1/2 Phenotype Predictors of Cognitive Outcomes in Geriatric Depression

https://neurodegenerationresearch.eu/survey/1-2-phenotype-predictors-of-cognitive-outcomes-in-geriatric-depression/

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Country

USA

Title of project or programme

1/2 Phenotype Predictors of Cognitive Outcomes in Geriatric Depression

Source of funding information

NIH (NIA)

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13/09/2016

Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

geriatric depression, appetite loss, Alzheimer's Disease, Cognitive, Cognition

Research Abstract
Among older adults, major depressive disorder with cognitive impairment (CI) is associated with increased disability, higher healthcare utilization, and increased risk of dementia. From a clinical

standpoint, gaining knowledge about proximate (i.e., within 5 years) predictors of adverse cognitive outcomes among currently depressed older adults is crucial to timely and targeted intervention for at-risk individuals. From a scientific standpoint, identifying phenotypes and genotypes associated with cognitive diagnostic outcomes—both positive and negative—will advance research on mechanisms, prevention, and treatment. The NIMH- supported Neurocognitive Outcomes of Depression in the Elderly (NCODE) Study at Duke University and Neurobiology of Late-life Depression (NBOLD) Study at the University of Connecticut (UConn) are among the few prospective studies that include both longitudinal cognitive diagnostic outcomes and a formal clinical diagnosis of major depression in late life (LLD). In addition, these studies share common features related to clinical and cognitive assessment, neuroimaging, and genetic analysis. Consistent with PAR-14-165, the objective of the proposed clinical collaboration is to complete a two-site prospective study of cognitive diagnostic outcomes of LLD that will capitalize on the power of the combined data to: 1) identify clinical and biological phenotypes that predict cognitive diagnostic outcomes, and 2) understand the neural and genetic mechanisms associated with them. We seek support to extend current 2-year study enrollments to a 5-year clinical follow-up period in order to increase sample sizes to identify clinical, neuroimaging and genetic predictors of three key diagnoses our data find in 90% of cognitive diagnostic outcomes over a 5-year period: 1) normal cognition (CN), 2) persistent cognitive impairment without dementia (PCI), and 3) Alzheimer's disease (AD). Our central hypothesis is that the 5-year likelihood of each cognitive diagnostic outcome is associated with distinct clinical, cognitive, and neural phenotypes during acute LLD, which in turn have distinct genotypic correlates. Specifically, CN individuals will have earlier first onset of depression relative to AD, report greater negative life stress compared to AD and PCI, and have greater white matter integrity; additionally, CN will be associated with the AA genotype of COMTval158met, which may confer both neuroprotection and higher sensitivity to stress. PCI will be associated with earlier age of depression onset relative to AD, greater frailty, and lesser white matter integrity than NC. AD will be associated with later age of depression onset, appetite/weight loss, lower anxiety, smaller hippocampal volume, and memory impairment. We propose to test all of these putative associations in our Specific Aims. The proposed research will identify and integrate biological and behavioral markers associated with proximate cognitive diagnostic outcomes in LLD (NIMH Strategic Objective 1), and has the potential to yield tools that better define and identify risk and protective factors for adverse outcomes of depression through the course of later life (NIMH Strategic Objective 2).

Lay Summary

The public health relevance of this project is that late-life depression and cognitive impairment are significant contributors to disability burden among older adults, and there is limited research to project which individuals presenting with depression in late life will develop persistent cognitive impairment or dementia, particularly within 5 years. This research is significant because it is a key step toward understanding phenotypic and genotypic factors that confer risk or protection against persistent cognitive impairment and dementia in older adults with major depression. The project is relevant to the mission of NIMH because it seeks to identify biomarkers with predictive value for diagnosis, prevention, and treatment of depression and its associated illness burden.

Further information available at:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

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