Plasma Amylin Impact on Cognitive Function and Brain Morphology in the Framingham Heart Study

https://www.neurodegenerationresearch.eu/survey/plasma-amylin-impact-on-cognitive-function-and-brain-morphology-in-the-framingham-heart-study-2/

Principal Investigators

QIU, WEI QIAO WENDY

Institution

BOSTON UNIVERSITY MEDICAL CAMPUS

Contact information of lead PI
Country

USA

Title of project or programme

Plasma Amylin Impact on Cognitive Function and Brain Morphology in the Framingham Heart Study

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,690,166.97

Start date of award

01/05/2015

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)... Behavioral and Social Science... Brain

Disorders... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Dementia... Endocrine System... Neurodegenerative... Neurosciences

Research Abstract

? DESCRIPTION (provided by applicant): Amylin is a gut-brain axis hormone, which readily crosses the blood brain barrier (BBB) and mediates activities including regulating glucose metabolism, relaxing cerebrovascular structure and modulating inflammation, all of which could be beneficial for Alzheimer's disease (AD). Recent studies have shown that mild cognitive impairment (amnestic MCI) and AD patients have a lower concentration of amylin in plasma than the elderly who had normal cognition. In cross-sectional analyses, higher concentrations of plasma amylin are related to better cognitive function, especially in memory and executive domains. Using AD mouse models, our recent study demonstrates that intraperitoneal injection (i.p) of amylin improves learning and memory as well as reduces indices of AD pathology in the brain. Although these studies suggest that exogenous administration of amylin type peptides may be beneficial for AD, amylin can also form amyloid in the pancreas of type 2 diabetes and in the cerebrovasculature of AD brain that may lead to worsened cognition. Thus, it is important and critical to study the longitudinal relationship between the baseline concentration of plasma amylin and cognitive decline during aging process. From the Framingham Heart Study Offspring and Omni Generation 1 cohorts, we propose using plasma samples collected from 1995- 1998 to relate to incident change in cognition and brain structure up to 15 years later. We posit that high levels of plasma amylin are protective for cognitive decline and brain atrophy in aging process. We have five specific aims including 1) studying the distribution of plasma amylin in FHS community based population; 2) determining the relationship between baseline plasma amylin and cognitive changes, including incident mild cognitive impairment and dementia; 3) examining the association between plasma amylin and changes in brain morphology; 4) stratifying these analyses by the presence of ApoE4 allele, diabetes and other vascular diseases and 5) studying the relationship between amylin, A?, lipids, other gut-brain axis peptides and inflammation in FHS. Pramlintide is an amylin analog and an FDA approved drug for diabetes with a favorable safety profile in clinical use. Should we find that high levels of plasma amylin are protective for the incidence of AD, our study will provide additional rationale for a large phase 2 or 3 trial with pramlintide to determine if amylin type peptides can prevent and treat AD. We anticipate that this study may help open a new and unconventional avenue for the therapeutic of AD.

Lay Summary

PUBLIC HEALTH RELEVANCE: The significance of the proposed study is to provide evidence in support of an alternative and innovative drug target to treat Alzheimer's disease (AD). Results from the study will be important for two reasons. First, the proposed study will use existing plasma samples and data on cognition and brain imaging from Framingham Heart Study (FHS) to test the concept that a high level of plasma amylin will be a protective factor for cognitive decline and brain aging. Positive findings will provide a rationale for opening a new therapeutic avenue for AD with amylin type peptides. Second, pramlintide is an amylin analog and an FDA approved diabetic drug with a favorable safety profile. Should this study show plasma amylin's protective effect on cognitive decline and the development of AD, it will serve as evidence for a large clinical trial of pramlintide. Repurposing of pramlintide for AD treatment will involve shortr trial time at a substantially lower cost than developing a new drug. Finally, this study can provid ""go or no go"" information regarding an amylin pathway as a target for the therapeutics of AD.

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