Dissociating Intrinsic and Extrinsic Motor Learning in Alzheimers Disease

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USA

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Dissociating Intrinsic and Extrinsic Motor Learning in Alzheimers Disease

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5

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Alzheimer's disease & other dementias

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Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Neurodegenerative... Neurosciences... Physical Rehabilitation... Rehabilitation

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) currently impairs an estimated 5 million people in the United States and that number is likely to double in the next 20 years. The social and economic burdens of AD are strikingly high, especially when patients lose independence as the disease progresses. AD is widely considered to be a disease of declarative memory. However, as it progresses motor deficits severely impair activities of daily living and largely determine when patients will lose independence and require nursing home placement. However, the mechanisms for the motor dysfunction in AD are poorly understood and little studied. Traditional neuroanatomical models maintain that AD damages areas critical for declarative memory but largely spares areas responsible for motor learning. However, more recent work challenges the idea of a single motor learning system, suggesting that there are at least two distinct neural systems encoding motor skill, one of which relies on areas damaged in AD. These systems are based on distinct coordinate frames for the representation of the spatial sensorimotor information that underlies motor learning. One reference frame is intrinsic (referenced to the body) and the other extrinsic (referenced to the environment). We hypothesize that the pathological changes observed in AD lead to a specific impairment in processing extrinsically-represented sensorimotor information. We propose to develop two complementary motor learning paradigms that can differentially measure the intrinsic and extrinsic components of motor skill acquisition: visuomotor rotation learning and motor sequence learning. Pilot studies with both paradigms suggest that healthy controls show a pattern where skill is acquired in both intrinsic and extrinsic frames. In contrast, preliminary dta from AD participants suggest a specific but profound impairment of extrinsic learning. These paradigms will provide converging evidence about which aspects of skill acquisition are preserved in AD and which are impaired. We will also use stereotactically-guided brain stimulation to determine the neuroanatomical specificity of intrinsic versus extrinsic reference frames for motor learning and to identify candidate sites for therapy. With this knowledge, retained forms of motor learning can be leveraged to maintain function, and innovative strategies such as noninvasive brain stimulation can be tested to ameliorate deficient forms of motor learning so that patients can prolong independence.

Lay Summary

The primary goal of this proposal is to determine whether intrinsically-based and extrinsically-based motor learning are differentially affected in Alzheimer’s disease (AD). We plan on using specifically designed motor learning task to differentially measure these two forms of motor learning in AD patients compared to demographically matched controls as this may lead to the development mechanism-specific treatment for motor deficits in AD.

Further information available at:

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Investments > €500k

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United States of America

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