Brain aging and treatment response in geriatric depression

https://www.neurodegenerationresearch.eu/survey/brain-aging-and-treatment-response-in-geriatric-depression/

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Country

USA

Title of project or programme

Brain aging and treatment response in geriatric depression

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,189,803.67

Start date of award

16/04/2013

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Escitalopram, geriatric depression, Memantine, aging brain, mild cognitive impairment

Research Abstract

DESCRIPTION (provided by applicant): Fewer than 50% of elderly depressed patients achieve remission and functional recovery in response to first-line antidepressant pharmacotherapy. The majority of patients are left with significant residual symptoms, putting them at risk of chronic,

relapsing illness, frailty, and suicide. Brain aging may be responsible fo poor treatment response. Our pilot data indicate that neurodegenerative changes with increased amyloid and tau protein binding, as well as microvascular brain changes frequently occur in older depressed individuals, as documented by using novel neuroimaging techniques (i.e., MRI and [F-18] FDDNP PET). Improved understanding of the neurobiology of brain aging in relation to treatment response can lead to the improved personalized treatment of depressed elderly with biomarkers of brain aging or with mild cognitive impairment (MCI). Cognitive impairment, especially, in the domains of memory and executive functions, persists even after amelioration of depressive symptoms in older adults, and these symptoms are poorly responsive to serotonergic treatment alone. There is a compelling rationale for the study of neuroprotective glutamatergic agents, such as memantine (MEM) that can target brain aging and provide cognitive enhancement. This is also supported by our pilot data that documented enhanced antidepressant response and improvement in executive cognitive function and memory tests to a combination of escitalopram and MEM. We hypothesize that the addition of memantine to the serotonergic drug, escitalopram, may result in better mood and cognitive outcomes of late life depression that will create a more personalized treatment strategy for a subgroup of older depressed individuals with neurodegenerative and microvascular brain changes or MCI. The current application will evaluate the predictors and moderators of treatment response to the combination of escitalopram and memantine compared to escitalopram and placebo in the 6 month randomized double- blind placebo controlled trial. We will determine whether brain structural changes, including 1. Volume and localization of white matter hyperintensities (WMH); 2.Regional gray and white matter volumes; 3. Hippocampal thickness; and 4.[F-18]FDDNP-PET total and regional binding are predictive of treatment response. We will also examine the role of amnestic mild cognitive impairment (MCI) and age of depression onset in predicting treatment response. We will recruit 134 elderly non-demented subjects with major depression. Participants will be randomly assigned to two treatment groups: one group will receive combination of escitalopram and memantine, the second group will receive escitalopram and placebo. All subjects will undergo MRI and PET at baseline and comprehensive medical, neuropsychiatric, and cognitive assessments at baseline and over the course of the study, including 12 months follow up to detect depression relapse. Our study will provide unique information on the use of memantine in geriatric depression, and will investigate the underlying mechanism of treatment response, and subgroups with preferential treatment to memantine.

Lay Summary

PUBLIC HEALTH RELEVANCE: The proposed project will evaluate the role of neuroimaging biomarkers of brain aging (i.e., neurodegenerative and vascular brain changes) and mild cognitive impairment in the patterns of treatment response to memantine combined with escitalopram compared to escitalopram and placebo. Memantine is likely to accelerate and enhance antidepressant response, to escitalopram and improve cognitive performance. Subjects with amnestic mild cognitive impairment or biomarkers of brain aging at baseline are likely to have preferential response to the combination of memantine and escitalopram compared to escitalopram and placebo, thus identifying a more personalized treatment approach in the high-risk subgroups for poor clinical outcomes.

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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