Exercise and Intensive Vascular Risk Reduction in Preventing Dementia

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Country

USA

Title of project or programme

Exercise and Intensive Vascular Risk Reduction in Preventing Dementia

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 13,140,022.94

Start date of award

15/01/2016

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)... Behavioral and Social Science... Brain Disorders... Cardiovascular... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Neurodegenerative... Neurosciences... Physical Activity... Prevention... Translational Research

Research Abstract
? DESCRIPTION (provided by applicant): We are facing one of the most significant challenges of the 21st century; how to maintain brain health and prevent dementia in our rapidly aging population. Alzheimer’s disease (AD) is the most common type of dementia. Currently, there is no treatment to prevent or cure AD. Mounting evidence indicates that late-onset AD is an age-related, multi-factorial disease(s), which has a complex genetic background and the onset and progression of AD are influenced to a large extent by modifiable factors such as cardiovascular risk factors and physical inactivity. However, at present, there is no direct evidence that reducing these modifiable risk factors prevents or slows AD. The overarching goal of this proposal is to conduct a rigorously designed randomized controlled phase II trial to determine the independent and combined effects of Intensive pharmacological Reduction of Vascular Risk factors (IRVR, blood pressure and lipids) and Exercise (Ex) on neurocognitive function in older adults at high risk of AD (primary outcome). Furthermore, we will determine the effects of these interventions on the neuroimaging, blood, and CSF biomarkers of AD (secondary outcomes). We will enroll 640 cognitively normal older adults age 65 to 79 with a family history (FH) of AD who have hypertension (SBP?140 mmHg) and dyslipidemia (according to the new 2013 ACC/AHA guidelines). They will be randomized into 2-yr interventions of IRVR (SBP?130mmHg, lowering lipids with atorvastatin), Ex, IRVR+Ex, and a control arm of standard care (a 2 x 2 factorial design). Aim 1: Determine the independent and combined effects of IRVR and Ex on neurocognitive function. Hypothesis: IRVR and Ex will improve global cognitive function, while IRVR+Ex will provide a greater benefit than either IRVR or Ex alone. Neurocognitive function will be measured using well-validated tests at baseline, 6, 12, 18, and 24 months to optimize study power using linear mixed effects models for analysis. Aim 2: Determine the independent and combined effects of IRVR and Ex on brain structural and neural network plasticity. Hypothesis: IRVR and Ex prevent or slow hippocampal and whole brain atrophy and improve brain default-mode network (DMN) functional connectivity, while IRVR+Ex will provide greater benefits than either IRVR or Ex alone. Changes in brain volume, structural and DMN functional connectivity will be measured using MRI at baseline, 12 and 24 months. Aim 3: Explore the underlying mechanisms by which IRVR, Ex and IRVR+Ex impact brain structure and function. Hypotheses: 1) IRVR and Ex reduce AD pathology as indicated by the changes in cerebrospinal fluid (CSF) A?42, tau and phosphorylated tau (p-tau), and CNS inflammation; 2) increases in brain perfusion and/or brain-derived neurotrophic factor (BDNF) mediate changes in brain structure and function; 3) IRVR+Ex will have greater impacts on improving AD biomarkers than either IRVR or Ex alone. Novel transcranial Doppler ultrasonography (TCD) methods will be used to assess cerebral autoregulation.

Lay Summary
PUBLIC HEALTH RELEVANCE: The multi-factorial nature of Alzheimer’s disease (AD) and the potential role of cardiovascular risk factors in AD onset and progression provide an opportunity for prevention and treatment. This project will determine whether a safe and pragmatic intervention of intensive pharmacological reduction of vascular risk factors (hypertension and

dyslipidemia), alone or combined with exercise, prevents or slows cognitive decline in older adults at high risk 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