Longitudinal Cognitive ERP studies: Advancement for AD Clinical Trials

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Principal Investigators

OLICHNEY, JOHN M

Institution

UNIVERSITY OF CALIFORNIA AT DAVIS

Contact information of lead PI
Country

USA

Title of project or programme

Longitudinal Cognitive ERP studies: Advancement for AD Clinical Trials

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

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01/09/2015

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2

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)... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences... Prevention... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): This proposal aims to validate cognitive event-related brain potential (ERP) biomarkers of disease progression in populations eligible to enroll in AD clinical drug trials. We will use a comprehensive ERP protocol which elicits 5 cognitive ERP components (P50, P300, N400, LPC and Frontal Positivity (FP)), each with demonstrated high sensitivity to early Alzheimer disease (AD). A systematic study which compares the relative sensitivity and stability of these ERP components is needed, in this era of validated amyloid biomarkers sensitive to early AD. We will study >200 elderly participants (60 pre-clinical AD, 50 amyloid biomarker – normal elderly, 50 amnestic MCI & 40 mild AD study completers) with longitudinal cognitive ERP/EEG, brain MRI and neuropsychological testing. The project will test the feasibility of multicenter ERP studies, develop infrastructure, refine methodology, and determine how ERPs can be best used to detect the AD pathophysiologic process and to measure changes over time. This study will advance our knowledge of how to use ERPs in AD treatment trials, e.g. for sample “”enrichment”” in prevention trials, and as outcome measures. Specific Aims: 1) To validate the utility of baseline ERPs in predicting longitudinal trajectories n cognitive decline and brain atrophy. 2) To test the hypothesis that our comprehensive ERP battery will assist the in vivo staging of the AD pathophysiologic process. 3) To test the hypothesis that ERPs are highly sensitive to changes in the AD pathophysiologic process over time and will provide useful biomarkers for tracking disease progression. Methods: We will recruit elderly subjects (age 60-90; n =252, 74 with Preclinical AD (Pre-AD), 62 amyloid biomarker-negative Normal Old (NO) subjects, 62 amnestic MCI, and 54 mild AD dementia). All enrolled subjects will receive an amyloid PET study, longitudinal ERP/EEG and brain MRI. All subjects will be studied with repeat annual ERP testing for 2 years and MRI 1 year after the baseline study, providing longitudinal ERP, structural MRI, neuropsychological and functional data. 32 channel ERP/EEG will be obtained using a comprehensive ERP battery which assesses automatic (P50) and controlled (P300) attention, language (N400) and memory (verbal and visual, with LPC and FP measures) processes. Significance: Sensitive, reliable markers of synaptic dysfunction and incipient AD in its preclinical stages are needed. This proposal, by validating ERP biomarkers of disease progression in populations most relevant to current AD clinical drug trials, will have important applications to primary prevention trials, disease-modifying and targeted cognitive therapies. This study will allow the rational application of specific ERP paradigms, best suited to preclinical vs. prodromal vs. demented populations. More wide application of sensitive ERP/EEG techniques could have major impact on reducing the requisite sample sizes and costs of AD treatment trials.

Lay Summary

PUBLIC HEALTH RELEVANCE: This multicenter proposal aims to validate cognitive ERP biomarkers of disease progression in populations eligible to enroll in Alzheimer’s disease (AD) clinical drug trials, with applications both to disease-modifying and targeted cognitive therapies. Combining the molecular specificity of amyloid biomarkers with the sensitivity of ERP measures of synaptic/cognitive dysfunction should advance our ability to stage AD and identify those at highest risk for decline. Detecting the earliest physiological changes of amyloid-related neurotoxicity, and understanding its timecourse, will be tremendously helpful for planning early intervention studies in AD, a condition which will grow sharply in the next 20 years.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

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Alzheimer's disease & other dementias

Years:
2016

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