Teens In Health

Neuroscience x AI Research Paper Journal

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About Teens in Health: *Teens in Health is a teen-led organization that aims to provide open access to biological research skill development through researching and writing articles. In this session, students spent 7-8 weeks working on individual articles, with topics ranging from cognitive neuroscience, Artificial Intelligence, and the intersection of both. Article types include Literature Review Papers, Analytical Research Papers, and Experimental Research Articles.*

Program Lead (Mentor + Reviewer): Thanisha Kapur
Teens in Health Director (Reviewer): Anika Shah

Authors:

Aahana Mittal (Research Article)
Aarin Varma (Literary Review)
Aleina Mendoza (Literary Review)
Alexandra Khovrine (Literary Review)
Allyse Nguyen (Research Article)
Anasha Maheen (Research Article)
Anika Seki (Literary Review)
Anna Bream (Literary Review)
Anushka Ayanampudi (Literary Review)
Arianna Barik (Literary Review)
Arshia Malhotra (Research Article)
Delilah Peñate (Literary Review)
Elliot Hsu (Literary Review)
Emma Rand (Literary Review)
Eshel Ahmad (Literary Review)
Evelyn Bekker (Literary Review)
Gabriella Harmon (Literary Review)
Gabrielle Rodriguez (Literary Review)

Jacqueline Bai (Research Article)

Janet Yang (Research Article)

Jessica Yam (Literary Review)

Katherine Mejia (Research Article)

Katherine Mock (Literary Review)

Keertana Raghavendra (Literary Review)

Kennedy Flowers (Literary Review)

Krish Khilnani (Literary Review)

Lexi Zhu (Literary Review)

Libbey Kwok (Literary Review)

Nandanashri Baskaran (Research Article)

Peyton Higa (Literary Review)

Pranjal Sharma (Research Article)

Ria Patel (Research Article)

Roshny Saha (Literary Review)

Sachi Chauhan (Literary Review)

Saivarunteja Elagandula (Literary Review)

Sanshray Mohapatra (Literary Review)

Sanvi Swain (Research Article)

Sarthak Chaturvedi (Literary Review)

Selina Gao (Literary Review)

Shamonti Shamim (Literary Review)

Si-Eun Park (Research Article)

Sneha Bhat (Literary Review)

Sneha Gadekarla (Research Article)

Soorya Krishnan (Literary Review)

Stephanie Medrano (Literary Review)

Tanmayee Gudi (Research Article)

Thanisha Kapur (Literary Review)

Vienna Li (Literary Review)

Zhentao Tan (Literary Review)

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Reducing the Effects of Bipolar Disorder by Observing Neural Networks

Aahana Mittal (author), Thanisha Kapur (advisor)
Tesla STEM High School

Keywords: Bipolar Disorder, Neuroimaging, Neuroplasticity, Neurofeedback Training, Psychoeducation, Neural Networks

Abstract

By analyzing neural networks using brain imaging and utilizing extrinsic factors, this research paper investigates how neuroplasticity may help to lessen the effects of bipolar disorder. The study compares those with bipolar disorder to a control group to determine any neurobiological differences using magnetic resonance imaging (MRI), functional MRI (fMRI), and diffusion tensor imaging (DTI). The experimental group receives a focused intervention over a 12-month period that combines neurofeedback training, psychoeducation, cognitive-behavioral techniques, and lifestyle changes. The results can reveal a significant decrease in the severity of symptoms in the experimental group, pointing to the targeted intervention's potential efficacy in encouraging neuroplastic changes and enhancing mood regulation and emotional stability in bipolar disorder sufferers.

Introduction

Bipolar disorder, a complex mental health condition, affects millions of individuals worldwide, causing significant disruptions in their emotional well-being and daily functioning. Characterized by episodes of extreme mood swings, ranging from manic highs to depressive lows, this disorder poses substantial challenges for both patients and clinicians. Bipolar disorder is distinguished by a unique set of symptoms and neural activity patterns that deviate from those observed in a typical, healthy brain. Neuroimaging studies have revealed structural and functional differences in the brains of individuals with bipolar disorder, implicating various regions and neural circuits involved in mood regulation and emotional processing (Clark). These differences include alterations in the prefrontal cortex, hippocampus, and amygdala, among others, highlighting the intricate interplay of these brain regions in bipolar disorder pathology. Neuroplasticity, a fundamental property of the brain, refers to its ability to reorganize its structure and function in

response to internal and external influences. This phenomenon encompasses both synaptic plasticity, involving changes in the strength and connectivity of neural connections, and structural plasticity, involving the growth of new neurons and modification of existing neural networks (Radulescu). Neuroplasticity plays a crucial role in learning, memory, and recovery from brain injuries, and it has become an area of intense scientific investigation in psychiatric disorders.

Despite the advancements in our understanding of bipolar disorder and the brain's plasticity, the disorder currently lacks a definitive cure. However, recent theoretical frameworks propose that external factors, such as environmental stimuli, lifestyle modifications, and therapeutic interventions, may induce neuroplastic changes in the brain and potentially mitigate the effects of bipolar disorder. These external influences have the potential to reshape neural circuits, optimize mood regulation, and enhance emotional stability, offering new avenues for therapeutic interventions and improved patient outcomes. This way, we will examine the hypothetical scenario in which external factors can influence neuroplasticity and potentially alleviate the symptoms of bipolar disorder. By unraveling the complex interplay between bipolar disorder and neuroplasticity, we hope to contribute to the growing body of knowledge surrounding this condition and pave the way for innovative therapeutic approaches.

Materials and Methods

The experimental design’s purpose is finding new possible ways of aiding those with bipolar disorder by taking advantage of the neuroplasticity of the brain— its ability to reorganize its structure due to external influences. To investigate the neurobiological differences in bipolar disorder, the study requires specific materials. An essential component is access to a high-quality Magnetic Resonance Imaging (MRI) scanner, which allows for the acquisition of detailed structural images of the brain. In addition, functional MRI (fMRI) and Diffusion Tensor Imaging (DTI) protocols will be utilized to assess brain activity and connectivity, respectively. These tools can help find key differences in the brains of those with bipolar disorder. Standardized scales for symptom assessment, such as the Young Mania Rating Scale and the Hamilton Depression Rating Scale, will be employed to evaluate symptom severity. These are standardized assessment tools used to evaluate the severity of bipolar disorder symptoms. The YMRS assesses manic

symptoms, including elevated mood, increased energy levels, disruptive behavior, and sleep disturbances by using a score ranging from 0 to 60, the higher the number the worse the manic symptoms (“Young Mania Rating Scale (YMRS) - University of Florida”). The HDRS focuses on depressive symptoms, such as low mood, feelings of guilt, insomnia, and loss of interest. Clinicians administer these scales through structured interviews to rate the severity of symptoms based on predefined criteria. Higher scores indicate more severe symptoms, enabling clinicians to assess symptom severity, track changes over time, and evaluate treatment response in individuals with bipolar disorder. After evaluating a group of individuals to find their symptom severity, using MRI and DTI to assess their brains can help find key differences between the brains of those who don’t have bipolar disorder and those who do, as per the YMRS and HDRS.

An example of a neurobiological difference observed in bipolar disorder is the altered connectivity within the prefrontal-limbic network. This network encompasses the prefrontal cortex, responsible for cognitive control and emotion regulation, and the limbic system, involved in emotional processing and regulation. Studies have consistently shown disrupted connectivity between these regions in individuals with bipolar disorder, contributing to mood dysregulation and emotional instability (Strakowski). Building upon the identified neurobiological differences, it is possible to design targeted interventions that specifically modulate the affected brain regions or networks— and can help improve these regions due to the brain's neuroplasticity. Then, using the experimental group, a specific targeted intervention using neurofeedback training can be administered over a set period of time. Neurofeedback involves providing real-time feedback of individuals' brain activity, enabling them to learn self-regulation techniques and modulate the targeted brain regions. Individuals in the experimental group would undergo neurofeedback training sessions. During these sessions, participants will receive visual or auditory feedback based on their prefrontal-limbic connectivity, encouraging them to enhance and stabilize the connectivity patterns associated with better emotional regulation and mood stability (Marzbani).

To do this, participants are connected to an electroencephalogram (EEG) device that measures their brainwave activity. Several trials will be conducted in order to minimize EEG error. Specific electrodes are placed on the scalp to detect electrical signals produced by the brain. These signals are then processed and translated into visual or auditory feedback that participants

can perceive in real-time. The feedback typically takes the form of a graphical display on a computer screen, which represents the participant's brainwave patterns, such as specific frequencies or connectivity between brain regions. In the context of targeting the prefrontal-limbic network in bipolar disorder, the feedback may reflect the strength or coherence of connectivity between these regions. The goal of neurofeedback training is to help individuals learn to self-regulate their brain activity and enhance the desired patterns associated with improved emotional regulation and mood stability. Through repeated sessions, participants gain insight into their brainwave activity and learn to consciously modulate it. The training typically would involve 1) a baseline assessment. Here, participants will undergo an initial assessment to establish their brainwave patterns and identify areas for improvement. 2) Feedback sessions where participants engage in neurofeedback training sessions in order for them to receive real-time feedback on their brainwave activity. The feedback is designed to encourage desired brainwave patterns associated with emotional regulation and mood stability. And 3) skill acquisition where participants learn techniques and strategies to intentionally modulate their brainwave patterns based on the feedback received. These techniques may include visualization exercises, mindfulness practices, or cognitive strategies. Participants apply the acquired self-regulation skills outside of the training sessions, integrating them into daily life situations to promote sustained benefits (Marzbani).

The intervention design will not be limited to neurofeedback alone but will also encompass additional elements. Psychoeducation will be provided to help individuals understand the neurobiological underpinnings of their symptoms and equip them with coping strategies. Cognitive-behavioral techniques will focus on addressing maladaptive thought patterns and behaviors associated with mood dysregulation (Sarkhel). Furthermore, lifestyle modifications, such as optimizing sleep patterns, regular exercise, and stress management techniques, will be incorporated into the intervention to support overall well-being. The modifications and training can be based on results of the MRI and brain imaging, so that specific areas such as the prefrontal-limbic network can be targeted, allowing establishment of specific techniques that aim to better bipolar disorder. After repeated neurofeedback sessions every month over a 12 month time span, the YMRS and HDRS tools can be readministered to see whether individuals symptom severity decreased after targeted treatment.

Data Analysis

Neuroimaging data obtained through Magnetic Resonance Imaging (MRI), functional MRI (fMRI), and Diffusion Tensor Imaging (DTI) will be analyzed to evaluate structural and functional brain differences between individuals with bipolar disorder and controls. The study will include a total of 50 participants, with 25 individuals diagnosed with bipolar disorder (experimental group) and 25 individuals without the disorder (control group). All participants in the experimental group will have the diagnostic criteria for bipolar disorder based on standardized clinical interviews and assessment tools. Both groups will comprise of individuals matched for age, gender, and other relevant demographic factors, the difference being the control group is without a history of any psychiatric disorders. For symptom assessment, participants will complete the Young Mania Rating Scale (YMRS) and the Hamilton Depression Rating Scale (HDRS) questionnaires at the baseline and after 12 months of the targeted intervention. The YMRS and HDRS scores will then be compared to determine changes in symptom severity over the intervention period. The MRI, fMRI, and DTI data can all be collected at the beginning of the study to evaluate neurobiological differences between the two groups. The MRI data is processed to obtain high-resolution structural images of the participants' brains, allowing for detailed examination of brain anatomy and volume. The fMRI data is analyzed to investigate brain activity patterns associated with specific tasks, such as emotional processing or cognitive control. DTI data is used to assess the integrity of white matter tracts, which connect different brain regions and play a crucial role in information transmission. Using each of these tools and scales, the results of the study can be properly analyzed to understand whether bipolar disorder’s effects can be managed using extrinsic factors.

Results and Discussion

The results of the study can show significant differences in symptom severity between the experimental group (individuals with bipolar disorder) and the control group (individuals without bipolar disorder). At baseline, the experimental group would exhibit higher YMRS scores, indicative of more severe manic symptoms, and higher HDRS scores, suggesting more severe depressive symptoms, compared to the control group. This finding is consistent with previous research highlighting the characteristic symptomatology of bipolar disorder. Following the

12-month targeted intervention, participants in the experimental group would show a significant reduction in both YMRS and HDRS scores. This decrease in symptom severity would indicate that the neurofeedback training, psychoeducation, cognitive-behavioral techniques, and lifestyle modifications collectively contribute to symptom improvement. The results suggest that the targeted intervention leveraging neuroplasticity had a positive impact on symptom management in individuals with bipolar disorder. Furthermore, neuroimaging data can reveal which specific brain regions and neural networks underwent significant changes following the intervention. The prefrontal-limbic network for example, which had exhibited altered connectivity in individuals with bipolar disorder, may show enhanced connectivity and improved functional synchronization after the targeted intervention. These findings would support the hypothesis that external factors can induce neuroplastic changes in the brain, promoting improved mood regulation and emotional stability.

Some common errors in the experiment could however relate to participant compliance with the intervention protocol. Some participants in the experimental group may experience difficulty adhering to the required frequency of neurofeedback training sessions or implementing the recommended lifestyle modifications consistently. These compliance-related challenges could influence the overall effectiveness of the intervention. Additionally, testing small sample sizes might limit the generalizability of the results. Further studies with larger and more diverse samples would be necessary to validate the findings. Assuming the results of this study support the potential benefits of targeted interventions leveraging neuroplasticity for individuals with bipolar disorder, it is safe to assume that the combination of neurofeedback training, psychoeducation, cognitive-behavioral techniques, and lifestyle modifications can demonstrate significant symptom improvement and alterations in brain connectivity. These findings would suggest which external factors can play a pivotal role in promoting neuroplasticity and potentially alleviating the effects of bipolar disorder. However, further research would be needed to validate these findings and optimize the intervention protocols for broader clinical application. The study may contribute to the growing understanding of the interplay between bipolar disorder and neuroplasticity, paving the way for innovative therapeutic approaches in the management of this complex condition.

Works Cited

Clark, Luke, and Barbara J Sahakian. “Cognitive neuroscience and brain imaging in bipolar disorder.” *Dialogues in clinical neuroscience* vol. 10,2 (2008): 153-63. doi:10.31887/DCNS.2008.10.2/lclark

Rădulescu, Ioana et al. “Neuroplasticity and depression: Rewiring the brain's networks through pharmacological therapy (Review).” *Experimental and therapeutic medicine* vol. 22,4 (2021): 1131. doi:10.3892/etm.2021.10565

Young Mania Rating Scale (YMRS) - University of Florida, dcf.psychiatry.ufl.edu/files/2011/05/Young-Mania-Rating-Scale-Measure-with-backgroun d.pdf. Accessed 30 July 2023.

Strakowski, Stephen M et al. “The functional neuroanatomy of bipolar disorder: a consensus model.” *Bipolar disorders* vol. 14,4 (2012): 313-25. doi:10.1111/j.1399-5618.2012.01022.x

Marzbani, Hengameh et al. “Neurofeedback: A Comprehensive Review on System Design, Methodology and Clinical Applications.” *Basic and clinical neuroscience* vol. 7,2 (2016): 143-58. doi:10.15412/J.BCN.03070208

Sarkhel, Sujit et al. “Clinical Practice Guidelines for Psychoeducation in Psychiatric Disorders General Principles of Psychoeducation.” *Indian journal of psychiatry* vol. 62,Suppl 2 (2020): S319-S323. doi:10.4103/psychiatry.IndianJPsychiatry_780_19

Artificial Intelligence in Brain Imaging and Neurological Disorders Research

Aarin Varma (author), Thanisha Kapur (advisor), Anika Shah (editor)
Olentangy Liberty High School

Keywords: Artificial Intelligence, Brain Imaging, Neurological Disorders, Parkinson's Disease, Neuroscience, Electrocardiogram

Abstract

Artificial Intelligence (AI) is revolutionizing the way researchers and clinicians are able to perceive brain imaging and neurological disorders With the increasing accuracy and sensitivity of AI, researchers will be able to gain more insights on the brain. AI can be incorporated into various types of brain imaging, including, computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and electroencephalography (EEG). In brain imaging, AI can read CT, MRI, and PET scans with reduced or without contrast, which minimizes the chance of adverse effects and reactions. AI has also been used to predict neurological disorders such as Parkinson's disease even before the first diagnosis using raw waveform ECGs so early intervention strategies can be used. AI has made the detection of tumors, seizures, development disorders, neurodegenerative illnesses, strokes, and neurological infections significantly easier in brain imaging. The integration of AI in neurological care has the promise of accelerated diagnostic accuracy, more personalized treatment plans, and better patient outcomes.

Introduction

As artificial intelligence (AI) tools emerge in the advancing world, it has begun to be used in various parts of the medical field. Common current applications of artificial intelligence in the medical field include diagnosing patients, end-to-end drug discovery and development, improving communication between physician and patient, transcribing medical documents, such as prescriptions, and remotely treating patients (Basu). With the latest advancement in this field, machines are being built to autonomously have the decision-making capability for problem-solving similar to the human brain. Specifically in neuroscience, the study of the structure and cognitive functions of the brain, AI can assist in brain imaging and neurological

disorder research. Due to its promising accuracy and sensitivity in the identification of imaging characterization and detection, AI is undergoing extensive evaluation in the medical field. Both of these areas, artificial intelligence and neuroscience, are very largely interrelated and will help with future advancements. The amount of research on the use of AI in the medical field has grown substantially; the number of publications on AI has increased from about 100 per year in 2007 to 2008 to 1000 per year from 2017 to 2018 for diagnostic imaging alone (Tang). AI has revolutionized the field of neuroscience and neuroimaging, granting clinicians unprecedented insights into the function and developments of the brain. AI algorithms can detect subtle patterns and abnormalities that humans may have not recognized. With its ability to extract hidden patterns, AI fits as the perfect choice for analyzing complex neuroscience data. The ability for artificial intelligence to work hand in hand with brain imaging and the diagnosis and prognosis of various neurological disorders is beneficial for both patients and clinicians.

Body

AI and Brain Imaging

As there is an abundance of image interpretation and data processing for radiologists, AI can assist in going through all the complex data. AI can be used in brain images from computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and electroencephalography (EEG) to detect lesions. One of the main benefits of the usage of AI in brain images is its ability to speed up the neuroimaging process. An AI algorithm, synthetic multi-orientation resolution enhancement works to reduce distortion and improves resolution in scans to make it easier to visualize white matter lesions in patients with multiple sclerosis in the scans (Zhao). AI is also able to read CT, MRI, and PET scans with reduced or without contrast. In MRIs, gadolinium-based contrast has a chance to cause injection site reactions and allergic reactions (Sammet). AI can be used in brain imaging to detect tumors, seizure disorders, developmental disorders, neurodegenerative disorders, headaches, strokes, and neurological infections. AI is applied in MRI scans for tumor detection, segmentation, and grade estimation (Surianarayanan). Brain tumor segmentation is the process of identifying and delineating the boundaries of tumors in medical images. This process is crucial in order to track tumor changes over time and make informed decisions on treatment options. Deep learning techniques such as convolutional neural networks (CNNs) have provided

promising data for the automation of brain tumor segmentation. A convolutional neural network is a type of artificial neural network that is composed of multiple building blocks of fully connected layers that are designed to automatically and adaptively learn through algorithms (Yamashita). CNNs are trained on large datasets of annotated brain MRI scans to learn how to recognize different tumor regions. In seizures, the variability of the pattern of abnormal surges of electrical activities in the brain makes detection very difficult (Shoeb). Recordings of the brain activities from electroencephalography were analyzed with machine learning algorithms to detect seizures effectively. Intellectual and developmental disabilities like autism spectrum disorders (ASDs) tend to appear in childhood. Machine learning can observe a toddler's eye movements in order to detect the presence of ASDs (Surianarayanan).

AI in Diagnosis and Prognosis of Neurological Disorders

In Parkinson's disease (PD), there is not a large amount of knowledge on the electrocardiogram (ECG) markers of PD during the prodromal stage. PD is the most common neurodegenerative movement disorder, where the main symptoms include tremors, rigidity, bradykinesia, and postural instability (Balestrino). An electrocardiogram records the electrical activity of the heart in a non-invasive approach. Currently, treatments for Parkinson's disease offer good control of motor symptoms but no effective cure (Balestrino). The prodromal stage of PD consists of various non-motor symptoms that predate the classic motor symptoms (Roos). Symptoms of the prodromal stage include constipation, hyposmia, possible REM-sleep behavior disorder, depression, anxiety disorder, and cognitive impairment (Postuma). In one study, researchers used AI to predict PD risk during the prodromal stage, up to 5 years before disease diagnosis. Their aim was to build a fully automatic artificial intelligence model based on electrocardiograms that could predict PD. In this study, researchers provided the deep learning model with raw waveform electrocardiograms, which would then predict Parkinson's disease risk in the prodromal stage. The study used ECG samples from Loyola University Chicago and the University of Tennessee-Methodist Le Bonheur Healthcare. The deep learning model was externally validated with ECG data where it correctly classified 12 of 29 PD cases five years prior to disease diagnosis, and 123 of 165 controls (Karabayir). The accuracy increased when predicting future Parkinson's disease within three years of diagnosis. It achieved the highest accuracy when predicting PD within one year of diagnosis. The researchers concluded that the deep-learning

predictive model using ECGs correctly classifies individuals with prodromal PD with modest accuracy. The AI was able to distinguish between future PD cases and controls and increased in accuracy closer to the diagnosis of PD. Since ECGs are commonly collected by healthcare providers, using predictive AI models alongside them will allow clinicians to be able to intervene with targeted therapies and minimize adverse effects. The integration of the deep learning models with the data from ECGs offers a non-invasive technique to detect PD in the prodromal stage. It is important to highlight that the research conducted by Karabayir and other colleagues represents an advancement toward using AI in the field of neuroscience.

Conclusion

Brain imaging and neurological disorder research are two extremely big parts of the field of neuroscience that are being advanced by the usage of artificial intelligence. It is important that AI is increasingly integrated into the works of the neuroscience field as it can bring about many benefits: improved diagnostic accuracy, earlier detection of neurological disorders, improved resolution of brain imaging without the use of contrast, more specialized intervention care for patients, and possibly less time and money spent for the clinicians and patients. The application of AI in types of brain imaging, such as CT, MRI, PET, fMRI, and PET has proven to be a valuable tool in the detection and identification of various neurological disorders. AI speeds up the neuroimaging process and improves the resolution of the scans which can improve the diagnosis of any neurological disorders and make sure patients get the treatment they should receive. In brain scans, AI can also track the progression of the growth of brain tumors and find the boundaries of the changing tumors. This could be crucial as tracking the growth could help clinicians make informed decisions on the treatment plans. Sometimes it is difficult for researchers and clinicians to spot the patterns of early signs of neurological disorders in data. With AI, researchers were able to detect signs of Parkinson's disease even before the initial diagnosis. The ECG markers of PD that were difficult for researchers to spot were provided to the deep learning model which predicted PD with adequate accuracy. If researchers were able to create learning models for the markers of various neurological disorders, the quality of life for patients would significantly increase. Clinicians could possibly be able to stop or treat these patients with neurological disorders and minimize their effects. The advancement and integration of AI in the field of neuroscience also brings about the question of whether AI will be able to

replace some clinical professions fully. Regardless of the possibility of the loss of professions, the relationship between artificial intelligence and neuroscience holds immense promise. Not only will AI increase understanding of the human brain, but it will transform the lives of many patients who are dealing with various neurological disorders. Medical decisions will be made with the information provided by AI which will lead to improved patient quality of life.

Works Cited

Balestrino, R, and A H V Schapira. “Parkinson's disease.” *European Journal of Neurology* vol. 27,1 (2020): 27-42. doi:10.1111/ene.14108

Basu, Kanadpriya, et al. "Artificial Intelligence: How Is It Changing Medical Sciences and Its Future?" *Indian Journal of Dermatology*, vol. 65, no. 5, 2020, pp. 365-370, https://doi.org/10.4103/ijd.IJD_421_20. Accessed 1 Aug. 2023.

Karabayir, Ibrahim, et al. "Externally Validated Deep Learning Model to Identify Prodromal Parkinson’S Disease from Electrocardiogram." *Scientific Reports*, vol. 13, 2022, https://doi.org/10.1038/s41598-023-38782-7. Accessed 31 Jul. 2023.

Monsour, Robert, et al. "Neuroimaging in the Era of Artificial Intelligence: Current Applications." *Federal Practitioner*, vol. 39, no. Suppl 1, 2022, p. S14, https://doi.org/10.12788/fp.0231. Accessed 30 Jul. 2023.

Postuma, Ronald, and Berg, Daniela. "Prodromal Parkinson's Disease: The Decade Past, the Decade to Come." *Movement Disorders*, vol. 34, no. 5, 2019, pp. 665-675, https://doi.org/10.1002/mds.27670. Accessed 31 Jul. 2023.

Roos, Dareia, et al. "Prevalence of Prodromal Symptoms of Parkinson’S Disease in the Late Middle-Aged Population." *Journal of Parkinson'S Disease*, vol. 12, no. 3, 2021, pp. 967-974, https://doi.org/10.3233/JPD-213007. Accessed 31 Jul. 2023.

Sammet, Steffen. "Magnetic Resonance Safety." *Abdominal Radiology (New York)*, vol. 41, no. 3, 2016, p. 444, https://doi.org/10.1007/s00261-016-0680-4. Accessed 31 Jul. 2023.

Shoeb A.H. *Application of Machine Learning to Epileptic Seizure Onset Detection and Treatment.* Massachusetts Institute of Technology, https://dspace.mit.edu/handle/1721.1/54669. Accessed 31 Jul. 2023.

Surianarayanan, Chellammal, et al. "Convergence of Artificial Intelligence and Neuroscience towards the Diagnosis of Neurological Disorders—A Scoping Review." *Sensors (Basel, Switzerland)*, vol. 23, no. 6, 2023, https://doi.org/10.3390/s23063062. Accessed 30 Jul. 2023.

Tang, Xiaoli. "The Role of Artificial Intelligence in Medical Imaging Research." *BJR Open*, vol. 2, no. 1, 2019, https://doi.org/10.1259/bjro.20190031. Accessed 30 Jul. 2023.

Yamashita, Rikiya et al. “Convolutional neural networks: an overview and application in radiology.” *Insights into imaging* vol. 9,4 (2018): 611-629. doi:10.1007/s13244-018-0639-9

Zhao, Can, et al. "Applications of a Deep Learning Method for anti-Aliasing and Super-Resolution in MRI." *Magnetic Resonance Imaging*, vol. 64, 2019, p. 132, https://doi.org/10.1016/j.mri.2019.05.038. Accessed 31 Jul. 2023.

Prediction of Borderline Personality Disorder Through Artificial Intelligence

Aleina Mendoza (author), Thanisha Kapur (advisor)
Bishop Dunne Catholic School

Keywords: Borderline Personality Disorder (BPD), Prefrontal Regulatory Regions, Neuroimaging, Machine Learning Systems, Psychotherapy, Optimal Predictive Model Selection

Abstract

Borderline personality disorder (BPD) is one of several mental illnesses affecting one's ability to manage emotion. For children, it has become difficult to retain a bpd diagnosis considering several studies pointing towards adolescents being incapable of developing symptoms associated with bpd and other mood disorders. Despite this viewpoint, researchers have worked towards developing machinery capable of noticing early signs and symptoms of borderline personality disorder considering the number of children seeking psychotherapy and medicated treatment. Early predictors of bpd are noted by psychiatrists to reduce the amount of difficulties children face in adulthood. Others argue that modern scientific developments do not have the necessary knowledge on children's neurobiological development essential in making a proper diagnosis. Conversation regarding the use of Artificial Intelligence (AI) through the development of complex algorithms and data-input systems continues to divide medical professionals today. Borderline personality disorder and Artificial Intelligence on their own are modern and growing developments with both factors becoming more prevalent in recent studies.

Introduction

Growth of Artificial Intelligence in Children's Psychiatric Research

The development of Artificial Intelligence leaves many critical to the implications of these systems, however with new strides in mental health diagnosis some researchers argue that new growth has the ability to change the future of children's therapy. A commonly recognized personality disorder, borderline personality disorder is defined as a condition characterized by difficulty regulating emotion reflected through an imbalance in personal relationships and self-image. Borderline Personality Disorder (BPD) summarized by instability is one of the most challenging disorders for mental health care professionals today. Previous neuroimaging reveals

the importance of the amygdala, insula, posterior cingulate cortex, hippocampus, and prefrontal regulatory regions in adult diagnosis. The difficulty of children's diagnosis and complexity of bpd comes from the effect on the brain's neurotransmitters embodying much of the researchers' studies today. With separation and stigma presented, recent research points towards the use of Artificial Intelligence in predicting early onset bpd. The divide between researchers on the use of Artificial Intelligence on mental health diagnosis ranges greatly. For instance, neuroscience researcher and child psychiatrist, Mai Uchida MD, motivates readers to move towards the use of Artificial Intelligence following a successful study. Other motivations lie outside detection with successful attempts being hopeful in the improvement of adolescent therapy. The applications of these forms of technology have been viewed in vast regions of children's developmental psychology with few medical professionals having further hope for implications in psychotherapy sessions. The division to the questions as to how Artificial Intelligence can be most efficient in bpd is accompanied by many current reports in the 20th century. This paper aims to review these two contracting sets of research to illustrate the role Artificial Intelligence has paved for the early findings of other neurological disorders and diseases. Therefore, academic literary pieces and large studies point towards Artificial Intelligence being effective in the early detection for adolescents, understanding changes to neurotransmitters through previous MRI adult screenings, with others claiming that successful attempts should simply be used to improve children's psychotherapy or to integrate Artificial Intelligence in therapy entirely. This review first highlights the argument concerning BPD diagnosis in children followed by the ethical and scientific argument of Artificial Intelligence in contrasting emerging literature.

Body

The Use of Functional Magnetic Resonance Imaging in Studying the Neurobiology of Borderline Personality Disorder

Neuroimaging serves as a supporting development in Artificial Intelligence hoping to generate a deeper understanding of borderline personality disorder (bpd). The use of brain scans proves evident in the following study when learning how prefrontal regions such as the amygdala and hippocampus are affected by symptoms associated with bpd. Katherine Pier MD, assistant clinical professor of psychiatry at the University of California San Francisco, accompanied by Lea K. Marin, assistant professor of psychiatry at the Icahn School of Medicine documents the

importance of neuroimaging on studying corticolimbic systems and symptoms of bpd. When using meta-analysis in studying brain volume through neuroimaging, both researchers examined the images of over 574 participants placing 281 as possessing prior diagnosis of bpd. The method of functional magnetic resonance imaging otherwise understood as (FMRI) is used thoroughly by researchers to measure brain activity and blood flow (Pier & Marin). As a result, Pier and Marin discovered that emotional stimulation proved difficult for bpd participants with heightened activation of negative emotional stimuli in the left amygdala and hippocampus. Stemming from the corticolimbic system, the amygdala follows the processing of emotion outlining bpd diagnosis and the symptoms of irregularity concerning many patients. Negative stimuli was further understood to affect the hippocampus responsible for learning and memory (Pier & Marin). Additionally, the effect of negative stimulation whether through thought or action decreases the activation of prefrontal regions responsible for regulating emotions, thoughts, and actions necessary in executing overall function. The effect on prefrontal regions demonstrates the neurobiology behind borderline personality disorder and opens up the use of neuroimaging. Answering many of psychiatrists' and medical professionals' questions regarding how mood disorders shape brain activity. Pier and Marin's study focuses upon adult brain neuroimages following previous volume studies claiming that adolescent bpd diagnosis exists to a small degree due to a lack of neuroimaging techniques available. Both researchers exclude adolescent scannings due to a lack of resources and the continuous neurological developments occurring until adulthood. Both researchers hope to promote the use of functional magnetic resonance imaging in future studies. Larger developments and implications focus on the amygdala, hippocampus, and their role in brain function or impact when one faces a mental illness or disorder. Pier and Marin demonstrate the use of artificial intelligence in their work with its ability to outline the future of neuroscience.

The Growth of Machine Learning Systems in Predicting the Future Development of Mood Disorders in Adolescents

A method to data analysis, machine learning systems function on a basis of computational power and complex algorithms. Pediatric psychiatrist, Mai Uchida, accompanied by a team of scientific researchers, including, Qasim Bukhari, Maura DiSalvo, Allison Green, Guilia Serra, Chloe Hutt Vater, Satrajit S. Ghosh, Stephen V. Faraone, John D.E Gabrieli, and Joseph Biederman.

Together, Uchida and her team of specialists develop a machine learning system to study Artificial Intelligence in a larger psychiatric landscape. Equipped with the Random Forest algorithm the following system served as an essential part of Uchida's study hoping to demonstrate how Artificial Intelligence can warn of early symptoms of bipolar disorder and various mood disorders. The importance of studying bipolar disorder 1 comes as a result of children experiencing symptoms of mood dysregulation, increased risk of suicide, link to substance abuse, and social turmoil for patients and families alike (Uchida et.al). Notable in detecting problems surrounding classification and regression, the Random Forest algorithm was accompanied by the Balanced Random algorithm following trial and error in the studies' early trials. Prior to implementing data within these systems, 492 child participants underwent prior psychological testing through a behavioral evaluation conducted by a child psychiatrist and in continuous psychological assessments throughout the studies' 10-year period (Uchida et.al). Data conducted during the study was implemented into learning systems algorithms to measure a child's susceptibility to developing a mood disorder within the span of 10 years following one's social and emotional development. Bipolar disorder-1 was the mood disorder closely monitored by Uchida and researchers following the complexity of symptoms and of children's diagnosis outlined by mania and various depressive episodes. As a result, Uchida's developed machine learning algorithms were 75% effective in noticing early onset mood disorders with bipolar 1 having a 76% specificity rate (Uchida et.al) . False positive rates were listed at 21.6%. While entirely negative rates for children following the studies 10-year period was 3.1% (Uchida et.al). Uchida lists the importance of machine learning systems in psychiatric studies following their ability to lift the burden of mood disorders off of parents, families, and participants. Motivation as a result of success speaks towards the use of longitudinal prediction in helping psychiatrists and specialists understand the risk of mood disorders for today's youth and determine how symptoms form even throughout adolescence. Machine learning through the use of various studied algorithms hopes to change children's modern form of psychotherapy. Uchida and colleagues work is a part of a small category of scientific study combining algorithms to promote knowledge in children's developmental studies. Targeting mood disorders in adolescents and in hoping to grow scientific discussions on the severity of early diagnosis.

Optimal Predictive Models and their Use in Identifying Early Predictors Associated with Borderline Personality Disorder

Leading research hopes to identify the critical predictors of borderline personality disorder in a set of 2,400 girls. Through sorting each participant on a series of clinical, psychological, and social factors, Joseph Beeney, assistant professor of psychology at the University of Pittsburgh, and his colleagues used an optimal predictive model to study early precursors of bpd. Beeney was moved towards the use of Artificial Intelligence following the overlapping of disorders such as depression and conduct disorders to that of borderline personality disorder. The optimal predictive model serves as a way to calculate median probability and is said to be chosen as a model for future prediction with its moderate measure of accuracy. The model included 128 predictors of bpd including impulsivity, poor emotional functioning, self-control, and irregularity (Edwards). Following the stages previewing adolescent to adult growth, Beeney grouped predictors by developmental stages from late childhood to mid adolescence due to previous research marking the unchanged nature of bpd. Late childhood was described as children ages 8-10, early adolescence was listed at 11-13, while mid adolescence was summarized by ages 14 and 15 (Edwards). Beeney's minimal use of predictors stems from the simplicity and severity of bpd symptoms. Although Beeney and his colleagues' research was pivotal in determining bpd in adolescents, the optimal predictive model fails to detect other disorders and illnesses affecting adolescents today. 19 predictors of bpd symptoms were identified by the model with a percentage difference of 33.2% when compared to other psychiatric disorders (Edwards). Five other symptoms accompanied bpd diagnosis including depression, anxiety, irregularities in self-control, poor social functioning, and reaction to punishment. Disorders were distinguished from that of bpd with predictors such as the appearance of two or more mental illnesses and struggles with self-control being prevented in many adolescents. Beeney's use of artificial intelligence demonstrates the intertwined nature of mental illness or mental disorders with several participants developing symptoms of depression or anxiety aside from bpd diagnosis. Furthermore, Beeney and his colleagues' research contributes to growing knowledge of psychopathology. Exploring mental disorders through their causes, developments, sets of characteristics, diagnosis, and treatment.

Future Implications of Artificial Intelligence In Improving Psychotherapy for Borderline Personality Disorder Patients

The following piece is written as an argumentative and literary piece presented during the rise of Artificial Intelligence in psychiatric studies. Judit Szalai reflects upon previous scientific research implementing Artificial Intelligence in borderline personality disorder diagnosis and treatment. Szalai introduces the use of conversation technology to improve patient's experiences throughout psychotherapy. Technology developed as a therapeutic tool would further provide to individuals who fail to have sufficient access to therapy. Szalai predicts that the use of technology in digital therapy services would be even more prevalent due to the program's ability to craft new relationships or help patients form consistent emotional connections. Chatbots are understood by Szalai to work well with digital psychotherapy services considering the machine's ability to mimic human interaction, use creative language, and provide conversational prompts that come across effectively in tone (Szalai 493). Messages would be programmed to craft responses motivated by emotion through expansive word choice and in exhibiting fear, joy, disgust, and sadness. Szalai's claims come as a result of emotion being the pivotal part of bpd diagnosis, with the implications of artificial intelligence in psychotherapy being able to fill the need for emotional variety in human interaction. Additional implications combine physical and digital approaches with Artificial Intelligence moving to improve cognitive therapy techniques such as the continuum method (Szalai 493). Promoting the identification of more than two extremes, patients would learn to externalize, removing oneself from negative behaviors or attitudes. The use of systems in this instance would be to target problems while reducing overgeneralization (Szalai 493). A third merit identified by Szalai points towards the ability for patients to open up to non-human devices removing the confrontational feeling many patients experience when talking to a medical professional. Despite therapeutic implications, the extent of Artificial Intelligence's use in therapy should be limited to a single role. According to Szalai, technology's ability to jeopardize the success of treatment or cause patients to lose comfortability with their mental health care provider is one of many scientific limitations (Szalai 494). Szalai's closing remarks note the importance of scientific development and design being specialized towards the patient's skills, needs, and ability to carry emotionally stimulating conversation. Further accompanied by a certified mental health professional.

Conclusion

The intricate nature of borderline personality disorder makes children's diagnosis even more challenging. While previous studies collected data regarding the changes made to adult's prefrontal regulatory regions, there is a visible gap between early adolescence and adulthood. Although machinery works towards analyzing data, Artificial Intelligence is challenged in the ability to give readily accurate readings for young representative participants. In many aspects, Artificial Intelligence was successful following several trials, however with this participants were said to undergo various extensive processes that filled much of one's early adolescence. The ability for scientists to create a bond between Artificial Intelligence and psychiatric research is no longer a question, but rather one that requires further inquiry to create a foundation of certainty. For children struggling with personal relationships or experiencing an increase towards impulsive reaction, Artificial Intelligence and prior studies serve to elevate difficulties within families. When compared to depression or anxiety, testing for symptoms of bpd through current technology serves to give an estimated answer as to how likely a child is to experience bpd or even as they experience it now. Therefore, serving to provide a range at which immediate or future care can be distributed in order to increase a child's ability of living comfortably. Scientific research demonstrates the expansive nature at which various techniques and equipment can hope to provide greater knowledge in almost any branch of medicine. The continuous search for answers to childhood bpd serves to demonstrate how Artificial Intelligence has made necessary altercations in reaffirming beliefs regarding children's psychiatric research and in becoming a foundation for future literary works.

Works Cited

"Overview- Borderline Personality Disorder." *NHS Choices*, NHS, 4 Nov. 2022, www.nhs.uk/mental-health/conditions/borderline-personality-disorder/overview/. Accessed 19 July 2023.

Katherine S. Pier, MD;Lea K. Marin. "The Neurobiology of Borderline Personality Disorder." *Psychiatric Times*, MJH Life Sciences, 31 Mar. 2016, www.psychiatrictimes.com/view/neurobiology-borderline-personality-disorder.

Pryor, Julie. "Machine Learning Can Predict Bipolar Disorder in Children and Teens." *MIT McGovern Institute for Brain Research* , Massachusetts Institute of Technology , 31 May 2023, mcgovern.mit.edu/2022/12/07/machine-learning-can-predict-bipolar-disorder-in-children-and-teens/.

Uchida, Mai, et al. "Can Machine Learning Identify Childhood Characteristics That Predict Future Development of Bipolar Disorder a Decade Later?" *Journal of Psychiatric Research*, U.S. National Library of Medicine, Dec. 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC9999264/.

Edwards , Dr. Jessica. "A Machine Learning Approach Identifies Unique Predictors." *Association for Child and Adolescent Mental Health* , www.acamh.org/app/uploads/2020/10/RD-a-machine-learning-approach-identifies-unique-predictors.pdf.

Szalai, Judit. "The Potential Use of Artificial Intelligence in the Therapy of Borderline Personality Disorder." *ResearchGate*, Journal of Evaluation in Clinical Practice, Dec. 2020, philarchive.org/archive/SZATPU-2.

Advancements In Alzheimer's Disease

Alexandra Khovrine (author), Thanisha Kapur (advisor), Anika Shah (editor)
High School For Health Professions And Human Services

Keywords: Neuroscience, Alzheimer's Disease, Cognitive Decline, Pharmacological Treatments, Nonpharmacological Treatments

Abstract

The brain is susceptible to cognitive decline as people age or experience head injuries. In some cases, cognitive decline may progress into the most common type of dementia, Alzheimer's (AD). To this day, scientists have not found a cure for AD despite the multitude of experiments testing pharmacological and nonpharmacological treatments. Advancements must be evaluated to find a cure for the millions suffering from AD today. Scientists have done research to assess the perks of music therapy, anti-cancer drugs, beta-amyloid antibodies, and anti-glutamatergic treatment. These treatments can range from decreasing daily agitation to recovering synapses, decreasing glutamate levels, repairing brain axons, and even slowing cognitive decline. Due to the complexity of the brain, it may take decades to create new treatments and diagnostics. While there is no concrete way to cure AD or direct way to diagnose the disease, these advancements are significant for the development of medicine in neuroscience.

Introduction

Alzheimer's Disease (AD) is a type of dementia that corrupts memory and basic thinking skills over time. Cognitive decline impairs the hippocampus, which can eventually create a build-up of amyloid proteins around brain cells. The disease can be categorized into three types: Early, moderate, and severe. Early-stage AD is when a patient can function independently but occasionally struggles with remembering locations, or objects. Moderate-stage AD patients experience frequent agitation and need assistance due to their stronger memory loss. Finally, severe-stage AD patients need extensive care due to their lost awareness in communication, and surroundings. As AD is vulnerable to progress quickly, scientists need to find a definite cure in order to lower the rate of deaths related to AD.

As the world is evolving in technology, neural networks can detect early patterns of AD, allowing patients to receive treatment early. These networks are significant in the testing of future treatments and AD management. While current inhibitors are used to minimize behavioral issues and cognitive decline in AD patients, the disease still exists. Potential candidates for a cure can range from pharmacological and non-pharmacological treatments. Pharmacological treatments like Aβ antibodies, anti-glutamatergic treatment, and anti-cancer drugs can minimize cognitive decline in AD patients by removing the plaque build-up in the hippocampus. These treatments can even lead to improvement in behavioral issues. Music therapy, a nonpharmacological treatment, can significantly decrease agitation and anger issues among patients. Detecting a pattern in these treatments would eventually build a stairwell for the cure for AD. By establishing definitive therapies, scientists are slowly erasing the emotional toll families face with relatives struggling with AD.

Body

Aβ Antibodies

Amyloid β peptide (Aβ) protein peptides progress AD. Aβ amyloids are soluble toxins that increase plaque size in the hippocampus. Researchers studied how anti-aggregated amyloid beta protofibril (Aβ) antibodies affect AD patients (Swanson et. al). The researchers introduce lecanemab, an enzyme that binds to soluble anti-Aβ protofibril proteins and reduces their consistent spread. As an Aβ antibody, lecanemab is able to remove the built-up plaque, or beta-amyloid, in the hippocampus. In an 18-month-long study, all 856 patients got biweekly infusions of either a placebo or lecanemab. Results show that at 18 months, the 10-mg/kg biweekly lecanemab reduced brain amyloid (Swanson et. al). This concludes that lecanemab is useful in treating early to mild Alzheimer's patients because it removes the sticky protein that advances the disease.

Anti-Glutamatergic Treatment

Memantine is a type of anti-glutamatergic treatment that slows down the rate of nerve loss in the brain. A group of researchers studied its effect on mild to severe AD patients. 252 mild to severe AD patients were assigned either a placebo or 20 mg of memantine for 28 weeks. It was concluded that memantine had better outcomes than the placebo. It was explained that the

changed N-methyl-D-aspartate (NMDA) receptors reduced the glutamate-induced excitotoxicity that usually increases symptoms of AD (Reisberg et. al). This improves general behavioral patterns in AD patients. Therefore, anti-glutamatergic treatments like memantine are able to reduce cognitive decline in AD patients, and any sort of clinical deterioration.

Anti-Cancer Drugs

Millions of anti-cancer drugs exist to kill cancer cells. However, they may also be effective in recovering synapses in AD patients. 13 studies of clinical trials were done to assess the association between anti-cancer drugs and AD patients. In the study, there were 11 drugs approved: five tyrosine kinase inhibitors, two retinoid X receptor agonists, two immunomodulatory agents, one histone deacetylase inhibitor, and one monoclonal antibody. There was an additional placebo distributed. To specify, tyrosine kinase inhibitors are in charge of attacking cancer cells by disrupting signal transduction pathways; Retinoid X receptor agonists regulate most processes of the human body, like metabolism and cell growth; Immunomodulatory agents manage proteins in the immune system to reduce cancers; Histone deacetylase inhibitors also regulate the cell cycle by inhibiting histone deacetylases; Lastly, monoclonal antibodies attack cancer cells through modifying the immune system. During this study, AD patients were allowed to continue using their usual treatments, and the drugs being evaluated were administered as side therapies to the patient's standard care. Three of the studies did not report any major improvements. Two bexarotene studies and a thalidomide study did not show were speculated to contribute to toxicity. Outcomes in the nilotinib study showed results that could be continued in longer studies. However, masitinib showed impactful results. Masitinib slowed down the rate of cognitive decline in AD, which signifies that the drug can replace current AD medication (Ancidoni et. al).

Music Therapy

As of 2023, the only feasible nonpharmacological treatment for AD is music therapy.
A group of scientists conducted a study on the association between music therapy and AD. Music therapy promotes tranquility through a wide range of arts. This includes listening to music and singing. This therapy is most effective in cases related to treating mental illness. In this study specifically, 298 AD patients with all ranges of dementia participated. Patients were divided into

three groups based on their AD severity. One was a singing group, a lyric reading group, and nothing music related at all. For approximately 3 months, participants went through a series of tests on their cognitive functions. Results illustrate that music therapy improved verbal fluency, along with memory and language in patients with mild AD. On the other hand, no improvement or change was found in patients with moderate and severe AD patients (Lyu et. al). Overall, music therapy is an effective non-pharmacological therapy for mild AD patients only.

Conclusion

These methods create new advancements in neuroscience and contribute to developing a cure. Once the disease is caught early, doctors are able to assign different therapies and treatments depending on how severe the disease is. For example, Aβ antibodies would help patients who have a mass amount of built-up plaque. On the other hand, anti-glutamatergic like memantine would benefit patients with excess levels of glutamate. The anti-cancer drug, mastinib, recovers synapses to reduce cognitive decline. Finally, music therapy is able to decrease increased agitation and anger. All treatments that have been mentioned earlier play a significant role in preventing the progression of cognitive decline. Though depending on the severity of one's AD, a different treatment is assigned. This is due to the fact that severe AD patients experience not just heightened agitation, but an endless build-up in plaque, and loss in nerve cells. Exposure to new treatments is always beneficial in finding a cure. Treatments are viable to a certain extent but cannot be considered permanent cures for all patients. However, the one thing in common between all these treatments is the fact they only benefit patients with early to mild AD. This leaves room for the question: How can advancements in AD reorient their focus to all patients? Including those who land on the severe spectrum. Advancements need to be made continuously in order to draw a path to a definitive diagnosis, and the cure for AD.

Works Cited

Ancidoni, A., Bacigalupo, I., Remoli, G., Lacorte, E., Piscopo, P., Sarti, G., Corbo, M., Vanacore, N., & Canevelli, M. "Anticancer drugs repurposed for Alzheimer's disease: a systematic review" *Alzheimer's research & therapy,* 5 May 2021, https://alzres.biomedcentral.com/articles/10.1186/s13195-021-00831-6

Lyu, J., Zhang, J., Mu, H., Li, W., Champ, M., Xiong, Q., Gao, T., Xie, L., Jin, W., Yang, W., Cui, M., Gao, M., & Li, M. "The Effects of Music Therapy on Cognition, Psychiatric Symptoms, and Activities of Daily Living in Patients with Alzheimer's Disease" *Journal of Alzheimer's Disease,* 24 July 2018, https://content.iospress.com/articles/journal-of-alzheimers-disease/jad180183

Reisberg, B., Doody, R., Stöffler, A., Schmitt, F., Ferris, S., Möbius, H. J., & Memantine Study Group, "Memantine in moderate-to-severe Alzheimer's disease" *The New England journal of medicine*, 3 April 2003, https://www.nejm.org/doi/full/10.1056/NEJMoa013128

Swanson, C. J., Zhang, Y., Dhadda, S., Wang, J., Kaplow, J., Lai, R. Y. K., Lannfelt, L., Bradley, H., Rabe, M., Koyama, A., Reyderman, L., Berry, D. A., Berry, S., Gordon, R., Kramer, L. D., & Cummings, J. L, "A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Aβ protofibril antibody" *Alzheimer's research & therapy*, 17 April 2021, https://alzres.biomedcentral.com/articles/10.1186/s13195-021-00813-8

Effects of Varied States of Awareness on the Presence of Spiral-like Wave Patterns

Allyse Nguyen (author), Thanisha Kapur (advisor)
Portola High School

Keywords: Insomnia, spiral brain waves, awareness, neocortex, dye imaging, EEGs

Abstract

Several recent discoveries have noted the existence of spiral-like waves in the neocortex of the brain, containing all 4 frontal, temporal, occipital, and parietal lobes, each responsible for different cognitive and sensory functions. This research article compares the prominence of their presence in three different states – sleep-like states, normal states, and focused states – in order to find linkage to insomnia and overall awareness. The injection of melatonin was used for sleep states, no substances were used for the normal state, and amphetamines were used for the focused state into rodents. Certain patterns were found repeatedly through a craniotomy and voltage sensitive dye imaging in the brain to detect wave shapes, as well as accompanying EEGs for each trial to confirm the state. It was discovered that states of normal awareness also had some levels of spiral waves, but less than the other two states on each end of the spectrum of awareness, as there was no specific activity prompted by a substance infusion. Although spiral waves were present in all states, states of higher awareness were associated with greatly longer lasting cycles, or epochs, which are groups of oscillations. Beta waves were observed as well, proving the state of attention. In contrast, states of lower awareness, such as sleep-like states, were associated with spiral waves of shorter durations. Delta waves were observed in these trials, matching what would be seen during deep sleep. These processes are examined and expanded on in this paper.

Introduction

Despite there being various known causes for the condition known as insomnia, such as environmental factors, mental illnesses, and sleep apnea, the problem remains persistent for millions of patients each year. The key to brain activity during sleep lies in various types of brain

waves measured by electroencephalography (EEGs), which can mark different sleep stages as well as disturbed sleep. As these two factors are strongly connected, discoveries about the presence of new brain waves could be relevant, as a recent study by the University of Sydney and Fudan University in China has discovered the presence of brain waves resembling the shape of spirals have been recorded in the neocortex, specifically in the outer layer of neural tissue.

These results were obtained through using functional magnetic resonance imaging (fMRIs) in 100 adults, with data demonstrating where high cortical activity and high concentrations of oxygenated blood are measured. The brain signals are complex circling around points called phase singularities at the center of each spiral resembling directional vortices in turbulence or circular pressure lines on a weather map (Watson). With the understanding that these types of waves in this area of the brain can greatly affect the reconfiguration of brain activity as well as memory and language processing, the possibility of a connection between a condition that may be affected by atypical brain waves such as insomnia and these patterns of waves is possible. This research is geared towards answering that question about the link between these two factors and determining if these emergent patterns can contribute to the activity found in those with insomnia, as well as the contrasting state of heightened awareness.

Materials and Methods

The experimental design involves injections of melatonin and amphetamine, as well as accompanying electroencephalographs into 24 common brown rats in order to examine patterns of spiral-like brain waves in different human states. The group of rodents exclude any animals with preexisting conditions that could affect their brain function, cognition, sleep, or awareness. Cognitive testing may be done if necessary to rule these possibilities out. The materials include at least about 3 mg of melatonin for each rodent, given the average weight of the common brown rat to be from 0.3 - 0.7kg, with the median being 0.5 kg. The amount of the chemical to be infused may vary in each animal based on the weight of the rat as well as its sex, as male rats weigh more on average. Additionally, at least 240 mg total of amphetamines are required for the rodents, with the amounts for each once again possibly varying based on the size and stature of the animal. Needles and syringes are necessary for the injection of these chemicals, as well as other supplemental blood tests, and need to be sterilized beforehand to avoid infection or any

other confounding variables that may impact the results of the study. This can be performed by placing the needles in a pot previously disinfected with both soap and water, and boiling water in it to at least 93.3 degrees Fahrenheit, or 200 degrees celsius (Weatherspoon et al.). At least 30 minutes are required between the cleaning and the time of use to ensure thorough disinfection. Flat metal discs called electrodes, their corresponding wires, and an electronic device, likely a computer, are all also needed for the completion of the electroencephalography. Anesthesia and the proper tools are needed in order to utilize the voltage sensitive dye imaging, and voltage sensitive dye is needed. For all processes, researchers will need lab coats, safety goggles, and medical gloves to avoid contamination. All proper lab protocols should be followed to ensure safety of the researchers and proper management of the experiment.

Epidural infusion of melatonin in 24 rodents is used to induce states similar to those occurring during sleep in humans. The initial dose given is 3 mg/kg, which is later supplemented by lower rate infusions through veins in the tail of 1 mg/kg when initial anesthetic levels waned after the passing of a few hours. EEGs are simultaneously taken for about 12-16 seconds to demonstrate the presence of both beta and delta waves, which are typically found in stages 1 and 2 of sleep, considered light sleep, as well as in stage 3 of sleep, considered deep sleep or REM sleep (TMSi). This is used as one experimental group. A separate experimental group of 24 rodents is then supplied with 10mg of amphetamine to induce states similar to those occurring during active concentration in humans. The goal is to enhance local excitatory connections, as they are essential for the prominence of spiral waves, as long range connections, such as thalamocortical or corticocortical connections, may interfere with rotors. An EEG for 12-16 seconds is taken to demonstrate the possible presence of gamma waves, found during active focus. A third group of 24 rodents is not supplied with any anesthesia to resemble a waking, normal state in humans. This is used as a negative control group in order to create a basis for comparison and identify any prominent effects in the experimental group. An EEG for 12-16 seconds is taken to demonstrate the presence of beta waves, found during states of awareness typical waking activities.

Voltage sensitive dye imaging is used to record the presence of spiral like waves for the same duration and compare their patterns in both waking rodents and those induced into a sleep-like state, in order to determine the existence of a relationship between spiral shaped waves and sleep

or the lack thereof. A high-speed sCMOS camera is needed to capture the fluctuating signals (Teledyne Photometrics). These waves rotate about a central point known as a rotor, and are organized around another central point known as a phase singularity (Turner). These centers then propagate across the brain cortex, coordinating the flow of activity and interacting to organize cognitive processing through their directions. Waves start at the area corresponding to where sensory stimuli was evoked, and then spread to greater primary and secondary cortical systems. Consequently, substantial amounts of neurons are depolarized, initiated by the opening of sodium ion channels within the plasma membrane, and the probability of action potentials, sequences of voltages, firing is increased (MIT). A craniotomy is then performed to surgically remove part of the skull to expose the brain and infuse voltage sensitive dye in order to receive the imaging.

The sensitivity and spatiotemporal resolution of voltage sensitive dye allows for the identification of the phase singularities that signify the presence of spiral waves (National Library of Medicine). The amplitude and phase maps formed by this imaging were examined in tandem with the visual depiction of the electroencephalographs. The independent variables were the three states of awareness induced, and the dependent variable was the concentration of spiral waves depicted in the dye imaging. The electroencapholgraphs were taken to ensure the proper function and activity of the chemicals in regards to the states they were creating and to match the results with occurrences identifiable to stages of sleep.

Data Analysis

Various tests are performed to determine the state of the experimental subjects and to ensure that all procedures could be properly followed through with. MRI and CT scans of the brains of each of the rodents are necessary prior to executing the experiment in order to verify that the animals did not possess any conditions, such as neurodevelopmental disabilities, deformations of the brain, or any other unusual circumstances that could impact the study. Conditions that affect parts of the brain stem, such as the reticular formation, which involves control of sleep and consciousness, or the pons, which affects the sleep cycle, could lead to situations where the chemicals bring the animals to a level of deep sleep or, on the contrary, awareness that far exceeds the other subjects (Mangold). Additionally, if these structures don’t function normally, the opposite could occur, where the chemicals fail to have significant effect and the animals are

at a level not comparable to the rest, making results from parts of the experiment population unreliable. Any concerning results should be noted.

Testing should also be done to check that none of the rodents have allergies or other extreme negative reactions to the chemicals so that they can be replaced if necessary. This can be done through patch testing or injections of a minimal amount of each of the chemicals, then monitoring the rats' statuses for at least 15 minutes. These examinations are also needed to make sure that the rodents don't have any complications that would severely interfere with the craniotomy that needed to be performed in order to infuse the voltage sensitive dye. Researchers should monitor symptoms and vitals before and after injection of substances to have a record of any significant findings that may be demonstrated, and to track any collateral harm that could occur to the animal.

Electroencephalography (EEG) is vital to the experiment. The electrodes are to be attached to the scalps of the rodents, as well as their corresponding wires, in order to detect electrical signals and translate them to visually viewable depictions on a computer for analysis (Mayo Clinic). The depictions appear as waves and spikes measured across time.

It would be beneficial to supplement the experiment with measurements of neurotransmitter levels through blood testing. Although they do not answer the main research question, they still remain very relevant to the topics being looked into, and could provide insight for other results or even prompt further findings.

Results and Discussion

Although this experiment has not been performed in a lab yet, predictions can be made on what the theoretical results would be based on other preexisting information.

In experimental group 1, where melatonin is injected into the rats, it is predicted that there would be high quantities of spiral-shaped brain waves, although they may appear for only a brief duration of time. Melatonin is a hormone secreted by the brain that manages the timing of the circadian rhythm, and is connected to the amount of light your eyes are exposed to through the

suprachiasmatic nucleus (National Library of Medicine). As 5 mg is appropriate for children, 3mg should induce the rats into a state of sleep (Cleveland Clinic). Delta waves in the neocortex are associated with sleep states as well as deep sleep and have the lowest frequency of zero point five to three hertz, so they would be expected to be recorded by the EEGs following the melatonin injections. In a study performed by Xiaoying Huang and Weifeng Xu, pentobarbital anesthesia was infused into the rodents and the EEGs did reflect a delta dominant state. Along with this state, 70 imaging trials, with 24 being held during the delta dominant state, demonstrated 132 cases of spiral waves, which was 65.35% of all cases found in the sleep state. The rate seen was 0.9 waves/second plusminus the standard deviation of 0.36 waves/ second, with N = 92 from five animals. However, it is true that during these sleep-like states the waves were very short lasting. Out of the 762 cases observed in 5 different animals, there were only 6 in which the waves lasted for a greater amount of time than two rotations, which is only 0.6%. The large majority of the waves, being 88%,were unable to complete one full cycle. Based on this information from a study with a similar framework, it is reasonable to assume that the infusion of melatonin would result in EEGs recording high amounts of both delta waves and patterns of spiral shaped waves; however they may be very short lived.

In experimental group 2, where amphetamines are injected into the rats, it is predicted that there would also be a significant level of spiral-like waves, although they may last for a longer duration. Amphetamines are a stimulant drug, rather than a depressant, meaning they speed up the rate of chemical messages being sent through neurotransmitters between the brain and the body. Specifically, the release of the neurotransmitter dopamine can be triggered by higher levels of amphetamines. Dopamines are partly responsible for thinking, movement, mood, and motivation (HealthDirect). Because of this, the organism receiving amphetamines can enter a more alert state with a more active brain; some of its common uses in the world are performance enhancement in sports or to boost attention for schooling (Medline Plus). As 20 mg of amphetamines is at the bottom of the dose range provided in tablets, 10mg should be appropriate for the rodents of smaller size. A state of higher awareness and focus was able to be replicated through amphetamines in the animals because of this fact. The EEGs would show beta waves, as they are waves of 14-30hz linked with increased awareness and intellectual activity. In the study performed by Xiaoying Huang and Weifeng Xu, local epidural application of carbachol and

bicuculline was used to enhance local excitatory connections in the brain, which has a similar effect to that produced by amphetamines. 433 trials found spontaneous clusters of oscillations of frequencies from 3 - 20 hz called epochs, each having anywhere from 3 to 100 cycles. Some epochs did not consist solely of spiral waves; other types were discovered. Although this is a significantly higher amount given that there were multiple epochs in comparison to those in sleep-like states, there were many more trials taken. However, a notable difference would be in the length of the wave cycles. Despite the fact that 81% of the spirals lasted between one and three cycles, the other 19% lasted between four and 25 cycles, which is substantially more than even the longest lasting waves found during states of sleep.

In the control group, no chemicals are infused into the subjects. Spiral waves have been linked to several functions in the neocortex, such as cortical processing, coordination of information flow, working memory, language processing, and reconfiguration of brain activity, according to a study published in Nature Human Behavior by the University of Sydney and Fudan University. Because of these important roles, it is likely that spiral brain waves would still be present; however, it is likely that they would be observed less often than when specific states or types of activity are stimulated by drugs such as melatonin and amphetamine.

Given these results, some conclusions can be predicted, especially in the focus of insomnia. Besides the delta and beta waves that have already been mentioned, there are two other main types, being gamma and theta waves. Gamma waves are high amplitude waves of 20 - 80 hz which " is considered to be the fastest brain activity…Prominence of this wave leads to anxiety, high arousal, and stress" (Mehrotra et. al.), while theta waves are low amplitude waves of 4-7hz that are seen during light sleep (Moawad). Based on this information, it is likely that these are the types of waves that would be distinguished on an electroencephalograph in a patient with insomnia. Gamma waves are the waves that would be present if the patient is purely unable to sleep, remaining in an awake state. Besides being unable to sleep, those with this condition also experience restless or interrupted sleep, which would be caused by the light sleep associated with theta waves. With results demonstrating that only the other two types of brain waves were recorded alongside the spiral waves, and no evidence of alpha and beta waves being present alongside them in the sleep states, it is possible that the lack of functions of spiral waves

contribute to inability to sleep. Since these waves have been suggested to manage cortical processing, the information processing model supports this idea (Ritchie). This model states that the brain utilizes the decrease in sensory information reception during sleep to process information (Wamsley et. al.).

Additionally, the time period distinction between the life of a spiral wave between the first and second experimental groups means it is possible that higher levels of awareness are connected with longer lasting wave patterns, and greater amounts of cycles or epochs. This understanding means that those suffering from this condition could focus on various strategies to slow their brain waves. Firstly, patients can use neurofeedback training through clinics or apps, which once again uses EEGs to stimulate the brain with visual and auditory cues, deliver brain wave recordings to the person, and then help them self-regulate and control their actions to achieve their goals. Studies have also shown that certain types of music can align brainwaves with the beat of the music, meaning songs with slower tempos can lead to a more relaxed state of mind (Wang). Another study has shown that listening to the song “Weightless,” designed to be anxiety reducing, led to a “65 percent reduction in participants' overall anxiety and a 35 percent reduction in their usual physiological resting rates” (Shepherd et. al.) Lastly, meditation has been proven to result in relaxed-state alpha waves (Kaushik et. al.). Alpha waves, the last type of brain wave, have a frequency of 8-12hz, and are responsible for calm, relaxation, and stress reduction. A 2020 study explained how participants experienced improved sleep quality when and lessened levels of stress when alpha waves increased to more prevalent levels. The results of this experiment can foster solutions and ideas for enhanced sleep in those with insomnia.

Another factor to be noted is the longer lasting spiral-shaped waves in states of attention and awareness. Although this research is focused on sleep and the lack of awareness, future research could further explore these relations, aiming to increase the time of these waves to improve focus. This could be very relevant in widespread physical and mental health issues in the modern world such as attention deficit hyperactivity disorder (ADHD), which affects 13% of teenagers and 5% of adults, hormone imbalances, fatigue, and more (NIMH).

Common mistakes in the procedure of this study could be failing to do appropriate testing to check for preexisting conditions, failing to monitor vitals for other reactions that could become confounding variables, not selecting animals of the same species, not sterilizing medical equipment between trials, therefore leaving medical residue that could change the amount of substance being given, and not providing the correct or equal amount of substance to each subject.

Works Cited

Abhang, Priyanka A., and Suresh C. Mehrotra. "Technical Aspects of Brain Rhythms and Speech Parameters." *Science Direct*, Elsevier B.V., 2016, https://www.sciencedirect.com/topics/neuroscience/gamma-wave#:~:text=A%20gamma%20wave%20is%20considered,%2C%20memory%2C%20and%20information%20processing. Accessed 27 July 2023.

"Attention-Deficit/Hyperactivity Disorder (ADHD)." *National Library of Medicine*, NIH, https://www.nimh.nih.gov/health/statistics/attention-deficit-hyperactivity-disorder-adhd. Accessed 27 July 2023.

"Dopamine | healthdirect." *Healthdirect*, https://www.healthdirect.gov.au/dopamine. Accessed 27 July 2023.

"EEG (electroencephalogram)." *Mayo Clinic*, 11 May 2022, https://www.mayoclinic.org/tests-procedures/eeg/about/pac-20393875. Accessed 27 July 2023.

Kaushik, Medha, et al. "Role of Yoga and Meditation as Complimentary Therapeutic Regime for Stress-Related Neuropsychiatric Disorders: Utilization of Brain Waves Activity as Novel Tool." *Journal of Evidence-Based Integrative Medicine*, vol. 25, 2020. *Sage Journals*, https://journals.sagepub.com/doi/full/10.1177/2515690X20949451. Accessed 27 July 2023.

Lall, Sabbi. "How do neurons communicate (so quickly)? - MIT McGovern Institute." *McGovern Institute for Brain Research*, 28 February 2019, https://mcgovern.mit.edu/2019/02/28/ask-the-brain-how-do-neurons-communicate/. Accessed 27 July 2023.

"Melatonin: What You Need To Know | NCCIH." *National Center for Complementary and Integrative Health*, https://www.nccih.nih.gov/health/melatonin-what-you-need-to-know. Accessed 27 July 2023.

Moawad, Heidi. "Alpha Brain Waves: What Are They and Why Are They Important?" *Healthline*, 9 October 2019, https://www.healthline.com/health/alpha-brain-waves#what-are-they. Accessed 27 July 2023.

"Neuroanatomy, Reticular Formation - StatPearls." *National Library of Medicine*, https://www.ncbi.nlm.nih.gov/books/NBK556102/. Accessed 27 July 2023.

Ritchie, Philip. "How Spiral Brain Signal Patterns Organize Cognitive Activity." *Neuroscience News*, 15 June 2023, https://neurosciencenews.com/cognition-swirl-brain-activity-23475/. Accessed 27 July 2023.

Shepherd, Daniel, et al. ""The most relaxing song in the world"? A comparative study." *Psychology of Music*, vol. 51, no. 1, 2022. *Sage Journals*, https://journals.sagepub.com/doi/abs/10.1177/03057356221081169. Accessed 27 July 2023.

"A study of the type and characteristics of relaxing music for college students." *ResearchGate*, 22 April 2023, https://www.researchgate.net/publication/265861608_A_study_of_the_type_and_characteristics_of_relaxing_music_for_college_students. Accessed 27 July 2023.

"Substance use - amphetamines." *MedlinePlus*, 30 April 2022, https://medlineplus.gov/ency/patientinstructions/000792.htm. Accessed 27 July 2023.

Turner, Ben. “Mysterious spiral signals in the human brain could be key to our cognition.” *Live Science*, 19 June 2023, https://www.livescience.com/health/neuroscience/mysterious-spiral-signals-in-the-human-brain-could-be-key-to-our-cognition. Accessed 27 July 2023.

“Voltage Imaging.” *Teledyne Photometrics*, https://www.photometrics.com/learn/electrophysiology/voltage-imaging. Accessed 27 July 2023.

Wamsley, Erin J., and Robert Stickgold. “Dreaming and Offline Memory Processing - PMC.” *NCBI*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3557787/. Accessed 27 July 2023.

Watson, Clare. “Mysterious Spiral-Shaped Signals Detected in The Human Brain.” *ScienceAlert*, 30 June 2023, https://www.sciencealert.com/mysterious-spiral-shaped-signals-detected-in-the-human-brain. Accessed 27 July 2023.

Weatherspoon, Deborah, and Corey Whelan. “How to Sterilize a Needle: Boiling Water, Alcohol, Fire, and More.” *Healthline*, 21 May 2019, https://www.healthline.com/health/how-to-sterilize-a-needle. Accessed 27 July 2023.

Wu, Jian-young. “Spiral wave dynamics in neocortex - PMC.” *National Library of Medicine*, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4433058/. Accessed 27 July 2023.

The Effects of Vitamin D on Oligodendrocyte Production

Anasha Maheen (author), Thanisha Kapur (advisor)
Texas Connections Academy at Houston

Keywords: Oligodendrocyte, Vitamin D, Multiple Sclerosis

Abstract

This research article and experimental design is targeted toward the effects of vitamin D on oligodendrocyte (OL) production in the brain. Oligodendrocytes are the producers of myelin in the brain, which allow neural impulses and messages to travel effectively. However, individuals suffering from multiple sclerosis lack myelin and face damage to myelin sheaths in their brains. Therefore, vitamin D was used to see if myelin can be produced. OL cell lines were established from guinea pig brain samples obtained through a biopsy. Cell isolation was then done to isolate OL cells from the rest of the brain biopsy sample. This was followed by the establishment of OL cell lines in cell culture dishes. Flow cytometry was then used to confirm the concentration of OL in the cell lines. Vitamin D was then applied to each cell line while observers waited for an appropriate amount of time to see the effects of VitD on the OL cell lines. To analyze the data, transmission electron microscopy and immunofluorescence (IF) microscopy was used. These processes confirmed that vitamin D increases the production of oligodendrocyte cells in the brain. This discovery is beneficial to the future of society because multiple sclerosis is a common neurological illness that affects a significant amount of the population. Vitamin D was already suspected to aid in the production of myelin, however, this experimental model may bring us closer to finding a cure. Through this discovery, vitamin D may be incorporated into MS patients' diets and could remove their symptoms and cure them of the illness.

Introduction

Over 1 billion people around the world have been affected by some type of neurological illness, with 2.8 million being diagnosed with multiple sclerosis, or MS. MS is a neurological disease that occurs when myelin, a protective sheath around the nerves in the brain and spinal cord, is damaged. The role of myelin in the brain is vital as it allows for the rapid and systematic transportation of electrical impulses through these brain nerves. When these nerves lack the

protection that myelin provides, messages may not travel as quickly or can even get lost in the transportation period. Although, naturally, the human body is capable of repairing myelin in the brain through the use of oligodendrocytes (OL), the extreme loss of myelin can severely harm the individual suffering from this deficiency. This can be caused by a break in the blood-brain barrier which allows the immune system and the brain to be exposed to each other. Hence, necessary structures, such as myelin, may be identified as a threat to the body and is the target of destruction. In these severe cases, MS occurs in the individual, causing symptoms such as muscle spasms, stiffness and weakness, fatigue, vision problems, cognitive disabilities, mobility issues, speech difficulties, and/or bladder/bowel problems, to appear. Although MS has been observed and identified for a long time, a cure has yet to be discovered. To find a remedy, the root problem of a lack of OL cells must be addressed. By increasing the production of OL cells in the brain, remyelination may occur. Additionally, experts have found that populations living closer to the equator have seen lower levels of MS patients. Excessive amounts of vitamin D have been suspected as the cause of this phenomenon. Therefore, this research is targeted toward the experimentation of vitamin D on oligodendrocyte production in individuals with multiple sclerosis.

Materials and Methods

Establishing Oligodendrocyte Cell Lines

This experimental model used samples from guinea pigs' brains to test vitamin D's effects on oligodendrocyte production in the brain in individuals with multiple sclerosis (MS). Guinea pigs were chosen because they are commonly used in neurological-related experiments and research, especially those focused on disorders and brain functions. To begin the experiment, OL cell lines must be established through cell culture. To do this, a brain sample was removed from the guinea pigs through a brain biopsy. Each of the four guinea pigs underwent an MRI scan which allows the surgeon to pinpoint the exact location of the biopsy. To begin the procedure, anesthesia with 2% isoflurane was administered to each guinea pig (Cuevas et al.). The dosage of anesthesia was determined according to each guinea pig's weight and previous medical history after consultation with an experienced veterinarian. Following all sanitary procedures and using appropriate equipment such as surgical gloves, gowns, masks, and caps, the surgeon begins the biopsy by making a burr hole, which is a small incision in the scalp to create an opening in the skull. Then,

using forceps purchased from Apiary Medical (Colorado, USA), the surgeon effectively obtains a small brain sample through the burr hole. This sample was taken from a portion of the brain that guinea pigs can safely live without according to consultation from a veterinarian. Once the biopsy is complete, interrupted sutures using nylon were used to close the burr hole and finish the procedure. This process was repeated for each guinea pig to gain four brain tissue samples. With consultation from a veterinarian, all four guinea pigs were placed in effective healing environments with an ideal temperature range. Additionally, the guinea pigs were fed a balanced diet that allowed for successful healing and aligned with the Institutional Animal Care and Use Committee's (IACUC) guidelines and approval.

The next step to establish an oligodendrocyte cell line is a process called cell isolation. This is done to isolate specific cells from a tissue sample. In this experimental design, OL cells were isolated through enzymatic digestion from the brain sample obtained from the guinea pigs previously. The chosen enzymes for enzymatic digestion were papain and trypsin, both purchased from Thomas Scientific (NJ, USA). Papain and trypsin were dissolved in an appropriately buffered solution to create a safe solution containing the enzymes. A buffered solution is necessary because it resists changes in pH levels and creates an environment in which the enzymes can maintain their attributes and carry out their appropriate functions. The brain tissue is then submersed in the enzyme solution to break down the extracellular matrix surrounding the OL cells. After the tissue sample has been digested by the enzymatic solution, the OL cells from the brain sample are released and become suspended in the papain and trypsin solution. To stop overdigestion of the sample, aprotinin and pepstatin A, buffers that inactivate trypsin and papain, respectively, are added to the enzymatic solution. Aprotinin and Pepstatin A were both purchased from MedChemExpress (NJ, USA). Enzymatic digestion is complete. To separate the OL cells from any tissue debris or remains that might not have been broken down by enzymatic digestion, the tissue suspension is spun in a centrifuge purchased from Thermo Fisher Scientific (MA, USA). After centrifugation, the isolated OL cells in the supernatant are aspirated with cation to obtain a refined cell population. To further eliminate any remaining cellular debris or enzymes, the OL cells are washed with a buffer solution. Then, they are counted and evaluated for viability to guarantee that they may be used in an experiment.

To establish OL cell lines, cell culture dishes purchased from Thermo Fisher Scientific were used. Using a sterilized dropper, DMEM/F12 cell culture media was poured into the cell culture dishes. DMEM/F12 cell culture media was purchased from Thermo Fisher Scientific. Basic fibroblast growth factor (bFGF), purchased from Sigma-Aldrich (MO, USA) was added to the media to increase the proliferation of OL cells. The OL cells obtained previously are then seeded into 4 cell culture dishes. As OL cells interact with the bFGF and the DMEM/F12 cell culture media in the dishes, the cells divide and multiply. After 5 days, the OL cells have completely covered the surface of the dishes and are ready for expansion. The OL cells are then detached from each of the dish's surfaces using trypsin, an enzyme ideal for separating cells from surfaces or other cells. Following detachment of the oligodendrocyte cells, an automated cell counter purchased from Thermo Fisher Scientific is used to count the number of OL cells. After counting, the cells are seeded into a different set of cell culture dishes with only DMEM/F12 cell culture media. Cell lines have been officially established.

Confirming the Presence of Oligodendrocytes in Cell Lines

Even though the brain tissue sample and cell lines are made up of oligodendrocytes, it is vital to scientifically confirm that the cell lines are composed of OL cells. To confirm the presence of OL cells in the cell culture dishes, flow cytometry, a process used to characterize cells in a sample, is used. To begin this process, the sample must be converted into a single-cell suspension. This is accomplished by harvesting the cells from the cell culture dishes and breaking apart the clumps in the sample. The cells are then evenly distributed in a buffer solution. Then, cell viability is assessed through a trypan blue exclusion test. To conduct a trypan blue exclusion test, a minuscule amount of trypan blue dye is incorporated into the cell suspension. Using a vortex mixer/vortex shaker purchased from Thermo Fisher Scientific, the cells are then mixed to verify that the blue dye has dispersed evenly. The sample is incubated for three minutes to ensure the dye has interacted with the cells. A hemocytometer, purchased from Thermo Fisher Scientific, is then used to hold a sample of the cell suspension. The hemocytometer is then placed under the AmScope T490B Microscope to distinguish blue cells from transparent ones. The AmScope T490B Microscope is purchased from Amazon. Cells that appear blue are considered dead, whereas transparent cells are considered living and viable. The non-viable cells are then counted and the percentage of the viability of the cell suspension is

determined. The trypan blue exclusion test is complete. To continue preparing the sample for flow cytometry, an automated cell counter is used to find the cell concentration and to make sure no additional clumps have formed. Fluorescent probes are then attached and used to find the correct structure of the OL cells and to confirm that they are existent in the sample. Once the harvested sample is prepared, it is then inserted into a flow cytometry machine; the flow cytometry machine was purchased from Bio-Rad Laboratories (CA, USA). Lasers from the flow cytometry machine then release light with specific wavelengths. This causes the fluorochromes previously attached to the cells to rapidly move around, which results in fluorescent signals being emitted from them. To guarantee that every single cell is monitored and analyzed carefully, the cells are placed in a sheath fluid. This causes the cells to travel in a single line through the laser beam so that the machine can individually observe and categorize each cell. Each cell produces scattering light along with fluorescence which then determines the type of cell through the use of a computer. In this experiment, the cells from the harvested sample were confirmed to be oligodendrocytes. A total of four cell lines have been established and each line is confirmed to be fully composed of OL cells.

Experimentation with Vitamin D

The four cell lines are then harvested and seeded into four separate cell culture dishes supplemented with fresh DMEM/F12 culture media. Each cell culture dish is also incorporated with 4 pumps (2 mL) of vitamin D liquid supplement. The brand of VitD is Designs for Health Liposomal D Supreme Liquid purchased from Amazon. Once the four cell lines are seeded into their respective cell culture dishes with VitD, they are placed in an appropriate environment with an ideal temperature that is constantly maintained. The cells must be incubated in the media with the VitD for a total of five days. The cell culture dishes are observed regularly by using the Celestron Labs CM800 Compound Microscope purchased from Amazon, and data is recorded with findings. Individuals participating in the experiment are qualified experts in their respective fields. For all aspects of the experiment, a sterile field was maintained, and ethical as well as hygienic procedures were observed.

Data Analysis

To observe the validity of the cells from the experiment, transmission electron microscopy, or TEM was used to analyze the effects of vitamin D on OL production and myelination. Using an ultramicrotome, a thin portion of the oligodendrocyte cell lines in the cell culture media must be cut to measure about 75 nanometers thick. Next, the appropriate electron beam used for TEM should be passed through the piece of the oligodendrocyte cell line obtained previously. This will cause the electrons from the beam to scatter. On the other side of the sample oligodendrocyte cell line, a detector is placed to record the transmitted electrons, which will form a black-and-white image of the internal structures. This procedure allows individuals to notice the healthiness of each of the cell lines and to determine if the results are valid. The TEM results from this experiment determine that the cell lines have not faced any damage during transfer or any other procedure. Additionally, oligodendrocyte production has increased due to VitD.

Although vitamin D has been confirmed to increase OL production, it is important to assess the functionality of the newly produced OL cells. This means that myelin sheaths should be able to form due to the new OL cells. To view myelinated axons, immunofluorescence (IF) microscopy will be used. First, formaldehyde, a chemical, will be applied to the OL cell lines from the cell culture dishes. Formaldehyde was purchased from Thomas Scientific. This is used to conserve the cell line formation and keep the protein content stable. The cell cultures are then permeabilized. Through permeabilization, the antibodies used in the future steps of IF microscopy will be able to use intracellular proteins. Each experiment will choose a different protein that bonds with the appropriate model being studied. In this experimental design, antibodies are chosen depending on the specific proteins in oligodendrocytes and myelin sheaths. The antibodies must be against the specific protein, which in this case is myelin basic protein (MBP). Purchased from Thermo Fisher Scientific, MBP antibody is chosen for this experiment. Fluorescent particles are then attached to the main antibodies to continue the process. The labeled antibodies are then uncovered and shown to light at a specific wavelength. This causes the labeled antibodies to emit light that has a wavelength that is in correlation with the light they were exposed to previously. The OL cell lines are then taken and incorporated with the labeled antibodies to bind to the myelin basic protein. Since the OL cell lines contain MBP, the antibodies will naturally be secured together. A fluorescence microscope, purchased from LabX,

is then used to analyze the results. An exciter filter is applied to the microscope to observe which wavelengths are allowed through the filter. A portion of the OL cell line is also placed underneath the fluorescence microscope for observation purposes. With consultation from a lab specialist, a specified light is shone on the OL cell line portion which causes the specific antibodies to shine fluorescence. After a photograph is taken by a specialist, it is run through filtering software to discover what proteins have been found and if the additional oligodendrocyte production is usable (creates usable myelin for myelin sheaths in the brain). In this experimental design, the OL cell line produced in the laboratory due to VitD is indeed beneficial; it creates myelin sheaths and repairs damaged portions of axons already in the brain. Hence, it can be concluded that OL production from vitamin D is beneficial to an individual.

Results & Discussion

This experimental design is completely hypothetical and has therefore never been conducted before. Hence, extreme caution should be observed before attempting the procedures in this research article.

This experiment has shown that VitD plays a role in the production of oligodendrocytes, cells in the brain responsible for producing myelin. Not only does VitD produce additional oligodendrocyte cells, but the newly produced cells also function effectively and produce myelin for developing myelin sheaths according to the immunofluorescence (IF) microscopy process in the previous section. The results of this hypothetical experiment can be backed up by the results of the transmission electron microscopy which was done earlier. This proves the validity of the sample. In individuals with multiple sclerosis (MS), this process of using oligodendrocyte precursor cells to produce myelin naturally is effective early on in the diagnosis. However, the process loses its effectiveness as MS attacks repeatedly occur. Based on this experiment, we can hypothesize that vitamin D can be taken by individuals diagnosed with MS to increase the production of oligodendrocytes in the brain. However, further research and experiments should be conducted by professionals in the field before vitamin D can be given to a patient suffering from a neurological disease such as multiple sclerosis. In turn, the production of myelin can be increased which can allow the myelin sheath to be replaced in neurons. Although this has been proven by the outline of the experiment and the hypothetical results, actual experiments done in

the lab are much more effective in proving this hypothesis. However, the effects of VitD on oligodendrocyte production have been experimented on previously and have found similar effects. Nevertheless, very few experiments were targeted toward oligodendrocyte cells like the experiment design outlined in this research article.

This information is beneficial because VitD can reduce the effects of multiple sclerosis on the body. With advice from a physician, if an individual diagnosed with multiple sclerosis incorporates vitamin D into their daily diet, the effects of the disease may be reduced according to the results from this experiment. Eventually, the number of attacks can decrease along with the severity. With further experimentation by professionals in many fields, the effects of vitamin D on oligodendrocyte production may even be tested in pregnant women to see if multiple sclerosis and other myelin-related diseases can be prevented completely.

Works Cited

Gomez-Pinedo U, Cuevas JA, Benito-Martín MS, Moreno-Jiménez L, Esteban-Garcia N, Torre-Fuentes L, Matías-Guiu JA, Pytel V, Montero P, Matías-Guiu J. Vitamin D increases remyelination by promoting oligodendrocyte lineage differentiation. Brain Behav. 2020 Jan;10(1):e01498. doi: 10.1002/brb3.1498. Epub 2019 Dec 13. PMID: 31837111; PMCID: PMC6955836.

"Immune System and MS." *Multiple Sclerosis Society UK*, www.mssociety.org.uk/research/explore-our-research/emerging-research-and-treatments/immunomodulation. Accessed 30 July 2023.

Jäkel S, Agirre E, Mendanha Falcão A, van Bruggen D, Lee KW, Knuesel I, Malhotra D, Ffrench-Constant C, Williams A, Castelo-Branco G. Altered human oligodendrocyte heterogeneity in multiple sclerosis. Nature. 2019 Feb;566(7745):543-547. doi: 10.1038/s41586-019-0903-2. Epub 2019 Jan 23. PMID: 30747918; PMCID: PMC6544546.

"Myelin Repair." *Multiple Sclerosis Society UK*, www.mssociety.org.uk/research/explore-our-research/emerging-research-and-treatments/myelin-repair. Accessed 30 July 2023.

Remaud S, Ortiz FC, Perret-Jeanneret M, Aigrot MS, Gothié JD, Fekete C, Kvárta-Papp Z, Gereben B, Langui D, Lubetzki C, Angulo MC, Zalc B, Demeneix B. Transient hypothyroidism favors oligodendrocyte generation providing functional remyelination in the adult mouse brain. Elife. 2017 Sep 6;6:e29996. doi: 10.7554/eLife.29996. PMID: 28875931; PMCID: PMC5779229.

Slavov GS, Trenova AG, Manova MG, Kostadinova II, Vasileva TV, Zahariev ZI. Vitamin D immunomodulatory potential in multiple sclerosis. Folia Med (Plovdiv). 2013 Apr-Jun;55(2):5-9. doi: 10.2478/folmed-2013-0011. PMID: 24191393.

Brain Spine Interface

Anika Seki (author), Thanisha Kapur (advisor), Anika Shah (editor)
Palisades High School

Keywords: Spinal Cord Injury, Digital Bridge, Brain Spine Interface, STIMO trials, Paralysis

Abstract

A spinal cord injury can be heavily fatal to one's bodily movement. When the spinal cord is injured, this trauma can interfere with the flowing signals from the brain to other destinations within the body. Therefore, with the obstruction of these signals, people can be victims of paralysis. With a new study that researchers have proposed, it was found that it was possible to reestablish signals between the brain and the body, leading to better chances of patients regaining mobility after injuring their spinal cord. This was possible through the digital bridge, a wireless brain spine interface which was vigorously studied through the STIMO trials. Although the digital bridge is currently limited to lower body paralysis, researchers believe the concept of creating an electronic bridge to restore damaged areas can lead to additional treatments for those with other spinal cord injuries.

Introduction

With the ever changing and evolving technology, AI has continuously become more integrated within the medical field. Recently, researchers have discovered the brain spine interface, otherwise known as the "digital bridge". This digital bridge refers to a two-part wireless electronic implant within the brain and spinal cord which transmits signals before translating them into actions. The digital bridge helps re-establish previously lost connection between the brain and the spine, which is the catalyst for lower body paralysis. This new brain spine interface has caused a large commotion as it allows those who are paralyzed within the lower region to walk again, which is a remarkable achievement in comparison to other known treatments.

Through this new AI system that helps decode signals between the brain and the spinal cord, a patient who was previously paralyzed within the lower region was able to swiftly recover,

showing the length to which this new treatment was useful. Although this digital bridge was only tested on one patient with lower body paralysis, it can be researched more in order to produce results that can be even more useful. Even though this treatment has limitations as does many other treatments, it is essential to address the importance of this research that has been done as it can potentially lead to further discoveries that could be used for other patients such as for those who have multiple sclerosis and more. This brain spine interface is an extraordinary discovery done through the use of technology, and thus should be studied further to reveal other potential treatments.

Body

STIMO Trials

The STIMO trials were put forth by Jocelyne Bloch along with Ecole Polytechnique Fédérale de Lausanne and Foundation Wings For Life. These trials differed from previous studies in regards to recovering paralysis as the STIMO trials focused on engineering aspects which had not already been done. The three known patients were reported to have been paralyzed in the lower body for 3 years, and they were completely unable to move their lower muscles voluntarily. The STIMO trials focused on two main implants: a 16-electrode array and a pacemaker. The 16-electrode array was carefully placed within the epidural space while the pacemaker was placed under the abdomen skin. Thus, by using technology through a device, researchers were able to create a series of signals turned into electrical pulses that were sent through the pacemaker to the electrodes within the epidural space to control a patient's muscles. The spinal cord is able to strengthen the relationship between the brain and lower body muscles, allowing more signals to pass and more mobility within the body. After these electronics were implanted and researchers were able to send electrical pulses through a device, the study resulted in patients being able to walk again. The STIMO trials were seen to be successful because this study relied on timed, calculated electrical pulses based on the body's natural movements. Although the patients continuously had to participate in physical therapy, they were able to regain most of their senses within their lower body. Researchers noted that the major difference in accomplishment between the STIMO trials and previous trials was the electrode array:" The array is longer and wider than the array most often used in other studies. This new electrode array can stimulate both the leg and trunk muscles because it allows access to a more extensive area of the spinal cord"

(Lovell). The limitation to the STIMO trials is that patients are only able to walk when devices are electrically stimulated, thus restricting patients from moving when devices are turned off. Researchers concluded that despite the fact that STIMO trials were able to gain new achievements with a new approach to countering paralysis, this topic must be studied more to promote more efficient ways of regaining mobility. This study confirmed that in order to take a step towards curing patients with such injuries, researchers must delve deeper into solutions that come from engineering.

STIMO-BSI Trials

In a study done by a group of scientists led by Gregoire Courtine from École Polytechnique Fédérale de Lausanne in Switzerland, Brain Spine Interface was utilized efficiently to counter a serious spine injury. Courtine and his scientists were able to discover the connection between Brain Spine Interface and paralysis whilst testing patient Gert-Jan Oskam, 38 year old male, suffering from a spinal cord injury that paralyzed his lower body. Oskam had been living with this spinal cord injury for over 10 years and had previously participated in the STIMO trials where electrical stimulation was used to successfully assist patients in walking again after paralysis incidents. Although the STIMO trials were revolutionary, they were found inefficient as Oskam did not fully recover, and thus he enrolled in the new study, STIMO-BSI. In this particular study, multiple implanted recording devices were used in order to decode signals within the brain before sending these signals to the spinal cord. These electronics consisted of two fundamental installments: a 64-channel electrode grid embedded in a 50 mm diameter titanium case and a 16-electrode paddle lead. Recording devices were meticulously implanted over the dura mater with the paddle lead on Oskam's lumbar spinal cord. Transmitter-receivers were given to the patient to pick up nerve impulses, giving insight into his body movement which then leads to the generation of nerve impulses that assist in carrying out these specific movements. Researchers were able to link ECoG signals to the lumbar region of the spinal cord, allowing nerve signals to reach paralyzed muscles within the lower body. As a final result, Oskam was able to walk independently with crutches. Although there was difficulty at first, there was much more improvement in Oskam's mobility compared to any previous trials. Oskam was able to walk on his own and over uneven surfaces such as stairs after competing 40 sessions with BSI. The patient's ability to regain mobility within his lower body after these BSI trials

demonstrates the wide impact of the digital bridge between the brain and the spine. This study with BSI heavily improved the patient's life, and researchers claim that this new technology can be utilized to help previously far-fetched treatments become true.

Comparative Analysis

Although the STIMO trials and the STIMO-BSI trials were similar in their goals, the outcomes heavily differed from each study. In a sense, though STIMO trials were a breakthrough in treating patients with spinal cord injuries, they were not able to thoroughly cure them of their paralysis. Thus, the STIMO-BSI trials were birthed from the results from the previous STIMO trials. Whilst STIMO trials focused on calculated signals of movement, STIMO-BSI trials relied on real-time signals instead. The STIMO-BSI trials directly scan the motor cortex, allowing patients to walk again. Artificial intelligence heavily aided in real-time decoding of the patient's intentions in relation to movement. The most significant difference between the two trials that were conducted were the results. After the STIMO trial study, the subjects were only able to walk a limited distance over flat surfaces. On the other hand, Oskam, subject of the STIMO-BSI trials, was able to move across uneven surfaces individually after weeks of testing, which could not have been done with the original STIMO study. Not only was Oskam able to gain better results of walking on his own from the newer trial, but as time passed he did not need excessive help from others to support his movement. As for the STIMO trials, patients were only able to move when devices were turned on, meaning that they did not have full control over mobility. STIMO-BSI trials created a new breakthrough for many researchers, and can be promising for the future. It was reported that not only does the brain spine interface help patients regain mobility within their lower body, but it also increases chances of neurological recovery. With new evidence of swift recoveries from patients subject to brain spine interface, researchers believe that this information can be utilized towards recovering different types of spinal cord injuries, as well as upper body paralysis. "Courtine and his team are also exploring other uses for their BSI system, including potentially restoring lost arm movement to tetraplegic spinal injury patients" (Nolan). Some studies suggest that although this brain-spine interface may not be able to help certain injuries, it can surely be used as a stepping stool for future studies, one injury being multiple sclerosis.

Conclusion

Through the trials and mistakes of many studies, researchers were able to build and create a brain spine interface which connects the spine to the brain to allow signals to pass through, promoting bodily function. Although the brain spine interface is extraordinary, it still has its limitations, as do most things. However, the digital bridge is only just the beginning of future studies. Even though the STIMO-trials do not address such things such as other common injuries that relate to the spine, it is possible that such a study can be utilized for other experiments as well. It allows the STIMO-trials to be the base for such future studies that can create a revolution, especially within the medical field. Thus, there is hope for the future that more treatments can be created with the assistance of previous knowledge and AI technology.

Works Cited

"Brain–Spine Interface Enables Natural Walking after Spinal Cord Injury." *Physics World*, 1 June 2023, physicsworld.com/a/brain-spine-interface-enables-natural-walking-after-spinal-cord-injury/#:~:text=Researchers%20have%20now%20developed%20a%20brain%E2%80%93spine%20interface%20%28BSI%29. Accessed 5 Aug. 2023.

CNN, Tasnim Ahmed. "New Spinal Cord Stimulation Study Puts People with Paralysis on Their Feet Again." *CNN*, www.cnn.com/2022/02/07/health/spinal-cord-stimulation-study/index.html

Daley, Jason. "How Implanted Electrodes Helped Paralyzed People Stand and Walk Again." *Smithsonian Magazine*, www.smithsonianmag.com/smart-news/implanted-electrodes-allow-paralyzed-people-walk-180970399/.

https://www.facebook.com/48576411181. "This Brain-Spine Interface Sidesteps Spinal Cord Injuries - IEEE Spectrum." *Spectrum.ieee.org*, spectrum.ieee.org/brain-spine-interface.

Lovell, Kristen . "New Spinal Cord Stimulator Technique Shows Promise." *Health Central* , 24 Mar. 2022, www.healthcentral.com/condition/back-pain/emerging/new-spinal-cord-stim.

Robertson, Sally. "Wireless Brain–Spine Interface Enables Primates with Spinal Cord Injury to Walk Again." *News*, 19 June 2019, www.news-medical.net/news/20161110/Wireless-brainspine-interface-enables-primates-with-spinal-cord-injury-to-walk-again.aspx#:~:text=Wireless%20brain%E2%80%93spine%20interface%20enables%20primates%20with%20spinal%20cord,aid%20the%20leg%20muscle%20movements%20required%20for%20walking.

"STIMO: Epidural Electrical Simulation (EES) with Robot-Assisted Rehabilitation in Patients with Spinal Cord Injury. - Full Text View - ClinicalTrials.gov." *Clinicaltrials.gov*, classic.clinicaltrials.gov/ct2/show/study/NCT02936453. Accessed 5 Aug. 2023.

Tobias, Ed. "Could a Digital Bridge to Link Brain and Spinal Cord Help Those with MS? | Multiple Sclerosis News Today." *Multiplesclerosisnewstoday.com*, 9 June 2023, multiplesclerosisnewstoday.com/columns/2023/06/09/could-digital-bridge-link-brain-spinal-cord-help-those-with-ms/. Accessed 5 Aug. 2023.

"Wireless Brain–Spine Interface Enables Primates with Spinal Cord Injury to Walk Again." *News-Medical.net*, 10 Nov. 2016, www.news-medical.net/news/20161110/Wireless-brainspine-interface-enables-primates-with-spinal-cord-injury-to-walk-again.aspx#:~:text=Wireless%20brain%E2%80%93spine%20interface%20enables%20primates%20with%20spinal%20cord. Accessed 5 Aug. 2023.

The Kappa Opioid Receptor as a Promising Tool to Addiction

Anushka Ayanampudi (author), Thanisha Kapur (advisor), Anika Shah (editor)
Woodbridge Academy Magnet School

Keywords: kappa-opioid receptor, addiction, opioids, G protein-coupled receptor, GPCR, schizophrenia, analgesics, dopamine

Abstract

As the opioid crisis worsens, researchers look to new alternatives to the addictive pain medications used in the past. The kappa-opioid receptor (KOR), specifically, has been a topic of interest because it may be an alternative to the mu-opioid receptor (MOR) used in the past, which can cause dangerous long term dependencies. This is because the KOR can inhibit pain signaling without having to create side effects of euphoric feelings. In doing so, many patients may not have to face addiction and other difficult withdrawal processes from prescribed drugs. However, there can be many dangerous side effects of using this receptor because not everything has been completely tested yet, and there are always outside elements that can potentially alter the behavior of certain KOR agonists or antagonists, making this a topic of further interest which can be crucial to discovering whether or not this seemingly well alternative is appropriate or not.

Introduction

Opioid addiction is a rising issue in the United States as well as all around the world. It is shown through the body's dependency to a substance. The process in which this occurs is a complex neurological issue having to do with the brain and its many receptors. The receptors of the brain are the main mechanisms of neurotransmission. Their many roles stretch from mood to motor control to memory and more. Each one of these receptors have agonists and antagonists. An agonist would be a drug that will bind to the receptor, producing the same or similar effect as the intended chemical. The antagonist would bind to a site that can be either the receptor itself, or even another site, and will prevent a response from the receptor, The kappa-opioid receptor specifically works with chemicals known as dynorphins, which are class of opioid peptides

related to pain stimuli. Researchers can utilize this mechanism to create medications that have the ability to reduce or even eliminate cravings or withdrawal symptoms. As a result, potential for drug abuse from opioids in the future can be reduced worldwide, making it a topic of interest for drug developers (Kosten and George).

Body

The G protein-coupled receptor (GPCR) family

As more and more pain management drugs are needed in the healthcare industry, the usage of opioid drugs as a solution has risen greatly, and over the last few decades, the addictive nature has become increasingly clear. The kappa opioid receptor (KOR) is a system that plays a role in this issue of opioid drugs ("Opioids and the Brain").

KORs, μ-opioid receptors (MORs), and delta-opioid receptors (DORs), are included in the G protein-coupled receptor (GPCR) family. A key difference between the three receptors is that KORs tend to inhibit neuronal activity and neurotransmission, whereas MORs and DORs will encourage it. KORs and MORs both can create pain relief, but a key difference being that the response to MORs has a higher tendency to cause euphoria in the user. It is also true that MORs and KORs exert contrasting influences on the management of motivational procedures, showing that KORs can be a promising solution to the current problem we have with our pain relief drugs today. By creating drugs that target the KOR in specific, we can reduce pain while still preventing the likelihood of an individual's dependence on that drug in the future (Lutz and Kieffer).

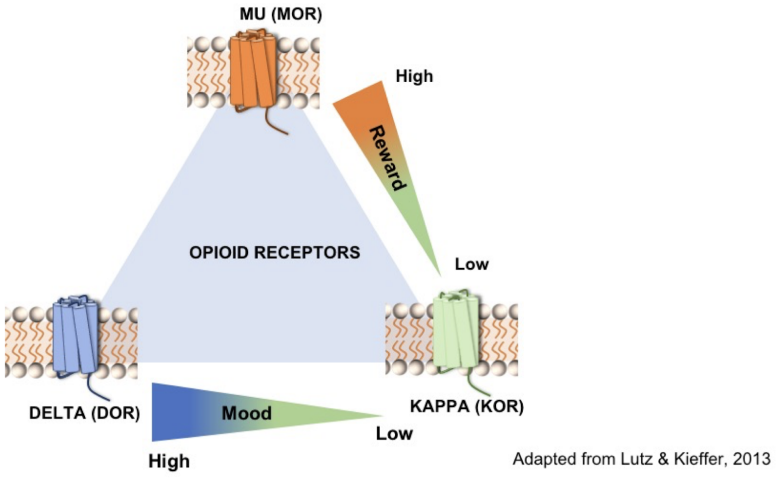
Addiction

Opioids receptors have the ability to flood the brain with dopamine. With a repeated use of dopamine from opioids, the body starts to adjust itself and adapt to the influx of these chemicals. It develops a need for those high levels of dopamine in order to maintain its hemostasis, and this dependance is otherwise known as addiction.

On the other hand, the appeal of the KOR is that this receptor can stop pain without giving the same release of dopamine, which over time usage is likely to not create a dependence from the

drug used. This is what creates the interest in this drug compared to the traditionally used receptors of the past.

Due to this reliance, an individual who was once consistently using opioid pain relievers would find great difficulties in trying to terminate their usage. Withdrawal symptoms are commonly seen among these long term users, making it very difficult to stop the medication, eventually leading many past users to find other methods such as using drugs that were not prescribed to them, or other illegal sources. “According to the Diagnostic and Statistical Manual of Mental Disorders (DSM–5) criteria, signs and symptoms of opioid withdrawal include lacrimation or rhinorrhea, piloerection "goose flesh," myalgia, diarrhea, nausea/vomiting, pupillary dilation, photophobia, insomnia, autonomic hyperactivity (tachypnea, hyperreflexia, tachycardia, sweating, hypertension, hyperthermia), and yawning” (Shah and Huecker).



In this image, it shows the different effects of the opioid receptors. Reward and Mood tend to be factors that drive up the risk of addiction. It is shown that both MORs are high in reward, and DORs are high in mood. This makes them seem to be bad choices when compared to the KOR, which is low in both reward and mood.

Relation to Schizophrenia

High levels of dopamine are known to cause schizophrenia. Because of the simulation of KOR constantly, the amount of dopamine released can be sufficient enough to cause

schizophrenia.These interactions between KORs and their agonist can create potentially psychotomimetic effects on individuals.

In the study *Effects of TRK-820, a selective kappa opioid receptor agonist, on rat schizophrenia models*, abnormalities in the dopaminergic and serotonergic neurotransmission in the forebrain can be treated using TRK-820 chemical compound, which is known to have a connection to certain schizophrenic mechanisms (Nakao, Kaoru, et al). Currently it is treated by blocking those receptors, however, it has negative side effects to the extrapyramidal system. The researchers used rats to test the effect of TRK-820, which was reversed with the usage of the KOR receptor. The rats had been treated with phencyclidine (PCP) in order to induce the schizophrenia-like behaviors. They were then administered TRK-820 to be the KOR agonist. The behaviors were observed and quantified, and overall evaluated to find the impact. They were then used in vivo microdialysis to measure the extracellular levels of dopamine and serotonin in the prefrontal cortexes of all the rats. The final findings were that TRK-820 has the potential to cure certain abnormal behaviors related to changes (from the dopamine or serotonin), proving to be a candidate for schizophrenia symptom treatment (Yoshikawa, et al).

However, this proves to be very inefficient when it comes to treatment of addiction. Activation of these receptors can produce dysphoria or aversive effects, which may discourage the addictive behaviors. In this way, kappa opioid receptor agonists have been explored as potential therapies for drug addiction, particularly in reducing drug cravings and relapse. Consequently, if the drugs cause a further issue with schizophrenia, it may not be a possibility to use them in finding treatments.

Conclusion

The KOR receptor is a great new tool to researchers developing alternatives to opioid medications. According to the Center for Disease Control and Prevention (CDC), there were 91,799 drug overdose deaths in 2020, and about 75% of them happened to involve opioid usage. The KOR is a receptor in the brain that has the property to create pain prevention, but without the addictive properties of the rest of its G protein-coupled receptor (GPCR) family including its MOR and DOR cousins, which all play a role in pain relief in different ways. The overuse of

those receptors is what created such a huge problem because of its addictive properties from the amount of dopamine released by the brain. Although the KOR seems to be such a promising tool, there are certain complications that can prevent this from being used. Other than the lack of field research that is happening at the time, there are also studies showing physiological side effects such as schizophrenic symptoms. Thus, the usage of the KOR receptor does not seem to be up to the standard it seems, and further research is expected before it is implemented into real world usage. Still, further studies and research must be done in order to fully acknowledge either side of the situation in this case.

Works Cited

Bai, Nina, and Dana Smith. "Body's "Natural Opioids" Affect Brain Cells Much Differently than Morphine." *Body's "Natural Opioids" Affect Brain Cells Much Differently than Morphine | UC San Francisco*, 10 May 2018, www.ucsf.edu/news/2018/05/410376/bodys-natural-opioids-affect-brain-cells-much-differently-morphine. Accessed 6 Nov. 2019.

Bruijnzeel, Adrie W. "Kappa-Opioid Receptor Signaling and Brain Reward Function." *Brain Research Reviews*, vol. 62, no. 1, Dec. 2009, pp. 127–146, www.ncbi.nlm.nih.gov/pmc/articles/PMC2787673/, https://doi.org/10.1016/j.brainresrev.2009.09.008.

Brust, Tarsis F., et al. "Biased Agonists of the Kappa Opioid Receptor Suppress Pain and Itch without Causing Sedation or Dysphoria." *Science Signaling*, vol. 9, no. 456, 29 Nov. 2016, pp. ra117–ra117, https://doi.org/10.1126/scisignal.aai8441. Accessed 10 Oct. 2021.

Carroll, F. Ivy, and William A. Carlezon. "Development of κ Opioid Receptor Antagonists." *Journal of Medicinal Chemistry*, vol. 56, no. 6, 14 Feb. 2013, pp. 2178–2195, www.ncbi.nlm.nih.gov/pmc/articles/PMC3612131/, https://doi.org/10.1021/jm301783x. Accessed 26 Apr. 2022.

CDC. "Understanding the Epidemic | CDC's Response to the Opioid Overdose Epidemic | CDC." *Www.cdc.gov*, 2 Oct. 2021, www.cdc.gov/opioids/basics/epidemic.html#:~:text=The%20number%20of%20drug%20overdose.

Chahl, Loris A. "Opioids - Mechanisms of Action." *NPS MedicineWise*, 1 July 1996, www.nps.org.au/australian-prescriber/articles/opioids-mechanisms-of-action.

Heinsbroek, Jasper A., et al. "A Single, Extinction-Based Treatment with a Kappa Opioid Receptor Agonist Elicits a Long-Term Reduction in Cocaine Relapse." *Neuropsychopharmacology*, vol. 43, no. 7, 22 Feb. 2018, pp. 1492–1497, https://doi.org/10.1038/s41386-017-0006-4. Accessed 17 Oct. 2022.

Kosten, Thomas, and Tony George. "The Neurobiology of Opioid Dependence: Implications for Treatment." *Science & Practice Perspectives*, vol. 1, no. 1, July 2002, pp. 13–20, www.ncbi.nlm.nih.gov/pmc/articles/PMC2851054/, https://doi.org/10.1151/spp021113.

Lutz, Pierre-Eric, and Brigitte L. Kieffer. “Opioid Receptors: Distinct Roles in Mood Disorders.” *Trends in Neurosciences*, vol. 36, no. 3, 1 Mar. 2013, pp. 195–206, www.sciencedirect.com/science/article/abs/pii/S016622361200197X, https://doi.org/10.1016/j.tins.2012.11.002.

Nakao, Kaoru, et al. “[Effect of TRK-820, a Selective Kappa Opioid Receptor Agonist, on Scratching Behavior in an Animal Model of Atopic Dermatitis].” *Japanese Journal of Psychopharmacology*, vol. 28, no. 2, 1 Apr. 2008, pp. 75–83. Accessed 1 Aug. 2023.

“Opioids and the Brain - How Do Changes in the Brain Begin?” *PursueCare*, 10 Apr. 2019, www.pursuecare.com/opioids-and-the-brain/#:~:text=When%20binding%20to%20the%20pain.

Akpan, Nsikan and Julia Griffin. “How a Brain Gets Hooked on Opioids.” *PBS NewsHour*, 9 Oct. 2017, www.pbs.org/newshour/science/brain-gets-hooked-opioids.

Shah, Mansi, and Martin R Huecker. “Opioid Withdrawal.” *Nih.gov*, StatPearls Publishing, 4 June 2019, https://www.ncbi.nlm.nih.gov/books/NBK526012/.

Yoshikawa, Satoru, et al. “Effects of TRK-820, a Selective Kappa Opioid Receptor Agonist, on Rat Schizophrenia Models.” *European Journal of Pharmacology*, vol. 606, no. 1-3, 15 Mar. 2009, pp. 102–108, https://doi.org/10.1016/j.ejphar.2009.01.043. Accessed 21 May 2023.

Neuroplasticity after TBI

Arianna Barik (author), Thanisha Kapur (advisor), Anika Shah (editor)
Amador Valley High School

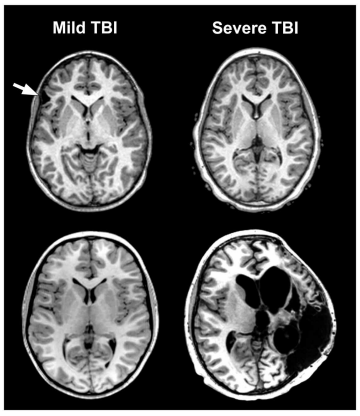
Keywords: Neuroscience, Traumatic Brain Injury, Neuroplasticity, Functional plasticity

Abstract

The brain is a complex and fascinating organ, able to control emotion, thoughts, motor functions, sensory input and much more. However, it is also delicate to injuries. Traumatic brain injury (or TBI) is common and can be caused by jolts to the head. It can cause damage to the brain in many different ways. However, the brain is able to recover due to its inherent quality of neuroplasticity. Neuroplasticity is commonly known as the reason why we can learn things, but it can also aid in recovery through a multitude of mechanisms, such as undamaged areas taking over the functions of damaged areas.

Introduction

The brain has the ability to change and make new connections based on experiences, which is called neuroplasticity. While this ability is most active during the early years, it continues well into adult years, bringing along many benefits, such as learning new abilities, "training" your brain, and recovering from brain injury. One type of brain injury is Traumatic Brain Injury (TBI), when a sudden external blow to the head can cause brain injury. Symptoms include headaches, convulsions, difficulty in memory, hearing issues, and new neurological deficits.



Specifically in cases of brain injury, neuroplasticity can be observed working in unique ways and can even be utilized in treatments. After TBI, synaptogenesis occurs, creating new connections between neurons. Also, neuronal regeneration can occur, which is neurons being created. There have been studies that indicate there is an increase in new neurons after injury (Perederiy et al.). Additionally, functional reorganization or "remodeling" of the brain can happen after TBI. If a cortical region is damaged, the function can move to an adjacent area.

Most importantly, neuroplasticity can be used to treat TBI in treatments such as stem cells, antioxidant therapy, and pharmacologic treatment along with new brain imaging techniques (Su).

Body

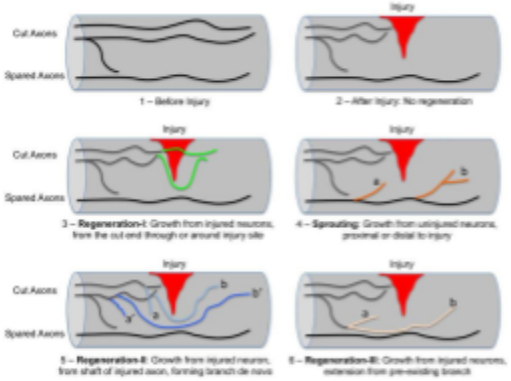
Understanding Traumatic Brain Injury (TBI)

A traumatic brain injury can occur when there has been an external jolt to the head (non-penetrating) or an object goes through the skull, entering the brain tissue (penetrating). This can happen due to sports injuries, car accidents, blunt trauma accidents, assaults, explosions, and more. TBIs can be primary or secondary. If primary, the damage is immediate. If secondary, the damage can take hours, days, or weeks to present themselves. Symptoms typically immediately after the injury are dizziness, headaches, fatigue, and disorientation, while long-term symptoms can be more behavioral such as irritation, mood changes, and frustration. TBI also has varying effects on consciousness. A severe TBI can cause minimally conscious state, vegetative state, coma, or even brain death. TBI's effects on the brain have been sorted into two categories: focal injury and diffusion injury. Focal injury is when the damage is only in one area of the brain, while diffusion injury is more widespread in the brain. One common effect of TBI is diffusion axonal injury, which is widespread damage to the white matter of the brain. White matter is made of axons, which are the "tails" of neurons that conduct electrical impulses to other cells. Diffusion axonal injury occurs when excessive twisting or force tears the axon bundles, causing interruption of neuron communication. TBIs can also cause hematomas, when a ruptured blood vessel causes the brain or area around it to bleed. Concussions are also a common effect of TBIs and typically take weeks to months to recover. Additionally when the brain moves back and forth in the skull, it can cause contusions, which are bruising or swellings either directly under the impact area– a coup injury– or on the opposite side of the brain from the impact area–a contrecoup injury. All of these primary effects can also lead to secondary effects such as increased intracranial pressure, infections, seizures, hemorrhagic progression (from a contusion) and more ("Traumatic Brain Injury (TBI)").

Neuroplasticity Further Explained

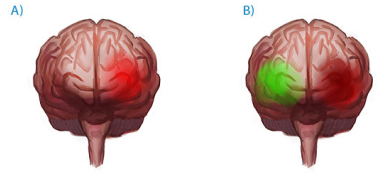
Neuroplasticity is the brain's ability to change neural networks through learning or experiences.

There are two types of neuroplasticity: structural plasticity and functional plasticity. Structural plasticity is when learning experiences alter the brain's physical structure, working on a cellular level (Cherry). Structural plasticity can range from myelination of axons (glial cells insulating the axon, allowing for faster signals) to neurogenesis(new neurons created). Synaptic remodeling can occur by modifying the dendritic spines, which are on the neuron's dendrite and will make contact with other neurons' axons to receive input, strengthening synapses with the help of functional synaptic remodeling; however, this process does decrease from childhood to adulthood(Adães). In addition, white matter –made of myelinated axons– also has the property of plasticity. Studies showed that increased activity of the neurons could proliferate oligodendrocytes, which produce myelin, allowing for faster conduction of the impulses traveling on axons (Gibson et al.). There is also neurogenesis, the creation of new neurons, but there has not been substantial evidence to prove that it is possible in human adults, though it is frequent in the developmental years. On the other hand, functional plasticity is when the brain moves functions from a damaged area of the brain to an undamaged area, thus working at a molecular level (Cherry). Examples of functional plasticity include the functional recovery after Broca's aphasia, in which many diagnosed patients recover their speaking abilities within months, despite damage to the Broca's area. Synaptic strengthening is the efficiency of synapses increasing due to increased activity/usage. However, synaptic weakening also exists, in which synapses become less efficient, making it harder for the neurons to communicate. This refers to the common phrase "use it or lose it." Axonal sprouting can also be an aspect of functional plasticity.



Axonal sprouting

Axonal sprouting occurs when undamaged axons grow new nerve endings to connect to the damaged neurons. Additionally, new neural pathways can be created when undamaged axons connect with each other to fulfill the same function as the damaged axons. Another form of functional neuroplasticity, more common in children, is when an area in one brain hemisphere, the function "transfers" to the other hemisphere, thus not losing the function completely. Another example of functional



A) A segment of one brain hemisphere is damaged (shown in red), resulting in a loss of a particular function.
B) Over time, the opposite hemisphere can take over the lost function in the damaged hemisphere (shown in green).

neuroplasticity is when a certain area of the brain is used extensively, that area will become larger physically, called map expansion. Cross-modal reassignment can also happen when an area of the brain normally used for a certain sensory input is instead used for a different sensory input. Similarly, compensatory masquerading is when the brain uses an area with lost function for a different usage than originally(Adães).

Neuroplasticity Phases After TBI

There are typically three phases to neuroplasticity after TBI (Burda). During the following 48 hours after the injury, cells die and cortical inhibitory pathways (pathways that block neural signals coming from the cerebral or cerebellar cortices) decrease. Then, this leads the brain to use secondary or new neural networks that may have been unmasked by the decrease (Nahmani). After a few weeks, the once inhibitory cortical pathways become excitatory, allowing recruitment of supporting cells to replace the damaged cells. Additionally, synaptogenesis (new connections made) and neuronal proliferation (neurons regenerated) occurs (Burda). After a few months, the brain, due to its neuroplasticity, continues to change, working around the injury, using axonal sprouting (Carmichael).

Impact on Healthcare: Music Therapy

Neuroplasticity's process after injury is important because it can be used to help patients recover. A study by Berit Marie Dykesteen, Geir Olve Skeie, and Karsten Specht showed a fascinating effect of stimulating activities on the brain after an injury. In this study, 7 volunteers affected by past mild TBIs were observed. In addition, there were two healthy control groups, one with music and one without. The volunteers affected by their TBIs had tried other rehabilitation that did not improve their issues with social behavior, focus, etc. Before the study began, participants had the following done: "neuroimaging, semi-structured interviews in the patient group only, self-report, training log and neuroimaging for all groups"(Vik). Then for 8 weeks, the music groups had two half-hour piano lessons every week with a thorough curriculum. In the end, out of the 7 participants, 6 reported improvement in cognitive difficulties. Additionally, after analyzing the MRIs, the researchers found functional neuroplasticity mostly in the orbito- and prefrontal cortex. The areas that showed improvement were areas having to do with cognitive control and social skills, and evidence showed that the

connectivity in these areas increased(Vik). While more research needs to be done to reach concrete conclusions, this study is a great example of the potential medical benefits of continuing to research neuroplasticity after TBIs.

Conclusion

All in all, research into the various mechanisms of neuroplasticity after brain injury is impacting the healthcare world. As more is learned about the brain, this knowledge can be applied to real-world patients. The research does not necessarily have to result in a novel complex surgery, but rather help us understand new ways to help patients recover from all types of brain injuries. For example, it has been studied how music can help rehabilitate people after traumatic brain injuries (Vik). By continuing the important work in the cross section of neuroplasticity and traumatic brain injury, researchers can change the course of many patients' lives through new therapies.

Works Cited

Adães, Sara. “What Is Neuroplasticity?-Mechanisms of Functional and Structural Brain Plasticity.” *Neurohacker Collective*, neurohacker.com/what-is-neuroplasticity-mechanisms-of-functional-and-structural-brain-plasticity. Accessed 30 July 2023.

Bigler, Erin D. “Systems Biology, Neuroimaging, Neuropsychology, Neuroconnectivity and Traumatic Brain Injury.” *Frontiers*, 8 June 2016, www.frontiersin.org/articles/10.3389/fnsys.2016.00055/full.

Cherry, Kendra. “What Is Neuroplasticity?” Edited by Shaheen Lakhan, *Verywell Mind*, 2022, www.verywellmind.com/what-is-brain-plasticity-2794886.

Geoffroy, Cedric, and Binhai Zheng. “Myelin-Associated Inhibitors in Axonal Growth after CNS Injury.” *PubMed*, 2014, www.researchgate.net/publication/260645285_Myelin-Associated_Inhibitors_in_Axonal_Growth_After_CNS_Injury.

Liou, Stephanie, and Stephanie Liou. “Neuroplasticity.” *HOPES Huntington’s Disease Information*, 5 Nov. 2016, hopes.stanford.edu/neuroplasticity/.

Puderbaugh, Matt, and Prabhu Emmady. “Neuroplasticity - Statpearls - NCBI Bookshelf.” *Neuroplasticity*, 2023, www.ncbi.nlm.nih.gov/books/NBK557811/.

Su, Sophie, et al. “Neuroplasticity after Traumatic Brain Injury - Translational Research ...” Edited by Laskowitz D. and Grant G., *Translational Research in Traumatic Brain Injury*, 2016, www.ncbi.nlm.nih.gov/books/NBK326735/.

"Traumatic Brain Injury (TBI)." *National Institute of Neurological Disorders and Stroke*, www.ninds.nih.gov/health-information/disorders/traumatic-brain-injury-tbi. Accessed 30 July 2023.

Vik, Berit Marie Dykesteen, et al. "Neuroplastic Effects in Patients with Traumatic Brain Injury after Music-Supported Therapy." Frontiers in Human Neuroscience, 25 June 2019, www.ncbi.nlm.nih.gov/pmc/articles/PMC6604902/#B41.

Effect of Gut Microbiota on a Neurological Condition

Arshia Malhotra (author), Thanisha Kapur (advisor)
Brentwood High School

Keywords: Gut Microbiota, Samples, rRNA

Abstract

This paper and research article examines the effect of gut microbiota on neurological conditions and its therapeutic implications. It also compares the function of the behavior of a group in which the gut microbiota has been altered. Through the extraction and separation of both mice groups, it was found that the group in which the addition of gut microbiota has been added, the neurological condition often sees a change in its severity. Additionally, the gut microbiota was found to have affected the behavior of these mice in which the additional strain was added. Gut microbiota is known to control part of the brain and influence the behavioral systems usually associated with stress response, anxiety, and memory function. If additional gut microbiota is added or a strain with a possible defect, it takes an influence upon the bodys' emotions and cognitive capabilities. This experiment aims to find the extent of the effect of the gut microbiota on the brain, as well as how it may alter behavior. Additionally, it gives the researcher the ability to determine which medication or probiotic can be taken to decrease the unusual behavior. Researchers have the flexibility to use a strain of their choice for the process. Through this research article, by determining the changed effects on the mice after the addition of a strain, it was found that the mice's behavior was altered due to the less frequent signals sent from those nerves to the brain.

Introduction

Due to one's original DNA, every individual has a completely unique microbiota, also known as gut bacteria. Gut bacteria is found in the intestines and is known for helping the human body by supplying necessary nutrients, synthesizing vitamin K (essential for the blood-clotting process), helping in the digestion of cellulose, and supporting nerve function. Likewise, gut bacteria is also known for causing harm to the human body when its composition changes due to the gut going through changes, often influenced by the host. With an imbalance of the gut microbiota, often the

body sees an arise in a neurological condition, or even the prior condition's severity increasing. Therefore, the evaluation of a condition is done through evaluating the functionality and complexity of the gut microbiota. Rather than the bacteria staying in the gut, it penetrates through the gut lining and reaches other bacteria. Additionally, this bacteria is known to reach the extent of affecting immune cells located in the body as well as the brain, increasing neurodegeneration process in conditions. Recently, it was discovered that the connection between the gut and brain happens through blood and nerves. Specifically through the nerves, the gut bacteria is able to send signals to the brain as well as making substances, ultimately having the potential to influence our emotions and cognitive abilities. This research is geared towards highlighting whether manipulating gut bacteria can have therapeutic implications for neurological conditions as well as possible solutions to limit gut bacteria's extent

Materials and Methods

(Results and procedure are purely hypothetical, they were not performed)

This experimental design used samples from mices' gut microbiota in order to study its effect on neurological conditions as well as its therapeutic implications. The materials, from PubMed Central, are as follows: adult germ-free (GF) mice, specific pathogen free (SPF) conditions, fecal samples, 16S rRNA gene sequencing, probiotic interventions, behavioral tests.

Have ten mice of the same species at hand, and divide them into two groups of 5. Throughout this procedure, ensure that all conditions are SPF, in order to ensure sanitation and allow for true results. First, take both groups of mice and collect their fecal samples in the early morning. Earlier in the day is recommended as it allows for the process to be quicker, in correlation with their eating behavior. For the process, take 1.5 ml cryovials and label them using a lab safe marker with each Mices' Information (name, group, number). Make sure to wear plastic gloves, and place one mouse in a clean cage with nothing else inside. Allow time for the mouse to defecate and once it has produced around 2-3 fecal pellets, remove the mouse from the cage. Next, collect at least two fecal pellets with a sample pick and place it within the labeled vial. Place the completed vial on ice until all samples are collected and/or are ready to be studied. After this has been completed for a single mouse, the steps can be repeated for the remaining

nine. It's important to note that you should change your gloves between the collection process of fecal matter from each mouse. Additionally, change the clean cage between both groups, rather than each mice. This helps to keep the experiment sanitary at all times, ensuring that all results are accurate.

After the collection of fecal samples from all mice, the fecal matter needs to be studied. First, it should be made uniform in phosphate-buffered saline (PBS) (1:50 w/v) and gram-stained, in order to allow for any bacterial infection to be detected. Once these steps are completed, the image can be observed using an ordinary optical microscope. When observing these images, divide them into three different sizes (64 x 64, 128 x 128, and 256 x 256 pixels) to show different perspectives of the samples. The different perspectives help to detect something new and allow for a clearer perspective of the sample. Once the images have been produced prior to conducting and procedure, then the RNA extraction can be started. Begin by thawing the fecal samples and attempt to create uniform and even suspensions. This suspension can be created through using TRIzol reagent or methods like beat-beating. To isolate the RNA from the fecal matter, follow the RNA extraction kit instructions. The procedures mentioned below should be similar. Begin by adding TRIzol reagent to the uniform fecal sample in a 1:5 ratio, making sure to keep the different units of measurements in mind. Mix both in a rapid circular motion to ensure the complete disintegration. Next, for the phase separation to occur, incubate the sample at room temperature for a few minutes. Once this time has passed, add chloroform to the mixture and use the help of a centrifuge to separate the aqueous RNA containing phase from the rest. Take this aqueous phase and place it in a new RNase-free tube. Within the new tube, precipitate the RNA by adding isopropanol and incubating the tube at -20°C or -80°C (according to the kit's directions). Use the help of a centrifuge after the incubation to transform the RNA within the tube to pellets. Once this state has been produced, wash the pellet with 75% ethanol to get rid of any contamination. Once again, use a centrifuge to help remove the ethanol within the tube again. Lastly, allow the RNA pellet to air-dry for a short period of time. This procedure allows for information about the mice's gene expression as well as their undergoing, if any, biological processes. Make sure to perform these steps for each test tube sample.

Once the gut microbiota has been studied and observed, the next step is to observe how influencing the gut microbiota can affect the mice's therapeutic implications. Introducing the new strain of gut microbiota is the choice given to the researcher in this experiment. This strain or gut microbiota can be introduced to the mice through fecal microbiota transplantation (FMT), engineered microbiota, or human microbiota-associated mice (HMA). When introducing the gut microbiota, ensure that it is administered completely to only one group, leaving the other group still GF. Allow the mice administered the addition of gut microbiota to recover for a few days, monitoring their health during intervals. Once the health recovers of the group in which the gut microbiota was added, repeat the RNA extraction process again from the fecal matter of each mice. This gives the researcher information as to what has changed when it comes to the mice's gene expression, molecular base, and cellular responses to stimuli.

After the group of mice has recovered, the experiment shifts to seeing the addition of the gut microbiota effect regarding neurological conditions. Place both groups, GF mice and the additional gut microbiota mice, into an open field activity box. For a time period of 60 minutes, measure its motor activity, both locomotor and rearing. Make sure to observe specifically which group of mice traveled longer distance, spent more time in both slow and fast locomotion as well as rearing activity, as well as the activity during the initial open field exposure. This provides the detail on the gut microbiota's affect on activity. To study if the microbial pathogen induces anxiety-like behavior within the mice, experiment has to be done involving both groups. Two rodent tests of anxiety can be performed: the light-dark box test and the elevated plus maze. Noting the mices' activity gives insight as to how altering gut microbiota affects the mices' neurological condition when it comes to anxiety.

Data Analysis

For the experiment, different data was measured using procedures and methods to examine the gut microbiota implication on the mice. Animal models, such as mice or rats, are often used to study the gut-brain axis due to ethical and practical considerations. Germ-free or gnotobiotic animals can be used to investigate the effects of specific gut microbiota on neurological disorders. Additionally when conducting experiments on mice, it's essential to make sure that conditions are all SPF, in order to keep things sanitary and eliminate confusion. The mice studied

in this experiment must be from the same genus, with a mic of female and males. Different genders allow for the analysis of which bacterial infections, if so, affect the mouse more severely or differently.

Collecting samples from the gut (fecal samples) is essential throughout this experiment. For human studies, volunteers or patients can provide stool samples and brain tissue can be obtained through biopsy. From the mice fecal samples, it is vital that both groups have their fecal matter examined before a new strain is added to the new group, as well as after the strain has been administered to see what has changed. As stated prior, studying the fecal matter through RNA sequencing offers insight regarding the mice's gene expression, molecular base, and cellular responses to stimuli.

The behavioral tests on animals to assess cognitive, emotions, and motor functions of the mice. This includes tests for learning and memory, anxiety, depression like behavior, social behavior, etc. The tests in this experiment are an open-field activity box and a light-dark box. Noting all aspects of the mices' behavior, as mentioned in the methods and materials section, allows for the researcher to acknowledge variations in the cognitive abilities between the original group versus the one where the additional strain was added.

Administering probiotics (substances that promote the growth of beneficial gut bacteria) help study their effects on neurological disorder in animal models or human subjects. In this experiment, the prebiotic administered is up to the choice of the researcher. This choice is made off of the mice's response to stimuli as detected in both behavioral experiments. The prebiotic adminsited will help balance the once disturbed gut microbiota levels, allowing for the mice behavior of the group altered to be similar to how it was before the experiment was conducted.

Results and Discussion

In order to analyze the gut microbiota's effect on the neurological condition and activity of the mice, the change in the body can be observed through the study of what changed with the mice group that had the addition of the extra strain/gut microbiota. Compare both groups after one has been changed and the other remains the same, through the fecal matter. As stated earlier, this

gives the researcher information as to what has changed when it comes to the mice's gene expression, molecular base, and cellular responses to stimuli.

Next, the physical effect on the mice can be studied through both behavior tests conducted after the RNA extraction process. For the light-dark box test, make sure to note which mice spend more or less time in the dark and light compartments, as well as willingness to explore the lit area. The mice who spent more time in the dark compartments are prone to having anxiety, when compared to the mice in the dark compartments. For the elevated plus maze test, observe which mice spent majority of the time in the open arm vs. the closed arm, which group took part in riskier behavior regarding the number of visits, as well as the number of entries as a total by each group. The mice that traveled throughout the maze and took part in risky behavior most likely did not have anxiety, compared to the ones that stayed in place. The results then can be studied by the original groups they were in, seeing if their gut microbiota was kept the same or altered.

Works Cited

Davis, University of California. *Gut Microbiota (GM) Fecal Collection and Fecal Sample Shipping*. https://mmrrc.ucdavis.edu/files/Gut-Microbiota-Collection-Kit.pdf

Fessi, Sophie. "Tinkering with Gut Microbes Boosts Brain Plasticity in Mice." *The Scientist Magazine®*, 13 Jan. 2022, https://www.the-scientist.com/news-opinion/tinkering-with-gut-microbes-boosts-brain-plasticity-in-mice-69606

Heijtz, R. D., et al. "Normal Gut Microbiota Modulates Brain Development and Behavior." *Proceedings of the National Academy of Sciences*, vol. 108, no. 7, 31 Jan. 2011, pp. 3047–3052 https://www.pnas.org/doi/full/10.1073/pnas.1010529108

Lupori, Leonardo, et al. "The Gut Microbiota of Environmentally Enriched Mice Regulates Visual Cortical Plasticity." *Cell Reports*, vol. 38, no. 2, Jan. 2022, p. 110212, https://www.cell.com/cell-reports/fulltext/S2211-1247(21)01716-2

Mukherjee, Suprabhat, et al. "Gut Microbes as Future Therapeutics in Treating Inflammatory and Infectious Diseases: Lessons from Recent Findings." *The Journal of Nutritional Biochemistry*, vol. 61, Nov. 2018, pp. 111–128, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7126101/

Singh, Rasnik K., et al. "Influence of Diet on the Gut Microbiome and Implications for Human Health." *Journal of Translational Medicine*, vol. 15, no. 1, 8 Apr. 2017, https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-017-1175-y

Artificial Intelligence's Role in the Diagnosis of Parkinson's Disease

Nandanashri Baskaran (Author), Thanisha Kapur (Advisor)
Saint Francis High School

Keywords: Parkinson's Disease, Diagnosing, Artificial Intelligence, Biomarkers, Blood Samples, Healthcare, Prospective Study, Neurofilament light chain, Malondialdehyde, 24S-Hydroxycholesterol

Abstract

Artificial Intelligence has the capability to efficiently diagnose Parkinson's Disease by analyzing certain biomarkers in a patient's blood samples. As of now, the traditional method of Parkinson's diagnosis is typically based on the observations of symptoms a patient is experiencing. However, traditional methods are often prone to error, as they rely on the evaluation of clinical signs that often go unnoticed, or are misclassified for other conditions. To improve the diagnostic accuracy of Parkinson's Disease, this research article has studied several biomarkers (Neurofilament light chain, Malondialdehyde, and 24S-Hydroxycholesterol) present in patients with the disorder, and how analyzing them in blood samples can successfully diagnose a patient years before symptoms arise. Using Artificial Intelligence, we can develop a machine learning tool that will ultimately create a composite data set featuring detected biomarkers from the laboratory samples. The result will be a highly accurate, less invasive, and less costly method of Parkinson's diagnosis.

Introduction

Did you know that Parkinson's Disease is one of the few neurological disorders with an unknown cause and no cure? Parkinson's Disease is a progressive neurological disorder that affects the nervous system and occurs commonly in elderly people, affecting approximately 10 million people worldwide. Parkinson's is most widely recognized by its symptoms of tremors, rigid movements, and slow movement, which affect the body gradually, in a declining manner. Diagnosing Parkinson's Disease early on is crucial, enhancing a patient's life quality and survival rate. In current events, early stages of Parkinson's Disease are often mistaken for arthritis. In

addition to this, the current methods of diagnosis with cerebrospinal fluid and neuroimaging are costly and invasive. The false diagnoses and limited resources present in everyday life result in the decline of a patient's quality of life. The concept of Artificial Intelligence has been recently making a debut in the field of healthcare, as it improves on traditional medical diagnoses and treatments by making them less costly, less invasive, and therefore more easily accessible. Previous researchers Dina Katabi, the Thuan (1990) and Nicole Pham Professor in the Department of Electrical Engineering and Computer Science (EECS) at MIT and principal investigator at MIT Jameel Clinic, and her team approached these problems by conducting a study at MIT and developing a device that uses AI to detect Parkinson's Disease by analyzing the subject's breathing patterns at night using radio signals, and using these signals to determine a diagnosis. Similarly, researchers have recently associated an increase of sebum secretion, the oily secretion of sebaceous glands, with Parkinson's Disease, and a study found that machine-learning algorithms were able to diagnose the disease from the smell of the sebum alone. (Fu et al.) We can make the conclusion from research that AI has the potential to turn the tides of the healthcare field for the better. Currently, Parkinson's Disease is primarily diagnosed by analyzing symptoms and viewing a patient's medical history. However, Artificial Intelligence may be able to successfully diagnose this disorder by conducting tests early-on to analyze possible indicators of this common disease. The research in this article is geared towards analyzing the potential AI has, and determining whether it can use laboratory tests to more efficiently diagnose Parkinson's Disease in patients.

Materials and Methods

To conduct this experiment, we would need to collect blood samples from a large group of healthy patients. By conducting a prospective study, we can analyze the certain biomarkers present in the blood samples of patients who were later on diagnosed with Parkinson's. A biomarker is defined as a characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention, including therapeutic interventions (FDA: Biomarkers, EndpointS, and other Tools (BEST) Glossary). They are often interpreted as signs of various conditions and diseases. Studies show that neurofilament light chain (NfL), malondialdehyde (MDA), and 24S-hydroxycholesterol

(24S-HC) are all biomarkers found at significant levels in patients diagnosed with Parkinson's disease.

Neurofilament light chain (NfL) is a noteworthy biomarker of several neurodegenerative conditions, including Parkinson's Disease. NfL is a structural protein found on a neuron's axon that, upon neuronal injury, is released into the cerebrospinal fluid and then into the blood, where it can be detected from laboratory tests. According to neurologist Alicia Algeciras, Ph.D., high levels of NfL in the blood correlates with neurodegeneration, and thus would prove as a useful biomarker for Parkinson's Disease (Toman).

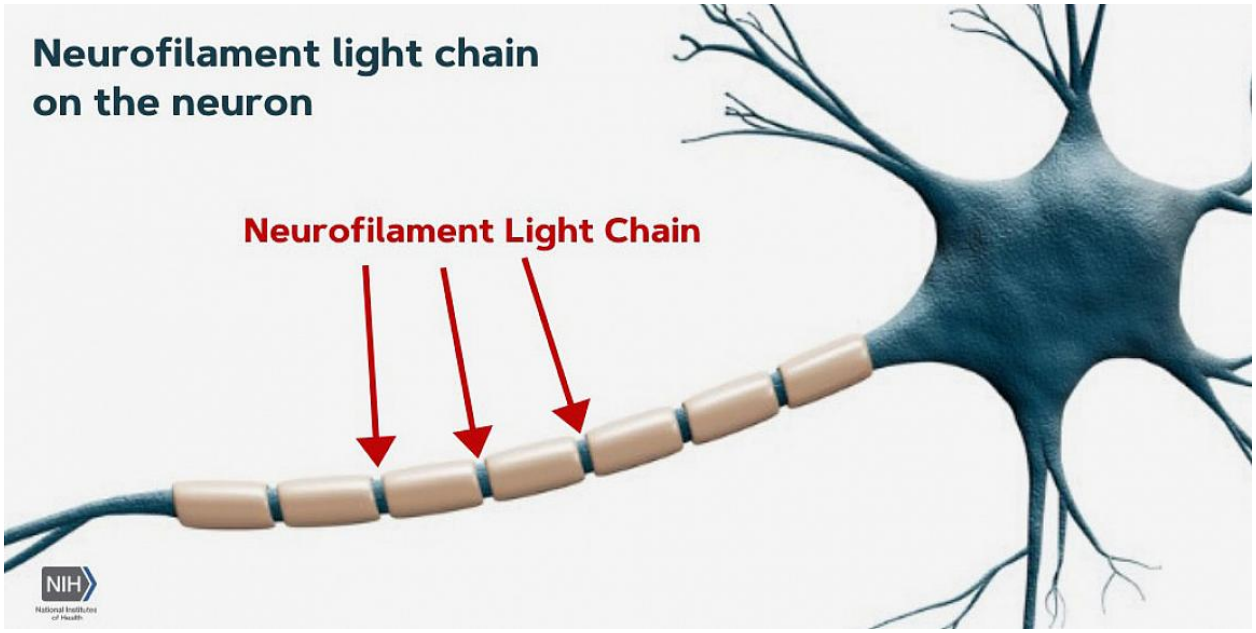


Figure 1: Neurofilament light chain on a Neuron (Credit: NIH Clinical Center)

Malondialdehyde (MDA) is commonly known to be a product of polyunsaturated fatty acid peroxidation in the cells. It is frequently correlated with oxidative stress in many health problems such as cancer, asthma, or cardiovascular diseases. Studies show that the accumulation of MDA is significantly increased in neurological diseases like Parkinson's.

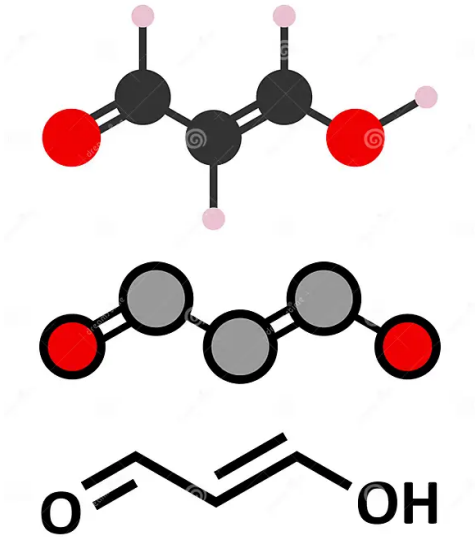


Figure 2: Malondialdehyde Molecule Structure (Credit: Dreamstime)

24S-Hydroxycholesterol (24S-HC), a major cholesterol metabolite in the brain, mainly serves as a vehicle for cholesterol removal. However, recent studies have discovered its effect on neuronal function. As cholesterol is located in many key brain structures, 24S-HC is a remarkable biomarker for neurodegenerative disorders like Parkinson's disease.

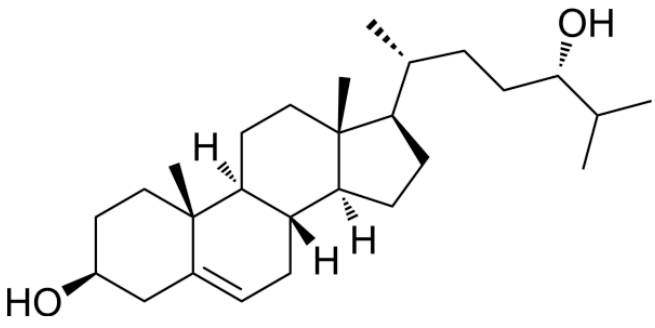


Figure 3: 24S-Hydroxycholesterol Molecule Structure (Credit: MedChemExpress)

The second part of this experiment involves machine learning. Here's where Artificial Intelligence steps in. In machine learning, a situation influences the initial data set for a model, making the model's predictions more accurate. Machine Learning systems can be used to develop accurate prediction models to successfully diagnose Parkinson's disease. This experiment would require the creation of a machine learning tool, potentially using gene expression profiling technologies (such as DNA microarrays and RNA sequencing), that can accurately analyze the biomarker data sets and diagnose a patient with Parkinson's disease. DNA microarrays and RNA sequencing are popular tools that can provide large gene expression data sets and are often used in biomarker discoveries.

Results and Discussion

In conclusion, the diagnostic performance of the machine learning tool in this experiment will be more accurate at diagnosing Parkinson's disease by analyzing biomarkers in blood samples compared to the traditional method of observing a patient's clinical signs and symptoms. The machine learning tool will hypothetically be able to create a composite data set featuring the detected biomarkers (NfL, MDA, and 24S-HC) from the blood samples using Artificial Intelligence, and it will give doctors an idea of the possible indicators of Parkinson's Disease and a headstart at diagnosing a patient's condition. Unlike traditional methods, this AI tool will be able to periodically input more data into the initial set in order to prevent errors and increase accuracy. The result will be a less costly, less invasive, more accurate, and easily accessible method of Parkinson's diagnosis that will be able to detect the disease years in advance, enhancing patients' survival rate and overall life quality.

Works Cited

"24(S)-Hydroxycholesterol." *MedChemExpress*, 5 Aug. 2023, https://file.medchemexpress.com/product_pic/hy-16940.gif

Fu, Wei, et al. "Artificial Intelligent Olfactory System for the Diagnosis of Parkinson's Disease" *ACS Omega*, 25 Jan. 2022, https://doi.org/10.1021/acsomega.1c05060

Molekuul. "Malondialdehyde (MDA, enol form) molecule." *Dreamstime*, 5 Aug. 2023, https://thumbs.dreamstime.com/z/malondialdehyde-mda-enol-form-molecule-marker-oxidative-stress-naturally-produced-lipid-peroxidation-191114910.jpg?w=576

Shahim, Pashtun. "Neurofilament Light Chain on the Neuron." *NIH Clinical Center*, 5 Aug. 2023, https://www.nih.gov/sites/default/files/styles/featured_media_breakpoint-large-extra/public/news-events/news-releases/2020/20200708-nfl-neuron.jpg?itok=BTl-Uu73&timestamp=1594155503

Shapiro, Lindsey. "3 blood biomarkers might identify Parkinson's, atypical parkinsonism" *Parkinson's News Today*, 28 Jun. 2023, https://parkinsonsnewstoday.com/news/biomarkers-diagnose-parkinsons-disease-atypical-parkinsonism/

Toman, Barbara J., "Neurofilament Light Chain: Answers from the Lab" *Mayo Clinic Laboratories*, 17 May. 2022, https://news.mayocliniclabs.com/2022/05/17/nflc-test-in-focus/

Yang, Yuzhe, et al. "Artificial intelligence-enabled detection and assessment of Parkinson's disease using nocturnal breathing signals" *Nature Medicine*, 22 Aug. 2022, https://doi.org/10.1038/s41591-022-01932-x

Zhang, Diana, et al. “Interpretable Machine Learning on Metabolomics Data Reveals Biomarkers for Parkinson’s Disease” *ACS Central Science*, 9 May. 2023, https://doi.org/10.1021/acscentsci.2c01468

Zhang, Xiaokang, et al. “Machine Learning Approaches for Biomarker Discovery Using Gene Expression Data” *Bioinformatics*, 20 Mar. 2021, https://www.ncbi.nlm.nih.gov/books/NBK569564/

Alpha-synuclein in Parkinson's Disease

Delilah Peñate (author), Thanisha Kapur (advisor), Anika Shah (editor)
Florida Atlantic University High School

Keywords: Alpha-synuclein, Parkinson's disease, proteins, neurodegenerative disorder, synucleinopathies, proteins

Abstract

Alpha-synuclein is a protein present in the brain that is known to be linked to rare hereditary versions of Parkinson's disease. Research on this rarer version of PD has allowed for progress to be made on discovering the cause, function, and possible treatment of much more common forms of Parkinson's disease. aSyn's interactions with lipid membranes, tubulin, and parkin may be linked to how it can cause Parkinson's disease in presynaptic terminals. Various genetic mutations may also interact with alpha synuclein, where mutations in these genes can often cause issues in the protein and heightened rates of Parkinson's disease. It is also currently being studied as a biomarker to identify Parkinson's disease risk early on. If alpha synuclein is able to be used for identifying Parkinson's earlier, this could greatly improve treatment for those affected. Additionally, some therapeutic treatments targeting alpha-synuclein have not yet cured Parkinson's, but have been able to slow progression of the disease in some parts of the body. Some treatments target the aforementioned mutated genes in an attempt to lower the amount of alpha synuclein produced within the brain.

Introduction

Parkinson's disease, or PD, is a progressive degenerative disorder of the brain that causes a lack of control of the motor system. A lack of dopamine due to nerve cell damage causes tremors, difficulty walking, and rigidity. While many have tried to find a particular cause or cure for Parkinson's, they have made some headway by looking at a protein quite prevalent in the human brain: *alpha-synuclein*, or aSyn. aSyn is a protein that is primarily in the brain, specifically in presynaptic terminals, thus prompting the release of neurotransmitters. The accumulation of alpha synuclein, therefore, could be connected to the degenerative symptoms we see in those diagnosed with Parkinson's disease. Additionally, since the alpha synuclein is being accumulated

surrounding the presynaptic terminals, an excess of them could be tied to the lack of dopamine present within the brain of PD patients, since it may cause the neurotransmitters, such as dopamine to be unable to release. Alpha-synuclein is also tied to a variety of other neurodegenerative diseases known as synucleinopathies, which are due to the accumulation of aSyn. Parkinson's, and other synucleinopathies, are not only being researched to find a better treatment or eventual cure, but also to better our understanding of these diseases, the brain in general, and how proteins work within it. This paper will review both the history of aSyn in our understanding of PD, as well as how aSyn can play a part in future Parkinson's disease research, along with possibly other synucleinopathies.

Body

Alpha-synuclein and its history

Alpha-synuclein is a protein linked to Parkinson's - but how did they find this? It first started with the discovery of a rare form of Parkinson's caused by a genetic mutation. In 1995, Parkinson's was generally believed to not be inheritable. While that is generally true, the NCHGR used positional cloning to find the gene that causes hereditary Parkinson's disease. Alpha-synuclein was linked to the region they had discovered ties to Parkinson's in, so they pursued it further. As they followed this trail to see what made this rare version of PD hereditary, they came across the protein involved not only in hereditary PD, but also in the far more common forms of Parkinson's. Since then, synuclein has popped up many more times both in Parkinson's and in other neurodegenerative disease research. For example, it was found that alpha-synuclein in sporadic Parkinson's was found outside of the central nervous system, meaning it may be related to some of the other symptoms and autonomic or enteric system dysfunction (Nussbaum). Understanding the ways that alpha-synuclein affects the brain in instances of Parkinson's disease is important, not just for making progress in Parkinson's research, but also in understanding the ways that similar diseases are affected. Additionally, this tests a theory that will be a recurring theme in alpha-synuclein research. To understand the common diseases and their variations, it can often be helpful to look to the rare forms and find their causes.

Alpha-synuclein's structure and interactions

aSyn is a small protein, which is able to interact with lipid membranes present in the brain. It has several series of repeating structures, which may be linked to its ability to disrupt lipid membranes. The middle section is involved in the creation of cross beta-structures. There are two distinct ends of the protein, one which is more positive called the N-terminal, and the more negatively charged acidic C-terminal. An increase in the protein can be found when the pH increases within the body, likely due to the fact that a rise in pH counteracts the acidity of this portion of the protein. Portions of aSyn are also related to other proteins that have protective capabilities, which suggest that aSyn in normal conditions may prevent the involvement of other proteins in the degenerative process. As for its interactions with the lipid membrane, aSyn most frequently interacts with small or large liposomes, which are spherical lipid bilayers. They are least likely to interact with very large liposomes (that is, liposomes larger than a micrometer in diameter). It also is more likely to bond to negatively charged liposomes using its N-terminal region, as this is the more positively charged part of the protein's structure. A few of its interactions are considered most likely to be linked to Parkinson's. First, with tubulin, the interaction of these proteins may lead to an inhibition of tubulin, causing cell death, which would lead to the degenerative effects seen in Parkinson's patients. It also may interact with dopamine receptors, causing increased amounts of dopamine in the brain, possibly leading to, once again, cell damage. However, aSyn would typically decrease the dopamine receptor activity to control the amount of dopamine. Therefore, the issue may be more linked to aSyn's neurotoxicity to dopaminergic cells. Mutated forms of the LRRK2 gene may also cause dysfunction in alpha-synuclein. There are also other genes where mutations may cause issues with alpha-synuclein, such as A53T, and a mutation in both genes severely increases the chances of Parkinson's and other synucleinopathies. Finally, aSyn also can interact with parkin, a protein that degrades other unneeded or harmful proteins. When parkin is mutated, it may be unable to clean out these harmful proteins. Although the specific mechanism is unknown, mutations in parkin are known to be linked to familial (autosomal recessive) Parkinson's disease. When this is mutated, it may allow aSyn to interact with it, causing deposition of other proteins, then a buildup, and ultimately affecting the structure of the brain and therefore neuronal dysfunction (Emamzadeh).

Alpha-synuclein in Parkinson's Disease

Alpha-synuclein is believed to contribute to PD in a few ways. One possible way is that protofibrils disrupt the ability of nearby cells to function. Specifically, that it can target the synapses, which would cause the degeneration in the brain needed for Parkinson's to occur. Additionally, excess alpha-synuclein may cause damaging effects on the surrounding portions of the brain, although an excess of aSyn is not consistent throughout all PD patients (Stefanis). However, it could be caused by issues in other proteins that would generally limit the quantity of aSyn. From this information, scientists have attempted to recreate an overexpression of alpha-synuclein in various ways. One of which is in using mice using promoters, which has caused traits similar to presymptomatic PD. Another done by transducing neurons with alpha-synuclein and has been able to cause the cell death frequently associated with Parkinson's disease. This is also used in testing how aberrant alpha-synuclein is able to have the effect it does. Alpha-synuclein is currently being studied as a biomarker to identify synucleinopathies and to differentiate between various kinds of neurodegenerative disease (Magalhães and Lashuel). However, this portion of it is still a work in progress, as consistent results have not yet been obtained. While some of the specific functions of alpha-synuclein are still being worked out, it is believed to be tied to Parkinson's, especially the rarer, mutation-origin, hereditary version. Being able to properly understand the functions of alpha-synuclein can not only point us in the direction of future Parkinson's treatments, but could also lead us towards other causes of Parkinson's.

Alpha-synuclein used in treatment

At the moment, they are investigating some possibly therapeutic strategies using alpha-synuclein for the treatment of Parkinson's disease. In some instances, the use of treatment that targets toxic components of alpha-synuclein have been successful in slowing the progression of the disease, however, not in curing it completely. For example, in some methods, there may be an attempt at reducing the amount of the SNCA present in the patient, to hopefully reduce the amount of alpha-synuclein expression (since the SNCA gene codes for it), to then lead to lower amounts of synaptic dysfunction. Alternatively, alpha-synuclein could be blocked from entering the cell in the first place. Clusters of alpha-synuclein could be broken apart. Or, types of immunotherapy could neutralize alpha-synuclein's effects. Although there haven't been any dramatic results yet, use of alpha-synuclein targeted therapeutic treatments were able to slow the progression of

Parkinson's in parts of the body for patients (Fields). While there is still much to be learned about alpha-synuclein's role in common Parkinson's, it is a contender for future treatment and research to benefit Parkinson's patients. Future therapeutic strategies could prove more effective. Or, in trying to find alpha-synuclein based treatments, even more about the protein, Parksinon's, and other synucleinopathies could be discovered. Regardless, Parksinon's research in general can benefit from learning more about alpha-synuclein.

Conclusion

Parkinson's disease is a neurodegenerative disorder responsible for a decline in the health and physical control of those who suffer from it. Although a proper cure or treatment has not yet been found, scientists have pinpointed alpha-synuclein as a possible contender for the disease's cause. This could be due to an excess of alpha-synuclein caused by inflammation in the brain. The alpha-synuclein then targets synapses in the brain, causing the degeneration in control that can be observed in patients who have Parkinson's disease. aSyn was initially discovered due to its presence in a rare, hereditary form of Parkinson's disease. However, its discovery as a linkage in genetic forms of Parkinson's disease led to further discovery about its role in the more common forms of Parkinson's. As we learn more about alpha-synuclein, we become closer to finding not only cures and causes of Parkinson's, but also to a variety of related diseases, known as synucleinopathies, due to their relation to alpha-synuclein. Therefore, Parkinson's, types of dementia, atrophy, and even some forms of Alzheimer's could be treated and learned about by investigating how alpha-synuclein works and how to treat it.

Works Cited

Emamzadeh, Fatemeh Nouri. "Alpha-Synuclein Structure, Functions, and Interactions." *Journal of Research in Medical Sciences : The Official Journal of Isfahan University of Medical Sciences*, 9 May 2016, www.ncbi.nlm.nih.gov/pmc/articles/PMC5122110/#ref58.

Fields, Carroll Rutherford, et al. "Targeting Alpha-Synuclein as a Therapy for Parkinson's Disease." *Frontiers*, 22 Nov. 2019, www.frontiersin.org/articles/10.3389/fnmol.2019.00299/full#h5.

Magalhães, Pedro, and Hilal A. Lashuel. "Opportunities and Challenges of Alpha-Synuclein as a Potential Biomarker for Parkinson's Disease and Other Synucleinopathies." *Nature News*, 22 July 2022, www.nature.com/articles/s41531-022-00357-0.

Nussbaum, Robert L. "The Identification of Alpha-Synuclein as the First Parkinson Disease Gene." *Journal of Parkinson's Disease*, 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5345646/.

Stefanis, Leonidas. "A-Synuclein in Parkinson's Disease." *Cold Spring Harbor Perspectives in Medicine*, Feb. 2012, www.ncbi.nlm.nih.gov/pmc/articles/PMC3281589/.

Differences Between The Autistic and Neurotypical Brain

Anna Bream (author), Thanisha Kapur (advisor), Anika Shah (editor)
Yorktown High School

Keywords: Neuroscience, Autism, Brain Structures, Neurotypical, Neurodivergent

Abstract

Autism is a developmental disorder affecting the central nervous system of the body with no known cure or cause. It causes characteristics including a high intelligence, difficulty socializing and maintaining eye contact, as well as identifying facial expressions and emotions. Researchers have begun investigating the autistic brain in search of potential causes for these symptoms. The hippocampus, amygdala, cerebellum, and cerebral cortex of the autistic brain were all found to be different in comparison to the neurotypical brain. The hippocampus was found to be increased in size in the autistic brain. This is assumed to cause the high intelligence pertaining to those with the disorder. Variety was also found in the amygdala. Autistic kids begin with a fast growing amygdala that quickly tapers off and, in some cases, even becomes smaller than that of a neurotypical person. This had been inferred by researchers to cause the social abnormalities in autistic people as the amygdala plays a vital role in social interaction and communication. Another explanation for the social differences in autistic people may lay in the cerebellum. The cerebellum, which aids in balance, implicit memories, and sociability, was found to have a lesser amount of brain tissue in compassion to neurotypical brains. Additionally, those with damage to the cerebellum often experience autism like symptoms of not maintaining eye contact or having a difficult time distinguishing facial expressions. Also contributing to autistic characteristics was the cerebral cortex, the very outer portion of the brain composed of gray matter. This gray matter has a key role in human survival as it holds memories, controls emotions and processes information. Those with autism were found to have a higher volume of gray matter which is associated with a higher IQ which may aid in explaining the intellectual abilities those with autism often have. Lastly, the autistic brain tends to be less or more connected with certain areas of the brain. This means some sections may lack connections with others whereas some may have a higher concentration of connections with other areas of the brain. The frontal lobe, which is known for controlling language and high levels of thinking, was found to be hypoconnected

between long distances which researchers think may aid in creating some of the social difficulties faced by autistic people.

Introduction

Autism is a common and fast growing neurological and developmental disorder affecting one in every thirty-six children in the United States that influences the central nervous system of the body. This disorder affects the development of assorted parts of the brain responsible for cognitive function, social interactions, and communication between peers. It is characterized by a high intelligence, fixated specific interests, as well as difficulty socializing with others. Autism is experienced on a spectrum, meaning severity and characteristics will range and differ in every person. There is currently no known cause that generates the disorder, however, researchers are working to further understand the condition and gain knowledge as to what may be the root of this condition. Researchers have begun to study the autistic brain in high hopes of discovering the cause for the disorder in addition to what may be causing these autistic traits. By using technology, including Magnetic Resonance Imaging (MRI's) which generates images, professionals have been able to get a look into the autistic brain and discover differences in a wide range of structures.

Body

The differences between autistic and neurotypical brains start in the limbic system. The limbic system is located deep in the center of the brain. It houses the hippocampus, amygdala, and hypothalamus. This region's role is to control memories, emotions and motivation for survival. This includes things like sleeping, eating, reproduction, and natural tendency of fight or flight. Those with autism have been found to have an enlarged hippocampus. This section of the brain is responsible for forming and processing memories. A larger hippocampus is assumed to create a longer lasting memory, which could play a key role in explaining the high intelligence characterized by autistic people. However, autistic people tend to have trouble recollecting daily events even though they have a very strong memory when it comes to facts, particularly those about their fixated interests. Varying sizes and abnormal growth of the hippocampus may be the cause for this difficulty in recalling social memories and events, however, more research is needed to verify this information.

Additionally, autistic people have been found to have amygdala's that fluctuate in size with age. Children tend to begin with fast growing amygdala that quickly slows down into adolescent years and may even become smaller in size. This almond shaped structure is in control of emotion and fear processing and also aids in enacting the fight or flight response. Wei Gao, a professor at Cedars-Sinai Medical Center, believes the amygdala plays a vital role in generating autistic traits and symptoms since the amygdala plays a large role in social interaction. Research has found that damage to the amygdala may cause difficulty understanding facial expressions as well as maintaining eye contact which are both very common autistic traits used to diagnose the disorder.

The cerebellum, also known as the little brain and located just below the back of the cerebrum, also had variance between autistic and neurotypical people. Using imaging studies, brain researchers found the cerebellum had a decreased amount of brain tissue compared to neurotypical brains. Although known for its role in implicit memories and motor movement, the cerebellum is also an important part in cognition and social contact. This may be a biological explanation for the communication difficulties those with autism face. In fact, those who experience damage to the cerebellum are at a high risk of obtaining autistic like characteristics, this includes social withdrawal, behavior issues, and difficulty paying attention.

Those with autism also tend to have a thicker cerebral cortex with a larger surface area. The cerebral cortex is the outer area of the brain which is composed of gray matter. Gray matter is highly concentrated neurons which play an essential role in human life. It is responsible for processing information, emotions, storing memories and controlling body movement. Autistic brains have a larger quantity of gyri and sulci, the ridges and grooves on the exterior of the brain, which creates a larger surface area of gray matter. Researchers have also found through brain scans that autistic people have a larger volume of gray matter in comparison to their neurotypical counterparts. An increase in gray matter is associated with higher neurological processing which may contribute to the autistic characteristics of having special interests and a high intelligence. For those with autism, connectivity levels between brain regions differ from that of neurotypicals. Some areas are more highly connected while some are hypoconnected. This means some sections may lack connections with others, whereas some may have a higher

concentration of connections with other areas of the brain. The frontal cortex aids in social processing and language. Those with autism have reduced long-distance connectivity with the frontal lobe which may explain social difficulties associated with autistic behavior including impairments in speech, communication, and emotion processing.

Conclusion

By looking at the anatomical brain differences, it begins to be more clear as to how autism works and manages to cause these wide ranges of characteristics. Although yet to be proven that these structures are the root cause of symptoms, it is no doubt that the brain plays a major role in the personality and traits of those with autism. Even though researchers are yet to find a cause or cure, medical research has largely assisted in helping to understand and improve the lives of those with autism.

Works Cited

"Amygdala, the Brain's Threat Detector, Has Broad Roles in Autism." *Spectrum | Autism Research News*, 14 July 2020, https://www.spectrumnews.org/news/amygdala-the-brains-threat-detector-has-broad-roles-in-autism/.

Autism Spectrum Disorder: Autistic Brains vs Non-Autistic Brains. 29 Nov. 2022, https://www.psycom.net/autism-brain-differences.

Autistic Brain Differences: Connectivity | Embrace Autism. https://embrace-autism.com/autistic-brain-differences-connectivity/. Accessed 30 July 2023.

Brain Changes in Autism Are Far More Sweeping than Previously Known, UCLA-Led Study Finds. https://www.uclahealth.org/news/brain-changes-autism-are-far-more-sweeping-previously-known. Accessed 30 July 2023.

"Brain Structure Changes in Autism, Explained." *Spectrum | Autism Research News*, 15 Oct. 2020, https://www.spectrumnews.org/news/brain-structure-changes-in-autism-explained/.

Spectrum | Autism Research News, 15 Oct. 2020, https://www.spectrumnews.org/news/brain-structure-changes-in-autism-explained/.

digitale@stanford.edu, <img src='https://med stanford edu/news/media-contacts/erin_digitale/_jcr_content/image img 620 high jpg/digitale-erin-90 jpg' alt='Erin Digitale'> Erin Digitale Erin Digitale is a senior science writer in the Office of Communications Email her at. "Brain wiring explains why autism hinders grasp of vocal emotion, says Stanford Medicine study." *News Center*, 28 Apr. 2022, http://med.stanford.edu/news/all-news/2023/01/brain-autism-speech-emotion.html.

D'Mello, Anila M., and Catherine J. Stoodley. "Cerebro-Cerebellar Circuits in Autism Spectrum Disorder." *Frontiers in Neuroscience*, vol. 9, 2015. *Frontiers*, https://www.frontiersin.org/articles/10.3389/fnins.2015.00408.

---. "Cerebro-Cerebellar Circuits in Autism Spectrum Disorder." *Frontiers in Neuroscience*, vol. 9, 2015. *Frontiers*, https://www.frontiersin.org/articles/10.3389/fnins.2015.00408.

"Grey Matter." *Cleveland Clinic*, https://my.clevelandclinic.org/health/body/24831-grey-matter. Accessed 30 July 2023.

Ha, Sungji, et al. "Characteristics of Brains in Autism Spectrum Disorder: Structure, Function and Connectivity across the Lifespan." *Experimental Neurobiology*, vol. 24, no. 4, Dec. 2015, pp. 273–84. *PubMed Central*, https://doi.org/10.5607/en.2015.24.4.273.

How Do Autistic Brains Work? https://www.crossrivertherapy.com/autism/how-do-autistic-brains-work. Accessed 30 July 2023.

"In Autism Brains, Neurons May Take up More Space than Usual." *Spectrum | Autism Research News*, 4 Nov. 2018, https://www.spectrumnews.org/news/autism-brains-neurons-take-space-usual/.

Leipold, Simon, et al. "Aberrant Emotional Prosody Circuitry Predicts Social Communication Impairments in Children With Autism." *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, vol. 8, no. 5, May 2023, pp. 531–41. *ScienceDirect*, https://doi.org/10.1016/j.bpsc.2022.09.016.

"Memory Hub Could Underlie Social, Cognitive Quirks of Autism." *Spectrum | Autism Research News*, 24 Aug. 2016, https://www.spectrumnews.org/news/memory-hub-underlie-social-cognitive-quirks-autism/.

Mercadante, Anthony A., and Prasanna Tadi. "Neuroanatomy, Gray Matter." *StatPearls*, StatPearls Publishing, 2023. *PubMed*, http://www.ncbi.nlm.nih.gov/books/NBK553239/.

"Neuroanatomy, Gray Matter." *StatPearls*, StatPearls Publishing, 2023. *PubMed*, http://www.ncbi.nlm.nih.gov/books/NBK553239/.

News. "UC Davis Study Uncovers Age-Related Brain Differences in Autistic Individuals." *News*, https://health.ucdavis.edu/news/headlines/uc-davis-study-uncovers-age-related-brain-differences-in-autistic-individuals/2023/03. Accessed 30 July 2023.

News, Neuroscience. "Are Bigger Brains Better?" *Neuroscience News*, 16 Jan. 2020, https://neurosciencenews.com/brain-size-memory-15497/.

The Autistic Brain :: Cambridge Neuroscience.
https://www.neuroscience.cam.ac.uk/research/cameos/AutisticBrain.php. Accessed 30 July 2023.

Mechanisms of Neurodegenerative Diseases and Alzheimer's

Elliot Hsu (author), Thanisha Kapur (advisor)
Saint Francis High School

Keywords: Neurodegenerative Disease, Proteotoxicity, Ubiquitin-proteasome system, Alzheimer's, Beta-amyloid Plaques, Neurofibrillary Tangles

Abstract

Neurodegenerative disease is a type of disease in which cells of the central nervous system stop functioning or die off because of the growth of misfolded proteins or harmed proteins that leads to their death. This article will talk about the cellular mechanism of different diseases. In these diseases there are different functions but one of the most important is the UPS system, which uses the route in which different useless and broken proteins take. In Alzheimer's there are two functions which cause the disease and what functions they provide in the system.

Introduction

This leads to the progressive deterioration of certain areas of the brain. Neurodegenerative diseases result in progressive damage to cells, more specifically proteins. These proteins and cells are essential for the body, for example, moving, coordination, stability, strength, cognition and others. These disorders, including Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis (ALS), have become relatively present in today's elderly, posing a significant social and medical challenge. Understanding the molecular and cellular mechanics of different neurodegenerative diseases is crucial for developing strategic solutions and helping and fixing the diseases that are present in the present elderly.

Body

The Overview of The Cellular Mechanism of Neurodegenerative Diseases

Through all of these different kinds of Neurodegenerative diseases, there is a common mechanism in proteotoxicity. Proteotoxicity is found in different regions of the affected brain. Therefore, this common mechanism of proteotoxicity could contribute to the learning, development, and progression of neurodegenerative diseases. It is when a cell is damaged

beyond repair and is caused by a collection of these damaged cells. Protein homeostasis (proteostasis) is maintained by many systems in a cell, most importantly, the ubiquitin-proteasome system (UPS).

The UPS system

The UPS is the route for damaged, degraded, unimportant, and useless protein. However, with the efficiency of the proteostasis and the UPS system, those damaged proteins can harm and disrupt normal cellular functions and can go as far to cause cell death. These decreased proteasome functions have been discovered in a broad array in many neurodegenerative diseases. However that is not always the case. Sometimes a small percentage of neurodegenerative diseases are caused by hereditary gene mutations, many of which affect the UPS system, leading to those diseases. “Despite these many efforts, an understanding of why and how the proteasome is so generally impaired in neurodegenerative disease has remained elusive. Understanding the mechanism of impairment will provide a basis for drug development to restore proteasome activity and proteostasis in the brain and is therefore an important effort.” (Anderson, Smith, Thibaudeau, A Common Mechanism Of Proteasome Impairment By Neurodegenerative Disease-Associated Oligomers). There is much more to learn about the neurodegenerative diseases than just the protein function and how it affects the cell and brain. By even furthering research and developing a basis for a solution for these diseases is a very important step and can impact what we discover. A study from the article explores the misfolded and damaged proteins, and goes into further detail about the proteostasis impairment in neurodegenerative diseases and they may share a common mechanism.

A Deeper Look: Alzheimer’s

Alzheimer’s is a common disease in today’s elderly and I have experienced living with a person with Alzheimer’s in my life. “Alzheimer’s disease remains a major therapeutic challenge despite a massive research effort over the past two decades. Applying quantitative mechanistic approaches to understanding the quantities and rates of Aβ amyloid production, accumulation and clearance may provide novel and more rigorous insights into developing rational therapeutic strategies.” (Alzheimer’s Disease: Toward a Quantitative Biological Approach in Describing its Natural History and Underlying Mechanisms). To summarize this paragraph, Alzheimer’s is

caused by the accumulation of the Aβ (β-amyloid) peptide. If we research how this protein is formed when Alzheimer's is diagnosed, we can take a step further into developing techniques and solutions for the disease.

Beta-amyloid and Neurofibrillary Tangles

Alzheimer's disease is a neurodegenerative disorder characterized by progressive cognitive decline and memory loss. At the molecular level, Alzheimer's is primarily associated with the accumulation of abnormal proteins in the brain. Two key causes in the disease are beta-amyloid plaques and neurofibrillary tangles. The research done on the Aβ production is still unclear, however the research on tangles can be dove in a little deeper. Neurofibrillary tangles are bundles or groups of tangled filaments found in neurons. These tangles are made up of proteins called tau. Some people also call these tangles "tau tangles". The tau proteins have different functions when healthy or when twisted. In healthy neurons, tau proteins provide positive functions and help the microtubules. These microtubules are part of the cell's structure support and help deliver different molecules and substances throughout the nerve cells. On the contrary, in Alzheimer's disease, the tau protein changes in a way that causes it to twist into pairs which are called "helical filaments" which then are referred to as tangles. Because of this, the microtubules can't function correctly and then they disintegrate and disappear. This disintegration can collapse the neuron transportation system and can cause a communication impairment between cells and can lead them to die. Even though the exact causes of Alzheimer's remain unclear, there are many different factors that can cause this disease to happen. Understanding the molecular and cellular intricacies of Alzheimer's disease is critical in the ongoing search for effective treatments and solutions to combat this neurological disease. Research on Alzheimer's still can provide hope for finding ways to detect the disease and find effective ways to prevent the spreading and the burden for other individuals and families.

Conclusion

As we all know, we have not found a cure for diseases such as neurodegenerative ones. Understanding the cellular function and mechanism of these diseases can greatly speed up the development of solutions and cures to these diseases. For example when studying Alzheimer's disease, we should dive deeper into the beta-amyloid and neurofibrillary tangles which are key

factors in the cause of Alzheimer's. By understanding the general functions of cells that are deteriorated we can find solutions for not only neurodegenerative diseases but other diseases such as cancer. It is now a case for our generation to study these factors and help provide for the generations after us.

Works Cited

"Alzheimer's Disease." *Stanford Health Care (SHC) - Stanford Medical Center*, 11 Sept. 2017, stanfordhealthcare.org/medical-conditions/brain-and-nerves/dementia/types/alzheimers-disease.html#:~:text=Alzheimer's%20disease%20is%20characterized%20by,of%20neurons%20and%20other%20cells.

Guo, Tiantian, et al. "Molecular and Cellular Mechanisms Underlying the Pathogenesis of Alzheimer's Disease - Molecular Neurodegeneration." *BioMed Central*, 16 July 2020, molecularneurodegeneration.biomedcentral.com/articles/10.1186/s13024-020-00391-7.

"The Molecular and Cellular Basis of Neurodegenerative Diseases." *ScienceDirect*, www.sciencedirect.com/book/9780128113042/the-molecular-and-cellular-basis-of-neurodegenerative-diseases. Accessed 6 Aug. 2023.

Thibaudeau, Tiffany A., et al. "A Common Mechanism of Proteasome Impairment by Neurodegenerative Disease-Associated Oligomers." *Nature News*, 15 Mar. 2018, www.nature.com/articles/s41467-018-03509-0#:~:text=The%20most%20 common%20 neurodegenerative%20 diseases,neurons1%2C2%2C3.

AI and its Applications in Healthcare

Emma Rand (Author), Thanisha Kapur (Advisor), Anika Shah (Editor)
Bayport-Blue Point High School

Keywords: artificial intelligence, clinical trials, diagnosis, debridement, suturing

Abstract

Artificial intelligence (AI) has many potential applications in the healthcare industry, but also raises many ethical concerns. For example, AI machines that use machine learning (ML) can diagnose skin cancer in patients, and aid in certain surgical procedures like suturing. Also, AI models can pick the best candidates for participation in clinical trials, which can streamline the clinical trial process and result in life-changing drugs hitting the market sooner. However, some patients may feel uncomfortable with AI models having such great responsibilities in caring for their health. In addition, some AI models have been found to contain gender and race bias. Ultimately, it is unlikely that AI will hold a prominent role in the healthcare industry within the foreseeable future.

Introduction

Artificial intelligence is a new and exciting technology that has the capability to drastically transform the world. Artificial intelligence is created when software (computer programming) is able to "think" independently, without any guidance or input from humans. Unlike other technologies, artificial intelligence does not run on a simple algorithm, taking one input and changing it based on the algorithm coded by humans to create an output. Instead, artificial intelligence takes an input and is able to *decide* which output to produce. As stated by Arend Hintze, a professor at Michigan State University, there are two main types of AI that currently exist: reactive machines and limited memory AI (Hintze). Reactive machines have no memory and cannot predict future events, they take in data and process it through an algorithm to produce very specific outputs. Examples of reactive machine AI include personalized ads that show up on social media feeds, such as Instagram and Snapchat. Limited memory AI functions in a way that is almost similar to the human brain, it is able to get "smarter" and improve over time as it is

given more data. However, pieces of data that are saved in this AI's memory are merely transient, they don't hold much meaning, only the meaning that the AI has been programmed for them to hold (Hintze). One example of this type of AI are self-driving cars. They are able to recognize the speeds and proximity of other cars only because they have "seen" other cars before and have "remembered" how fast they were going.

AI has many potential applications in the field of healthcare. The use of AI in healthcare has many benefits, but also many drawbacks. This article will review the current literature on the most significant benefits that AI offers to healthcare, and will also review some of the prominent ethical concerns over the implementation of AI in health care.

Body

AI and Diagnosing Patients

Artificial intelligence, particularly machine learning models, have been proven to be extremely accurate when it comes to diagnosing patients. In fact, one study conducted by Jonathan Richens, Ciaran Lee, and Saurabh Johri from Babylon Health and University College London found that AI was 72% more accurate than physicians when it came to diagnosing patients. This study used a machine-learning algorithm that was able to recognize symptoms in patients and not immediately associate these symptoms with a specific disease or medical issue, which is a unique feature compared to other AI algorithms that were designed to do the same thing. Essentially, the algorithm that this study used was able to "think outside the box", so that when a patient described their sore throat, the algorithm did not automatically diagnose them with streptococcal pharyngitis (Richens et al.). This ability to disconnect correlation from causation is called causal reasoning, and it allowed the AI algorithm to be more accurate in its diagnoses (Richens et al). This study proved to be a breakthrough in AI diagnoses, as former algorithms were consistently less accurate than physicians when tasked with diagnosing patients (Liang et al; Jiang et al; Zhang et al.)

In addition, AI has been successful at recognizing skin cancer, which is the most common cancer, causing approximately 10,000 deaths each year in the United States (Fogel et al.). Andre Esteva et al. developed an AI algorithm, specifically a convulsion neural network (CNN), able to

differentiate between malignant and benign skin lesions. The CNN was trained using a data set of over 12,000 clinical images, containing over 2,000 different diseases (Esteva et al.) . When put to the test against 21 U.S. board-certified dermatologists, the CNN algorithm was just as accurate as the dermatologists in differentiating between cancerous and non-cancerous skin lesions (Esteva et al.). However, the sample size of dermatologists that the study used was small so further studies must be done in the future to more accurately determine the effectiveness of this particular AI model.

AI and Clinical Trials

Bringing a new drug into the market is no easy task, and it's getting increasingly more difficult. In fact, within the past 9 years, the amount of drugs that have gained regulatory approval per billion USD spent has been cut in half (Harrer et al.). One of the main causes of this problem is the high fail rate of clinical trials. The main reasons for the high failure rate of clinical trials include the inadequate selection of patients who participate in the trial, and the inability to monitor patients effectively during the trial (Harrer et al.). Regarding patient selection, it is absolutely crucial that the right patients are selected to participate in clinical trials. The reasons for this vary across different trials, but, for instance, perhaps if a drug that only treats people who have a specific stage of a disease is being tested, the clinical trial for that drug has to consist of people who are in that specific stage of that particular disease, otherwise, the results of the trial will be compromised and actual efficacy of the drug will remain unknown. Also, patients' medical history can disqualify them from participating in a clinical trial (Harrer et al.). Thankfully artificial intelligence algorithms, specifically machine learning algorithms, can be used to select the appropriate patients by combining omic data (genetic data) and electronic medical record (EMR) data for each patient and making sure that combined data aligns with the specifications of the clinical trial (Harrer et al.). Although, even if the right patients are selected, it can be difficult to motivate them to consent to participate in the trial. Oftentimes the confusing medical vernacular can make it difficult for patients to understand what exactly is going on, which lowers their motivation to participate in trials, especially because trials are often long and require participants to invest a considerable amount of their time. However, Natural Language Processing (NLP) AI can convert the intense medical language into something more understandable, which can increase patients' sense of what clinic trials are trying to accomplish

and why exactly they are eligible to participate in them, which may increase their motivation to participate (Harrer et al.).

AI and Surgery

Robotic surgery is something that already exists, with more than one million surgeries performed by robots each year (Tindera). However, these robots are not autonomous, they are completely controlled by surgeons, and they do not have AI. Although, recently researchers have been working on adding AI to surgical robots to make them more effective and improve patient outcomes. For instance, the process of debridement (removal of damaged or foreign tissue) is long and it is easy for a surgeon to miss a piece of tissue, which could lead to an infection (Yip et al.). A medical robot powered machine learning (ML) AI would be able to recognize damaged or foreign tissue and have the capability to debride autonomously, which has the potential to save a lot of time and possibly lower the patient's risk for infection. Autonomous debriding robots have been successful in laboratory conditions, however it is unlikely that they will appear in operating rooms within the near future, as further research must be done to ensure complete safety and reliability (De Luca).

In addition, researchers are also developing an autonomous robot for surgical suturing, a tedious task that involves stitching tissues together. Although current models are not completely autonomous, they fall under the category of supervised autonomous robots, they use machine learning technology. The robot functions when a surgeon touches the area that needs suturing with a medical instrument, the AI will then produce the points of needle exit and entry on the wound that would make the most effective suture (Yip et al.; Peng et al.).

Ethical Concerns

It is understandable that patients may feel uncomfortable with machines performing tasks that directly relate to a patient's health and may have serious implications in a patient's life. It is likely that patients will want to know how these AI models work, especially the machine-learning tools that can diagnose skin cancer. However, it can be very difficult to explain exactly how these machines work, even professionals have difficulties delivering concise and understandable answers to these questions (Davenport et al.). Because of this, patients may not feel comfortable

with AI treatment and may decide to refuse AI treatment. In addition, AI machines are capable of making mistakes. In fact, some AI models have been proven to have algorithmic bias which causes them to take patients' gender and race into consideration during diagnosis, even in cases when gender and race are not factors that make individuals more or less likely to have a certain disease/ medical problem (Davenport et al.). What exactly causes this gender and race bias is not precisely known yet, making AI models that possess this bias unfit to be introduced into commonplace healthcare environments.

Conclusion

AI has a plethora of exciting applications in the healthcare industry; from streamlining clinical trials to diagnosing skin cancer. However, artificial intelligence is not perfect. AI has many flaws, especially when it is put within the context of the healthcare industry, an industry that is so essential and highly specific with its guidelines and principles. AI models will have to be flawless in order to be seriously implemented in the healthcare industry, and AI flawlessness is not something that is feasible for scientists today. Also, it must be taken into consideration that many patients just do not feel comfortable putting their trust into non-human intelligence, especially concerning matters that have a significant impact on something so important as their health. For these reasons, it is very unlikely that AI will hold a significant position in the healthcare industry.

Works Cited

Davenport, T., Kalakota, R. (2019). The potential for artificial intelligence in healthcare. Future healthcare journal, 6(2), 94–98. https://doi.org/10.7861/futurehosp.6-2-94

De Luca, A. (2016). IEEE International Conference on Robotics and Automation.

Esteva, A., Kuprel, B., Novoa, R. et al.(2017). Dermatologist-level classification of skin cancer with deep neural networks. Nature 542, 115–118 . https://doi.org/10.1038/nature21056

Fogel, A.L., Kvedar, J.C. (2018).Artificial intelligence powers digital medicine. npj. Digital Med 1, 5 . https://doi.org/10.1038/s41746-017-0012-2

Harrer, S., Shah, P., & Antony , B. (2019, July 17). Artificial intelligence for clinical trial design. Cell.com. Retrieved July 29, 2023, from https://www.cell.com/trends/pharmacological-sciences/fulltext/S0165-6147(19)30130-0?dgcid=raven_jbs_etoc_email

Hintze, A. (2016, November 14). Understanding the four Types of AI, from reactive robots to self-aware beings. Theconversation.com. Retrieved July 29, 2023, from https://theconversation.com/understanding-the-fou

Jiang F., Zhi H., et al (2017).Artificial intelligence in healthcare: past, present and future Stroke and Vascular Neurology;2:doi: 10.1136/svn-2017-000101

Liang, H., Tsui, B.Y., Ni, H. et al. (2019) Evaluation and accurate diagnoses of pediatric diseases using artificial intelligence. Nat Med 25, 433–438. https://doi.org/10.1038/s41591-018-0335-9

Richens, J.G., Lee, C.M. & Johri, S. (2020).Improving the accuracy of medical diagnosis with causal machine learning. Nat Commun 11, 3923. https://doi.org/10.1038/s41467-020-17419-7

Peng, X. B., Andrychowicz, M., Zaremba, W., & Abbeel, P. (2018). 2018 IEEE international conference on robotics and automation (ICRA).

Tindera, M. (2019). Robot Wars: $60 B Intuitive Surgical Dominated Its Market for 20 Years. Now Rivals Like Alphabet Are Moving In. Forbes.

Yip, M. et al. (2023). Artificial intelligence meets medical robotics.Science381,141-146 .DOI:10.1126/science.adj3312

Zhang Z., Chen, P., McGough, M. et al. (2019).Pathologist-level interpretable whole-slide cancer diagnosis with deep learning. Nat Mach Intell 1, 236–245. https://doi.org/10.1038/s42256-019-0052-1

The Effect of Anxiety on the Brain

Eshel Ahmad (author), Thanisha Kapur (advisor)
Drexel University

Keywords: Anxiety, Microglia, Central Nervous System, Brain, Prefrontal Cortex, Hippocampus, Amygdala, Chronic Stress, Neurocircuitry

Abstract

Anxiety, a mental illness that causes feelings of fear and worry, often without reason, affects the lives of millions across the world. It, like many other mental conditions, can actually have physical effects on the brain. Microglia are immune cells in the brain that are essential to investigate because of the role they play in anxiety. Multiple studies conducted on rats and mice have found that these cells are activated when anxious behaviors are displayed. Optogenetics is also a groundbreaking tool that has been used in many studies researching anxiety. It utilizes light to control the activity of neurons. The neurocircuitry of the brain, as well as the hippocampus, lateral septum, and amygdala in specific, are also vital to note when understanding how anxiety works. These specific regions contain cells that have been found to be activated during anxiety and as a result, these parts of the brain are directly involved in anxiety. During chronic anxiety, certain parts of the brain can undergo physical changes in addition to altered functions.

Introduction

One of the most common mental illnesses in the world results in feelings of unease and fear. This disorder that affects millions of people is called anxiety. To a certain extent, anxiety is necessary for survival. This biological feature kept humans alive when they lived in the wild and danger was around every corner. However, many people experience more than the “normal” amount of anxiety in their everyday lives. Though the condition is commonly referred to as just “anxiety” there are actually many disorders that exist under this umbrella term. These include generalized anxiety disorder, social anxiety, and separation anxiety among others. Some conditions cause people to experience anxiety because of a particular situation, like in social settings (social anxiety) or being in situations where one feels as though they will be unable to get help if they

need it (agoraphobia). Others feel scared without explanation or trigger. The experience of anxiety is complicated when looked through a neuroscience lens as several cells are thought to be activated and controlling the anxiety while other areas of the brain temporarily shut down. Dealing with anxiety, especially over prolonged periods of time, can physically impact the brain. Certain parts of the brain can deteriorate and degenerate when in a constant state of anxiety. Researching the ways anxiety causes the brain to adapt is essential to understanding the condition and finding ways to effectively treat it.

Body

Microglia

The human body consists of multiple systems that are made up of organs and cells. These systems work to carry out separate functions that make the human body operate and perform as needed. Two of these systems, the immune system which is the network that protects the body from outside invaders like infections and pathogens, and the central nervous system, the network that controls the body's functions, are actually closely related. These two systems are connected by microglia, immune cells located in the brain. Microglia function as cells that execute inflammatory responses in the body.

Multiple studies have found microglia to be closely related to anxiety and anxious behavior but it has also been found to be related to chronic stress. Chronic stress activates a reaction from the immune system. This is where microglia play a role in chronic stress. Exposure to chronic stress has been found to alter the phenotype of the microglia after long periods of activation, resulting in changes to their functional properties and even resulting in a deteriorating number of microglia within the brain (Schramm and Waisman 2023).

Both anxiety and chronic stress result in activation of certain parts of the brain, often for prolonged periods of time. This can result in neuroinflammation, though it is essential to note that neuroinflammation is often caused by other factors like infection and disease. During neuroinflammation, microglia and other cells of the immune system produce cytokines, proteins that aid in growth of immune system cells. Extended periods of neuroinflammation can result in

an accumulation of inflammatory cytokines. In humans, high amounts of inflammatory cytokines have been found to be correlated with depression. (Yirmiya et al., 2000).

In a study conducted at the University of Utah School of Medicine, Naveen Nagarajan and Mario R. Capecchi regulated an experiment on mice where they tested the impact of microglia on anxious behavior. They utilized optogenetic stimulation to stimulate a specific population of microglia called Hoxb8 microglia. The researchers stimulated the Hoxb8 microglia in different parts of the brain to test if stimulating different areas of the brain would result in different responses in the mice. They engaged the medial prefrontal cortex, central amygdala, and hippocampus with optogenetic stimulation. Nagarajan and Capecchi found that activated microglia in the medial prefrontal cortex resulted in obsessive grooming behaviors, in the central amygdala resulted in anxious behavior and the hippocampus demonstrated both grooming, anxiety, and freezing. This study found that in mice, Hoxb8 microglia is most likely what controls anxiety and the part of the brain stimulated is what affects the particular behavior. They also observed that anxious behavior was more extreme in the female mice.

Another study, conducted at the University of Southern Carolina and published in *Brain, Behavior, and Immunity*, experimented specifically on the microglia of female rats. Lead Researcher Brittany S. Pate and her team experimented specifically on female rats because in humans, women are more susceptible to anxiety disorders and sufficient research investigating the microglia of females had yet to be conducted. This study focused on the microglia located in the brain stem and specifically in the locus coeruleus. The researchers activated the microglia in two ways, the first being a microglial stimulant that was distributed to the rats and the second being a stressful social situation. The study identified that locus coeruleus microglia are a key component to female response to social stress.

Hippocampus

When the brain is experiencing stress and anxiety, it focuses on dealing with what is the cause of stress. The amygdala is the part of the brain that is responsible for processing information and emotions. During times of anxiety and stress, the function of the amygdala is enhanced to deal with what the brain has identified as immediate danger. As a result, other functions of the brain

are temporarily halted so that all focus and attention can be directed towards handling what is causing anxiety. The hippocampus is a structure of the brain that is a part of the temporal lobe. This region of the brain is essential to memory and learning. This means that during stressful situations, the functions of the hippocampus are paused so that the body can focus on surviving the immediate threat. When the brain is fighting stress and anxiety for long periods of time, for example if one is experiencing chronic anxiety or chronic stress, the hippocampus, and other regions of the brain that are nonessential when reacting to stress, remain inactivated for long periods of time. This results in impaired function of the hippocampus as well as degeneration. The hippocampus has also physically shrunk in size in people who have experienced long periods of anxiety and stress because of long periods without use.

Specific cells within the hippocampus have also been discovered to be closely tied with anxiety and anxious behavior. Researchers at Columbia University and University of California, San Francisco discovered neurons located specifically in the hippocampus that are “anxiety cells” in mice. Their study utilized optogenetics to control cells of the hippocampus and found that anxious behavior in the mice was dictated by the activity of these specific cells. This study also found that anxiety can be reduced when altering hippocampus activity (Jimenez et. al., 2018). Though this experiment was conducted in mice, these findings are ground breaking and could lay the foundation for future anxiety treatment. These findings could also translate to understanding “anxiety cells” in the human hippocampus. More research needs to be conducted on these cells to further understand the implications of these findings and if targeting anxiety cells could potentially transform anxiety treatment.

Lateral Septum

The neurocircuitry of the brain is the system of control mechanisms in the brain. Each part of the circuit works to execute functions. A study has found that anxiety occurs throughout the neurocircuitry of the brain (Anthony et. al., 2015) and the lateral septum is another important area to study. The lateral septum functions as a hub for regulation and function and it connects the hippocampus with other subcortical regions. Previously, the lateral septum was thought to repress feelings of anxiety. Using optogenetics, researchers investigated Crfr2+ cells within the lateral septum to test if they are activated during anxiety and this study found that the Crfr2+

cells were supplementing feelings of anxiety and anxious behavior. Crfr2+ is another important cell to conduct further research with to further understand its role in anxiety.

Amygdala

The amygdala is one of the main sections of the brain that remains activated and is involved when the body undergoes stress and anxiety. This is because the amygdala is essential when dealing with emotions. In cases of chronic anxiety or stress, the amygdala remains operative for extended periods of time to respond to the perceived threat. As a result, the amygdala can become larger in those who experience chronic stress or anxiety. This small structure within the brain has its own substructures that are also involved in anxiety.

A study conducted by Stanford University School of Medicine investigated subregions of the amygdala to understand the roles of each area of the amygdala in the experience of anxiety. The subsections they experimented with were the basolateral amygdala and centromedial amygdala. The researchers discovered patterns in the amygdala's communication with other parts of the brain. Crossover in connections could result in feelings of anxiety, overwhelming emotion, and worry. The connections that are involved in anxiety go beyond just within the amygdala and its subsections. That being said, it is thought that the amygdala is the starting and ending point of the neural circuit of anxiety. The amygdala sends the initial signal which then is transported throughout the brain and then the circuit reverses and the signal returns back to the amygdala (Calhoon and Tye 2020).

Conclusion

The nervous system is incredibly complicated and the parts of the brain that are engaged during anxiety go beyond the few that were discussed in this review. That being said, the amygdala is one of the essential emotional processing centers of the brain and it plays a large role in anxiety. Long periods of anxiety can result in the amygdala increasing in size as it regulates emotions. As a result, other parts of the brain that aren't needed during a time of anxiety, like the hippocampus, can actually shrink in size. This is because when someone experiences chronic anxiety, certain parts of their brain remain inactive for extended periods of time. In both the amygdala and hippocampus, as well as other areas of the brain, immune cells called microglia

have been discovered to be key components in anxiety. Multiple experiments conducted on mice and rats found that when these cells were active, anxious behavior was displayed. Optogenetics is also a tool that has been used often when studying anxiety as it can control the activity of cells. It is essential to research anxiety because through understanding how anxiety works within the brain and investigating the effects and changes that occur in the mind after experiencing anxiety and stress for prolonged periods of time, more effective treatment could potentially be discovered.

Works Cited

AJ;, Mah L;Szabuniewicz C;Fiocco. “Can Anxiety Damage the Brain?” Current Opinion in Psychiatry, pubmed.ncbi.nlm.nih.gov/26651008/. Accessed 31 July 2023.

Anthony, Todd E, et al. “Control of Stress-Induced Persistent Anxiety by an Extra-Amygdala SEPTOHYPOTHALAMIC Circuit.” Cell, 30 Jan. 2014, www.ncbi.nlm.nih.gov/pmc/articles/PMC3982923/.

Anxiety Cells in a Hippocampal-Hypothalamic Circuit: Neuron - Cell Press, www.cell.com/neuron/fulltext/S0896-6273(18)30019-9. Accessed 31 July 2023.

Bachiller, Sara, et al. “Microglia in Neurological Diseases: A Road Map to Brain-Disease Dependent-Inflammatory Response.” Frontiers, 29 Nov. 2018, www.frontiersin.org/articles/10.3389/fncel.2018.00488/full.

Calhoon, Gwendolyn G, and Kay M Tye. “Resolving the Neural Circuits of Anxiety.” Nature Neuroscience, Oct. 2015, www.ncbi.nlm.nih.gov/pmc/articles/PMC7575249/#R97.

Felger, J C, and F E Lotrich. “Inflammatory Cytokines in Depression: Neurobiological Mechanisms and Therapeutic Implications.” Neuroscience, 29 Aug. 2013, www.ncbi.nlm.nih.gov/pmc/articles/PMC3741070/.

León-Rodríguez, Ana, et al. “Anxiety-like Behavior and Microglial Activation in the Amygdala after Acute Neuroinflammation Induced by Microbial Neuraminidase.” Nature News, 8 July 2022, www.nature.com/articles/s41598-022-15617-5.

Nagarajan, Naveen, and Mario R. Capecchi. “Optogenetic Stimulation of Mouse Hoxb8 Microglia in Specific Regions of the Brain Induces Anxiety, Grooming, or Both.” Nature News, 10 Apr. 2023, www.nature.com/articles/s41380-023-02019.

News Center. “Brain Scans Show Distinctive Patterns in People with Generalized Anxiety Disorder in Stanford Study.” News Center, 7 Dec. 2009, med.stanford.edu/news/all-news/2009/12/brain-scans-show-distinctive-patterns-in-people-with-generalized-anxiety-disorder-in-stanford-study.html.

Pate, Brittany S., et al. “Site-Specific Knockdown of Microglia in the Locus Coeruleus Regulates Hypervigilant Responses to Social Stress in Female Rats.” bioRxiv, 1 Jan. 2022, www.biorxiv.org/content/10.1101/2022.10.03.509934v1.full.

Schramm, Eva, and Ari Waisman. “Microglia as Central Protagonists in the Chronic Stress Response.” Neurology Neuroimmunology & Neuroinflammation, 1 Nov. 2022, nn.neurology.org/content/9/6/e200023.

Van Deren DA;De S;Xu B;Eschenbacher KM;Zhang S;Capecchi MR; “Defining the Hoxb8 Cell Lineage during Murine Definitive Hematopoiesis.” Development (Cambridge, England), pubmed.ncbi.nlm.nih.gov/35452096/. Accessed 31 July 2023.

Yirmiya R;Pollak Y;Morag M;Reichenberg A;Barak O;Avitsur R;Shavit Y;Ovadia H;Weidenfeld J;Morag A;Newman ME;Pollmächer T; “Illness, Cytokines, and Depression.” Annals of the New York Academy of Sciences, pubmed.ncbi.nlm.nih.gov/11268375/. Accessed 31 July 2023.

“‘Anxiety Cells’ Identified in the Brain’s Hippocampus.” Columbia University Irving Medical Center, 31 Jan. 2018, www.cuimc.columbia.edu/news/anxiety-cells-identified-brains-hippocampus.

Alzheimer's Disease and Down Syndrome Comorbidity

Evelyn Bekker (author), Thanisha Kapur (advisor), Anika Shah (editor)
Northwood High School

Keywords: Down Syndrome, Alzheimer's Disease, comorbidity, animal models, synteny, trisomy, target genes, RCAN1, DYRK1A, SOD1

Abstract

Alzheimer's disease is hypothesized to be caused by the buildup of a peptide, amyloid beta, in the brain. Amyloid beta is produced by a gene, APP, located on chromosome 21. Thus, Down syndrome, or the trisomy of chromosome 21, has an extremely high comorbidity with Alzheimer's disease. However, research has proven that APP is not the only gene on chromosome 21 that causes neurodegeneration characteristic of Alzheimer's disease. Researchers have used the link between the two conditions to explore the relationship between chromosome 21 and Alzheimer's disease. By understanding the role of specific genes in neurodegeneration, drugs can target novel proteins to improve our ability to treat dementia. This review provides an overview of the comorbidity between the two conditions, as well as genetic findings relating to it.

Introduction

Down syndrome (DS), or trisomy 21, occurs predominantly when chromosome 21 is randomly triplicated instead of replicated during meiotic division. It is the leading genetic cause of intellectual disability, affecting 1 in every 700 births ("Down Syndrome"). The life expectancy of DS patients has increased dramatically in the past decades, from an average of 10 years in 1960 to 47 in 2007 ("Data and Statistics on Down Syndrome"). With this, countless findings have emerged connecting DS to age-dependent conditions. During their 40s and 50s, many DS patients will develop a variety of conditions that are usually seen in older populations, a phenomenon known as premature aging that connects genes on chromosome 21 to certain aging factors. Dementia, specifically that which parallels Alzheimer's disease (AD), is an extremely common symptom of premature aging in DS patients. By 35 to 40 years of age, all DS patients exhibit amyloid plaque and tau tangles. By their 50s, 30% of DS patients are diagnosed with AD,

which is characterized by memory loss and general cognitive decline and very rarely occurs before the age of 65 in non-DS populations, at around 5% (Hendrix) (“Down Syndrome and Alzheimer's | Symptoms & Treatments | alz.org”). The widely accepted amyloid cascade hypothesis of AD development appears to explain this discrepancy; it asserts that the first step towards mass neuronal death, which causes the behavioral symptoms of AD, is overproduction and dysregulation of amyloid beta peptide (A□). Because the gene that creates A□ and codes for amyloid precursor protein (APP) is located on chromosome 21, it can be expected that its overexpression will cause A□ buildup, plaques, and cell death. Thus, all DS patients exhibit hallmarks of AD. However, even with a third APP gene, 10% of DS patients never develop AD, showing shortcomings in our understanding of the cascade.

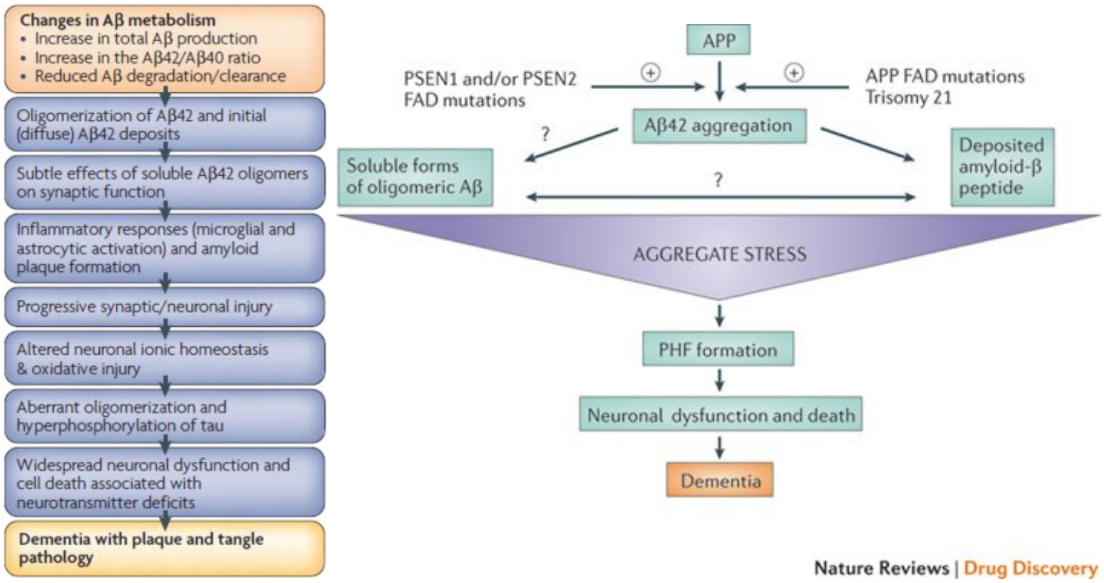


Image Credit: https://www.sciencedirect.com/science/article/abs/pii/S0143417915000657, https://www.nature.com/articles/nrd3505

Body

Mouse Models of AD-DS

Human chromosome 21 (Hsa21) has synteny with mouse chromosomes 10, 16, and 17 (Mmu 10, 16, 17), with the APP gene found on Mmu 16. To model DS, scientists tried triplicating the entire Mmu16 chromosome and found that the resulting mice had phenotypes similar to human DS, both systemically and neurologically. However, these mice all died in utero, making studies of their neurodevelopment impossible, and contained parts of Mmu16 shared not with Hsa21 but

other human chromosomes, making phenotype analysis difficult. To fix these issues, scientists turned to partial trisomy, creating the Ts65Dn mouse, with 3 copies of two-thirds of the genes homologous between Mmu16 and Hsa21 and 5% of those of Mmu17 ("001924 - Ts65Dn Strain Details"). Though the mice showed impaired cognitive ability and increased APP expression in neurons, amyloid plaques never formed (Reeves). Thus, to assess Hsa21 for other genes that may contribute to the formation of amyloid plaques, researchers used transgenic mice: (i) the Tc(Hsa21)1TybEmcf (Tc1) mouse, which has a freely segregating Hsa21 which makes it 75% trisomic for the chromosome's genes but importantly, not APP, models DS (ii) the Tg(PDGFB-APPSwInd)20Lms (J20-tgAPP) mouse, which overexpresses a human APP transgene, causing it to experience amyloid deposition from 4 months of age. By studying the abundance of amyloid plaques in wild type, Tc1, J20-tgAPP, and Tc1;J20-tgAPP mice, scientists determined that the cross gained significantly more buildup compared to the APP-only mouse. They concluded that, though APP is necessary for A□ buildup, it is accelerated by other genes present on Hsa21. Behaviorally, the cross mice showed exacerbated APP-related hyperactivity. Additionally, when presented with a T-maze, the cross mice performed poorly compared to the other progeny types, demonstrating memory deficits. Thus, the A□ buildup caused by trisomy 21 is correlated with cognitive decline, as proposed by the amyloid cascade hypothesis (Wiseman).

Specific Hsa21 Genes Associated with AD

Upon further study of Hsa21, multiple other genes have been linked to AD. One such gene is the Regulator of Calcineurin Activity 1 gene (RCAN1), implicated in AD development by genome wide association studies. To study the connection, scientists developed RCAN1 transgenic mice that had either overexpressed or ablated RCAN1. They found that RCAN1 regulates exocytosis through the number of vesicles undergoing exocytosis and the speed at which the fusion occurs. Reduced rates of vesicle endocytosis is associated with enlarged early endosomes, a phenomenon observed in the neurons of the Ts65Dn mouse model, DS patients, and some AD patients. This indicates that the expression of RCAN1 is directly involved in the development of AD hallmarks (Keating). Research has also implicated DYRK1A, a gene that plays a significant role in neural development and cognitive function, in both DS and AD phenotypes. It encodes a protein kinase that regulates various cellular processes, including neurogenesis and synaptic plasticity.

Scientists analyzed the brains of two DS patients with associated AD using paraformaldehyde-fixed cryoprotected sections and anti-DYRK1A antibodies. They concluded that in the nuclei and cytoplasms of certain neurons of people with Alzheimer's disease and those with adult Down syndrome and Alzheimer's pathology had enhanced Dyrk1A immunoreactivity. However, when they looked at the overall brain tissue, there was no general increase in Dyrk1A protein levels, suggesting that the changes are specific to only a few neurons and not widespread throughout the brain (Ferrer). Superoxide Dismutase 1 (SOD1) is a gene responsible for converting superoxide radicals into less harmful substances like hydrogen peroxide and molecular oxygen. Its overexpression in DS may contribute to increased the characteristic susceptibility to oxidative stress. Interestingly, when scientists compared SOD-1 protein levels in the brains of healthy controls, adult DS patients, and those with AD, they found higher SOD-1 levels in DS patients' temporal, parietal, and occipital cortex, possibly due to the trisomic state's overexpression response to oxidative stress, and lower SOD-1 levels in the AD temporal cortex, suggesting cell loss in the brain. This indicates a difference between DS-related AD and general AD (Gulesserian).

Conclusion

Currently, AD is an incurable condition. Patients are oftentimes unaware of their neurodegeneration until they begin exhibiting behavioral symptoms, which tend to occur in the later stages. Consequently, many treatments have proven unable to slow AD significantly. Most drugs that aim to treat AD are monoclonal antibodies that target amyloid plaque, such as lecanemab and donanemab. Though these drugs have been proven in clinical trials to reduce amyloid markers and partially slow cognitive regression, they are also associated with cerebral hemorrhage and edema, side effects known as amyloid-related imaging abnormalities (Sterling). In order to understand DS-specific AD, DS patients should be included in these trials. DS-AD comorbidity implicates Hsa21 genes outside of APP in AD development. By identifying new genes that contribute to AD, such as RCAN1, DYRK1A, and SOD1, we gain new drug targets that lead us closer to an effective treatment.

Works Cited

"001924 - Ts65Dn Strain Details." *The Jackson Laboratory*, 6 January 2023, https://www.jax.org/strain/001924. Accessed 22 July 2023.

"Data and Statistics on Down Syndrome." *CDC*, https://www.cdc.gov/ncbddd/birthdefects/downsyndrome/data.html. Accessed 22 July 2023.

"Down Syndrome." *Boston Children's Hospital*, https://www.childrenshospital.org/conditions/down-syndrome. Accessed 22 July 2023.

"Down Syndrome and Alzheimer's | Symptoms & Treatments | alz.org." *Alzheimer's Association*, https://www.alz.org/alzheimers-dementia/what-is-dementia/types-of-dementia/down-syndrome. Accessed 22 July 2023.

Ferrer, Isidro. "Constitutive Dyrk1A is abnormally expressed in Alzheimer disease, Down syndrome, Pick disease, and related transgenic models." *Science Direct*, https://www.sciencedirect.com/science/article/pii/S0969996105000835?casa_token=qbfQRXTKEIcAAAAA:ocFke53ng7E6Z2hDc70ipgkpz1jaZVIB9YZInsF7frsfP5nDe_EnZHqd0uF3paaIwa7Wxcg#aep-section-id20.

Gulesserian, Talin. "Superoxide Dismutase SOD1, Encoded on Chromosome 21, but Not SOD2 is Overexpressed in Brains of Patients with down Syndrome." *Sagepub*, January 2001, https://journals.sagepub.com/doi/abs/10.2310/6650.2001.34089.

Hendrix, James A. "Cross-Sectional Exploration of Plasma Biomarkers of Alzheimer's Disease in Down Syndrome: Early Data from the Longitudinal Investigation for Enhancing Down Syndrome Research (LIFE-DSR) Study." *MDPI*, 28 April 2021, https://www.mdpi.com/2077-0383/10/9/1907. Accessed 22 July 2023.

Keating, Damien J. *Academic*, Human Molecular Genetics, 1 4 2008, https://academic.oup.com/hmg/article/17/7/1020/870196#85562989.

Reeves, Roger H. “A mouse model for Down syndrome exhibits learning and behaviour deficits.” *NPG*, vol. 11, 1995.

Sterling, Reisa A. “Amyloid Related Imaging Abnormalities (ARIA) in Amyloid Modifying Therapeutic Trials: Recommendations from the Alzheimer's Association Research Roundtable Workgroup.” *NCBI*, 4 7 2011, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3693547/. Accessed 30 July 2023.

Wiseman, Frances K. “Trisomy of human chromosome 21 enhances amyloid-β deposition independently of an extra copy of APP.” *NCBI*, 26 June 2018, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6061702/. Accessed 22 July 2023.

Recognition and Response of First Responders to Stroke

Gabriella Harmon (author), Thanisha Kapur (advisor)
Mount Olive High School

Keywords: Stroke, First Responder, Emergency Medical Service (EMS,) EMT

Abstract

Strokes remain a leading cause of death in the United States, and, characterized by a rapid death of brain cells as a result of blocked blood flow, require rapid response times to produce the best results possible. Emergency Medical Services (EMS) play a large role in response times of stroke patients, from recognizing initial symptoms of stroke, to creating a proper response to ensure the best possible chances of survival for the patient. Statistics derived from US citizens suggest that the population is commonly unaware of stroke warning signs, and similarly suggest that EMS providers are unable to correctly identify all cases of stroke, increasing the time it takes for stroke patients to get to the hospital or another facility to receive proper care. Studies done on the responses of EMS to strokes have suggested that response times are often too long, or protocols are not set in place to allow for rapid action to be completed in necessary periods. This decreases the ability of stroke patients to qualify for specific treatment types that require treatment at least 3 hours after onset of symptoms. For these reasons, it is necessary for EMS responders to be able to quickly and effectively recognize and respond to stroke cases in order to ensure the best chances of survival for a patient.

Introduction

As of 2023, stroke is the fifth leading cause of death in the United States, according to the Centers for Disease Control and Prevention (CDC.) Each year, over 795,000 Americans have a stroke, with a majority of this statistic experiencing a stroke for the first time, making a majority of this population more vulnerable to not recognizing the occurring event. A stroke includes rapid death of brain cells, as they deteriorate without a supply of blood flow. For this reason, seconds count in prevention of death and disability in stroke victims, strengthening the importance of recognizing the early signs of stroke (Marc A. Lazarro.) Strokes often lead to disability associated with long-term brain damage, including speech impairment, communication

issues, loss of physical ability, and more. Often, the first trained response to stroke victims are the Emergency Medical Services (EMS,) being trained emergency services that provide pre-hospital care and services to those experiencing medical emergencies. Between 38%-65% of stroke cases are first evaluated by EMS before being transported to the hospital (Opeolu Adeoye et al.) EMS responders, being the first trained link to the process of healthcare in these cases, become vital in assessing the vital first seconds of a stroke emergency. With seconds counting in stroke response, it is important that quality services are delivered, and the symptoms of stroke are recognized quickly. Addressing stroke response among EMS systems is important to victims and future victims of strokes, their families, and the future of stroke care and EMS response systems.

Body

Recognition

Statistics show that an alarming number of Americans are unable to identify signs of stroke, with nearly 1 in 3 young adults being unable to provide knowledge of common stroke symptoms (Stroke Journal Report.) With seconds making a difference, it is critical for Americans to recognize the warning signs of stroke, and call 911, summoning first responders. For example, a 2003 study intended to assess public awareness of warning signs of a stroke. Data was collected from 61,019 adults that had participated in a state-based telephone survey, the Behavioral Risk Surveillance System. Respondents were given a list of common alarming symptoms, and asked to decipher which symptom was a sign of stroke. Furthermore, respondents were also asked to describe their path of action if they believed someone was having a stroke. Results from this study suggested that only 17.2% of respondents were able to correctly identify all stroke symptoms, and indicate that they would call 911 in the situation of recognizing a stroke occurring.

If 911 is called, the responsibility of properly recognizing the warning signs of stroke fall into the hands of EMS services. In September 2009 and December 2012, retrospective studies were performed to assess statistics associated with EMS recognition of stroke symptoms. Databases associated with both hospital and EMS systems were used to compile data. 399 cases of stroke, specifically ischemic attack, ischemic stroke, or intracerebral hemorrhage, were included in the

assessed data. Results suggested that, in 56.7% of the cases, EMS providers correctly recognized the presence of stroke related conditions. This study then went on to assess the correlation of correct recognition of stroke symptoms by EMS providers to time spent by EMS evaluating patients on scene, transporting patients, and getting to professional assistance. Compared to EMS that missed the correct case diagnosis, correctly identified cases were associated with longer on scene times, shorter transport times, and faster door-to-door physician and CT times. Another study assessing stroke recognition and accuracy was completed in 2015. This study also used compiled data from both hospital and EMS systems, focusing on 441 EMS-transported patients who had unidentified strokes, correctly identified strokes, or cases incorrectly identified as strokes (all by EMS providers.) This study suggested that 75% of cases of stroke (ischemic stroke and transient ischemic attack) were recognized by EMS providers, but 50% of EMS identified strokes were false positives.

Overall, the two studies suggest that, while EMS providers are often capable of recognizing stroke symptoms among cases, many cases still occur in which EMS providers are unable to correctly recognize a case as a progressing stroke. These studies also suggest the correlation between the recognition of stroke cases by EMS providers and rapidness of being able to get professional care.When seconds matter, it is important, therefore, that EMS providers recognize the warning signs of stroke in order to increase the possibility of survival and recovery among patients.

Response

When dealing with a stroke, speed of response is necessary to improve chances of survival or recovery. Therefore, the proper response of EMS is vital. A 2016 study assessed the response of EMS to recognized stroke symptoms. This study used the National EMS Information database, subjecting 184,179 that EMS determined as stroke, to assess response times. The response time was determined by the study to be 36 minutes, including call center and EMS dispatch time, time to scene, time on scene, and transport time. This result was taken with the statistic that 22%-46% of responses by EMS were unable to meet stroke guidelines. A common aspect of response by EMS is protocol of the EMS system. A 2013 study sought to assess the effect and prevalence of protocol in EMS stroke response. The protocols of 100 EMS systems in North Carolina were

analyzed. Results were analyzed alongside data from North Carolina Prehospital Medical Information System in 2009 of suspected stroke events. Results included that 23 of the systems had no instruction on scene time, 73 had general instruction on minimizing scene time, and 4 had specific instructions on scene time limits. When analyzed with 9,723 stroke cases within the area, little significant difference was found in response time between the protocols with no instruction and those with general instruction, with only a difference of about 0.7 seconds. However, the difference in response time between the protocols with no instruction and those with specific instruction were found to be relatively significant, with a difference of 2.2 minutes. While it may seem like a short period of time, these minutes and seconds are essential to survival and rehabilitation of stroke patients. A 2005 study demonstrates the importance of response time in stroke cases, as the quicker the response time, the faster stroke patients can receive thrombolytic treatment. Thrombolytic treatment is an effective treatment method of ischemic stroke, when received within the first 3 hours of symptom onset, which is a very minimal number of cases. The method of this study included collecting all initially-diagnosed ischemic stroke patients at 11 California hospitals over 3 months. All factors delaying treatment at initial symptoms were factored into the study, including EMS response. Overall, of the 374 patients, only 88 arrived at the hospital within the 3 hour period, with only 16 receiving the thrombolytic treatment. If all patients had arrived within 1 hour of symptom onset, 57% of them, statistically, could have likely been cured. While EMS isn't the only factor in response since symptom onset, EMS is an important factor in recognizing and quickly transporting stroke patients.

Conclusion

EMS is the platform relied on by United States citizens to be the first step in receiving proper medical care. With strokes being within the top 5 leading causes of US deaths, it is necessary that the EMS are effective in recognizing and responding to strokes. Studies indicate that, while EMS are commonly more qualified than other bystanders to recognize signs of stroke, many EMS still miss the early signs of stroke, or incorrectly identify strokes. Other research shows that response times of stroke patients are often long enough to cause damage to stroke patients, as they are unable to receive certain treatments as a result of having long response times. Overall, it would likely be beneficial to excel in training for EMS in order to assure that they are qualified to be the first link of emergency services to see a patient.

Works Cited

Marc A. Lazzaro. "Stroke: When Seconds Count." *Froedtert & the Medical College of Wisconsin*, www.froedtert.com/stories/stroke-when-seconds-count. Accessed 1 Aug. 2023.

Adeoye, Opeolu, et al. "Emergency Medical Services Use by Stroke Patients: A Population-Based Study." *The American Journal of Emergency Medicine*, Feb. 2009, www.ncbi.nlm.nih.gov/pmc/articles/PMC2686130/.

Kurt J Greenlund PhD a, et al. "Low Public Recognition of Major Stroke Symptoms." *American Journal of Preventive Medicine*, 17 Oct. 2003, www.sciencedirect.com/science/article/abs/pii/S074937970300206X.

California Acute Stroke Pilot Registry (CASPR) Investigators. "Prioritizing Interventions to Improve Rates of Thrombolysis for Ischemic Stroke." *Neurology*, 22 Feb. 2005, https://n.neurology.org/content/64/4/654.short

Clinical Predictors of Accurate Prehospital Stroke Recognition, https://www.ahajournals.org/doi/full/10.1161/STROKEAHA.115.008650. Accessed 2 Aug. 2023.

Contemporary Prehospital Emergency Medical Services Response Times For ..., https://www.tandfonline.com/doi/abs/10.3109/10903127.2016.1139219. Accessed 2 Aug. 2023.

"FASTSTATS - Leading Causes of Death." *Centers for Disease Control and Prevention*, 18 Jan. 2023, www.cdc.gov/nchs/fastats/leading-causes-of-death.htm.

Implementation Strategies for Emergency Medical Services within Stroke ..., https://www.ahajournals.org/doi/full/10.1161/STROKEAHA.107.186094. Accessed 2 Aug. 2023.

Recognition of Stroke by EMS Is Associated with Improvement In ..., https://www.tandfonline.com/doi/abs/10.1080/10903127.2016.1182602.

Apolipoprotein E, Alzheimer's, and Artificial Intelligence

Gabrielle Rodriguez (author), Thanisha Kapur (advisor), Anika Shah (editor)
Saint Brendan Highschool

Keywords: APOE4, AI, Alzheimer's, Amyloid, Pathogenesis

Abstract

Alzheimer's disease, a complicated neurodegenerative disease, is a major health concern that affects millions of people around the world. The APOE4 gene has been discovered as a critical contributor to Alzheimer's disease susceptibility, and considerably boosts vulnerability to the condition. This research dives into the APOE4 gene's influence on Alzheimer's pathology, investigating the molecular mechanisms that support its role in disease initiation and progression. Furthermore, this study highlights the potential of Artificial Intelligence (AI) in Alzheimer's research. AI-driven approaches have been shown to be promising in the areas of analyzing vast amounts of genetic imaging, and clinical data to identify complex patterns and biomarkers linked to the disease. By manipulating machine learning algorithms and deep neural networks, researchers can gain deeper insights into the relationship between APOE4 gene variants and Alzheimer's pathogenesis. The use of AI in combination with genomic data makes it easier to identify the therapeutic targets and personalize the development of treatment strategies for people carrying the APOE4 gene. Finally, this work underlines the crucial function of the APOE4 gene in Alzheimer's disease progression while fighting for the possibility of AI-powered research methods to accelerate our understanding of this complicated disease. We can pave the way for breakthrough diagnostic tools and specialized medicines by utilizing and embracing AI-driven approaches and fostering collaboration between researchers, ultimately aiming for a future in which Alzheimer's can be better avoided, managed, and cured.

Introduction

Often regarded as one of the most complex neural diseases, Alzheimer's affects 1 in every 10 individuals over the age of 65. The symptoms include: memory loss, difficulty participating in daily tasks, and a gradual cognitive decline. In the 1990's the Apolipoprotein E (APOE), a

protein whose function is to bind lipids, was discovered to have a significant effect on a person's risk of developing Alzheimer's. The APOE gene, which is found on chromosome 19, encodes the apolipoprotein E (APOE) protein, which is essential for lipid metabolism and neuronal repair in the brain. There are three variants of this gene; APOE2, APOE3, and APOE4 each with varying "effects". The APOE2 variant has protective factors against the disease, while APOE4 increases the risk of developing it. Having one copy of the APOE4 gene doubles your risk of disease, while having two copies can quadruple and even octuple your chances. However, it's important to note this is not a cause, it is simply a correlation. Studying these genes can be helpful in order to reduce the number of Alzheimer's cases, find a definite cause, and uncover a cure for the disease. With new advances in technology artificial intelligence proves to be a promising tool for research in the realm of neuroscience, Alzheimer's, and Apolipoproteins.

Body

Apolipoproteins and Alzheimer's

Alzheimer's is a degenerative disease that occurs when an excess of amyloid precursor protein (APP) beta is present, overcrowding neurons and preventing them from firing, ultimately causing the neuron to die. An article written by Jungsu Kim, Jacob M. Basak, and David M. Holtzman with the Washington University of School and Medicine suggests that apolipoproteins affect the process of amyloid-beta aggregation directly. This is due to the large presence of apolipoproteins in the brain which work towards cholesterol homeostasis. Once the apolipoprotein has completed receptor mediated endocytosis (the importation of macromolecules from the outside of the cell to the inside) it can either deteriorate or be recycled. This process releases cholesterol which is used to maintain synaptic health (synaptogenesis and synaptic connections). Apolipoprotein E4 causes an overproduction of cholesterol which is linked to accelerated Alzheimer's pathogenesis. The apoE4 gene also expedites the onset of Amyloid beta deposition into amyloid plaques causing the overcrowding of neurons to occur more frequently. Another study written by a team of highly esteemed neurologists including; Yang Shi, Kaoru Yamada, Shane Antony Liddelow, et. al describes how the apoE4 gene interacts with and affects tau, a protein that causes the neurofibrillary tangles that are commonly associated with the disease. In vitro, ApoE has been demonstrated to directly bind to tau, and in vivo,

neuronal expression of human ApoE results in tau hyperphosphorylation, a fully saturated biochemical with multiple phosphorylation sites . After controlling for the effect of APOE on Beta-2 microglobulin levels, recent GWAS studies demonstrate a robust and significant relationship of APOE with CSF tau and p-tau. ApoE4 allele frequency has been shown to be significantly raised in frontotemporal dementia (FTD) patients, a major number of whom have tauopathy. Carriers had more shrinkage in affected brain regions as well as aggravated behavioral deficits. These findings imply that ApoE may have a direct impact on tau pathology and tau-mediated neurodegeneration. On top of that, new research studies suggest that APOE4 may also alter cerebrovascular health in regards to the blood-brain barrier (BBB) and its integrity. BBB dysfunction can result in increased permeability and hazardous chemical buildup in the brain, which in conjunction with the amyloid and tau pathologies, can result in a complex interplay that leads to the neurodegenerative process we know as Alzheimer's disease.

Artificial Intelligence and Medicine

Artificial intelligence is the ability for a machine to learn in a similar way as humans and animals hence the term “artificial”. Yongjun Xu among others highlight the innovative impact that AI may have on various fields of scientific research in their article "Artificial Intelligence: A Powerful Paradigm for Scientific Research ". They describe perceptual intelligence, cognitive intelligence, and decision-making intelligence as part of the AI development process. Perceptual intelligence means that a machine has the basic human capacities of vision, hearing, touch, and so on. Cognitive intelligence is a greater level of competence in induction, argumentation, and knowledge acquisition. Artificial intelligence also has algorithms known as machine learning and deep learning which allow these machines to process extensive amounts of data, identify patterns, and make predictions with exceptional accuracy. This can be useful when researching Alzheimer's because the disease involves several intricate interactions between genetic, molecular, and environmental factors that can be analyzed by artificial intelligence. Ramesh, Kambhampati, Monson, and Drew delve into the specific applications of AI in the medical domain in their paper titled "Artificial Intelligence in Medicine."The

paper looks at a variety of AI applications, such as image analysis, natural language processing, and predictive modeling. This means that AI can help evaluate neuroimaging data to detect early indicators of the disease, forecast disease progression, and aid in the discovery of new treatment targets when applied to Alzheimer's research. By analyzing all that AI is capable of and applying it to Alzheimer's the possibilities of what can be accomplished are endless. For example, machine learning algorithms can identify an individual's genetic risk for Alzheimer's disease, allowing for early intervention and individualized treatments. Furthermore, AI can find additional genetic relationships, providing vital insights into the disease's complicated interplay of genes and pathways. Early detection and accurate diagnosis are two of the greatest difficulties in Alzheimer's research. AI-powered technologies should also be able to examine a wide range of datasets, including neuroimaging scans, genetic data, and cognitive tests, to uncover minor patterns that indicate illness development. According to the various capabilities of AI, it should be able to detect structural brain changes and foreshadow the progression of what is known as moderate cognitive impairment (MCI) to Alzheimer's disease using its deep learning algorithms. Moreover, AI can make it easier to integrate multimodal data, such as imaging, genomics, and clinical records. This integration allows for a more thorough and exact understanding of the disease, potentially leading to earlier intervention that can slow the progression of the disease or even stop it in its course. By searching enormous chemical databases, AI may speed up the process of discovering certain chemicals that may work as a drug against the disease. There can also be AI algorithms that are made to study biochemical connections between APOE4 and other genetic variables and potentially improve target identification. Additionally, AI models may be able to simulate certain pharmacological interactions with specific gene variants, which can assist in the development of personalized treatment methods for APOE4 gene carriers. AI algorithms are able to examine longitudinal data which can allow it to predict illness trajectories based on genetic profiles, environmental factors, and lifestyle choices in a process called "predictive modeling." This predictive power should be able to warrant more precise prognostic assessments, helping physicians and caregivers in the development of individualized treatment plans for patients who are at increased risk due to APOE4. AI-powered platforms enable the collection and analysis of massive amounts of data from a

variety of sources. Sharing such data between research institutes and international databases can stimulate collaboration and accelerate discoveries in Alzheimer's research. This, in turn, allows for a more thorough understanding of the role of the APOE4 gene in illness progression and opens up new paths for inquiry.

Conclusion

The APOE4 gene impacts the pathogenesis of Alzheimer's disease significantly. Its association with amyloid-beta pathology, tau hyperphosphorylation, and an altered lipid metabolism contributes to the cognitive decline and neurodegenerative aspects observed in Alzheimer’s disease. Understanding the certain mechanisms of the brain through which APOE4 influences Alzheimer's is crucial in the development of targeted therapies for patients with the gene. The more time that passes by the more progress is achieved in the realms of personalized medicine medication, AI analysis, and treatment strategies which in turn offers hope to the families of individuals with the gene and or the disease.

Works Cited

Kim, Jungsu, et al. “The Role of Apolipoprotein E in Alzheimer’s Disease.” *Science Direct*, 12 Aug. 2009, www.sciencedirect.com/science/article/pii/S0896627309005492?ref=pdf_download&fr=RR-2&rr=7ef14964cddcb3e3.

Ramesh, A N, et al. “Artificial Intelligence in Medicine.” *Annals of the Royal College of Surgeons of England*, Sept. 2004, www.ncbi.nlm.nih.gov/pmc/articles/PMC1964229/.

Shi, Yang, et al. “ApoE4 Markedly Exacerbates Tau-Mediated Neurodegeneration in a Mouse Model of Tauopathy.” *Nature*, 28 Sept. 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5641217/.

Xu, Yongjun, et al. “Artificial Intelligence: A Powerful Paradigm for Scientific Research.” *The Innovation*, 28 Oct. 2021, www.sciencedirect.com/science/article/pii/S2666675821001041?ref=pdf_download&fr=RR-2&rr=7ef15343fe3a67da.

Comparison of AuNF vs. Polysorbate-80 Nanoparticles on L-DOPA Transport

Jacqueline Bai (author), Thanisha Kapur (advisor)
The Bear Creek School

Keywords: Parkinson's Disease, L-DOPA, Nanoparticles, AuNFs, Polysorbate-80

Abstract

Parkinson's Disease (PD) is the second most common neurodegenerative disorder that affects a vast amount of people, especially with progressing age. A common drug to alleviate the symptoms of Parkinson's Disease is L-DOPA. However, L-DOPA has many side effects that result in its inefficient crossing of the blood brain barrier (BBB). This paper researches the effects of gold-seed nanoparticles (AuNF) and polysorbate-80 coatings as possible methods to deliver the drug L-DOPA across the BBB in order to increase drug efficacy. L-DOPA is one of the most common treatments for Parkinson's disease, but because of the selective permeability of the BBB, the drug has severe side effects, as well as a gradual loss of efficacy as the patient continues taking it. Nanoparticles are a new way to transport large molecules across the BBB. Through the testing of only AuNFs, only a polysorbate-80 coating, and a combination of both on five groups of albino Wistar rats, it was found that a combination of both AuNF and a coating of polysorbate-80 resulted in the most efficient delivery of L-DOPA across the BBB. To measure the levels of L-DOPA in the rats, high performance liquid chromatography was used where we first extracted and isolated the L-DOPA, and then compared them using a machine calibrated to 1 mg/L of L-DOPA.

Introduction

Parkinson's Disease is a common neurodegenerative disorder that is caused by a dopamine deficiency, specifically in the substantia nigra pars compacta (SNpc) that is characterized by resting tremors as well as a loss of motor coordination among others. The most common treatment for PD is L-DOPA, a drug that acts as a precursor to dopamine that many use as a replacement for dopamine. However, patients require more frequent doses over the years due to the loss of efficacy of levodopa, and one of the main side effects of the drug is dyskinesias, which is akin to the original symptoms of PD (Armstrong et al., 2020). This loss of efficacy and

increased dyskinesias is largely due to the blood brain barrier (BBB), a selectively permeable membrane that does not allow large proteins or other molecules to enter the brain. To combat this, scientists have developed nanotechnology made of both organic materials such as polymeric nanoparticles, liposomes, and dendrimers, as well as inorganic materials such as gold, silica, and carbon to deliver larger drugs into the brain that are unable to cross the BBB by themselves. Previous studies have been done with both organic and inorganic materials. For example, Dr. Gonzalez-Carter et al. found that the application of L-DOPA using gold nanoparticles (AuNF) was a way to efficiently deliver therapies into the brain. Other studies have shown that particles can successfully cross the BBB when coated with organic molecules such as polyethylene glycol (PEG), polysorbate, or other polymers (Kretuer et al., 2002). The goal of this study is to discover the best way to deliver dopamine across the BBB and into the brain–whether it is only inorganic materials, only organic materials, or a combination of both.

Materials and Methods

Preparation of AuNF with L-DOPA:

Preparation of AuNFs was done according to a previous study done by Gonzalez et al.

The AuNFs were synthesized using the Turkevich method (reduction of gold chloride using sodium citrate: spherical gold seeds (14 nm) were prepared by mixing a solution of HAuCl4·3H2O with sodium citrate acting as a reducing agent). Then, mPEG thiol was added to the AuNF dispersion to modify the surface properties of the AuNF to facilitate the attachment of other molecules or ligands onto its surface, and a solution of L-DOPA was added shortly after while stirring.

Preparation of polysorbate-80 with L-DOPA:

Preparation of polysorbate-80 was done according to a previous study done by Chandran et al.

A lipid solution was prepared by dissolving soy lecithin and cholesterol in a 9:1 molar ratio in diethyl ether. An L-DOPA solution was then prepared in a phosphate buffer solution (PBS) in a concentration of 2mg/ml. The L-DOPA solution was then added to the lipid solution along with the polysorbate 80 and span 80 in a molar concentration of 9:1:1:4. The solution was then converted to a fluid consistency and hydrated by first homogenizing the formulation (using a homogenizer at 5000 rpm for 20 mins at 50 degrees celsius), agitating the mixture using a vortex

mixer and adding PBS to produce a suspension of multilamellar vesicles (MLV). The MLV was then sonicated using a microtip probe sonicator for 30 minutes at 40% frequency to produce a homogenous liposome formulation.

Preparation of AuNF and polysorbate 80 with L-DOPA:

The AuNF was prepared in the same method shown above. A solution of polysorbate 80 was diluted to a concentration of 9:1 molar, and will functionalize the AuNF by combining the two solutions and mixing thoroughly in a 1:1 ratio. The L-DOPA solution was prepared in the same way it was with just the polysorbate 80 mixture, and will be incorporated to the AuNF/polysorbate 80 solution by mixing thoroughly.

Animal Testing:

Testing was performed on albino Wistar rats (180-200g) that had access to food and water ad libitum. The rats were divided into five groups. The first group received only L-DOPA diluted with normal saline, the second received the AuNF/L-DOPA mixture, the third received the L-DOPA transported by nanoparticles coated in polysorbate 80, and the fourth received the AuNF/polysorbate 80 combination. The fifth group received no drug treatment at all and was only injected with saline solution. All groups were administered via i.v. in the tail vein (except group 5). After 2 hours, the rats were anesthetized with ethyl ether and sacrificed by decapitation. The brains of the rats were then collected and L-DOPA levels were extracted and analyzed using High-Performance Liquid Chromatography (HPLC).

High-Performance Liquid Chromatography (HPLC) Analysis:

All methods of HPLC were done according to the previous study done by Riggin et al.

We are able to analyze levels of L-DOPA in brain blood plasma and tissue using HPLC. For every 1 ml of blood plasma, 3.5 ml of saturated sodium chloride solution and 100 ul of concentrated hydrochloric acid in a 15-ml polypropylene centrifuge tube. The tube was shaken well and then centrifuged for 15 minutes at 15,000xg to precipitate the protein. The supernatant was then poured into a 12-ml glass centrifuge tube. We would then hydrolyze the sulfate conjugates by heating it in a 90 degrees Celsius water bath for 20 minutes. The tubes were then cooled and 0.5 g of ammonium sulfate was added. The solutions were then extracted twice with

ethyl acetate, once with hexane (5-ml portions of each), centrifuged briefly, and then aspirated. The non-aqueous layers were discarded.

The aqueous layers were then placed in a 10-ml beaker with a magnetic stirrer, and 100 ul of ethylenediaminetetraacetate and sodium metabisulfite solutions were added. While stirring the mixture, the pH was adjusted to 8.5 ± 0.1 by rapid addition of 3 mol/L sodium hydroxide and then 1 mol/L sodium hydroxide. The solution was then shaken with 60 mg of acid-washed alumina in a 5-ml conical screw-cap vial for 12 min. The alumina was settled and then aspirated, discarding the serum solution. The alumina was then washed once with a phosphate buffer, twice with distilled water, and then dried in a vacuum oven for 10 min at 40 degrees Celsius.

The L-DOPA was then eluted from the alumina with 300 ul of 1 mol/L acetic acid. The vials were then gently shaken for 10 min on a mechanical shaker. 200 ul of the eluent was then transferred to the second vial. 20 ul was injected onto the chromatographic column. Peak heights were measured and the concentrations were calculated using the comparisons with the peak heights obtained for the working standard containing a known concentration (1 mg/L) of L-DOPA.

Results and Discussion

Although this experiment has not been tested in the real world, given current information, it is likely that the combination of both gold nanoparticles and the polysorbate-80 coating would result in the most efficient transportation of L-DOPA past the BBB. As previous studies have shown (Gonzalez-Carter et al., 2019, Chandran et al., 2015), both AuNFs and a polysorbate-80 coating has provided a statistically significant increase in L-DOPA levels past the BBB, and it is highly likely that the combination of both would result in better facilitation across the membrane. The group that was administered only L-DOPA with no saline solution would exhibit normal baseline levels with no significant increase, and the group that was administered no L-DOPA and only saline solution exhibited no L-DOPA levels at all.

In general, nanoparticles help facilitate the transportation of larger drugs through three ways: (1) the binding of nanoparticles to the inner endothelial lining of the brain capillaries could provide a

drug concentration gradient, thus improving passive diffusion (2) brain endothelial cell uptake of nanoparticles may occur through endocytosis or transcytosis (3) apolipoproteins (APO) are involved in the brain penetration of nanoparticles over those coated with polysorbate-80 (Karanth et al., 2008). Polysorbate-80 is a molecule composed of fatty acid esters of sorbitol-derived cyclic ethers with approximately 20 mols of ethylene oxide per mol of polysorbate 80 (Amani et al., 2011). In this scenario, the coating of polysorbate-80 mimics the low-density lipoproteins which allows the nanoparticles carrying L-DOPA to be transported across the capillary wall and into the brain via the low-density lipoprotein receptors (Kreuter et al., 2002). Because AuNFs are synthesized using inorganic materials, the transportation of L-DOPA across the BBB is mediated through an energy-dependent endocytosis, not through diffusion. As a result, the combination of the polysorbate-80 coating with the AuNFs might result in an increase in opportunities for L-DOPA to cross the BBB, utilizing the advantages that both types of nanoparticles provide.

Specifically for AuNFs, there is the risk that the brain will suffer from inflammation due to its characteristics as an inorganic material. Brain macrophages (microglia), however, remedy this problem, clearing foreign entities within the brain and capturing/processing exogenous nanomaterials. To prove this, Gonzalez-Carter et al. quantified the capacity of AuNF in the brain after BBB penetration and clearing using light transmission microscopy and confocal reflectance microscopy analysis of microglia cells treated with L-DOPA-AuNF. Z-stack analysis revealed that L-DOPA-AuNF could be detected throughout the cell, showing cellular internalization.

Furthermore, while HPLC analysis is an efficient way to analyze L-DOPA levels in the brain, it is limited to only analyzing quantity. Other factors such as internalization of L-DOPA, or the location of where the drug appeared, remain unknown through this method of analysis alone. However, performing analysis methods that would allow us to determine factors such as these would be difficult, especially at the same time as HPLC. Other studies such as one performed by Gonzalez-Carter et al. utilize in vitro models instead of in vivo models that allow for multiple tests to be performed simultaneously. Further research on this topic using in vitro models might reveal more about the efficacy of AuNFs coated with polysorbate-80.

However, the results of this testing does suggest that utilizing nanoparticles as carriers for L-DOPA can significantly improve transport to the brain, especially when using a combination of AuNFs and a polysorbate-80 coating. L-DOPA uptake in the brain is further enhanced, possibly due to the synergistic effects of both the carrier and the permeation enhancer. These findings will have important implications for the treatment of neurological disorders, especially Parkinson's Disease, for which L-DOPA is one of the main treatments. Utilizing AuNFs with a polysorbate-80 coating as a drug carrier could offer a promising approach to increase the efficacy of L-DOPA, as well as decreasing its side effects. It is, however, crucial to acknowledge the limitations of this study, especially since it was done hypothetically and only on animal models. Because animal models do not fully encompass the complexity of human physiology, the drug response in humans may differ. We must also thoroughly investigate the long term effects of these nanoparticles, since this study was performed in a relatively small time window. However, the present study demonstrates that the use of AuNF as a carrier alongside a polysorbate-80 coating holds promise as a potential strategy to enhance L-DOPA delivery to the brain.

Works Cited

Amani, Amir, et al. "Molecular Dynamics Simulation of a Polysorbate 80 Micelle in Water." *Soft Matter*, vol. 7, no. 6, 7 Mar. 2011, pp. 2900–2908, pubs.rsc.org/en/content/articlelanding/2011/SM/c0sm00965b#, https://doi.org/10.1039/C0SM00965B. Accessed 10 Nov. 2020.

Armstrong, Melissa J., and Michael S. Okun. "Diagnosis and Treatment of Parkinson Disease." *JAMA*, vol. 323, no. 6, 11 Feb. 2020, pp. 548–560, https://doi.org/10.1001/jama.2019.22360.

Bansal, Ranju, et al. "Quantitative Analysis of Doxorubicin Hydrochloride and Arterolane Maleate by Mid IR Spectroscopy Using Transmission and Reflectance Modes." *BMC Chemistry*, vol. 15, no. 1, 24 Apr. 2021, https://doi.org/10.1186/s13065-021-00752-3. Accessed 4 Oct. 2021.

Chandran, Sarath, and Pichandy Prasanna. "Targeting Dopamine Liposome to Brain Using Polysorbate 80 for Parkinson's Disease." *International Journal of Biosciences*, vol. 7, no. 5, 30 Nov. 2015, pp. 107–115, citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=3b2e5a4406de417270b2bba8d44a95cf385f7a24, https://doi.org/10.12692/ijb/7.5.107-115. Accessed 24 July 2023.

Gonzalez-Carter, Daniel, et al. "L-DOPA Functionalized, Multi-Branched Gold Nanoparticles as Brain-Targeted Nano-Vehicles." *Nanomedicine: Nanotechnology, Biotechnology, Medicine*, vol. 15, no. 1, 1 Jan. 2019, pp. 1–11, https://doi.org/10.1016/j.nano.2018.08.011. Accessed 1 June 2023.

Kreuter, Jörg, et al. "Apolipoprotein-Mediated Transport of Nanoparticle-Bound Drugs across the Blood-Brain Barrier." *Journal of Drug Targeting*, vol. 10, no. 4, Jan. 2002, pp. 317–325, https://doi.org/10.1080/10611860290031877. Accessed 16 Nov. 2020.

Riggin, Ralph M, et al. “Liquid Chromatographic Method for Monitoring Therapeutic Concentrations of L-Dopa and Dopamine in Serum.” *Clinical Chemistry*, vol. 22, no. 6, 1 June 1976, pp. 782–784, https://doi.org/10.1093/clinchem/22.6.782. Accessed 23 Apr. 2023.

Silva, Gabriel A. “Nanotechnology Approaches to Crossing the Blood-Brain Barrier and Drug Delivery to the CNS.” *BMC Neuroscience*, vol. 9, no. S3, Dec. 2008, https://doi.org/10.1186/1471-2202-9-s3-s4. Accessed 30 Aug. 2019.

Teleanu, Daniel, et al. “Blood-Brain Delivery Methods Using Nanotechnology.” *Pharmaceutics*, vol. 10, no. 4, 11 Dec. 2018, p. 269, https://doi.org/10.3390/pharmaceutics10040269.

AI Therapists: Effectiveness as Therapeutic Support

Janet Yang (author), Thanisha Kapur (advisor)
Central High School

Keywords: Artificial Intelligence, Therapy, Mental Health, Traditional Therapy, Digital Therapy, Stress, Anxiety, Depression

Abstract

Artificial intelligence has had a prominent effect on society. It has been explored in multiple aspects. In this research article, it discusses and reviews whether or not Artificial Intelligence will be more or less beneficial to a human therapist and the overall healthcare industry, specifically regarding mental health. The experiment investigates the use of artificial intelligence (AI) as therapists to offer emotional support to those suffering from mental health issues. The choice of interacting with AI therapy versus real therapists was made at random for each participant. Prior to the experiment, participants will complete evaluations and pre-assignments regarding the severity of their mental health condition that will be compared with the post-assignment after the experiment. This data will be used to see whether or not AI have the ability to become therapists. Both groups will be asked to implement coping mechanisms, professionalism, activities, and maintain a positive and uplifting environment for participants. The findings demonstrated that stress and anxiety levels were significantly reduced by both human and artificial intelligence therapy. Participants were asked to participate in surveys, interviews, and evaluation techniques after the experiment had been concluded. They gave relatively positive feedback on the accessibility and understanding nature of the AI therapists, and in general had effective sessions with them. In contrast to human therapists, several participants did notice limitations within the AI's ability in fully understanding the necessary needs from the participants. This research is aimed to study whether or not AI therapists have the potential to be an additional resource for mental health care, but based on results, further research and considerations is required.

Introduction

Artificial intelligence was first presented in the late 1900s and has grown exponentially over the last few decades. With the rise of artificial intelligence (AI) as an engine of change in several fields, the field of mental health has seen considerable advancements in recent years. The concept of implementing AI as therapists is gaining traction in the field of therapy and mental health care. AI-powered therapy has the potential to transform the way emotional support and psychological treatments are offered by making them flexible, affordable, and easily available to a larger and diverse population. AI therapists are intelligent programs that can analyze human speech and use advanced algorithms to respond and understand human languages. These systems are intended to communicate with users, giving compassionate replies, have both psychological education, and treatments suited to each user's requirements. AI therapists hope to establish an environment that encourages emotional understanding in a more accessible setting. However, this newly found concept of AI therapists has raised questions on whether or not it will be more beneficial compared to traditional therapy sessions with licensed therapists. This introduction is the beginning of a more in-depth examination of AI therapists via an experiment that analyzes their effectiveness in giving emotional support to those experiencing stress and anxiety. The research aims to add useful insights about the role of AI in mental health care and to develop responsible AI-based treatment approaches. By investigating the possible benefits and limitations of AI therapists, this experiment is aimed to suggest more creative solutions that improve mental health support for people all around the world.

Materials and Methods

A varied sample of people seeking therapy or mental health support will be recruited for this project, a total of 200. Participants will be randomly placed into one of two groups: AI therapy or human therapy, 100 in each, varying from 18-60 years old. An AI-based treatment group with advanced natural language processing and machine learning capabilities will be created in the AI therapy group. The artificial intelligence model will be trained to communicate with multiple therapy sessions, have therapeutic approaches, and advanced psychological knowledge. The goal is to ensure that the AI therapist has the knowledge and abilities necessary for effective therapy. In addition, a user-friendly interface will be built to allow participants to comfortably interact with the AI therapist. Similar to texting, it will be presented in the same format but with limited features. There will not be the ability to send emojis and gifs as the goal is for the AI to respond

to words and respond appropriately. There will be implemented breaks throughout the session for the participants who request longer sessions. We respect our participants' wishes and make sure they are fulfilled. The AI therapist will maintain user privacy and confidentiality throughout the experiment. The human treatment group will be made up of professional and skilled human therapists who will provide participants with traditional therapy sessions. These therapists will be expected to follow professional guidelines and ethical standards. Participants will be asked to attend regular sessions for six weeks. To measure quantitative data, each participant will be given an assessment before the 6-week experiment to identify the specific mental concerns of that person, whether it is anxiety, depression, etc., to ensure quality, effective, and focused therapy sessions from either a therapist or AI. Participants will have completed the Patient Health Questionnaire (PHQ-9) and Generalized Anxiety Disorder 7-item scale (GAD-7). This information will be given to the therapists and AIs prior to their sessions in order to measure any changes with these scales after the following sessions. After a few sessions, surveys and interviews will be held to collect the qualitative data of the experiment. These will ask the participant how they feel about their assigned group, if the overall sessions were effective, etc. At the end of the experiment, all these components will be compared, a conclusion will be formed, as well as possible limitations. During the sessions, psychological assessment tools, such as questionnaires, will be present to measure the effectiveness of the session such as the severity of their concerns and well-being scores.

Psychological Tools During Therapy

During the treatment sessions, both AI and human therapists will be expected to use appropriate psychological methods. This includes, but is not limited to, active listening, empathy, mindfulness, and with the aim of making the person feel safe and have a healthy way of approaching problems. Mindfulness-based therapy teaches individuals to be present in the moment, increasing self-awareness and decreasing stress. Individuals can use this strategy to better understand their emotions, fostering personal growth and resilience. Clients can express their feelings and thoughts nonverbally through numerous artistic approaches in art therapy. This type of therapy can be very effective for people who struggle to express their emotions verbally. Deep breathing exercises and muscular relaxation can also assist people control anxiety and create a sense of peace. Aside from that, both groups will practice both coping techniques and

implement activities into their sessions, based on the participants' interests and hobbies. Both groups should be engaged during their sessions and respond in a respectful and thoughtful manner. These psychological tools, among others, are useful resources for healing during treatment and better personal development.

Cognitive-Behavioral Techniques (CBT)

Both the AI and human therapy group will be asked to implement a few cognitive-behavioral techniques (CBT) in their sessions. CBT is based on the idea that our thoughts, emotions, and behaviors are all connected and can impact one another. CBT attempts to identify and repair dysfunctional thought patterns and behaviors in individuals experiencing emotional discomfort or mental health difficulties in order to bring about beneficial improvements in emotions and overall well-being. This includes scheduling and partaking in recreational activities, identifying and acknowledging automatic negative thoughts (ANTs), as well as thought patterns and behavior.

Patient Health Questionnaire (PHQ-9)

The Patient Health Questionnaire-9 (PHQ-9) is a popular self-report tool for determining the severity of depression, developed by multiple professors. It was adapted from the Primary Care Evaluation of Mental Disorders (PRIME-MD) questionnaire, which was used in medical settings to diagnose a range of mental health disorders. The PHQ-9 is the "depression module, which scores each of the 9 DSM-IV criteria as '0' (not at all) to '3' (nearly every day)" (Kroenke, Spitzer, Williams). In addition, a study was conducted by Bernd Löwe that reviewed the sensitivity of the PHQ-9 in terms of detecting any diagnostic and severity changes. They found that the PHQ-9 was an effective way to measure changes in depression diagnostic over time, suggesting that the PHQ-9 can be utilized for "longitudinal as well as for cross-sectional studies" (Löwe, 2004). This questionnaire will be used during the experiment to measure the severity of the participant's symptoms.

Generalized Anxiety Disorder-7

The Generalized Anxiety Disorder-7 is a tool developed by the same professors in order to determine the severity of generalized anxiety disorder. Prior to publishing the "7-item anxiety scale (GAD-7)," professors Robert L. Spitzer, Kurt Kroenke, Janet B.W. Williams, and Bernd Löwe did their own experiment, studying its sensitivity to new changes based on one's mental health severity. In this case, it specifically measures the severity of anxiety. The results of the experiment claimed that, overall, the GAD-7 "had good reliability, as well as criterion, construct, factorial, and procedural validity." The conclusion states that the "GAD-& is a valid and efficient tool for screening for GAD and assessing its severity in clinical practice and research" (Spitzer, Kroenke, Williams, Löwe). This will be used during the experiment for those who are or previously diagnosed with anxiety of any severity.

Results and Discussion

The experiment was not hypothetical. It was conducted with a goal to compare and contrast human and AI therapy. There was no hypothesis prior to the experiment. The overall results are seen to be beneficial regarding both groups. Based on the various assessments and tools used throughout the experiment, the data found that both the AI therapy and human therapy participants' mental health has significantly improved when compared to their pre-assignments. In both groups, participants reported having less severe symptoms throughout the experiment. There were no significant statistical differences between the two groups; both groups reported a positive reaction towards their sessions. Participants in the AI group reported having an enjoyable experience with the AI therapist. The AI's empathetic and human-like nature allowed them to express themselves more freely and develop a sense of trust and companionship with the therapist. A few participants, during their interview, claimed they felt less self-conscious and more open to discuss more sensitive and difficult topics with the AI. Similarly, the human therapy group found traditional therapy sessions just as beneficial and allowed them to talk in a comfortable environment. The traditional sessions also allowed them to partake in physical activities and have hands-on practice with various different coping mechanisms, breathing exercises, and more (Molina, Rosenblatt). Although many participants were satisfied with their sessions, others reported having issues regarding the AI and specifically, its ability to understand more complex emotions and thought processes. There were many instances in which participants weren't able to express how they were feeling that could have potentially been identified

physically or through body movements. The AI couldn't establish the tone they said it in as well, which can lead to misconceptions regarding how someone is feeling about specific topics. For example, a participant could say that they are comfortable going over a specific topic but in reality, they may not. The AI therapist wouldn't be able to decipher whether or not it was factual. We also found a difference with how different age groups react to the specific two groups. More younger participants were able to work with the AI therapist more efficiently and openly compared to the older participants, who were more reluctant due to their unfamiliarity with new technology. We found that these participants had a lower change of symptom severity since time was taken for them to get used to the complex AI systems. The format of the AI therapists was similar to texting on a regular cellular device, however, we found that this format can still be challenging and confusing for older generations compared to the younger generations.

Based on these results, the future of artificial intelligences being used as individual therapists seems to be reachable. However, before any actions are performed, more research and considerations must be made. The development and rising popularity of AIs is promising but there are many factors to consider before deeming them just as effective as traditional therapy. These topics must be further explored so AI therapy can evolve into a safe option, similar to traditional therapy. First, technical issues. They are more prone to potential bugs, troubleshooting, system breaches, and maintenance if not organized carefully. In this experiment, the AI worked with a more private setting, thus these potential issues were not taken into consideration. The AI therapist must be able to be used both domestically and globally. It must also be able to be used by multiple people at the same time, providing both quality and efficiency. Second, ethical concerns. Once more, the AI presented was developed by scientists for this specific experiment so all the information is kept between the program and the individual, but this is not guaranteed for other AI therapy bots that are developed in the future. Understanding culture and diversity may be complicated for AIs, especially if one of the leading factors that may be causing specific reactions or symptoms is rooted deeply in their cultural identity and complexity. The accessibility and overall design of the AI therapists should appeal to all age groups, considering those who may not be familiar with the concept of AIs as therapists or in general. In conclusion, the concept of artificial intelligence acting as therapists

may be extremely beneficial for those who lack access to traditional therapy. However, multiple precautions are needed to move forward with this idea.

Works Cited

Löwe, Bernd et al. “Measuring depression outcome with a brief self-report instrument: sensitivity to change of the Patient Health Questionnaire (PHQ-9).” *Journal of affective disorders* vol. 81,1 (2004): 61-6. doi:10.1016/S0165-0327(03)00198-8

Kroenke, Kurt, et al. “The PHQ-9.” *NCBI*, 2001, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1495268/. Accessed 30 July 2023.

Löwe, Bernd, et al. “A brief measure for assessing generalized anxiety disorder: the GAD-7.” *PubMed*, 22 May 2006, https://pubmed.ncbi.nlm.nih.gov/16717171/. Accessed 30 July 2023.

Molina, Olga, and Kate Rosenblatt. “12 Rewarding Benefits of Therapy — Talkspace.” *Talkspace*, 18 October 2021, https://www.talkspace.com/blog/benefits-of-therapy/. Accessed 30 July 2023.

Mace, Ryan A., et al. “Older adults can use technology: why healthcare professionals must overcome ageism in digital health.” *NCBI*, 8 September 2022, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9494377/. Accessed 30 July 2023.

Alzheimer’s Detection Through Artificial Intelligence, Methods and Effectiveness

Jessica Yam (author), Thanisha Kapur (advisor), Anika Shah (editor)
Mills High School

Keywords: Nervous System, Neuron, Brain, Central Nervous System (CNS), Beta-Amyloid, Tau, Detection, Classify, Algorithm, Machine Learning, Artificial Intelligence (AD), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), Natural Language Processing (NLP), Convolutional Neural Networks (CNNs), Support Vector Machines (SVMs)

Abstract

Alzhemier’s disease is one of the most common types of neurological disorders that occurs in the brain of the nervous system. Alzheimier’s diseases (AD) is a neurological disorder that’s neurodegenerative as the cells in the brain slowly die and is most prone to develop in age groups 65 and older. As a result, those affected experience a loss of memory and cognitive functions. Since AD is fatal, it’s important to study how it can be detected early-on to allow the initiation of treatment and interventions to help manage the symptoms and slow the disease progression. With the use of artificial intelligence (AI), the incorporation of various AI strategies and methods can improvise the accuracy and reliability of results to identify AD early-on.

Introduction

Alzhemier’s disease is a progressive neurological disorder that’s the most common type of dementia. Dementia is a characterized neurodegenerative condition that slowly consumes a person’s cognitive skills in the brain. As a result, this affects one’s ability to read, learn, think, remember, speech, and to carry a simple task. This is because Alzhemier’s disease releases abnormal proteins including beta-amyloid plaques and tau tangles. The tangles block the neuron’s transport system, which interferes with the neurons from communicating and impair electrical signals transmission across synapses. While the presence of plaques create an inflammatory response in the system, which triggers an immune response in the immediate area. Neurons are made of three components, their cell body, dendrites, and an axon. The cell body contains the neuron’s genetic information, maintains the neuron's structure, and controls the

neuron's activities. Dendrites extend from the cell body and collect the information from the signals synapses receive. Axons are the elongated portion of the neuron with a cable-like structure that's in charge of transmitting the messages from the signals to other neurons. When a neuron receives signals from other neurons, it generates an electrical charge that travels through an axon and releases neurotransmitters across a synapse. As a result, a disruption between the neurons' communication inhibits the neuron's ability to perform its functions. However, Artificial Intelligence(AI) has been exponentially growing in recent years as it enlightens with its continued advancements in technology. As AI continues to grow, AI has been essential to many fields including the healthcare industry. With proposed methods, solutions, and identified sources, researchers have developed advanced technology to detect Alzheimier's disease early-on. Even though there is no supported evidence to cure or prevent this disease, identifying the disease early can allow the initiation of treatment and interventions to help manage the symptoms and slow the disease progression. This is important to review because there are about 500,000 new cases every year and 1-in-9 people suffer from Alzheimer's disease aged 65 and older.

Body

Overview of Alzheimer's Disease and Methods

Traditionally, AD has been detected through a combination of medical history evaluation, clinical assessments, cognitive tests, and neuro-imaging techniques. Physicians would conduct a thorough interview on an individual's medical history allowing them to assess the changes in a patient's behavior and functional abilities. They would also evaluate the presence of risk factors such as the individual's genetics, lifestyle, and environment. Cognitive testing was also incorporated by using the standardized examinations. These included the Mini-Mental State Exam (MMSE), Montreal Cognitive Assessment (MoCA) and the Neuropsychiatric Inventory Questionnaire (NPI-Q) to assess memory, attention, speech, and function. Physicians would also conduct a neurological examination to assess an individual's neuromotor, neuroimaging techniques via magnetic resonance imaging (MRI) to visualize the brain's structure and detect abnormalities associated with AD, and positron emission tomography (PET) scans with specific tracers such as amyloid or tau to measure the presence of amyloid plaques and tau tangles in the brain, which are the characteristics of AD pathology. Although these methods were effective

traditionally to a certain extent, they often relied on subjective interpretation, the influence of the personal opinion's of physicians, which limits the accuracy and specificity. However, with the integration of AI, machine learning, and deep learning algorithms, AD detection via AI has shown the improvement of accuracy in results and provides quantitative analysis of cognitive assessments, biomarkers, and neuroimaging data enhancing the early detection and treatment approaches for AD. Though, what is machine learning and deep learning? Machine learning is a branch of AI, which primarily focuses on the use of data and algorithms, a process or set of rules through calculations and other problem-solving operations via a computer to mimic the way humans learn and improve accuracy. Deep Learning is a type of machine learning that consists a neural network with 3 types of layers: the input layer that consists the initial data for the neural network, hidden layers in between the input and output layer where the computation is optimized, refine for accuracy, and finalized, and the output layer whose role is to produce the results for the given inputs. The DL algorithm is a structure of layers that build on top of each other. Given an image of a fruit, the DL will extract the raw data. Then, the hidden layers in between would view in depth and extract the subtle features of the fruit. Finally, the output layer will summarize and develop an extract of what it has learned from the given data.

AI-Based Approaches in Alzheimier's Detection

Neuroimaging Data

Advances in artificial intelligence have enabled current approaches to analyze neuroimaging data, voice and speech patterns, and cognitive assessment data to aid the research of detections and treatments in Alzheimier's disease. Magnetic resonance imaging(MRI) and positron emission tomography(PET) scans are imaging techniques that are often used to examine the nervous system, but not limited to. Some common AI algorithms used in analyzing brain images in AD are convolutional neural networks(CNNs), autoencoders, support vector machines(SVMs), random forest classifiers, and deep learning networks. CNNs is a subtype of neural networks and is commonly used to identify patterns that could lead to pathology or progression of AD. Its phenomenal layer allows the high dimensionalities of images to be reduced by preserving characterizations of massive neuronal activities and insights to miniature features in the brain without losing its information. Autoencoders are unsupervised neural networks that learn to compress the representations of neural images that can be used to identify

subtle features via the data for progression. This is important because it can extract biomarkers of AD through brain scans. SVMs are supervised learning models and random forest classifiers are applied to categorize brain images enabling both techniques to distinguish between a brain with Alzheimier's versus a healthy brain to scan for distinct features. DL networks can extract features from a 4D brain imaging data that may serve as biomarkers for AD. While there are a number of AI methodologies applied, it is important to understand that the extraction of subtle signatures and changes in the data of brain imaging can serve as biomarkers for detection and progression in AD.

Voice and Speech Analysis

Alongside neuroimaging data analysis, voice and speech patterns are also analyzed through AI via speech patterns and linguistic markers. Natural language processing (NLP), automated speech recognition, and machine learning algorithms are AI techniques that are often implemented to analyze the voice and speech of an individual. NLP is a subfield in linguistics that concerns the interaction between the language of humans and AI. Automated speech recognition is the process of converting a spoken language to text by learning and inputting the words spoken to transcribing the words as a text and comparing its accuracy as its output. They are applied to detect speech and voice recordings in order to identify linguistic or vocal biomarkers that could be associated with the cognitive impairment of AD. These techniques can analyze features including tone, voice, pitch, pauses, semantic and synaptic patterns, filler words, fluency, naming ability, and recalling. ML models are also used to compare between a healthy speech pattern without Alzheimier's and with Alzheimier's given a sample to classify. Therefore, the progression of Alzheimier's and detection could be noticed by AI through the change of speech of certain speech features such as the richness in vocabulary and the ability to recall, which can be tracked to record the cognitive decline overtime.

Cognitive Assessment Data

Moreover, cognitive performance is another aspect and current approach AI uses to analyze the psychosocial presentation of individuals. Similarly to traditional cognitive assessments via paper, computer-based cognitive tests also test for cognitive impairments such as memory, attention, language, problem-solving, and speech. However, these tests are adapted into a digital format by

assessing users through interactive tasks. The data is then processed using AI algorithms that extract the cognitive performance of users reflecting their memory assessment, attention, how they may execute things, and etc. Similarly to all three approaches, machine learning models are used to compare between a cognitive performance from a healthy brain and a brain potentially affected by Alzheimier's to detect.

Effectiveness of AI in Alzheimier's Detection

Neuroimaging analysis is effective for early diagnosis and tracking progression as technological scans conducted by advanced imaging modalities such as MRI and PET can reveal subtle brain changes and biomarkers associated with Alzheimier's. These potential biomarkers studied include abnormal amy-betaloid and tau levels in the cerebrospinal fluid (CSF). Its impressive ability through neuroimaging technologies offers remarkable insights into the structure and function of the brain as it can visualize the intricate anatomy and connections between the different brain regions. This allows researchers to explore and study the relationships between various parts of the brain and how they influence each other. The detailed functional and structural map offered by neuroimaging empowers scientists to understand this complex organ health and diseases through this invaluable tool. Voice and speech analysis is effective in early detection through AI because it provides more reliable and accurate results. Although subtle abnormalities of vocabulary, phrase length, and complexity may be easily identified through observations, AI techniques such as NLP and speech recognition can analyze the subtle difference in tone and pronunciation, which human observations can't necessarily be noticed alone. Furthermore, utilizing computer cognitive tasks enables the software to effectively and accurately log an individual's performance as it can time, track, and recognize speech inputted into the system. Therefore, its accuracy could provide physicians and researchers much more accurate results compared to traditional cognitive tests.

Early Detection and Prognostic Value

The nervous system is the most vital system in the human body, responsible for regulating both voluntary and involuntary responses. It comprises the CNS as well as the peripheral nervous system (PNS) of nerves that delivers signals throughout the body. Nevertheless, the complex interconnected web of neurons enables communication pathways between the regions. However,

this means that such diseases, disorders, or injury can damage one area and rapidly lead to disruptions in multiple neural networks. Studying these connectivity patterns of neurons is therefore crucial for understanding how pathogenesis in certain brain regions or neural pathways can lead to broader effects. With AI, it enables the analysis of the complexity of neural relationships that drives neurological diseases. The various techniques and machine learning algorithms AI offers combined provides valuable insights, in depth analysis, and efficiency thus, assisting with better detection, decision making, and accuracy.

Limitations and Challenges

AI can efficiently process a vast amount of information, can provide, and predict accurate results. While the application of artificial intelligence tools in neuroscience to analyze complex data holds potential, there are limitations as it's highly dependent on the quality of the data. Algorithms trained on incomplete or biased datasets are liable to the same errors and assumptions. In addition, some ethical concerns are that the potential misuse of neural data can violate privacy, promote biases, or cause harm. Furthermore, there are also challenges in using AI to detect Alzheimier's disease including individual variability, model biases, ethical issues, and accessibility. Finding consistent predictive signals can be difficult as Alzheimer's disease can affect each patient differently. Algorithms trained improperly may exclude certain genders, age, or have racial biases increasing the risks of inaccurate diagnoses. Ethical issues may rise as patient's privacy, data security, and accountability may be at risk of exposure. Accessibility may also be a limiting factor as not all communities share an equal amount of access and opportunities to resources. Communities with lack of resources may face a disadvantage to those with. However, addressing these limitations may encourage researchers and developers to carefully design new softwares/tools, algorithms, and evaluation. Thus, utilizing AI tools in neuroscience could be greatly advanced.

Conclusion

Overall, AD is a characterized neurodegenerative condition that slowly consumes a person's cognitive skills in the brain. This is because Alzhemier's disease releases abnormal proteins including beta-amyloid plaques and tau tangles. Even though there is no supported evidence to cure or prevent this disease, identifying the disease early with the help of AI can allow the

initiation of treatment and interventions to help manage the symptoms and slow the disease progression. This is important to review because there are about 500,000 new cases every year and 1-in-9 people suffer from Alzheimer's disease aged 65 and older. Techniques such as machine learning, deep learning, and AI algorithms have enabled current approaches to analyze neuroimaging data, voice and speech patterns, and cognitive assessment data. AI's ability to process large datasets and identify subtle patterns allows researchers to explore and study the relationships between various parts of the brain and how they influence each other. Moreover, neuroimaging technologies offer a detailed visualization of the brain, voice and speech analysis enables the detection of subtle abnormalities, and computer cognitive tasks enable the software to effectively and accurately log an individual's performance. Though misuse of neural data can elevate ethical problems and resource accessibility are limited in some communities, continued research and responsible development of AI tools for neuroscience can lead to improved outcomes for patients. Therefore, AI has proven to be a valuable analysis tool for early-detection for Alzheimier's disease.

Work Cited

N/A, N/A. "Diagnosis." *Alzheimer's Disease and Dementia*, www.alz.org/alzheimers-dementia/diagnosis#:~:text=Testing%20for%20Alzheimer%27s%20or%20other,neurological%20exams%20 or%20 other%20 assessments.

N/A, N/A. "What Is Deep Learning?" *IBM*, www.ibm.com/topics/deep-learning.

Melchionna, Mark. "AI Model Enables Alzheimer's Disease Detection from Brain Mris." *HealthITAnalytics*, 9 Mar. 2023, healthitanalytics.com/news/ai-model-enables-alzheimers-disease-detection-from-brain-mris#:~:text=March%2009%2C%202023%20%2D%20Published%20in,MRIs)%20to%20detect%20Alzheimer%27s%20disease.

Sarvamangala, D R, and Raghavendra V Kulkarni. "Convolutional Neural Networks in Medical Image Understanding: A Survey." *Evolutionary Intelligence*, 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC7778711/.

Monsour, Robert, et al. "Neuroimaging in the Era of Artificial Intelligence: Current Applications." *Federal Practitioner : For the Health Care Professionals of the VA, DoD, and PHS*, Apr. 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC9227741/.

N/A, N/A. "How Biomarkers Help Diagnose Dementia." *National Institute on Aging*, www.nia.nih.gov/health/how-biomarkers-help-diagnose-dementia.

N/A, N/A. "Nervous System - Reflex Action, Voluntary and Involuntary Action." *BYJUS*, 20 Aug. 2020, byjus.com/biology/nervous-system-coordination/#:~:text=Both%20involuntary%20and%20voluntary%20actions,frontal%20lobe%20of%20the%20cerebrum.

Steward, Cindy. "AI and Neuroscience: Roots, Limitations, and Future Improvements." *Medium*, 21 Dec. 2022, medium.com/@cindysteward/ai-and-neuroscience-roots-limitations-and-future-improvements-f975b4ffed04.

Lovinger, David M. “Communication Networks in the Brain: Neurons, Receptors, Neurotransmitters, and Alcohol.” *Alcohol Research & Health : The Journal of the National Institute on Alcohol Abuse and Alcoholism*, 2008, www.ncbi.nlm.nih.gov/pmc/articles/PMC3860493/#:~:text=Communication%20between%20neurons%20occurs%20at,to%20allow%20for%20chemical%20transmission.

The effects of mental health on a patient's family members/caregivers

Katherine Mejia (Author), Thanisha Kapur (Advisor)
City College of San Francisco

Keywords: Mental Health, Mental Illness, Caregivers, AI

Abstract

In a year, 43.8 million adults experience mental illness. Mental illness also affects 5 million kids a year. In order to keep them safe and in stable conditions, their family members often take on caregiver roles in order to help them sustain their treatment and keep them safe. This paper and research article digs into the effects on people whose family members suffer from mental health illnesses and diseases. Though it's certain that a specific mental illness such as bpd, bipolar disorder, schizophrenia or any sort of psychosis isn't "contagious" or physically transmissible between people according to the National Library of Medicine, it has been known that one's emotions could affect another. Spending time and taking care of loved ones with a mental health illness could lead to stress and loss of sleep which could lead to depression when being a caregiver. The Family Caregiver Alliance agrees that loss of sleep is often seen as a result of caring for a loved one suffering from mental health disorders and could often lead them to develop a serious depression. This topic may be one that's not talked about enough, some people may not even know the way being a caregiver may affect their own mental health. This research article attempts to dig more into ways in which caregivers could receive the help they need, including AI benefits. With the help of AI, parents / caregivers could have the necessary room in order to be able to properly provide themselves with the time and space they need in order to maintain a healthy mindset and be ready to help with anything their child or family member needs. Having to vicariously take in what a family member or child might be experiencing in a negative way is never easy. You have to be able to support them with whatever they're going through, and AI could help support you in a way you might not even know you need help in. Having time to reach out for help yourself, or take in a moment of silence should be considered a necessity when you're a caregiver negatively and vicariously living through a mental health patient. You can't take care of someone when you are not taking care of yourself.

Introduction

Mental health illnesses or diseases affect 1 in 5 Americans a year. One of the most important things for people who suffer from mental health illnesses is to get the help and the treatment they need. People often talk about the people suffering from a mental health illness or disorder, but not many people talk about how it affects the people around them, especially their family members who become their number one supporters through their treatment. With this experiment I'd like to, not exactly answer, but instead at least get an understanding of the effects of mental health on caregivers. According to Priory Group, an extension of a selection of Hospitals in the UK, a survey they conducted on whether or not a patient with a mental health illness affects their family as well resulted in 80% of patients agreeing. When a family member is diagnosed with a mental illness or disorder, ranging from adhd to schizophrenia and psychosis, the top priority should be seeking them treatment. But what many people forget, is how this diagnosis doesn't only affect the patient, but also their caregivers, and surrounding family members. Though it's not the most common occurrence, it's possible for preteens and teens to be diagnosed with an early onset mental illness such as schizophrenia. Dealing with a mental health illness this serious alone is never a good option. When a child is diagnosed with a mental illness or diagnosed with early signs of one, all a parent can do then is take care of them, keep them safe, and help them get the treatment that they need. It's never easy news to hear. A parent always wants to keep their child safe from the world, but what do you do when you have to start keeping them safe from themselves? Many of the symptoms for schizophrenia for example include, the flat effect which is when a person has a vacant facial expression almost as if they've been paused. Positive symptoms include delusions, hallucinations, and thoughts of danger; some thoughts may even invoke fear of their parents wanting to hurt them. This not only puts stress on the person experiencing the symptoms and feeling scared of not knowing what's real and what's not, feeling disconnected from reality. This also puts stress and fear on their parents and or caretakers who can't help control their thoughts and can only rely on the treatment working.

Materials and Methods

When it comes to AI and mental health, there have been a lot of trials, experiments and attempts to allow AI to treat patients. But there are no methods that have been used in order to help people who are caregivers for their family members who suffer from mental health illnesses and

diseases. If there were any specific methods used in an AI's attempt to aid people dealing with mental health problems or their caregivers, it would most likely have an outcome measured by data analysis. Taking notes on how their response to each day is would play a big role in one's ability to get better and make sure that the treatment is working. Not only for mental health patients, but for their caregivers as well. Marking results that include information on times when they seeked help for themselves, were able to take care of themselves, and talk about what was going on with them as caregivers. AI being capable of monitoring changes, patterns and any notable occurrence would benefit caregivers by allowing them to notice any changes whether they be small or significantly noticeable. Being a caregiver of someone who suffers from mental health illnesses, especially harder ones to deal with including psychosis and schizophrenia, is not easy at all; taking care of their medication, staying alert incase they go into an episode, and never being able to predict their next move is a scary place to be in. With this heavy responsibility at hand, it's not difficult to feel the stress; stress that could eventually lead into depression. Let it be known that the caregivers couldn't have "caught the illness" when it comes to falling into depression. But instead, the experience of living with and taking care of a mental health patient could provoke them excess stress, with a result of depression if not properly taken care of. Stress wouldn't be the only factor contributing to a caregiver dealing with their own mental health, but lack of sleep and unintentionally unhealthy eating habits. With the help of AI, and their contribution to caregivers by helping them keep notes of, and track of medications given and times, it would very likely help alleviate some weight off their shoulders.

Results and Discussion

The hypothetical results could vary from simple improvements in a caregivers life, to a grand positive change in both their everyday lives and their mental health as well. An Entrepreneur article titled "How AI Can Enable and Support Both Caregivers and Patients" talks about the benefits artificial intelligence would have on a caregivers life. Though in some instances it might seem like AI could replace or take over human run healthcare, it's highly unlikely the human touch would ever disappear from the healthcare world.

What could potentially happen and looks like it is already in the process of happening, is that AI helps "lighten the load" on caregivers by freeing up time in places such as keeping track of

medication, symptoms, and possibly being able to predict occurrences based on their data. Having an algorithm [in AI] could potentially help with patient predictions, allow for a stable routine to be set in place and would even help reduce the cost and timeline of a treatment.

Caregivers and family members who are responsible for their family members who suffer from a mental health illness don't "have it easy" when they are monitoring their medication, making sure they're safe, and protecting their loved ones as best they can. It's not uncommon for caregivers to feel stressed out and overwhelmed when taking care of someone with a mental illness, especially with their unpredictableness. This often leads to a loss of sleep which could potentially end in depression. Caregivers provide their time to help take care of others, but it's not uncommon for them to innocently forget to take care of themselves as well. They can't properly help others unless they are properly helping themselves too.

In conclusion, the research article is a simplified form mentioning a couple of benefits AI would contribute a caregiver with, if assigned to help. The topic of the effects of a mental health illness or disorder on a patient's family member and caregiver is one that's not normally talked about. The attention is often directed at the patient, which is necessary; but it's important that the family members, the ones taking care of a mental health patient, are also taken care of and in a healthy state of mind. They can't properly take care of someone when they aren't well themselves. Simple tasks that an AI can run such as monitoring medication, taking in notes and data points on the patients wellbeing and current health and habits would be essential in order to track their treatment plan and help diagnose any future episodes early enough. The well being of everyone is always a healthcare provider's first point of focus. It's important for patients to get the treatment they need and deserve in order to get better. But it's also important that the person that is helping them get better and is keeping track of their treatment, taking care of them, and keeping a close eye on them doesn't develop sleep deprivation, excess stress nor eventually falls into depression. It's important for everyone to be taken care of, and an AI would help assist caregivers in order to maintain it that way.

Works Cited

MacLeod, Beth. “Depression and Caregiving.” *Family Caregiver Alliance*, https://www.caregiver.org/resource/depression-and-caregiving/. Accessed 30 July 2023.

“Mental Health Facts in America.” *NAMI*, https://www.nami.org/nami/media/nami-media/infographics/generalmhfacts.pdf. Accessed 30 July 2023.

Reynolds, Akilah, and Timothy J. Legg. “Schizophrenia in teens: Signs, treatment, and more.” *Medical News Today*, 20 June 2023, https://www.medicalnewstoday.com/articles/schizophrenia-in-teens. Accessed 30 July 2023.

“Social contagion of mental health: Evidence from college roommates.” *NCBI*, 11 October 2012, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4381550/. Accessed 30 July 2023.

Terry, Jeff. “How AI Can Enable and Support Both Caregivers and Patients.” *Entrepreneur*, 7 January 2022, https://www.entrepreneur.com/leadership/how-ai-can-enable-and-support-both-caregivers-and-patients/402458. Accessed 30 July 2023.

Mimicking Olfaction Using Artificial Intelligence

Katherine Mock (author), Thanisha Kapur (advisor), Anika Shah (editor)
Eastside High School

Keywords: Olfaction, Artificial Intelligence, Deep Learning, Machine Learning, Neural Networks

Abstract

Recent developments in artificial intelligence have yielded potential for growth in mimicking olfaction, the body's sense of smell. Researchers have uncovered that the structure of the olfactory system is organized in a multi-dimensional structure of sparse neural networks that closely mirrors other brain regions like the hippocampus and central cortex. Thus, advancements in deep learning algorithms in connection to olfaction could yield real-world applications to entirely new brain functions. Researchers at Drexel University have recently developed a program that is capable of categorizing and identifying specific odors by analyzing their chemical makeup with accuracy comparable and even superior to that of human test subjects. Using a system called a Principle Odor Map, these researchers have made it possible to concretely measure abstract characteristics of odor perception. Similarly, at MIT, several researchers turned to the organization of the olfactory system in the fruit fly in order to better understand how the process of olfaction works. From there, they went on to create an AI capable of mimicking the structure and functions of the human olfactory system. Through researching the process of olfaction, scientists are gaining a better understanding of the structure of the human brain, as well as how this structure can be translated into complex deep learning algorithms.

Introduction

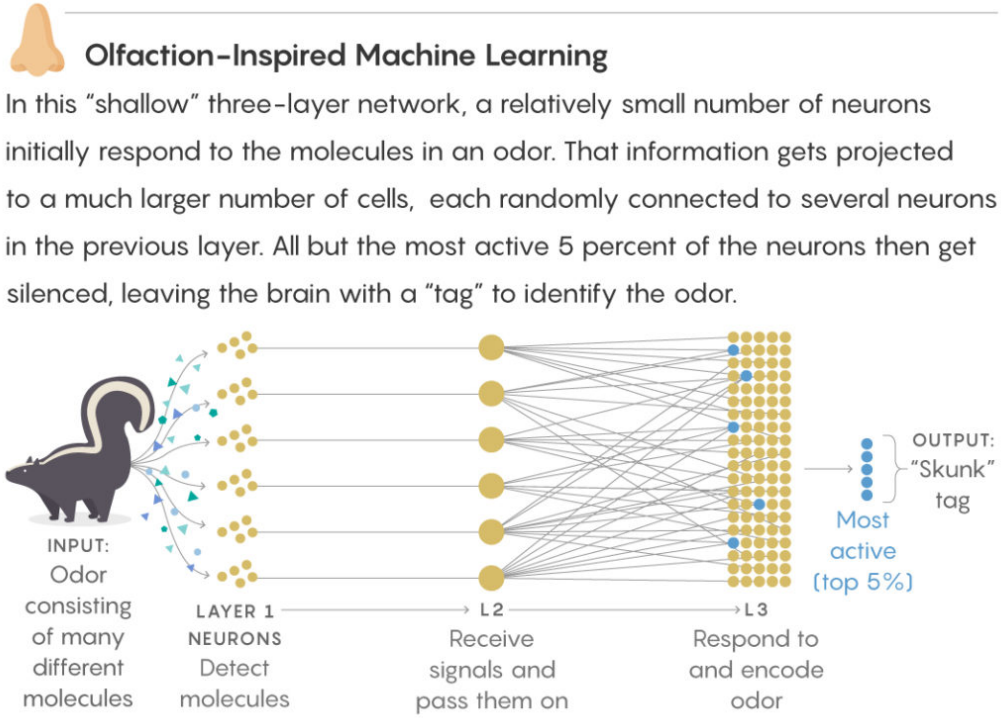
As new advancements progress in the field of artificial intelligence (AI), researchers are beginning to gain more insight as to how we might use AI to mimic the process of olfaction, the body's sense of smell. Olfaction, scientists have discovered, operates in a completely different way from the typical neuronal processes in the brain. Using a process of random organization and sensory feedback, the brain uses what researchers have termed an "antimap" to establish

associations between neurons and specific sensations of smell. In practice, this recent research has given way to a multitude of new inventions—from an AI system capable of mimicking the olfactory circuits of a fruit fly to deep learning algorithms that are now able to detect and identify subtle toxins within the air that the human nose remains blind to. While the sensation of smell remains difficult to categorize, scientists have now found ways to effectively identify and describe various odors simply through the use of AI. Thus, further research could have great implications in terms of understanding the complex and unique process of olfaction, as well as furthering capabilities of artificial intelligence in the medical field. Olfaction is beginning to interact with artificial intelligence in ways never before thought possible, presenting significant implications in the development of new technology.

Potential for Deep Learning Algorithms in Neurology

Jordana Cepelewicz of Quanta Magazine speaks in depth on the challenges presented by adapting deep learning algorithms to the structure of olfaction—while these programs excel at completing specific, concrete tasks, it is a much more challenging task to ask AI programs to categorize and understand the concept of smell. Tasks such as optimizing efficiency when playing chess or solving equations, which have concrete limitations, are much easier to navigate than tasks requiring meaningful and abstract reasoning when it comes to artificial intelligence. While the neurons in many parts of the brain are encoded with rigid structure and organization (i.e., each type of neuron carries out a specified task and is correlated to a specific type of information), neurons involved in olfaction operate quite differently. To this end, Cepelewicz cites the structure of the visual cortex: hierarchical and linear, first identifying smaller features of visual information, such as texture, and passing through layers of cortical neurons until the brain can fully interpret the visual stimuli. Conversely, scientists have coined the organization of neurons involved in olfaction as adhering to an "antimap," a multidimensional model of thinking that is powered by randomized, sparse neural networks. At its core, an antimap is usually used to portray a region of the brain in which the location of neurons does not indicate the neuron's function. Conversely, in areas such as the visual cortex, the location of a neuron can directly indicate its purpose and the type of information that it carries. While this enables the brain to have a more nuanced perception of sensory information, it is inherently difficult to adapt into deep learning algorithms due to the fact that odors, unlike visual stimuli, are difficult to

categorize concretely. However, Cepelewicz notes that scientists have recently made great progress in further understanding the nature of olfaction through the study of fruit flies. When a fruit fly encounters a particular scent, 50 neurons, each receptive to different molecules or "scents," receive this sensory input and become active if they are coded to be receptive to the given odor. From there, the sensory information is passed along to 2,000 Kenyon cells that code for the sensation of specific odors. In this way, scientists are able to emulate the process of olfaction with artificial intelligence by mimicking the organization of the olfactory system's antimap.



(Cepelwicz)

Ultimately, as scientists are progressively learning more about the process of olfaction and how this translates into machine learning problems, there is still much to be understood about the structure of the olfactory system and mimicking olfaction beyond the simplistic brains of fruit flies. As far as real-world applications for these algorithms, Cepelwicz notes that similarities in the olfactory system to other areas in the brain, such as the hippocampus and the cerebellum, could potentially allow researchers to apply our current understanding of olfaction to entirely new brain functions, such as memory, navigation, and motor control. However, Cepelwicz also points out that much of this remains as speculation, and that in order for these new technologies

to have impactful implications in the real world, efforts to better understand the process of olfaction must continue. While olfaction represents a potential gateway into broader implications in mimicking different brain functions, improvement in current deep learning algorithms and artificial intelligence must first be achieved.

Mapping Qualitative Data Using a Principal Odor Map

A study performed by Brian K. Lee of Drexel University et al demonstrates how researchers are now able to predict what certain chemicals will smell like to humans using artificial intelligence. For example, compounds containing sulfur are often perceived by people to smell similar to garlic. In this way, researchers are able to analyze the chemical makeup of specific compounds and assign adjectives to these compounds based on the way they would be perceived by a person during olfaction. Using what researchers call a graph neural network (GNN), researchers can categorize chemical compounds using descriptive adjectives such as “medicinal” or “earthy.” Lee and collaborators used the GNN in order to create a Principal Odor Map (POM), which allows software to better analyze odors based on their molecular compositions. The POM was shown to be comparable in accuracy to a human when it comes to categorizing and identifying odors in an analysis comparing model generated odor profiles to that of humans. Lee argues that current modes of mapping odors using physical properties are inadequate, citing the example of Sell’s triplets, a trio of molecules that, when paired together, do not correspond to their typical perceived odors. The newly developed POM, which functions at a level of accuracy higher than that of humans when it comes to odor detection, provides a more functional mode of mapping and interpreting odors based on their physical properties. With further development of technologies that can map abstract sensory stimuli, potential for real-world implications beyond that of olfaction emerge. Although the POM currently surpasses any other mode of odor mapping, more research is required in order to improve the accuracy and odor capacity of the POM. Furthermore, the POM created by Lee et al proves to be more effective in odor quality prediction than chemoinformatic model when tested on a variety of odor prediction tasks, suggesting that the POM is a highly successful mode of categorizing and analyzing odors using deep learning algorithms. Researchers note that this deep learning software is still in development and has many limitations, but are hopeful that there is much more to be explored in using AI to understand olfactory networks.

Translating Brain Processes into Neural Networks

Similarly, a new study performed by Guangyu Robert Yang of MIT's McGovern Institute for Brain Research et. al has revealed that we are much closer than we previously imagined in terms of creating deep learning algorithms that can imitate and perform functions of the olfactory system. Although Yang notes that the process used by AI does not accurately reflect the brain's process of evolution, the end result is nearly identical in its efficiency in modeling the brain's olfactory system. In order to do this, Yang and his collaborators first turned to fruit flies in order to understand the basic organization of the brain's olfactory circuitry, revealing what is presently known to be true: the olfactory system is multidimensional, using sparse networking signals that make up the brain's perception of smell. Next, they began to construct what is called a neural network—a system of artificial neurons that are rewired in order to fulfill a given task, usually in an effort to mimic that of the human brain. Teaming up with Columbia University student Peter Yiliu Wang and neuroscientists Larry Abbot and Richard Axel, Yang creates a neural network that closely mirrors the olfactory circuits observed in the fruit fly. The result was a success—this neural network quickly learned how to classify sensory data and correctly identify specific odors. Within minutes, the researchers reported this model of the olfactory system functioning nearly identically to that of the fruit fly. Yang and others are hopeful that this progression will be helpful in learning more about the human brain's olfactory circuits in the future, as they are now able to very accurately mimic the inner workings of the olfactory circuits in fruit flies.

Discussion

While Cepelwicz speaks in depth on the potential for developing deep learning software mimicking the olfactory system, many researchers have since gone on to create such software with great success. However, most investigation done on the organization and structure of the olfactory system has been built upon the foundations of the principles established by Cepelwicz—the olfactory system is a multidimensional system of neurons connected by sparse networks and unlike any other sensory system in the brain. While the visual cortex is structured with more linearity, the antimap adheres to a structure that presents challenges to researchers when it comes to translating olfaction to artificial intelligence. Additionally, like Cepelwicz and Yang, many researchers begin by analyzing the brain of the fruit fly—a more simplistic version

of the human brain. By first analyzing the organization of the olfactory system, researchers are better enabled to mimic the structure of the brain in deep learning algorithms. Lee's POM demonstrates an extension of the principles established by Cepelwicz and Yang and a potential for complex deep learning algorithms mimicking the function of the brain. Lee and collaborators overcome a pervasive hurdle in the realm of neuroscience—mapping physical characteristics of stimuli to the stimuli's perceived sensation. Lee notes that although stimuli such as sound can be concretely measured—frequency mapping pitch—odors are much more difficult to categorize, which presents a major challenge when attempting to adapt olfaction to artificial intelligence. As AI algorithms such as Lee's POM and Yang's neural network become more advanced, there emerges further potential for implicating these algorithms in alternate brain regions, as suggested by Cepelwicz. If abstract stimuli such as scent can be categorized based on physical characteristics, then perhaps so, too, can abstract brain functions such as memory, motor control, and navigation be effectively categorized and subsequently translated into AI.

Works Cited

Cepelewicz, Jordana. "New AI Strategy Mimics How Brains Learn to Smell." *Quanta Magazine*, 10 Oct. 2022, www.quantamagazine.org/new-ai-strategy-mimics-how-brains-learn-to-smell-20180918/.

Lee, Brian K., et al. *A Principal Odor Map Unifies Diverse Tasks in Human Olfactory Perception*, 2022, https://doi.org/10.1101/2022.09.01.504602.

Michalowski, Jennifer. "Artificial Networks Learn to Smell like the Brain." *MIT News | Massachusetts Institute of Technology*, https://news.mit.edu/2021/artificial-networks-learn-smell-like-the-brain-1018.

Parry, Wynne. "AI Predicts What Chemicals Will Smell Like to a Human." *Scientific American*, 27 Oct. 2022, www.scientificamerican.com/article/ai-predicts-what-chemicals-will-smell-like-to-a-human/.

Wang, Peter Y., et al. "Evolving the Olfactory System with Machine Learning." *Neuron*, vol. 109, no. 23, 2021, https://doi.org/10.1016/j.neuron.2021.09.010.

AI Transforming Stroke Care

Keertana Raghavendra (author), Thanisha Kapur (advisor), Anika Shah (editor)
Skyline High School

Keywords: Support vector machine (SVM), Artificial neural network (ANN), Machine Learning (ML), Large-vessel occlusion stroke (LVO), Mechanical Thrombectomy (MT), Computed Tomography (CT), Magnetic Resonance Imaging (MRI)

Abstract

In 2021, 1 in 6 deaths from cardiovascular disease was due to stroke (Stroke Facts). Making stroke one of the leading causes of death in the US. AI using different algorithms and codes like Machine Learning has improved stroke diagnosis, treatment, and prognosis, saving many lives. AI being able to store and analyze data rapidly has allowed it to detect and produce clinical suggestions in a small amount of time, revolutionizing stroke care for patients. CT and MRI scans have always been used to diagnose and treat LVO stroke. This article explores the different ways AI is used in stroke care to provide better care for patients with stroke.

Introduction

AI dominates the world, from daily cleaning tasks to groundbreaking scientific discoveries. AI is rapidly evolving in the medical field. Stroke being a common cause of morbidity and mortality globally, AI is being used to transform stroke care. It is a brain attack caused by the weakening and death of brain cells due to a blood spill in the brain. That said, stroke can cause permanent brain damage. Every minute counts when having a stroke, so AI being coded to perform activities without errors is transforming stroke care. AI using machine learning algorithms is revolutionizing stroke care.

Body

AI in Stroke Diagnosis

In research funded by the Korea Health Technology R&D Project and Ministry for Health & Welfare, researchers performing a scoping review of AI techniques in stroke imaging for diagnosis found that AI is indeed promising in stroke diagnosis because of the large databases of

imaging and other parameters are exponentially being accumulated improving the diagnosis timeliness. The two algorithms, the support vector machine (SVM) and the artificial neural network (ANN), are revolutionizing stroke diagnosis. SVM is a supervised machine learning for developing a model to allocate objects to various categories. So SVM is widely used in clinical imaging analysis to categorize or classify a diagnosis. SVM also constructs a hyper-plane in a high-dimensional space as the decision surface using the kernel technique, that converts the input features into high-dimensional feature spaces. SVM is revolutionizing stroke care by stabilizing error rates in diagnosing stroke. ANN is an inspired biological neural network where an artificial neuron gets inputs from other neurons, combines the inputs with weights, and activates when a defined condition is satisfied (Deep into the Brain: Artificial Intelligence in Stroke Imaging). ANN consists of output, input, and hidden layers. The multiple layers ANN produces are used by Deep learning to mimic the human brain, which simulates a patient's brain to diagnose without affecting the patient. However, ANN has limitations; it is susceptible to data overfitting and requires a long computation time. Machine learning techniques showed promising results comparable to manual segmentation in chronic stroke. Machine learning-based diagnosis utilizing computed tomography (CT) has also been attempted and showed a non-inferior performance. However, regarding intracranial hemorrhage (ICH), automatic segmentation of CT lesions has been successfully achieved (Deep into the Brain: Artificial Intelligence in Stroke Imaging). Imaging findings can also be used as an input feature for predicting stroke prognosis. AI techniques in stroke imaging could change the milieu of stroke diagnosis and management. The machine-based diagnosis would be helpful for medical staff not accustomed to stroke imaging, such as general practitioners or paramedics, revolutionizing stroke diagnosis.

AI in LVO detection

Large-vessel occlusion (LVO) is an attractive field to use AI, specifically machine learning (ML), due to the Optimal outcomes after LVO stroke are highly dependent on prompt diagnosis, effective communication, and treatment. Mainly Machine learning (ML), a subset of AI involving computer problem-solving using data-driven algorithms derived from large data sets without explicit human programming, has become particularly prominent because of the potential for rapid automatic evaluation of patients with stroke. In a systematic review of the PubMed, Embase, and Scopus databases, ML techniques proved vastly accurate in identifying

LVO on computed tomography with ML algorithms that were convolutional neural networks (CNN). Large-vessel occlusion (LVO) comprises 29.3% of AIS cases and has an incidence of 24 per 100,000 people annually. Randomized controlled trials have provided evidence that timely mechanical thrombectomy (MT) in patients with LVO is safe and effective in improving functional outcomes, as MT has become the standard of care for LVO. Determination of treatment strategy is critical because MT must be timely, given that "time is brain. ML methods for better triage study found that transporting patients with stroke directly to a comprehensive stroke center for tissue plasminogen activator and MT (if indicated) rather than to a primary stroke center was favored in most real-world scenarios regardless of formal LVO screening. LVO diagnosis on computed tomography (CT) imaging using AI models has primarily involved the prediction of clot signs or infarction volume. CT data, in addition to demographic and clinical data, had superior performance in detecting LVO to extreme gradient boost using demographic and clinical data and to RF and SVM models. The advantages of AI can be seen in the triage and diagnosis of patients with LVO. One of the most crucial factors in predicting good patient outcomes is the timely arrival and triage of probable patients with stroke. Due to this, most triage AI applications have been focused on prehospital transport, given the prognostic importance of timely arrival. Regarding diagnosis, AI has primarily been used to accurately identify LVO on CT using ML that identifies clot signs or infarction volume. However, inputting additional information, such as demographics and clinical factors, improves accuracy. The use of AI in patient selection and prognostication by predicting clinical and angiographic outcomes of MT for LVO is one of the most important applications of ML. A combination of radiomic features from various imaging modalities also provides a valuable prediction of recanalization. The role of AI in LVO stroke is expanding; however, several strides regarding critical decision-making and patient selection need to be made. Even though AI is useful for triaging and diagnosing LVO, it is still at the investigational stage. But the quality of the ML model, and its subsequent adoption in medical practice, is proof of clinical improvement and good outcomes.

AI in Prognosis

Many factors can affect stroke prognosis and mortality. Compared to conventional methods, ML methods have advantages in improving prediction performance. ML techniques that are used to identify factors influencing predictions in brain arteriovenous malformation are treated with

endovascular embolization have showed better results. The use of the synthetic minority oversampling process to reduce the stroke outcome prediction bias has been caused by a between-class imbalance among multiple data sets. Brain images have been analyzed to predict the outcome of stroke treatment. In addition, a CT scan evaluating cerebral edema following hemispheric infarction built to identify cerebrospinal fluid and examine the shifts automatically is more efficient and accurate than conventional methods. Functional connectivity from available MRI data, ridge regression, and multitask learning were used for cognitive deficiency prediction after stroke. The relationship between lesions taken from MRI images and the treatment outcome via the Gaussian process regression model has been used to predict the dangers of cognitive impairments after stroke and the course of recovery over time (Artificial intelligence in healthcare: past, present, and future). Knowing the stroke prognosis also assists in making clinical decisions. Prediction of treatment complications may help screen a high-risk group receiving accurate treatment, such as thrombolysis, whereas predicting neurological long-term outcomes may guide stroke management. Imaging findings can be used as an input feature in machines for predicting stroke prognosis.

Conclusion

In conclusion, stroke management has been a and is still a complicated process with a series of clinical decision points. Traditionally, clinical research focused on a single or limited clinical question while ignoring the continuous nature of stroke management. Taking advantage of copious amounts of data with rich information, AI is helping with studying much more complicated yet closer to real-life clinical questions, leading to better decision-making in stroke management. Researchers have recently started working in this direction and gained promising results. Although AI is attracting attention in medical research, its real-life implementation still faces obstacles. Nevertheless, a healthcare revolution is underway in the medical field.

Works Cited

Amann J;Vayena E;Ormond KE;Frey D;Madai VI;Blasimme A; "Expectations and Attitudes towards Medical Artificial Intelligence: A Qualitative Study in the Field of Stroke." *PloS One*, pubmed.ncbi.nlm.nih.gov/36630325/. Accessed 22 July 2023.

Bivard, Andrew, et al. "Artificial Intelligence for Decision Support in Acute Stroke - Current Roles and Potential." *Nature News*, 24 Aug. 2020, www.nature.com/articles/s41582-020-0390-y.

Jiang, Fei, et al. "Artificial Intelligence in Healthcare: Past, Present and Future." *Stroke and Vascular Neurology*, 21 June 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5829945/.

Lee, Eun-Jae, et al. "Deep into the Brain: Artificial Intelligence in Stroke Imaging." *Journal of Stroke*, Sept. 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5647643/.

Shafaat O;Bernstock JD;Shafaat A;Yedavalli VS;Elsayed G;Gupta S;Sotoudeh E;Sair HI;Yousem DM;Sotoudeh H; "Leveraging Artificial Intelligence in Ischemic Stroke Imaging." *Journal of Neuroradiology = Journal de Neuroradiologie*, pubmed.ncbi.nlm.nih.gov/33984377/. Accessed 22 July 2023.

Shlobin, Nathan A, et al. "Artificial Intelligence for Large-Vessel Occlusion Stroke: A Systematic Review." *World Neurosurgery*, Mar. 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC9172262/.

"Stroke Facts." *Centers for Disease Control and Prevention*, 4 May 2023, www.cdc.gov/stroke/facts.htm.

"Stroke." *National Institute of Neurological Disorders and Stroke*, www.ninds.nih.gov/health-information/disorders/stroke. Accessed 22 July 2023.

AI Technology and Bias in Detecting Psychiatric Disorders

Kennedy Flowers (author), Thanisha Kapur (advisor)
Pioneer High School

Keywords: Artificial Intelligence (AI), Mental Health, Epigenetics, Intersectionality, schizophrenia

Abstract

The brain's frontal and temporal lobes are responsible for our social skills, memory, behavior, audio, emotional, and language processing. People with schizophrenia, however, experience shrinkage in both their frontal and temporal lobes, impairing the social and processing capacity of their brains and affecting their ability to concentrate and perform everyday tasks. Schizophrenia affects a disproportionate amount of Black men compared to other ethnic and racial groups. While this trend can be partially explained by genetic and environmental factors such as family history, childhood health complications, urbanicity, substance abuse, etc., a prominent reason that Black men are diagnosed with schizophrenia is due to racial bias present in the AI (Artificial intelligence) technology used to aid physicians in detecting and diagnosing psychiatric disorders, as well as systemic racial bias present in America's healthcare system.

Introduction

Artificial Intelligence and Mental Health

AI (Artificial Intelligence) technology has seeded its place in the healthcare field as a benevolent asset to physicians and scientists examining psychiatric disorders. Presently, AI technology is used to aid neuroscientists in testing hypotheses and physicians in processing imaging data and diagnosing diseases via machine learning (surface-level problem-solving using algorithms) and deep learning (analyzing multiple layers of data to extract specific info from a data set) respectively. In a similar vein, AI-aided psychiatric-based resources improve a patient's accessibility to mental health resources. They can even detect and treat psychiatric disorders, such as autism spectrum disorder, schizophrenia, bipolar disorder, and more. However, all patients do not enjoy these monumental developments equally. Time and time again, we see disastrous results when patients are misdiagnosed due to an inherent racial bias present in

AI-based algorithms. Without proper treatment, untreated patients often turn to illegal substances to numb their pain, creating a spiral of abusive, toxic, or fatal events. This harmful trend is one excessively felt by minority patients, who are frequently misdiagnosed and mistreated in America's healthcare system.

As previously stated, recent developments in AI software are intended to combat these issues and improve access to quality mental health resources. Still, if AI technology disproportionately misdiagnoses minority patients, its usefulness becomes negligible. In this article, I examine the history of psychiatric disorders in minority communities and analyze the bias involved in psychiatric-based AI systems.

Body

What schizophrenia is

Schizophrenia is a chronic brain disorder impacting 1 in every 300 people. The onset or predominant stage of this disorder is categorized as a mild form of psychosis in which a person may voice abnormal beliefs or behaviors, hallucinate, experience delusions or catatonic (sporadic or withdrawn) behavior, or cannot perform daily activities, such as keeping up with their hygiene. Before someone is officially diagnosed, a doctor performs a physical exam, looking through their medical and family history before having them describe their experiences. A blood test or MRI may also be conducted to better understand a person's mind and body. Affecting 24 million worldwide, active schizophrenia causes those afflicted to suffer hallucinations, speech impairment, and cognitive issues. Furthermore, unhealthy coping mechanisms, such as smoking and substance abuse, increase these symptoms exponentially by increasing the chances that a patient will develop heart disease, which accounts for one-quarter of deaths for people with schizophrenia.

Epigenetics

In 2019, a study of 1,647 patient's at a community behavioral healthcare clinic was conducted at Rutgers University. The study, which examined patients' medical records, investigated the use of depression screening when assessing and diagnosing schizophrenia in new patients. The study, led by psychiatry professor Michael Gara, found that "There [was] a tendency for clinicians to

overemphasize the relevance of psychotic symptoms [while overlooking] symptoms of major depression in African-Americans compared with other racial or ethnic groups." Unfortunately, this tendency is the reason that many black patients are often misdiagnosed and mistreated for schizophrenia when they are *actually* suffering from a major depressive disorder. This experience is especially common in black men, who are often seen as "threatening" or "irrationally aggressive" due to racial stereotypes. These stereotypes, whether we like them or not, flow through our brains subconsciously. This is the reason why many clinicians failed to weigh mood symptoms effectively when making their diagnoses in this study and is reflective of a trend throughout America.

The root cause of this trend is tied to *Epigenetics* and *intersectionality*. In simple terms, Epigenetics is the study of intergenerational trauma. At its core, Epigenetics is the exploration of the trauma that an offspring inherits from their parents and ancestors as a result of a repeated history of extremely traumatic events (such as slavery, torture, serial rape, etc). While memories themselves are not passed from generation to generation, many African-American children experience symptoms of PTSD concerning certain topics or situations from the moment they are born. This trauma is passed through DNA and/or gene transcription (making an RNA copy of a DNA sequence during egg fertilization). This trauma has both a biological and physical effect on the body and can cause chronic stress and hypertension, among many other health issues.

Dr. Joy DeGry puts the concept of Epigenetics into a racial context in her book, *"Post Traumatic Slave Syndrome: America's Legacy of Enduring Injury & Healing."* Dr. Degry defines P.T.S.S. as "a condition that exists as a consequence of multigenerational oppression of Africans and their descendants resulting from centuries of chattel slavery." This condition is not a new idea: scientists around the world have been researching ancestral trauma for years. Slavery perpetrated the idea that Blacks were genetically inferior to Whites, leading to institutionalized racism that further fuels this idea.

For the Black community, hundreds of years of unaddressed, inherited trauma still impact our day-to-day lives. Being Black in America means carrying a heavy burden: inherited P.T.S.D.; caused not by our parents or grandparents or their behaviors but by the trauma that our enslaved

ancestors endured that fundamentally altered the genes of black Americans. This chronic stress coupled with subconscious biases in the Healthcare system lead to the harmful trend found in the Rutgers study.

Intersectionality

Many people do not belong to a single minority. The term intersectionality is an all-encompassing term that accounts for the existence of "double" or "triple" minorities (people who belong to multiple minority groups). Intersectionality is important because it helps explain the trends in mental health diagnoses that we often see with African-American men and women and people of color in general. Various socioeconomic factors, like poverty, ancestral and lived traumas, and stereotyping that affect people of color (particularly African-Americans) influence the negative stigmas in healthcare, making Black Americans more reluctant to seek treatment and care for their mental (and physical) health.

Artificial Intelligence (AI) and Mental Health

Researchers use AI to analyze electronic health records (alongside blood tests and brain images), questionnaires, voice recordings, behavioral signs, and more alongside supervised machine learning, deep learning, and Natural Language Processing (NLP) models to gain a deeper understanding of a patient's mental and physical state. Additionally, virtual therapists like Woebot, Replika, and Wysa offer personalized therapy by acting as AI "chatbots" where patients can describe their feelings to the therapists. AI chatbots make care more accessible and affordable for patients and increase the efficiency of existing systems by taking phone calls, making appointments, and delivering health education. However, the potential **bias** in AI systems can render chatbots and virtual therapists insufficient and decrease their quality significantly.

AI and Implicit Bias

Researchers have discovered that current NLP models in leading AI-assisted Mental Health resources may widen existing health inequalities. Popular language learning algorithms include GloVe and Word2Vec, which assesses psychiatric terms and demographic labels. Researchers examined these NLP models by analyzing how the algorithms relate the terms to the labels and

found distinct religious, racial, gender, nationality, sexuality, and age-related biases embedded in the programming of both GloVe and Word2Vec. As shown in *Figure 1*, the algorithms directly correlated Black patients with a schizoaffective disorder diagnosis *without* any patient input, suggesting an implicit bias present in these models. The implicit biases in these NLP models are not inherently permanent, however. A major reason for these biases is the lack of minority representation in the early trials of these systems. In addition, key developers of these models can also influence the biases in these algorithms by implementing their own subconscious prejudices.

Ethnicity Label	Most Closely Related Mental Health Diagnosis	Vector Similarity
Irish	alcoholism	0.14398772
African_american	schizoaffective_disorder	0.1818381
American	obsessive_compulsive	0.07114809
Chinese	obsessive_compulsive	0.13045943
Italian	obsessive_compulsive	0.103272386
Polish	alcoholism	0.098870605
German	obsessive_compulsive	0.07460512
English	schizoaffective_disorder	0.12912744
Asian	compulsive_hoarding	0.0947723

Figure 1. Image from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7745984/

Conclusion

Artificial Intelligence is used in a multitude of ways to aid physicians in diagnosing schizophrenia and many other psychiatric disorders. AI technology in the form of Natural Language Processing models is used to assess and interpret data collected by physicians and neuroscientists alike. However, researchers at the National Institute of Health found that many popular models such as GloVe and Word2Vec have been found to contain inherent racial, gender, and age biases. The models diagnosed patients under the “African-American” label with a schizoaffective disorder diagnosis solely based on their ethnicity label. This unfortunate model defect, coupled with a physician’s implicit bias, leads to a disproportionate amount of Black men who are diagnosed (or simply misdiagnosed) with schizophrenia. To rid these models of their inherent biases the data processed by these models must be balanced. This can be achieved by employing one of three de-biasing techniques: *data manipulation, fine-tuning biases,* or *increasing representation in early development teams*. Data manipulation involves using data augmentation algorithms that will create more data for minority patients. Data from particularly large sets can be removed if found to contain biases as well, balancing out the overall system. Fine-tuning biases involves re-purposing an existing model using a balanced, unbiased dataset, thus ridding the existing model of inherent biases. The third technique is based on the idea that

the existing biases in these models are influenced by those who created the models. The amount of diversity present in the teams that make these models has been found to correlate directly with the amount of biases present in the systems created. Therefore, increasing the diversity of the teams working on these systems will help to create a balanced set of data to be used by these models.

Works Cited

"African-Americans More Likely to Be Misdiagnosed with Schizophrenia, Study Finds." *ScienceDaily*, 21 Mar. 2019, www.sciencedaily.com/releases/2019/03/190321130300.htm

Straw, Isabel, and Chris Callison-Burch. "Artificial Intelligence in Mental Health and the Biases of Language-Based Models." *PloS One*, 17 Dec. 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC7745984/

"Diagnosing Schizophrenia." *Patient Care at NYU Langone Health*, https://nyulangone.org/conditions/schizophrenia/diagnosis#:~:text=At%20least%20one%20of%20the,MRI%20scan%20or%20blood%20test. Accessed 22 July 2023.

Ringen, Petter Andreas, et al. "Increased Mortality in Schizophrenia Due to Cardiovascular Disease - a Non-Systematic Review of Epidemiology, Possible Causes, and Interventions." *Frontiers in Psychiatry*, 26 Sept. 2014, www.ncbi.nlm.nih.gov/pmc/articles/PMC4175996/

"Untimely Deaths in People with Schizophrenia." *Columbia University Irving Medical Center*, 28 Oct. 2015, www.cuimc.columbia.edu/news/untimely-deaths-people-schizophrenia

"What Is Schizophrenia?" *Psychiatry.Org - What Is Schizophrenia?*, www.psychiatry.org/patients-families/schizophrenia/what-is-schizophrenia Accessed 22 July 2023.

Machine Learning and Deep Learning for Parkinson's Disease Diagnosis

Krish Khilnani (Author), Thanisha Kapur (Advisor)
Round Rock High School

Abstract

As a unique and complex neurological disorder that shows itself differently in each patient, Parkinson's Disease (PD) has become a significant problem in the modern world. Part of the reason for this is that it has been difficult to identify PD in the past with typical plasma tests. As a result, the use of non-invasive brain scans such as fMRI scans have been applied to better diagnose the disorder. Despite this, accuracy rates are still not up to a golden standard and scholars are experimenting with Artificial Intelligence (AI), specifically Machine Learning (ML) and Deep Learning (DL), to boost accuracy rates of non-invasive technological diagnosis. This paper goes over multiple ML and DL methods as well as studies that have been conducted on them to determine if the techniques would provide an advantage to professionals in clinical situations as they try to diagnose PD. The studies have revealed that some methods individually or in conjunction with other methods have significantly increased accuracy rates, with the range being anywhere from 87% to 94%. This contrast in accuracy rates of diagnoses with ML and DL methods versus without is incredibly steep with the latter having an accuracy rate around 67%. These advancements have great potential to decode brain signals and help with the understanding of preclinical studies to improve the efficiency of distinguishing diseases, making them an important tool to combat PD and relieve millions of patients.

Introduction

Around 7 million to 10 million people in the world experience the frustrating symptoms of the disease known as Parkinson's Disease (PD) and the number of instances is only expected to increase within the next decade (Dixit et al.). PD is a neurological condition that is identified with multiple symptoms relating to the nervous system with common signs being loss of motor control and speech. In any case, PD is a severe condition that is progressive with later stages of the disease being very difficult to respond to and therefore must be identified in its early stages to prevent the further degradation of the neurological systems. The most pressing issue relating to the disorder is the fact that there is no definitive cure to the disease; only symptom-relieving

measures, particularly for less severe cases. A vital tool that has been used to identify neurological disorders in preclinical studies since the 1990s is the functional Magnetic Resonance Imaging (fMRI) technique, a non-invasive technique that records brain scans determined by blood-oxygenation-level-dependent (BOLD) signals (Yin et al.). The fMRI has quickly become one of the most effective tools in the neurological diagnosis arsenal as it allows for the precise imaging of brain functions which help detect disorders such as autism, schizophrenia, and PD. However, with the complexity of the neurological systems and functions, neurologists and scientists have found it difficult to decode images efficiently and distinguish the disorder at hand. Recent innovations in Machine Learning (ML) and Deep Learning (DL) have allowed academics in neurology to skyrocket with the diagnosis of neurological disorders being a main focus. Scientists and researchers in the medical field across the world have been experimenting with the use of DL techniques, specifically in the diagnosis of neurological diseases, such as PD. This paper will identify DL techniques that allow for the classification and sorting of brain signals received from non-invasive neuroimaging, such as fMRI scans.

Body

PD Diagnosis using fMRI

In situations relating to degenerative diseases like PD, forms of motor loss depend on the severity of the case. More advanced cases can include symptoms such as tremors, bradykinesia, dyskinesia, stiffness, loss of postural balance, as well as other non-motor symptoms such as restlessness, constant tiredness, excessive sweating, constipation, and more (Dixit et al.). This disease is the 2nd most common neurological disorder after Alzeihmers and affects countless lives daily. The disease itself is caused by a loss of neurons in the substantia nigra, the part of the brain which creates dopamine. Dopamine is an essential hormone required to coordinate with the rest of the brain and body to perform actions and the loss of this hormone causes irregular brain function resulting in the many symptoms seen in PD cases. PD is triggered by a mix of environmental factors and genetic factors with genetic changes being the primary reason for PD cases. PD can also be inherited from generation to generation through the passing of faulty genes.

PD can be diagnosed by observing patient symptoms or identifying the genetic biomarkers found in those affected by PD. While it is difficult to do so, identifying PD biomarkers is the most accurate method of diagnosing PD (Vyas et al.). As a result, neurologists and healthcare professionals make use of fMRI scans to capture brain signals and signs of PD biomarkers. The fMRI has been used to diagnose various neurological disorders and to check up on a patient's vital brain systems, as the fMRI records a series of brain signals or images. It does this by measuring the blood-oxygenation-level-dependent (BOLD) signs or the changes in blood flow in the brain in response to neurological activity. The fMRI is known for having a high level of spatial specificity or spatial resolution, meaning that the fMRI is capable of retrieving brain signals as images in high definition (Tang et al.). This allows experts and analyzers to differentiate between brain scans for a more accurate diagnosis. However, despite the accuracy of this diagnosis method, it has proven to have low-efficiency levels. Researchers have found that the process of measuring the BOLD signals is incredibly slow due to the fMRI's high spatial resolution. As a result, achieving a definitive result or diagnosis in a short amount of time would be very difficult to do. Additionally, the interpretability of some brain scans in certain PD cases has shown to be very poor to the point where experts can even miss specific systemic brain changes in the images (Dixit et al.). The complexities involved in analyzing brain signals have also been known to extend the time it takes to reach a conclusive diagnosis.

Machine Learning and Deep Learning Classification Techniques

The need for new perspectives in almost every field has brought about many advancements in Artificial Intelligence (AI). As a result, the use of Machine Learning (ML) and Deep Learning (DL) is becoming increasingly more viable, and the use of ML in neurological disorder diagnosis is no exception. Machine Learning is a concept in which AI systems leverage algorithms and patterns to learn certain skills and constantly upgrade their knowledge. In other words, ML can perform a skill and improve in executing that action by using past data. Deep Learning is a branch stemming from ML and involves a more advanced version of ML that serves to imitate the neural network of a human brain (Fan et al.). DL uses algorithms to learn similar to ML, but it also involves the stacking of different layers of networks which means that DL is capable of performing tasks that require the consideration of many factors. These tasks are often very

complex such as driving a car, playing a high-level game of chess, and in the case of PD diagnosis, the classification of fMRI images.

Several studies in recent years have shown that the disadvantages of fMRI such as the poor temporal resolution can be overcome using ML and DL. The application of neural networks has not only proven to make the use of fMRI diagnosis more time efficient but also more accurate as it rules out potential neurological disorders. This paired with its cost-effectivity makes ML and DL truly a powerful tool. There are several types of classification techniques or algorithm-based ML or DL techniques, each with its advantages. Most techniques serve to classify fMRI scans based on the typical signs that would be found in the diagnosis of a particular neurological disorder, and in this case, PD. Deep learning methods have also been used to identify particular biomarkers of PD that would otherwise be missed by a human brain. This is made possible by the classification techniques' tendencies to follow algorithms that they use to analyze neural images or large datasets to provide an accurate result or prediction. The exceptional power of ML and DL is reinforced by the idea that the classification methods can constantly learn through past and new data to adapt and improve. Deep Learning techniques specifically can be even more powerful due to their neural network-like structure made to imitate the human brain. Their ability to handle large amounts of data and different variables at once makes them incredibly suitable for diagnosis purposes.

Machine Learning and Deep Learning Models

Support Vector Machine

The Support Vector Machine (SVM) ML technique is a classification model which creates a hyperplane and uses regression analysis algorithms to create optimal and accurate predictions based on a given dataset (Jukkula 1). When using an SVM hyperplane, a large gap between data points denotes little to no error or a high accuracy rate. As a result, when performing an SVM-based diagnosis, the general goal is to maximize the gap between data points (Dixit et al.).

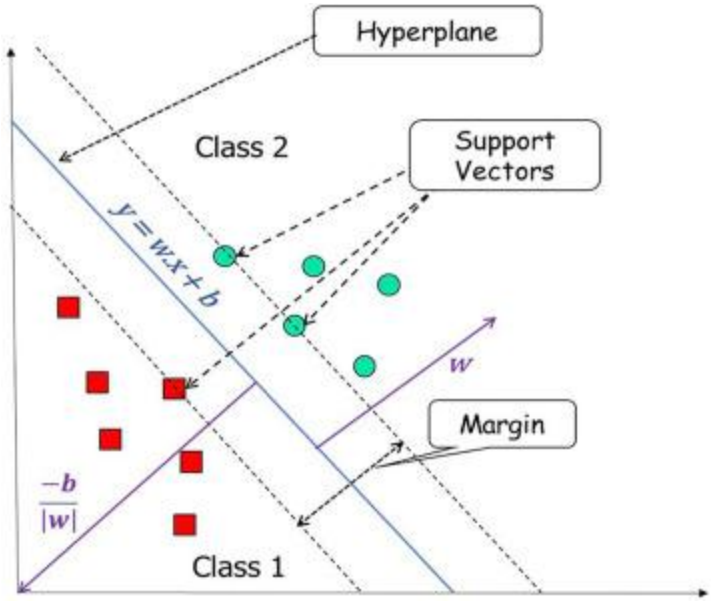


Image From: https://www.sciencedirect.com/topics/computer-science/support-vector-machine

Scientists from the University of Magna Graecia of Catanzaro, University of Cagliari, Dalhousie University, Halifax, NS, Canada, Sapienza University of Rome, and Giustino Fortunato University, Benevento, Italy focused on the use of SVM to diagnose Schizophrenia, another specific neurological condition. The article explains how SVM can be implemented in the analysis of fMRI scans of potentially schizophrenic patients to identify specific genetic biomarkers to determine the diagnosis of a patient and the severity of the condition (Steardo et al.). The study included several schizophrenic patients and healthy controls (HC) or individuals that participated in the experiment. Varying samples or fMRI scans were taken from each of the participants to simulate a realistic situation with many features from different areas of the brain being used as inputs for the SVM. The areas of the brain that were focused on were the evaluated frontal, temporal, and occipital brain regions. The experiment found that the SVM Machine Learning technique successfully exposed brain connectivity differences between schizophrenic patients and healthy control individuals.

While the article mainly focuses on SVM's connection to schizophrenia, a similar process can be used in the case of PD, as PD is also a neurological genetic disease and can be diagnosed by its unique genetic biomarkers. This was proven by two researchers from technological institutes in India, a researcher from the Mayo Clinic, and a researcher from the UAE. The researchers

performed a study in which they used the SVM technique to accurately diagnose PD using non-invasive brain scans. They began by using a PD feature selection strategy and incorporated SVM to classify the images or scans. The SVM technique plotted data based on the collected feature selection values on hyperplanes and classified them for a high-accuracy result. What they found is that the SVM model significantly increased accuracy for diagnosis, reaching a 92.75% accuracy (Dixit et al.). The process needs refinement, however, the initial tests proved to be time efficient and effective with few inaccuracies. Furthermore, room for improvement is always available as the ML technique is capable of adapting using knowledge from previous experiments and data.

Convolutional Neural Network

The Convolutional Neural Network (CNN) is another DL technique made up of multiple layers. CNN uses linear algebra or matrix multiplication to find patterns within data to classify information correctly (Dixit et al.). CNN is excellent for analyzing images as it can handle large amounts of data. Moreover, the CNN method's many layers allow data to be extracted from many types of data making it a versatile tool. The CNN has three layers: the convolutional layer, the pooling layer, and the fully-connected layer ("What Are Convolutional Neural Networks? | IBM"). The convolutional layer is the base of the CNN and it is also where most of the computing happens. The convolutional layer requires three components to function. The first is the input data. The input data can vary depending on the use of the CNN, but it is most commonly derived from images such as brain scans. Second, there is a 3 by 3 matrix filter which is a 2-D array of weights that hones in on specific, smaller parts of the data and studies it. Lastly, there is a feature selector or kernel parameter which is what the filter uses to separate the data. The filter would go through the data and check for specific features to determine the status of the data. In the case of PD diagnosis, the data would be taken from the pixels of the patient's brain scans and the filter would look for PD biomarkers or signs. The pooling layer adds to the efforts of the convolutional layer. In this layer, pixels that are checked by the filter and are determined to have the specific feature are added to an output array. This output array would contain the separated data that the user is looking for. This is important because most CNN models have multiple convolutional layers. After each pooling layer groups data based on the feature selection system, another convolutional layer can be run on the array to further classify the data. As a

result, the pooling layers become essential to reduce complexity and improve efficiency. Finally, the fully-connected layer is the layer that connects the previous or filtered layers and is also the layer where the actual classification occurs.

Several researchers from the Institute of Technology at Nirma University in Ahmedabad, India conducted a study in which they collected 318 MRI scans from HC and PD patients to test the viability of using the CNN for diagnosis purposes. They set the CNN classification method to identify PD progression markers along with many factors considered on different neural network layers. The DL method was able to use the training images to successfully learn how to diagnose PD with high accuracy, reaching an accuracy percentage of 88.9%. Another study performed a similar experiment in which they focused on the reduction of dopamine-producing neurons in the brain as the selective feature being classified by the CNN. The results revealed that with some refinement, the accuracy rate could be roughly 91.17% (Vyas et al.). Currently, CNN is one of the most explored DL methods relating to neurological disorder diagnosis and has shown to be one of the most promising methods. CNN shows incredible potential to improve the diagnosis process of PD and improve the overall care of PD patients.

Limitations of ML and DL Methods

Despite the strength of ML and DL as a tool in healthcare, the application of these tools is still being explored seeing as it is a fairly new revelation. Researchers and scientists want to improve their understanding of the subject as much as possible to ensure that the concepts are ready for practical use. In diagnosis applications especially, mistakes must be minimalized as much as possible as millions of lives may be affected by the technology. One caveat with using ML and DL to diagnose PD using fMRI scans is the need for a non-invasive device. While the application of ML and DL itself is fairly cheap, the non-invasive diagnostic technology can become very expensive with high-end MRI machines costing millions in USD. This is especially a problem in the less developed parts of the world as the technology is limited in those areas and is not easily attainable due to the price. Without the non-invasive diagnostic technology, there would be no data for ML and DL methods to sort through making them ineffective.

Along with the previously mentioned drawbacks, Deep Learning also has its limitations due to its recent emergence in the medical field. First of all, DL is a very complex subset of ML. As a result, applying DL for the diagnosis of PD can become very difficult for scholars to do

effectively. Before DL can be used properly, DL must be studied for much longer, most likely more than the use of DL due to the complexity of the concept. However, the incredible potential that the use of DL holds makes it a very worthwhile angle to research.

Research efforts are necessary to bring about the full-scale use of ML and DL for diagnostic purposes, however, there is an issue that arises in research as well. Collecting data from real-world patients in the medical field is one of the most challenging tasks in the research industry (Dixit et al.). The same is true for experiments in which data from PD patients must be extracted as data relating to diseases, especially neurological diseases, are often imbalanced. Results achieved by DL methods are often affected by these imbalanced datasets and managing the result can be a struggle for this reason (Dixit et al.). Moreover, the complexities involved in collecting data and verifying the validity of the data can slow down the data collection process. DL models specifically require a large number of datasets which can take time to collect. This drawback, although simple in concept, impedes the immediate use of DL.

Connections

ML and DL methods can also be used in conjunction as studies from Iran have shown. Three researchers from Hakim Sabzevari University in Iran conducted an experiment where they collected electroencephalogram (EEG) data, a form of non-invasive neuroimaging, which they classified using several ML methods at once to predict possible cases of epilepsy seizures. A similar concept has been initiated for the diagnosis of PD as well.

Other researchers are using multiple ML and DL methods in different ways. Rather than using the models together, researchers are comparing the results of using different techniques. This can also be very important as it lets scientists know which techniques are most reliable, both in accuracy and consistency. For example, the SVM machine learning method has shown to be the greatest in terms of accuracy for neurological diagnosis using non-invasive imaging data. However, the deep learning technique, CNN, has also been shown to be very promising and is currently going under more experimentation. A researcher in Punjab, India collected non-invasive brain scans and performed classification on the data using SVM along with a few other ML methods. In this case, he performed the analysis with the methods individually to compare which was best. While most researchers have seen the best results with SVM, this

researcher found that random forest models, a separate type of ML model, had the best results with an accuracy rate near 91% (Tiwari 6). Yet the main takeaway from these studies is that ML and DL models individually or together can play a large role in nullifying the negative aspects of using an fMRI diagnosis.

Conclusion

As explained, fMRI is one of the greatest tools used to diagnose neurological disorders, but the low temporal resolution is a severe drawback associated with this diagnosis method. ML and DL have shown that they can invalidate this drawback by speeding up the analysis program. BOLD signals are incredibly complex, which allows brain images to be outputted in high detail, yet this also makes them difficult to analyze if done by a human. ML and DL techniques have been designed to imitate humans with instructions that allow them to perform the analysis instead of humans, however, the computerized aspect of the technology allows the speed of the analysis to happen much faster than if done by a professional. Furthermore, in some cases, analysis steps are automated which means that these steps can happen without supervision while more complex tasks can be monitored by professional individuals. These models are also constantly adapting and learning based on new data which increases reliability levels overall.

Essentially, the use of DL and ML-assisted diagnosis of PD using non-invasive neuroimaging has the potential to forever change the decision-making of clinical situations. Quick and easy analysis of brain scans allows for the uncovering of biomarkers and PD signs that inevitably allow for the early detection of the disease. Such a revolution would allow professionals to give care to PD patients early to slow progression and possibly find a cure for PD. However, it is essential to note that there is a long way to go before ML and DL can be completely incorporated into a medical setting consequently making researching and enhancing these methods will surely help achieve the goal of early PD diagnosis.

Works Cited

Aspinall, MARY Jo. “Use of a Decision Tree to Improve Accuracy of Diagnosis.” Nursing Research, vol. 28, no. 3, May 1979, p. 182, journals.lww.com/nursingresearchonline/Abstract/1979/05000/Use_of_a_Decision_Tree_to_Improve_Accuracy_of.14.aspx.

Dixit, Shriniket, et al. “A Comprehensive Review on AI-Enabled Models for Parkinson’s Disease Diagnosis.” *Electronics*, vol. 12, no. 4, Multidisciplinary Digital Publishing Institute, Feb. 2023, p. 783. https://doi.org/10.3390/electronics12040783.

Fan, Jianqing, et al. “A Selective Overview of Deep Learning.” *Statistical Science*, vol. 36, no. 2, May 2021, https://doi.org/10.1214/20-sts783.

Jakkula, Vikramaditya. "Tutorial on support vector machine (svm)." School of EECS, Washington State University 37.2.5 (2006): 3.

Khodatars, Marjane, et al. “Deep Learning for Neuroimaging-based Diagnosis and Rehabilitation of Autism Spectrum Disorder: A Review.” *Computers in Biology and Medicine*, vol. 139, Elsevier BV, Dec. 2021, p. 104949. https://doi.org/10.1016/j.compbiomed.2021.104949.

Mohammadpoory, Zeynab, et al. “Epileptic Seizure Detection in EEGs Signals Based on the Weighted Visibility Graph Entropy.” *Seizure-european Journal of Epilepsy*, vol. 50, Elsevier BV, Aug. 2017, pp. 202–08. https://doi.org/10.1016/j.seizure.2017.07.001.

Noirhomme, Quentin, et al. “Biased Binomial Assessment of Cross-validated Estimation of Classification Accuracies Illustrated in Diagnosis Predictions.” *NeuroImage: Clinical*, vol. 4, Elsevier BV, Jan. 2014, pp. 687–94. https://doi.org/10.1016/j.nicl.2014.04.004.

Rana, Arti, et al. “Imperative Role of Machine Learning Algorithm for Detection of Parkinson’s Disease: Review, Challenges and Recommendations.” *Diagnostics*, vol. 12, no. 8, Multidisciplinary Digital Publishing Institute, Aug. 2022, p. 2003. https://doi.org/10.3390/diagnostics12082003.

Steardo, Luca, et al. “Application of Support Vector Machine on fMRI Data as Biomarkers in Schizophrenia Diagnosis: A Systematic Review.” *Frontiers in Psychiatry*, vol. 11, Frontiers Media, June 2020, https://doi.org/10.3389/fpsyt.2020.00588.

“Support Vector Machine - an Overview | ScienceDirect Topics.” *Www.sciencedirect.com*, www.sciencedirect.com/topics/computer-science/support-vector-machine.

Tang, Jerry, et al. “Semantic Reconstruction of Continuous Language From Non-invasive Brain Recordings.” *bioRxiv (Cold Spring Harbor Laboratory)*, Cold Spring Harbor Laboratory, Sept. 2022, https://doi.org/10.1101/2022.09.29.509744.

Tiwari, Arvind Kumar. "Machine learning based approaches for prediction of Parkinson’s disease." Mach Learn Appl 3.2 (2016): 33-39.

Vyas, Tarjni, et al. “Deep Learning‐based Scheme to Diagnose Parkinson’s Disease.” *Expert Systems*, vol. 39, no. 3, Wiley-Blackwell, May 2021, https://doi.org/10.1111/exsy.12739.

What Are Convolutional Neural Networks? | IBM. www.ibm.com/topics/convolutional-neural-networks.

Yin, Wutao, et al. “Deep Learning for Brain Disorder Diagnosis Based on fMRI Images.” *Neurocomputing*, vol. 469, Elsevier BV, Jan. 2022, pp. 332–45. https://doi.org/10.1016/j.neucom.2020.05.113.

How Ambient Clinical Intelligence Reduces Physician Burnout (The Neurobiological Perspective)

Ruoxi Zhu (author), Thanisha Kapur (advisor)
The College Preparatory School

Keywords: Ambient Clinical Intelligence, Artificial Intelligence, Biology, Neurobiology, Neuroscience, Physician Burnout

Abstract

Physician burnout is a dire problem in healthcare and medical communities all around the world. In recent years, ambient clinical intelligence (ACI) has emerged as a promising approach to alleviate symptoms of burnout by relieving medical providers of their bureaucratic burdens and letting them focus on the patient and their story, strengthening the physician-patient bond while improving the physician's control over their own time and lives. As a result, the prefrontal cortex (PFC) of the human brain is positively impacted by the reduction in stress and improvement in control, leading to an overall improvement in symptoms of physician burnout. Despite being at a relatively early stage, examples of ACI have already empirically reduced symptoms of physician burnout by nearly 70%, a percentage that will improve in the future as ACI technology advances and researchers better understand the neurobiological reasoning behind why ACI works to reduce physician burnout.

Introduction

Neuroscience is the study of the nervous system, including how it develops, its structure, and what it does, with a focus on the brain and its impact on its cognitive and behavioral functions (Department of Neuroscience), and neurobiology is the specific branch of biology that deals with the anatomy, physiology, and pathology of the nervous system (Merriam-Webster). Due to the complexities of the human brain, factors such as uncontrollable stress can often overwhelm it and incapacitate aspects of its performance, as is the case with physician burnout, in which uncontrollable stress evokes a series of chemical events in the brain that rapidly disconnect circuits in the prefrontal cortex (PFC) and causes human PFC synaptic connections to waste

away, while those in more primitive brain circuits expand, effectively leading to a diminished working memory, inadequate attention regulation, poor decision-making, and many other cognitive deficits, all of which are prominent traits of physician burnout (Arnsten & Shanafelt, 2021). However, examples of artificial intelligence have recently been leveraged to battle symptoms of physician burnout in recent years, and have been proven successful on multiple occasions. Though physician burnout and its connection to forms of artificial intelligence such as ambient clinical intelligence (ACI) have been widely studied, this paper aims to address in detail the neurobiology and reasoning behind why ACI can help reduce physician burnout, which could not only help researchers improve existing ACI technology to better combat burnout symptoms but also aid them in understanding the logic and neurobiology behind using ACI in clinics.

Body

ACI in Healthcare

ACI is a form of artificial intelligence that is capable of adapting to and supporting physicians in how they deliver care. It builds on speech recognition technologies that have been used by doctors for the past two decades, using voice biometrics to authenticate clinical users and other technologies to identify the clinician, patient, and others in the patient room by their voices, providing real-time responses whenever the doctor asks to view patient histories or test results. Another perk of the technology is that it helps with prescribing medications, ordering tests, and scheduling follow-up appointments between the clinician and the patient, cutting down on much of the busywork that each physician must do during the patient's visit. Through integrating conversational AI, machine learning, speech synthesis, natural language understanding, and cloud computing, ACI is also able to help provide accurate diagnostic guidance and clinical intelligence, including highlighting potentially overlooked diagnoses based on the patient's history, symptoms, and possible interactions with drugs, as well as recommending alternative medical prescriptions. As soon as the patient's visit is over, the ACI system is then able to create a summary of the visit, update the patient's digital health record, and enter the appropriate billing codes, which the physician can then edit, review, and then submit to the electronic health record (EHR), which stores all of the patient's data (Ash, Petro, & Rab, 2019).

Furthermore, ACI-collected data could hypothetically be integrated into EHR workflows so that

physicians can receive a more complete picture of patient health for clinical decision support and care coordination, monitoring patient health status and care trajectory. In particular, healthcare organizations would be able to use contactless, ambient sensors for the continuous and nuanced monitoring of Intensive Care Unit (ICU) patient mobility in an attempt to improve the quality and efficiency of care (Nelson, 2021), which is especially important because early patient mobilization can help reduce the relative incidence of ICU-acquired weaknesses by as much as 40%, a critical step to reducing mortality and hospital rates (Haque, Milstein, & Fei-Fei, 2020). The ACI-powered mobility assessment would be superior to the current in-person assessment, which is limited by cost impracticality, observer bias, and human judgment error. Though organizations have attempted to use wearable devices to monitor patient movement in the ICU, this technology is limited to detecting pre-ambulation maneuvers, and is unable to detect external assistance or interactions with the physical space, unlike ACI (Nelson, 2021).

Physician Burnout

Physician burnout rates are on the rise for physicians all around the world, with as many as two-thirds of physicians experiencing at least one symptom of burnout (Whang, 2022), and is diagnosed in physicians who experience emotional exhaustion, no longer find work meaningful, feel ineffective, and tend to view patients, students, and colleagues as objects rather than as human beings (Fred & Scheid, 2018). Though each individual physician's makeup (commitment level, upbringing, role models, expectations, moral values, stress tolerance, & resiliency) always plays an important role in deciding their susceptance to burnout, external influences such as loss of autonomy, a sense of treating the data instead of the patient, countless rules, asymmetric rewards, a sense of powerlessness, and inconveniences with the EHR system, all of which feed into additional stress for the physician, will overwhelm even the best of the best (Fred & Scheid, 2018).

A loss of autonomy has been identified as a leading cause of stress for physicians, and, in turn, physician burnout. Autonomy is characterized as the basic ability of an individual to exercise their judgment in terms of how to spend their time, attention, and resources, which include the ability to decide when to schedule a patient visit, how long each visit is, what questions to ask, when to schedule the next appointment, what types of tests are needed, and which treatments are

fitting. Unfortunately, this view of autonomy is almost completely in opposition to the current state of affairs in the practice of medicine, which emphasizes less time spent with patients in favor of more information to manage. As such, physicians are forced to spend more time focusing on the monitor rather than on the patient, reducing both the quality of care that each patient feels like they receive as well as the physician-patient connection.

The countless rules that each physician must learn when entering the practice is also a big contributor to stress and physician burnout. Stress is especially prominent in young physicians who are taught in medical school to focus on the patient but must adjust to focus on the business aspects of medicine once they start working. These business aspects often include rules from the government, insurance companies, and hospitals, all of which limit the time that these physicians can spend with their patients and puts additional pressure on program directors who diligently monitor and enforce work-hour limits for trainees, as well as physicians who must check the correct boxes on the EHR in order to maximize the bill for each encounter. As a result, upwards of 50% of medical students, residents/fellows, and physicians are already burned out early into their careers.

Yet another reason for physician burnout is asymmetric rewards. In the medical profession, the asymmetry of reward and punishment is especially notable; exacerbated by an explosion of information about each patient, treatment, and disease, physicians are punished more harshly whenever they make a mistake, yet rarely receive praise when they live up to expectations. Though physicians choose a life of service and therefore don't necessarily think of "insufficient reward" as an important factor in career satisfaction, long-time exposure to harsh criticisms and little praise steadily feed into growing stress for many physicians.

For many physicians, especially those who work with populations in poor socioeconomic situations, the sense of powerlessness that stems from an inability to fix the root cause of a patient's medical issue is also a leading cause of burnout and stress. Every physician will inevitably encounter a situation where they are unable to solve a health problem that is initially derived from factors that they cannot control such as poverty and marginalization. To someone who has chosen to dedicate their life to that very purpose, the realization that they cannot save

everyone is a cold wake-up call.

Last but not least, the inefficiency of the current EHR system utilized by healthcare organizations is considered the final straw for many physicians, as it causes the absence of the necessary social and behavioral factors between the patient and the physician that are fundamental to treatment. Though it was originally designed to replace paper records, EHRs are now more focused on the process rather than the outcome, adding to the individual physician's workload while the quality of patient care remains stagnant. In fact, one study found that for every single hour the doctor spends facing their patients, they spend an additional two hours entering data on the computer, in addition to the one or two hours that they spend at home every night attempting to keep up with their work. Another study of family medicine physicians found that they consistently spend more than half of their workday, which is nearly six hours, working with the EHR system. According to the same study, two-thirds of that time was spent on doing clerical and inbox work. Furthermore, due to the hundreds of different communication and nomenclature standards used by health information technology developers all over the world, many digital health records are unable to be translated across competing EHR platforms, complicating the healthcare system beyond what is necessary. It is also worthy of note that the point-and-click design of the EHR system also prompts errors from the physician, encouraging them to check off more boxes even when they may not be completely accurate for the patient. Thus, the EHR is a major source of stress for many physicians, often leading to burnout (Fred & Scheid, 2018).

Neurobiology Behind Stress Reduction

At the very core of physician burnout is stress. The factors mentioned in the above section all result in uncontrolled stress for physicians, leading to burnout. In situations such as the COVID-19 pandemic, the perceived loss of control and overwhelming workloads that each physician must take care of every day can also further exacerbate this process.

Though chronic occupational stress is often triggered by characteristics in the physicians' work environments, it ultimately affects biological functions as well, especially in the PFC. The PFC is the part of the brain that governs high-order reasoning, social cognition, and complex decision-making, including the integration, conceptualization, and critical evaluation of

information. Prolonged exposure to uncontrollable stress drastically impairs PFC functioning, which is harmful since the PFC is crucial for attentional regulation, planning, organization, guiding appropriate social behaviors, maintaining integrity despite challenges, metacognitive abilities, moral conscience, emotional intelligence, and empathy, all of which are important for optimal physician performance.

Uncontrollable stress exposure includes an acute stressor if the subject feels threatened by a situation, evoking a series of chemical events in the brain that rapidly disconnects PFC circuits and causes human PFC synaptic connections to waste away, while those in more primitive brain circuits expand. For example, high levels of norepinephrine and dopamine are released within the brain during instances of uncontrollable stress, impairing PFC cognitive functions and resulting in diminished working memory, inadequate attention regulation, poor decision-making, and other cognitive deficits. Indeed, human subjects with symptoms of burnout such as occupational exhaustion have thinner PFC gray matter than their counterparts. Fortunately, studies show that both human and animal PFC connections can regrow during sustained periods when stress is avoided, which allows the return of top-down control to the physician.

Looking at the neurobiological perspective of physician burnout helps provide a more rational understanding of why burnout symptoms happen, and can also be used to help create strategies for burnout prevention and treatment. Impaired PFC self-regulation can explain many burnout symptoms, including reduced motivation, unprofessional behavior, decreased compassion, and poor communication with patients, especially during a time when the physician has an overwhelming load of work. However, researchers have found that maintaining a sense of control can protect against cognitive deficits and PFC impairment during prolonged stress exposure, implying that strategies to restore control to physicians may be particularly helpful to reduce burnout. These strategies could include creating organization and structure during times of chaos, advocating for change, identifying inefficient processes and leading efforts to improve workflows, working part-time, gaining perspective by engaging in meaningful and refreshing activities, learning about the underlying neurobiology of the stress response to reduce self-blame, and deliberately fostering work-life integration (Arnsten & Shanafelt, 2021).

Why ACI Works For Burnout Prevention

One of the strategies to return a sense of control and autonomy to physicians is through using ACI to reduce stress and increase physician-patient connection. As ACI can help physicians efficiently diagnose and monitor patients, detect and predict illness, accelerate drug development, improve the patient experience, and expand access to care, the technology has a significant positive impact on time management and efficiency for many physicians.

For example, the Nuance® Dragon® Ambient eXperience™, or DAX™, is an ACI system that automatically documents patient encounters accurately and efficiently during each patient visit. Since ACI systems such as DAX ensure that the primary focus of each patient visit is the patient instead of documentation, patient-physician bonds are often strengthened during visits to offices that use ACI. Furthermore, these ACI systems also provide physicians with relief from much of their administrative burdens, improving their overall efficiency. As a result, ACI not only strengthens the physician-patient relationship but also removes hours of daunting documentation work for the physicians, giving the physicians more control over how they choose to spend their time (Nuance Communications, 2023).

Indeed, a survey of the DAX system showed that clinicians reduced time spent on documentation by 50% and felt a 70% reduction in feelings of burnout and fatigue (Nuance Communications, 2023). Furthermore, a medical provider was not only able to cut their time spent on clinical documentation from two hours to 15 minutes with the help of a different type of ACI in the form of microphones attached to eyeglasses, they were also able to double the time that they spent with patients (Haque, Milstein, & Fei-Fei, 2020).

Importantly, feeling more in control of their everyday life is an important factor in protecting physicians from cognitive deficits and PFC impairment during prolonged stress exposure, as mentioned above. As such, by helping physicians regain more control over their own time, the ACI systems are able to positively impact the PFC and reduce symptoms of physician burnout. As ACI technology continues to improve, we can expect to see this percentage rise in the near future (Nuance Communications, 2023).

Conclusion

Physician burnout is a pressing problem among doctors in the United States, and results in emotionally exhausted physicians who no longer find their work meaningful or effective, viewing their peers and patients as objects rather than human beings. Though there are many common causes of physician burnout, they all feed into one main problem: stress. To relieve some of the pressure on physicians, ACI has emerged as a promising approach. ACI helps take care of various bureaucratic tasks, an overload of which has been identified as a leading feeder into stress, and ensures that each patient visit is focused on the patient instead of note-taking or documentation. This shift not only empirically strengthens the physician-patient relationship, but also removes hours of daunting documentation work for the physicians, giving the physicians more control over how they choose to spend their time. From the neurobiological perspective, the resulting stress relief from the usage of ACI positively impacts the PFC of the brain, restoring gray matter connections in the PFC that are lost due to chronic stress exposure and thus helping alleviate symptoms of physician burnout. ACI is still a fairly new technology that has been implemented in the healthcare field. As further research is done and technology advances, we can expect even more improvements in ACI technology and its impact on reducing physician burnout.

Works Cited

Arnsten, Amy F.T. and Tait Shanafelt. "Physician Distress and Burnout, the Neurobiological Perspective." *Mayo Clinic Proceedings*, Mar. 2021, https://doi.org/10.1016/j.mayocp.2020.12.027.

Ash, Michael, Joe Petro, and Shafiq Rab. "How AI in the Exam Room Could Reduce Physician Burnout." *Harvard Business Review*, 12 Nov. 2019, https://hbr.org/2019/11/how-ai-in-the-exam-room-could-reduce-physician-burnout.

Datta, Dibyadeep and Amy F.T. Arnsten. "Loss of Prefrontal Cortical Higher Cognition with Uncontrollable Stress: Molecular Mechanisms, Changes with Age, and Relevance to Treatment." *MDPI*, 17 May 2019, https://doi.org/10.3390/brainsci9050113.

Department of Neuroscience. "About Neuroscience." *Georgetown University Medical Center*, https://neuro.georgetown.edu/about-neuroscience/.

Fred, Herbert L. and Mark S. Scheid. "Physician Burnout: Causes, Consequences, and (?) Cures." *The Texas Institute Heart Journal*, 1 Aug. 2018, https://doi.org/10.14503/THIJ-18-6842.

Haque, Albert, Arnold Milstein, and Li Fei-Fei. "Illuminating the dark spaces of healthcare with ambient intelligence." *Nature*, 09 Sep. 2020, https://doi.org/10.1038/s41586-020-2669-y.

Merriam-Webster. "neurobiology." *Merriam-Webster Dictionary*, https://www.merriam-webster.com/dictionary/neurobiology.

Nelson, Hannah. "Ambient Clinical Intelligence: What It Means for the EHR Industry." *EHR Intelligence*, 20 Oct. 2021, https://ehrintelligence.com/features/ambient-clinical-intelligence-what-it-means-for-the-ehr-industry.

Nuance Communications. “Reducing burnout and improving patient care with ambient clinical intelligence.” *www.kevinmd.com*, 28 Feb. 2023, https://www.kevinmd.com/2023/02/reducing-burnout-and-improving-patient-care-with-ambient-clinical-intelligence.html.

Whang, Oliver. “Physician Burnout Has Reached Distressing Levels, New Research Finds.” *The New York Times*, 29 Sep. 2022, https://www.nytimes.com/2022/09/29/health/doctor-burnout-pandemic.html.

The Implications of Generative AI on Mental Health

Libbey Kwok (author), Thanisha Kapur (advisor), Anika Shah (editor)
Burlingame High School

Keywords: Neural Language Processing, Artificial Intelligence, Emotional AI, Generative AI, Psychotherapy, Risks

Abstract

Artificial Intelligence (AI) is used to problem solve and perform human tasks through its ability to learn and mimic human intelligence. Mental health is defined as one's ability to handle the daily stressors of life. Artificial Intelligence has a propitious future in the field of Mental Health as a result of its sound personalization, and abilities such as detecting patterns over a large period of time, natural impersonation of human speech, and understanding of human emotion. These abilities could potentially find a permanent solution to the unpredictability and uniqueness of an individual's mental health struggles. Although the future benefits are innumerable, widespread use of AI blurs the line between ethicality and has shown cases of extreme bias, misinformation, and dehumanization of AI. Only future research can reveal a definite answer as to if the rapid development in AI today is productive.

Introduction

In the 21st Century, Artificial Intelligence is a rapidly growing field that will impact many aspects of future generations. Artificial Intelligence, more commonly known as AI, is defined as computers' emulation of human intelligence to problem-solve and make decisions. Through deep analysis of syntax, pragmatics, and other language-related factors in its dataset, AI forms rules about language that it applies to new input. This creates a positive feedback loop that ultimately allows for human language comprehension and increasing accuracy. The method described above is called neural language processing(NLP). ChatGPT, OpenAI's newest innovation, is an AI chatbot that uses natural language processing to respond to virtually anyone or anything in a natural manner.

The latter half of its name ‘GPT’ stands for ‘Generative pre-trained transformer’ meaning that the chatbot is built to generate new content utilizing prediction algorithms based on its training dataset. The training process is often very intense and long but eventually gives the chatbot the ability to emulate human language. The mind-blowing naturality and responsiveness of AI technology seemingly makes it the perfect tool to increase accessibility in mental health.

Although the benefits of generative AI seem boundless, it would be ill-intentioned to discount the risks. Because the main goal of Chat GPT is to naturally respond to inquiries with the most probabilistic next words, biases can occur that doubt our trust in Artificial intelligence. These behaviors cause serious ethical and technical concerns in the future of AI and cast doubt on the worthwhile potential of today’s AI innovations. As AI technology for mental health today relies heavily on human interaction, it’s crucial that the risks are accurately analyzed to make sure generative AI helps individuals in vulnerable states more than it hurts. The lack of direct human control that is present among chatbots makes it unpredictable, and thus able to lead customers towards the wrong paths. It has the ability to be life-altering which is why it is so important that risks are prevented before it is too late.

As mental health awareness has increased greatly, society is starting to realize the huge problem that it is. Approximately 20 percent of adults suffer from a diagnosable mental illness yet they fail to receive the help and support they need in order to get better. The copious amounts of stigma, lack of accessibility, and lack of self-awareness are the biggest factors regarding why individuals are not proactive about their mental health. Although often unrecognized, mental health has a dramatic effect on one’s quality of life and if these issues are able to be solved using generative AI, lives could be improved and potentially even saved. This paper explores our potential future relationships with AI technology and weighs the dangers and potential “what ifs” when it is used as a tool to impact the field of Mental Health. It primarily explores this idea through ChatGPT and other chatbots but also talks generally about artificial intelligence as a whole.

How Generative AI is being used in Mental Health as of 2023

In a world of intense technological revolution, AI is a field that has defied many boundaries. What was once set to resemble a human mind is now a machine built on association rather than thoughts of its own. In recent research, Health Care Professionals converse with and compare AI models on their outlook regarding mental health in a study by the Psychiatric Times titled "Conversations With Artificial Intelligence: Mental Health vs Machine". This particular study found that Open AI's ChatGPT gave excellent and conversationally understandable general information on what patients could do when struggling with various mental health issues but that users should be cognizant of the risks it poses and always refer to a professional when needed. Another study detailed a conversation between psychiatrist Ronald W. Pies and ChatGPT competitor, Google's Bard. The results further demonstrate the success that AI can bring in a mentally stable population. The ChatGPT competitor gave very original analyses and responses that were backed up by extensive amounts of information and were even able to personalize responses towards an individual. This critical point of originality is especially exciting as we are shown AI's potential to not only produce reliable information but also be used for users to understand their emotions in their own unique ways. These insights can potentially become something even professionals can learn from and utilize as a teaching tool.

Beneficial Use Cases of Artificial Intelligence in Mental Health

Another article, "Emotion AI: Why It's The Future Of Digital Health" talks about the beneficial use cases of emotion AI in healthcare. Emotional AI deals with a field of computer science that allows machines to grasp the concept of human feelings. If done right, development in Emotional AI will benefit us for generations. This futuristic world could encompass new innovations like ways to monitor the resilience of conditions such as cancer and alleviate the emotional burden caregivers take on when providing support to people with dementia or other mental illnesses. Given the ability to accurately and efficiently respond, AI could be even better than caregivers with their extremely structured approach to learning things. This relieves caretakers of the burden they take on and instead, allows them to focus on other tasks or career goals. Other examples include Twill, a personalized care bot, and LUCID, an AI music recommendation system that bases its recommendations on one's detected mental states. All in all, Emotional AI can help significantly when it comes to serving patients more effectively, eventually even helping humans understand what they're feeling at times.

As a result of its highly algorithmic approach, Artificial intelligence has been found to have huge success in one particular area, diagnosing mental illnesses. When dealing with virtual therapy, AI uses Emotion AI to detect emotions such as depression, anxiety, and stress. This helps decipher the usual subtlety of human language and detect the early symptoms of a mental illness. To highlight the importance of this, the National Institute of Health states, "It is estimated that more than one in five U.S. adults live with a mental illness". Here, it is shown the staggering amount of individuals living with a mental illness and shines a light on the cruciality of seeking the adequate support and help needed. Additionally, it is also helpful in detecting changes in emotion over time and exploring somebody's emotional journey.

To add on, its algorithmic approach combining Emotion AI and Natural Language Processing makes it the perfect tool to improve a patient's awareness of their mental state. It is a global thought that mental states change quite frequently so from a human perspective, a depressive state could very possibly just be a depressive state rather than a mental illness. Making patients aware of what their change in mental states could be is a very beneficial preemptive step in a mentally stable society. People are often reluctant to ask for help despite the stigma surrounding mental health issues. Because of the often not physical changes of mental illness, it is hard for others to empathize. Thus, asking for help can seem very daunting; therefore, a machine removes the fear and human-to-human interaction that usually induces fear in the regular person. ChatGPT and other chatbots provide an alternative where others don't have to be ashamed of getting the help they need.

The Dangers and Risky Use Cases of AI on Mental Health

The below section references information from the article, "AI Chatbots Could Help Provide Therapy, but Caution Is Needed" published by Scientific American. While the future of AI is filled with a plethora of unignorable benefits, several drawbacks have left many more concerned rather than excited. Firstly, users report feeling a sense of understanding when engaging with AI machines contrasted with human interaction. The world of digitization has already brought up the concern of not being present at the moment and replacing humans with inanimate objects. Obvious concerns like bias, falsified information, and privacy are increasingly becoming

researched more in-depth as AI embeds itself deeper into everyday society. ChatGPT is a model that is trained on finding the next best word as its priority rather than providing accurate information which makes it easy for machines to have “hallucinations” or falsify information. These drawbacks re-emphasize the fact that humans should be alongside this AI revolution. Humans trust machines with vulnerable information and tend to accept machines’ information as the truth. Chatbots don’t have the flexibility to personalize advice to every individual and have limited advice prone to promoting dangers like self-harm. With the right specialists alongside these technologies, reinforcement could be given to the machines and guide them in the least harmful direction to humans.

Another notable danger would be the dehumanization of mental health that could occur. When models are implemented in place of therapists or licensed psychologists, not only are humans lost, but we also lose the special bond and empathy that patients usually form with professionals. This bond is very unlikely to be formed or be able to be emulated by an algorithm. Concerns with this are that a certain demographic might not feel open to discussing their emotions with a machine. A connection with a human is known as the core success for certain therapies and treatments and it is feared that without it, AI would only be making the problem worse.

The mental health field will also become exacerbated when AI potentially endorses factually inaccurate actions. When dealing with individuals who are mentally unstable, it is incredibly crucial that the most up-to-date, relevant, and accurate information is brought to the table as the information you feed to the individual could end up being a matter of life or death rather than a guessing game. As of 2023, AI is still very much in its developmental stages, and when dealing with susceptible individuals, developers should be conscious of what they put out for public use as it could dramatically impact lives. Until we have a solid grasp and control of what AI can do and can get rid of the large amounts of biases that we see today, it is best practice to wait for further development to be done in cooperation with humans to ensure a positive impact on citizens in the future.

An exciting use case: Psychotherapy

A scholar from Stanford University's Institute for Human-Centered AI highlights the exciting research that is currently being done with AI to improve therapies. Psychotherapy is defined as the use of psychology and repeated human interactions to treat conditions. Although investing in AI is a high-risk area, the potential is also something that cannot be ignored. An article by the Human-Centered Artificial Intelligence at Stanford University researches the use of Psychotherapy to improve mental health. AI can help make our lives easier by aiding in basic tasks in the healthcare industry including documentation and notes. Additionally, they could help in making psychotherapy more interactive between sessions which will skyrocket success rates. The most important thing is to not rush into developing AI without considering the vast risks it comes with. His steps start with assisting others, go on to suggesting options for therapy, and then eventually, become fully autonomous.

Conclusion

Using Artificial Intelligence in such a high-risk field as mental health is a particularly difficult topic. There are a plethora of ways in which it could quite literally change the landscape of how we process and understand emotions yet on the other hand, the current states of AI chatbots are prone to dangerous outputs that could cost a vulnerable individual's life. To make the technology better, there are not many options in which a human test subject would not be needed. Unfortunately, testing it on actual human subjects proves to be very risky. The common advice when dealing with new technologies with lots of risks is to minimize the weight of outputs on actual results. In the case of AI, this means taking responses minimally and not letting it shape one's thoughts on the subject. The reason for doing this is because we do not know the accuracy of the results, and thus, can't trust them. By minimizing the weight responses have on results, false results are less probable. However, mentally unstable humans are not in the correct mindset to do so and take whatever they see as the truth. Because they are so vulnerable at times, it is not a safe idea to test it on mentally unstable individuals as the potential of ChatGPT perpetuating dangerous paths is a risk.

Works Cited

Khullar, Dhruv. "Can A.I. Treat Mental Illness?" *The New Yorker*, 27 Feb. 2023, www.newyorker.com/magazine/2023/03/06/can-ai-treat-mental-illness . Accessed 23 July 2023.

Labbé, Aaron. "Council Post: Emotion AI: Why It's the Future of Digital Health." *Forbes*, 23 Nov. 2022, www.forbes.com/sites/forbestechcouncil/2022/11/23/emotion-ai-why-its-the-future-of-digital-health/?sh=6d98adfa6516 . Accessed 23 July 2023.

"Mental Illness." National Institute of Mental Health, www.nimh.nih.gov/health/statistics/mental-illness#:~:text=It%20is%20estimated%20that%20more,mild%20to%20moderate%20to%20severe . Accessed 29 July 2023.

Nicholas Pratt, M. D., et al. "Conversations with Artificial Intelligence: Mental Health vs Machine." *Www.psychiatrictimes.com*, 12 June 2023, www.psychiatrictimes.com/view/conversations-with-artificial-intelligence-mental-health-vs-machine. Accessed 24 July 2023.

Nilsen, Per, et al. "Accelerating the Impact of Artificial Intelligence in Mental Healthcare through Implementation Science." *Implementation Research and Practice*, vol. 3, Jan. 2022, p. 263348952211120, https://doi.org/10.1177/26334895221112033.

Reardon, Sara. "AI Chatbots Could Help Provide Therapy, but Caution Is Needed." *Scientific American*, 14 June 2023, www.scientificamerican.com/article/ai-chatbots-could-help-provide-therapy-but-caution-is-needed/ . Accessed 23 July 2023.

Walsh, Dylan. "A Blueprint for Using AI in Psychotherapy." *Stanford HAI*, 21 June 2023, hai.stanford.edu/news/blueprint-using-ai-psychotherap. Accessed 24 July 2023.

Ulotaront: A New Method of Treating Schizophrenia

Peyton Higa (author), Thanisha Kapur (advisor)
Hillsdale High School

Keywords: Ulotaront, SmartCube, Psychogenics, schizophrenia, Parkinson Disease, Parkinson Disease Psychosis, psychosis, depression, anxiety, dopamine system, TAAR1, 5HT2A, D_2

Abstract

Schizophrenia is a serious mental disorder that is characterized by hallucinations, delusions, feeling demotivated, and trouble thinking or speaking. While there is currently no cure, it is treatable with medication, such as ulotaront. Ulotorant is a novel prescription created by PsychoGenics using breakthrough automated technology SmartCube. It is different from other psychiatric medications, which typically target the dopamine D_2 receptor. Although this eases positive symptoms (hallucinations, delusions, disorganized motor behavior), it does not treat negative symptoms (lack of motivation, emotion, and social withdrawal). Ulotorant is unique because it is a TAAR1 receptor agonist, meaning that it activates a different signaling pathway. Using this different system, it treats both positive and negative symptoms of schizophrenia. This article evaluates ulotorant and its efficacy as an indicator that automated tools are the future of psychiatric research.

Introduction

For years, the status quo of antipsychotic medication has been incomplete. Schizophrenia is a debilitating mental disorder involving alterations in one's brain chemistry, mood, and connection to reality. While there is no cure for schizophrenia, it can be treated. Side effects either fall under the category of positive symptoms and negative symptoms. Positive symptoms are effects that "add on" something, such as hallucinations or paranoia. On the other hand, negative symptoms "take away" normal functions, resulting in apathy and reduced motivation. For years, treatment for schizophrenia has focused on dopaminergic modulation, which only resolves positive symptoms. However, the pharmaceutical lab PsychoGenics used the breakthrough technology SmartCube to create ulotaront, a medication that aids with both positive and negative symptoms. Two thirds of people suffering from psychosis do not receive the healthcare needed to treat their

illness. This literary review will evaluate the potential of ulotaront, considering that it functions differently from most treatments and was created using the new SmartCube new technology.

Body

Highthroughtput Analysis for Antipsychotics

The SmartCube® is a high-throughput system, meaning that it uses automation to collect millions of data samples on organisms. During the process, a mouse is placed in the box and exposed to a sequence of anxiogenic, or startling, challenges. The machine records and analyzes every slight change in position and behavior to detect activity in the central nervous system. Every session, around half a million data points are recorded and pieced together into 2000 target features (Alexandrov et al.). All compounds tested by Psychogenics are stored in a database that recognizes unique "signature" responses to different compounds. Based on features that the drug evokes, each compound is categorized into a Class and a Subclass. Thus, the SmartCube can determine the efficacy of a new drug without bias by referencing it with other medications that are already tested and on the market.

Trace Amine-Associated Receptor 1:a New Target for Psychogenic Medicine

Treatments for schizophrenia typically involve blocking the D_2 receptor, which regulates the creation, storage, and release of dopamine in the brain. This is effective in reducing positive symptoms (i.e. hallucinations, hearing voices, paranoia) but does not reduce negative symptoms (reduced motivation or emotion) or repair cognitive function. As of February 2022, using the "typical antipsychotics" for schizophrenia, only around 70% of patients given D_2 antagonists responded to treatment (Nair et al.). In addition, typical antipsychotics caused significant neurological side effects. Newer antipsychotics using 5HT2A-receptor antagonism alongside D_2 blockade were safer, but still yielded similar efficacy. Ulotaront is unique because it induces trace-amine-associated receptor 1 (TAAR1). TAAR1 medications are different from other antipsychotics that focus on the dopamine system. TAAR1 is not part of the dopaminergic system, yet still plays a crucial role in the neurotransmission that schizophrenia disrupts. While 16% of the general public experiences drug or alcohol abuse, nearly half of all schizophrenia patients have substance abuse issues (Nair et al.). It is not clear what causes such a high comorbidity rate between schizophrenia and substance abuse disorders, but some theorize that it

is due to their overlap in the brain's "reward circuits." Ulotaront may help with patients dealing with both of these disorders because TAAR1 agonists reduce amphetamine cravings and other behaviors associated with addiction. TAAR1 medications may carry less side effects and help with substance abuse comorbidity and metabolic syndrome common in schizophrenia patients.

Long Term Effectiveness and Safety of Ulotaront for Schizophrenia

After showing efficacy in a 4 week, double blind, placebo controlled study, 193 patients continued to participate in an open-label extension study. For 26 weeks, 193 patients were evaluated to test the long-term safety of ulotaront for treating schizophrenia. The study concluded that daily doses of 25-75mg of ulotaront resulted in minimal change in weight and metabolism, a high completion rate, and a decrease in the baseline of the mean Positive and Negative Symptoms Scale (PANSS) (Correll et al.). Pictured below is the change in mean PANSS score for patients treated with the placebo during the double blind trial, then switched to ulotaront (light green) compared to the patients who were treated with ulotaront for the entire duration of both trials (dark green). During the study, 56.4% of patients experienced adverse effects, which are unwanted side effects of treatment (Correll et al.). However, most of the AEs were mild to moderate in severity. In addition, the treatment proved to make no change in prolactin levels, which are significant to the symptoms of schizophrenia. The mean change from the PANSS baseline in the open-line group was -22.6 (Correll et al.).

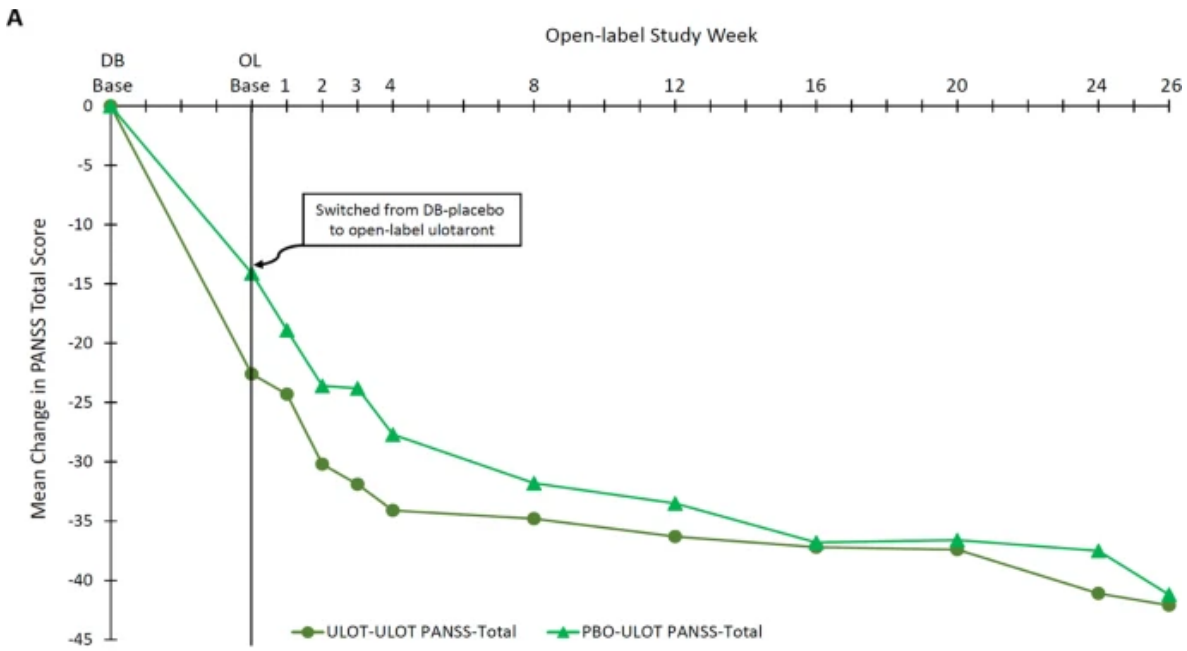


Image from www.nature.com/articles/s41537-021-00190-z

Ulotaront for Parkinson's Disease Psychosis

In a study of 38 patients, 24 were treated with ulotaront and 14 with a placebo to analyze its efficacy in treating Parkinson disease psychosis (PDP). 25% of patients given ulotaront found that their PDP symptoms had gone into complete remission (Crandall et al.). It is unique from most other antipsychotic drugs because it does solely function on dopamine or serotonin blockades. Ulotaront is a trace amine-associated receptor 1 (TAAR1) agonist, meaning it induces the same response as the molecule that naturally binds to it. The TAAR1 receptor could be a future target for developing other psychiatric drugs, due to its broad control over neurotransmission. The central focus of the study was to determine whether ulotaront reduced the frequency and intensity of hallucinations and delusions. Symptoms of PDP showed significant reduction within the first week and maintained until week 6. The most common reasons for patients' withdrawal from the study were adverse events (AEs). 1 out of 14 patients administered the placebo and 5 out of 25 dosed with ulotaront discontinued due to AEs (Crandall et al.). The figure below demonstrates the least squares mean difference from baseline in SAPS-PD. Scale for the Assessment of Positive Symptoms of Parkinson Disease (SAPS-PD) is a measure of the severity of symptoms of Parkinson Disease based on a numerical scale. The graph below illustrates that patients treated with ulotaront showed a greater decrease from the baseline

than did the placebo group. However, this was not a statistically significant decrease because the difference between the SAPS-PD scores did not exceed the standard error. However, the ulotorant group demonstrated a trend of greater improvement.

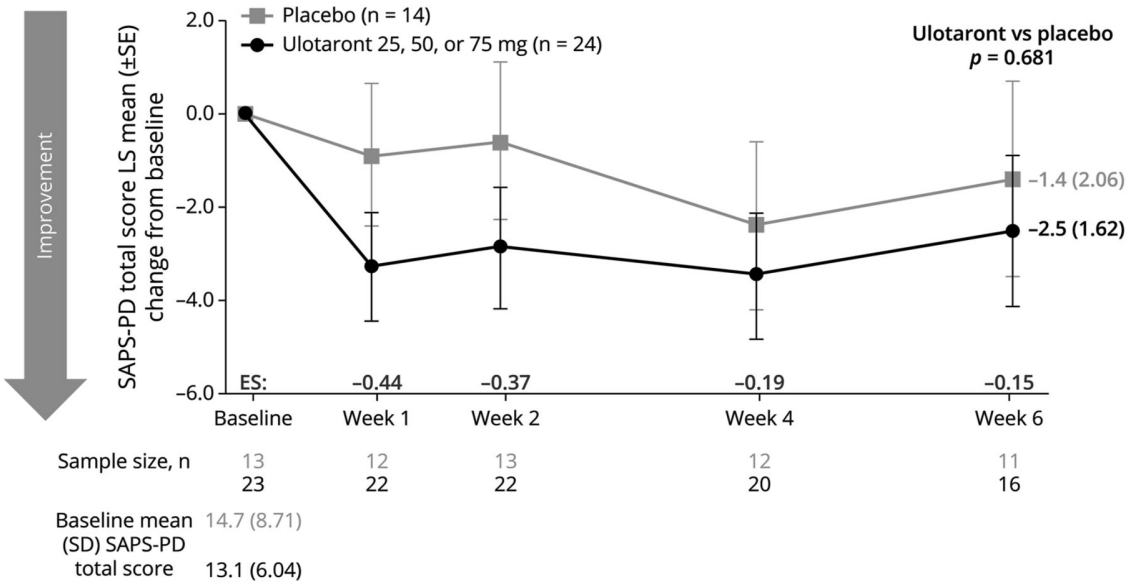


Image from https://pubmed.ncbi.nlm.nih.gov/37273942/

Conclusion

All articles concurred that ulotorant is a novel solution for a quality that many neurological treatments are lacking: treating negative symptoms, especially in schizophrenia. Ulotorant's unique function stems from the fact that it involves the TAAR1 receptor, instead of only focusing on the D_2 receptor. Article 2 displays ulotorant's efficacy as it resulted in a mean change from baseline in the PANSS of -22.6. In addition, Nair (et al.) discusses how ulotorant may aid with issues separate from the symptoms of schizophrenia, such as substance abuse. Also, Correll (et al.) states that there was not a statistically significant change in ulotorant versus the placebo, there was a nonsignificant trend favoring ulotorant. This opens the door for future use of TAAR1 agonists in neurological disorders other than ulotorant. Overall, the sources convey that ulotorant may propose new opportunities for schizophrenia and other products to come from the SmartCube technology.

Works Cited

Alexandrov, Vadim, et al. "High-Throughput Analysis of Behavior for Drug Discovery." *European Journal of Pharmacology*, 5 Mar. 2015, www.ncbi.nlm.nih.gov/pmc/articles/PMC4552324/.

Correll, Christoph U., et al. "Safety and Effectiveness of Ulotaront (Sep-363856) in Schizophrenia: Results of a 6-Month, Open-Label Extension Study." *Nature News*, 9 Dec. 2021, www.nature.com/articles/s41537-021-00190-z.

Isaacson SH;Goldstein M;Pahwa R;Singer C;Klos K;Pucci M;Zhang Y;Crandall D;Koblan KS;Navia B; ; "Ulotaront, a Trace Amine-Associated Receptor 1/Serotonin 5-HT1A Agonist, in Patients with Parkinson Disease Psychosis: A Pilot Study." *Neurology. Clinical Practice*, 25 May 2023, https://pubmed.ncbi.nlm.nih.gov/37273942/

Nair, Pramod C, et al. "Trace Amine-Associated Receptor 1 (TAAR1): Molecular and Clinical Insights for the Treatment of Schizophrenia and Related Comorbidities." *ACS Pharmacology & Translational Science*, 18 Feb. 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC8922295/.

Effect of Gut Mechanosensation on Cognitive Disorders in Depressed Alzheimers' Patients

Pranjal Sharma (author), Thanisha Kapur (advisor)
Ballard High School

Keywords: Mechanosensation, Gut-Brain Axis, GBA, Alzheimer's, Brain, Microbiome, Parieto-Occipital region, Depression, Cognitive Disorders, Gastroduodenal Stimulation, Gut

Abstract

The Gut-Brain Axis (GBA) has long intrigued researchers, but it has always been challenging to study due to the inaccessibility of the body's interior. Extensive research has revealed a link between the brain and the gut with possible effects on neurological and gastrointestinal disorders. The microbiome found in the gut has closely been related to neuropsychiatric disorders and neurodegenerative disorders. Therefore this microbiome-gut-axis can be a potential target point for the reduction of symptoms of such diseases, if not the treatment. In the various external studies referenced in this paper it has been found that depressed patients have a decreased Parieto-Occipital activation in the brain as compared to health groups and how that can be an initiating factor for cognitive disorders. Alzheimer's disease is one of the leading cognitive disorders, and affects over 6 million Americans. Additionally, in a study referenced in this paper states that the stimulation of the gastrointestinal area, specifically the gastroduodenal area can increase the potential of the same region (Parieto-Occipital). Therefore this study focuses on how the gastroduodenal stimulation using a minimally invasive vibrating capsule can affect the Parieto-Occipital activation in depressed patients, to finally study the effects it can have on the possibility of them developing Alzheimer's disease.

Introduction

The GBA crosstalk is a complex communication system that can be a key factor for neurological disorders. The gut functions based on mechanical stimuli to work in unison. The sensing of mechanical stimuli is mechanosensation. It is the conversion of mechanical stimuli into neural

signals, which is responsible for the sensation of pain, light touch, hearing, etc. The mechanosensory cells in the gut are responsible for transduction through signal amplification. This occurs through the microbiome-gut-brain axis or GBA, which is a bidirectional pathway which connects the gut to the brain. In a study performed by Toledo, A.R.L.; et al, this pathway has been considered as a possible pathological and therapeutic target region for certain neurodegenerative disorders, such as Alzheimers. In another study by Mayeli, Ahmad, et al., the stimulation of the gastrointestinal tract, especially the gastroduodenal region resulted in neural responses, called evoked response potential (ERP), in the parietal-occipital region of the brain. The use of capsule stimulation on normal and enhanced vibratory settings was used to elicit this response. Furthermore, in a study conducted by Li, Jianying et al., they found that decreased activation of the occipital region of the brain might be an initiating factor of cognitive disorders in depressed patients. Depressed patients and patients with Alzheimer's disease have an altered composition of gut microbiome compared to healthy patients. Both the disorders show a decrease in protective bacteria such as *Lactobacillus* and *Bifidobacteria* as per studies 3 and 4, which again connects back to the microbiome-gut-brain axis.

Therefore, based on the studies described above a decrease in protective gut bacteria and occipital activation in the brain can be linked to the development of cognitive disorders, like Alzheimers. The present study focuses on the effect of gastroduodenal stimulation to increase the activation of the occipital region of the brain and its possible effect on Alzheimers.

Materials and Methods

Since this experiment is hypothetical and does not take place in real life, the materials and methods have been extracted from research articles written by Li, Jianying et al., from a paper published under the NIH and by Mayeli, Ahmad, et al., researchers at the Laureate Institute for Brain Research (LIBR).

To study the decreased occipital activation in depressed patients:

In the current study using the experiment design inspired by Li, Jianying et al.,42 major depressive disorder patients completed the study, which consisted of 16 males and 26 females.

The average age range of 32.4 ± 10.1 years. The control group of 38 healthy human participants with a median age of 32.9 ± 9.2 years was also considered. The depressed patients had an average Hamilton Depression Rating Scale of 24.26 ± 6.47 and the control group had an average of 1.74 ± 2.15. Test of normality showed normal distribution in age, education duration and gender in two groups, with no significant differences (age, $t = –0.24$, $P = 0.811$; education duration, $t = –1.56$, $P = 0.122$; gender, $X2 = 0.456$, $P = 0.499$). (Li, Jianying et al.)

The participants were given negative, positive and neutral pictures to recognise. The total correct rate and misrecognition range was recorded of both the groups. Furthermore, those patients went through a functional MRI during the period of recognition of the pictures, to record the activation levels and regions of the brain.

To study the effects of gastroduodenal stimulation on the Parietal-occipital region of the brain:

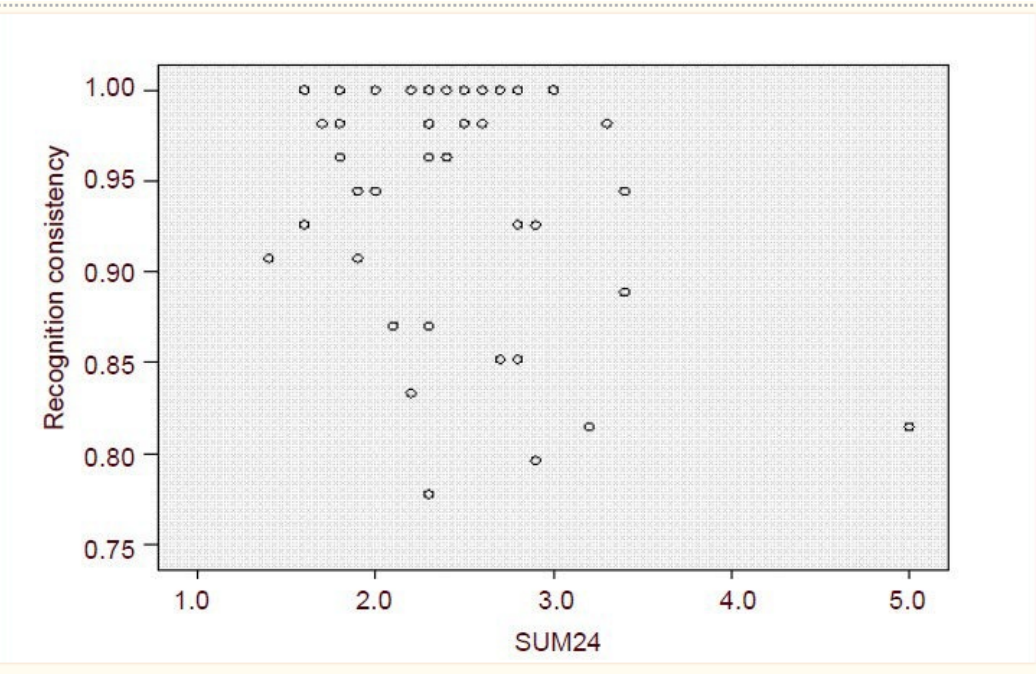
In the current study using the experiment design inspired by (Mayeli, Ahmad, et al.) ,40 healthy human participants, including 19 females and 21 males completed the study. The females had an average age of 22.90 ± 4.56 years and the males had a mean age of 24.3 ± 3.24 years, and the average BMI recorded of the whole group was 24.18 ± 3.03. To achieve gastroduodenal stimulation a non-invasive vibrating capsule was administered. The capsule had normal and enhanced settings. After the administration of the capsule, the participants were to press a button every time they felt some sensation. The perceptual accuracy of various other regions of the gut was also recorded which was accompanied with Gastrointestinal imaging to pinpoint the location of the capsule. Lastly, the effects on the brain as measured by evoked response potential (ERP) with the use of EEG. A 32-channel scalp EEG was used.

Results

Although the experiments conducted in this study are a replication of other experiments (Mayeli, Ahmad, et al.) and (Li, Jianying et al.), the study is hypothetical.

Depressed patients showed an increase in misrecognition of the images:

The depressed group had a lower total correct rate than the control group by $P < 0.05$. Additionally, the depressed group showed to have a higher misrecognition rate of 17.21 ± 12.97, where they recognized positive pictures as negative. There was a significant difference in the misrecognition rates between the two groups, as the control group had a misrecognition rate of 11.43 ± 8.30. This portrays their negative bias as well. Additionally, it was discovered that the misrecognition rate was directly proportional to the rating on the Hamilton Depression Scale. In other words, the recognition consistency is negatively proportional to the HAMD value, which means that the more the depressed patient, the more the misrecognition frequency. In the Hamilton Depression Rating Scale, scores of 8–20 represent normal, 20–35 represent possible depression, and > 35 represent depression (Zhang ZJ).

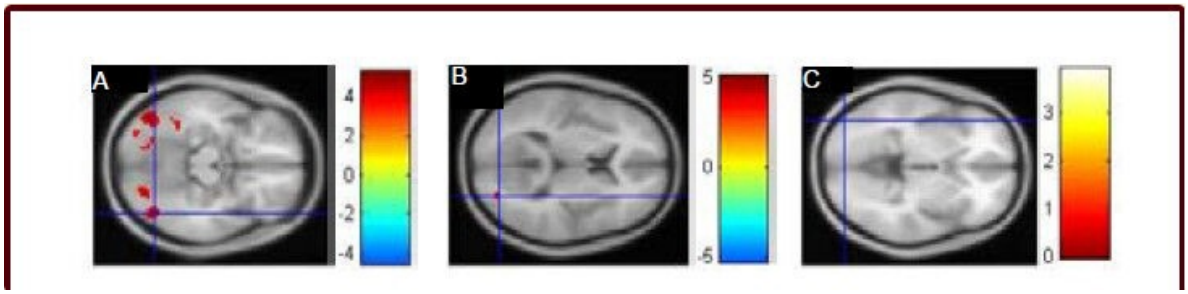


This figure taken from the experiment performed by Li, Jianying et al. shows that the recognition consistency is negatively proportional to the SUM24, which is the sum of the 24 items on the HAMD

Abnormal brain activity in depressed patients:

The participants of experiment 1 were put through a functional MRI scan and they were shown positive, neutral, and negative images, to record brain activity of different regions to compare the results with the control group. When the patients were recognizing positive and neutral images

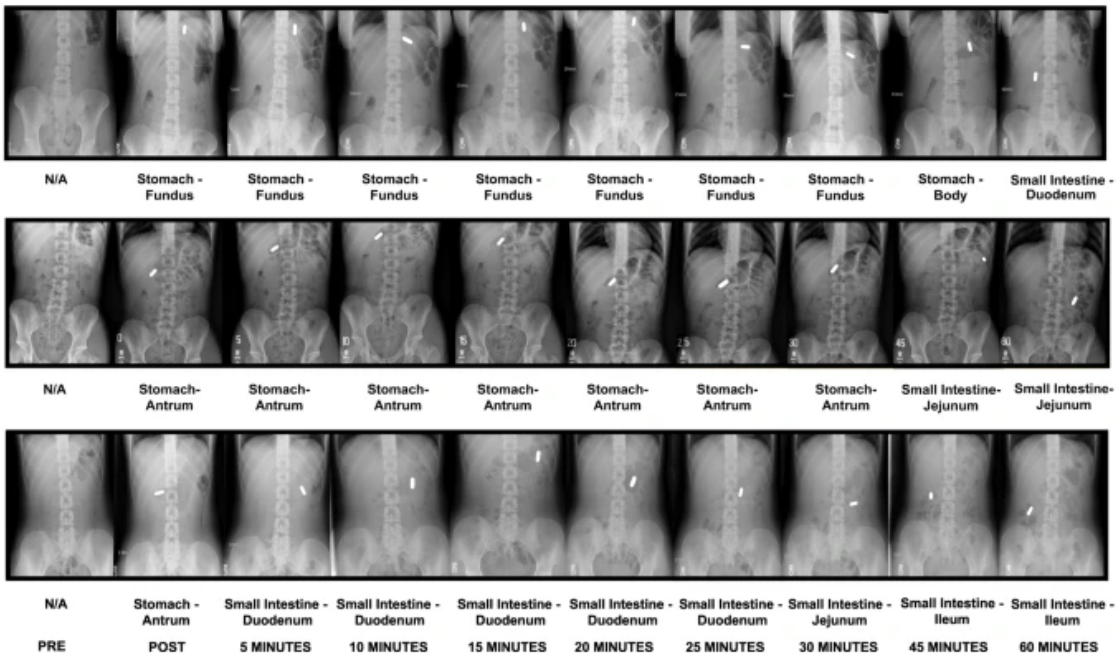
there was a comparative decrease in the activation of the parietal-occipital region of the brain, when compared to the control group. And when the patients were shown the negative pictures, a decrease in the activation of the occipital region was recorded in the depressed set, whereas the control group had a higher activation. Therefore, overall there was a general decrease in the occipital activation in depressed patients while they were recognizing pictures.



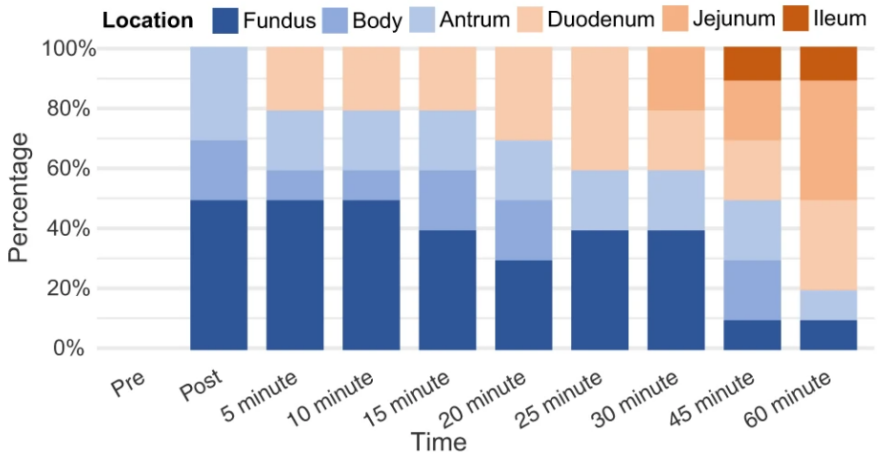
This figure taken from the experiment performed by Li, Jianying et al. show the decreased activation in the occipital region of the brain of depressed patients. The patients are shown positive (A), neutral (B), and negative (C) pictures. Colored bars reflect *T* scores for each analysis: higher *T* values represent higher intensity.

Perceptual accuracy and latency in response to intestinal sensations by the vibrating capsule: The study showed that the participants could detect sensations at normal and enhanced vibration frequency, but there was an increase in accuracy with the enhanced setting. The patients, however, also show a latency in response in both the normal and enhanced setting of an average of 1.06 ± 0.33 seconds and 0.74 ± 0.23 seconds respectively. This shows that there was a decrease in latency in the enhanced conditions.

A subset of the patients were also given abdominal X-rays to track the location of the capsule. When the effect on the brain due to stimulation was studied with the use of EEG, it was found that the stimulation caused the formation of GEPs in the parieto-occipital region of the brain and most of these signals (80%) originated due to a stimulation in the gastroduodenal region.



This image is taken from the study performed by Mayeli, Ahmad, et al. and it portrays the position of the vibrating capsule in 3 patients over the time period of 60 minutes while lying supine.



This graph from the same study shows a detailed illustration of the location of the capsule in the small intestine. It relates the percentage of patients and the location of the capsule with respect to time.

Discussion

From the above experiments and results, we know that depression causes a decrease in the activation of the parieto-occipital region in the brain and that the stimulation of the

gastroduodenal region of the brain. As studied by (Li, Jianying, et al.), depressed patients that have decreased occipital activation might have a risk of developing cognitive disorders like Alzheimer's.

Therefore with the use of gastroduodenal stimulation, there will be an increase in Parieto-Occipital stimulations in patients with depression, which with further detailed studies can be linked to having an effect on the development of Alzheimer's.

The different mechanosensory properties of the gastrointestinal region can be further studied in detail to discover its effects on other neurological or cognitive disorders. This method of non-invasive mechanosensory stimulation can further pose an integral base for the study of the GBA in the future.

Works Cited

Mayeli, Ahmad, et al. “Parieto-Occipital ERP Indicators of Gut Mechanosensation in Humans.” *Nature News*, 13 June 2023, www.nature.com/articles/s41467-023-39058-4#citeas.

Griffiths, Jessica A., and Sarkis K. Mazmanian. “Emerging Evidence Linking the Gut Microbiome to Neurologic Disorders - Genome Medicine.” *BioMed Central*, 21 Dec. 2018, genomemedicine.biomedcentral.com/articles/10.1186/s13073-018-0609-3.

Gut–Brain Axis as a Pathological and Therapeutic Target For ..., www.semanticscholar.org/paper/Gut%E2%80%93Brain-Axis-as-a-Pathological-and-Therapeutic-Toledo-Monroy/63d6c171f3f2901c9669620128c76d4cd19c194a. Accessed 27 July 2023.

Siba, Isadora P., et al. “When Gut Hormones Influence Brain Function in Depression.” *Applied Biosciences*, vol. 2, no. 1, Feb. 2023, pp. 31–51. *Crossref*, https://doi.org/10.3390/applbiosci2010005.

Carabotti, Marilia et al. “The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems.” *Annals of gastroenterology* vol. 28,2 (2015): 203-209.

Li, Jianying et al. “Abnormal activation of the occipital lobes during emotion picture processing in major depressive disorder patients.” *Neural regeneration research* vol. 8,18 (2013): 1693-701. doi:10.3969/j.issn.1673-5374.2013.18.007

Mercado-Perez, Arnaldo, and Arthur Beyder. “Gut feelings: mechanosensing in the gastrointestinal tract.” *Nature reviews. Gastroenterology & hepatology* vol. 19,5 (2022): 283-296. doi:10.1038/s41575-021-00561-y

Zhang ZJ. Beijing: Chinese Medical Multimedia Press; 2005. Behavioral Medicine Scale Manual.

Exploring the Impact of Cultural Stimuli on Brand Packaging through Neuromarketing Insights

Ria Patel (author), Thanisha Kapur (advisor)
Hightstown High School

Keywords: Neuromarketing, Cultural Stimuli, Product Packaging, Product Stimuli, Emotions

Abstract

This paper examines the application of neuromarketing and its impact on consumer preferences, specifically focusing on the role of cultural stimuli in product naming. A mixed-method approach was used to study this, including blindfolded product sampling and emotional response questionnaires. Results from 25 participants indicated that cultural stimuli significantly influence consumer perceptions and emotional responses to products. Branding is essential for building brand recognition, which can negatively or positively affect a consumer's behavior. This study underscores the significance of strategically incorporating cultural stimuli to enhance product design and brand loyalty.

Introduction

Neuromarketing refers to "the measurement of physiological and neural signals to gain insight into customers' motivations, preferences, and decisions, which can help inform creative advertising, product development, pricing, and other marketing areas" (Harrell). Although the ancient Egyptians created the term neuroscience, the term neuromarketing was coined when, in 2002, Dutch marketing professor Ale Smidts established the technique as an integral method of product communication (Wiktionary). As neuromarketing became more popular, brain imaging techniques were used to watch which neural circuits lit up or went dark during the purchasing process. To do this, functional magnetic resonance imaging machines (fMRI) and the electroencephalogram (EEG) were used (Harrell). The fMRI measures the small changes in blood flow that occur with brain activity ("Functional MRI (fMRI) of the brain"), and the EEG detects abnormalities in brain waves ("Electroencephalogram (EEG)"). As the development of neuromarketing became more widespread as it revealed insights into the subconscious mind, many marketers started implementing neuromarketing into product design testing, optimizing

“call to actions,” and rebranding campaigns (Lutkevich). Yet, it is important to recognize that neuromarketing is not a “one-size-fits-all approach” and can significantly vary across different industries and product categories based on cultural stimuli. Cultural values and norms shape individuals’ preferences and perceptions, resulting in different cultures’ unique value systems and means influencing consumer preferences and decision-making processes. Neuromarketing studies help uncover how cultural stimuli interact with consumers’ neural responses, which sheds light on the underlying mechanisms of consumer behavior. Therefore, it is necessary for marketers and researchers to understand these differences in individuals as it allows them to tailor their strategies based on neuroscientific findings, resulting in improved product design, more impactful marketing campaigns, and an overall satisfactory consumer experience. Therefore, this paper intends to study the application of neuromarketing to reveal and impact consumer preferences for products based on cultural stimuli.

Materials and Methods

Study Design

This study aims to investigate how factors such as sensory perception and cognitive decision-making processes influence neuromarketing applications. By investigating these factors, marketers can better understand how consumers respond to different stimuli. This knowledge can help develop more effective marketing strategies aligning with consumers' sensory perceptions and preferences. To investigate the application of marketing on different product categories, a two-part, mixed-method approach consisting of an experiment of different branded products and a participant-filled questionnaire was conducted to analyze the emotional and cognitive aspects of marketing.

Subjects

The chosen individuals for this experiment included students from various schools and adults outside the educational field. This demographic of participants was selected to participate in an experiment and fill out a questionnaire to receive an overall conclusion on the influences of cultural stimuli on consumer perception regardless of confounding variables such as age, gender, or race. A total of 25 participants took part in the experiment.

Research Instruments

The experiment included the following products and compared their differences: Packaged water (Poland Spring versus Nestle water), chocolate (Hershey versus Cadbury), sunscreen (Coppertone Sport versus Equate), gum (Extra versus Trident), and concealer (Nars versus Maybelline) to have a diversity of different product types and styles. Each participant was given the same quantity of each product to eliminate possible confounding variables. Participants were first asked to rate their emotions on the products before knowing the brand names. Then participants used the same survey and were asked to rate their feelings and favorite brand from the two choices after knowing the product names.

Subjects

The experiment was administered to people living in the tri-state area. For ethical considerations, participants were asked for their consent. Then participants were blindfolded and invited to sample two products in the same category, and this process was done to all five categories (water, chocolate, sunscreen, gum, and makeup). For example, in the water category, Poland Spring was water bottle one, and Nestle was water bottle two. After tasting both waters, participants were asked to record which water bottle brand they preferred. This process was done for all the different product categories. Looking at Table 2, Product 1 is the first listed in the parenthesis under the research instruments category, and Product 2 is the second listed in the parenthesis (Coppertone Sport- Product 1 and Equate-Product 2). After recording their responses, participants repeated the same procedure with their blindfolds off so they could see the brand names of the products. From there, participants recorded the emotions they felt in the same questionnaire they were given before.

Data Analysis

Table 1 presents a selection of emotional responses obtained from participants who viewed the products. The emotions are categorized as positive or negative based on Plutchik's Wheel, which encompasses eight primary emotions, including joy, trust, fear, and surprise, as well as negative emotions like sadness, anticipation, anger, and disgust (Karimova & Millacci, 2017). This categorization system allows marketers and advertisers to understand the extent of cultural stimuli on emotional response.

Table 1: Positive or Negative Connotations of Emotions

Emotion	Positive or Negative
Anger/Irritation	Negative
Contempt/Scorn	Negative
Disgust/Repulsion	Negative
Envy/Jealousy	Negative
Guilt/Remorse	Negative
Embarrassment/Shame	Negative
Worry/Fear	Negative
Sadness/Despair	Negative
Pity/Compassion	Positive
Involvement/Interest	Positive
Amusement/Laughter	Positive
Pride/Elation	Positive
Happiness/Joy	Positive
Enjoyment/Pleasure	Positive
Tenderness/Feeling Love	Positive
Wonderment/Feeling Awe	Positive
Feeling Disburdened/Relief	Positive

Astonishment/Surprise	Positive
Longing/Nostalgia	Positive

Table 2 illustrates the percentages of positive and negative responses obtained from participants before their knowledge of the brands. As explained in Table 1, participants were presented with various products and asked to choose an emotion from Plutchik's Wheel, which includes both positive and negative emotional responses. The emotion they selected was associated with the product type. The percentages of positive and negative emotions were then calculated. For each product, the category (positive or negative) that received the highest number of responses determined the overall connotation associated with the product.

Table 2: Percentages between product types (Positive or Negative) n=25

Product Type	Positive	Negative	Overall
Poland Water: Water Bottle 1	56.7%	43.3%	Positive
Nestle Water: Water Bottle 2	61.4%	36.8%	Positive
Cadbury Chocolate Bar (milk chocolate) Chocolate 2	70.9%	29.1%	Positive
Hershey Chocolate Bar (milk chocolate): Chocolate 2	66.39%	33.6%	Positive
Coppertone Sport Sunscreen (Spray):	84.4.%	15.5%	Positive

Sunscreen 1			
Equate Sunscreen (Spray): Sunscreen 2	41%	59%	Negative
Extra Spearmint Gum: Gum 1	59.8%	40.1%	Positive
Trident Spearmint Gum: Gum 2	63%	37%	Positive
Nars concealer: Concealer 1	69.2%	30.8%	Positive
Maybelline concealer: Concealer 2	47%	53%	Negative

Table 3 presents the percentages of positive and negative responses for various products, taking brand knowledge into account. As explained in Table 1, participants were provided with a range of emotions based on Plutchik's Wheel, encompassing both positive and negative emotional responses when viewing specific products. Participants were then asked to associate an emotion with each product category (e.g., water bottle, sunscreen, etc.). Subsequently, the positive and negative emotions percentages were calculated based on participants' selections. The category (positive or negative) that received the highest number of responses determined the overall connotation associated with each product.

Table 3: Percentages between product types with knowledge of the brands (Positive or Negative) n=25

Product Type	Positive	Negative	Overall
Poland Water: Water	68.2%	31.8%	Positive

Bottle 1			
Nestle Water: Water Bottle 2	43%	57%	Negative
Cadbury Chocolate Bar (milk chocolate) Chocolate 1	82.7%	17.3%	Positive
Hershey Chocolate Bar (milk chocolate): Chocolate 2	34.7%	65.3%	Negative
Coppertone Sport Sunscreen (Spray): Sunscreen 1	94%	6%	Positive
Equate Sunscreen (Spray): Sunscreen 2	31%	69%	Negative
Extra Spearmint Gum: Gum 1	61.5%	38.5%	Positive
Trident Spearmint Gum: Gum 2	27.6%	72.4%	Negative
Nars concealer: Concealer 1	70.4%	29.6%	Positive
Maybelline concealer: Concealer 2	13%	87%	Negative

Results and Discussion

After viewing the results of participants' perceptions of two-similar-like products without

knowledge of their brands, it appears that most products positively impact consumers. According to Table 2, both water bottles, chocolate bars, and gum products all received a positive connotation. For example, 56.7% of participants rated the Poland Spring water bottle, while 43.3% rated it as negative. Similarly, 61.4% of participants rated the Nestle water bottle as positive, and 36.8% rated it as negative. However, with the sunscreen and concealer, product 1 received a positive connotation compared to product 2, which received a negative connotation. For example, 69.2% of participants viewed Nars as positive, while only 47% viewed the Maybelline concealer as positive. Therefore, this table shows that prior knowledge of product branding does not significantly impact skin and makeup products' positive or negative impact but rather the product itself. These results indicate for food products, two similar products generally receive a positive connotation and that branding and cultural stimuli do not alter results. However, for skincare and makeup, the connotation is based on the quality of the product rather than the similarities between the two products. Therefore from this table, it can be concluded that for the beauty industry, marketers should focus on the product type and quality rather than the branding itself.

The results also indicate that knowledge of the brands alters consumers' positive or negative brand connotations. Regardless of their categories, knowledge of the brandings did indicate negative responses for all product number 2 types. According to Table 2, the Hershey Bar before brand knowledge received 66.39% of participants viewing it as positive, while 33.6% of participants viewed it as negative. The Cadbury bar similarly received 70.9% of participants viewing it as positive, with only 29.1% viewing it as negative. However, when participants learned about the brands, their perception of the Hershey and Cadbury bars changed. According to Table 3, compared to the Cadbury chocolate bar, Hershey received 34.7% of the same participants rating the bar as positive but 65.3% rating the bar as negative. The difference between the Hershey Bar's percentages of 33.6% of negative responses before the knowledge of the Hershey brand to 65.3% with the knowledge indicates that the cultural stimuli of brand marketing do influence consumer's perception of products. Although the results indicate that the perception of skin care products is not necessarily influenced by product name, the distribution of percentages suggests that the brand name and cultural stimuli play a role in consumers' product preferences. For example, before the participants learned the brand names, Concealer 1

received 69.2% of participants rating it as positive and 30.8% as negative. However, Concealer 2 received 47% of participants who viewed the product with a positive connotation, and 53% of participants regarded the product as negative, giving Concealer 2 a negative connotation. Although the positive connotation for Concealer 1 (Nars) and Concealer 2 (Maybelline) did not change with the brands' knowledge, the percentage distribution was drastic. According to Table 3, Nars received 70.4% of participants rating it positively, while 29.6% viewed it as negative. However, Maybelline received 13% of respondents viewing it as positive, while 87% viewed the product as negative. The difference between 47% positive and 13% positive for the Maybelline concealer indicates that although cultural stimuli do not change the perception of a product as being either positive or negative, the amount of emotional responses and their percentages varies significantly. Therefore it can be concluded that through the application of neuromarketing and participants' emotional responses to different products, cultural stimuli impact consumer preferences for different categories as people tend to have a pre-existing bias on certain products based on their branding.

Limitations

It is worthwhile to mention that some participants abstained from participating in the experiment. Participants were asked on a local scale, but only some who were asked completed the experiment. Although the data of 25 participants were proportionally analyzed, more data could have been examined had all prospective respondents participated. Additionally, another limitation of this study was the resources permitted. In this experiment, had a fMRI machine and EEG been available, participants' brain waves and blood activity could have been measured. Without these two machines, the full extent of studying the neurological effects of brand packaging could not be analyzed. However, based on pre-existing research such as the Coca-Cola and Pepsi experiment, the Product 1 category (Poland Spring, Cadbury, Coppertone Sport, Extra, and Nars) would have exhibited a stronger brain response in the ventral putamen when participants were unblinded just how Coca-Cola did.

Implications

The findings of this study offer valuable insights for marketers and advertisers, highlighting the importance of deliberately incorporating strong cultural stimuli in packaging and branding to

enhance business promotion. The brand name subconsciously impacts consumers' emotional responses and behavior, influencing sales and brand recognition positively or negatively. By strategically using cultural stimuli, marketers can create a sense of urgency and excitement in consumers, leading them to favor one product over another. Furthermore, cultural stimuli play a vital role in establishing brand recognition, making it easier for consumers to recall and choose a specific product. This recognition can result in repeat purchases and long-term loyalty. Understanding the interplay between cultural stimuli and consumers' neural responses can also improve product design, ensuring products resonate more effectively with their target audience. Importantly, this study emphasizes to marketers and advertisers the significant role of brand names in shaping consumer product preferences. It is valuable to mention that awareness of the intentional use of brand names to increase profits can empower consumers to make more informed choices about their purchases, encouraging them to consider the underlying influences behind their decisions.

Conclusion

The results from the experiment and the survey strongly suggest that cultural stimuli do play a role in consumer preferences in the product section. In the study conducted by neuroscientists at the Baylor College of Medicine in Houston, it was found that when Pepsi and Coca-Cola were both compared, the “Coca-Cola brand [was] so attractive [because] it [overrode] what our taste buds [tells] us” (The Lancet Neurology). This study extends the Coca-Cola and Pepsi experiment; via this study, it is evident that brand naming increases consumers’ emotional responses, and the emotional response is what overrides consumers’ taste buds. This study included only the visual aspect of neuromarketing: brand name. Researchers wishing to continue this research area should explore the other senses and their impacts on consumer purchasing decisions. Although this study aimed to research cultural stimuli globally, most participants were from the United States. Therefore, future researchers should explore the cultural differences between stimuli and brand marketing. Also, future researchers can specifically look at different cultural stimuli, including packaging, logos, and colors, and their differences among people. Expanding research in these areas can lead to a more comprehensive understanding of how neuromarketing and cultural stimuli interact to shape consumer preferences and inform effective marketing strategies worldwide.

Works Cited

"‘." ′ - *Wiktionary*, https://www.boonmind.com/a-brief-history-of-neuromarketing. Accessed 9 July 2023.

".,:;"-.'" .,.:;"-′ - *YouTube*, 22 June 2023, https://www.thelancet.com/action/showPdf?pii=S1474-4422%2803%2900643-4. Accessed 30 July 2023.

"Electroencephalogram (EEG)." *Johns Hopkins Medicine*, https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/electroencephalogram-eeg. Accessed 9 July 2023.

"Functional MRI (fMRI) of the brain." *RadiologyInfo.org*, https://www.radiologyinfo.org/en/info/fmribrain. Accessed 9 July 2023.

Harrell, Eben. "Neuromarketing: What You Need to Know." *Harvard Business Review*, 23 January 2019, https://hbr.org/2019/01/neuromarketing-what-you-need-to-know. Accessed 9 July 2023.

Karimova, MA, and Tiffany Sauber Millacci. "The Emotion Wheel: What It Is and How to Use It [+PDF]." *Positive Psychology*, 24 December 2017, https://positivepsychology.com/emotion-wheel/. Accessed 30 July 2023.

Lutkevich, Ben. "What is Neuromarketing? Definition & Examples." *TechTarget*, https://www.techtarget.com/searchcustomerexperience/definition/neuromarketing. Accessed 9 July 2023.

"Pepsi vs Coke: A Neuromarketing Study." *Neuroscience*, 29 November 2019, https://www.neuroscience.org.uk/pepsi-vs-coke-a-neuromarketing-study/. Accessed 21 July 2023.

Effects of Sexual Abuse in Children

Roshny Saha (author), Thanisha Kapur (advisor)
High School for Health Professions and Human Services

Keywords: Child sexual abuse, developmental psychopathology, neurobiology, neuroimaging

Abstract

Child sexual abuse (CSA) is a major public health issue that has long been associated with neurobiological, developmental, and psychiatric problems. The current review examines the long-term effects of CSA from the perspectives of development, psychiatric morbidity, neurochemistry, and neurobiology. The role of several neurotransmitters affected by CSA, including serotonin and dopamine, is explored. Serotonin abnormalities have been identified in several investigations among CSA individuals. Prefrontal cortex, superior temporal gyrus, corpus callosum, parietal lobes, hippocampus, and cerebellum all show volumetric and structural alterations in response to CSA trauma. This review attempts to construct a developmental trajectory framework that is unique to each scenario where CSA exposure may result in psychopathology and psychiatric morbidity later in life.

Introduction

Child sexual abuse is a global issue that frequently defies beliefs and prejudices, and it does not appear to be lessening with time. There are several definitions of CSA, which complicates testing, assessment, and therapy. Globalization and contemporary technology may raise the potential of abuse and exploitation, but they may also provide opportunities to enhance our responses, especially in low-resource countries. There are many different types of CSA which assure that there'll be different outcomes on how it affects the child. In addition, the age of the child and assaulter along with the gender and relationship will affect the outcome. The relationship between the child and the assaulter and how often the abuse happens will affect the outcome as well. Neuroimaging studies have uncovered a plethora of evidence linking childhood sexual abuse to structural abnormalities in the brain. Childhood sexual abuse impacts brain development, resulting in changes in brain structure and functioning that have long-term implications for mental health.

Body

What are the risks of CSA?

Identifying risk factors for childhood sexual abuse (CSA) is essential for developing preventative strategies. This study explored the relationship between a range of putative risk factors and CSA in a community sample of women using multivariate analysis and completely operationalized variables. Physical abuse, having a mentally ill mother, not having someone to confide in, and being socially isolated all had a significant impact on CSA. With the exception of physical abuse, there were several predictors of abuse before and beyond the age of 12. Before the age of 12, social isolation and the loss of a mother were major predictors of abuse, whereas physical abuse and a mentally ill mother were strong predictors of CSA after the age of 12. Physical abuse, no one to confide in, a lack of loving female adults, and an alcoholic father were all significant predictors of CSA for family member abuse. Physical abuse, social isolation, mother loss, and having an alcoholic mother were all strong indicators of maltreatment by someone other than family for boys and girls. These risk factors also come along with effects when growing up. Child sexual abuse is an issue on a national and global scale. The authors of this review note that, while empirical research has clearly shown that child sexual abuse has a negative impact on social, psychological, and sexual functioning later in life, it has also been reported that some individuals remain asymptomatic despite a history of child sexual abuse. This means that unfavorable consequences later in life are not unavoidable, emphasizing the crucial need to understand how resilience might mitigate the detrimental effects of child sexual abuse. This review, in addition to emphasizing the role of resilience, emphasizes the importance of cultural context in understanding child sexual abuse, as there are recognized risk factors and protective variables particular to different cultures. The percentage of CSA survivors reported to have a normal level of functioning despite a history of sexual abuse ranged from 10% to 53% in the research included in this study. Education, interpersonal and emotional competence, control beliefs, active coping, optimism, social connection, external attribution of blame, and, most crucially, support from family and the wider social environment were shown to have the best empirical support. Preventive and therapeutic therapies for CSA survivors should include psychoeducation and cognitive methods that are tailored to the victim's developmental level and aim to increase social support from important people. Future research should concentrate on

longitudinal designs that see resilience as a dynamic process with numerous aspects in a social and developmental context.

Brain Impact

To know what kind of help to give a victim of child abuse, you need to know what exactly happened to the child. The impact of sexual abuse can take many forms, such as emotional, social, and also physiological. Your stress reaction and alertness to danger work together to keep you safe in a typically "balanced" neurological system. When you go through a traumatic event, like CSA, it stresses your brain. Victims of CSA usually go through “body dysregulation” which is when children and adult survivors respond to stimuli in their everyday lives to an exaggerated degree. Within the human mind, the brain structure can be affected. The human brain is the central nervous system hub. You experience fear or panic in situations when you should experience fear or panic. Many survivors are hypersensitive to noises, smells, tastes, and sensations that are generally harmless or do not warrant such a strong reaction. Sexual abuse has an impact on numerous systems inside the human psyche. These structures serve specialized functions during a kid's development, and injury to them as a youngster, while not irreparable, poses significant cognitive issues as they age. For nearly a decade, neurophysiological research on child survivors has been continuing. Neuroscientists such as Dr. Martin Teicher of Harvard and Dr. Bruce Perry of the Child Trauma Academy in Houston demonstrated direct links between childhood maltreatment and aberrant brain development at the time. The amygdala, for example, is an almond-shaped region in the brain that manages the brain's response to stress. As previously stated, the neurological system of a sexually abused person tends to respond to safe occurrences and ordinary sensations with a "Code Red" stress reaction. Damage to the amygdala has been linked to these out-of-control emotions, according to research. Essentially, the amygdala transmits messages of danger to the child's brains even when there is no risk. According to Dr. Bruce Perry, an abused child's amygdala causes them to "recoil in fear at the drop of a hat". They are "hypersensitive" to tiny dangers. Other brain areas are also affected by childhood sexual abuse. The cortex is in charge of the vast bulk of our logical decision-making, planning, and analytical skills. The hippocampus is a deep-brain region that aids in emotion and memory processing. These frameworks collaborate to assist children and adults in learning new skills. The stress of abuse weakens certain areas of the brain. With a harmed capacity to learn,

abused children and adult survivors have an uphill struggle in learning coping strategies and new ways to frame their experiences, with or without treatment. Brain structures are not the only ones that are abused. Chemicals within the brain are critical for development and are also under threat. Cortisol, for example, is the hormone responsible for our stress response. Cortisol is created more in the brains of abused children and adults than in the brains of persons who have never been mistreated. Other neurotransmitters including serotonin, adrenaline, and dopamine help govern our positive moods and sense of accomplishment. Abused brains produce less of these neurotransmitters, which can contribute to sadness or "impulsive aggression" later in life. Furthermore, extremely high doses of stress hormones alter a child's brain circuitry.

Neurocognitive Findings.

Recent cognitive neuroscience and cognitive psychology research may help explain why recovered memories of trauma are sometimes illusory. Current neuroscience research is centered on developing techniques to avoid or counteract the negative effects of childhood stress on the central nervous system. The discovery of the neurological foundations of early unpleasant experience is critical for developing innovative therapies for children, adolescents, and adults. Significant progress has been made in understanding the neurological foundation of mood and anxiety disorders, as well as the impact of life events on risk and resilience. Persistent sensitization of neural circuits involved in the regulation of stress and emotion as a result of early life stress may represent the underlying biological substrate of an increased vulnerability to subsequent stress as well as the development of depression and anxiety. The concept of poor source monitoring, in particular, has been utilized to explain a wide range of recently established memory distortions and illusions. Alternatively, the findings of a number of studies, including those revealing lower hippocampus volume in survivors of sexual abuse and recovery from functional and organic retrograde amnesia, may be related to forgetting and recovery of accurate memories.Other recent discoveries of interest include the idea that stress-related hormones can create state-dependent memory, new pharmacological models of dissociative states, and evidence for "repression" in patients with right parietal brain damage. The Cambridge Neuropsychological Test Automated Battery and the Wide Range Achievement Test-3 were used to examine cognitive function and individual achievement in 47 healthy adults who were identified as part of a larger study from the general population. The findings show that physical and emotional abuse

may be linked to adult memory problems, which may be a risk factor for the development of psychopathology. One hypothesized mechanism by which these contextual events influence aggressive behavior during adolescence is changes in social cognition. Maltreated children have adversely biased socio-cognitive processing styles, which may increase their chance of reacting aggressively in uncertain social settings. It has been observed that memory changes in the form of dissociative amnesia are a significant component of traumatic stressors such as childhood abuse. Stress has a long-term impact on memory. These findings could give a model for understanding the mechanics underlying dissociative amnesia, as well as a justification for occurrences like delayed recall of childhood maltreatment. Investigating the impact of CSA on intellect, memory, cognitive skills, and cognitive processing is an intriguing avenue of research.

Conclusion

Child Sexual Abuse is one of the most damging to the neurological development a child can have. This is because of how many different outcomes a child can have based on the circumstances as it happened. Sexual abuse can have a variety of effects, including emotional, social, and physiological effects. In a usually "balanced" neurological system, your stress reaction and vigilance to danger work together to keep you safe. Abuse stress impairs key parts of the brain. Abused children and adult survivors have an uphill battle in learning coping mechanisms and new ways to frame their experiences, with or without treatment. Physical and emotional abuse is connected to adult memory impairments, which is a risk factor for the development of psychopathology. Changes in social cognition are one suggested mechanism through which these environmental events impact aggressive behavior during adolescence. Children who have been abused have negatively biased socio-cognitive processing styles, which may enhance their likelihood of behaving violently in uncertain social contexts. Memory abnormalities in the form of dissociative amnesia have been reported to be a prominent component of traumatic stresses such as childhood abuse. Stress has a long-lasting effect on memory. Learning more about how CSA affects the child as they grow older is interesting because there is so much that can happen to damage them both physically and mentally.

Works Cited

De Sousa, AvinashA, et al. "Child Sexual Abuse and the Development of Psychiatric Disorders: A Neurobiological Trajectory of Pathogenesis." Industrial Psychiatry Journal, vol. 26, no. 1, 2017, p. 4, www.ncbi.nlm.nih.gov/pmc/articles/PMC5810166/, https://doi.org/10.4103/ipj.ipj_38_15.

Edwards, Damyan. "Childhood Sexual Abuse and Brain Development: A Discussion of Associated Structural Changes and Negative Psychological Outcomes." Child Abuse Review, vol. 27, no. 3, May 2018, pp. 198–208, https://doi.org/10.1002/car.2514.

McKillop, Nadine, et al. "Comparing the Onset of Child Sexual Abuse Perpetration from Adolescence into Adulthood: Are There Unique Risks, and What Does This Mean for Prevention?" Child Abuse & Neglect, vol. 107, Sept. 2020, p. 104630, https://www.sciencedirect.com/science/article/abs/pii/S0145213420302854?via%3Dihub

Murray, Laura K., et al. "Child Sexual Abuse." Child and Adolescent Psychiatric Clinics of North America, vol. 23, no. 2, 2014, pp. 321–337, www.ncbi.nlm.nih.gov/pmc/articles/PMC4413451/ , https://doi.org/10.1016/j.chc.2014.01.003.

Putnam, Frank. Ten-Year Research Update Review: Child Sexual Abuse. pdfs.semanticscholar.org/754a/984815c7fab512e651fc6c5d6aa4864f559e.pdf, https://doi.org/10.1097/01.CHI.0000037029.04952.72.

The Effects of Child Abuse on the Developing Brain – Keep Kids Safe. https://keepkidssafe.org/effects-of-child-abuse/

"What Places Youth at Risk? | Joshua Center on Child Sexual Abuse." Uwjoshuacenter.org, https://uwjoshuacenter.org/what-places-youth-risk Accessed 30 July 2023.

Exploring the Impact of The Gut-Brain Axis on Parkinson's Disease

Sachi Chauhan (author), Thanisha Kapur (advisor), Anika Shah (editor)
Del Norte High School

Keywords: The Gut-Brain Axis, Parkinson's Disease, alpha-synuclein, Neurodegenerative diseases

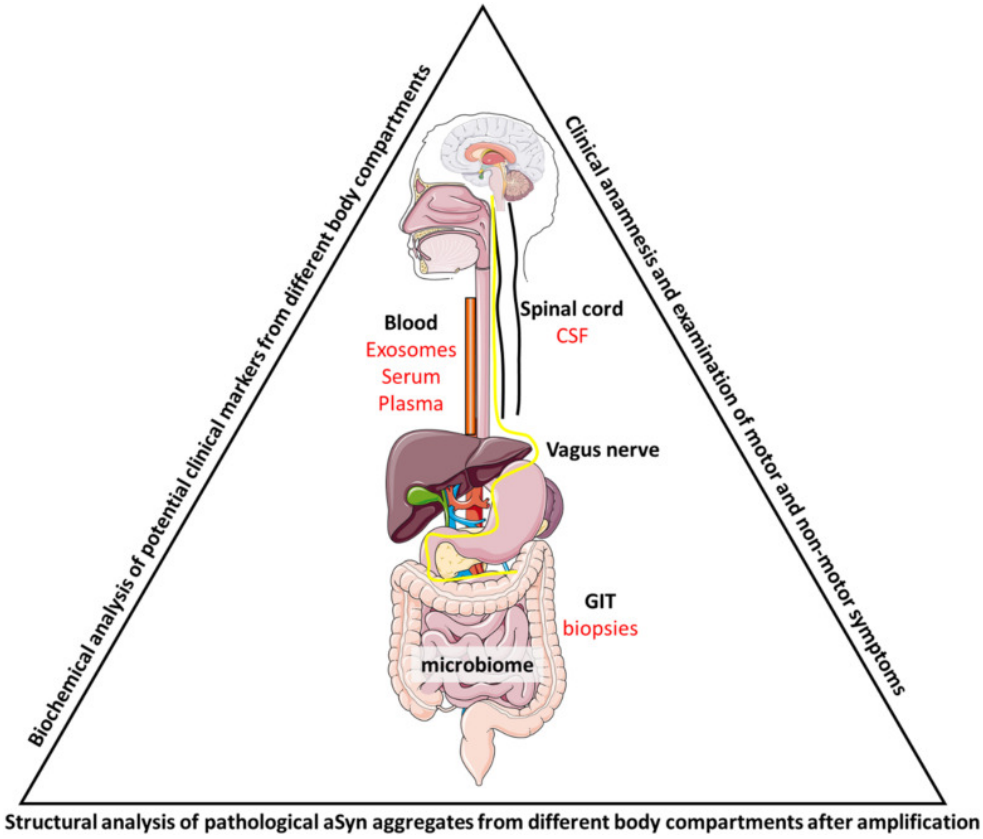
Abstract

Parkinson's Disease is a neurological disorder that causes uncontrollable movements and tremors. While its symptoms are caused by an irregular aggregation of alpha-synuclein protein in the brain, the primary trigger of the aggregation is largely unknown. However, recent studies have shown that Parkinson's Disease (PD) has some correlation with the gut, a possible location for the start of these protein aggregates. The connection between PD and the gut is facilitated through the Gut-Brain Axis. To investigate this theory, researchers have been conducting experiments on rodent models to understand the processes behind the aggregation, and whether or not the gut is something they can target in terms of treatments. Research behind this link holds promise not only for developing therapies for PD, but also for enhancing our understanding of various other neurological disorders and overall health.

Introduction

When making decisions the common advice is to "go with your gut", and nervousness often manifests itself as "butterflies in your stomach". While these expressions may sound idiomatic, recent studies have shown that there is an intricate connection between the gut and the brain known as the Gut-Brain Axis. This axis relies on bidirectional interactions between the enteric nervous system (ENS) and the central nervous system (CNS). The ENS is made up of a lining of neurons in the gastrointestinal tract, and is capable of some processes without the help of the CNS. The CNS, made of the brain and the spinal cord, communicates with the ENS through the vagus nerve, proteins, and neurotransmitters. This communication is integral to maintaining homeostasis and regulating various physiological and psychological processes. However, disruptions in the delicate balance of these microbiota, also known as dysbiosis, have been

increasingly associated with various neurodegenerative disorders, most notably Parkinson's Disease (Peterson, et al.). To unravel the intricacies of this relationship, scientists have been researching the cause of Parkinson's Disease and its possible relationship to the gut. By researching this new outlook on the disease, researchers aim to deepen their understanding of the disorder, uncover potential preventative measures, and ultimately, tailor personalized treatments.



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Body

What is Parkinson's Disease?

Parkinson's disease (PD) is a neurological disorder that causes involuntary or uncontrollable movements ("Parkinson's Disease: Causes, Symptoms, and Treatments | National Institute on Aging"). The symptoms of this disorder result from the death of neurons in the substantia nigra, a region of the midbrain that supplies dopamine to the basal ganglia, the part of the brain responsible for motor control. The exact cause of this cell death is poorly understood, but it involves the aggregation of a protein known as alpha-synuclein (α-Syn), into clumps called

Lewy bodies within neurons (Stefanis et al.). While the aggregation of α-Syn is understood, the primary trigger for this response is not.

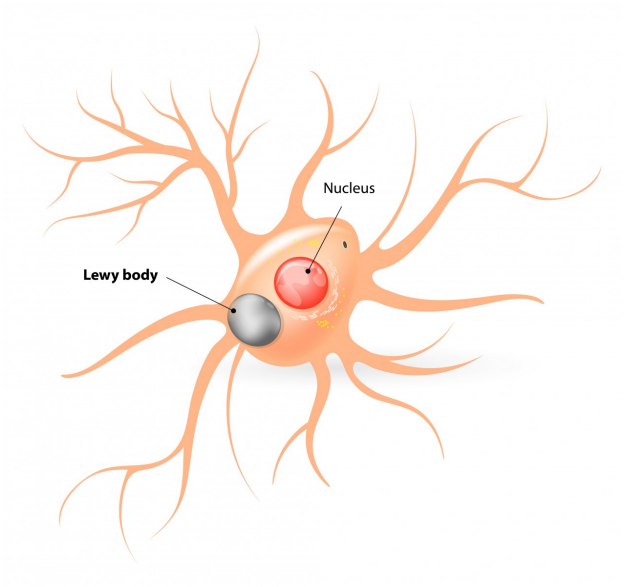


Image from:
https://alzheimersnewstoday.com/news/new-insights-into-dementia-with-lewy-bodies-parkinsons-disease/

The Gut and Parkinson's Disease

Patients are often diagnosed when they exhibit symptoms of movement impairment, but by this stage, they have already lost around 80 percent of the dopamine-producing cells in their substantia nigra ("Parkinson's Disease: Challenges, Progress, and Promise | National Institute of Neurological Disorders and Stroke"). To find a way to diagnose PD earlier, researchers surveyed some PD patients regarding their earlier symptoms. What they found was that 4 out of 5 patients were affected by at least one gastrointestinal issue before being officially diagnosed with PD (Schaeffer et al.). This symptom suggested a major correlation between the gut and PD, leading to research being done regarding their link. To explore this connection, two research teams conducted studies using rodent models to investigate the spread of α-Syn pathology from the gut to the brain. In the first study, conducted at Johns Hopkins University School of Medicine, researchers injected α-Syn preformed fibrils (PFFs), which are "pre-made" replications of the α-Syn protein, into the duodenum of the rodents (Kim, et al.). Around 1 month later, aggregates of α-synuclein were detectable in the dorsal motor nucleus of the vagus (DMV), a specific nucleus located within the lower part of the brain stem known as the medulla oblongata.

Afterwards, more aggregates were detected in the substantia nigra, which resulted in the loss of dopamine-producing neurons and also the emergence of motor and non-motor symptoms of PD. The spread of the α-synuclein pathology from the gut to the brain relied on the vagus nerve, which established that the nerve was the main facilitator of substances between the gut and the brain. In the second study researchers at Aarhus University in Denmark used transgenic rats with an overexpressed human form of α-synuclein, or rats that already contained some α-Syn protein prior to the injection (Van den Berge, et al.). These rats were injected with PFFs into the wall of their duodenum. The researchers anticipated that the excess gene in the rats would lead to α-synuclein aggregates, resulting in PD. When they conducted the experiment their hypothesis was affirmed and the rodent models showed that the α-synuclein pathology transferred from the gut to the brain, further confirming that the primary trigger for PD likely begins in the gut. But what researchers also found was that the α-Syn aggregates could move in the opposite direction, from the brain to the gut. This was significant as it proved that the connection between the gut and the brain is bidirectional, meaning the two impact each other equally. Both these studies have thus shown that a likely starting location for these aggregates is the gut and that going further, therapies and other forms of treatments could target the gut rather than the brain for safer and more efficient results.

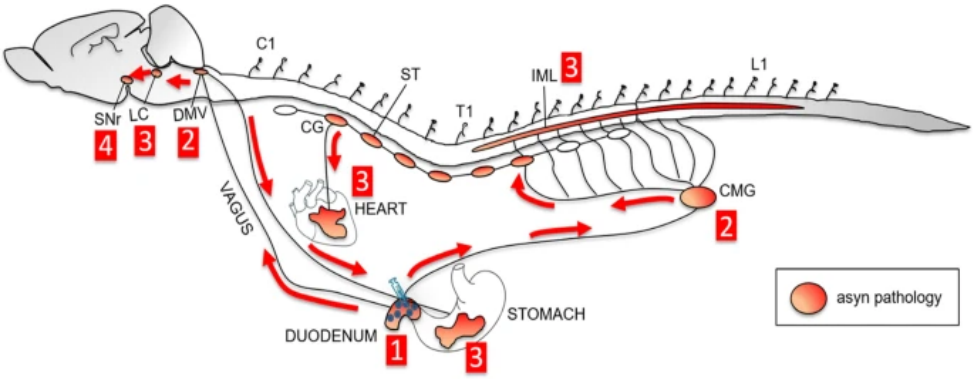
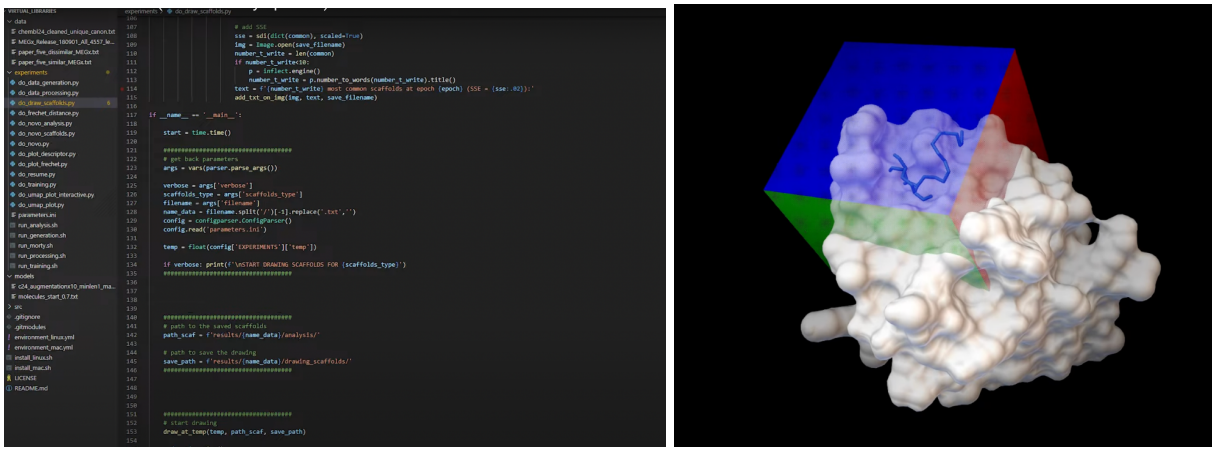


Image from: https://link.springer.com/article/10.1007/s00401-019-02040-w

Using AI to Treat Parkinson's Disease

Using the relationship between the gut and the brain, scientists have been trying to uncover new treatments and preventative strategies for Parkinson's Disease with the help of advanced technology. At the University of Queensland, scientists are in the process of creating an inhibitor molecule that can eliminate α-synuclein aggregates in the gut, to prevent the spread to the brain.

To accomplish this, they have been utilizing machine learning algorithms to generate hundreds of molecules for the α-Syn protein (Jewell, et al.). By inputting the protein target, an AI software produces a wide array of molecules with similar structures and high binding affinity. Then, from this vast pool of generated molecules, the research team selects the most chemically stable ones, and discards those that are unsuitable. When going through this process they take various factors into consideration, including the molecule's ability to cross the blood-brain barrier and its ability to pinpoint the α-Syn aggregate. Ultimately, their goal is to develop an optimal treatment that can effectively slow or halt the progression of Parkinson's disease.



Images from: https://www.thescienceofpsychotherapy.com/the-gut-brain-axis-documentary/

Conclusion

Looking forward, the Gut-Brain Axis seems to be a huge field of research that could result in possible treatments and preventative measures for not only Parkinson's Disease, but other neurological disorders as well. Many researchers have devoted their efforts to develop these treatments into drugs and test kits, aiming to make healthcare more accessible and widely available to the general public. One notable example is BrilliantBiome: a company founded by Dr. Sierra Simpson, a researcher at the University of California, San Diego, who focuses on creating gut microbiome test kits. These kits function in a way that is similar to DNA test kits; patients send over a sample of their microbiome, a lab analyzes it, and then creates a personalized report that simplifies the findings into more easily understood language. The reports include ways in which patients can balance mood and wellness, improve energy levels and metabolism, reduce bloating, and identify future disease risks. Altogether, kits like

BrilliantBiome can make healthcare more accessible and inform people on a healthy lifestyle that is best suited for their body.

Works Cited

Dahlitz, Matthew, director. "The Science of Us." *Episode 1 - The Gut-Brain Axis*, season 1, episode 1, The Science of Psychotherapy, 2021. *YouTube*, https://www.thescienceofpsychotherapy.com/the-gut-brain-axis-documentary/. Accessed 30 July 2023.

Inacio, Patricia. "New Insights Into Dementia with Lewy Bodies, Parkinson's Disease." *Alzheimer's News Today*, 3 December 2014, https://alzheimersnewstoday.com/news/new-insights-into-dementia-with-lewy-bodies-parkinsons-disease/. Accessed 30 July 2023.

Jewell, Shannon. "Inflammasome Activation in Parkinson's Disease." *PubMed*, 13 July 2022, https://pubmed.ncbi.nlm.nih.gov/35848038/. Accessed 30 July 2023.

Kim, Sangjune. "Transneuronal propagation of pathologic α-synuclein from the gut to the brain models Parkinson's disease." *Neuron*, 26 June 2019, https://www.cell.com/neuron/fulltext/S0896-6273(19)30488-X?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS089662731930488X%3Fshowall%3Dtrue. Accessed 30 July 2023.

"Parkinson's Disease: Causes, Symptoms, and Treatments | National Institute on Aging." *National Institute on Aging*, 26 July 2023, https://www.nia.nih.gov/health/parkinsons-disease. Accessed 30 July 2023.

"Parkinson's Disease: Challenges, Progress, and Promise | National Institute of Neurological Disorders and Stroke." National Institute of Neurological Disorders and Stroke, 30 January 2023, https://www.ninds.nih.gov/current-research/focus-disorders/focus-parkinsons-disease-research/parkinsons-disease-challenges-progress-and-promise. Accessed 30 July 2023.

Peterson, Christine Tara. “Dysfunction of the Microbiota-Gut-Brain Axis in Neurodegenerative Disease: The Promise of Therapeutic Modulation With Prebiotics, Medicinal Herbs, Probiotics, and Synbiotics.” NCBI, 22 October 2020, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7586271/. Accessed 30 July 2023.

Schaeffer, Eva. “Alpha Synuclein Connects the Gut-Brain Axis in Parkinson's Disease Patients – A View on Clinical Aspects, Cellular Pathology and Analytical Methodology.” NCBI, 8 September 2020, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7509446/. Accessed 30 July 2023.

Stefanis, Leonidas. “α-Synuclein in Parkinson's Disease - PMC.” *NCBI*, February 2012, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3281589/. Accessed 30 July 2023.

Van den Berge, Nathalie. “Evidence for bidirectional and trans-synaptic parasympathetic and sympathetic propagation of alpha-synuclein in rats.” *Springer Link*, 26 June 2019, https://link.springer.com/article/10.1007/s00401-019-02040-w. Accessed 30 July 2023.

Comparing Two Different Approaches for TBI Recovery and Neurogeneration

Saivarunteja Elagandula (Author), Thanisha Kapur (Advisor)

Bentonville High School

Keywords: intersection, TBI, bio-materials, Computational , Therapies, Neuroregeneration , Brain Damage, Limitations

Abstract

This literary review will discuss the intersection between computational therapeutics and biomaterial-based approaches for TBI recovery and neuroregeneration, which refers to the intertwining of two major technologies in the field of TBI recovery to develop a more personalized and targeted approach to recovery. In a person with a neurotypical brain, all of the neurons are working together and there is no damage to the nervous tissue. When a TBI happens, it can lead to lesions, the loss of crucial brain tissue, or cell death which can leave a patient heavily disabled or dead . When this damage occurs, the brain is slow to recover due to its restrictive abilities to regenerate neurons and nervous tissue. To assist in the recovery of neurons many biomaterials can be used to help with this process and deliver the necessary support or materials needed to regenerate damaged tissues. However biomaterial-based approaches come with inconsiderable amounts of variability and uncertainties. The additive tool of computational models can help to considerably decrease the gray area of biomaterial-based approaches and better understand how to treat the damaged tissue using biomaterials.

Introduction

Traumatic brain injuries result from a sudden jolt or blow to the skull. This sudden impact, delivered from an object or force, can cause bruising and hemorrhaging to the brain, leading to long term complications and complete loss of brain function. Approximately, 176 TBI-related deaths occur each day in 2020 (Peterson AB & Zhou H & Thomas KE, 2022). Along with the lethal outcomes of TBIs, 80% of many TBI related cases are miscategorized as mild head injuries. TBI mislabelling is a result of quick diagnoses and a lack of sophisticated and accurate understanding of the brain's present condition and mechanisms. TBIs are categorized into many forms including concussions, extra-axial hematoma, contusion, traumatic subarachnoid hemorrhage and diffuse axonal injury(Alan Georges & Joe M Das, 2023). Each type of injury damages nervous tissue in ways that affect different areas of the brain. Since different parts of the brain have different neurons that exhibit structural and functional diversity across various brain regions (Das & Ramanan, 2023), a targeted therapy would prove to be most effective. Additionally, a more personalized approach to TBI care is needed as patients can present with unique symptoms and reactions to treatments. Today's therapies lack this sense of a targeted approach and are more systemic. Commonly used therapies that are currently in practice include anticonvulsant therapy, osmotherapy, decompressive craniectomy, and anitibiotic therapy. All of these therapies are targeted towards helping relieve symptoms or prevent further damage to the brain, very few are tailored to each person. In this review, we are investigating the intersection between computational neuroscience and biomaterial-based approaches for traumatic brain injury for the development of more individualized therapies.

Body

Biomaterials and their limitations

Once a neuron is damaged there are many factors that hinder its ability to repair the damage. Some of the main factors are that the central nervous system has limited stem cell supply, growth signals may be impeded, and inflammation or scarring can slow the process down significantly. One of the main solutions to tackle these factors are biomaterial-based approaches that allow for neuroregeneration and the restoration of neuronal function (Galgano et al., 2017). These approaches can also provide structural support and guidance for axonal regeneration by facilitating the registration of stem cells and growth factors to the area of injury (Pepper et al. 2017, Wu et al., 2011). This can be particularly useful for diffuse axonal injury related TBIs as these are TBIs where the axon is injured or harmed, which would require the rebuilding and regeneration of parts of the neuron. Additionally, biomaterials can be engineered to mimic the extracellular matrix allowing for support in nervous tissue regrowth (Xiong et al., 2018). One type of therapeutic process is through the registration of mesenchymal stem cells which can be used to regenerate nervous tissue within the body as these cells can differentiate into cells needed for nervous tissue repair (Daniele Tartarini & Elisa Mele. 2016). Despite the vast amounts of research and promise biomaterials hold, many biomaterials face challenges such as biocompatibility issues, aggressive immunoreactivity, and struggles with the preservation of the biomaterial. However this issue can be solved by combining computational techniques to find the best biomaterial for the individual's anatomy and physiology. (Hasan Uludağ1, 2014)

Computational Therapies

Computational therapeutics refers to the use of computational models and simulations of the brain to understand the underlying mechanisms of certain TBI cases. Therapeutic measures can then be used to develop a personalized treatment plan (Xiong et al., 2015). These models can help in identifying genetic factors associated with TBI recovery and predicting the effectiveness of different therapeutic approaches, as well as provide an individualistic prognosis for the patient (Kurowski et al., 2017). By incorporating data from various sources, such as genomics, proteomics, and neuroimaging, computational models can explain the hidden mechanisms in the brain that are affected by a TBI (Kurowski et al., 2017). Computational models, however, still do have limitations. Computational models regularly oversimplify the mechanisms of the nervous system which obviously does not perfectly mimic this incredibly complex system. A secondary limitation comes from increasing the complexity of the model then decreases the readability of the model, which leads to increased difficulty with understanding the findings of the model. Finally running and creating these models are time extensive and require extensive financial support and expertise.

The intersection of Computational therapeutics and Bio-material Based Approaches

The combination of computational therapeutics and biomaterial-based approaches can enhance the effectiveness of TBI recovery and neuroregeneration strategies by allowing a deeper understanding of the cell's growth and how scaffolding biomaterials can be effectively chosen (Daniele Tartarini & Elisa Mele. 2016). Computational models can be used to optimize the design and delivery of biomaterials, taking into account factors such as administration route, dose, and time window (Galgano et al., 2017). These models can also predict the interactions

between biomaterials and the injured brain tissue allowing for a more personalized and specific selection of biomaterials for the brain region without subjecting patients to multiple failed surgeries. Many of today's computational models consider individual patient characteristics and genetic factors which can further increase the models' predictability of future outcomes. (Xiong et al., 2015). Using neuroimages, obtained by devices such as a 18-Fluoro-deoxyglucose positron emission tomography(FDG-PET), these models can detect any changes that are related to the TBI which can then be useful in deducing the specific needs of the patient(García-Panache et al., 2011).

Conclusion

In summary, the intersection between computational therapeutics and biomaterial-based approaches for TBI recovery and neuroregeneration involves the use of a computational model with a biomaterial based approach that can be effectively used to help heal the injury. As these technologies intertwine, a more personalized therapy emerges which is especially useful for the wide variety of TBIs.The future of medicine lies within individualized care and we need to continue to look for ways to center our treatments around our patients.

Works Cited

Das, Soumen, and Narendrakumar Ramanan. “Region-Specific Heterogeneity in Neuronal Nuclear Morphology in Young, Aged and in Alzheimer’s Disease Mouse Brains.” Frontiers, 20 Jan. 2023, www.frontiersin.org/articles/10.3389/fcell.2023.1032504/full.

Georges, Alan, and Joe M Das. “Traumatic Brain Injury - Statpearls - NCBI Bookshelf.” NIH, 2 Jan. 2023, www.ncbi.nlm.nih.gov/books/NBK459300/.

Peterson, Alexis B, et al. “Disparities in Traumatic Brain Injury-Related Deaths-United States, 2020.” *Journal of Safety Research*, Dec. 2022, www.ncbi.nlm.nih.gov/pmc/articles/PMC9795830/.

Uludağ, Hasan. “Grand Challenges in Biomaterials.” *Frontiers in Bioengineering and Biotechnology*, 17 Oct. 2014, www.ncbi.nlm.nih.gov/pmc/articles/PMC4202113/.

Ye Xiong, Yanlu Zhang, Asim Mahmood & Michael Chopp (2015) Investigational agents for treatment of traumatic brain injury, Expert Opinion on Investigational Drugs, 24:6, 743-760, DOI: 10.1517/13543784.2015.1021919

The Gut Microbiome's Effect on Neurological Disorders

Sanshray Mohapatra (author), Thanisha Kapur (advisor)
BASIS Peoria

Keywords: Gut Microbiome, Depression, Anxiety, Parkinson's Disease, Autism Spectrum Disorder

Abstract

The gut microbiome consists of all the microorganisms that live in the gastrointestinal tract of the human body. These microorganisms in the body don't just aid in digestion, but also partake in multiple signaling pathways. Some of these signaling pathways include the central nervous system(CNS). Many articles have already discussed the link between the gut microbiome and the nervous system through something called the gut brain axis. However, if the gut microbiome and the CNS can affect each other, this means that the gut microbiome can have an effect on many neurological diseases and disorders. Three disorders being looked at in this article are depression/anxiety, Parkinson's disease and autism spectrum disorder. When it comes to depression/anxiety, mouse models of this neurological disorder show that changes in the gut microbiota via fecal microbiota transplants(FMTs) have a direct impact on depression related symptoms. Microbiome changes in both Parkinson's disease and autism spectrum disorder mouse models/patients have shown to have an impact on their respective symptoms.

Introduction

What is the gut microbiome?

The gut microbiome includes all of the microorganisms that live in the gastrointestinal (GI) tract of the body. These microorganisms, mostly bacteria, interact with the body in a multitude of ways, ranging from communication with immune cells all the way to participating in signaling pathways. Most of these bacteria are commensal, or in other words, are neutral or beneficial bacteria, but in most cases harmful bacteria can also exist in the microbiome. The term dysbiosis refers to an imbalance between the beneficial and harmful bacteria of the gut microbiome, and it has been linked to many different diseases. Specifically, dysbiosis has been seen as a major indicator and factor in certain neurodegenerative diseases such as Parkisnon's disease, but it also

has been linked to other neurological problems such as depression, anxiety and even schizophrenia. However, dysbiosis becomes a confusing term as the gut microbiome becomes so variable from individual to individual, so it becomes extremely difficult to establish what constitutes a healthy gut. The main link between the central nervous system and the gut is facilitated through the gut-brain axis, in which bacteria in the gut can affect and mediate certain neural signaling pathways in a variety of ways. Most articles in the current literature have established a link between the gut-brain axis and diseases like Parkinson's. However, more study needs to be done to further explore this link. It becomes extremely important to review this link between the gut and the central nervous system in the context of neurodegenerative diseases as the gut microbiome may play a vital role in the diagnosis of such diseases or perhaps as a therapy treatment.

Body

The Gut Microbiome and Anxiety/Depression

The gut microbiome can communicate with the brain in many ways. Many articles have discussed how the gut microbiome affects numerous signaling pathways through the gut-brain axis. For example, Microbially derived molecules like short-chain fatty acids, secondary bile acids, and tryptophan metabolites play a key role in transmitting signals by interacting with cells in the gut and even neural networks.

The gut microbiome can affect many different aspects of neurology. For example, anxiety and depression are often associated with irritable bowel syndrome. Furthermore, there have been many preclinical studies that show some type of link between the gut microbiota and emotional behaviors and parameters that are related to depression. Due to this link, researchers are trying to affect the gut microbiota using fecal microbiota transplants. Studies show that transferring fecal microbiota from depressed individuals to rodents have caused similar emotional and depressive symptoms in these animal models. They also have looked at prebiotics and probiotics to improve these symptoms. In some individuals, prebiotics and probiotics have improved anxiety and mood. Looking more into certain bacteria, it has been seen that subtypes of E. Coli have actually exacerbated depressive symptoms.

Researchers took various mouse models of depression/anxiety and used behavioral tests to observe them. The first model used was a social defeat model which was achieved via fecal microbiota transplant or FMT. The behavioral test used was the forced swim test. The findings of this test were that the rats that underwent FMT from the vulnerable rats displayed depression-like characteristics compared to the control rats that got FMTs from the non-stressed rats. Researchers also took fecal microbiota from human depressive donors and placed it into mouse models vs FMT. They then took the animal models through a variety of tests (Elevated plus maze test Open field test Forced swim test) and the results showed that the transplantation of fecal microbiota from depressed patients to microbiota-depleted rats resulted in the recipient animals displaying behavioral and physiological characteristics typical of depression. Additionally, depression was linked to reduced richness and diversity of gut microbiota. In a chronic social defeat stress model, researchers found that chronic social defeat induced behavioral changes that were associated with reduced richness and diversity of the gut microbial community.

In conclusion, the gut microbiome can drastically increase the chances of and in some cases directly cause depression/anxiety. However, there needs to be further study into if and how FMTs can be used as potential treatments for drastic cases of depression/anxiety.

Parkinson's Disease

Another aspect of neurology that the gut microbiome can affect is Parkinson's disease. In Parkinson's disease, symptoms pertaining to the gut microbiome can drastically affect the patient and their quality of life. More importantly, symptoms like constipation appear years before the motor dysfunction that Parkinson's disease is known for. For this reason, studies have been looking into how the gut microbiome can be used to either diagnose or treat patients with Parkinson's disease (PD).

Researchers have specifically identified metabolites that induce PD symptoms FOr example, when FMT from PD patients were transferred into mice, there was a greater extent of motor dysfunction when compared to FMTs from healthy individuals. These results show a strong correlation between the gut microbiome and PD.

To further investigate this, a certain study took fecal samples from 6 PD patients and 6 controls and transplanted them into recipient mice. They proceeded to analyze these mice 16S rRNA sequencing was performed to analyze the microbial communities. The results showed that the mice profiles resembled their respective human donors' microbial profiles. More importantly, the disease status of the human donors had a major effect on the recipient mice, suggesting that human gut microbes can influence the constitution of other microbial communities. Furthermore, when testing the function of these microbiota, in four of six donor pairs, microbiota from PD patients led to increased motor dysfunction in the mice. This observation provides evidence supporting the functional contribution of the microbiota to neurodegenerative diseases, particularly in depleting motor deficits in the tested mouse model.

Autism Spectrum Disorder

The last neurological condition to be discussed is autism spectrum disorder , or ASD. ASD is a group of neurodevelopmental disorders that are known by difficulties in social interaction, verbal and nonverbal communication, and repetitive behavioral patterns. ASP patients can have other conditions like anxiety, depression, seizures , gut dysbiosis, and other gastrointestinal related issues such as diarrhea, constipation, abdominal pain, vomiting, bloating, reflux, or foul-smelling stools . Dysbiosis in particular which can be thought of as an unhealthy gut that contributes to disease-like symptoms happens independently of ASD gastrointestinal symptoms.

In one study, researchers used *Lactobacillus plantarum* which resulted in changes to the gut microbiota of ASD patients . This supplementation of this bacteria led to improvements in some GI symptoms and also surprisingly had an effect on the autistic behavior. In another study, supplementation of *Lactobacillus acidophilus* led to improvements in the cognitive ability to concentrate and follow instructions. Another study looked at *Lactobacillus rhamnosus* and supplemented this bacteria to infants during their first 6 months. This resulted in a reduced risk of developing Asperger's. Bacterial cocktails are starting to be looked at as therapy treatments for the GI symptoms of ASD patients. For example, a mixture of *Lactobacillus, Bifidobacterium,* and *Streptococcus* improved the quality of gut microbiota in autistic children and their severity of autism.

In conclusion, targeting the gut microbiome via bacterial supplementation can be used as a form of therapy for not just GI symptoms but also severity of autism in ASD patients.

Conclusion

The gut microbiome is heavily included in the function of the central nervous system. Microorganisms from the gut release metabolites that insert themselves into different signaling pathways that then go and affect some type of neurological function. Because of this phenomenon, neurological disorders are being studied in the light of the gut microbiome. In three neurological disorders, depression/anxiety, Parkinson's disease and autism spectrum disorder, the gut microbiome seemed to have a drastic effect on the respective symptoms. For example, in mouse models, gut microbiota from depressive human donors caused depression in mice. Furthermore, mouse models that had FMTs from Parkinson's disease patients showed increased motor dysfunction. Bacterial cocktails that affect the microbiome composition had a drastic effect on reducing the severity of autism in ASD patients. There is lots of promise in using FMT and gut microbiota changes to perhaps diagnose and even treat these neurological conditions, but more clinical studies have to be done in order to completely transform these preclinical studies into working treatments that are safe and effective for humans battling these conditions.

Works Cited

Martin, Clair. “The Brain-Gut-Microbiome Axis.” Science Direct, 19 November 2017, https://www.sciencedirect.com/science/article/pii/S2352345X18300602#sec6.

Sampson, Timothy. “Gut Microbiota Regulate Motor Deficits and Neuroinflammation in a Model of Parkinson’s Disease.” Science Direct, 29 June 2016, https://www.sciencedirect.com/science/article/pii/S0092867416315902.

Socała, Katarzyna. “The role of microbiota-gut-brain axis in neuropsychiatric and neurological disorders.” PubMed, August 24 2021, https://pubmed.ncbi.nlm.nih.gov/34450312/.

Using Artificial Intelligence to Pre-diagnose Alzheimer's Based on Multicentric MRI Imaging

Sanvi Swain (author), Thanisha Kapur (advisor)
Westmont High School

Keywords: Alzheimer's, Behavioral Variant Frontotemporal Dementia (bvFTD), Atlas-Based Volumetry (ABV), Support Vector Machine (SVM), Clinical Dementia Rating (CDR)

Abstract

Over five million Americans have Alzheimer's disease without knowing, according to the *AWARE* foundation (Aware). As research and time progresses our capacity to identify the initial symptoms of Alzheimer's improves; on the other hand, the total number of individuals rapidly inclines. The focus of the research article is to examine how artificial intelligence can be used to pre-diagnose Alzheier's based on multi-centric magnetic resonance imaging. Researchers at the German Research Consortium of Frontotemporal Lobar Degeneration used MRI and atlas-based volumetry data to classify different dementia subtypes. They distinguished behavioral variant frontotemporal dementia from other variants based on specific brain regions and clinical characteristics. As more data is given to the machine, the better results appear as this study successfully differentiated behavioral variant frontotemporal dementia from other dementias using Support vector machine algorithms, providing valuable information for diagnosis and treatment. The purpose of the experimentation of the lab is to utilize artificial intelligence to predict and detect early signs of Alzhemiers, ultimately saving lives.

Introduction

Alzheimer's disease, the most prevalent form of dementia, proves to be challenginging in terms of detection and intervention. According to the Alzheimer's Association "around one in nine people (10.7%) aged 65 and older have Alzheimer's" (Alzheimers). In recent years, artificial intelligence (AI) and medical computer vision imaging has sparked a new era of advancements in the initial detection and pre-diagnosis of Alzheimer's disease. Among the promising approaches, the integration of AI algorithms with multi-centric volumetric magnetic resonance imaging has emerged as a transformative game-changer. An Elsevier study focuses on the

utilization of artificial intelligence in pre-diagnosing multiple Alzheimer's syndromes using magnetic resonance imaging (MRI). The researchers applied atlas-based volumetry (ABV) to MRI data from 426 patients and 51 healthy controls. Support vector machine (SVM) classification was employed for both binary and multi-syndrome classification. The binary classification models achieved high prediction accuracies, reflecting disease-specific atrophy patterns. The multi-syndrome model outperformed the chance level, although accuracies varied across the different dementia syndromes tested. The study highlights the potential of automated methods using AI and MRI data to support physicians in diagnosing dementia syndromes, including Alzheimer's disease, and emphasizes the importance of differential diagnosis. The research contributes to the tremendous amount of evidence that AI algorithms can aid in the detecting and differentiating neurodegenerative diseases based on the structural MRI data. This combination empowers more precise and reliable pre-diagnosis by harnessing the potentially embedded in diverse datasets from multiple imaging centers. The prevalence of Alzheimer's disease underscores the urgency for innovative diagnostic approaches. As the population ages, early detection becomes increasingly crucial for their intervention and personalized care. AI algorithms trained on diverse datasets encompassing different imaging protocols and patient demographics can uncover subtle patterns and biomarkers indicating an early stage of Alzheimer's. By processing multi-centric volumetric MRI data, these algorithms enhance the accuracy and reliability of pre-diagnostic predictions. On the other hand, the use of AI with multi-centric volumetric MRI imaging offers an ample shift in the pre-diagnostic process. By utilizing the power of AI algorithms, which are capable of analyzing vast amounts of data and harnessing the information from multiple imaging centers, healthcare professionals gain a more comprehensive understanding of the early progression of this disease.

Materials and Methods

The experiment took place in a German Research Consortium of Frontotemporal Lobar Degeneration, when they used structural MRI data and Atlas-based volumetry (ABV) to analyze brain region volumes. The following materials and methods presented below have been adopted from prior scholarly works of *European Journal of Radiology*.The study involved a cohort comprising of 426 cases and 51 healthy patient controls who were linked from the multi-centric German Research Consortium of Frontotemporal Lobar Degeneration. The patient group were

measured by various neurological conditions, involving Alzheimer's complaint, behavioral variant frontotemporal derangement, the three subtypes of primary progressive aphasia (semantic, logogenic, and nonfluent-agrammatic variant), as well as unusual parkinsonian runs (progressive supranuclear palsy and corticobasal pattern).

Structural MRI head reviews were obtained from multitudinous university hospitals utilizing T1-burdened three dimensional magnetization prepared rapid acquisition gradient echo. (MPRAGE) sequences with a high spatial conclusion of 1 mm isovoxel. The imaging data was collected from a plethora of centers such as Bonn, Erlangen, Goettingen, Hamburg, Homburg, Leipzig, Munich (Ludwig Maximilians University and Technische University), Rostock, Tuebingen, Ulm, and Wuerzburg.

The researchers predicted the ABV on the T1 burdened MRI data to estimate brain region volumes or areas. ABV allotted the images into gray matter, undyed matter, and cerebrospinal fluid chambers at a voxel situation. The dissection assumed the LONI Probabilistic Brain Atlas (LPBA40) in convergence with fresh masks derived from it. ABV eased the introduction of autochthonous brain volumes or areas predicated on predefined regions of interest in a standardized template room.

Support Vector Machine (SVM) type was perceived to discern between nonidentical patient groups and controls (double-barreled type) and among all seven individual groups (multi-class type). SVM, an operative engine mastering algorithm predicated on the Library for Support Vector Machines (LIBSVM), determined the separating hyperplanes for categorizing subjects into nonidentical runs. The researchers executed the SVM models utilizing the e1071 package in the R fiefdom.The e1071 package in R is a popular tool for machine learning, particularly for support vector machines and other classification tasks. Linear kernels with a “cost” parameter value of 0.25 were assumed for SVM training predicated on the ABV effects of the 64 brain regions.

To ensure the safety and responsibility of the SVM classifier and palliate overfitting, a Leave-One-Out Cross-Validation (LOOCV) path was utilized. This path involved iteratively

barring data from one motive at a time and training the SVM classifier on the remaining data to codify the left eschewal motive. LOOCV enabled the researchers to charge the generalizability of the SVM classifier to unseen data and address implicit imbalances in group sizes.

The primary measures comprehended brain region volumes or areas derived through ABV, along with various SVM type criteria. For double-barreled SVM models (cases with one pattern vs. healthy controls), the researchers calculated perceptivity, particularity, positive predictive value, inhospitable predictive value, model delicacy, and clear headed delicacy. Also, the researchers assumed the correlation measure to esteem for imbalanced group sizes and luck predictions in double-barreled classifiers. In the case of multi-class SVM models, the seat was on perceptivity, positive predictive value, and the F1-score, which provides a combined measure of perceptivity and positive predictive value (PPV). An F-1 score is a metric used to calculate the harmonic mean (precision) of a classification model and the PPV shows how many of the predictions are actually correct. Model delicacy for the multi- class SVM was also determined.

The study stuck strictly to the principles of the declaration of Helsinki and penetrated ethically from the initial moral councils of all sharing centers. The Declaration of Helsinki is a set of principles for medical research involving human participants, ensuring their rights and safety are protected. Informed consent was given by all impersonators, involving cases, caregivers, or legit representatives, former to their extension in the study.

Data Analysis

The objective of this data analysis was to categorize various forms of dementia including behavioral variant frontotemporal dementia (bvFTD) which correlates to Alzheimer’s.
The data was categorized based on the clinical, demographic characteristics of patients, as well the brain regions. Based on the characteristics of patients and the significance of specific brain regions, the data was analyzed based off of the different types of dementia, including behavioral variant frontotemporal dementia (bvFTD), which colates to Alzheimer's. Using a binary support vector machine, the researchers were able to differentiate between dementia patients and healthy controls. They additionally classified the different subtypes using a multi-syndrome methodology. The analysis of behavioral variant frontotemporal dementia (bvFTD) results

revealed several important conclusions that were backed up by evidence and specifics. The study discovered a significant age gap between patients with bvFTD and those with other dementia syndromes. People who have bvFTD are said to be younger than people who have Alzheimer's disease , progressive supranuclear paralysis (PSP), logopenic variant primary progressive aphasia (lvPPA), and nonfluent variant primary progressive aphasia (nfvPPA). When compared to other dementia subtypes, bvFTD tends to strike people when they are still relatively young, according to statistical analysis (0.05). Second, in separating bvFTD from some other dementia subgroups, the clinical dementia rating (CDR) scores were extremely important. Patients with bvFTD had significantly lower CDR scores than those with lvPPA and nfvPPA (between 0.05 and 0.001). In contrast to lvPPA and nfvPPA, patients with bvFTD had higher CDR scores, which indicated a more serious level of cognitive and functional impairment. Below is a model metrics test for multi-syndrome classification conducted by the laboratories (Elsevier 23).
Additionally, the multi-syndrome classification analysis correctly and precisely classified the

Table 3. Model metrics for multi-syndrome classification.

	Sensitivity (Recall)	Positive predictive value (Precision)	F-score
AD	0.42	0.43	0.42
bvFTD	0.60	0.51	0.55
CBS	0.08	0.18	0.11
lvPPA	0.20	0.40	0.27
nfvPPA	0.36	0.34	0.35
PSP	0.54	0.51	0.53
svPPA	0.65	0.61	0.63

bvFTD. The performance indicators listed in Table 3 provided evidence in favor of the bvFTD

classification's accuracy. The classifier correctly identified 60% of the cases as having bvFTD, according to the sensitivity recall of bvFTD classification, which was 0.60. The classifier correctly predicted bvFTD 51% of the time, according to the positive predictive value (precision) of 0.51. The F- score of 0.55 reflected the overall delicacy of the bvFTD bracket, considering a combination of perfection and recall criteria.

Also, the brain region analysis provided perceptivity into secerning bvFTD from other madness runs. The anterior cortex surfaced as a vital brain region for the bvFTD bracket, parallel to the former exploration of the typical pattern of atrophy in bvFTD. The involvement of the anterior cortex in bvFTD has been well-proven in the literature (Schroeter etal., 2007, Schroeter etal., 2014.), and this finding aligns with the given neurodegenerative processes characteristic of this pattern.

Discussion

Alzhemiers tends to be the most prevalent condition of dementia and poses significant threats when it comes to pre-diagnosing. AI algorithms with multi-centric volumetric MRI imaging can aid in the rapid detection and differentiation of neurodegenerative diseases based on structural MRI data. Data was collected from diverse centers such as Bonn, Erlangen, Hamburg, Homburg, and Munich.The Elsevier study focuses on the utilization of AI algorithms in pre-diagnosing multiple syndromes of Alzheimer's using an MRI. Atlas-based volumetry ABV was used to analyze brain region volumes in MRI data from 426 patients including 51 patients for control. The Support vector machine classification was used for both binary and multi-syndrome classification, with high prediction accuracies for disease specific patterns.

The main purpose of the data analysis was to categorize various forms of dementia, including behavioral variant frontotemporal dementia, which is a clear factor in Alzheimers .Scientist utilized a used a binary support vector machine to differentiate between dementia patients and the Structural MRI head reviews were obtained from multitudinous university hospitals utilizing T1- burdened three-dimensional magnetization prepared rapid acquisition gradient echo sequences with a high spatial conclusion (1 mm isovoxel). The experiment shows that there is a significant age gap between patients with bvFTD and those with other dementia syndromes. It is evident that bvFTD strikes people when they are still relatively older. Clinical dementia rating scores were extremely important in separating bVFTD from other dementia subgroups, the

patients usually had significantly lower CDR scores than those with lvPPA and nfvPPA. Additionally, the study found that the anterior cortex is a vital brain region for the bvFTD bracket and is parallel to the former exploration of the typical pattern of atrophy.

In this scientific trial fastening on medical trial runs, it is important to remember that several implicit miscalculations could impact the delicacy and trustability of the results. These include sample bias, where an uneven representation of certain dementia subtypes could dispose of the findings, and a small sample size, reducing statistical power and generalizability. Variables like comorbidities may impact the issues, and inaccurate data collection could introduce faulty results. Insufficient longitudinal data changes the comprehension of symptom progression, while overfitting of models might diminish their relevance. Variability in complaint submissions and missing data could also impact the findings, along with any assumptions made during the analysis. To address these challenges, it is crucial to implement rigorous experimental designs, structured data collection, and extreme statistical analysis. Utilizing larger, diverse samples and conducting replication studies can enhance the credibility and validity of the research findings, making this study more credible .

In conclusion, the results of the analysis provided ample substantiation and specific details regarding bvFTD, showcasing its unique clinical and demographic characteristics, as well as its distinct pattern of brain region involvement. The accuracy of bvFTD classification using the chosen methods supports the potential utility of this approach in clinical diagnosis and research on dementia subtypes.

Works Cited

Alzheimer's Association, 2 October 2022, https://www.alz.org/alzheimers-dementia/facts-figures#:~:text=About%201%20in%209%20people,other%20dementias%20as%20older%20Whites

Brandon Chase MGH Communications. "Using AI to Target Alzheimer's." *Harvard Gazette*, 3 Mar. 2023, https://news.harvard.edu/gazette/story/2023/03/using-ai-to-target-alzheimers/

"Join the Cause." *AWARE Dallas*, Accessed 1 August 2023, https://www.awaredallas.org/join-the-cause/

Lampe, Leonie, et al. "Multiclass Prediction of Different Dementia Syndromes Based on Multi-Centric Volumetric MRI Imaging." *NeuroImage: Clinical*, vol. 37, 1 Jan. 2023, https://www.sciencedirect.com/science/article/pii/S2213158223000098#bb0190

Yao, Zhaomin, et al. "Artificial Intelligence-Based Diagnosis of Alzheimer's Disease with Brain MRI Images." *European Journal of Radiology*, vol. 165, 1 Aug. 2023, https://www.sciencedirect.com/science/article/abs/pii/S0720048X23002486

Neuroplasticity in Language Regions of the Brain

Sarthak Chaturvedi (author), Thanisha Kapur (advisor)
Bentonville High School

Keywords: Neuroplasticity, Aphasia, Broca's area, Wernicke's area, Stroke, Left hemisphere, Right hemisphere

Abstract

This literary review will discuss the causes of neuroplasticity in language regions of the brain. The brain may undergo neuroplasticity when it is damaged, learning, or gaining new experiences. The left hemisphere of the brain processes sentences, while the right hemisphere processes tone of voice. When a stroke occurs, it can cause lesions and the loss of vital brain tissue. If the left hemisphere is affected, it can result in aphasia, affecting language abilities. However, the brain can trigger neuroplasticity after a stroke, allowing it to adapt to injuries or unique situations like bilingualism, serving a biological and evolutionary purpose. It allows the brain to reorganize its neural connections and form new pathways activating alternative regions to compensate for the loss of function in damaged areas. The brain's ability to adapt and reroute neural circuits allows individuals to overcome challenges and continue essential functions, such as communication, even after sustaining brain damage. While there is no exact measure of how successful brain plasticity is, many instances and rehab techniques have shown to trigger brain plasticity. The occurrence of plasticity in language regions of the brain can be attributed to aphasia, stroke, bilingualism, etc.

Introduction

Neuroplasticity pertains to the brain's capacity to reorganize and establish novel neural connections in response to environmental changes or injury (Kiran & Thompson, 2019). The brain's neuroplasticity significantly impacts the recovery of language functions after a stroke and the language skills of bilingual individuals. Aphasia, characterized by language impairment or loss, commonly arises after a stroke. Rehabilitation interventions have demonstrated the potential to trigger neuroplastic changes, leading to language function improvements. Broca's and Wernicke's areas are crucial regions in language processing. In right-handed individuals, the

areas are located in the left hemisphere. For left-handed individuals, they are located in the right hemisphere. Bilingualism in individuals also demonstrates neuroplasticity because when a person has to switch between languages, they have to use different amounts of cognitive effort than monolinguals. New studies have given us important knowledge about how language-related neuroplasticity works. This understanding has significant implications for language learning, acquisition, and the recovery of language skills after experiencing impairments.

Body

Aphasia after stroke

A common symptom after a left hemisphere stroke is aphasia, which involves the impairment of language functions. Neuroplasticity can play an important role in language recovery after a stroke, but the effectiveness and strength of neuroplasticity varies depending on the stroke's age and many other variables (Kiran & Thompson, 2019). Research indicates that the most substantial changes in neural architecture for language occurs in the early stages of recovery, but even in chronic aphasia, neuroplasticity continues to take place despite the completion of neurophysiological repair processes (Kiran & Thompson, 2019). After a stroke, language regions are activated along with other domain-general regions which leads to heightened cognitive effort. Due to neuroplasticity, previously unengaged tissue can assume functions. However, it remains uncertain whether the engagement of these domain-general regions alongside language regions correlates with improved language recovery in patients (Kiran & Thompson, 2019). Various methods have been used to study neuroplasticity following a stroke. One of these studies in 2017 used an electroencephalogram to observe brain activity. This helped to recognize neuroplasticity for language abilities after a stroke in the left side of the brain. They recorded an EEG from patients with stroke lesions to the left temporal lobe and matched controls during context-driven word retrieval. (Piai et al., 2017) After strokes in the lateral frontal cortex, scientists have seen changes in brain flexibility related to working memory and attention. These neuronal oscillations have the potential to serve as biomarkers for monitoring neurorehabilitation and recovery of language function (Piai et al., 2017). In children, neuroplasticity in language regions after a stroke can lead to different outcomes. Children with left hemisphere language regions spared by or recovered after stroke may develop normal or

near-to-normal language functions, whereas those with language regions affected by stroke may develop bilateral or right language lateralization as a compensatory mechanism (Fischmeister et al., 2019). However, this substitution of language areas is associated with reduced efficiency (Fischmeister et al., 2019). The critical role of the left hemisphere in language recovery even after a left hemisphere stroke supports the view of an ontogenetic predisposition of the left hemisphere for the maturation of linguistic functions (Fischmeister et al., 2019). The left and right hemisphere both handle different functions; the left is responsible for processing sentences as we listen to words while the right is responsible for processing the emotion of the voice. In children who suffer a left-hemisphere stroke shortly after birth, neuroplasticity enables the right hemisphere to take on language abilities that are typically managed by the left hemisphere. Despite this adaptation, the right hemisphere retains its original language capabilities as well. Participants, who suffered medium to large perinatal arterial ischemic stroke, from the age of 9 to 26 were given language tests. The results were compared to people with no stroke. An MRi scan revealed which areas of the brain were involved in sentence comprehension (Newport et al., 2022). The stroke patients resulted in a consistent pattern of language activation in the right hemisphere while the control participants processed sentences on the left side. However, not all stroke patients go through successful neuroplasticity as one of the patients in the study with a small stroke did not show clear right hemisphere activation. (Newport et al., 2022). Rehabilitation interventions have been found to trigger changes in brain plasticity in patients with aphasia, leading to improvements in language functions. Language recovery after a stroke is viewed from a network perspective, emphasizing the importance of maintaining a balance between language-specific regions within and between the brain's hemispheres (Sebastian et al., 2016). In cases of post-stroke aphasia, language tasks involve both regions remaining within the typical language network and regions outside of it in both the left and right hemispheres (LaCroix et al., 2021). The production and comprehension of language following a left hemisphere stroke involve different parts of the brain, with language production activating the right frontal and temporal cortices (LaCroix et al., 2021). Successful naming in individuals with chronic post-stroke aphasia is connected to the involvement of regions in the right hemisphere related to motor speech planning, while difficulties in naming are associated with the engagement of the right inferior frontal gyrus, which is a region associated with general cognitive processes (LaCroix et al., 2021).

Bilingualism

Bilingualism's effects on brain structure in relation to neuroplasticity has been explored with different methods of research.. Gray matter and white matter are two components of brain tissue. Gray matter contains the nerve cell bodies which process sensation, perception, speech, cognition, etc. White matter provides the exchange of information between the parts of gray matter in the brain. Learning and using additional languages have been found to reshape both gray and white matter in the brain. However, the specific patterns of these structural changes can differ, with some regions showing increased volume and diffusivity while others demonstrate reductions (Pliatsikas, 2019). According to the Dynamic Restructuring Model (DRM), the structural adaptations in the bilingual brain depend on the amount and quality of language learning and switching experiences (Pliatsikas, 2019).

Bilingualism has the ability to adjust the structure of subcortical regions, such as the basal ganglia and thalamus, which are involved in language selection and speech monitoring. (Pliatsikas et al., 2016). One study compared brain activity in fluent bilinguals and monolingual controls. They participated in linguistic tasks in their first language. The results demonstrated that bilinguals experienced increased activity in left-hemisphere brain areas related to language. This shows that bilingualism requires more cognitive effort even though the bilinguals were being tested in their first language. (Costa & Sebastián-Gallés, 2014). Additionally, another study found that bilinguals showed increased activation in the left inferior frontal cortex during comprehension tasks, suggesting a unique brain activity pattern specific to bilingualism (Costa & Sebastián-Gallés, 2014). Language proficiency also influences bilingual language organization in the brain. Neural differences were observed in bilingual brains based on their language proficiency in each language, with regards to all ages of acquisition (Kovelman et al., 2008). Moreover, a meta-analysis of studies comparing bilingual and monolingual speakers on language lateralization discovered that bilinguals, particularly proficient ones, demonstrated greater right hemisphere involvement compared to monolinguals (Hull & Vaid, 2006).

Researchers have also investigated the control networks involved in language-switching among bilingual individuals. Arabic-English bilingual participants took part in language switching tasks It was found that neural networks for production and comprehension processes diverge during auditory word recognition and word production. Bilingual individuals rely on adaptive

cognitive control in language-switching. When one switches language or category of words during speech, the dorsolateral prefrontal cortex regions are activated. However, when a bilingual individual trying to understand 2 alternate languages, the anterior cingulate cortex is activated, but this doesn't happen when switching between word categories. The dorsolateral prefrontal cortex is an important region for handling language switching since one language needs to be inhibited in order to activate the other. Frequent switching of language correlates to increased involvement of each cortex. This demonstrates that bilinguals use adaptive strategies to control how they understand and produce the different languages. (Blanco-Elorrieta & Pylkkänen, 2016).

Environmental factors

Not all forms of neuroplasticity are in order to recover from damage and improve neural networks. Environmental factors such as stress, linguistic exposure, and cultural background can negatively influence neuroplasticity. When there is an increase of stress, many sectors in the amygdala grow while the hippocampus and prefrontal cortex do the opposite. One research paper found that orphans may experience cognitive impairment if they are not placed in foster care on time. There is no set amount of time before a child goes through brain plasticity due to such stresses. Another example from the same study is when rats were placed in more complex living spaces daily showed increased dendritic branching. (Davidson & McEwen, 2012) Increased branching could lead to improved learning, memory, and cognitive function which could be applied to other situations by the rats. An increase in glial cells was also noticed. This demonstrates that there may be boosted synaptic communication which would again lead to increased cognitive function. Neurotransmitters would be able to reach the next neuron faster leading to more efficient neural processing. Positive environmental exercise as the one with the rats can trigger positive changes in brain plasticity; this demonstrates neuroplasticity.

In humans, early life stress can significantly impact the way the brain develops. A sample of 31 physically abused teenagers was taken along with a control of 41 normal teenagers. Researchers found that the abused children had smaller orbitofrontal volumes. This region in the frontal cortex handles emotional processing, decision making, and social aspects. These smaller volumes directly correlated to poorer academic functioning and poorer family functioning. (Davidson & McEwen, 2012). Contrary to the rat study, here is an example of how negative

stresses can also lead to brain plasticity which at times may be irreversible.
In another example, the amygdala of a sample of 10 year old children who were repeatedly exposed to maternal depressive symptoms from their mothers was compared with a control sample that had not been exposed to these symptoms. Children who experienced depressive symptoms since birth had larger amygdalae than the control group of children (Davidson & McEwen, 2012). A larger amygdala could hint at more difficulty in emotional processing since the amygdala is known to process emotions such as fear and anxiety. Further research into the amygdala could confirm the significance.

Conclusion

Various factors, including stroke, aphasia, and bilingualism, can influence neuroplasticity in the brain. In patients with aphasia, rehabilitation interventions have been observed to induce changes in brain plasticity, resulting in better language abilities. Interestingly, the production and comprehension of language after a left hemisphere stroke engage distinct brain regions, with language production involving the right frontal and temporal cortices. (LaCroix et al., 2021). Successful naming in individuals with chronic post-stroke aphasia is connected to the involvement of regions in the right hemisphere related to motor speech planning, while difficulties in naming are associated with the engagement of the right inferior frontal gyrus, which is a region associated with general cognitive processes. Brain neuroplasticity is an amazing process that fosters resilience and aids in the recovery from injuries, revealing the brain's remarkable ability to adjust and cope with the effects of neurological disorders, including aphasia. This is a crucial topic for research in order to understand the way the brain rewires itself. It can also potentially improve treatments for those who have suffered from aphasia or even relieve symptoms.

Works Cited

Kiran, Swathi, and Cynthia K. Thompson. *Neuroplasticity of Language Networks in Aphasia: Advances, Updates, and Future Challenges*. Apr. 2019, https://doi.org/10.3389/fneur.2019.00295. Accessed 1 Aug. 2023.

Vitória Piai, et al. *Neuroplasticity of Language in Left-Hemisphere Stroke: Evidence Linking Subsecond Electrophysiology and Structural Connections*. no. 6, Mar. 2017, pp. 3151–62, https://doi.org/10.1002/hbm.23581. Accessed 1 Aug. 2023.

News, Neuroscience. "After Stroke in an Infant's Brain, Right Side of Brain Compensates for Loss of Language in Left Side - Neuroscience News." *Neuroscience News*, 10 Oct. 2022, neurosciencenews.com/stroke-infant-language-21610/. Accessed 1 Aug. 2023.

Bartha-Doering, Lisa, et al. *Atypical Language Representation Is Unfavorable for Language Abilities Following Childhood Stroke*. no. 1, Jan. 2019, pp. 102–16, https://doi.org/10.1016/j.ejpn.2018.09.007. Accessed 1 Aug. 2023.

Sebastian, Rajani, et al. *Cerebellar TDCS: A Novel Approach to Augment Language Treatment Post-Stroke*. Jan. 2017, https://doi.org/10.3389/fnhum.2016.00695. Accessed 1 Aug. 2023.

LaCroix, Arianna N., et al. *Auditory Attention Following a Left Hemisphere Stroke:*

Comparisons of Alerting, Orienting, and Executive Control Performance Using an Auditory Attention Network Test. no. 4, Oct. 2020, pp. 238–51, https://doi.org/10.1080/25742442.2021.1922988. Accessed 1 Aug. 2023.

Christos Pliatsikas, et al. *The Effect of Bilingualism on Brain Development from Early Childhood to Young Adulthood*. no. 7, July 2020, pp. 2131–52, https://doi.org/10.1007/s00429-020-02115-5. Accessed 1 Aug. 2023.

Christos Pliatsikas, et al. *Immersive Bilingualism Reshapes the Core of the Brain*. no. 4, Sept. 2016, pp. 1785–95, https://doi.org/10.1007/s00429-016-1307-9. Accessed 1 Aug. 2023.

Costa, Albert, and Núria Sebastián-Gallés. *How Does the Bilingual Experience Sculpt the Brain?* no. 5, Apr. 2014, pp. 336–45, https://doi.org/10.1038/nrn3709. Accessed 1 Aug. 2023.

Esti Blanco-Elorrieta, and Liina Pylkkänen. *Bilingual Language Control in Perception versus Action: MEG Reveals Comprehension Control Mechanisms in Anterior Cingulate Cortex and Domain-General Control of Production in Dorsolateral Prefrontal Cortex*. no. 2, Jan. 2016, pp. 290–301, https://doi.org/10.1523/jneurosci.2597-15.2016. Accessed 1 Aug. 2023.

Davidson, Richard J., and Bruce S. McEwen. Social Influences on Neuroplasticity: Stress and

Interventions to Promote Well-Being. no. 5, Apr. 2012, pp. 689–95, https://doi.org/10.1038/nn.3093. Accessed 1 Aug. 2023.

How Can AI diagnose Alzheimer's Through Various Medical Scans

Selina Gao (Author), Thanisha Kapur (Advisor)
High School of Health Professions and Human Services

Keywords: Alzheimer’s, Machine Learning, Un/supervised Machine learning, Positron Emission Tomography

Abstract

Alzheimer's disease is a global health concern with no known cause currently. Therefore it’s emphasized to many doctors the need for early detection and precise diagnosis. So far, the research that has been done by artificial intelligence (AI) and by various medical scans has shown a promising future in identifying and predicting Alzheimer's disease. This literary review will explore different ways AI can be used to detect glucose levels in the brain through medical scans. Glucose is specifically used other than other types of molecules, since its abnormalities have been linked to Alzheimer's progression, making them potential predictive biomarkers. Researchers have developed AI techniques like VoxelMorph for PET scans, allowing early detection and intervention. The use of AI in PET scans can then possibly lead to improved treatment strategies and reduced healthcare costs in the future. Along with, better outcomes for affected individuals and their families. Two-sample t-tests and unsupervised machine learning have been used to analyze MRI and PET scans, to identify relevant brain regions and point out features for Alzheimer's diagnosis. The successful application of AI-powered PET scans has the potential to transform how Alzheimer's is diagnosed and managed in the future.

Introduction

A major global health issue is heavily correlated back to the progressive neurological disorder: Alzheimer's disease. Due to its unknown cause, early detection and a precise diagnosis of Alzheimer's are now essential for successful treatment and intervention as the elderly population continues to grow. Thankfully, with the beneficial outcomes of this new era of technology, artificial intelligence (AI) and neuroscience in positron emission tomography (PET) scans can now identify and anticipate Alzheimer's disease. The fusion of these technologies has recently demonstrated considerable promise for changing medical imaging procedures. Researchers have

created new methods such as VoxelMorph (an AI technique) to detect and predict Alzheimer's disease. The focus of this review will show how AI can effectively identify glucose levels in the brain through pet scans. Glucose plays a crucial role in how a brain functions. You may have advised before tests to eat a big breakfast or perhaps to consume candy. Many advise this since your brain is only able to function when there's energy provided. This goes for many other parts of your body, but as you stop using a specific part of your body, you will also be using less glucose in that area, hence the reason we are zooming in on glucose levels. PET scans, combined with AI algorithms, allow for the detection of these abnormalities. With such advanced technology in this era, researchers can now uncover vital information that helps with identifying and staging Alzheimer's disease. Ultimately, AI has the potential to change the way we approach Alzheimer's care: offering opportunities for earlier interventions, personalized therapies, and improved outcomes for individuals and their families affected by this progressing disease.

Body

Alzheimer's Explained

Alzheimer's is the most common type of dementia that causes memory loss, cognitive decline, language impairment, disorientation and confusion, behavioral changes, impaired motor skills, and loss of independence. This is a progressive disease found amongst elders, it can affect one's lifestyle and simple tasks that need to be done in a day. Although there is no cure, treatments can help manage symptoms. Early detection is crucial for better care.

How AI be a changing factor in diagnosing Alzheimer

The growing body of evidence showed the relevance of poorly functioning glucose metabolism and oxidative stress plays a crucial role in Alzheimer's progression. In other words, glucose uptake differences in the brain can serve as predictive biomarkers for Alzheimer's disease. By fusing PET scans with machine learning algorithms, researchers can detect these glucose abnormalities, allowing doctors to be alert to the presence and progression of the disease. An example of this was done by Stanford University researchers, who developed VoxelMorph, an artificial intelligence approach specifically made for PET scans for Alzheimer's. The fusion of AI and PET scans to diagnose Alzheimer's has shown promising results for detecting glucose abnormalities. These findings offer opportunities for early prediction and intervention. As a

result, glucose abnormalities can then be observed even before the beginning of characteristic symptoms. Early detection through AI-powered PET scans can enable healthcare providers to initiate appropriate treatments and interventions to slow down the destructive progression of the disease.

When comparing the idea of AI and no AI involvement in diagnosing, with no AI involvement it's often more challenging. In case studies found: the challenges associated with community-acquired PET scans include issues related to scan quality, variability in imaging protocols, limited availability of radiotracer agents, and the lack of standardized interpretation criteria. These factors can contribute to difficulties in accurately interpreting the PET scan results and making appropriate clinical decisions. With AI involvement, neuroimaging in PET scans could lead to early detection, improved treatment strategies, and reduced healthcare costs for Alzheimer's disease. The first case emphasized the need for standardization and collaboration to overcome the challenges associated with community-acquired PET scans and enhance their integration into routine clinical care.

Furthermore, without the involvement of AI, a separate branch of researchers has developed another technique called amyloid PET scans. Amyloid PET scans are a new type of imaging scan that was able to detect amyloid plaques in the brain. Amyloid plaques are another type of biomarker of Alzheimer's. However, the availability and accessibility of these scans are limited, due to their cost; resulting in differences in access and potentially widening health inequities. In comparison with the new approach to analyzing PET scans, it's much more accessible, convenient, and accurate.

However, as much as there is praise for AI involvement in the medical field, AI technology is extremely costly for a huge project. This makes AI-involved projects impractical for small-scale businesses. Even for companies with substantial revenues, the development cost can be high due to the complexity of features and regular hardware and software updates. Secondly, the advancement of AI has led to increased unemployment, as automation replaces traditional jobs, causing a significant human toll. This not only affects livelihoods but also diminishes the sense of community and purpose derived from meaningful employment. Nevertheless, AI can never

replace the employed population, since we will always need someone to confirm the results. Moreover, if the AI results in inaccurate information, we need a person to point to in court.

AI machine learning used to diagnose Alzheimer's

When we use AI to analyze models for us, we use this through supervising or unsupervised machine learning techniques for the AI. Supervising machine learning is where the machine can analyze an algorithm based on a labeled dataset, meaning the input data and their corresponding correct output values are provided during the training process. The goal of supervised learning is for the algorithm to learn a mapping between the input features and the target output based on the provided labeled examples. Once the algorithm is trained, it can then make predictions or classify new, unseen data based on the patterns it learned during training. On the other hand, unsupervised machine learning is where there is no data inputted before the analysis begins. The input data does not have corresponding output labels or target values. Unlike supervised learning, there is no guidance or guidelines when analyzing and learning the data given. Instead, the algorithm is tasked with finding patterns, relationships, and structures within the data on its own. In recent research done in May 2023, Yuyang Liu, Suvodeep Mazumdar, and Peter A Bath used two-sample t-tests using unsupervised machines in Magnetic Resonance Imaging (MRI) scans of a patient who has Alzheimer's. The t-test that was conducted was to confirm the differences we found between the control group and the experimental group weren’t based on luck. It's a standard tool used in different areas to make comparisons and draw conclusions from data. The t-test was used to detect the relevant regions of the brain that are closely associated with Alzheimer's. Then the researchers employed an unsupervised learning neural network to extract features of the areas. Finally, a clustering algorithm was used to determine the differences between a Cognitively Normal patient (CN) and a patient who has Alzheimer’s data based on the extracted features. This method that was discussed was assessed using baseline brain structural MRI scans from the 429 participants that have enrolled in the Alzheimer's Disease Neuroimaging Initiative (ADNI). Among these participants, 231 individuals were classified as Cognitively Normal (CN), while 198 individuals were diagnosed with Alzheimer's disease (AD).
Another research was led by Sohn, a radiologist who used PET scans along with a machine learning program his team of researchers developed specifically zoomed into glucose levels of the brain. PET scans have been studied as a diagnostic tool for Alzheimer's disease before the

patient begins to experience the symptoms. These scans measured specific molecules, such as glucose molecules found in the brain. Glucose is the main energy source for cells, so applying this knowledge, when the brain is active, so are the cells. If the cells are active, the glucose levels are much higher. However, as brain cells become affected and deteriorate, their glucose consumption decreases, and in further evolved stages, they stop using glucose altogether. By detecting these changes in glucose usage, PET scans may help in early Alzheimer's diagnosis. In this group of researchers' experiments, the algorithm was trained on 1,921 scans.

Comparisons across the different experiments done

The way AI is used to diagnose Alzheimer's patients is used through machine learning techniques. In all three methods discussed, machine learning in AI has to be unsurprised for the machine to learn what's given. Researchers won't be able to use a supervised learning approach due to the lack of information about Alzheimer's. Comparing the three different research done, the first one associated with the new programming approach called VoxelMorph and the third one mentioned regarding radiologists both closely zoomed into one part of the research. Instead of inputting no exact subject for the unsupervised AI to identify, the data clusters will be messy. It won't be easy to differentiate much of its data from CN patients. By drawing closer attention to one idea that we already know can be easily compared with a CN and AD patient it's much easier to find its cause. The first and third research closely examines glucose levels, hence the successful promising results.

Conclusion

In conclusion, this review stresses the idea of the promising role that AI can provide in diagnosing Alzheimer's disease through various medical scans. While Alzheimer's remains a demanding global health concern, AI-powered algorithms combined with techniques like PET and MRI scans have shown potential for early intervention by detecting distinctive biomarker patterns related to glucose metabolism and amyloid plaques. Despite the potential, challenges such as AI implementation costs and social impacts should not be overlooked. The intersection of AI and medical imaging offers a path to Alzheimer's diagnosis, encouraging hope for improved interventions and personalized care for affected individuals and families.

Works Cited

"What Is Alzheimer's?" Alzheimer's Disease and Dementia, *www.alz.org/alzheimers-dementia/what-is-alzheimers*. Accessed 30 July 2023.

"Pros & Cons of Artificial Intelligence - Insights from AI Experts." Intellipaat Blog, 24 July 2023, https://intellipaat.com/blog/pros-and-cons-of-ai/?US

Stanford University. "AI Improves Alzheimer's Imaging." Stanford University. Human-Centered AI Institute, 12 Feb. 2020. *https://hai.stanford.edu/news/ai-improves-alzheimers-imaging*.

University of California, San Francisco (UCSF). "Artificial Intelligence Can Detect Alzheimer's Disease in Brain Scans Six Years Before a Diagnosis." UCSF News. University of California, San Francisco, 2 Jan. 2019. *https://www.ucsf.edu/news/2019/01/412946/artificial-intelligence-can-detect-alzheimers-disease-brain-scans-six-years*.

Liu, Yuyang, Suvodeep Mazumdar, and Peter A. Bath. "Using Unsupervised Machine Learning to Classify Alzheimer's Disease Stages." PubMed Central (PMC), 25 Jul. 2023. *https://pubmed.ncbi.nlm.nih.gov/36921480*.

"What Is Machine Learning?" IBM, *www.ibm.com/topics/machine-learning*. Accessed 30 July 2023.

"Artificial Intelligence (AI) vs. Machine Learning." CU-CAI, 3 Mar. 2022, *https://ai.engineering.columbia.edu/ai-vs-machine-learning/*

Developments of Neuroscience: Brain Organoids

Shamonti Shamim (author), Thanisha Kapur (advisor), Anika Shah (editor)
Townsend Harris High School

Keywords: Brain Organoid, Cerebral Organoid, Pluripotent Stem Cells, Embryonic Brain, Neurological Conditions, Vitro Models, Consciousness, Informed Consent, Electrical Activity

Abstract

The field of neuroscience continues to expand as it implements new technology into the healthcare industry in order to provide improved services for patients. Researchers have struggled to explore many aspects of the brain, including its different mechanisms, the effects of neurodegenerative and neurodevelopmental diseases, and both the structural and functional abilities. However, through the introduction of brain organoids, a vitro model of the brain made up of induced-pluripotent stem cells, these opportunities are in-reach for researchers. Brain organoids provide scientists with a lab-grown brain that is separated from the experimental subject, allowing for an ethical application of neuroscience. Despite this, researchers have come across ethical concerns that create difficult circumstances regarding the nature of the brain and the manner in which research may be conducted, limiting the studies and its implementations. These concerns consist of how the usage of stem cells may result in the brain potentially gaining consciousness and difficulties obtaining informed consent from donors. Although these ethical concerns can affect the research being conducted, brain organoids serve as significant models that can shed light on drug responses, therapeutic interventions, and the impacts of brain disorders, providing the healthcare industry with significant information that can alter and shape our current understanding of neuroscience.

Introduction

Contributions of Brain Organoids

According to Elizabeth Di Lullo and Arnold Kriegston, researchers from the Department of Neurology at the University of San Francisco, our current understanding of the brain is extremely limited as the information can only be tested and collected from studies on deceased non-human primates (Kriegston and Di Lullo 573). Due to the maintenance of ethics, these

limitations are posed and make it difficult to explore the human brain and its development effectively; however, with the development of cerebral organoids, researchers can now form their own brains without the need of a patient, whether dead or alive. These brain organoids, also known as cerebral organoids, have emerged as a new form of research and exploration in the neuroscience field, allowing scientists to thoroughly understand the brain's functions and structure (Goldman). According to Momoko Watanabe and their team of researchers at UCLA, blood cells or human skin are needed to act as a base for the production of induced pluripotent stem cells, which occurs through the process of reprogramming (Buth, et al. 2220). The process of "reprogramming" consists of introducing transcription into somatic stem cells that can become differentiated and thus, take on different roles as if the organoid were an embryonic organ (Dinella, et al. 1). Nuclear reprogramming allows for these cells to maintain their genetic memory, providing a greater success for the mature development of an organism (Abbar, et al. 121). With the production of brain organoids, they serve as an accurate and effective three -dimensional representation of the human brain (Benito-Kwiecinski and Lancaster). These models are used to investigate the development of the human brain and allows researchers to gain insight into certain brain disorders as well (Wang).

Despite its immense contributions to the healthcare industry, the ethicality of brain organoids continues to be questioned due to informed consent and the nature of the brain itself. Researchers have presented the possibility of these brains expanding their functionality by becoming conscious. As induced pluripotent stem cells differentiate, the cerebral cortex can become developed and create neuron connections that form consciousness within these organoids, known as "neuronal correlates" (Lagercrantz and Changeux 255). The connections can allow for electrical activity to take place, creating interactions and development between the spinal cord and the cerebral structures (Lavazza and Reichlin 1). Through its development of consciousness, the brain can experience both pain and discomfort from experimentation as well as have thoughts and feelings associated with them (Hyun, et al.). However, these chances are seen as slim due to the Furthermore, these methods require either autonomy or de-identification of the individual, however, this cannot be maintained as it becomes difficult to investigate the brain without acknowledging whom these cells belong to (Chen). If the patient had any health complications, these would be expressed heavily in the genetic material contained in the cells, thus forming a

brain that will express these genetics as well. By gaining personal information before studies are conducted, it provides researchers with a clearer understanding of how these conditions may affect the brain's responses (Benito-Kwiecinski and Lancaster). Although these results impact what can be applicable during many studies, brain organoids closely resemble human embryonic brains, providing the world with accurate interpretations and information. Overall, cerebral organoids remain significant and provide insight into the development of the human brain by replicating its functions and structure effectively while serving as a three-dimensional model.

Body

Brain Organoids and its Implications

As brain organoids serve as a real-life model of the human brain, it allows researchers to study its development, functions, and structure in-depth without harming a patient. Cerebral organoids are comprised of pluripotent stem cells that are capable of differentiating into various cell types (Benito-Kwiecinski and Lancaster). During the early 21st century, Madeline Lancaster and Jürgen Knoblich were the first individuals to develop the cerebral organoid and report their findings, suggesting that pluripotent stem cells are capable of becoming different types of brain cells that aid in the evolution of a human brain (Bicknell, et al. 373). With these new heights reached, the team was capable of using differentiation in order to develop cells for all parts of the brain, thus, providing the brain with similar functions and structures to that of an embryonic brain (Li, et al.). In order to create these structures, a simpler version of the vitro model is implemented to fully capture the essence of an embryonic human brain.

These vitro models are first composed with the collection of embryonic stem cells [ESCs] from human embryos and induced pluripotent stem cells [PSCs] from adult cells (Ming, et al.). In the lab, these cells are placed under controlled conditions in order to ensure that they develop properly, including the maintenance of essential nutrients, hormones, oxygen concentration, and components of the extracellular matrix (Ming, et al.). These aspects encourage the cells to undergo self-renewal, allowing stem cells to divide and reproduce accordingly (Goldman). To create the organoid, these cells are then exposed to conditions that allow for differentiation to occur, ultimately producing the cell types found throughout the brain. Afterwards, the neural progenitor cells are placed into cultures to promote interactions between the cells and thus, create

self-organization (Li, et al.). As time passes, the stem cells continue to differentiate and make up different areas of the brain, thus forming the basis of the brain organoid (Benito-Kwiecinski and Lancaster). With the development of cerebral organoids, it provides research advantages that are difficult to match when studying brains that have undergone surgery or post-mortem.

Furthermore, in many studies regarding the human brain, primates that are similar to humans are often used as experimental subjects to prevent the interference of ethical concerns. However, these animals pose a limitation as they don't experience human cognitive and behavioral diseases, including autism, schizophrenia, and Parkinson's disease (Kriegston and Di Lullo 573). Due to this, these 3-dimensional models serve as significant advancements within the neuroscience field by providing insight into neurodegenerative and neurodevelopmental diseases (Choi, et al. 617). As they offer "live and functioning tissue," scientists can easily observe and study the negative implications of neurological disorders, which can lead to possible cures and treatments being developed (Kreigston and Di Lullo 573). In addition, the neural tissue creates realistic interactions within the brain, including synaptic connections and electrical impulses, allowing for an improved approach to studying the brain. Through the ability to have both a conceptual and structural representation of the brain, researchers can use genome-editing technology to change the DNA genome sequence and thus, implement diseases into the brain. These improvements in technology allow scientists to gain insight into how mutations and changes in the genetic material impact the brain's structure and its functions (Li, et al.).

Ethical Concerns and Complications

Despite the scientific breakthrough of the cerebral organoid, there are ethical concerns regarding the nature of the brain and the research conducted that may limit the studies conducted and its potential implementations. As pluripotent stem cells form the structure of brain organoids, these cells can create a fully functioning brain that experiences a sense of consciousness. Due to the complexity of the structure, it is difficult to avoid the brain from developing consciousness, causing the brain to encounter thoughts and feelings of pain and uncomfort due to the experimentation conducted (Bassil and Horstkotter 1). Consciousness is developed through the "neuronal correlates" within the brain, allowing for thalamocortical connections to be made and thus, introducing brain activity into the organoids (Li, et al.). Although the organoids cannot

directly demonstrate its behaviors, feelings, and thoughts through verbal means, brain activity itself is seen as a possible contributor to consciousness. The complexity of neuronal and cerebral structures allow for the processing of information, forming links between an individual's self-awareness, sensory input, and memories (Gabrielsen). According to Dr. Alysson Muotri, a professor in the Department of Cellular and Molecular Medicine at the University of California, her studies have suggested that a brain organoid that is merely six-weeks old can develop electroenceph -alogram activity, signaling electrical impulses that occur within premature infants that are around 25-39 weeks old (Hyun, et al.).

As supported by the peer-reviewed journal Science, researchers have suggested that infants gain both memory and consciousness at as little as 5 months old, meaning that cerebral organoids have a large chance of developing these senses similar to how an infant would (Gabrielsen). Despite this, many have argued that without enough information regarding the brain waves found in a premature infant, it's difficult to compare these findings to the development of brain organoids (Hyun, et al.). Many researchers have stated that brain organoids are not intricately designed and merely comprise the basic functions and structures of the brain, making it difficult to develop a sense of consciousness. Furthermore, the term "conscious" is ambiguous and associated with different meanings, creating controversy on whether the issue at hand can be considered as an ethical matter (Lavazza and Reichlin 1). The word itself has subjective meanings, yet is usually attributed to the idea of a living being due to the fact that consciousness allows one to experience feelings, including pain and suffering (Assanelli, et al.). Rather than the development of consciousness, researchers describe the state of brain organoids as "sentient," referring to one's capacity to experience different mental states, including a negative mindset (Lavazza and Reichlin 1).

Moreover, another ethical issue that research has highlighted concerns the usage of stem cells and the informed consent needed to form cerebral organoids. Within these studies, the person who's stem cells are being used must either provide informed consent or be anonymized to protect the person's privacy and basic rights (Fessl). However, these regulations are difficult to follow with the nature of brain organoid studies as many have argued. Although de-identification can protect the interests of the donor, it poses limitations to the research that can be conducted as

their tissue may contain mutations and diseases (Assanelli, et al.). Due to these issues, gaining anonymity of one's tissue and cells is not possible nor desirable for research purposes. Scientists claim that identification is needed in order to study the cerebral organoid significantly without the need for speculation (Koplin and Savulescu 760). Thus, it creates less useful research on brain organoids and a reduced accuracy in the information, diagnoses, and medications that can be formed through the experiments that may be conducted.

Furthermore, informed consent, which refers to informing the patient of the procedure along with the possible outcomes and risks, is difficult to obtain in these circumstances. As brain organoids are still being explored currently through research, the details regarding its applications and risks are changing unknowingly, making it difficult to describe the process to patients (Assanelli, et al.). Additionally, the clinical usage of cerebral organoids creates more concerns when considering informed consent (Goldman). As the healthcare industry consists of biobanks, institutions in which biological substances are stored for research purposes, they may be connected to companies that commercialize brain organoids (Assanelli, et al.). With this risk, donors may be skeptical of providing consent to such practices as they are influenced to participate in the research for an improvement in healthcare rather than being exploited for monetary purposes (Fessl).

Future Implementations of Brain Organoids

Although cerebral organoids may be subject to ethical complications, using these methods for research can allow for further progress in the neuroscience field. Brain organoids offer scientists a platform to observe and evaluate potential drug responses, therapeutic interventions, and disease mechanisms within the brain, curating important research that can change the trajectory of neuroscience (Shonkoff and Phillips). With the introduction of drugs in the brain, there are differing gene expressions associated with such changes, which can be observed with cerebral organoids. Researchers can observe patterns in neural activity as well, specifically the electrical impulses of the brain, to view the implementations of drugs and its potential (Kaykas, et al. 67). Through the use of imaging techniques, advancements in technology provide accurate visualizations of the brain to understand the changes in neuron connections that are caused by drugs. As more experiments are conducted, drug screening and efficacy can be evaluated in order

to identify treatments for a range of conditions (Wang). Additionally, these alterations in the brain can be viewed through therapeutic interventions, allowing for the production of personalized medication.

Brain organoids are composed of pluripotent stem cells that are derived from the organs of human individuals, including somatic cells from various areas of the body (Ming, et al.). These cells contain the genetic material of the subject, meaning that the drug responses gathered from the experiments would mostly pertain to the individual at hand, especially if they are suffering from any potential condition (Di Lullo and Kriegstein 573). Treatments can be developed through extensive analysis of the subject, allowing researchers to combine different regimes to optimize the success rates of these new potential medications. Furthermore, as the structure of cerebral organoids closely resembles an embryonic human brain, it can exhibit the characteristics of certain neurological conditions, thus shedding light on disease pathology (Wang.).

Many believe that brain organoids offer a deeper understanding of the concepts of heterogeneity as well through the production of various organoids (Badsha, et al. 15672). When many models of the brain are created with a different pluripotent stem cells, the DNA genome encryptions within these cells allow for varying protein expression, thus, providing researchers with a wide range of information regarding a disease's subtypes, inter-individual variability, and treatment options (Di Lullo and Kriegstein 573). Despite these advantages, there are shortcomings to the technology of organoids, revealing possible areas of improvement in terms of its structure and design. When engineering brain organoids, there is an apparent lack of vascularization, which refers to the formation of vessels, specifically blood vessels (Di Lullo and Kriegstein 573). These blood vessels have the responsibility of delivering nutrients and oxygen to the brain in order for it to function effectively (Brandt, et al. 97). According to Mayo Clinic, without a sufficient blood flow to the brain, many can develop life-threatening brain damage or strokes that are difficult to recover from (Shonkoff and Phillips). Although these disadvantages pose limitations to the potential use of brain organoids, with further research and knowledge regarding the subject, these issues can become resolved.

Conclusion

In essence, brain organoids serve as significant milestones within the neuroscience field as they provide us insight into the development of the human brain along with the implications of certain neurological conditions. These accurate three-dimensional models provide both a structural and conceptual understanding of the brain, providing researchers with a tool to explore the brain extensively (Wang). The structure of the brain offers realistic interactions, such as synaptic connections, which can be thoroughly observed and studied due to the developing and functioning tissue (Li, et al.). The formation through induced pluripotent stem cells allows for the interconnected functioning of the brain to be similar to that of an embryonic brain, allowing researchers to treat the brain organoid as such. Despite its ability to transform the biomedical field, there are ethical concerns regarding cerebral organoids, including the possibility of developing consciousness and gaining informed consent (Lavazza and Reichlin 1).

These issues are difficult to combat due to the nature of brain organoids and the composition of their structure, creating inevitable circumstances for donors and researchers. As brain organoids are still being studied, its clinical applications and setbacks are constantly changing, making it difficult for both parties to have a true understanding of the procedure involved (Assanelli, et al.). Researchers argue however that cerebral organoids have significant contributions to future discoveries, especially in the field of neuroscience, allowing many to continue their research and experimentation. Brain organoids provide researchers with the opportunity to evaluate the effects of drug responses, disease mechanisms, and therapeutic interference within the brain, changing the course of the medical field prominently. As research continues to prosper in the healthcare industry, brain organoids may begin to serve more purposes than originally intended, changing the medical opportunities that are yet to arrive.

Works Cited

Abbar, Akram, et al. “Induced Pluripotent Stem Cells: Reprogramming Platforms and Applications in Cell Replacement Therapy.” *BioResearch Open Access*, vol. 9, no. 1, 1 Apr. 2020, pp. 121–136. *Mary Ann Liebert*, www.liebertpub.com/doi/10.1089/biores.2019.0046, https://doi.org/10.1089/biores.2019.0046. Accessed 28 July 2023.

Assanelli, Simone, et al. “Organoids: A Systematic Review of Ethical Issues.” *Stem Cell Research & Therapy*, vol. 13, no. 1, 23 July 2022. *Springer Link*, https://doi.org/10.1186/s13287-022-02950-9. Accessed 11 July. 2023.

Badsha, Farhath, et al. “Human Cerebral Organoids Recapitulate Gene Expression Programs of Fetal Neocortex Development.” *Proceedings of the National Academy of Sciences*, vol. 112, no. 51, 7 Dec. 2015, pp. 15672–15677, https://doi.org/10.1073/pnas.1520760112. Accessed 12 July. 2023.

Bassil, Katherine, and Dorothee Horstkötter. “Ethical Implications in Making Use of Human Cerebral Organoids for Investigating Stress—Related Mechanisms and Disorders.” *Cambridge Quarterly of Healthcare Ethics*, 17 Feb. 2023, pp. 1–13. *Cambridge University Press*, https://doi.org/10.1017/s0963180123000038. Accessed 6 July. 2023.

Benito-Kwiecinski, Silvia, and Madeline A. Lancaster. “Brain Organoids: Human Neurodevelopment in a Dish.” *Cold Spring Harbor Perspectives in Biology*, 25 Nov. 2019. *Pubmed Central*, https://doi.org/10.1101/cshperspect.a035709. Accessed 6 July. 2023.

Bicknell, Louise S., et al. “Cerebral Organoids Model Human Brain Development and Microcephaly.” *Nature*, vol. 501, no. 7467, 28 Aug. 2013, pp. 373–379. *Pubmed Central*, www.research.ed.ac.uk/portal/en/publications/cerebral-organoids-model-human-brain-development-and-microcephaly(0ca40c0c-c197-4a79-b461-e453bbee838d)/export.html, https://doi.org/10.1038/nature12517. Accessed 5 July. 2023.

Brandt, Reuven, et al. “Brain Organoids, Consciousness, Ethics and Moral Status.” *Seminars in Cell & Developmental Biology*, vol. 144, Mar. 2022, pp. 97–102. *ScienceDirect*, https://doi.org/10.1016/j.semcdb.2022.03.020. Accessed 5 Apr. 2022. Accessed 10 July. 2023.

Buth, Jessie , et al. “TGFβ Superfamily Signaling Regulates the State of Human Stem Cell Pluripotency and Capacity to Create Well-Structured Telencephalic Organoids.” *Stem Cell Reports*, vol. 17, no. 10, 1 Sept. 2022, pp. 2220–2238. *Cell Press*, doi.org/10.1016/j.stemcr.2022.08.013, https://doi.org/10.1016/j.stemcr.2022.08.013. Accessed 28 July. 2023.

Choi, Baekgyu, et al. “Past, Present, and Future of Brain Organoid Technology.” *Molecules and Cells*, vol. 42, no. 9, 1 Sept. 2019, pp. 617–627. *Pubmed Central*, www.ncbi.nlm.nih.gov/pmc/articles/PMC6776157/, https://doi.org/10.14348/molcells. 2019.0162. Accessed 12 July. 2023.

Di Lullo, Elizabeth, and Arnold R. Kriegstein. “The Use of Brain Organoids to Investigate Neural Development and Disease.” *Nature Reviews Neuroscience*, vol. 18, no. 10, 7 Sept. 2017, pp. 573–584. *Pubmed Central*, www.nature.com/articles/nrn.2017.107, https://doi.org/10.1038/nrn.2017.107. Accessed 10 July. 2023.

Dinella, Jason, et al. “Use of Induced Pluripotent Stem Cells in Dermatological Research.” *Journal of Investigative Dermatology*, vol. 134, no. 8, 28 July 2023, pp. 1–5. *Pubmed Central*,www.ncbi.nlm.nih.gov/pmc/articles/PMC4527532/#, https://doi.org/10.1038/jid.2014.238. Accessed 28 July. 2023.

Gabrielsen, Paul. “When Does Your Baby Become Conscious?” *www.science.org*, Science, 18 Apr. 2013, www.science.org/content/article/when-does-your-baby-become-conscious. Accessed 5 July. 2023.

Goldman, Bruce. “Neural Organoids Mimic Developing Brains in a Lab Dish.” *Stanford Medicine Magazine*, Stanford University, 26 Feb. 2018, stanmed.stanford.edu/lab-grown-brain-balls-could-aid-understanding-of-neurological-diseases/. Accessed 11 July 2023.

Halley, Catherine. “Is It Ethical to Grow a Brain in a Petri Dish?” *JSTOR Daily*, JSTOR, 11 Dec. 2019, daily.jstor.org/is-it-ethical-to-grow-a-brain-in-a-petri-dish/. Accessed 6 July 2023.

Hyun, Insoo, et al. “Ethical Issues Related to Brain Organoid Research.” *Brain Research*, vol. 1732, Apr. 2020. *Pubmed Central*, https://doi.org/10.1016/j.brainres.2020.146653. Accessed 12 July. 2023.

Kaykas, Ajamete, et al. “The Future of Cerebral Organoids in Drug Discovery.” *Seminars in Cell & Developmental Biology*, vol. 111, July 2020, pp. 67–73. *ScienceDirect*, https://doi.org/10.1016/j.semcdb.2020.05.024. Accessed 26 Oct. 2020. Accessed 5 July. 2023.

Koplin, Julian J., and Julian Savulescu. “Moral Limits of Brain Organoid Research.” *The Journal of Law, Medicine & Ethics*, vol. 47, no. 4, Dec. 2019, pp. 760–767. *Sage Journals*, https://doi.org/10.1177/1073110519897789. Accessed 5 July. 2023.

Lagercrantz, Hugo, and Jean-Pierre Changeux. “The Emergence of Human Consciousness: From Fetal to Neonatal Life.” *Pediatric Research*, vol. 65, no. 3, Mar. 2009, pp. 255–260. *Nature*, www.nature.com/articles/pr200950, https://doi.org/10.1203/pdr.0b013e3181973b0d. Accessed 28 July 2023.

Lavazza, Andrea, and Massimo Reichlin. “Human Brain Organoids: Why There Can Be Moral Concerns If They Grow up in the Lab and Are Transplanted or Destroyed.” *Cambridge Quarterly of Healthcare Ethics*, 8 June 2023, pp. 1–15. *Cambridge University*, www.cambridge.org/core/journals/cambridge-quarterly-of-healthcare-ethics/article/human-brain-organoids-why-there-can-be-moral-concerns-if-they-grow-up-in-the-lab-and-are-transplanted-or-destroyed/CCC979E2F69341BA096779C28493D16B, https://doi.org/10.1017/S096318012300021X. Accessed 5 July 2023.

Li, Xuekun, et al. “The Application of Brain Organoids: From Neuronal Development to Neurological Diseases.” *Frontiers in Cell and Developmental Biology*, vol. 8, 22 Oct. 2020. *Frontiers*, https://doi.org/10.3389/fcell.2020.579659. Accessed 16 July. 2023.

Ming, Guo-li, et al. “Brain Organoids: Advances, Applications and Challenges.” *Development*, vol. 146, no. 8, 15 Apr. 2019. *The Company of Biologists*, https://doi.org/10.1242/dev.166074. Accessed 18 July. 2023.

Setia, Harpreet, and Alysson R. Muotri. “Brain Organoids as a Model System for Human Neurodevelopment and Disease.” *Seminars in Cell & Developmental Biology*, vol. 95, Nov. 2019, pp. 93–97. *ScienceDirect*, https://doi.org/10.1016/j.semcdb.2019.03.002. Accessed 18 July. 2023.

Shonkoff, Jack P, and Deborah A Phillips. “The Developing Brain - from Neurons to Neighborhoods.” *Nih.gov*, Pubmed Central, 2019, www.ncbi.nlm.nih.gov/books/NBK225562/. Accessed 12 July. 2023.

Wang, Hansen. “Modeling Neurological Diseases with Human Brain Organoids.” *Frontiers in Synaptic Neuroscience*, vol. 10, 8 June 2018. *Frontiers*, https://doi.org/10.3389/fnsyn.2018.00015. Accessed 10 July. 2023.

AI's Interfere with Human Brain

Si-Eun Park (author), Thanisha Kapur (advisor)
North Gwinnett High School

Keywords: Brain-Computer Interfaces, Motor Cortex, Electroencephalography, Non-Invasive BCI, Mu Rhythm, Beta Waves

Abstract

In this research paper, the investigation of Brain-Computer Interfaces (BCI) based on Electroencephalography signals to classify motor imagery tasks as a step toward controlling external devices with one's cognitive process. Twenty healthy participants took part in the conducted experiment. The experiment settings involved recording EEG data while participants were performing the task. Using EEGLAB, the artifacts from acquired EEG recordings were removed and later processed through Python. The featured extracted signals showed a frequency of 8-13 Hz of mu rhythm and exhibited mu suppression as well. Results revealed that fifteen out of twenty participants succeed in controlling external devices with their neural activities, demonstrating a 75% success rate from the result. These findings demonstrated the capability of BCIs and the beneficial insights for the future implication and development of BCI. Though more research is necessary, this work establishes the comprehension of motor-control BCI based on EEG into assistive technology and neurorehabilitation applications.

Introduction

Various science-fiction movies, dramas, or any media have been demonstrating futuristic artificial intelligence that is completely absorbed with human life. Some of the displayed imaginations have been researched and are in fact happening in real life as well: from the earliest AI program, a checkers-playing program, to now assisting surgery and diagnosing diseases in the human body. As AI technology is contributing massive effects on the physical human body, it has attracted many scientists and researchers to wonder if AI technology can interfere with humans neurologically. Nowadays, psychological disorders have been problems for countless people; indeed, about 1 in 5 U.S. adults live with mental disorders. Many experts have been claiming that those disorders are due to imbalances or malfunctions of the neurons in the brain.

Though causes for these disorders vary, the distinct treatments are yet to be found due to reasons such as the complexity of the brain, limited knowledge of brain functions, animal models' limitation, or ethical considerations. Despite these limitations, researchers and scientists are taking various approaches and experiments with fast-advancing technology such as utilizing software, programs, or AI. One of the rising technologies in the field of neuroscience is Brain-Computer Interfaces (BCIs), a computer-based system collaborated with Artificial Intelligence that allows transmission between external devices and one's brain. BCI enables one to control external devices only by using their neuronal activity. Neurons, a fundamental unit of the nervous system in the brain, allows nerve cells to send messages all over one's body with chemical signaling and electrical impulse. In this sense, BCIs read the electrical signal in the brain, and transmit and translate the acquired signal to the device, allowing one to move the device with any physical effort. This research paper examines the effectiveness of BCI based on Electroencephalography (EEG) and its possibility to play a role in the treatment of neurological disorders, specifically, neuromuscular disorders.

Materials and Methods

The brain that will be analyzed throughout the experiment is recruited from a clinical setting from collaborating hospitals, the participants who do not have any concerning health conditions or medical histories, volunteered for the experiment. Before the experiment, a detailed explanation of the experiment procedure, potential risks or aftereffects, purpose, and benefits were thoroughly clarified: including consent from each of the participants. A total of 20 healthy volunteers' (10 males, 10 females, right-handed, and age 40 ± 10) motor imagery movements of the right hand were conducted through this BCI experiment. The recordings of neural activities were done by an electroencephalogram (EEG). EEG records electrical currents that are generated when neurons communicate with each other. The electrodes were specifically placed in an area of primary hand area, C3 and C4 as an array of electrodes covering motor and somatosensory areas. Before placing the electrodes on the scalp, conductive gel is applied to improve electrical contact between the scalp and EEG, providing accurate signal recording. Participants were asked to visually perform two tasks as they got instructions on each performance virtually by television screen in a relaxed position: they were asked to perform drawing a circle and writing short words with 4 letters with their right hand. The experiment was conducted in a 20-30 seconds duration

with 3 minutes break and was instructed to perform 10 experiments each day for 10 days to minimize the experimental error. While participants are performing the tasks, recorded EEG will provide activity patterns that are generated from the participants' movements, especially beta waves and mu rhythms in the frontal or central area of the brain. EEG recording often gets debased from external signals called artifacts, a source that usually comes from physiological movements such as eye, muscle, or heartbeat movement, and other environmental settings.Therefore, the recorded EEG must go through filterings for an accurate and clear signal. In this setting, software tools and programming libraries such as EEGLAB are used to eliminate artifacts, including eye movements or blinks, and to separate brain activities from artifacts.
In this experiment, EEG signals were filtered from 4 to 50 Hz using MNE-Pythold, a Python library for EEG and MEG data analysis. This programming tool not only provides tools for time-frequency analysis, but also provides statistical analysis and source localization, which helps to focus on brain signals that are specifically needed to convert into commands. When determining the tasks that will be used to generate commands, Python is used for designing and controlling the experimental tasks, which also allows the synchronization of EEG recording systems. After these processes, recorded neural activities are calibrated to interpret the signals and map them into specific commands for an external device to follow. This step is critical for BCIs when extracted, the calibration phase allows the external device to 'learn' and 'recognize' the pattern. Throughout the rest of the BCI experiment, participants are engaged in the actual BCI task, which are the tasks the participants have already demonstrated visually without moving any muscles. The experiment ended with the feedback and training using BCI2000, a software platform that allows researchers to design personalized feedback paradigms and adaptive training scenarios. The method used to work on feedback-and-learning is *the operant conditioning approach*, in which an EEG signal decoder/classifier is fixed and unknown to the user, and the user has to figure out how to control the device with their brain activities.

Data Analysis

The data analysis from the experiment will be from amplification, processing, interpretation, and visualization of recorded EEG signals along how these processed signals cooperate with external devices. The EEG signals are first converted into Common Average Reference (CAR) to filter and decrease the outsourcing noise such as background electrical noise or muscle activity, when

recording the brain activity in the motor cortex, frontal lobe. Then, the raw EEG signals that are processed from neural activity are converted into Frequency-Domain Signals, which offers insights into brain rhythms and activity patterns by representing the power of amplitude of various frequency bands overtime. The converted signals are studied with frequencies such as Alpha, Beta, Theta, and Low Gamma, as these brain waves provide different states of mental condition. Theta waves associated with such deep meditation, or internal focus; Alpha waves associated with a state of awakeness, eyes closed, or overall mental coordination; Beta waves are associated with eyes opened, thinking, high energy or arousal; and last Gamma waves are associated with higher brain functions like cognition and memory. As the main focus of this experiment is the motoric movement, the result is specifically focused on Beta waves. Normal Beta waves range should fall into 12-38 Hz. Low beta waves (15-20 Hz) are associated with increase in energy, anxiety, and performances, and high beta waves (18-40 Hz) are associated with significant stress, anxiety, high energy and arousal. Within the beta waves, the mu rhythms, a specific type of beta waves that shows the rhythm of mirror neurons, mu rhythms, are majorly focused to convert into the command: Mirror neurons are the most prominent features of the brain that allows one to encode others' actions, feelings, or intentions. The recorded mu rhythms showed a range of 8-13 Hz throughout the experiment, though, when participants were performing the tasks, the amplitude of the mu rhythm significantly decreased. The decrease of amplitude in the mu rhythms is a phenomenon called mu suppression, which is exhibited when one is performing or perceiving specific movement or motor imagery : "It [mu] decreases or disappears completely when the subject changes his position on his seat or when he readjusts his tonus. It also disappears when the subject identifies himself when an active person is represented on the screen" (Gastaut & Bert). With these acquired signals, the processings of extracting EEG was performed with EEGLAB, MNE-Python, and BCI2000 as listed in the materials and method section. Out of 20 participants, fifteen of the participants succeeded in controlling devices, and others struggled to control the devices. Despite this result, the intended users are patients with neurological disabilities, meaning that they may have never performed such tasks in their life. This indicates that the actual users might struggle in controlling devices or even imagine these tasks. For example, suppose asking one who has never ridden a bike to imagine riding a bike, and another one who previously has experience of riding a bike. Obviously, one who previously

had an experience of riding a bike could imagine better. In this sense, it is necessary for the BCI field to improve the strategies for feedback-and-learning.

Discussion and Results

With current technology, there are several limitations in utilizing BCI in real life. Human brain is still complex, and the complete understanding of the brain is extremely challenging. Reading the currents of about 100 billion neurons, each playing different roles, and converting it to command is still a huge challenge. Not only this, but the equipment for BCIs are also not as portable. The ultimate goal of BCI technology is to establish a ‘seamless’ communication pathway between the human brain and external devices or systems. Majority of the current BCI technologies still requires wired-connection to equipment, and the computers that are used for BCIs might weigh more than around 10 pounds, which makes it hard to use it in real life situations. However, those with neurological disorders struggle to perform simple yet customary movements in their daily lives, and just being able to perform those simple tasks can totally change one’s life. With fast-developing technology, the field of BCI applications are expected to rapidly extend and improve.

Works Cited

Fox, Nathan A, et al. "Assessing Human Mirror Activity with EEG Mu Rhythm: A Meta-Analysis." *Psychological Bulletin*, vol. 142, no. 3, 2016, pp. 291–313, www.ncbi.nlm.nih.gov/pubmed/26689088, https://doi.org/10.1037/bul0000031.

Gastaut, Henri J, and Jacques Bert. "EEG Changes during Cinematographic Presentation (Moving Picture Activation of the EEG)." *Electroencephalography and Clinical Neurophysiology*, vol. 6, Jan. 1954, pp. 433–444, https://doi.org/10.1016/0013-4694(54)90058-9.

Hobson, Hannah M., and Dorothy V. M. Bishop. "The Interpretation of Mu Suppression as an Index of Mirror Neuron Activity: Past, Present and Future." *Royal Society Open Science*, vol. 4, no. 3, Mar. 2017, p. 160662, https://doi.org/10.1098/rsos.160662.

Hwang, Han-Jeong, et al. "Neurofeedback-Based Motor Imagery Training for Brain–Computer Interface (BCI)." *Journal of Neuroscience Methods*, vol. 179, no. 1, Apr. 2009, pp. 150–156, https://doi.org/10.1016/j.jneumeth.2009.01.015.

Javaid, Muhammad Adeel. "Brain-Computer Interface." *SSRN Electronic Journal*, 2013, https://doi.org/10.2139/ssrn.2386900.

Lotte, Fabien. *On the Need for Alternative Feedback Training Approaches for BCI*. June 14AD, inria.hal.science/hal-00834391/document.

Ye, Hui, and Amanda Steiger. "Neuron Matters: Electric Activation of Neuronal Tissue Is Dependent on the Interaction between the Neuron and the Electric Field." *Journal of NeuroEngineering and Rehabilitation*, vol. 12, no. 1, 12 Aug. 2015, https://doi.org/10.1186/s12984-015-0061-1.

Musical Therapy in the Treatment of Alzheimer’s Disease

Sneha Bhat (author), Thanisha Kapur (advisor)
John F. Kennedy Memorial High School

Keywords: Alzheimer’s, Musical Therapy, Memory

Abstract

Alzheimer's disease is a general neurological illness causing memory loss, cognitive decline, and changes in conduct amongst thousands and thousands worldwide. However, music has emerged as a new, promising, treatment for this ailment. This literary review presents an exploration of the healing power of music in Alzheimer's treatment, going based on considerable research and systematic reviews. Musical therapy has proven to have profound results in the improvement of cognitive abilities, emotional well-being, and quality of life for those affected byAlzheimer's disorder. Active musical interventions, which includes singing and playing an instrument have proven effective, fostering social connections and cognitive stimulation. Even as the evidence for the musical effect on memory loss stays inconclusive, it has been validated as effective in treating cognitive symptoms in various types of dementia. Having musical education and background expertise offer extra advantages, enriching the lives of individuals with Alzheimer's. Incorporating music therapy into Alzheimer's care holds fantastic potential to offer valuable support, wish, and step forward satisfactory life for patients and their caregivers alike.

Introduction

Alzheimer's disease is a widespread neurological disorder that influences hundreds of thousands of individuals globally, mainly causing memory loss, cognitive decline, and changes in behavior. It impacts an approximate 5% of men and 6% of women over the age of 60 internationally. Difficult conversations, emotionally demanding situations, and diminished quality of life often accompany the illness. Nevertheless, the therapeutic power of msuic has emerged as an incredible device in enhancing the lives of individuals living with Alzheimer's. Relevant studies suggest that musical remedy has profound effective outcomes on cognitive talents, emotional well-being, and averagenice of existence for those suffering from Alzheimer's. This study explores the healing advantages of music in Alzheimer's treatment, examining the clinical proof

and highlighting the transformative effect it has on individuals with the illness. Understanding the position of music in Alzheimer's care can offer wish and progressed aid for those navigating the demanding situations of this complicated disease.

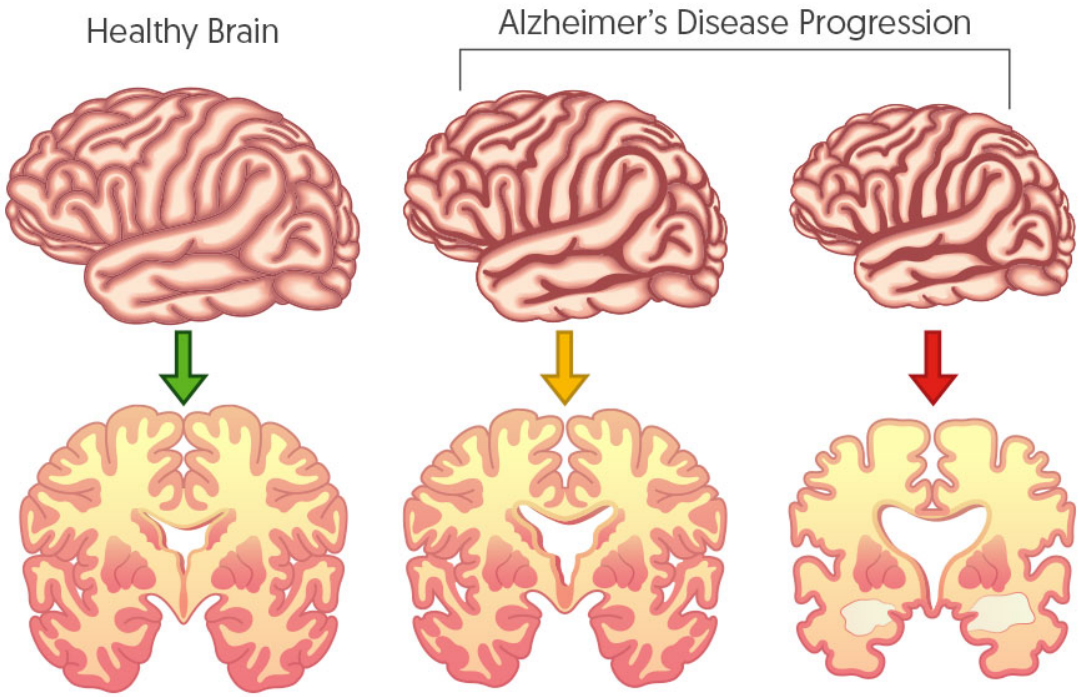


Image from: https://advancedbrain.com/blog/alzheimers-and-memory-loss-natural-ways-to-protect-your-brain/

Body

Music Therapy as a Complementary Treatment

In a systematic evaluation performed through researchers, eight randomized managed trials were analyzed to assess the effect of musical therapy on cognitive functions in advert patients (Article 1). The trials, encompassing 689 individuals from numerous international locations, revealed promising outcomes. The findings suggested that musical therapy, whether or not used alone or alongside pharmacological treatments, had a wonderful impact on cognitive functions. Furthermore, active musical interventions, along with singing and gambling tunes, demonstrated extra effectiveness. The overview highlighted the capacity of musical therapy as a complementary treatment choice for individuals with Alzheimers, even though similar research is needed to decide the greatest intervention techniques and evaluate lengthy-term effects. The

positive impact of track therapy on cognitive capabilities in patients with Alzheimer's can be attributed to its multifaceted outcomes on the brain. Neurobiological studies have proven that music engages various areas of the mind, primarily memory, attention, emotion, and language processing. The auditory cortex, hippocampus, and prefrontal cortex are many of the key mind regions that reply to music stimuli. Additionally, these areas often undergo degeneration, cognitive decline and memory deficits. Music remedy appears to spark off neural networks that remain extraordinarily preserved in the early levels of the disease, allowing individuals to get admission to recollections and feelings related to familiar tunes.

Moreover, music has been found to stimulate the release of neurotransmitters like dopamine, which might be important for reward and pleasure processing. This dopamine launch at some stage in musical reports can enhance mood and decrease strain and anxiety, common signs experienced with the aid of Alzheimer's patients. Moreover, music therapy can foster a feel of social connection and emotional assistance, as organization classes regularly schedule interactions and bonding amongst participants.

The lively music interventions, which often include singing and playing music are immensely effective in comparison to passive listening periods. Listening to this music requires the coordination of motor competencies, auditory processing, and cognitive features, which lead to heightened neural plasticity. This neuroplasticity is critical for maintaining cognitive capabilities and could doubtlessly slow down the progression of cognitive decline in patients.

Music and Dementia

Other systematic overviews explored the outcomes of music therapy on memory deficits in Alzheimer's patients (Bleibel "The Effect of Music Therapy on Cognitive Functions in Patients with Alzheimer's Disease"). After reading 4 studies regarding 179 patients, the researchers located evidence supporting the advantages of musical remedy in treating memory deficits. but, because of the restricted number of randomized managed trials held, the proof stays rather inconclusive. Furthermore, music therapy has proven effectiveness in enhancing memory in addition to behavior and cognitive signs in patients with dementia. It is seen as a non-pharmacological remedy that could improve cognitive functions and temper. Exposure to

music has been determined to elicit emotional responses, provoke social connections, and serve as an effective link to a person's life in the past. The concept of procedural reminiscence allows individuals with dementia to interact in music-related sports, such as playing an instrument or dancing, regardless of severe memory impairment. Customized music sports and track remedy have confirmed positive outcomes on temper, behavior, and cognition in people with dementia, together with those with Alzheimer's (Moreira "Can Musical Intervention Improve Memory in Alzheimer's Patients? Evidence from a Systematic Review").

Moreover, the impact of music knowledge and musical schooling on aging cognition and dementia has been investigated ("Music and Dementia: An Overview"). Preliminary findings suggest that musical schooling may have a defensive effect in opposition to dementia. However, much more extensive research is needed to set up a clearer knowledge of the relationship among music expertise and cognitive decline.

Conclusion

To conclude, Alzheimer's is a progressive neurological disease that affects millions worldwide, causing cognitive decline and diminished satisfaction of life. However, the therapeutic power of music has emerged as a new, yet valuable tool in enhancing the lives of people suffering from Alzheimer's. Countless studies suggest that musical treatment has profound positive consequences on cognitive abilities, emotional well-being, and quality of life for the ones suffering from this illness. The engagement of numerous brain regions, stimulation of neurotransmitters like dopamine, and promoting neural plasticity make contributions to musical therapy's effectiveness in improving cognitive functions in patients. Active musical interventions, like playing instruments or singing, have also proven worthwhile, fostering social connections and cognitive stimulation. By incorporating musical therapy into Alzheimer's treatment, we can provide invaluable care and assistance for both patients and their caregivers.

Works Cited

Bleibel, Malak, et al. “The Effect of Music Therapy on Cognitive Functions in Patients with Alzheimer’s Disease: A Systematic Review of Randomized Controlled Trials - Alzheimer’s Research & Therapy.” *BioMed Central*, 27 Mar. 2023, alzres.biomedcentral.com/articles/10.1186/s13195-023-01214-9#:~:text=In%20addition%20to%20 eliciting%20 positive,assess%20and%20evaluation%20 behavioral%20 symptoms.

Moreira, Shirlene Vianna, et al. “Can Musical Intervention Improve Memory in Alzheimer’s Patients? Evidence from a Systematic Review.” *Dementia & Neuropsychologia*, 2018, www.ncbi.nlm.nih.gov/pmc/articles/PMC6022981/.

“Music and Dementia: An Overview.” *Practical Neurology*, practicalneurology.com/articles/2017-june/music-and-dementia-an-overview. Accessed 26 July 2023.

Effect of AI on the Function of EEG Based Brain-Computer Interfaces

Sneha Gadekarla (author), Thanisha Kapur (advisor)
The Quarry Lane School

Keywords: Brain-computer interfaces, Artificial Intelligence, Brain Signal Analyzation, Feature Extraction, Electroencephalogram, Brain

Abstract

This paper and research article examines the effects of using artificial intelligence to analyze brain signals collected in EEG based brain-computer interfaces. It goes over the function and uses of brain-computer interfaces, along with their possible applications in the medical field. It also describes the process brain-computer interfaces go through in order to perform their function and the step where artificial intelligence can be added to improve the efficiency of the interface. Brain signals are collected in the study using the electroencephalogram cap participants are wearing, and artificial intelligence is used to find patterns within the collected signals and the actions that must be performed based on the patterns. Participants play a game using a brain-computer interface not using artificial intelligence in the signal analyzation stage first. Then, they play the same game while using a brain-computer interface that does use artificial intelligence. Through this research article, by comparing the efficiency of both brain-computer interfaces and the performance of participants between both interfaces, it is shown that artificial intelligence can improve the interface.

Introduction

A type of technology currently being studied and improved upon by researchers are brain-computer interfaces. Brain-computer interfaces (BCIs) are computer systems that collect brain signals from the user, analyze them, and then translate the signals in order to send commands to the device and do a certain action. Popular brain-computer interfaces are EEG based BCIs, which collect signals using scalp recorded electroencephalogram (EEG), such as a scalp based EEG, that can then be analyzed. Scalp based EEG is non-invasive, which makes it easier to use and research. All BCIs follow a process, going from signal acquisition to feature extraction, feature translation, and finally device output. There are various applications of

brain-computer interfaces. One application is in somatosensation, where brain-computer interfaces are used to help people who have lost abilities to feel or process what they feel. Another way that BCIs can be used is in terms of cochlear implants, which can help people with hearing loss. Such applications can have a great impact on patients who have suffered from brain injuries and increase their quality of life. Scientists are looking at ways artificial intelligence can be combined with brain-computer interfaces to improve their function and reliability. However, some problems with using AI with BCIs is that machine learning algorithms may cause a difference between the user's thoughts and the actual technology because of its process. This paper aims to observe the effect of using artificial intelligence in the process of analyzing brain signals that are collected by the EEG in brain-computer interfaces.

Materials and Methods

The experiment will use 10 females and 10 males living in the United States as participants. All participants will have to live around the same location in order for them to use the brain-computer interface. Participants will all be from the age of 25 to 30. The experiment will also use one laptop with Windows 10 Professional (64 bit), a minimum of 2GHz for a 20-30 GB harddisk, 4GB RAM, Bluetooth 2.1 + EDR support, NET Framework 4.7.1, Desktop development with C++ workload, and Microsoft Visual Studio. The experiment will also involve 1 Unicorn Hybrid Black, which includes a Unicorn Brain Interface amplifier, the Unicorn Suite Hybrid black containing a Unicorn Recorder, Unicorn .Net API, and Unicorn C API, a Unicorn EEG Cap, 8 Unicorn Hybrid EEG electrodes, 50 Unicorn Sticky electrodes, a Unicorn Bluetooth dongle, and a Unicorn Micro USB charging cable ("Technology of Unicorn Hybrid Black").

Each participant will wear the Unicorn EEG cap. The 8 electrodes will then be connected to the corresponding locations on the cap and Unicorn EEG gel will be added. The electrodes should be in positions over the parietal, occipital, and central areas of the brain. The sticky electrodes will be attached on the mastoids of the user. After the Unicorn Recorder shows that all electrodes are connected properly by turning green, the game can be started. All materials can be found and ordered on the Unicorn website by ordering the Unicorn Hybrid Black from the shop ("Technology of Unicorn Hybrid Black").

All participants will first do the game using the brain computer interface with no AI used in the brain signal analyzation stage. The game will involve a 2D object on a screen. Participants will be able to move the object left, right, up, and down. There will also be a target that the participants must direct the 2D object towards that is set randomly on the screen. However, the target should be the same distance away from the object in every trial. Afterwards, the participants will do the same game except with AI being used in the BCI's brain signal analyzation stage. This process will be repeated 5 times per participant. By repeating the process, participants will be able to gain practice with using the brain-computer interfaces and more data can be collected on the efficiency of the brain-computer interfaces (Garcia-Molina 111).

Results will be determined based on the change in speed and accuracy for participants in the completion of the game from having no AI and to then using AI. The speed taken for the brain-computer interfaces to detect patterns from the brain signals participants produce will also be measured and compared to see which interface is more efficient.

Results and Discussion

All results in this research article are hypothetical, as the experiment is based on similar past experiments and has not been done before. Based on previous experiments, it seems that scalp based EEG brain-computer interfaces using artificial intelligence in the brain signal analyzation stage would perform better than brain-computer interfaces that do not use artificial intelligence because of their quicker speed at detecting patterns in the signals produced. In one paper, the experiment uses artificial intelligence in the brain signal analyzation stage and in the conclusion states that the artificial intelligence that is used helped improve the process of finding patterns in the brain signals given off of the EEG. To recognize these patterns, Kernel functions were used (Garcia-Molina 95). While the paper did not compare the brain-computer interfaces using artificial intelligence with those that are not, it was stated that the use of better artificial intelligence networks did help the performance of how the brain-computer interfaces analyzed data and that continued improvement on these artificial intelligence models would likely cause even better brain-computer interfaces to be created (Garcia-Molina 135).

However, there are multiple errors that could happen in the experiment. Participants who have experience with brain-computer interfaces before might have a better performance in the experiment, creating an outlier in the data. Furthermore, the EEG cap participants wear have electrodes that need Unicorn EEG gel to clear up noise and allow for better signal acquisition. Because of the need for a human to apply the gel and attach the electrodes to participants, there would be variation between each participant in terms of the attachment of the electrodes and the gel application. This could create large differences between participants and trials in the signal acquisition stage, which could be the cause for the better performance of one brain-computer interface over the other. Overall, while the use of artificial intelligence in the brain signal analyzation stage of brain-computer interfaces seems promising, there needs to be more research to understand its effects and improve the accuracy of the interfaces.

Works Cited

Garcia-Molina, Gary. “Direct brain-computer communication through scalp recorded EEG signals.” (2004). doi:10.5075/epfl-thesis-3019.

Li, Zina et al. “Advances in Hybrid Brain-Computer Interfaces: Principles, Design, and Applications.” *Computational intelligence and neuroscience* vol. 2019 3807670. 8 Oct. 2019, doi:10.1155/2019/3807670

Liang, Xinbin et al. “Convolutional Neural Network with a Topographic Representation Module for EEG-Based Brain-Computer Interfaces.” *Brain sciences* vol. 13,2 268. 5 Feb. 2023, doi:10.3390/brainsci13020268

Ponce, Hiram et al. “Editorial: Artificial intelligence in brain-computer interfaces and neuroimaging for neuromodulation and neurofeedback.” *Frontiers in neuroscience* vol. 16 974269. 15 Jul. 2022, doi:10.3389/fnins.2022.974269

Shih, Jerry J et al. “Brain-computer interfaces in medicine.” *Mayo Clinic proceedings* vol. 87,3 (2012): 268-79. doi:10.1016/j.mayocp.2011.12.008

“Technology of Unicorn Hybrid Black.” *Unicorn*, 15 Dec. 2022,www.unicorn-bi.com/brain-interface-technology/.

Zhang, Xiayin et al. “The combination of brain-computer interfaces and artificial intelligence: applications and challenges.” *Annals of translational medicine* vol. 8,11 (2020): 712. doi:10.21037/atm.2019.11.109

Neuroplasticity in Children

Soorya Krishnan (author), Thanisha Kapur (advisor)
WW-P High School South

Keywords: Neuroplasticity, Neural Networks, Neural Circuits, Cognitive Development, Multisensory Experience.

Abstract

This article aims to explore the concept of neuroplasticity in one's childhood, which refers to the brain's ability to change and adapt as we grow. It discusses the importance of this process in education, cognitive development, and overall well-being. The review highlights how neural circuits form and refine over time, and how experiences shape the brain's connections. It puts emphasis on the significance of creating learning environments that leverage neuroplasticity through multisensory experiences, hands-on activities, and enriching learning opportunities. The article also puts emphasis on the role of a nurturing and supportive classroom atmosphere in promoting the brain's growth. Understanding and utilizing neuroplasticity could lead to improved education and better opportunities for young students.

Introduction

Functions of Neuroplasticity in Childhood

Neuroplasticity, defined as the brain's ability to reorder and adapt throughout life, has captivated researchers and educators alike, particularly in the context of childhood development. This review will explore the extensive research on neuroplasticity in children, particularly into its mechanisms, implications, and enhanced potential. Understanding neuroplasticity during childhood has dynamic implications for education, cognitive development, skill acquisition, and overall life By revealing the dynamic nature of the developing brain, we can optimize early learning environments, support language acquisition, deepen sensory skills, and promote positive outcomes for children that might be born with neural conditions, which could otherwise inhibit their education.

During childhood, the brain undergoes an extraordinary phase of growth and development, usually defined by heightened neuroplasticity. Neural circuits form and refine which creates a complex network that supports cognitive processes, sensory perception, motor skills, and emotional development. Through structural and functional changes, the brain adapts to experiences, optimizing its function and the refinement of neural circuits in coordination with specific tasks and skills moving forward.

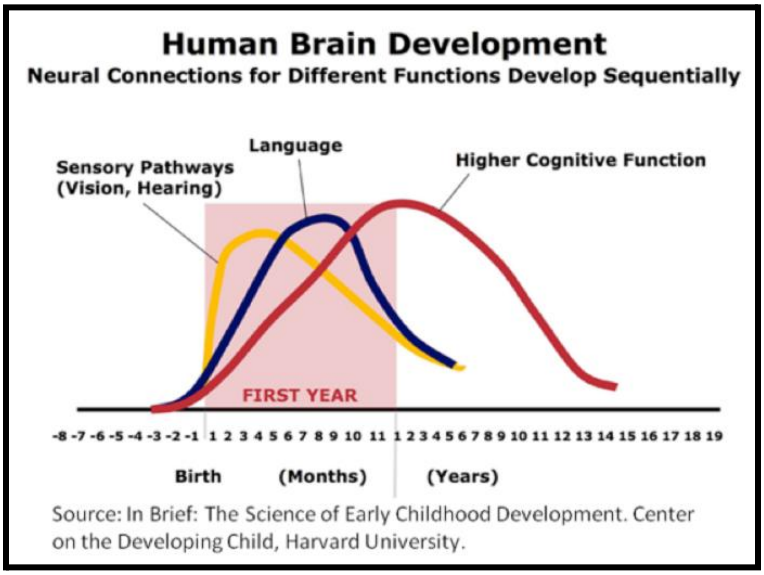


Image from https://karenpapemd.com/can-you-stimulate-baby-brain-neuroplasticity/

The full understanding of neuroplasticity holds immense significance for elementary level education. By recognizing the vulnerability and responses of children's brains, educators can tailor instructional strategies to optimize a child's neuroplasticity and help a student reach their full academic potential. Incorporating multisensory experiences, hands-on activities, and enrichment to students can create open grounds for neural growth, facilitating the acquisition of knowledge, critical thinking skills, and problem-solving abilities of children to aid their transition to high levels of education.

Body

Formation and Development of Neural Circuits

Neuroplasticity during childhood encompasses the dynamic processes involved in the formation, strengthening, and refinement of neural circuits. As children engage with their environment, their brains undergo immense shuffling. This shuffling occurs through the establishment of new connections between neurons and the strengthening of existing connections, known as synaptic plasticity. These structural changes allow the brain to optimize its functioning and tailor its neural architecture to specific tasks and skills, which come from experience.

The formation of neural circuits is a fundamental aspect of neuroplasticity in childhood. When children explore their environment and interact with various stimuli, new connections between neurons are made. These connections are formed by the experiences and environmental demands the child encounters. For example, when a child learns to recognize and respond to faces, specific neural circuits involved in facial recognition develop and strengthen through synaptic plasticity.

To add on, neuroplasticity involves the refinement of neural circuits through a process called synaptic pruning. During this process, weaker or redundant synapses are eliminated, allowing the brain to filter its neural connections and optimize its efficiency. Through synaptic pruning, the brain ensures that its resources are being used effectively, optimizing its neural structure to ensure a child has specific competencies.

Neuroplasticity in Education: Tailoring Instructional Strategies

Understanding the relationship between neuroplasticity and childhood brain development holds immense significance for the future of elementary education. By recognizing the brain's malleability and its rapid response to experiences, teachers can design instructional strategies that use neuroplasticity to enhance learning outcomes.

Tailoring instructional strategies to capitalize on neuroplasticity is crucial for optimizing learning. An effective example of this could be to incorporate multisensory experiences into lessons. By engaging multiple neural networks simultaneously through visual, auditory, and

kinesthetic elements, educators stimulate different regions of the brain, facilitating deeper learning, and improving neuroplasticity.

Another effective strategy could be to promote hands-on activities and learning by experiences. These approaches provide opportunities for engagement, practical application of knowledge, and reinforcement through feedback and reflection. By engaging students in real-world problem-solving tasks, teachers develop critical thinking skills, creativity, and adaptability, which are essential for success in higher levels of education.

Promoting Cognitive Development

Enrichment activities that expose children to diverse experiences promote neuroplasticity and enhance the child's cognitive development. By offering opportunities for exploration in various subjects, typically in arts, music, sports, and languages, educators stimulate different regions of the brain, facilitating the formation of new connections.

Enrichment activities are flexible, field trips, guest speakers, and extracurricular programs and all beneficial. These activities increase a child's exposure to different experiences and provide opportunities for more specific learning. For example, engaging in art can enhance creativity and heighten individuality, while learning a musical instrument can improve the sense of hearing

Learning Environments

A forgiving and supportive learning environment is crucial for optimizing neuroplasticity. Positive relationships, emotional well-being, and reduced stress levels have been found to facilitate brain development and learning. Teachers can promote these factors by holding strong qualities of respect and tolerance within their classrooms, as well as teaching stress management techniques.

Building positive relationships with students can create a supportive learning atmosphere. When children feel valued, respected, and emotionally supported, they are more likely to engage in learning and take risks. This emotional connection enhances neuroplasticity by reducing stress

and promoting a sense of safety and well-being, which would help the previously formed neural networks.

Additionally, teaching stress management techniques gives children the strategies to regulate their emotions and cope with challenges effectively. Mindfulness exercises, deep breathing techniques, and physical activities can help reduce stress levels and create a balanced state for neuroplasticity, but more importantly, learning.

Conclusion

In conclusion, neuroplasticity is an amazing ability of the brain that helps it change and adapt during one’s childhood. By understanding and using neuroplasticity in education, teachers can create better learning experiences for students. Activities that use multiple senses and hands-on learning are great for the brain. Enriching experiences, like exploring different subjects, can also help the brain develop. A caring and supportive environment is essential for the brain's growth, and it's something teachers can create in the classroom. Understanding neuroplasticity can lead to better education and brighter futures for students. As technology advances, it is more likely that kids will be chronically online, ensuring that their brains are effectively developed in school will keep a constant flow of effective, intelligent, and hardworking students into higher levels of education.

Works Cited

Davidson, Richard J. "Childhood adversity and the brain: Harnessing the power of neuroplasticity." Biological psychiatry 90.3 (2021): 143-144.
https://www.biologicalpsychiatryjournal.com/article/S0006-3223(21)01302-0/abstract

Schlaug, Gottfried, et al. "Training‐induced neuroplasticity in young children." Annals of the New York Academy of Sciences 1169.1 (2009): 205-208.
https://nyaspubs.onlinelibrary.wiley.com/doi/abs/10.1111/j.1749-6632.2009.04842.x

Asby, Dana. "Why early intervention is important: neuroplasticity in early childhood." Preuzeto s (2018).
https://www.researchgate.net/profile/Dana-Asby/publication/326690391_Why_Early_Intervention_is_Important_Neuroplasticity_in_Early_Childhood/links/5b5f3f74aca272a2d6755774/Why-Early-Intervention-is-Important-Neuroplasticity-in-Early-Childhood.pdf

Celentano, Alexis M. "Neuroplasticity: the impact of age and injury." (2017).
https://soar.suny.edu/handle/20.500.12648/1353

Pal, Ria, and Jorina Elbers. "Neuroplasticity: The other side of the coin." Pediatric Neurology 84 (2018): 3-4.
https://www.pedneur.com/article/S0887-8994(18)30249-2/abstract

Watt, Toni, et al. "The unique nature of depression and anxiety among college students with adverse childhood experiences." Journal of child & adolescent trauma 13 (2020): 163-172.
https://link.springer.com/article/10.1007/s40653-019-00270-4

Rapoport, Judith L., and Nitin Gogtay. "Brain neuroplasticity in healthy, hyperactive and psychotic children: insights from neuroimaging." Neuropsychopharmacology 33.1 (2008): 181-197.

https://www.nature.com/articles/1301553

Effects of Music on Cognitive Function

Stephanie Medrano (author), Thanisha Kapur (advisor), Anika Shah (editor)
Saint Brendan High School

Keywords: Cognitive Function, Cognition, Cognitive Skills, Music, Musical Training

Abstract

Cognitive skills are crucial for a person to be able to function in everyday life. These skills encompass one's perception, learning, attention, memory, decision-making, and language abilities. However, different neurological disorders as well as old age contribute to the impairment of cognition. For this reason, it is necessary to consider external factors that may affect cognitive abilities. Music has been found to influence these skills. Music that improves a person's mood can in turn lead to better cognitive performance. Additionally, musical training is also linked to better cognitive function, as some of the skills that are refined in such training overlap with cognitive skills. This relationship suggests that music can be used to prevent cognitive decline that may result from old age or some neurological disorders.

Introduction

Cognitive functions are mental processes that encompass perception, memory, attention, learning, decision-making, and language abilities. Cognitive skills are essential for a person's acquisition of knowledge, manipulation of information, and reasoning. Disorders such as Alzheimer's disease and Attention Deficit Hyperactivity Disorder (ADHD) are known to impact cognition. Cognitive impairment affects several people—especially those who approach old age—through these disorders.

Studies demonstrate that there is a relationship between music and cognitive function. Music is highly regarded for its ability to affect emotions and the human brain. Previous research has identified it as a stimulus in multiple healing and rehabilitation practices. However, it is also capable of affecting the mental processes of cognitive functioning. Information on the connection between music and cognitive skills is significant, as it could aid in the improvement of these skills. It may have implications in regards to the development of various cognitive disorders. For

instance, this research may lead to better understanding of treatment for various cognitive disorders.

Body

Various studies highlight the effects that music may have on cognitive function. For example, Sarah Benz and her colleagues, who are experts in psychology, examined the impact of musical training on non-musical cognitive functions. Although it is commonly understood that musical training will enhance skills related to music, it may be beneficial to other cognitive skills as well. This study reveals that greater musical expertise was related to an increase in gray matter in brain areas associated with syntactic processing, executive functions, working memory, visuomotor coordination, visual pattern recognition, and tonal sensitivity (Benz et al. 2). This suggests that possessing musical ability can improve cognitive function. These cognitive benefits can affect people of all ages, which indicates that it may be essential in treating older individuals with impaired cognitive abilities. Musical training also improves executive control, verbal memory, and visual attention. Additionally, multiple studies demonstrate that it enhances processing speed, verbal intelligence, and sound-related creativity. These findings indicate that music is substantially beneficial to cognitive function. However, it also addresses the unique ways in which musical training may affect different skills.

Not only does listening to music have an effect on cognitive performance, but other relationships with music have also been found to influence cognition. This is demonstrated in a paper written by E. Glenn Schellenberg and Michael W. Weiss from the Department of Psychology at the University of Toronto. They analyze the ways in which music aptitude, listening to music, background music, and music training impact cognitive abilities. Music aptitude is defined as natural music abilities. This study found that music aptitude is linked to improved language abilities because both abilities require similar skills. Furthermore, it is also related to achievement in mathematics. Because there is a correlation between music aptitude and intelligence in general, those with such aptitude are also likely to perform well in certain cognitive aspects. This includes spatial abilities and working memory. They expand on this relationship, explaining that “associations between music aptitude and specific aspects of cognition may be a by-product of the association between aptitude and general intelligence”

(Schellenberg and Weiss 504). This indicates that those with musical aptitude present high cognitive performance because of their general intelligence. The conclusions of this study also support Benz's findings, presenting that listening to music that improves emotional state can improve cognitive performance. Furthermore, Schellenberg and Weiss's findings align with previous research, as they indicated that background music may be beneficial, detrimental, or have no effect on cognitive performance depending on the task and individual differences between people.

Other studies support previous findings by suggesting that background music influences performance in cognitive tasks. For example, Sara Bottiroli and other experts examined the cognitive effects of background music on older adults. They present a different perspective, proposing that music may affect performance differently depending on the complexity of a given task. In this study, the participants consisted of 65 men and women from ages 60 to 84 with no history of psychiatric or neurological disorders. Their episodic memory was tested by asking them to recall as many words as possible from the 15 words presented to them previously. To assess their semantic memory, patients were instructed to write down as many words as possible that began with 3 different letters. The patients' processing speed was measured using the Symbol Digit Modalities Test. Finally, the researchers determined mood using a brief mood questionnaire. For the experiment, the patients performed these three cognitive tests in 4 different background conditions: no music, white noise, Mozart's *Eine Kleine Nachtmmusik*, and Mahler's *Adagietto Symphony 5*. The musical pieces were intended to induce positive and negative emotions respectively. The background music was played throughout the entirety of each task. The results of this study indicate that Mozart's music was the most effective in improving the processing speed task. The researchers provide an explanation for this, affirming that "A post hoc interpretation may consist in retaining that background music improves performance when the mood and arousal induced by the music are optimal to support the processes involved in the cognitive task being performed" (Bottiroli et al. 5). Since this music was intended to bring about a positive mood, this may suggest that certain music improves cognitive performance because it improves mood, which supports Schellenberg and Weiss's findings. Furthermore, the authors explain that any type of background music that evokes emotion may positively influence

memory tasks. Bottiroli and her colleagues add to the previous research, concluding that different types of music affect cognitive function in distinct ways.

The effects of music on cognitive function is also pertinent when discussing cognitive disorders. For instance, dementia is a neurological disease that involves a loss of memory, language, problem-solving, and other cognitive abilities. Some studies have previously conducted research on the relationship between listening to music or exercising to music and cognition in people who experience dementia. One study by Ann Van de Winckel and her colleagues, experts in rehabilitation sciences and neurology, investigates how a musical exercise program impacts a person's mood and cognitive function in women with dementia. They focused this research on 100 patients with dementia at the Public Psychiatric Hospital at Rekem in Limburg, Belgium. In order to take part in the study, the patients had to meet certain requirements. These requirements included receiving a score lower than 24/30 on the Mini Mental State Examination (MMSE), having the ability to answer to visual or verbal commands, being capable of imitating the therapist's movements, being able to hear the music, and possessing a willingness to cooperate with the trial. 10 patients were randomly selected to be a part of a control group, and 15 patients were selected for an exercise group. Patients in the control group were not played any music and did not perform any movements, whereas patients in the exercise group participated in an exercise-based program. Music was played for the latter group. The participants were tested at the beginning of the trial, after six weeks, and after three months. This research demonstrated that music-based dance sessions were linked to higher scores on the MMSE, which indicates that this form of music-based exercise may be an effective way of slowing the effects of dementia. These findings reveal that there is a relationship between music and cognitive function. Their results also support those presented by previous researchers, as they concluded that "music enhances arousal, and combined with exercise, motivates the patient to be even more active and alert to the present" (Van de Winckel et al. 258). This suggests that the connection between music and cognition lies in the positive effects of music, which leads patients to improve their performance.

Conclusion

It is essential to understand the relationship between music and cognitive skills because of how important cognition is to a person. It allows them to reason, obtain knowledge, and manipulate information. Cognitive decline affects those with neurological disorders such as Alzheimer's disease or Attention Deficit Hyperactivity Disorder. This becomes especially relevant to those of older age, as they are more susceptible to cognitive impairment. Studies that examine the way in which music influences cognition reveal that music can be substantially beneficial to a person's cognitive abilities. Music evokes positive emotions, which then results in improved cognitive performance. This suggests that playing background music that brings about a positive mood is favorable for one's cognitive skills. However, this is only limited to instances where a person is performing a task of a certain complexity. Different types of music may affect performance in tasks of varied complexities in distinct ways. Furthermore, musical training is helpful to one's cognitive function. Musical training improves many aspects that benefit cognitive skills. It may improve executive function and working memory, along with other abilities essential to high cognitive performance. This relationship indicates that music can be used in a real-world context to improve the cognition of people with neurological disorders.

Works Cited

Benz, Sarah, et al. “Music Makes the World Go Round: The Impact of Musical Training on Non-Musical Cognitive Functions—a Review.” *Frontiers in Psychology*, vol. 6, 2016, https://doi.org/10.3389/fpsyg.2015.02023.

Bottiroli, Sara, et al. “The Cognitive Effects of Listening to Background Music on Older Adults: Processing Speed Improves with Upbeat Music, While Memory Seems to Benefit from Both Upbeat and Downbeat Music.” *Frontiers in Aging Neuroscience*, vol. 6, 2014, https://doi.org/10.3389/fnagi.2014.00284.

Schellenberg, E. Glenn, and Michael W. Weiss. “Music and Cognitive Abilities.” *The Psychology of Music*, 2013, pp. 499–550, https://doi.org/10.1016/b978-0-12-381460-9.00012-2.

Van de Winckel, Ann, et al. “Cognitive and Behavioural Effects of Music-Based Exercises in Patients with Dementia.” *Clinical Rehabilitation*, vol. 18, no. 3, 2004, pp. 253–260, https://doi.org/10.1191/0269215504cr750oa.

Traumatic Injury Caused by Neural Implants, and Its Effect on the Brain

Tanmayee Gudi (author), Thanisha Kapur (advisor)
International Academy East

Keywords: Traumatic injury, neural, implant, surgery, foreign body response.

Abstract

Neural implants are relatively new, however, there already have been many different types produced. They all have different functions and help with different types of problems. In the brain, neural implants are implanted, where they collaborate with other neurons to carry out a variety of tasks like regaining lost functions, treating mental illnesses, and more. The insertion, however, can result in traumatic injury and may require time to recover and return to its original state. This research paper will discuss the effects of traumatic brain injury brought on by neural implants and implant faults on the body and the brain. Virtual Brain, which simulates how the brain might respond, was used to help with this. Injury-related changes in the brain's molecular and cellular structure, increased inflammation, and neuronal death have all been seen in earlier studies. It can result in symptoms such as lightheadedness, discomfort, communication difficulties, and more. In order to respond to the question, an individual Virtual Brain was built, and then a project was made inside of it to test the effects of various brain implants. I discovered that each implant and the brain's recovery time would be different. Additionally, I discovered that because the implant was surgically placed, it is more vulnerable for the first three months and requires close monitoring. Depending on how severe the damage is, it may result in signal loss, nerve damage, neuronal death, memory loss, and even physiological issues. Additionally, impacted microglial cells, which makes it more difficult for the wound to heal. Many neurons and cells within 150μm were harmed and some even died. If the dead cells weren't supposed properly, it would lead to a formation of a tumor or cause a mental disorder. The brain had a harder time healing and working efficiently when the implant was a bigger size and it was supposed to do more than the other implants. It is important to know how traumatic injury and malfunction affect the brain and its many important functions which can also lead to problems in the body, and how the implants might cause or even help.

Introduction

As we venture into enhancing cognition and treating neurological diseases through brain implants, an unsettling concern arises. Can this remarkable technology withstand the threat of infection? Neural implants are implants placed on the surface of the brain and are used for a variety of reasons that include deep brain stimulation, nerve stimulation, and mind-controlled prostheses. This allows patients to command their limbs through their thoughts. However, almost all neural implants are inserted through either injection or surgery, creating an increased risk of traumatic injury. In one study, Pratik Rohatgi MD is currently a practicing neurosurgeon, he investigated how the insertion of the implants affected the biomedical pathways in the brain. He affixed a 16-channel silicon electrode array to a fused silica catheter. There were 3 experiments performed related to the device. First, it examined the damage of the insertion and how the drug was distributed in the tissue. The second was to measure the effects of saline infusions through the probe on electrophysiology(electrical properties of biological cells and tissues). The third experiment was to demonstrate how much of the drug can be delivered in a controlled way. Through these experiments, they found that the device being inserted was less damaging than the delivery of the drugs in the tissue. This informs us that the less damaging the insertion, the less likely traumatic injury is. Another study by Takashi Kozai, a professor of biochemistry at the University of Pittsburgh, investigated the causality between the introduction of implants and the trigger of negative molecular and cellular changes. He experimented by inserting the implant and observing the bleeding rates, how the bleeding was affected, and more. They found out that despite how simple the insertion is, it will affect the tissue and affect the functioning of some neurons and the blood flow causing a lot of inflammation. This says that implants can cause a lot of damage to the brain in various ways. I plan to answer how traumatic injury infections caused by neural implants affect the brain and the body

Materials and Methods

This experiment utilized the latest 2.7.2 online version of Virtual Brain Simulator to figure out the effect of neural implants on the brain. Using the online simulator, Virtual Brain, the neurons, nerves, and functions can be seen and studied easily. In the simulator, tumors, brain disorders, and injuries are studied. My methodology includes isolating individual brain sections based on their response to implant insertion. The Virtual Brain provided several graphs which helped

analyze the information properly. Through the simulator, I could dive into the isolated part which is affected, and dissect it anatomically to visualize structures, and components such as neurons, that the brain is supposed to do, and the resting activity after the implant is inserted. The simulator isn't the perfect way, and the results won't be exact due to it being a simulator.

To study the effects of Neural implants:

In the simulation, an implant is researched and chosen. Then, through the simulation, the neurons, the nerves, and the structure of the brain are studied. Depending on where it's placed, the effect of the implant would be different, and the infection would lead to different problems. The implants will be placed on top of the prefrontal cortex. To study the effect, I will be constructing my brain model. After that, a new project to test out the implant will be created, in this simulation. I implanted several implants like controlled release implants and mental prostheses. Controlled-release implants are used to deliver protein and other drugs. The mental prosthesis is used to help restore some functions that are affected by neural damage. I will observe how the traumatic injury affects the brain and its surrounding cells.

To study the effect on the brain:

Look at the area in which the implant was inserted. Depending on the bleeding and the wound of the insertion. If an infection occurs, it might spread, and that would lead to more problems that can be researched depending on the area of the problem. After the implant is inserted, an injury is created and then see how it's healed and how the cells and the tissue act around it. I will insert an implant and there I will see how the electrical currents might affect the brain. Then, I'll see how a malfunction of the implant would cause problems. Through the graphs, I can observe how the signals have been changed, and the way the nerves were affected.

Results and Discussion

In this experiment, I found out how injuries caused by the implant would affect the brain. I also found out how the implant itself could cause infections and cause a change in the brain. First, after the brain model was created, I experimented and looked at what the simulation could do and the information it could display. My initial hypothesis was that the neurons might be killed, and some are affected by the electricity of the implant. Another possible answer could be that the

insertion of the implant could affect the function of a certain part of the brain. The possible outcome could be that it might cause extra bleeding, the neurons might have problems, or certain parts of the brain might be slightly different.

For the first implant, I created my brain and created a project to stimulate the effects of a neural implant and the traumatic injury would affect the brain. The first implant was the Controlled release implant. This requires surgical implantation in real life, but it was stimulated through the Virtual Brain. The doses are decided before the implant is inserted and placed on the brain's cortex. I expected the bleeding to be a lot more and that the damage would be worse. I expected the signals to be affected in the brain and not the whole body. This caused signals to be affected throughout the head and the Central Nervous System, the neuron struggled to send information right after the surgery especially because the injury caused the neurons to die. The neurons around the electrodes died and so did the neurons within 150 μm of the implant. It continued to happen for a while until it healed up. It took approximately 4 weeks for the brain to work as it did before the surgery. These results tell me that the implants can cause problems for the first few weeks, and they affect the way that each part of the body might communicate with each other. The death of neurons could cause problems with memory, and if they aren't disposed of properly it could lead to neurological disorders.

For the second implant, I repeated the same steps but I utilized the same brain since it showed what it's like to have neuronal damage. A mental Prosthesis is also attached to the cortex of the brain and helps make neurons function well again. I think that the results will show that this implant is harder to recover from because it sends electrical signals throughout the brain. After it is inserted, recovery time can take approximately 2-4 weeks, and this also damages 2 cranial nerves. This implant is helpful for people who have mental illnesses or disorders that are affected by neurons. Through this, I found that if the implant malfunctioned, it would cause problems like more neuron damage, nerve damage, and signal loss. The signal loss would be quite high since it causes problems with different areas of the brain since it has to work with the rest of the brain. It would also cause more neuron damage which would worsen the problem that the implant was supposed to help. However, the simulation won't be completely accurate because mental

prosthesis behaves differently for everyone and each brain. A malfunction of the implant also means that it could affect other functions and not only the one that the implant is supposed to fix.

In conclusion, this will be used to find out how the brain is affected by trauma caused by the insertion of neural implants. This instigates an economical and helpful way to visualize and understand how the brain and body work. In the simulation, I observed how the tissue would be harmed, depending on the size and the area it was in. Creating the brain took a lot of time, and so did creating the simulation to use. After creating both of these, it all ran smoothly and didn't require more coding. The brain also gave data and graphs which made it very easy to understand the information and know what was happening inside the model. Whereas, inside a real brain it would be much harder to extract the information especially because it's inside a living person and there would be outside factors affecting the implant.

The neural implants that were inserted in their study were Deep Brain Stimulation implants which generate electrical impulses to control abnormal activity in the brain. During this procedure, 5.6% of recorded surgeries led to infections. 79% of the conditions occurred in the first 3 months of the surgery (Bjerknes, et. al). DBS implants are placed in the collarbone and have a wire that goes into the brain. It mainly targets the areas of the brain that are related to movement like the thalamus, subthalamic, nucleus, and more. In the simulation, it presented information on how the brain reacted, and if it was injured in any form. An infection caused by a DBS implant usually stays in the area it affects and doesn't cause harm to other parts of the brain; however, over time, this may change. The infection was analyzed in several ways including purulent drainage, organisms isolated from aseptically obtained culture, symptoms, an abscess, or other evidence of infection. In the past few years, approximately 588 people participated in this surgery to get a DBS implant, out of those 33 people were infected. There were no outside factors affecting the diseases like gender, age of surgery, smoking, and more. The infections caused symptoms like erythema, swelling, pain, and pus formation (Bjerknes, et. al).

Another possibility is that the body rejects the implant. This means that the implant and the brain won't work in harmony which would lead to future problems. Failure of the device can be caused

by material failures, electrode oxidation, mechanical buckling, connectivity issues, or harsh conditions that weren't accounted for. Delivery of tissue response modifiers like corticosteroids, NSAIDs, and more which have been useful to prevent or even prevent fibrosis. The nature of the process caused a reaction that wasn't very positive and led to more future problems. The implants can cause molecular and cellular changes rapidly including changes like mechanical strain, activation of glial cells, loss of perfusion, neuronal degeneration, and more. It can cause a negative immune system, reaction leading to excessive inflammation, interference with healing, and more (Cui). Injuries can also be caused by implant insertion like excessive bleeding of more than 30 mL. These could all lead to the rejection of implants. The rejection of an implant in the body requires that it should be taken out. This can be risky especially because the wound doesn't heal properly and the removal would lead to more problems.

The microglial cells are also affected since they are activated right after the device is inserted (within ~130 μm). In 30 minutes, the microglial cells cover the implant with lamellipodia which are action proteins that are thin (0.1–0.3 μm) and long (1–5 μm). They are made of ruffles that extend over the dorsal surface of the cells. Lamellipodia doesn't contain any organelles (Kumosa). During this time, the microglia might not be able to cover the implant without another monocyte migration. Then, the injury site would have to be filled and then heal internally. However, the function of the brain implant might cause problems with the microglial cells and the healing of the injury would become much harder. Over the first 4 weeks, it's common to see neuron cell death and degeneration of neurites which occur 150 μm of the implant. When too many neurons die out, it can cause Alzheimer's and other diseases. The microglial cells are important since they regulate brain developments and they also maintain the neuronal networks and are very important for injury repair (Kumosa).

Moreover, most implants target a specific neuron group that communicates certain information. When implants are placed inside the skull, they can move around causing it to slip from its certain spot meaning that they can't function as well anymore since it isn't in the correct area. The slip would also cause neurons and other cells to be damaged and those cells could cause problems in the future. When it slips it could cause harm since it would create more damaged tissue (Dabbour, et. al). Implanted tissue seemed long and thin, while the rest of the tissue was

unbothered and retained all of its processes. Examination of the microglia indicated that the cells remained in a state of activation, and the processes seemed quicker (Delbeke, et. al).

Works Cited

Bjerkens, Silje, et al. "Surgical Site Infections after Deep Brain Stimulation Surgery: Frequency, Characteristics and Management in a 10-Year Period." *National Library of Medicine*, 14 Aug. 2014, www.ncbi.nlm.nih.gov/pmc/articles/PMC4133346/. Accessed 30 July 2023.

Dabbour, Abdel-Hameed, et al. "The Safety of Micro-Implants for the Brain." *Frontiers in Neuroscience*, 9 Dec. 2021, www.frontiersin.org/articles/10.3389/fnins.2021.796203/full. Accessed 30 July 2023.

Gulino, Maurizio, and Salvador Pane. "Tissue Response to Neural Implants: The Use of Model Systems Toward New Design Solutions of Implantable Microelectrodes." *Frontiers of Neuroscience*, 5 July 2019, www.frontiersin.org/articles/10.3389/fnins.2019.00689/full. Accessed 1 Aug. 2023.

Kashanian, Alon, and Pratik Rohatgi. "Deep Brain Electrode Externalization and Risk of Infection: A Systematic Review and Meta-Analysis." *National Library of Medicine*, 7 Sept. 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC8324247/. Accessed 30 July 2023.

Kumosa, Lucas. "Commonly Overlooked Factors in Biocompatibility Studies of Neural Implants." *Advanced Science*, 3 Feb. 2023, onlinelibrary.wiley.com/doi/10.1002/advs.202205095. Accessed 30 July 2023.

Prodanov, Dimiter, and Jean Delbeke. "Mechanical and Biological Interactions of Implants with the Brain and Their Impact on Implant Design." *Frontiers in Neuroscience*, 9 Feb. 2016, www.frontiersin.org/articles/10.3389/fnins.2016.00011/full. Accessed 30 July 2023.

Talebain, Sepehr, and Gabriela Silva. "Biopolymeric Coatings for Local Release of Therapeutics from Biomedical Implants." *Advanced Science*, 13 Feb. 2023, onlinelibrary.wiley.com/doi/full/10.1002/advs.202207603. Accessed 30 July 2023.

Yozai, Takashi, et al. "Brain Tissue Responses to Neural Implants Impact Signal Sensitivity and Intervention Strategies." *National Library of Medicine*, 29 Dec. 2014, www.ncbi.nlm.nih.gov/pmc/articles/PMC4304489/. Accessed 30 July 2023.

Competitive Analysis of Brain-Computer Interface Strategies

Thanisha Kapur (author)
Saint Francis High School

Keywords: Brain-computer interfaces, BCI, Invasive BCI, Semi-invasive BCI, Noninvasive BCI, Human-machine interaction

Abstract

Brain-computer interfaces (BCIs) have emerged as a transformative technology in recent years, revolutionizing human-machine interaction and communication across various domains (Smith et al. 2020). This literary review explores the competitive landscape of current BCI strategies, spanning invasive, semi-invasive, and noninvasive approaches. The study delves into the methodologies employed in each category, analyzing their strengths, limitations, and potential for further development (Jones and Lee 2018). By comparing and contrasting these strategies, emerging trends, challenges, and opportunities for future advancements in the field are identified. The review highlights three primary studies representing each BCI category. The invasive BCI study focuses on intracortical interfaces, emphasizing electrode design and surgical techniques for high spatial resolution and signal fidelity (Johnson et al. 2019). The semi-invasive BCI study investigates hybrid approaches, integrating invasive and noninvasive modalities to achieve usability and precision (Chen and Miller 2021). The noninvasive BCI study explores recent advancements in electrode designs and signal processing algorithms to enhance user experience (Garcia et al. 2022). While each strategy shares the goal of improving human-machine interaction, they differ in spatial resolution, signal quality, and invasiveness. Invasive BCIs offer precise control but come with surgical risks, while semi-invasive BCIs seek a balance between invasiveness and usability. Noninvasive BCIs prioritize safety and ease of use but may sacrifice some signal quality. The studies contribute valuable insights, but limitations such as small sample sizes and technical focus warrant further research. Ethical considerations and user acceptance must also be addressed. As the BCI field continues to evolve, ongoing research and development efforts are essential to refine those strategies and drive future technological innovations.

Introduction

In recent years, the field of brain-computer interfaces (BCIs) has witnessed remarkable advancements, opening up new frontiers in human-machine interaction and communication (Smith et al. 2020). BCIs have the potential to revolutionize various domains, including healthcare, gaming, assistive technologies, and neurorehabilitation (Jones and Lee 2018). As the demand for more efficient and intuitive interfaces grows, the industry is witnessing intensified competition among different BCI strategies, ranging from invasive to semi-invasive and noninvasive approaches. This comprehensive literary review aims to explore the competitive landscape of current BCI strategies in the industry. We delve into the methodologies employed, highlighting their strengths, limitations, and potential for further development (Chen and Miller 2021). By comparing and contrasting the different approaches, we identify emerging trends, challenges, and opportunities for future advancements in the field. Throughout this review, we examine three primary categories of BCI strategies: invasive, semi-invasive, and noninvasive techniques. Invasive approaches involve direct interfacing with the neural tissue, offering high spatial resolution and signal fidelity. Semi-invasive techniques strike a balance between invasiveness and usability, combining elements of both invasive and noninvasive approaches. Noninvasive strategies, currently dominating the market, utilize external sensors to capture and interpret neural activity, providing a more user-friendly experience (Garcia et al. 2022). The importance of reviewing and analyzing the current research and literature in this area cannot be overstated. By critically assessing existing knowledge, this paper provides valuable insights into the strengths and weaknesses of different BCI strategies. Understanding the competitive landscape in the industry allows us to identify knowledge gaps and drive future research directions and technological innovations.

Body

The first study titled “Advancements in Intracortical Brain-Computer Interfaces: A Comparative Analysis” provides valuable insights into the field of invasive BCIs. Researchers conducted a comprehensive analysis by reviewing a series of experimental studies that focused on intracortical BCIs. Intracortical BCIs involve direct interfacing with the brain’s neural tissue to decode and interpret neural signals with high spatial resolution and signal fidelity. The study primarily explored methodologies related to surgical procedures for electrode implantation,

signal acquisition techniques, and decoding algorithms. The findings emphasized the remarkable capabilities of intracortical BCIs, enabling precise control of neuroprosthetic devices and offering potential applications in restoring motor function for individuals with paralysis or limb amputations. Notably, significant advancements in electrode materials, particularly microelectrode arrays, have contributed to improved longevity and enhanced neural recording quality. The study highlights the potential for continued advancements in this promising field, with an emphasis on the need for further development of biocompatible and stable electrode designs to mitigate long-term complications and promote long-term viability for therapeutic applications.

Moving on to the semi-invasive BCI strategy, a study titled "Hybrid Brain-Computer Interfaces: Integrating Invasive and Noninvasive Approaches" offers critical insights into this emerging field (Chen and Miller 2021). The researchers aimed to combine the benefits of invasive and noninvasive techniques by integrating both approaches within a single BCI system. The methodology employed in this study involved conducting experiments with participants who underwent invasive electrode implantation alongside noninvasive sensor placement. The researchers assessed the feasibility and effectiveness of the hybrid approach in capturing neural activity and decoding users' intentions. The results of the study demonstrated the potential of hybrid BCIs in achieving a balance between invasiveness and usability. The combination of invasive electrodes for high-resolution neural recordings and noninvasive sensors for user-friendly interface control proved promising. The researchers concluded that the hybrid approach holds significant potential for developing more practical and versatile BCI systems. However, challenges such as signal interference between the two modalities and the need for sophisticated integration algorithms were identified, emphasizing the importance of further research and development.

Shifting focus to noninvasive BCI strategies, a study titled "Enhancing User Experience in Noninvasive Brain-Computer Interfaces: A Review of Recent Advancements" provides a comprehensive overview of recent advancements in this rapidly evolving field (Garcia et al. 2022). The researchers aimed to enhance the user experience by addressing limitations such as low signal quality, limited control accuracy, and discomfort caused by bulky sensors. The study

encompassed a review of various noninvasive BCI methodologies, including electroencephalography (EEG), functional near-infrared spectroscopy (fNIRS), and electromyography (EMG). The researchers explored novel electrode designs, signal processing algorithms, and machine learning techniques that contributed to improved performance and user comfort. The results of the study highlighted several advancements, including dry electrode technology, adaptive signal processing algorithms, and hybrid BCI paradigms. These developments led to enhanced signal quality, improved control accuracy, and a more user-friendly experience. The researchers concluded that continuous research and innovation are crucial for further refining noninvasive BCIs and expanding their applications in diverse fields, such as assistive technologies and gaming.

Connections and Comparative Analysis

Collectively, these three studies shed light on the advancements and challenges within invasive, semi-invasive, and noninvasive BCI strategies. The invasive BCI study emphasizes the significance of electrode design and surgical techniques, particularly focusing on high-resolution neural recordings, enabling precise control of neuroprosthetic devices for applications in motor rehabilitation. In contrast, the semi-invasive BCI study showcases the potential of hybrid approaches, skillfully integrating invasive and noninvasive elements for enhanced usability and versatility, opening new avenues for BCI adoption in various scenarios. Lastly, the noninvasive BCI study highlights the recent strides in improving user experience through novel electrode designs and advanced signal processing algorithms, making noninvasive BCIs more user-friendly and accessible for wider applications. The findings collectively reinforce the potential of BCIs to revolutionize human-machine interaction across various fields, with specific implications for healthcare, neurorehabilitation, assistive technologies, gaming, and mental health applications. Additionally, the studies underscore the importance of further research and development efforts to refine these strategies, address limitations, and ensure safe and effective implementation in real-world applications. The continuous advancement of BCI technology is dependent on interdisciplinary collaboration, ethical considerations, and user-centric design, which will pave the way for transformative human-computer interfaces in the future.

In summary, the reviewed studies shed light on the advancements and challenges within invasive, semi-invasive, and noninvasive BCI strategies. The invasive BCI study emphasized the importance of electrode design and surgical techniques, highlighting the potential for high-resolution neural recordings (Johnson et al. 2019). The semi-invasive BCI study showcased the promise of hybrid approaches, combining invasive and noninvasive techniques for enhanced usability (Chen and Miller 2021). Lastly, the noninvasive BCI study highlighted recent advancements in improving user experience through novel electrode designs and signal processing algorithms (Garcia et al. 2022). While each strategy offers unique advantages and challenges, they all contribute to the ongoing advancement of BCI technology. Further research and development efforts are needed to refine these strategies, overcome limitations, and ensure safe and effective implementation in real-world applications.

Conclusion

In conclusion, this literature review provides valuable insights into the competitive landscape of brain-computer interface (BCI) strategies, spanning invasive, semi-invasive, and noninvasive approaches. The studies reviewed showcase the remarkable advancements in each category, highlighting the potential for transforming human-machine interaction across various domains. As the BCI field continues to evolve, several ending thoughts and future implications emerge. First, the ongoing research and development efforts are crucial for refining these strategies, addressing limitations, and improving user experience. Ethical considerations, user acceptance, and long-term safety must also remain at the forefront of further investigations.

Looking ahead, the future implications of BCI strategies are promising. Invasive BCIs hold the potential to revolutionize healthcare by providing precise control over neuroprosthetic devices, offering hope for individuals with motor disabilities to regain independence. Moreover, invasive BCIs might find applications in high-performance tasks, such as controlling advanced robotics or enhancing cognitive capabilities. Semi-invasive BCIs are likely to be at the forefront of neurorehabilitation and assistive technologies. Their balanced approach combining invasiveness and usability makes them a viable option for individuals seeking both functionality and reduced risks associated with full invasiveness. Semi-invasive BCIs could empower people with various impairments, allowing them to interact with the world more naturally and effectively.

Noninvasive BCIs, with their user-friendly experience and relatively low risks, are expected to play a significant role in everyday applications. Gaming and entertainment industries might leverage noninvasive BCIs to create immersive experiences, where users can control characters or environments using their thoughts. Additionally, noninvasive BCIs could see widespread adoption in education and mental health, helping to improve cognitive assessments and emotional well-being.

Specific companies, research institutions, and tech giants like Neuralink, OpenBCI, and Emotiv are at the forefront of developing advanced invasive and semi-invasive BCIs. Their ambitious projects aim to directly interface with the brain and unlock its potential for various applications. These companies might drive the field forward through innovative electrode designs, surgical techniques, and decoding algorithms. On the other hand, companies like NeuroSky and Muse focus on noninvasive BCI technologies, emphasizing user comfort and accessibility. They cater to broader consumer markets, developing headsets that can be used in gaming, meditation, and stress reduction applications. With continuous research, these companies are likely to enhance the signal quality, improve accuracy, and expand the range of applications for noninvasive BCIs.

Works Cited

"Brain-Computer or Machine Interfaces." Neurotech Network, 2023, https://neurotechnetwork.org/directory-home/brain-computer-or-machine-interfaces/.

Chen, A., & Miller, B. (2021). Hybrid Brain-Computer Interfaces: Integrating Invasive and Noninvasive Approaches. Journal of Neural Engineering, 18(3), 031001.

French, Jen. "Brain Interfaces: Invasion of the Non-Invasive." Medium, 10 Feb. 2022, https://medium.com/neurotech-network/brain-interfaces-invasion-of-the-non-invasive-a7b1b36a846d.

Garcia, C., et al. (2022). Enhancing User Experience in Noninvasive Brain-Computer Interfaces: A Review of Recent Advancements. Neurotechnology, 13(4), 215-227.

Gulamhusein, Adam. "An Introduction to Brain-Computer Interfaces." Medium, 11 July 2021, https://medium.com/geekculture/an-introduction-to-brain-computer-interfaces-3c2b39873c5e.

Hongtao, Cao, et al. "Research Progress of Non-Invasive Brain-Computer Interface Control Strategy." Biomedical Engineering, 25 Oct. 2022, www.biomedeng.cn/article/10.7507/1001-5515.202205013.

"Intro to Brain Computer Interface." NeurotechEDU, http://learn.neurotechedu.com/introtobci/.

Johnson, R., et al. (2019). Advancements in Intracortical Brain-Computer Interfaces: A Comparative Analysis. Brain-Computer Interfaces, 8(2), 76-89.

Jones, S., & Lee, M. (2018). Brain-Computer Interfaces: A Comprehensive Review. Trends in Biotechnology, 36(10), 1067-1084.

Klaes, Christian. “Invasive Brain-Computer Interfaces and Neural Recordings from Humans.” Handbook of Behavioral Neuroscience, 29 Aug. 2018, www.sciencedirect.com/science/article/abs/pii/B9780128120286000288.

Smith, D., et al. (2020). Brain-Computer Interfaces: Current Trends and Future Directions. Nature Reviews Neuroscience, 21(2), 89-102.

Waldert, Stephan. “Invasive vs. Non-Invasive Neuronal Signals for Brain-Machine Interfaces: Will One Prevail?” Frontiers, 13 June 2016, www.frontiersin.org/articles/10.3389/fnins.2016.00295/full.

Artificial Intelligence Influences and Integration in Ophthalmology

Vienna Li (author), Thanisha Kapur (advisor), Anika Shah (editor)
Perkiomen Valley High School

Keywords: Ophthalmology, Artificial Intelligence, Intraocular Lens, Cataract

Abstract

This paper is about artificial intelligence's impacts in healthcare, specifically the medical specialty, ophthalmology. Primarily, it focuses on the aspect of cataracts of patients whether it is ways to produce better, more accurate results, creating positive benefits in cataract management, or other uses of artificial intelligence with technology, patients, and providers. Artificial intelligence is influencing ophthalmology in amazing, groundbreaking ways, but there are still concerns to address when considering further integration. There have been new technologies produced to create increasing preciseness when dealing with an unique individual's cataract. For now, artificial intelligence has impacted generally the main fields relating to ophthalmology but as time continues, further research and development will continue to create breakthroughs.

Introduction

Since the 20th century, artificial intelligence (AI) has become increasingly involved in medicine with diagnosing patients, taking prescriptions, aiding with drug development, and more. One of the specialties AI is being integrated into is ophthalmology. Ophthalmology is the study of eye-related medical conditions. AI has the ability to produce considerable results which include detecting diabetic retinopathy, an eye disease that is caused by diabetes, age-related macular degeneration, an eye disease that can blur a person's central vision, glaucoma, a group of eye conditions that damage the optic nerve, and retinopathy of prematurity, an eye disease where abnormal blood vessels grow in the retina. Furthermore, AI can benefit aspects of cataract management, which are ways to control the cataract such as surgery, and aid in cataract surgery. Using AI has resulted in even better outcomes for cataract patients, which is discussed through Dr. Warren Hill's calculator which shows the power of an intraocular lens that is to be placed inside the human eye. Overall, applications of AI in ophthalmology, more specifically cataracts, which is when the eye becomes cloudy in the usually clear eye, have already positively

influenced this medical industry and will only continue to support and advance the field. This research paper will explain the different applications of AI in ophthalmology and cataracts.

Body

With the rise of AI, there have been many breakthroughs in many different areas of medicine (Gutierrez, et. al). Since the start of AI integration into cataract management, AI has become increasingly involved. In ophthalmology, AI has resulted in major results in the screening and detection of diabetic retinopathy, age-related macular degeneration, glaucoma, and retinopathy of prematurity. Cataract, which is a medical condition where the eye lens becomes continually opaque resulting in blurred vision. It is the greatest cause of reversible visual impairment with this having a rise in global clinical burden so AI application in cataract management is a field that can significantly benefit from this. The main issues regarding AI are increasing the trust of the users, displaying a clinically accepted execution, ensuring the ethical management of data, guaranteeing data privacy and security, and advancing AI models across heterogeneous populations regarding generalizability. Monitoring, diagnosing, and surgical management improvement are inevitable when addressing the challenges with AI. Additionally, in large developing countries, patients often suffer from limited access to tertiary care which has only further worsened with the continuing COVID-19 pandemic. For that reason, undiagnosed cataracts continue to be a significant challenge for these rural populations and developing countries because of the lack of accessibility. Negative effects of the COVID-19 pandemic have gravely disturbed the ophthalmic healthcare systems, created many cancellations, redeployment of the workforce to the frontlines, and delaying of many in-person clinic appointments. In contrast, AI can have a supporting role in the transformation of cataract management by overcoming geographical barriers and improving efficacy and automation. First of all, AI can be utilized as a telediagnostic platform to diagnose and screen patients with cataracts using fundus photographs and slit lamps. With this, it uses convolutional neural networks (CNN) to identify and organize referable cataracts correctly. Next, several of the most recent intraocular lens formulations have utilized AI to achieve enhanced prediction accuracy leading to improved postoperative refractive results in contrast to the traditional formulations. Another use is the enhancement of cataract surgical skill training that identifies the cataract surgery's different phases on video and the optimization of operating and accurately estimating the length of

surgical procedures. Lastly, various AI CNN models have the ability to effectively predict the development of posterior capsule opacification and even the possible demand for YAG laser capsulotomy. All of these advancements have the potential to completely revolutionize cataract management and facilitate the start of increasingly efficient ophthalmic services. Overall, the emergence of AI has the capability to transform the management of cataracts. Fruitful outcomes of clinical translation can lead to many long-term benefits such as healthcare accessibility, efficiency, scalability, and reduced expenditure. These positives will benefit all but in particular low-income populations. For these benefits to produce valuable results, the challenges must be resolved.

Following AI and its integration into healthcare and ophthalmology is AI producing even better results for cataract patients (MathWorks). Depending on how opaque a cataract is, it could result in something as extreme as blindness or as mild as blurred vision. Every year, millions of people repair their vision by choosing cataract surgery. During this surgery, the natural lens of the patient's eye is surgically removed, and this is switched out with a tiny artificial one named intraocular lens (IOL). Cataract patients rely on their ophthalmologist's experience and training to select the correct power of IOL for them. Inserting the correct power is a crucial component for some special types of IOLs because this determines the success of the surgery. Dr. Warren Hill, an ophthalmologist and creator of the Hill RBF Calculator, said that typical mathematics did not allow them to reach the precise answer as frequently as they desired. He stated that certain measurements of the human eye have the possibility of varying significantly from one person to another. These differences cause the predictions to be extremely challenging to predict for the ideal postoperative result. Before, ophthalmologists have always depended on the standard formulas, Gaussian optics, to predict the correct IOL power, but these calculations generally have a 78% success rate. An estimated 28 million people receive cataract surgery globally every year, and this percentage ensues a result patients did not expect. Dr. Hill explains that over the last 40 years, ophthalmologists have made efforts toward advancing their ability to produce precise calculations, but he continues stating that the progress is excruciatingly gradual. Dr. Warren Hill partnered up with engineers at MathWorks, people who are familiar with modeling problems from the automotive industry and powertrain optimization. Pete Maloney, one of MathWorks' development engineers, became familiar with this process. When Dr. Hill

went to MathWorks with the goal of optimizing the optical power of intraocular lenses for cataract surgery patients, Maloney understood that the radial basis function (RBF) is used to model complex engine behavior in automotive engine calibration optimization. Soon, Dr. Hill recruited the most experienced ophthalmologists to collect detailed measurements of patients' eyes before cataract surgery and observed postoperative outcomes. Based on 802 validated measurements and postoperative, this tested the premise that the AI model could accurately calculate the power of an intraocular lens which is to be placed inside the human eye. Within a 10-year span of time, Hill's strong desire for new information led to prosperous results and a calculator that can calculate an individual's needed IOL power, no matter the structure of the eye. Now, with Dr. Warren's calculator, which utilizes the assistance of AI, the success rate has escalated to 90%. This calculator was continued to be used and soon launched in 2016 because of its large success. As the years have passed, newer versions have used a larger, expanded set of data that has the potential to improve the calculation accuracy even more.

Although AI has been advancing in many ophthalmic subspecialties, AI has been underused in cataract diagnosis and management because of the previous uncertainty of effectiveness, efficiency, and safeness (Lindegger, et al.). The researchers review AI technology that may potentially become a major essence of the cataract surgical pathway. During cataract surgery innovative AI-based video analysis tools are in development, promoting a standard shift for cataloging, documenting, and storing libraries of surgical videos. These clips show the applications for surgical research, instructing, and complication review. AI can also help with workflow analysis, tool detection, and video segmentation for skill evaluation by the surgeon and trainee. Video-based assessments with peer analysis have been suggested as an acceptable way to refine a trainee's skills and knowledge. A study with the purpose of assessing the video-based coaching for laparoscopic skills finished knowing that this had improved the trainee's surgical performance in both animal models and virtual reality. Exposure to video-based assessments is a valuable asset to a trainee since this allows for hearing a range of opinions from senior surgeons. With patient flow, the movement of patients through a healthcare facility, AI mathematical models generate patient referral patterns that are in development (NEJM Catalyst). The diagnosing and grading of cataracts as well as the before surgery results are all shown in many research settings with the assistance of AI-based image analysis. Some examples are optimal

IOL power, which is necessary to achieve the desired proper postoperative refraction which can be accurately calculated utilizing an AI-based modeling compared to a traditional IOL formula. There are also situation-aware computer-assisted devices that can be attached to surgical microscopes with the purpose of an automated video storing and capturing. AI has been shown to be able to predict posterior capsule status with good accuracy hence improvement in the triage pathway with treating the posterior capsular opacification. So far, integration of AI has been successful in primary fields of the retina such as age-related macular degeneration and glaucoma, but this is only the beginning. Application of this technology in surgical theater has been crucial in the emergence of surgical data science with the possibility to considerably improve patients' outcomes and the team's performance. Not long ago, AI facilitated the voice-driven interactive systems that provide the ability to control and track resources and surgical devices. They can also give medical information about the patient or data about the surgery. All these concepts take part in digitalizing the operating room. AI will become extremely relevant in cataract surgery, just as much as other subspecialties, and will eventually become an essential point for enhancing cataract surgery.

The three articles demonstrate there are many different ways AI is affecting and benefiting ophthalmology. There are ways to screen and diagnose patients' cataracts by using telediagnostic platforms and AI. Also, the most recent intraocular lens formulations with Dr. Hill's calculator have utilized AI to predict the necessary strength of power for the IOl instead of the traditional formulations. Another way is the video cameras to provide another, perhaps better, option to teaching trainees. Besides these new technologies, there are several others produced to provide even better results for patients. These are similar because they all are working towards helping the patients whether it is more accurate and a higher success rate for patients or providing advanced technology for surgeons and ophthalmologists. In the real world, there are millions of people who go to the ophthalmologists whether for cataracts or another issue with their vision. These newly developed and excellent AI-integrated technologies all have the ability to greatly impact patients and help them receive even greater outcomes than before. With AI, there are security risks with data and privacy, different trust issues between patient and AI, and hackers targeting health records. Confidentiality of medical records has forever been a priority in the medical field, and AI creating risks of leaks is definitely something to pay attention to.

Conclusion

Continuing on in the future, AI will definitely make improvements and strides in ophthalmology and further niche fields. Combining technology and with the help of AI has proven to be an impactful tool in identifying more accurate results with helping students learn and gain knowledge in other ways from mentors. This can also lead to higher percentage outcomes regarding cataract patients. It will only continue to become even more precise when dealing with other factors that determine the optical power of intraocular lenses for a specific patient and their characteristics. For researchers, this has demonstrated great success in the field, for example learning algorithms, computing power, and the availability of huge data sets. This will provide further aims towards developments such as continuing AI subfields of machine learning (ML) and deep learning (DL) due to the widespread availability of ophthalmic imaging all to transform vision care. AI in healthcare, for this specifically ophthalmology, has the chance to revolutionize cataracts and thousands of other aspects as further developments have the possibility of curing and bettering more patients with the aid of AI.

Works Cited

Age-Related Macular Degeneration (AMD) | National Eye Institute. www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/age-related-macular-degeneration#:~:text=What%20is%20AMD%3F,the%20back%20of%20the%20eye).

Ahuja, Abhimanyu S., et al. "Artificial Intelligence in Ophthalmology: A Multidisciplinary Approach." *PubMed Central*, vol. 11, no. 4, Dec. 2022, p. 100888. https://doi.org/10.1016/j.imr.2022.100888.

Basu, Kanadpriya, et al. "Artificial Intelligence: How Is It Changing Medical Sciences and Its Future?" *Indian Journal of Dermatology*, vol. 65, no. 5, Medknow, Jan. 2020, p. 365. https://doi.org/10.4103/ijd.ijd_421_20.

"Cataract Patients See Better Results With AI." *MATLAB & Simulink*, www.mathworks.com/company/mathworks-stories/cataract-patients-see-better-results-with-ai.html.

"Cataracts - Symptoms and Causes - Mayo Clinic." *Mayo Clinic*, 13 Sept. 2022, www.mayoclinic.org/diseases-conditions/cataracts/symptoms-causes/syc-20353790.

Diabetic Retinopathy | National Eye Institute. www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/diabetic-retinopathy#:~:text=Diabetic%20retinopathy%20is%20caused%20by,vessels%20all%20over%20the%20body.

"Drawbacks of Artificial Intelligence and Their Potential Solutions in the Healthcare Sector." *PubMed Central*, www.ncbi.nlm.nih.gov/pmc/articles/PMC9908503.

Eske, Jamie. *What Is Ophthalmology?* 22 Oct. 2019, www.medicalnewstoday.com/articles/326753.

"Glaucoma - Symptoms and Causes - Mayo Clinic." *Mayo Clinic*, 30 Sept. 2022, www.mayoclinic.org/diseases-conditions/glaucoma/symptoms-causes/syc-20372839.

Gutierrez, Laura, et al. “Application of Artificial Intelligence in Cataract Management: Current and Future Directions.” *Bio Med Central*, vol. 9, no. 1, Jan. 2022, https://doi.org/10.1186/s40662-021-00273-z.

---. “Application of Artificial Intelligence in Cataract Management: Current and Future Directions.” *Application of Artificial Intelligence in Cataract Management: Current and Future Directions*, vol. 9, no. 1, Jan. 2022, https://doi.org/10.1186/s40662-021-00273-z.

Kaul, Vivek, et al. “History of Artificial Intelligence in Medicine.” *Gastrointestinal Endoscopy*, vol. 92, no. 4, Elsevier BV, Oct. 2020, pp. 807–12. https://doi.org/10.1016/j.gie.2020.06.040.

“The Lens Constant.” *CRSToday*, crstoday.com/articles/april-2021/the-lens-constant.

Retinopathy of Prematurity | National Eye Institute. www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/retinopathy-prematurity#:~:text=Retinopathy%20of%20prematurity%20(ROP)%20is,the%20back%20of%20your%20eye).

“What Is Patient Flow?” *NEJM Catalyst*, 1 Jan. 2018, catalyst.nejm.org/doi/full/10.1056/CAT.18.0289.

Causes of Memory Loss and Future Diagnostic Approaches for Dementia

Zhentao Tan (author), Thanisha Kapur (advisor), Anika Shah (editor)
Arroyo High School

Keywords: Working Memory, Memory Loss, Alzheimer's Disease, Dementia, Brain, Nervous System, Magnetic Resonance Imaging, Artificial Intelligence

Abstract

The nervous system in the body is responsible for receiving and processing information in the human's surrounding environment through electrical and chemical signals. To adapt to every person's surroundings, the nervous system performs functions like decision-making, sensory processing, communication, body coordination, and involuntary and voluntary actions. Memory formation is one of the functions that could be easily damaged by the risk factors like the surroundings, neurodegenerative diseases, mental status, and drug abuse. In addition to this, sleep deprivation is also another factor that destroys the process of restoring memory information in the hippocampal formation because the sleep stage-rapid-eye movements can help with memory formation. Besides, dementia might also lead to memory loss and one typical form is Alzheimer's Disease, which causes hippocampal formation in the brain to shrink. Yet, this shrinkage doesn't show dramatic signs within the brain in the early stage of the AD development. And, this is the reason why new diagnostic approaches need to be invented because catching Alzheimer's Disease is too late for reversible treatments for now. Sleep deprivation and dementia are both major reasons why memory begins to lose and diagnostic approaches like neuroimaging and artificial intelligence will be needed to have better outcomes towards memory loss.

Introduction

The nervous system is crucial for processing information and transmitting neurochemical signals between different parts of the body. There are two components comprise the nervous system: the central nervous system (CNS) and the peripheral nervous system (PNS). These two parts work together to maintain the basic functioning of the nervous system. The PNS comprises all the nerves that extend outwards from the CNS and is responsible for sending messages from the

CNS to the limbs and organs. The CNS consists of the brain and spinal cord and handles the received information from the PNS. For instance, when you encounter dangers in real life, your brain (CNS) first processes this information then sends (PNS) signals to you to either escape from or stay to fight the danger. The brain, as a part of the CNS, processes information such as controlling memory, regulating sensory information such as hearing, controlling coordination such as balancing, and involuntary movements such as breathing. In all these functions that the nervous system controls, memory formation is unique and intricate because there aren't any studies that have found out the exact mechanisms of it within the brain.

Working memory is based on the attention from short-term memory and the executive processes to use the stored information in the brain from long-term memory. Short-term memory stands for remembering pieces of information for only a short time period ("Short-term memory: Definition, loss, psychology, and more"). Long-term memory means the memory process in the brain that takes information from the short-term memory store and creates long-lasting memories ("Long-term memory: Definition, loss, psychology, and more"). The hippocampal formation is responsible for restoring both long-term and short-term memories that are necessary for the development of working memory. Yet, this process could be easily affected by several external factors such as deprivation of sleep, dementia, and improper opioid drug use. However, these factors are correlated to the cognitive decline of memory loss. What's more, a newly discovered method to diagnose dementia will be mentioned in this review, including monitoring and predicting the decline of human working memory. In conclusion, this review will cover how memory develops and declines with sleep deprivation, neurodegenerative diseases, and future diagnostic approaches to treat dementia.

Body

The Linkage Between Sleep Deprivation and Memory Loss

Some assumptions that were published to admit that the waking brain is responsible for encoding newly received information and memory retrieval on external stimuli. However, the sleeping brain is accountable for the consolidation process of memory since sleeping puts newly received information into long-term storage. Slow-wave sleep (SWS) and rapid eye movement (REM) sleep are both sleeping stages that work together to help with the formation of long-term memory

in the brain. In one study, the electroencephalogram (EEG) detects memory consolidation during the REM sleep stage in the brain. Along with that, the participants in this study asserted that they experienced vivid dreams after waking. Research has also shown that during human sleep, SWS emerges in early periods, and REM shows up in the late period of sleep (“About Sleep’s Role in Memory”). Studies were conducted using animal trials such as rats, mice, and cats to resolve the relationship between REM and memory consolidation. Studies imitate the human learning process and alter this process for animals to easily adapt. For instance, they use complicated tasks like shuttle box avoidance and complex mazes. Then, they put a group of animals to sleep after learning these tasks. Finally, researchers put these animals back to these activities to see whether their level of completing the tasks would be the same as the learning period. The result of this study shows that sleeping after learning helps the consolidation of memory in the brain. However, waking after learning suggests an exponential decrease in patterns in memory recall. Thus, sleep and memory are closely linked together though researchers have not yet found out the exact biochemical reason.

An essential part of the memory process in the human brain is the ability to remember. Yet, the erasure of information in memory has also become a significant part (or a coping mechanism) in certain situations. Many scholars have asserted that sleep might help with deleting or filtering information that is devastating to a person’s health. Based on a neurocomputational model of associative learning, dreaming when a person is in REM sleep aids in the forgetting of "parasitic modes" of activity, thus ensuring an efficient mode of operation of the brain during waking (“About Sleep’s Role in Memory”). Research shows dreaming reduces unwelcome forms of representation in memory. These forms of representation in memory include trauma, depressive events, or instant embarrassment. Then, the brain integrates the memory development during the day and the recall of memories acquired before sleep. Once the person wakes up, they won’t remember the trauma or certain events they experienced that are threatening to their mental status. Memory erasure might provide relief by removing distressing memories for people who go through severe traumatic events. Post-Traumatic Stress Disorder (PTSD) patients are an example of memory erasure since they typically have a severe trauma (“Intrusive Memories of Trauma: A Target for Research Bridging Cognitive Science and Its Clinical Application”). Removing the distressing and mental struggles of the trauma, this fact could hypothetically

improve the PTSD patient's quality of life. Even so, in some of these cases, the people who "forget" certain memories from the trauma might reveal that distress if facing similar situations again, which is known as re-experiencing symptoms. Re-experiencing symptoms could be highly distressing and disruptive to daily life, including distressing memories, flashbacks, nightmares, and intense emotional or physical reactions.

Overall, current studies link sleep deprivation, memory loss, and dementia closely together. Insufficiency of sleep leads to the failure of memory formation in the brain and might eventually cause dementia. Researchers can deepen the understanding of the relationship between the REM sleep stage and memory consolidation in the brain and clinicians should promote better sleep patterns to reduce the chance of memory loss.

Memory Loss in Alzheimer's Disease

Alzheimer's Disease (AD) is known as the most common form of dementia ("Alzheimer's Disease: Causes, Symptoms, Treatment & Stages"). Its clinical symptoms include memory loss and other cognitive impairments. All of these impairments and malfunctions ruin AD patient's daily life. AD results from the buildup of proteins like amyloid and tau that causes the development of cortical atrophy over decades. Current theories believe that a group of genetic and environmental factors may contribute to the formation of these proteins. The apolipoprotein E4 (ApoE4) genotype is one possible genetic risk factor in AD. The ApoE4 carriers have a 4- to 10-fold increased odds ratio of developing AD. However, the chance of ApoE3 and Apo32 carriers developing AD is significantly less than ApoE4 carriers, which is also the reason why these two genotypes are possibly an advantage to have gained prevalence in human populations so quickly ("Alzheimer's risk factors age, APOE genotype, and sex drive distinct molecular pathways").

Cortical atrophy means degeneration of cells that happens in the cortices of the brain. The neuropathological signs of the atrophy process in AD include the presence of senile plaques (amyloid-P) and neurofibrillary tangles (hyperphosphorylated tau protein) in autopsied brains ("Memory Loss in Alzheimer's Disease"). Because of the fast atrophy in poorly myelinated areas of the brain, AD patients often experience memory loss as the first show-case symptom. The first

lesions characteristic of AD appear in brain areas where memory and learning are grouped by poorly myelinated limbic neurons in the hippocampus and association cortex. Both regions are responsible for memory and the generation of behaviors. Compared to a healthy person's brain, the rate of atrophy in an AD patient's brain is ten times faster according to the current research. In vulnerable regions like hippocampal formation, AD patients' atrophy rates surpass 10% per year. Physicians in Germany monitored the brain of an AD patient for over 4 years and noticed a reduction of gray matter (contains brain cell bodies), a decline in the left hippocampal volume, and an expansion of a lateral ventricle volume. Beginning in the entorhinal cortex and hippocampal formations, these neuropathological alterations later progressed to the other temporal, parietal, and frontal association cortices. According to research, hippocampal shrinkage and the formalization of previous disease phases begin before dementia becomes visible. However, memory loss appears to be an apparent symptom in an AD patient before catching it in the progressive development of the preclinical stage of AD.

Alzheimer's Disease and other forms of dementia have been difficult to diagnose over decades. Gradual onset, non-specific symptoms, overlapping with normal aging, lack of awareness, and misdiagnosis are the reasons why this issue would happen. Once physicians catch the disease, it's either already in the late stage or as far as no further treatment or procedure could reverse the deficits these neurodegenerative diseases have made. Future studies should focus on looking for more certain causes for dementia and methods to detect them early enough to avoid its progressive impact on the patients.

Future Diagnosis Approaches for Dementia

Current study started using magnetic resonance imaging (MRI) to create a classifier for different dementia disorders. Atlas-based volumetry was performed on T1-weighted MRI data of 426 patients and 51 controls from the multi-centric German Research Consortium of Frontotemporal Lobar Degeneration including patients with behavioral variant frontotemporal dementia, Alzheimer's disease, the three subtypes of primary progressive aphasia, i.e., semantic, logopenic and nonfluent-agrammatic variant, and the atypical parkinsonian syndromes progressive supranuclear palsy and corticobasal syndrome ("Multiclass Prediction of Different Dementia Syndromes based on Multi-centric Volumetric MRI Imaging"). In the purpose of comparing each

patient group to controls to all seven diagnostic groups in a multi-syndrome classifier, the researchers employed support vector machine classification. Results show the binary classification models reached high prediction accuracies between 71 and 95% with a chance level of 50% (“Multiclass Prediction of Different Dementia Syndromes based on Multi-centric Volumetric MRI Imaging”). In contrast, the multi-syndrome model achieved accuracy levels that were more than three times greater than the level of chance of the binary classification. Further, the multi-syndrome model has better predictions of regionally specific atrophy patterns compared to its performance on dementia syndrome. This result means that the detection of early-stage progression of dementia in certain brain regions has a better prediction in the current model so far.

Overall, AI algorithms can process vast amounts of MRI data and extract patterns that might not be observed by humans. Magnetic Resonance Imaging (MRI) will be promoted in modeling the prediction of various neurodegenerative diseases and hopefully help clinicians in diagnosing diseases before becoming irreversible. With the integration of advanced artificial intelligence into MRI analysis, there is a great chance that physicians can detect subtle changes in brain structure and function before the emergence of clinical symptoms. Thus, research should integrate current artificial intelligence with the MRI to increase the accuracy of the diagnosis. Furthermore, AI models can become increasingly accurate in recognizing unique disease signatures, thus leading to earlier interventions and the implementation of personalized treatment plans.

Conclusion

Electrical and chemical signaling in the brain controls everything humans do, including behavior, thinking, emotions, and memory. The brain integrates and processes long-term and short-term memory into a working memory which is the instant thought process and recall that helps humans to cope with their surroundings. However, the causes of memory loss are various, involving dementia, sleep deprivation, and mental status. Sleep is a “temporary shelter” which delays the consequences of memory traces because research revealed the REM sleep stage helps the brain to restore memory. Dementia like Alzheimer’s Disease also causes memory loss due to the shrinkage of the hippocampal formation because of the buildup of abnormal proteins. Though

diagnosis for dementia is difficult now because physicians struggle to notice the minor symptoms dementia has, researchers are integrating AI with current medical devices to detect changes in patients' brains easier. Research is needed in understanding how the signaling of memory works in the brain exactly and to innovate medical devices with AI to assist physicians with diagnosis.

Works Cited

"Alzheimer's Disease: Causes, Symptoms, Treatment & Stages." *Cleveland Clinic*, https://my.clevelandclinic.org/health/diseases/9164-alzheimers-disease.

Chai, Wen Jia, et al. "Working Memory from the Psychological and Neurosciences Perspectives: A Review." *Frontiers*, 9 Mar. 2018, www.frontiersin.org/articles/10.3389/fpsyg.2018.00401/full.

Iyadurai, Lalitha, et al. "Intrusive Memories of Trauma: A Target for Research Bridging Cognitive Science and Its Clinical Application." *Clinical Psychology Review*, Apr. 2019, www.ncbi.nlm.nih.gov/pmc/articles/PMC6475651/.

Jahn, Holger. "Memory Loss in Alzheimer's Disease." Dialogues in *Clinical Neuroscience*, Dec. 2013, www.ncbi.nlm.nih.gov/pmc/articles/PMC3898682/.

"Long-Term Memory: Definition, Loss, Psychology, and More." *Medical News Today*, www.medicalnewstoday.com/articles/long-term-memory#:~:text=Long%2Dterm%20memory%20refers%20to,an%20indefinite%20period%20of%20time.

"Multiclass Prediction of Different Dementia Syndromes Based on Multi-Centric Volumetric MRI Imaging." *NeuroImage: Clinical*, 5 Jan. 2023, www.sciencedirect.com/science/article/pii/S2213158223000098.

Rasch, Björn, and Jan Born. "About Sleep's Role in Memory." Physiological Reviews, Apr. 2013, www.ncbi.nlm.nih.gov/pmc/articles/PMC3768102/.

"Short-Term Memory Loss: Definition, Loss, Psychology, and More." *Medical News Today*, www.medicalnewstoday.com/articles/short-term-memory#:~:text=Short%2Dterm%20memory%20refers%20to%20the%20memory%20systems%20in%20the,often%20up%20to%2030%20seconds%20.

"Sleep Deprivation and Memory Loss." *WebMD*, www.webmd.com/sleep-disorders/sleep-deprivation-effects-on-memory#:~:text=Both%20acquisition%20and%20recall%20are,absorbing%20and%20recalling%20new%20information.

Zhao, Na, et al. "Alzheimer's Risk Factors Age, APOE Genotype, and Sex Drive Distinct Molecular Pathways." *Neuron*, 3 June 2020, www.ncbi.nlm.nih.gov/pmc/articles/PMC7388065/.

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