Deep Brain Stimulation for Alzheimers Disease

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Country

USA

Title of project or programme

Deep Brain Stimulation for Alzheimers Disease

Source of funding information

NIH (NIA)

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30/09/2012

Total duration of award in years

5

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Assistive Technology... Bioengineering... Brain Disorders... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Mental Health... Neurodegenerative... Neurosciences... Rehabilitation... Translational Research

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is a major and rapidly

growing public health problem for which few effective therapies are available. Treatment development has focused on the amyloid hypothesis. Unfortunately, disappointing results have emerged from trials of the “”anti-amyloid”” therapies. The urgent need for the development of novel, non-amyloid therapies, the efficacy of deep brain stimulation (DBS) in neuropsychiatric disorders (e.g. Parkinson’s disease and depression), and the striking improvement in memory in an individual who underwent fornix DBS was the impetus for a Phase 1 clinical trial of DBS-F in AD. The fornix is a major inflow and outflow tract of the hippocampus. Studies of the earliest phases of AD in humans and animal models indicate that one of the first areas affected is the hippocampus, most likely resulting from cortical pathology that leads to dying back of neurons and the spread of the disease into the hippocampus. Recent research from our group suggests that loss of fornix integrity is an early event in AD that is followed by later reduction of hippocampal volumes. Targeting therapies at the fornix, especially ones that affect other brain areas such as hippocampus, is a novel and potentially important therapeutic approach. We hypothesize that DBS placed anterior to the columns of the fornix (DBS-F) during early AD electrically stimulates the hippocampus leading to improvement in clinical and biological outcomes. This hypothesis is supported by our promising preliminary results from the Phase 1 clinical trial in AD that demonstrated the safety and tolerability of DBS-F, as well as a sustained increase in cortical glucose metabolism over one year, in contrast to the natural course of AD, and in excess of the effects of chronic cholinesterase inhibitors. Furthermore, studies in rodents demonstrated that DBS-F leads to improved memory and hippocampal neurogenesis. The logical next step is a Phase 2b trial of DBS-F in AD to gain additional experience focused on safety, preliminary estimation of efficacy, and response predictors. Specifically, we propose to evaluate in a masked, randomized clinical trial the safety and tolerability of DBS-F for the treatment of mild AD (AIM 1). We also will examine the efficacy of DBS-F for mild AD by comparing clinical and neuro-imaging outcomes of patients started on active DBS-F after surgery to those in patients in whom DBS-F activation is delayed by 12 months (AIM 2). Finally, we will examine intra-individual effects of DBS-F by comparing outcomes in the 12 months before to the 12 months after activation in patients assigned to delayed activation (AIM 3). The study’s innovation relates to the use of DBS in AD, targeting the fornix, an area closely linked to the hippocampus, affected very early in AD, and surgically accessible at relatively low risk. Data from the Phase 1 trial together with findings that stimulation in rodents leads to improved memory and hippocampal neurogenesis provide support for a proposed Phase 2b investigation of this novel therapy.

Lay Summary
PUBLIC HEALTH RELEVANCE: Alzheimer’s disease (AD) is a major public health problem with few effective treatments. Disappointing results have emerged from studies of medications for AD focused on removing brain amyloid. New non-amyloid therapies will be critical to finding a cure. Deep brain stimulation (DBS) holds promise as a treatment for AD. Building on early findings from our group with DBS in AD patients, also supported by results from animal studies, we propose a two-year clinical trial of DBS to target a part of the brain known as the fornix to evaluate its safety and efficacy in 20 patients with mild AD.

Further information available at:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

Years:
2016

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