Correlation of brain atrophy to decreased CBF and CVR in coronary artery disease patients.

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Introduction: Neurodegeneration and cognitive impairment are often associated with aging[1] and, as recent evidence suggests, they are also associated with vascular disease and vascular disease risk factors[2]. Decrease in regional gray matter volume (GMV), cerebral blood flow (CBF) and cerebrovascular reactivity (CVR) have been linked to vascular disease risk factors, such as hypertension, and diabetes[2]. However, little is known of the impact of cardiovascular disease on brain structure and function. Recently, we demonstrated with voxel-based morphometry (VBM) decreased regional GMV in brains of coronary artery disease (CAD) patients, including regions associated with cognition [3]. In this study, we examined 1) evidence of reduced regional CBF and CVR in CAD, since increased vascular resistance, common in CAD, will diminish CVR, and 2) the relationship between perfusion changes and brain atrophy in regions revealed from VBM and from cortical thickness analysis. Regional CVR and CBF were measured with pseudocontinous ASL (pCASL).

Materials and Methods: 35 CAD patients (age 58 ± 8 years) and 20 controls (age 58 ± 9 years) were scanned on a Siemens 3.0T Verio system using a 32-channel array coil. 2D-pCASL[4] imaging parameters include 1.5s label duration, 1.0s post-label delay, TR/TE =3500ms/12ms, FOV=24cm, matrix=64x64, and 12 axial slices. Patients breathed room air for 5 min, followed by 5 min of inhaling a mixture of $CO_2/O_2/N_2$ (6:21:74%). The CO_2/air mixture was delivered by a facemask attached to a large reservoir bag, and end-tidal CO_2 ($ETCO_2$) was monitored continuously. 1.0mm^3 isotropic T1-weighted MPRAGE data was acquired for cortical thickness analysis (CTA).

CTA was performed with Brainvoyager QX (Brain Innovation, NL) and pCASL images were processed using SPM8 (UCL, London, UK) and in-house MATLAB scripts. Average perfusion-weighted images for normo- and hypercapnia were generated by surround subtraction and smoothed. Gray matter (GM) mask containing 80% GM voxels was applied to CBF images. CVR was defined as the change in CBF divided by the change in $ETCO_2$ ($\Delta ETCO_2$). Independent t-test was conducted across the whole brain and in a priori ROIs to compare CTA, CBF and CVR between patients and controls ($p<0.05$). Whole brain mean CBF and CVR, and mean regional values of CBF and CVR were correlated to CTA.

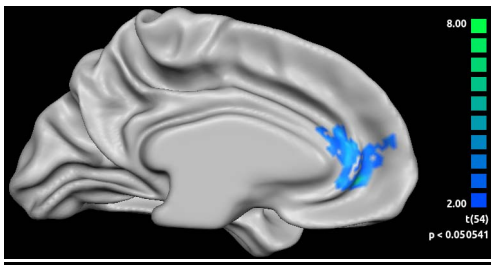
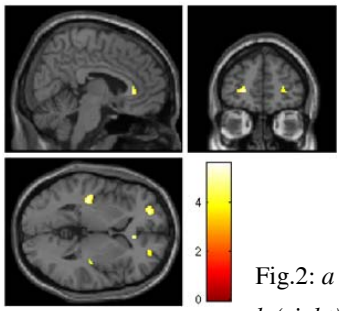


Fig.1: Areas (blue) of cortical thinning in CAD patients.



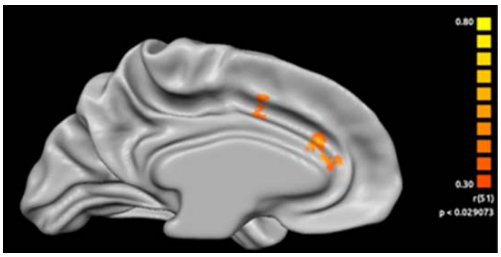


Fig.2: *a (left)* Areas (yellow) <CBF in CAD ($p<0.05$, FDR); *b (right)* correlation of mean CBF to CTA.

Results: Mean $\Delta ETCO_2$, GM CBF and CVR were 10.75 ± 3.69 mm/Hg, 50.83 ± 11.68 ml/100g/min and 5.65 ± 1.76 %/mm/Hg in controls and 12.69 ± 4.36 mm/Hg, 46.49 ± 13.88* ml/100g/min and 5.92 ± 1.99 %/mm/Hg in patients (* = significance). Cortical thinning was observed in patients in right (R) inferior parietal, R medial frontal, left (L) anterior cingulate and L insula (*Fig.1, L side shown*). Hypoperfusion was observed in the same regions and in bilateral middle frontal, superior temporal, middle temporal and postcentral gyrus (*Fig. 2a*). CTA was correlated to CBF in regions mentioned above (*Fig. 2b, L*) but not to CVR. Compared to controls, patients had higher CVR in all regions measured.

Discussion and Conclusion: Brain atrophy in CAD patients recently reported with VBM [3] was confirmed with CTA. Regional cortical thinning was associated with hypoperfusion. However, CAD patients had higher regional CVR compared to controls, an unexpected finding possibly related to the potential of statin to improve vascular dynamics [5]. Nearly all patients were on statin therapy and no difference was found between groups in measures of vascular dynamics such as compliance, resistance and wall thickness. In general CAD is associated with abnormalities in brain structure and function.

Reference: [1] Kastrup et al. *J NeurolSci,* 1999. [2] Abete et al. *Ageing Res. Rev.* 2014. [3] Anazodo et al. *NeuroImage Clinical 2013* [4] Wang, *Proc ISMRM*, 2007; 15:2974. [5] Malik et al. *Cardiovasc. Res*, 2001.