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Biomarker and Neural System Effects in Calcineurin Inhibition with Tacrolimus

This Phase Ib/IIa study will evaluate Tacrolimus- a drug used in organ transplant- in people with Alzheimer's.

PI

- M.D., Boston University, 1983
- Translational Neurology Head of the Interdisciplinary Brain Center at Mass General, Harvard Medical School, 2015
- Authored over 250 scientific articles, reviews and chapters

STUDY

- CADRO category: Translational Research & Clinical Interventions

Background

Calcium plays a critical role in the health, survival and actions of many types of cells in the body, and especially in nerve cells and immune cells. Previous studies suggest calcium imbalances in the brain disrupt nerve cell communication, and may contribute to cognitive symptoms in Alzheimer's. Nerve cells communicate with each other through specialized cell structures called synapses. For nerve cells to communicate, the synapses contain specific balance of molecules that move between nerve cells and throughout the brain system. One molecule that plays a key role in regulating nerve cell communication is calcium.

Calcium activates an important brain protein (called an enzyme) known as calcineurin, which can become overactivated during Alzheimer's. Dr. Steven Arnold and colleagues found that treating genetically engineered Alzheimer's-like mice with a drug called tacrolimus - approved by the FDA to prevent organ transplant rejection - blocks calcineurin in the brain, and prevents it from becoming overactivated. The researchers found that Alzheimer's-like mice treated with the drug have reduced memory loss as well as reduction in brain changes such as accumulation of beta-amyloid plaques and tau tangles, which are hallmark brain changes observed in Alzheimer's.

Research Plan

Building on their laboratory work, Dr. Arnold and colleagues will evaluate the brain with changes associated with Alzheimer's, safety and tolerability of the drug tacrolimus in a phase 1b/IIa study in 12 individuals with mild cognitive impairment, a condition of subtle memory loss, due to Alzheimer's disease. The researchers will assign the study participants to receive either a low or high dose of the drug for twelve weeks.

The researchers will also evaluate the impact of the drug in the study participants by measuring proteins in blood samples and cerebrospinal fluid (a biological fluid sample found in the brain and spinal cord). The proteins will serve as biological markers (biomarkers) to help the researchers track inflammation, nerve cell functions, nerve cell death and Alzheimer's progression over the course of the trial. They will also

measure any brain changes with brain scans, electroencephalography or EEG (used to measure electrical signals in the brain) and cognitive tests over the course of the trial.

Impact

This clinical trial represents an important step to determine if an FDA-approved organ transplant drug could be repurposed as a potential therapy for Alzheimer's. If successful, the results of this work could lead to future large-scale clinical trials to evaluate whether the drug is able to delay, or stop progression of mild cognitive impairment and Alzheimer's disease.

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