# Genes, Exercise, Neurocognitive and Neurodegeneration: Community-Based Approach

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**Country**

USA

**Title of project or programme**

Genes, Exercise, Neurocognitive and Neurodegeneration: Community-Based Approach

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NIH (NIA)

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3

**The project/programme is most relevant to:**

Alzheimer's disease & other dementias

**Keywords**

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Behavioral and Social Science... Brain Disorders... Cardiovascular...

Cerebrovascular... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Health Disparities for IC Use... Heart Disease... Mind and Body... Minority Health for IC Use... Neurodegenerative... Neurosciences... Physical Activity... Prevention... Translational Research... Vascular Cognitive Impairment/Dementia

**Research Abstract**

DESCRIPTION (provided by applicant): Although anticholinesterase therapies have greatly improved the symptomatic treatment of Alzheimer's disease (AD), they have not been demonstrated to significantly slow the disease progression; and amyloid- directed therapies have produced disappointing results. A promising evidence-based and relatively side-effect free lifestyle approach is emerging as an alternative or adjunct to drug therapy. In cross-section and prospective studies, and a few randomized controlled trials; aerobic exercise-training has been demonstrated to improve cognition in older subjects. However, the mechanisms of these effects remain poorly understood. Because it is now recognized that cardiovascular disease (CVD) risks can catalyze AD development, it is vital to test whether lifestyle adaptation shown to reduce CVD risks can favorably modify cognitive trajectories and markers of neurodegeneration. Such interventions may benefit those at an early and clinically discernible prodromal stage of AD such as mild cognitive impairment (MCI). Notably, such data are currently lacking in African Americans (AA)s who harbor higher rate of CVD risks and AD. For ~10 years, the Principal Investigator has conducted studies on the effects of fitness adaptation on cardiovascular (CV) health. Recently, he received 2 years of funding to examine the effects of 3-times/week 6-month aerobic exercise-training on cognition in the laboratory setting. This ongoing study has allowed the Principal Investigator to demonstrate the ability to recruit, enroll, test, collect and manage related neuroimaging pilot data in a predominantly AA sample. While such a laboratory approach to exercise intervention study is required to prove causation, such a design may not lend itself to real-life application, and is demanding for many economically and educationally disadvantaged older AAs experiencing early symptoms of cognitive deterioration. To logically extend this ongoing work, he seeks to initiate an 18-month study, testing real-life applicability o the effects of exercise adaptation on memory in a more ideal community setting. Collection of outcome measures at baseline, 3- month, 6-month, 9-month, 12-month and 18-month will provide pilot data to inform dose and duration effects of exercise on outcome measures. In addition to augmenting enrollments, the proposed approach will bolster retention. The objectives of this pilot study, therefore, are to examine the feasibility of a community-based 18-month study (6-month active intervention and 12-month passive follow-up) aerobic exercise-training on neurodegeneration in AAs MCI subjects. We will test our hypotheses by randomizing subjects into one of 2 groups: 1.) aerobic-exercise; and 2.) stretch-exercise (control). We proposed that the aerobic-exercise group will perform better than control group on cognitive measures. Secondarily, we will determine whether training- induced changes in cognition relate to increases in brain volume. Explanatorily, we will also investigate intervention effects on cerebrospinal fluid (CSF) biomarkers, selected CVD risk factors and biomarkers, cerebral oxygenation and Hypoxia-Inducible Factors (HIF-1?) gene expression, and Apolipoprotein E gene (APOE), to assess their mediation of training-induced changes in cognition. A team of experienced investigators in neuroimaging, neurology, cognitive neuroscience, and exercise physiology has been assembled to conduct this study. Working collaboratively with the District of Columbia Office on Aging (DCOA), the Directors of the Ward 6 Senior Wellness Center operated by DCOA, and the lead agencies on aging (community grassroots organizations supported by DCOA), we will recruit, enroll, randomize, and train participants at the wellness

center. After obtaining informed consent and completing an initial assessment, participants will undergo initial exercise screening to determine their ability to exercise safely. Following randomization of 80 volunteers into aerobic-exercise (40) and control (40); baseline neuropsychological, neuroimaging and biomarker measurements will be obtained. Both groups will undergo 3 times/week supervised group-specific intervention at the wellness center for 6 months. After the initial 6 months of active intervention, the aerobic-exercise group will follow a prescribed but free living 40 minutes, 3 time/week exercise regimen, while the control group returns to usual care. Baseline tests will be repeated at 3 month, after 6 months (active intervention period); and at 9, 12 and 18 months (passive follow-up period). Treadmill, lumber puncture (LP) and brain magnetic resonance imaging (MRI) tests will occur only at baseline and 6 months. Between groups changes in cognitive performance, biomarkers, and neuroimaging measurements will be compared using appropriate multivariate methods. While we remain cognizant of other planned or ongoing fitness and memory trial, the proposed study is unique in the sense that: it is a logical extension of our ongoing work; tests the proposed hypotheses in predominantly AA sample in whom paucity of data remains, and therefore, will advance reduction in health disparity; will obtain data at multiple time-points (baseline, 3, 6, 9, 12 and 8 months) and therefore allow for the assessments of the effects of duration and dose of intervention on outcome measures; test the real-life applicability of the proposed intervention in a community setting; and generate pilot data on the mechanisms by which these interventions affects memory. Importantly, outcomes from this study may lead to practical and effective strategy to delay cognitive decline in populations at most risk, and can prevent or attenuate the physical, psychological and the economic burden associated with dementia in AAs.

**Lay Summary**
PUBLIC HEALTH RELEVANCE: Alzheimer’s disease is the most common type of dementia constituting ~2/3 of all late-life cases. Based on 2011 estimates, the annual health care cost for dementia is ~$183 billion. Given this staggering cost, and the projected increase in elderly population by the year 2030, identifying effective mechanisms to ward off structural and functional declines associated with AD is an important public health goal as evidenced by recent presidential initiatives (reduce the morbidity and costs associated with, and maintain or enhance the quality of life for, persons with dementia, including Alzheimer’s disease). Unfortunately, this well-intended public health goal cannot be achieved without an effective dementia preventive strategy. Fortunately, lifestyle-induced preservation of intellectual dexterity among those showing earliest symptoms of cognitive deterioration may ameliorate the physical, emotional, and economic burden associated with loss of cognitive vitality. If proven and properly directed in African Americans, such intervention can further reduce health disparity.

**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:**
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