

Impaired Cerebro-Vascular Reserve in Carotid Artery Disease correlates with deficits in cognitive functions

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Purpose: In carotid artery disease (CAD) information about cerebral blood flow identifies areas with reduced perfusion due to the flow restriction of a feeding vessel. Arterial Spin Labeling (ASL) has proven to provide similar information about altered perfusion in vascular territories like PET with the advantage of its non-invasiveness [1]. More recently, cerebro-vascular reserve (CVR) in ASL was suggested as of value in CAD [2]. CVR indicates the capacity of the vasculature to increase cerebral blood flow (CBF) in a specific region, which is a necessity for proper brain function and is achieved by administration of a vasodilatory agent. In CAD this CVR is often reduced which is suggested to be the physiological basis for observed cognitive deficits. Therefore, in this study we investigated CBF and CVR in the watershed areas of CAD patients and correlated them with neuropsychological performance.

Methods: 32 patients with CAD (grade of stenosis >70%) were investigated using pseudocontinuous ASL (pCASL [3]): Hanning window-shaped RF pulse with duration 0.5 ms and space between RF pulses of 0.9 ms, flip angle = 25°, slice-selective gradient = 6 mT/m, tagging duration (τ) = 1720 ms, postlabeling delay (PLD) = 1500 ms and TR/TE 4000ms/13ms, 120 volumes. Fourteen axial slices with 6mm thickness were placed parallel to the anterior-posterior commissure line. Labelling block was 9cm below the isocenter of the readout slices. Acquisitions were performed in resting condition with ambient air and during vasodilatation stimulated with either 7% CO₂ enriched air or Diamox. CBF was quantified for both conditions within gray matter voxels (estimated after segmentation of a T1 weighted image and coregistration in SPM8). Region of interest analysis was performed in the anterior watershed (AW) areas as defined with the WFUPickatlas (according to [4]). By subtraction of the CBF values for vasodilatation and baseline the patient's CVR was estimated. In addition to the MR measurements all participants were tested for neuropsychological performance (language skills, executive functions, visual and verbal memory) by expert neuropsychologists.

Statistical analyses were performed with SPSS (Version 19). A repeated-measures ANOVA with within subject factors Hemisphere (left/right) and Condition (baseline/vasodilatation) and between subject factor AffectedSide (left/right) was performed (post hoc tests were calculated with 1-sided t-tests for significance). Partial correlations between CBF / CVR and neuropsychological performance were done, using global baseline perfusion as control variable. In addition, the patients were grouped into terciles (3-quantiles) based on CVR in the AW on the stenotic hemisphere.

Results: ANOVA revealed significant effects of Condition ($F(1,29)=13.50$; $p=0.001$) and significant interaction effects of Hemisphere*AffectedSide ($F(1,29)=10.69$; $p=0.003$) (Figure1). A t-test showed significant reduction of CVR in the AW on the stenotic side ($t(31)=-1.83$; $p=0.039$). ANOVA of terciles showed a significant interaction effect of Subgroup*Hemisphere $F(2,29)=7.37$ $p=0.003$ (Figure2). Post Hoc tests revealed that only the group with lowest CVR showed a significant difference between stenotic and healthy hemisphere. However, both, lowest and average CVR group showed reduced CVR on both hemispheres as compared to the highest CVR group. Significant negative correlations between AW-CVR on the stenotic side and the neuropsychological performance were found in the domain of verbal working memory (Digit span; $r=-0.37$, $p=0.035$, one-sided) as well as for executive functions (processing speed i.e. TMT A time; $r=-0.45$ $p=0.015$; inhibition i.e. Stroop inference time; $r=-0.38$, $p=0.033$)

Discussion: Our results indicate reduced baseline perfusion as well as impaired CVR in the anterior water shed areas of the affected side in CAD patients. Moreover, patients showed deficits in cognitive functions (working memory and executive functions) that could be associated with reduced CVR.

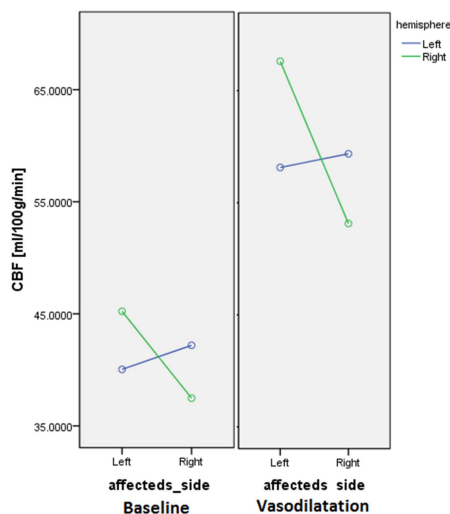


Figure1: ANOVA results for CBF in AW area for within subject factors condition [rest/stimulation] and hemisphere (left/right) and between subject factor affected side (left/right)

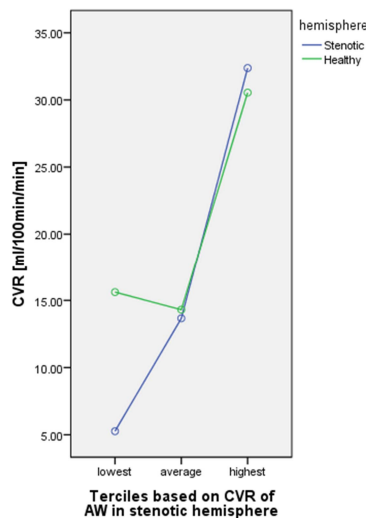


Figure2: ANOVA results for CVR in AW area for within subject factor hemisphere (stenotic/healthy) and between subject factor CVR-subgroup (low/average/high).

References:

[1] Ye et al. (2000) Magn Reson Med; [2] Bokkers et al. (2011) J Neurol Neurosurg Psychiatry; [3] Dai et al. (2008) Magn Reson Med; [4] Maldjian et al (2003) Neuroimage

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