Differences in Cerebrovascular Reactivity in Posterior Circulation Territories obtained with BOLD and ASL MRI using Hypercapnic Challenges

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Purpose: Assessing cerebrovascular reactivity using hypercapnia with BOLD and ASL MRI in posterior circulation territories

Introduction: Posterior circulation stroke and transient ischemic attacks (TIA) account for 20% of all stroke and TIA occurrences [1,2]. Recent studies have indicated that the risk of recurrent stroke is high in patients with vertebrobasilar artery disease [3]. Therefore identification of tissue features related to recurrent stroke prevention is of primary concern. Non-invasive methods that can assess and isolate cerebrovascular from non-vascular/metabolic causes, and can track progression of symptoms and disease state are ideal [4]. Measuring the cerebrovascular reactivity (CVR) using ASL or BOLD MRI is becoming a popular method for investigating cerebrovascular disease, however it has been mostly aimed at carotid artery territories [5,6]. Here, we use BOLD and ASL to investigate CVR in posterior circulation territories (cerebellum, occipital lobe, thalamus) in healthy subjects using two hypercapnic challenges ($5\%C0_2+95\%O_2$ and $5\%C0_2$+room air). We hypothesise that differences in CVR assessed with BOLD (modulated by changes in CBF, cerebral blood volume (CBV) and cerebral metabolic rate of oxygen ($CMRO_2$)) and ASL (CBF changes) may yield important information pertaining to the tissue vascular and metabolic condition.

Materials and Methods: *Data acquisition:* Subjects (N=10) were scanned on a Philips 3T system (8-channel head coil) *ASL*; pCASL data were acquired GE-EPI with background suppression: TR/TE=3900/13 ms, α=90°, SENSE factor=2, spatial resolution =3.5mm, FOV=240×240×127 mm^3, 17 slices, slice thickness=7 mm, label duration/post label delay=1650/1525 ms, scan-time=9.1 min. An additional M_0 scan was acquired for CBF quantification. *BOLD*; GE-EPI with background suppression: TR/TE=2000/35 ms, α=80°, SENSE factor=1.8, spatial resolution=3mm, FOV=240×240×124 mm^3, 31 slices, slice thickness=3.5 mm, scan-time=12.1 min. *Hypercapnic paradigm*: for both the ASL and BOLD session two datasets were obtained using either carbogen ($5\%C0_2$, $95\%O_2$) or $5\%C0_2$ + room air (CO_2-air) delivery via a facemask. The ASL scan consisted of 4.5min of baseline followed by 4.5min of hypercapnia (carbogen or CO_2-air). The BOLD scan consisted of 90s of baseline, 3min hypercapnia, 3min baseline, 3min hypercapnia, 90s baseline. *Analysis:* ASL and BOLD data were corrected for motion. CBF values were computed using a single-compartment kinetic model [7]. We included a reduction in blood water T_1 from 1.7 to 1.2s in the model in carbogen data to correct for the hyperoxic effect on blood water T_1. CBF-CVR was defined as the percentage increase of the average CBF during hypercapnic condition with respect to the average CBF for the room air condition. BOLD-CVR was estimated similarly using a GLM approach in FSL (FEAT). Regions of interests (ROI) for the occipital lobe and thalamus were obtained from the MNI atlas after co-registering the data to the MNI space. ROIs for cerebellum were drawn manually for each subject and scan, as a MNI based approach revealed poor delineating of the cerebellum.

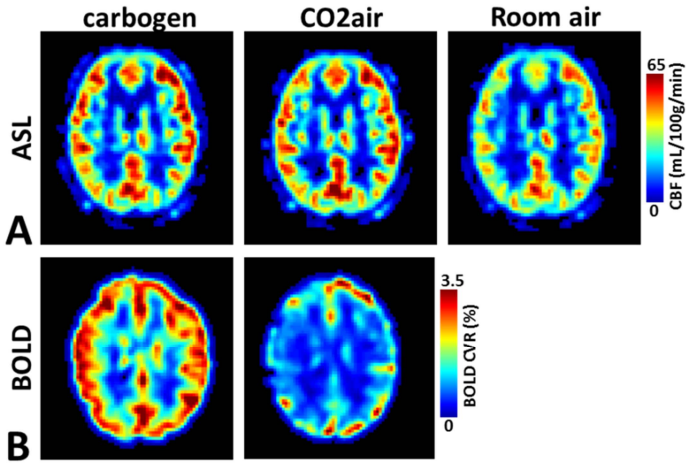

Figure1 ***A)*** *ASL computed CBF maps for the carbogen, CO_2-air and room air condition for a single subject.* ***B)*** *BOLD signal increase (%) for the carbogen and CO_2-air*

Results & Discussion: Figure 1A shows the CBF maps of the carbogen, CO_2-air and room air condition for a single subject. The vasodilatory effect of administered CO_2 gas results in an increase in the overall CBF for the carbogen and CO_2-air condition relative to room air. Comparison of the carbogen with the CO_2-air CBF maps reveals a slight reduction in the CBF increase for the carbogen task. This can be attributed to a vasoconstrictive effect of the high O_2 (95%) content in the carbogen gas mixture. **Figure 1B** shows the BOLD-CVR maps in the carbogen and CO_2-air condition for the same subject. Higher BOLD signal changes are observed for the carbogen task due to hyperoxia during the carbogen task which reduces the relative venous deoxyhemoglobin content compared to room air (and hence increases the BOLD signal [8]). These effects are also observed in **Figure 2** which shows, for all subjects, the computed CBF-CVR (**Fig.2A**) and BOLD-CVR (**Fig.2B**) for the carbogen and CO_2-air conditions in posterior circulation territories (cerebellum, occipital lobe and thalamus). For the CBF-CVR we observe significant differences between cerebellum, thalamus and occipital lobe gray matter. The cerebellum and thalamus show higher CVR compared to the occipital lobe. The regional trends between CBF and BOLD-CVR appear similar, however the BOLD CVR differences did not reach significance - perhaps owing to lower range or contrast to noise ratio. Differences between CBF and BOLD-CVR may be explained by variations in arterial arrival time which may bias CBF results. However, this effect is likely minimal for the long post label delays used in this study. The mismatch between CBF and BOLD may also indicate differences in vascularization and metabolic condition between these regions as BOLD is also modulated by changes in CBV and $CMRO_2$.

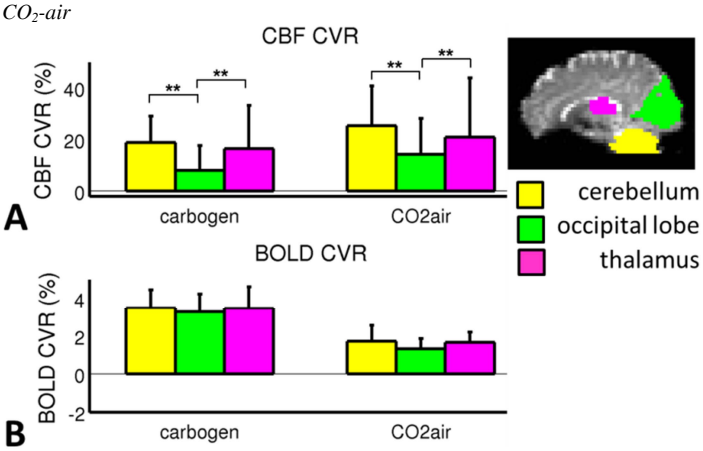

Figure2 *Regional differences in CVR for* ***A)*** *CBF based CVR, however less apparent in* ***B)*** *BOLD based CVR which could be due to differences in vascularization and metabolic condition. Data shown are mean ± standard deviation values across all subjects. ** denotes significant differences p<0.005.*

Conclusion: We performed cerebrovascular reactivity measurements in healthy subjects using BOLD and CBF for different hypercapnic and hyperoxic conditions, focussing on posterior circulation territories. Results demonstrate that CVR in posterior circulation territories is regionally dependent, at least for CBF. Observed differences between CBF and BOLD based CVR may indicate differences in vascular and metabolic condition. Future work will aim at elucidating and separating these effects by comparing healthy subjects and patients with posterior circulation pathology.

References.

[1] Bogousslavsky et al. Stroke 1988,[2] Cloud et al. QJM 2003, [3] Gulli et al. Stroke 2013, [4] Markus et al. LancetNeur. 2013, [5] Detre et al. JMRI 1999, [6] Mandell et al. Stroke 2008, [7] Buxton et al. MRM 1998,[8] Chiarelli et al. NI 2007