MRI based quantification of cortical responses to exercise

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TARGET AUDIENCE: Researchers, physiologists and clinicians interested in the physiological response to exercise.

PURPOSE: Low to moderate intensity dynamic exercise in healthy, young individuals increases global cerebral blood flow (CBF) and oxygenation, which has been directly linked to enhanced cerebral neuronal activity[1, 2]. At high exercise intensities global CBF and oxygenation have been reported to plateau, or decline in line with the hyperventilation-induced fall in arterial carbon dioxide tension[1].

Aim: (1) To assess the feasibility of using MRI to measure both global and regional changes in CBF in response to low, moderate and high intensity steady-state exercise in healthy, young volunteers. (2) To determine whether there is an uncoupling of regional blood flow compared to blood flow in active brain regions.

METHODS: Following ethics approval, 6 male subjects were recruited to the study (age 22-27 years, BMI 24 ± 2). All exercise tasks were performed using an MR compatible, electrically braked, supine cycle ergometer (Lode B.V, Groningen, Netherlands). *VO2max:* Prior to MR based experiments, all volunteers underwent a continuous, incremental supine exercise test to determine maximal oxygen consumption ($VO2_{max}$) using the supine ergometer and on-line gas analysis system (Cosmed, Rome, Italy) (Fig. 1A).

Exercise task: MR data was acquired at rest and during 10 min of steady-state exercise at workloads of 30, 50 and 75% $VO2_{max}$ (Fig. 1B). Heart-rate (HR) was measured throughout.

MR acquisition: Data was acquired on a Philips Achieva 3 T MR scanner using a 32 channel receive coil. Sagittal and coronal 2D PC-MRA data sets were initially acquired to locate the R and L internal carotid arteries (ICA) and the vertebral artery (VA). During baseline and each workload level, global and regional cerebral blood flow (CBF), and BOLD contrast was assessed. *PCA data*: Blood flow (velocity and flux) in L/R ICA and VA was measured using a vectorcardiogram (VCG) gated, 2D PC-MRA (TR/TE = 15/6.5 ms, FA = 25°, FOV = 280 x 77 mm^2, 0.75 x 0.75 x 6 mm^3 reconstructed, SENSE 4, v_{ENC} = 0 and 100 cm/s, scan duration = 1 min 25 s, NSA = 2). *Regional CBF and BOLD data:* A Double Acquisition Background Suppression (DABS) sequence was used to acquire simultaneous CBF and BOLD data (GE-EPI at TE = 13ms/40 ms for ASL and BOLD respectively), 10 slices of in-plane resolution 2.94 x 2.94 mm, slice thickness 8 mm, post-label delay (TI) = 1550 ms, TR = 2600 ms per label/control, total acquisition time ~ 5 min); a base M_0 image was acquired at each $VO2_{max}$ level. Following the exercise protocol, a T_1-weighted MPRAGE anatomical image was acquired.

Data Analysis: PCA data was analysed using Q-Flow (Philips) to determine vessel area, velocity and flux in the left and right ICA and VA, flux measures were summed to estimate total brain blood flow. DABS data were separated into BOLD and ASL time-series. BOLD data was motion corrected (FSL, fMRIB, Oxford) and motion parameters applied to ASL images. Perfusion weighted images were then formed from subtraction of label and control data. BOLD data was analysed using FEAT (FSL) to identify brain areas associated with the exercise task (GLM analysis, FDR corrected Z > 3.89). These areas were used to form a binary mask of BOLD active areas. BOLD (% change) and CBF (ml/100g/min) was then assessed in 4 masks: global grey matter (GM_{global}), BOLD active regions ($BOLD_{act}$), GM portion of BOLD active regions (GM_{act}), and GM excluding BOLD active regions (GM_{ex}).

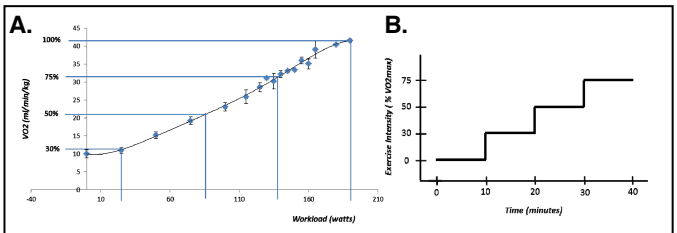

Figure 1: A) VO2max versus workload showing 30, 50 and 75 % levels. B) Exercise protocol performed inside scanner.

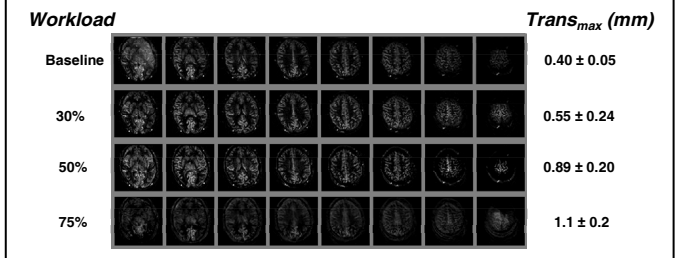

Figure 2: ASL images at 30, 50 and 75%$VO2_{max}$, and mean translation across subjects, showing motion artefacts at 75%$VO2_{max}$

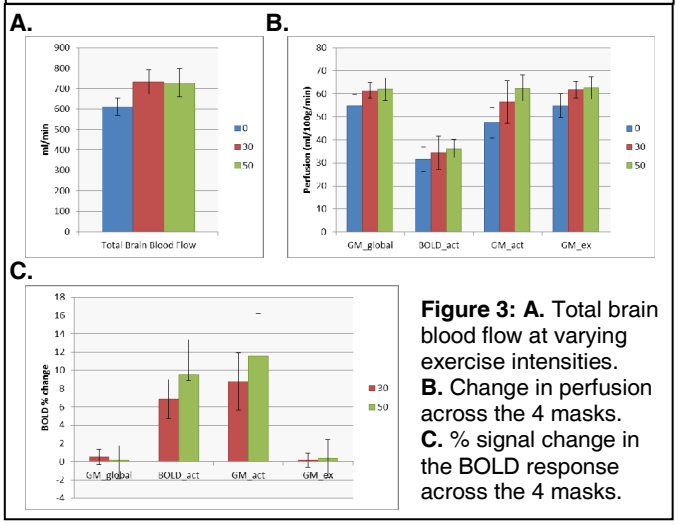

Figure 3: A. Total brain blood flow at varying exercise intensities. **B.** Change in perfusion across the 4 masks. **C.** % signal change in the BOLD response across the 4 masks.

RESULTS: Steady-state heart rate increased across workloads (rest: 57, 30%$VO2_{max}$: 71, 50%$VO2_{max}$: 84, 75%$VO2_{max}$: 114 bpm). Motion was assessed across workloads, with significant motion observed at 75 % (Fig.2), leading to poor ASL quality and PCA acquisition at this exercise intensity. Fig. 3A shows an increase in total brain blood flow with increasing workload, with a significant increase between baseline and 30%$VO2_{max}$ (P=0.05). Fig.3B shows the corresponding mean regional CBF as measured using ASL across each of the masks. In the active regional mask, a significant increase in CBF was found from baseline to 30 and 50% $VO2_{max}$, whilst GM outside these areas showed a significant increase in CBF between baseline and 30% $VO2_{max}$. Fig.3C shows the mean BOLD % signal change across each mask.

DISCUSSION: This study has demonstrated that it is possible to assess global and regional brain responses to exercise involving a large muscle mass at workloads of up to 50% $VO2_{max}$ without significant detrimental effects from motion artefacts influencing data acquisition. Moreover, the difference in CBF between non-active GM and the active GM varies superlinearly with increasing workloads suggesting that the coupling of regional blood flow and brain activity is modulated by the underlying changes in CBF due to changes in cardiac output, which warrants further investigation.

References: **[1]** Ide K & Secher NH, *Prog Neurobiol* **61,** 397–414, 2000. **[2]** Secher NH et al. *J Appl Physiol* **104,** 306–314, 2008.

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