

Hypertension angiotensin receptor blockers and cognition: effects and mechanism

<https://neurodegenerationresearch.eu/survey/hypertension-angiotensin-receptor-blockers-and-cognition-effects-and-mechanism/>

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Country

USA

Title of project or programme

Hypertension angiotensin receptor blockers and cognition: effects and mechanism

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,794,902.75

Start date of award

15/08/2013

Total duration of award in years

5

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)... Basic Behavioral and Social Science... Behavioral and Social Science... Brain Disorders... Cardiovascular... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Clinical Trials and Supportive Activities... Dementia... Diagnostic Radiology... Hypertension... Neurodegenerative... Neurosciences...

Research Abstract

DESCRIPTION (provided by applicant): Hypertension is associated with cognitive impairment even in the absence of dementia. These vascular-related mild cognitive impairments are undetected and are commonly characterized by executive dysfunction. To date, no specific treatment is available for executive mild cognitive impairment which is associated with poor outcomes in hypertension. The PI has recently completed, with support from a K23 award, a preparatory pilot study (n=47) to test the feasibility, safety and effect size of candesartan, an angiotensin receptor blocker, compared to hydrochlorothiazide and lisinopril, in individuals with hypertension and mild cognitive impairment characterized by executive dysfunction. Our preliminary analysis which was recently accepted for publication in the Archives of Internal Medicine, suggests that, independent of blood pressure, candesartan is superior to other antihypertensives in preserving executive function. Candesartan was also associated with an increase in cerebral blood flow velocity that only reached significance in those with low flow velocity at baseline (n=23). We hypothesized based on these data to further test the effect of angiotensin receptor blockers on cognitive function by conducting a 1-year double blind randomized active-control trial of candesartan vs. lisinopril in 160 individuals with hypertension and evidence of mild cognitive impairment in the executive domain. The specific aims of this proposal are to investigate the effects of candesartan on executive function decline and on change in cerebral perfusion, cerebrovascular reserve and microvascular brain injury. We also aim at identifying potential underlying mechanisms related to vascular structure and function by which candesartan may affect the cognitive and cerebrovascular outcomes. Participants will be recruited from the greater Los Angeles Area and evaluated at the University of Southern California. Cognitive tests that assess executive function and other cognitive domains will be administered at baseline and 12 months after treatment. Neuroimaging which includes perfusion (continuous arterial spin labeling) and micro-structure (diffusion tensor imaging), carotid ultrasound (carotid intima-media thickness), and endothelial and vascular inflammatory markers will be performed at baseline and after 12 months of treatment. This trial will shed more light onto the potential therapeutic effects of angiotensin receptor blockers on executive dysfunction and related vascular brain injury. This project will also improve our understanding of the possible mechanisms of action of this class of antihypertensives.

Lay Summary

Hypertension is associated with a pattern of cognitive decline characterized by executive dysfunction. Although great advances have been made in treating hypertension, cognitive decline is on the rise. This study investigates the effect and mechanism of action of an angiotensin receptor blocker compared to an angiotensin converting enzyme inhibitor (an antihypertensive medication) on executive function and related cognitive domains. The effects of this medication will also be assessed based on cerebral circulatory function and structure.

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