Brain-Gut Communication in Alzheimers Disease

https://www.neurodegenerationresearch.eu/survey/brain-gut-communication-in-alzheimers-disease/

Principal Investigators

COMBS, COLIN K

Institution

UNIVERSITY OF NORTH DAKOTA

Contact information of lead PI
Country

USA

Title of project or programme

Brain-Gut Communication in Alzheimers Disease

Source of funding information

NIH (NIA)

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15/08/2015

Total duration of award in years

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)... Biotechnology... Brain Disorders... Dementia... Digestive Diseases... Genetics... Immune System... Neurodegenerative... Neurosciences

Research Abstract

? DESCRIPTION (provided by applicant): Although amyloid precursor protein (APP) is ubiquitously expressed, much of the focus on APP biology with respect to Alzheimer's disease (AD) has focused on the brain due to high levels of neuronal expression. However, the enteric nervous system of the gastrointestinal tract also expresses APP. Moreover, the gastrointestinal tract is filled with a plethora of immune cell types that broadly affect not only the function of te gut but also other organ systems including the brain. Recognition of this comparison forces one to consider whether or not Aß aggregation/deposition with subsequent inflammation characteristic of the brain during AD occurs in parallel in the digestive tract. This suggests an opportunity for peripherally monitoring APP-related biology or therapeutic interventions as well as a novel understanding of the pathophysiology of AD. Even more exciting is the possibility that the two organ systems influence disease phenotype in one another based upon not only immune cell interactions but also the direct autonomic innervation of the gastrointestinal tract. Our preliminary data using a transgenic mouse model of AD demonstrated increased APP levels, Aß deposition and immune dysfunction in the intestines similar to findings from brains. Moreover, manipulation of the peripheral immune system with therapeutic antibodies was sufficient to attenuate brain microgliosis in these mice. Most importantly, we observed APP immunoreactivity, Aß plaques, and phospho-tau containing tangles in AD large intestines validating the relevance of the mouse model. In comparison to human diseased intestines, we will continue using the most relevant mouse models of AD to define the temporal relationship between brain and gastrointestinal disease identifying both neuronal and immune changes in correlation with both memory performance and gut function. We will also determine the specific role of APP and its metabolites in regulating both intestinal epithelial and immune cell phenotypes. Finally, by altering gut-brain communication we will determine whether it is possible to regulate disease progression in either organ by manipulating immune or nervous communication.

Lay Summary

PUBLIC HEALTH RELEVANCE: This study will define temporal changes in the gastrointestinal tract compared to the brain during the progression of Alzheimer's disease using for comparison to human, diseased intestine. This novel disease characterization focusing on the digestive system will identify not only a novel disease phenotype but also therapeutic targets outside of the brain. The possibility of targeting the peripheral changes to affect brain disease will be directly tested using mouse models of disease.

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

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