Blood pressure, cardiac biomarkers and cognitive function in old age

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Chapter 1

General introduction

Introduction

With the increase in life expectancy, the prevalence of cognitive disorders is expected to further rise the coming years.(1) The number of people suffering from dementia worldwide is estimated to almost double every 20 years, with prevalence numbers of 65.7 million in 2030 and 115.4 million in 2050.(1) Accumulating evidence of the last years highlights the role of cardiovascular risk factors in the pathogenesis of cognitive disorders.(2-4) Epidemiological, pathological and neuroimaging studies show that cardiovascular risk factors in middle age associate with an increased risk of brain aging and cognitive impairment in later life.(5, 6) In older people, however, the contribution of cardiovascular risk factors in the development of cognitive impairment is still a matter of debate.(7) Furthermore, although a variety of mechanisms have been proposed to explain the association of cardiovascular risk factors with cognitive disorders, the underlying pathways have not been fully understood.

An example of a cardiovascular risk factor in middle age that is associated with cognitive impairment in later life, is high blood pressure.(8) Numerous studies demonstrate that midlife high blood pressure is a risk factor for cardiovascular events, brain atrophy, and cognitive decline.(9-12) In addition, some randomized controlled trials show favorable effects of midlife antihypertensive treatment on risk of cognitive impairment.(13, 14) However, recent evidence shows that this association attenuates with increasing age and it has even been reported that in older age, low instead of high blood pressure relates with increased risk of cognitive disorders and cardiovascular events.(6, 15-17) In particular people who are biologically older seem to suffer from low blood pressure values.(18-20)

Besides blood pressure, cardiac disease is associated with increased risk of cognitive disorders and dementia. Patients with coronary artery disease, atrial fibrillation, and chronic heart failure have worse cognitive function and a higher risk of progression to dementia. (3, 21-23) A possible explanation behind this association is reduced cardiac output, leading to cerebral hypoperfusion and subsequently to impairment of delivery of oxygen and nutrients to the brain.(3) Concordantly, it has been shown that in patients with severe systolic heart failure, cognitive function significantly improved after a cardiac transplantation, or after implantation of a left ventricular assist device.(24, 25) However, whether people with early signs of cardiac disease are also at increased risk of cognitive impairment, has poorly been studied.

The aims of this thesis are 1) to further investigate whether blood pressure in older people is a risk factor for cardiovascular events and cognitive impairment; 2) to study whether early markers of cardiac disease are related with cognitive impairment; and 3) to evaluate the feasibility of home blood pressure monitoring using smartphone-assisted technology, which might eventually assist to prevent cognitive impairment.

Outline of this thesis

This thesis is divided in three parts. The first part consists three studies evaluating the association of blood pressure and blood pressure variability with cardiovascular events and cognitive function in older age, respectively. **Chapter 2** evaluates whether the association between (diastolic) blood pressure and cardiovascular events differs in people with and without a history of cardiovascular disease. Besides average blood pressure, visit-to-visit blood pressure variability has been associated with cardiovascular events and cognitive impairment. In **chapter 3**, we therefore study the association of visit-to-visit blood pressure variability with cognitive function. Furthermore, we investigate potential explanations behind this association in a magnetic resonance substudy. **Chapter 4** further elaborates on this topic by studying how blood pressure lowering medication is related to both visit-to-visit blood pressure variability and cognitive function; and whether blood pressure lowering medication could explain the relation between visit-to-visit blood pressure variability and cognitive impairment.

The second part of this thesis consists of two studies addressing the association between early markers of cardiac disease and cognitive function. In **chapter 5**, we evaluate the relation of N-terminal pro-brain natriuretic peptide (NT-proBNP), a neurohormone that is commonly used in the diagnosis of clinical heart failure, with cognitive function and decline. Furthermore, **chapter 6** investigates whether cardiac troponin T (cTnT), routinely used in the diagnosis of acute myocardial infarction, associates with cognitive function.

Part three includes the translation of results of previous studies into an innovative method, focused on the prevention of cognitive impairment. The online research platform iVitality, that comprises a website, a smartphone-based application and health sensors, was designed to perform large-scale studies in an aging population at risk for cognitive impairment. **Chapter 7** describes the first results of a proof-of-principle study, in which we evaluated the feasibility of home blood pressure monitoring using iVitality.

In **chapter 8** the main conclusions of this thesis are summarized and discussed, and future perspectives are proposed.

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