

Monkeys, Machines, and MPTP: Discovery for the Parkinsonian Brain

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AUTHOR BIO

This paper was written by Daniel Joshi, a student at Sage Hill High School in Newport Beach who found a passion for neuroscience after participating as a research assistant in a Parkinson's Longitudinal Study. He enjoys leading his school team as a captain of varsity cross country and track and field, and he also relishes the competition he faces as a starter for the varsity soccer team. Outside of physical activity, Daniel loves hanging out with friends, watching TV, and eating delicious foods. In the future, Daniel hopes to major in neuroscience or biomedical engineering, and he plans to research Parkinson's specifically.

ABSTRACT

Parkinson's Disease (PD) is a brain disorder characterized by tremors, bradykinesia, and dyskinesia. Although discovered in the early 20th Century, to this day there remains no cure. This research paper highlights the neural identifiers in people diagnosed with PD, the history of artificial intelligence (AI), and several existing methods to improve the lifestyles of PD patients. Also reviewing the history of PD, the paper ventures through some history, discoveries, and breakthroughs surrounding the condition. The goal of this paper is to explain several Parkinsonian experiments and review the capabilities of AI in PD treatment. Finally, the present paper will discuss the limitations of AI in this field and hypothetical treatments to the neurological disorder.

Keywords: Parkinson's disease, Neurological disorder, AI, Treatments.

INTRODUCTION

With nearly one million people diagnosed with Parkinson's disease (PD) in the United States, the disease is quite prevalent and widespread in today's society. Patients living with PD suffer from gradually worsening symptoms. The condition typically makes it harder for people to walk and talk, as balance and coordination deteriorates with time. Additionally, those with PD are prone to gastrointestinal and psychiatric symptoms along with sleeping issues during the long term progression of the disease. As their lifestyle declines, the dopamine medications patients are prescribed also slowly lose effect. Most patients only live for 10 to 20 years after their PD diagnosis.

History of PD

In 1817, James Parkinson first described the symptoms of the disease in an essay about his patients. Although the namesake of the disease, Parkinson never found a cure or had the disease. Although PD became well-known, treatments were essentially non-existent until the mid-20th Century. In the 1950s, a treatment known as a pallidotomy saw some success, in which the globus pallidus internus (GPi) of the brain was removed to relieve some PD symptoms. However, the addition of L-dopa effectively put pallidotomies out of use (Vitek & Johnson, 2019). Currently the United States spends 52 billion dollars annually on PD treatment (Parkinson's Foundation, 2023). In this research paper, I will summarize our understanding of PD, review current treatments, and look into potential future treatments to Parkinsons' with AI.

The Monkey Experiments

In 1971, a study run by Mahlon DeLong conducted a seminal study for the role of the pallidum in movement with monkeys. After years of studying monkey anatomy and electrophysiology, scientists were able to describe the basal ganglia, a part of the brain responsible for motor control, in terms of functionality in the year 1986. By this time, scientists had already gained an understanding of the motor, oculomotor, limbic, and associative circuits of the brain. Based on the studies, scientists developed accurate models of the basal ganglia. Also during the 1980s, scientists discovered MPTP, which proved to be critical in analyzing the changes in dopamine state in PD patients. Researchers experimented with MPTP to develop a monkey model of a subthalamic nucleus (a part of the basal ganglia responsible for circuitry; STN) comparable to a Parkinsonian brain. With this developed model of the STN, researchers observed the levels of dopamine activity in the globus pallidus externus (GPe) and GPi (Vitek & Johnson, 2019).

MPTP and the Rate Model

Through the monkey experiments and models, scientists found that the exposure to the neurotoxin MPTP tended to decrease the brain activity utilized in motor control and increased the likelihood of an individual getting PD. Certain occupations increased risk of exposure to this PD-correlated chemical. When human basal ganglia were used, the results mirrored those of the monkey brains. A rate model hypothesis was developed based on the monkey model. This reflected how scientists found that the basal ganglia with PD produced dopamine in a different quantity and rate. This in turn caused the direct dopamine pathway (thalamocortical) to decrease flow and the indirect dopamine pathway (GPi) to have an

excessive amount of dopamine which caused the dopamine levels sent throughout the body to change. However, compared to the PD brain, a brain with an ibotenic acid lesion of the STN showed a removal of the imbalance of dopamine in a PD patient (Vitek, Johnson, 2019).

The History of Related AI

With the advancement in understanding of the brain, researchers looked for ways to apply the knowledge. However, long before the development of the PD brain rate model, scientists had been developing brain-related AI that possessed the ability to analyze the human brain. In 1943 Warren S. McCulloch wrote a paper titled “A logical calculus of the ideas immanent in nervous activity”. He described a mathematical model known as MP neuron created to perform computation with binary commands. In 1949, Donald Hebb discovered that when two nerve cells fire simultaneously, connection is stronger, and that neural pathways strengthen with use. Following this, in 1954 Farley and Clark created the first randomly connected reverberatory network. In 1960, Roserberg introduces MADALINE (Multiple Adaptive Linear Elements), which is the first learning machine capable of identifying optical patterns. This paved the way for diagnosis of PD with the help of AI (Chandrabhatla, 2022).

Current Treatment

Currently, AI is mainly used to diagnose or monitor PD in patients. Because doctors are not as accurate as machines in determining the stage or progression of PD, AI has taken prominence in the initial diagnosis. Computer-based algorithms are used to measure the symptoms and stage of the condition. Magnetometers are used to quantify the tremors

of PD patients to classify the extent of the disease and track gait freezing as well. Monitors on the body, which include biosensors, are used to track vitals and activity of the patient for the caregiver to see and to help provide feedback for healthcare professionals to limit the degradation of the body. Additionally, an autoremind AI has been developed to take care of schedules for PD patients. They use reinforcement learning to produce an efficient schedule that tracks habits, includes exercise for maintaining health, and to help keep the patient independent.

Deep Brain Stimulation Machine Learning

As a current PD treatment, deep brain stimulation (DBS) is a risky surgery that yields different levels of benefit from patient to patient (Mayo Clinic 2021). It involves implanting a neurostimulator that sends electrical signals throughout the brain to reduce symptoms of PD. However, DBS is quite inconsistent among individuals and is far from perfect. Perhaps in the future researchers could launch experiments with a brain model, whether from a monkey or human, to test the use of AI in the development of DBS. Using reinforcement learning to help adjust electric signals based on the reaction of the brain could prove to be monumental in the development of PD treatment. With AI, patients could improve their lifestyles just with the addition of AI inside their head. Perhaps with the knowledge of the brain, AI could learn to target electrical signals at parts of the brain such as the GPi to remove excess dopamine activity. However, with the vast complexities of the brain, AI would not have many examples to learn from. Additionally, this poses moral problems as having AI in an individual's head would effectively make them a cyborg. After the addition of AI for medical purposes, researchers would not know where to stop the line at. This

could lead to the addition of AI to someone for non-therapeutic purposes, which would emerge as a difficult ethical controversy to deal with.

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Conclusion

Since its discovery in 1817, PD has been a prominent enigma that scientists have struggled to find a cure for. Through the studying of monkey brains, the neuroscience community discovered the difference in brain activity that PD causes. However, with a greater understanding of the brain, the causes, and the symptoms of PD, researchers have been able to develop different treatments to the brain with varying success. However, with the advancement of AI, there have been ways to improve the lifestyles of patients. In the future, AI has great potential to change the entire field of neuroscience, but researchers must be careful in their use of their treatments. Focusing on AI will prove crucial for revolutionary progress in the foreseeable future.

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