Keeping the heart in mind: Cardiovascular determinants of neurocognitive functioning in old age

Bertens, A.S.

Chapter 8

Summary

Aim

The aim of this thesis was to investigate cardiovascular determinants of neurocognitive functioning in old age, in particular cognitive dysfunction, depressive symptoms, and apathy. First, we investigated whether the Geriatric Depression Scale (GDS)-3A, comprising the three apathy items of the GDS-15, can be used to measure symptoms of apathy in research settings. We further explored the role of cardiac function by investigating the relation between high sensitivity troponin T (hs-cTnT), a cardiac biomarker, and neurocognitive functioning in the Leiden 85-Plus Study. Next, by using data from the DANTE Study Leiden and the AGES-Reykjavik Study, we investigated how blood pressure was related to symptoms of apathy, depressive symptoms, and cognitive dysfunction. We tested the hypothesis that particularly in older persons with impaired capability to maintain optimal cerebral blood flow, such as individuals with poor functional ability and with a higher burden of cerebral small vessel disease (CSVD), lower rather than higher blood pressure would be related to worse neurocognitive functioning.

The validity of the GDS-3A to measure apathy in research settings

In **chapter 2,** we investigated the scale properties of the GDS-3A, a sub-set of the three 'apathy' questions of the frequently administered GDS-15, as compared to the Apathy Scale in both the DANTE Study Leiden and the PROMODE Study. In both studies, the GDS-3A only moderately discriminated between presence and absence of apathy; the sensitivity for apathy according to a cut-off of 2 or higher was low (29-33%), while specificity was high (89-93%). These findings suggest that, while not a useful instrument to screen for apathy in clinical practice, the GDS-3A can be used in research to study associations with risk factors. In case of non-differential misclassification, using the GDS-3A will yield estimates that are biased towards the null.

High sensitivity cardiac troponin T and neurocognitive functioning

In **chapter 3,** we studied the longitudinal association between the cardiac biomarker hs-cTnT and neurocognitive functioning in the oldest old, using data from the Leiden 85-Plus Study. During four years of follow-up, those older persons with the highest levels of hs-cTnT had a steeper annual decline in Mini Mental State Examination (MMSE) score. We demonstrated that this association is independent of sociodemographic

and cardiovascular risk factors. Moreover, the relation between higher levels of hs-cTnT and worse cognitive function was also found in those participants without a history of clinically overt cardiac disease, suggesting that hs-c-TnT may be a marker of microvascular coronary artery disease or global microvascular disease underlying processes of cognitive decline in older people. Levels of hs-cTnT were not related to more symptoms of apathy and inconsistently with symptoms of depression. Thus, hs-cTnT may be a more specific marker for cognitive dysfunction than for apathy and depression.

Blood pressure and neurocognitive functioning

In **chapter 4,** we used data from the DANTE Study Leiden to investigate the relation between blood pressure and symptoms of apathy measured with the Apathy Scale, and depressive symptoms measured with the GDS-15. We demonstrated that lower systolic and diastolic blood pressure were related to more symptoms of apathy in older persons with lower functional ability, while blood pressure measures were not related to apathy in older persons with higher functional ability. Blood pressure measures were not related to depressive symptoms in either stratum.
In **chapter 5** we used data from the DANTE Study Leiden MRI Sub Study to demonstrate that the association between a lower systolic and diastolic blood pressure and symptoms of apathy was present in those with a higher burden of CSVD, but not in those with a lower burden of CSVD. Blood pressure was not associated with depressive symptoms in the entire population, nor in either of the subgroups.
In **chapter 6**, we demonstrated that in the population-based AGES-Reykjavik Study, a lower systolic blood pressure was associated with more symptoms of depression measured with the GDS-12D. No clear association between blood pressure and cognitive measures was found. Blood pressure was not related to apathy as measured with the GDS-3A in the entire study sample. When we stratified for the presence of CSVD, lower blood pressure was related to symptoms of apathy only in those participants with a higher burden of CSVD. The associations between blood pressure on the one hand and depressive symptoms and cognitive function on the other hand, were not influenced by the burden of CSVD. Results from this study further add to the notion that cognitive dysfunction, symptoms of depression, and symptoms of apathy in older age may have different risk factor profiles.
In **chapter 7**, the main findings of this thesis are discussed. Our findings are placed in the light of the literature and we discuss methodological strengths and limitations. We propose hypotheses that might explain our findings and make recommendations for clinical practice and future studies.

In conclusion, we found that cardiovascular risk factors are important for neurocognitive functioning in older persons. Moreover, we found that specific cardiovascular determinants, such as blood pressure and hs-cTnT, have different associations with apathy than with depression and cognitive function.