Stress Mental Disorders Accelerated Aging and Dementia a 35 year Cohort Study

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Country

USA

Title of project or programme

Stress Mental Disorders Accelerated Aging and Dementia a 35 year Cohort Study

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NIH (NIA)

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€ 3,371,286.24

Start date of award

01/09/2016

Total duration of award in years

1

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)... Anxiety Disorders... Basic Behavioral and Social Science... Behavioral and Social Science... Brain Disorders... Burden of Illness... Clinical Research... Clinical Research - Extramural... Dementia... Depression... Epidemiology And Longitudinal Studies... Genetics... Human Genome... Mental Health... Mental Illness...

Minority Health for IC Use... Neurodegenerative... Neurosciences... Prevention... Rehabilitation... Sleep Research

Research Abstract
? DESCRIPTION (provided by applicant): Numerous studies demonstrate links between depressive symptoms or disorders and poor cognitive and functional outcomes. Anxiety symptoms and disorders, poor sleep, and stressful life events are common and correlated with depression, but little is known about their association with cognitive and functional decline, such as occurs in Alzheimer's disease (AD). These stress-related exposures are also associated with medical morbidity and disability, but the mechanisms linking them to poor health outcomes are unclear. Cross-sectional studies suggest that these exposures might lead to these outcomes by hastening cellular aging, measured by shortening of telomeres. Prospective studies in cohorts with well-characterized histories of stress-related exposures and repeated measures of cellular aging are needed to investigate this possibility. We propose to analyze these issues using data already collected in the Baltimore Epidemiologic Catchment Area (ECA) Followup Study cohort, adding another wave of data collection. The Baltimore ECA Study began collecting structured diagnostic interview data on depressive and anxiety disorders in 1981 in a representative sample of East Baltimore residents, and did so over three additional waves, most recently in 2004 (Wave 4). In addition to measures of anxiety and depressive symptoms and disorders, the diverse (35% African American) ECA cohort has completed repeated measures of poor sleep, life stressors, trauma exposure, cognition, and functional impairment. In 2004, when all participants were aged ?40 years, they donated blood and buccal samples. All ECA subjects are now aged ?50 (estimated mean = 68, range 52-96). We will locate and interview an estimated 601 participants from Wave 4, repeating structured diagnostic interview assessment of mental disorders, and measuring life stressors, trauma exposure, and poor sleep by both self-report and wrist actigraphy. Participants will complete neuropsychological tests and functional measures, and will again donate blood and buccal samples. This will enable us to determine the association of 35-year histories of stress- related exposures, from mid to later life, with cognitie and functional decline, adjudicated mild cognitive impairment and dementia diagnoses, including probable and possible AD, and biomarkers of cellular aging: shortening of telomeres and increases in p16ink4a levels from 2004 to 2016. We will also determine if these exposures are associated with epigenetic modification of genes in the ECA that we select based on novel genome-wide association and methylation analyses we will conduct in existing data from the Baltimore Longitudinal Study of Aging (BLSA) and the InCHIANTI cohorts. We will examine whether methylation of these candidate sites, and measures of inflammation (measured in blood in 2004 and 2016) in the ECA, mediate hypothesized predictive associations in the ECA cohort. Results will clarify the link between stress-related exposures from mid to later life and aging-related outcomes, advance knowledge of mechanisms linking these exposures to disease and disability, and provide clues to avenues for preventing these outcomes.

Lay Summary
PUBLIC HEALTH RELEVANCE: Depression and anxiety disorders, poor sleep, and stressful life events are prevalent and may increase the risk for poor cognitive and functional outcomes and medical illness in older adults; however, methodological limitations of prior studies hinder our understanding of these associations and the mechanisms linking these stress-related exposures to poor health outcomes. We propose to leverage existing data from the Baltimore Epidemiologic Catchment Area Study and to collect new data in this cohort to study the association of 35-year histories of stress-related exposures (from mid to later life) with cognitiv

and functional decline, including diagnosis of probable or possible Alzheimer’s disease (AD), and biomarkers of cellular aging. We will also investigate inflammation and epigenetic modification as mediators, and AD risk genes as moderators of these associations, advancing understanding of stress-related exposures as potentially modifiable risk factors for poor aging-related health 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

Database Tags:
N/A