

Episodic memory protection in apolipoprotein E (APOE) knockout rats

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USA

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Episodic memory protection in apolipoprotein E (APOE) knockout rats

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Research Abstract

? DESCRIPTION (provided by applicant): The long-range goal is to understand how animals process and remember events in time and provide a neuroanatomically guided theoretical framework for understanding memory disorders. The objective of the present exploratory R21

application is to assess the memory impairing or enhancing effect of the apolipoprotein E gene (APOE) in an animal model of cognitive decline in aging. The central hypothesis is that APOE deletion protects memory. Our preliminary studies, which show that APOE deletion protects spatial working memory (while controlling for spatial perception, learning, motivation, motor control, and other non-specific factors), support this hypothesis. The PI will test the central hypothesis by accomplishing two specific aims: (1) To identify the impact of APOE deletion on episodic memory in young adult rats. We will test the working hypothesis that APOE deletion protects episodic memory in young adult rats. We will test young adult APOE +/+ and -/- rats using two models of episodic memory, namely what-where-when memory and source memory. Elements of episodic memory include memory for features of specific unique events, such as what happened, where it took place, and when in time the event occurred (i.e., what-where-when memory). Source memory is the aspect of episodic memory that encodes the origin (i.e., source) of information acquired in the past. (2) To identify the impact of APOE deletion on age-related decline in episodic memory in old rats. We will test the working hypothesis that APOE deletion protects against age-related cognitive decline in aged rats. We will test young adult and old APOE +/+ and -/- rats using what-where-when and source-memory preparations, in longitudinal and cross-sectional designs. Health relatedness of the project: Episodic memory is impaired in Alzheimer's disease and normal aging. APOE is the major genetic risk factor for Alzheimer's disease. APOE is unequivocally the most important susceptibility gene for Alzheimer's disease. Because the loss of episodic memory is the most debilitating cognitive impairment in Alzheimer's disease, development of preclinical models of episodic memory is critical for translational research. Improving memory is an important objective for therapies of Alzheimer's disease and age-related cognitive decline. Ultimately understanding and exploiting protective effects on the specific types of cognition that are impaired in Alzheimer's disease and normal aging may yield novel therapeutic approaches to Alzheimer's disease and age-related declines in cognition.

Further information available at:

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