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2020 Part the Cloud: Translational Research Funding for Alzheimer's Disease (PTC) - \$992,093

Mitochondrial function and BBB leakage as a novel treatment for Alzheimer's

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- Ph.D., Imperial College London, UK, 2009
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STUDY

- CADRO category: Translational Research & Clinical Interventions

This Phase 2a clinical trial will test whether a chemical compound can improve functionality of structures inside cells and reduce the progression of Alzheimer's.

Background

A specialized structure called the blood-brain barrier (BBB) is a highly selective barrier that helps maintain a healthy brain environment by tightly regulating what goes in and out of the brain from the circulating blood. The BBB is comprised of different cells that help clear toxic debris from the brain. Normal functioning of the BBB is essential to protect the brain from harmful changes. Studies show that in Alzheimer's and other brain disease, the BBB may become leaky and this may contribute to disease-related changes.

Dr. Edison and his team believes that abnormal functioning of the BBB cells may lead to a leakage through barrier. This could be associated with increased immune response seen in Alzheimer's and other brain diseases. Leakage in the BBB has been found to be higher in individuals with the APOE-e4 genetic variation, which is thought to impact the risk of developing Alzheimer's in some populations. Using genetically engineered Alzheimer's-like mice, the researchers found that a chemical compound - by repurposing a drug frequently used to treat complications of diabetes - may improve BBB leakage.

Research Plan

Building on their initial findings, Dr. Edison and colleagues will conduct a clinical trial to test the safety of their compound in 60 participants with the APOE-e4 genetic variation and early stage Alzheimer's. Participants in the study will receive either a daily dose of the compound or a placebo (not the actual compound but an inactive substance that has no benefits and also no risk for the participant) for one year. The researchers will measure the safety and tolerability of the compound. The researchers will administer brain scans before and after the clinical trial to measure the impact of the chemical compound on the functionality of BBB and

the mitochondria. The research team will also use these scans to study the impact of compound on brain volume and brain blood flow. Furthermore, the participants will be given cognitive tests to evaluate the effect of the compound on cognition. Dr. Edison's team will then prepare to test this compound in larger clinical trials.

Impact

If successful, the study results may pave the way of identifying novel therapeutic targets such as mitochondria and blood brain barrier function to tackle neurodegenerative diseases, including Alzheimer's.

Made possible through the generous funding from the Part the Cloud benefiting the Alzheimer's Association.