Early imaging markers for elderly individuals with high risk to develop Alzheimers disease

https://neurodegenerationresearch.eu/survey/early-imaging-markers-for-elderly-individuals-with-high-risk-to-develop-alzheimers-disease/

Principal Investigators

LU, HANZHANG

Institution

JOHNS HOPKINS UNIVERSITY

Contact information of lead PI
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USA

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Early imaging markers for elderly individuals with high risk to develop Alzheimers disease

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1

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Research Abstract

Project Summary/Abstract: Early diagnosis of Alzheimer’s disease (AD) is important, as therapeutic interventions such as amyloid immunization are thought to be most beneficial at this stage of the disease. Therefore, the emphasis in AD research is shifting toward understanding

the process by which high-risk elderly individuals begin to develop brain abnormality, at a time when they are still cognitively normal. Apolipoprotein E allele 4 (APOE4) is the largest known genetic risk factor for sporadic Alzheimer's disease. Carriers of APOE4 gene have between 10 and 30 times the risk of developing AD, as compared to those not carrying APOE4. Therefore, understanding neurobiological differences between APOE4 carriers and non-carriers will have a significant benefit in this high-risk population and will also help elucidate early AD mechanisms in general. Brain metabolism has been hypothesized as one of the earliest imaging markers of AD in the recent consensus model. To date, brain metabolism in AD is primarily measured with Fludeoxyglucose (FDG) PET. However, the presence of ionizing radiation and the lack of absolute quantification make the technique less frequently used in studies of cognitively normal subjects. Our laboratory has recently developed and validated a technique to measure the brain's oxygen extraction fraction and metabolism with MRI. The technique does not require any exogenous tracer, can be completed within five minutes on a standard 3T, has a high test-retest reproducibility, and has recently been evaluated in a multi-site setting. This project represents the first application of this novel technique in prodromal AD. The central hypothesis of this project that elderly individuals with high risk to develop AD, e.g. APOE4 carriers, will show abnormal brain metabolic features, at an early time when their cognition is still normal. We have a cost-effective, time-limited window of opportunity to test this hypothesis, by leveraging rich resources of the NIH-funded "Biomarkers for Older Controls at Risk for Dementia (BIOCARD)" study. The BIOCARD Study is a longitudinal, observational study of 278 elderly individuals. We have obtained approval from the BIOCARD study to include the brain metabolism sequences in the MRI protocol, and the preliminary studies have shown a potential effect of APOE4. Therefore, we are in a unique position to thoroughly examine the role of imaging markers in the onset of neurodegeneration in high-risk individuals. Our Specific Aims are 1) Examine the relationship between brain oxygen metabolic markers and APOE4 in cognitively normal elderly individuals; 2) Investigate whether the association between high AD risk and aberrant brain metabolism can be extended to other risk factors such as tauopathy and amyloid protein. Impact: The impact of this work is that we will establish an early biomarker to detect neurodegeneration in individuals with a high risk to develop Alzheimer's disease, at a time when they are still cognitively normal and when intervention may be most effective.

Further information available at:

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United States of America

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