Effect of Aging on Efficacy of Alzheimer-focused Therapeutic Strategies

https://neurodegenerationresearch.eu/survey/effect-of-aging-on-efficacy-of-alzheimer-focused-therapeutic-strategies/

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Country

USA

Title of project or programme

Effect of Aging on Efficacy of Alzheimer-focused Therapeutic Strategies

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 550,454.13

Start date of award

30/09/2016

Total duration of award in years

4

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Human Amyloid Precursor Protein, age effect, Levetiracetam, Alzheimer's Disease, network dysfunction

Research Abstract

Alzheimer’s disease (AD) is the most common neurodegenerative disorder, affecting over 5

million people in the U.S. No effective treatments are available to prevent, halt, or reverse the disease. Although aging is the most important nongenetic risk factor for AD, young mice have been used for the vast majority of preclinical studies in AD-related mouse models, mainly for practical and financial reasons. Even at young ages, these models share several pathological features with AD. However, they clearly do not simulate the full complexity of the human condition. We hypothesize that aged mouse models will simulate the human condition to a greater extent than young mouse models and that assessing candidate therapies in aged mouse models will better predict the efficacy of these therapies in later clinical trials. In this UH2/UH3 proposal, we will elucidate the phenotypic impact of natural aging in human amyloid precursor protein (hAPP) transgenic mice from line J20—one of the most extensively used AD-related mouse models. In addition, we will compare the efficacy of promising candidate therapies in young and old mice from this line. While strategies targeting amyloid-? (A?) have justifiably received considerable attention over the past decade, it is still unclear whether they will turn out to be both efficacious and safe in ongoing clinical trials. We reported in well-cited publications that treatment with the anti-epileptic drug levetiracetam and genetic reduction of tau ameliorate synaptic, network and cognitive dysfunction in hAPP-J20 mice, and these findings have been confirmed by other groups in independent mouse models. However, it remains to be determine whether these strategies also have beneficial effects in aging brains that have had longer exposures to pathologically elevated levels of A?. We therefore propose to investigate the efficacy of levetiracetam treatment and genetic reduction of tau in old hAPP-J20 mice.

Lay Summary

Aging is the best established nongenetic risk factor for Alzheimer’s disease (AD). Mouse models of AD simulate key features of the disease even at young ages, but the effect of aging on these models is unknown. The current proposal aims to determine how natural aging affects AD-related abnormalities and to compare the efficacy of promising candidate therapies at young and old ages in a widely used mouse model.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A