Alzheimer's Disease with A.I: Insights from Neural Network Damage and Adaptation

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***Abstract*—Alzheimer's disease is a progressive neurodegenerative disorder that affects millions of people worldwide. Unfortunately, there is currently no known cure for this progressive condition to date. Therefore, early detection and intervention are crucial in enhancing patient outcomes. This paper highlights the importance of continuous research and development on the potential of artificial intelligence (AI) to revolutionize Alzheimer's disease care. AI holds promise in providing accurate and efficient diagnostic tools, as well as personalized treatment options. To illustrate this, the paper investigates the response of the nervous system to injury, the correlation between neural network damage, and accuracy using a neural network model trained with the MNIST dataset [1]. Additionally, it delves into how a damaged network can restore functionality through the assistance of another neural network, providing valuable insights into the nervous system's ability to adapt to changes and respond to injury, contributing to the ongoing efforts to understanding more of the Alzheimer's disease.**

***Index Terms*—Alzheimer's disease, artificial intelligence, machine learning, diagnosis, treatment, neural network, neural injury,**

I. Introduction

A.I. techniques have been found in a wide range of applications in the clinical and biomedical fields. Alzheimer's Disease is currently an active research field and is one of the most prevalent and costly diseases to manage in developed nations. The disease has been a devastating neurologic disorder that affects millions of people worldwide. It is an irreversible neurodegenerative disease that progressively destroys cognitive skills causing the brain to undergo atrophy that results in the brain shrinking and the brain cells to die, eventually fatal for the patient. Its common symptoms are characterized by progressive memory loss, cognitive decline, behavioral changes, and dementia. Globally, over 50 million people are living with dementia, one in eight person over the age of 65 is affected by it. Every year more than 200 billion dollars are spent on its research, making it the third most expensive disease. Diagnosis is extremely difficult because even though clinical signs only start to show up after the age of 65, the changes in the brain can begin years or decades in advance. [2]

A. Background

From the biological standpoint, Alzheimer's Disease is caused by abnormal deposits of protein in the brain. In an Alzheimer's brain, beta-amyloid plaques and tau tangles are formed which damages the nerve cell in the brain, leading to neurodegeneration and cognitive decline, and brain shrinkage. The hippocampus, which is used for forming memories, is usually the first area of the brain to be affected. So someone in the early stage of Alzheimer's may struggle to remember recent memories. Since brain cells cannot be revived, there is currently no cure for Alzheimer's, and the currently available treatments only provide limited symptomatic relief. Therefore, early diagnosis and intervention are crucial for improving patient outcomes, since alternative treatments have not been commonly accepted by medical professionals. [3]

The clinical diagnosis of Alzheimer's Disease is based on brain imaging and cognitive tests which required the presence of significant cognitive loss, but since AD also shared some common clinical features with other neurodegenerative diseases, this makes early and differential diagnosis difficult. Moreover, Alzheimer's Disease pathology is also characterized by high complexity and heterogeneity. It is multifactorial where many conditions can influence the individual risk of onset. These factors can include genetics, lifestyles, age, and environmental factors. This shows that the traditional method of classifying neurodegenerative diseases based on symptomatology is difficult in the diagnostic process due to the occurrence of both clinical and neuropathological features defined in one individual at the same time, and sometimes for separate neurodegenerative disorders. [2] This implies that diverse and personalized treatment options may be required for each individual patient.

B. OpenSource Datasets

In the last 20 years, many open data-sharing initiatives have grown in the field of neurodegenerative disease research.

Clinical and biological data from electronic health records and multi-omics sciences represent a potentially unlimited amount of information about biological processes which can be explored through Big Data exploitation. These large and highly complex dataset generated from biological experiments can far exceed the human ability to make sense of the disease. [4] [5] Using AI to process these datasets can offer a huge opportunity to explore and provide insight into mechanisms that drive Alzheimer's pathogenesis. [6]

C. AI in Alzheimer's

In this context, AI technology represents a promising approach to investigating the pathological mechanisms of AD by analyzing such complex data. AI has the potential to revolutionize Alzheimer's care by providing more accurate and efficient diagnostic tools and personalized treatment options. Machine learning algorithms can analyze large datasets of brain imaging and biomarker data to identify early signs of Alzheimer's and predict disease progression. These algorithms can also be used to develop personalized treatment plans based on an individual's unique genetic, lifestyle, and environmental factors. AI-based interventions, such as virtual reality and cognitive training, have also been developed to help patients with Alzheimer's manage their symptoms and improve their quality of life.

II. Objective

In recent years, there has been a rapidly accelerating rate of new publications in this field. Synthesizing the updated literature to provide insights into the current status, challenges, and future directions has revealed a pressing need in advancing this important research field. [5] This paper focuses on some recent AI technologies for Alzheimer's research to specifically answer the following questions: 1. Can AI be used to diagnose Alzheimer's Disease 2. Can AI monitor the disease progression between patients? 3. Will AI be able to help in finding a cure for Alzheimer's Disease? Then the paper will discuss the current shortcomings with AI and then explores its future directions in the field.

III. AD detection with AI

Machine Learning techniques and Neural Networks have been used and tested in attempt of early detection of the disease. These methods consist of combing different kinds of data such as brain images or neuropsychological assessments to help train the AI model to have a more comprehensive understanding of disease heterogeneity. These datasets are usually in the form of Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), Diffusion Tensor Imaging (DTI) and 18F-fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) which are helpful to identify the anatomical structures of the brain for diagnosis. One of the feature extraction methods is called "eigenbrain" when the algorithm is applied with SVM was able to achieve a mean accuracy of 92.36% for Alzheimer's Disease diagnosis using MRI data. [6] It can be observed that combining neural imaging, and other available neuropsychological data can ensure high accuracy in classifying AD patients from cognitively normal elders. However, it is harder for some patients with mild cognitive impairment (MCI) to be detected if their symptoms will be converted to AD in the future. Their other limitations include their high cost and lack of diffusion in non-specialized centers.

IV. AD diagnosis with AI

The conversion from Mild Cognitive Impairment to Alzheimer's Disease dementia is a binary diagnostic categorization that does not capture the heterogeneity among patients. Common proposed machine learning model usually combines info from risk factors, clinical assessments, and anatomical MRI images. But the research done till date shows a high probable detection rate in which they used the pattern classifier built on various longitudinal data. Papers have found that by adding a time point of a second assessment gives a significantly better prediction of the patient's status in brain atrophy and is able to identify individuals at risk of Alzheimer's and predict their symptom progression over the next 5 to 6 years in order to conduct decision making, treatment, lifestyle changes and even drug trials at the individual level. [7]

V. AD treatment with AI

As mentioned, AD patients have a highly heterogeneous pathology in terms of clinical manifestations, disease progression and response to pharmacological treatment. Machine Learning techniques and Deep Neural Network models are used to identify sub-groups of individuals with similar features. Research in this area has discovered that various applications of unsupervised learning can highlight the complex patterns ranging from patients to disease progression, which even experts may find difficult to discern. [8] Using AI to accurately model the disease stages in the varied phenotypes of mild AD is a crucial task for the development of new treatments and optimal patient stratification in the field. [9]

VI. AD cure with AI?

Even though there is currently no cure for Alzheimer's disease, there are methods and ideas proposed in which AI research could contribute to the advancement in potential pharmacological treatments to delay the progression of the disease or soothe symptoms. The idea of using AI to attack the effects of the disease has in the brain as a possible cure for AD might not be out of the picture. Pharmacology researchers have been using AI to assist their research on Alzheimer's Disease at a molecular level to identify diverse and subtly-differentiated morphologies. They used deep metric learning to explore the similarity spaces and landscapes of the molecules in order to understand the disease mechanism. The study can be used to better hypotheses for the protein in question and for drug discovery. [10]

VII. Ethical Considerations

Even though AI posed great potential in the field of diagnosing and managing of AD, other than the issue with dataset privacy, bias, and diversity, most papers have brought up the concern about the trustworthiness of the AI approach. In order to provide trust and confidence in the prediction results for the patient and medical professionals, the transparency and explainability of complex models are needed. This area of concern is in the rise for its research phase, a few papers have been trying to solve this problem with the use of XAI. The study of Alzheimer's Disease Prediction with XAI has been conducted in various Neural Network Models such as such as vgg-16 and CNN, and is even able to identify the stages of Alzheimer using Layer wise relevance propagation method. [7] [11] Using XAI with the corresponding feature explanation is able to help deliver the justification for the model's decision in a way that humans can understand and interpret it quite easily so that the prediction can be finalized by the medical expert for proper prescription and further diagnosis as required by the patient's circumstance. However, like most current XAI models, the margin of loss for sacrificing accuracy for an explainable model is the main limitation of this approach. [3]

VIII. Mimicking damages in neural network

In recent years, neural networks have gained widespread adoption as tools for understanding the human brain. However, the response of the neural system to injury remains a challenging problem. To address this issue, researchers have conducted a range of experiments that involve damaged trained neural networks. Meyes et al. performed experiments to examine the robustness versus structural damage in the neural network. [12] Cun et al. discovered that removing unimportant weight improves learning speed and slightly in accuracy. [13] Such experiments offer valuable insights into the impact of neural injury on neuron function, and may lead to the development of novel approaches for treating neural injuries.

To further understand the impact of the damage on neural networks, such as Alzheimer's disease, this study emulates the impact of the simulated neural injury on a trained neural network with MNIST dataset using two distinct experimental approaches. The first approach selectively damages specific neurons, and the second approach selectively damages the outputs of a specific layer of neurons. The network's performance is evaluated after simulated neural injury, providing insight into how the brain responds to injury and adapts to changes in neural networks.

Lastly, the neuron damage experiments were reversed to investigate whether a neural network could repair a damaged network. Such an approach may provide insights into the self-repair mechanisms of the brain and inspire the development of new treatment strategies for neural injuries.

A. Experiments

1) Noisy neuron: To replicate the characteristics of an injured nervous system, the experiment employs a fully connected two-layer neural network comprising an input layer and an output layer. The network is evaluated based on two critical parameters - noise probability and noise level - in terms of accuracy. Additionally, the study introduces two types of damage, namely neuron damage and output damage. The former impacts all outputs from the affected neuron, while the latter only affects certain outputs from the neural layer.

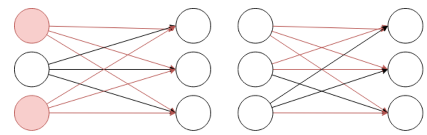

Fig. 1. Neuron damage (LHS) and Output damage (RHS). The red neuron and output are those affected

In Figure 1, both networks exhibit a 66% noise probability in their first layer. However, the network on the left-hand side has incurred neuron damage, resulting in the 1st and 3rd neurons being affected, and consequently, all their outputs being replaced with noise. On the other hand, the network on the right-hand side has experienced output damage, where 66% of its outputs in the first layer have been impacted. In this example, as there are a total of 9 outputs from the first layer, 6 outputs have been affected by the damage, which may or may not originate from the same neuron and the noise may or may not be the same. In output damage, despite some neurons in the layer being impacted, a portion of the correct signals of the damaged neurons are still able to be transmitted instead of producing all noise.

$$Noise(i) = X(i) \times noise\_level \tag{1}$$

The relationship between the noise level and the noise is depicted in Eq. 1, where $X \sim \mathcal{N}(0, 1)$ and i is either the index of a neuron or index of output depending on the experiment performed. Please notes that the affected outputs or neurons have their value replaced, not added, by the noise.

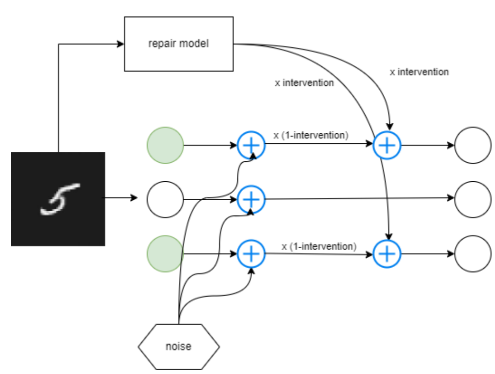

Fig. 2. Simplified structure for neuron repair

2) Neural repair: A comprehensive set of experiments is conducted to explore the effects of varying combinations of noise probability and level on neuron damage. Additionally, a restorative experiment is conducted, wherein noise is added to all the outputs of the first layer, while leaving the underlying structure of the neural network unaltered. A three-layer neural network model, which possesses complete knowledge of both the input, prediction, and label, has partial access to alter all the output per neuron as in neuron damage. This access is quantified by the term "neuron access density" which is similar to the concept of noise probability while the "intervention" is defined as the percentage of the impact on the damaged model output after the noise. Figure 2 shows a simplified structure for neuron repair experiments where the neuron access density of 66%. The repair model has its parameter train based on the loss between the label and the final output of the damaged model.

B. Results

1) Noisy neuron: Figure 3 depicts the outcome of the two-layer neuron damage experiment, which examines the impact of different noise levels and probabilities on accuracy. As the noise probabilities increase, more neurons are either injured or affected by the noise, leading to a decrease in accuracy. Moreover, the accuracy decreases at a faster rate as the noise level increases.

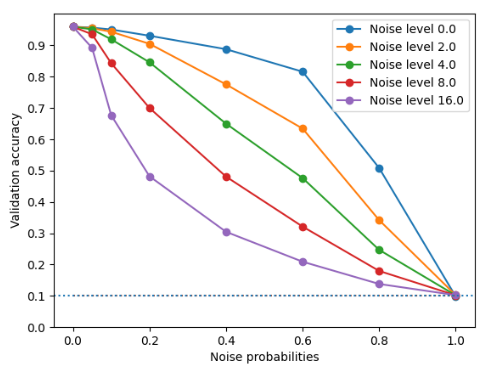

Fig. 3. Noise Probability vs. Accuracy with different noise levels on entire neurons of a single layer in a two-layer neural network model for neuron damage

Figure 4 depicts similar results to those presented in Figure 3. However, in the former, the accuracy drops at a much faster rate. One interesting observation is that noise level 0.0 decreases more rapidly than noise levels 2.0 and 4.0. This phenomenon is possibly due to the weight in the next layer being unable to propagate since the weight is multiplied by 0, and the bias is insufficient for the model to arrive at the correct answer.

2) Neural repair: The findings presented in Figure 5 demonstrate the efficacy of neuron repair in restoring accuracy to neural networks. Accuracy improves as the neuron access density increases and as the intervention increase, highlighting the viability of repairing damaged or inaccessible neurons. The restoration neural network was able to achieve significant accuracy improvements even after only one epoch, indicating the efficiency and effectiveness of the repair mechanism, and thus showing the repair mechanism has the potential to be dynamic in the human nervous system. However, to effectively repair the neural network, above 0.5 intervention has a much

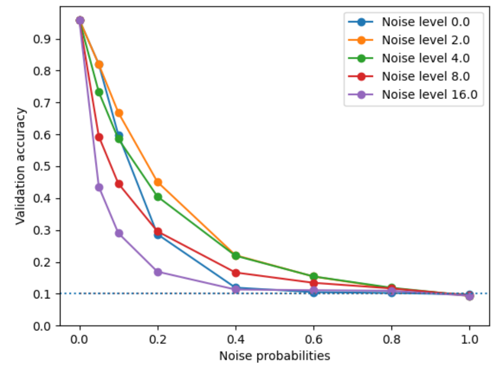

Fig. 4. Noise Probability vs. Accuracy with different noise levels on a portion of outputs of a single layer in a two-layer neural network model for output damage

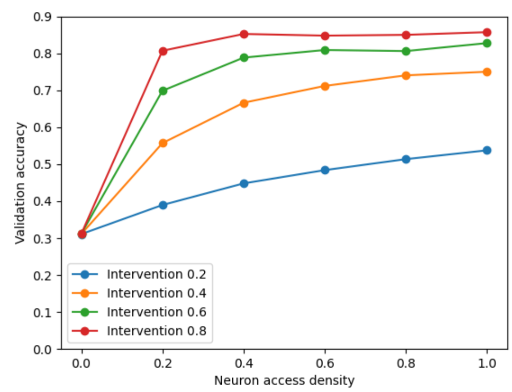

Fig. 5. Noise access density vs. Accuracy with 1 epoch on two-layer neural network model

better effect, indicating that the key to neuron repair is not only based on the number of neurons controlled but also on how much control the restoration model has on individual neurons.

IX. Discussion

Artificial neural networks are computing systems inspired by the biological neural networks that constitute animal brains and is based on a collection of connected units or nodes called artificial neurons. The connections in the ANN are like the synapses in a biological brain, transmitting a signal to other neurons. These artificial neuron receives signals, processes them, and signals the other neurons connected to them. [14] While there is currently no direct equivalent damage model for artificial neural networks that mimics the effects of neurodegenerative diseases, there are some ways in which artificial neural networks can be damaged or degraded that could be represent the effects of neurodegenerative diseases. For example, if an artificial neural network is exposed to corrupt or incomplete data, it may become less accurate or completely fail to perform its intended function, similar to how neurodegenerative diseases can lead to cognitive impairment and other neurological symptoms. Additionally, artificial neural networks can suffer from "catastrophic forgetting", where they forget previously learned information when presented with new data, which could be considered analogous to the memory loss seen in Alzheimer's disease and other forms of dementia. Assimilating such an approach in computational neuroscience can be crucial in helping researchers to understand more of the brain and neurodegenerative diseases in cognitive domains that Alzheimer's Disease impacts. However, the mechanisms of neurodegenerative diseases' damage to the brain are complex and multifaceted, involving various factors such as genetic, environmental, and lifestyle factors. There may also need for a more specific way to better replicate the pathology involving the loss of neurons, synaptic dysfunction, and abnormal accumulation of proteins, beta-amyloid, and tau in the artificial neural network.

X. Conclusion

In conclusion, AI continues to play a critical role in aiding neuroimaging analysis for the diagnosis of Alzheimer's Disease, and monitoring disease progression and transition. With the increasing availability of open-source databases, AI has been able to produce more advanced and accurate approaches. New research for XAI on the application of AD has provided more validity and reliability for physicians to communicate and explain AI findings in decision-making. While most current AI technologies have made significant progress in classifying Alzheimer's disease and stratifying patient treatments, they can also be served as a tool for scientists to better understand the disease mechanism and conduct studies and hypotheses for the protein in question.

The study investigated the correlation between the probability and level of noise and their respective effects on accuracy, which simulates the cognitive performance of individuals with tangles and plaques in the AD brain. The results revealed a significant decline in accuracy with an increase in noise probability, and a steeper decline was observed with an elevated noise level. The findings also indicated that the output damage had a more pronounced effect on accuracy than neuron damage, despite having identical levels and probabilities of noise. The neural repair is able to successfully restore functionality in the damaged model. As the restoration model has more access to the damaged model, the accuracy of the damaged model increases. The implications of these observations provide valuable insights into the intricate mechanisms underlying the impact of injuries on the nervous system and can be further used to understand and analyze to develop a cure for Alzheimer's disease with more in-depth brain function modeling.

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