reference region. Quantitative MRI 3 measured the volumes of cerebral gray matter, hippocampi, and white matter hyperintensities (WMH) on MRI scans obtained nearest to PiB PET. Mixed effects regression models of individual trajectories of memory and executive functioning were estimated with random effects of baseline level and rate of change. Demographic variables, baseline clinical diagnosis, global amyloid burden defined as the average DVR from cortical regions associated with Alzheimer's amyloid pathology 1, MRI variables, and vascular risk factor burden defined as the simple sum of vascular risk factors present were entered into the model as fixed effects in a stepwise fashion. All fixed effects whose association with memory or executive function passed a p-value threshold of 0.01 were carried forward to subsequent models. **Results:** In the first model, baseline diagnosis was significantly associated with both baseline level and rate of change in memory and executive function. Global amyloid burden, when added to this model, was significantly associated with baseline level and rate of change in one or both cognitive domains. When MRI measures were further added to the model, only hippocampus volume was a significant predictor of baseline level and rate of change in cognitive domains. When total vascular risk factor burden was further added to the model, it significantly predicted baseline level of executive function. When total vascular risk factor burden was replaced with individual risks factors, only hyperlipidemia was significantly associated with baseline level of memory performance (Table). **Conclusions:** In a cohort of community based, predominantly nondemented individuals, greater vascular risk factor exposure was significantly associated with baseline level of executive function in a model that included amyloid burden and MRI measures of vascular and neurodegenerative disease. We conclude that modifiable vascular risk factors are important to cognitive health even after adjusting for the concurrent effects of cerebral amyloid burden.1. Marchant NL, Reed BR, DeCarli CS, et al. Cerebrovascular disease, beta-amyloid, and cognition in aging. Neurobiol Aging 2012;33:1006 e1025-1036.2. Marchant NL, Reed BR, Sanossian N, et al. The Aging Brain and Cognition: Contribution of Vascular Injury and Abeta to Mild Cognitive Dysfunction. JAMA neurology 2013:1-8.3. DeCarli C, Reed BR, Jagust W, Martinez O, Ortega M, Mungas D. Brain behavior relationships among African Americans, white, and Hispanics. Alzheimer Dis Assoc Disord 2008;22:382-391.

IC-01-05 REGIONAL CEREBRAL BLOOD FLOW PATTERN ASSOCIATED WITH SUBCLINICAL COGNITIVE DECLINE AND VASCULAR RISK FACTORS IN HEALTHY, MIDDLE-AGED MALES

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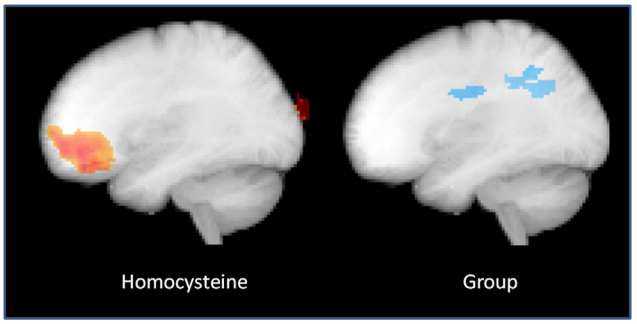
Background: Age related cognitive dysfunction and structural brain changes have been associated with both cerebral blood flow (CBF) changes and vascular risk factors such as homocysteine, suggesting a role of cerebrovascular function in the brain aging process and neurodegenerative disease. However, little is known about the interplay between these factors in normal brain aging preceding overt cognitive dysfunction. We investigated the relationship between cognitive function, structural brain changes, vascular risk factors and CBF in a group of 175 middle aged malesubject with or without life-time decline in cognitive function. **Methods:** The Metropolit cohort consists of all men born in Copenhagen in 1953, with a cognitive examination at age approx. 20 years. Among 2000 healthy participants retested at age 57, we included those with highest relative increase (Group A, n=87) or decrease (Group B, n=88) in cognitive function. Subjects underwent cognitive testing, blood sampling and structural MRI. Regional CBF measurements were obtained using the QUASAR arterial spin labeling sequence and boht absolute and normalized perfusion maps were calculated using FSL tools taking individual hematocrit values into account. Phase contrast mapping was used to measure global brain blood flow, and by normalizing to brain volume a measure of mean global CBF was obtained. Structural brain changes were assessed by calculation brain parenchymal fraction (BPF) and Fazeka's white matter lesion score. **Results:** The two groups did not significantly differ with regard to mean global CBF or structural brain changes. Also no correlation between vascular risk factors or structural brain changes with mean global CBF were observed. Cognitive decline was associated with significantly lower perfusion in the precuneal area in voxelwise analysis ($p<0.001$ uncorr), and in regional analysis ($p<0.05$) also in post. cingulate and calcarine areas. Further, homocysteine was associated with relative hyperperfusion in the inferior mesial frontal areas ($p<0.001$ uncorr.) independently of the group effect. **Conclusions:** The main findings are that both pre-symptomatic lifetime cognitive decline and homocysteine are independently associated with specific regional CBF patterns but not to global CBF changes or structural measures of brain aging.



IC-01-06 AORTIC BLOOD PRESSURE IS ASSOCIATED WITH WHITE MATTER HYPERINTENSITY FRACTION IN POSTMENOPAUSAL WOMEN WITH NORMAL BLOOD PRESSURE

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Background: White matter hyperintensity (WMH) load on T2-weighted MRI is a risk factor for cognitive impairment. Hypertension is associated with high WMH load, suggesting a vascular etiology. However, the relationship of blood pressure (BP) within the normal range and WMH is not established. Elevations in aortic hemodynamics precede the appearance of clinically-diagnosed hypertension. In normotensive individuals, noninvasive measurements of aortic hemodynamics provide information on vascular function. Early alterations in aortic hemodynamics may be mechanistically linked to the development of WMH. In this context, the hormonal shifts during menopause accelerate vascular dysfunction in women, putting postmenopausal women at increased risk for both hypertension and WMH. Our objective was to determine the association between aortic hemodynamics and WMH in healthy, postmenopausal women with normal blood pressure. **Methods:** We examined 39 nonhypertensive postmenopausal women (age 60±3 yrs; body mass index 27±4 kg/m 2). Mean arterial blood pressure (MAP) was determined using a brachial arm cuff and was within normal range (88±7 mmHg). Aortic hemodynamics were estimated using beat-by-beat tonometry (Sphygmocor). WMH was calculated from fluid-attenuated inversion recovery MRI using a semi-automated segmentation algorithm. WMH volume was divided by the total white matter volume to calculate WMH fraction in each subject. **Results:** Aortic hemodynamics included systolic BP (112±10 mmHg) and diastolic BP (74±7 mmHg). WMH fraction was positively associated with aortic systolic BP ($r=0.40$;$p<0.01$) and aortic diastolic BP ($r=0.33$;$p<0.05$). After adjusting for age, aortic systolic BP and WMH remained significantly associated ($p=0.03$). Age and diastolic BP had a significant interaction ($p=0.02$), with WMH fraction increasing less with aortic diastolic BP in older ages. **Conclusions:** In postmenopausal women with normal blood pressure, higher aortic systolic pressure was associated with greater WMH load. Because increases in aortic hemodynamics precede changes in brachial cuff BP measurements, our results suggest that monitoring aortic hemodynamics may identify individuals at accelerated risk for WMH and guide early treatment to reduce development of WMH and cognitive impairment.