Hypertension, Arterial Health and Neuronal Integrity in Midlife

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Introduction

Increased carotid artery intima-media thickness (IMT) is a noninvasive marker of systemic arterial disease (1) as it has been associated with atherosclerosis, abnormal arterial mechanics, myocardial infarction and stroke. In addition, elevated IMT is related to diminished cognitive function in the elderly (2,3). Given evidence of the importance of arterial health for cognitive function even in non-demented older adults, the purpose of this study was to search for early markers of cognitive vulnerability by examining IMT in relation to neuronal integrity as measured by cerebral N-acetyl-aspartate (NAA) concentrations in midlife.

Participants and Methods

A total of 42 middle-aged adults (17 men, 25 women; 50±6 yrs) were studied. Participants were at variable risk for cardiovascular disease based on current hypertension (35%), family history of hypertension (29%), concurrent hypertension and type II diabetes (7%), obesity and hypertension (16%), or concurrent obesity, hypertension and diabetes (0.2%). ^{1}H MRS data were collected on a 3T GE Signa Excite MRI system (PROBE-P: TE/TR = 35/3000 ms, 128 excitations, 5000 Hz spectral width, volume ~6 cm^3) from the posterior cingulate gyrus. The region of interest was selected based on evidence that changes in posterior cingulate function may be an early indication of cognitive vulnerability in healthy young individuals at risk for hypertension (4). LCModel was used to quantify and separate the metabolite resonances from the macromolecule background (5).

Metabolite concentrations were calculated using creatine (Cr) as an internal reference. Participants also underwent a neuropsychological evaluation and high-resolution B-mode carotid ultrasound scanning (Philips iE33, Bothel, WA). IMT was calculated using scans of the far wall of the left common carotid artery and was defined as the distance between the luminal-endothelial interface and the junction between the media and the adventitia.
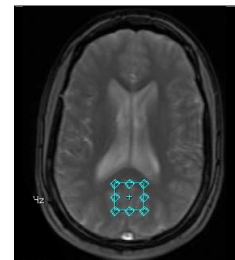
Results and Discussion

Mean NAA/Cr was 1.45±0.09, and mean IMT was 0.58±0.12 mm. Hierarchical linear regression analysis was used to estimate the independent contribution of carotid IMT to variance in NAA/Cr. Age, sex and full-scale IQ were entered in the first step of the analysis, systolic blood pressure was entered in the second step, and IMT was entered in the third step. Results revealed that increased IMT was significantly related to lower NAA/Cr independent of age, sex, IQ or systolic blood pressure [$F(5,35)=2.59$, $p=0.043$, IMT $\beta=-0.53$, $p=0.003$, Fig. 1].

Our results are consistent with findings that increased IMT relates to diminished cognitive function in the elderly. However, previous work involving paper-and-pencil measures of cognition has highlighted the fact that a certain threshold of pathology may need to be reached before IMT consistently relates to poor neuropsychological test performance (i.e., IMT≥0.9 mm). The present study extends the previous findings significantly by indicating that even IMT levels below clinical thresholds for end-organ damage (<0.9 mm) may be relevant to cognition when sensitive markers of neuronal health and viability are employed.
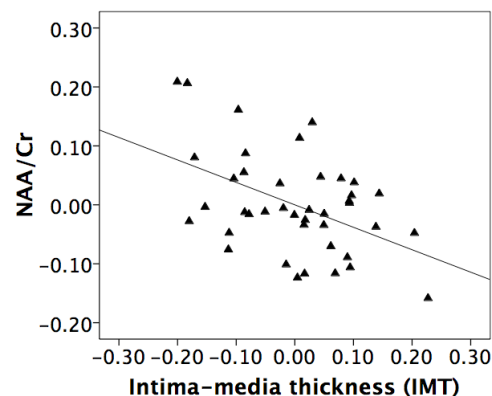

Fig. 1. Partial correlation plot indicating that higher IMT is significantly related to lower cerebral NAA/Cr in middle-aged adults at risk for cardiovascular disease

Conclusion

The present study bridges the gap between midlife hypertension and late-life cognitive impairment, a relationship that has long been documented but remains poorly understood. We demonstrate that midlife hypertension and associated arterial thickening relate to cerebral measures of neuronal health and viability in middle-aged adults with intact cognitive performance. The value of midlife IMT and NAA/Cr to predict future cognitive impairment should be further explored as well as the cognitive benefits of interventions targeted towards improving arterial health in midlife.

References

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