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Aromatase inhibition in Alzheimer's disease: Phase 2 study

This Phase 2 clinical trial will examine whether a FDA-approved drug used to treat breast cancer can be repurposed to reduce cognitive decline and delay the progression of Alzheimer's.

PI

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Background

Aging is the biggest risk factor for Alzheimer's disease. Aging may be associated with progressive or abrupt decline in the levels of the sex hormones testosterone and estrogen in the blood in men and women respectively. Sex hormones levels in the blood as well as in the brain are regulated by a protein (enzyme) called aromatase, which converts testosterone to estrogen. Studies have shown increased levels of aromatase may result in excessive estrogen and diminished testosterone levels in individuals (both men and women) with Alzheimer's.

Several research groups have observed an increase in the level of aromatase in brain tissue samples from individuals with Alzheimer's. Furthermore, Dr. Anat Biegon and colleagues have found high levels of aromatase in the hippocampus (a brain region responsible for memory formation), which were associated with the severity of brain changes observed in Alzheimer's. A recent study shows that blocking the action of aromatase using chemical compounds could reduce the risk of Alzheimer's. Based on these findings, Dr. Biegon believes that blocking this enzyme may halt the progression of Alzheimer's.

Research Plan

Dr. Biegon and her team will conduct a Phase 2 study by recruiting 100 older adults with mild or moderate Alzheimer's from the Stony Brook Center for Excellence in Alzheimer's disease. Two-thirds of these participants will receive a drug (letrozole) which is a hormonal treatment approved for breast cancer treatment by the Food and Drug Administration (FDA). This drug blocks the action of aromatase, reducing estrogen production and increasing testosterone levels in all organs including the brain. In the research team's study, the remaining third of the participants will receive a placebo (not the actual drug but an inactive substance). Dr. Biegon's team will evaluate the safety of the drug in the participants. They will also administer Positron Emission Tomography (PET) and Magnetic Resonance Imaging (MRI) brain

scans and cognitive tests to the participants before the clinical trial and afterwards in order to evaluate the impact of the drug on aromatase, loss of brain tissue and cognitive decline. The researchers will then prepare to test the drug in a larger clinical trial.

Impact

If successful, the study results may give rise to a new approach to reduce cognitive decline and delay the progression of Alzheimer's.

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