Cerebral Perfusion Response to Graded Levels of Inspired Hyperoxia

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Introduction

Hyperoxia induced via increased inspired fractions of oxygen (FiO2) has been used as a minimally invasive form of contrast in MRI [1]. In comparison to the effects of hypoxia, the detail of the CBF-FiO2 curve for hyperoxic conditions is not well known [2]. T2*-weighted imaging techniques are very successful at detecting such signal changes, however, care needs to be taken as the Haldane effect reduces the CO2-carrying ability of haemoglobin at higher levels of FiO2, resulting in numerous physiological changes [3]. Significantly, a reduction in cerebral perfusion occurs; thus in order that hyperoxia be effective as a passive agent, it is essential to determine the maximum FiO2 which can be administered without affecting perfusion levels.

Methods

Normal, healthy volunteers (N=6, 2♀) with a mean age of 25.7±3.6 years were studied using a Varian 3T MRI scanner. A Magnex head-dedicated gradient insert coil was used in conjunction with a birdcage coil tuned to 127.4MHz. Perfusion imaging was performed using a QUIPSS2 sequence [4], TR=2s, TE=22ms, tag-excitation time (TI2) 1.4s, tag-saturation time (TI1) 0.7s, 10cm inversion slab 1.5cm from the imaging slab. 1804 volumes were acquired in 5 axial slices, 6mm thick extending in a superior direction from the thalamus. An EPI whole-brain scan and a T1-weighted whole-brain structural scan were also acquired for registration.
Respiratory composition was monitored using (AEI Technologies, PA) gas analysers. Inspired gases were delivered via a multi-tube system which mixed humidified medical oxygen and compressed air to a mixing chamber 30cm from the subject's mouth at a total delivery rate of 30 litres per minute. Subjects wore a close fitting mask over the mouth and nose. Gases were exhaled into a large re-breathing chamber in combination with an open vacuum extraction system for safety. A protocol of graded steps of FiO2 was administered consisting of 12 minutes at each level (FiO2 = normal i.e. 0.21, 0.4, 0.6, 0.8, and 1.0). This enabled the subject to reach a steady-state of blood flow, blood volume and metabolism (after ~2 minutes) and provide sufficient power for a perfusion measurement. Perfusion data were analyzed using FSL [5] incorporating motion correction (MCFLIRT), brain extraction (BET), and a GLM-based estimation of activation intensity (FEAT). Temporal sinc-interpolation was applied to perfusion images prior to pair-wise subtraction of control and tag. Masks of segmented grey and white matter were calculated from high resolution T1 structural scans of each subject using FAST (FMRIB automated segmentation tool).

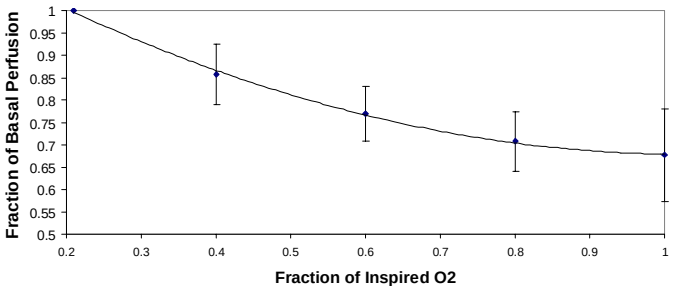

Figure 1: Fractional change in perfusion signal from normoxic baseline with increasing FiO2.

Results and Discussion

The mean of the voxels in each segmented region of the subtracted images were calculated for each slice and each subject at the different oxygen levels. Changes in perfusion under hyperoxic conditions were seen to be very regional in nature and from the segmentation interrogation were shown to occur predominately in grey matter, with little or no measurable change in white matter regions, in agreement with other studies [6]. The mean fractional change in signal in grey matter regions from the baseline value recorded during the initial normoxic phase, averaged over all slices and all subjects at each FiO2 is shown in Figure 1. The value of an approximately 32% decrease in perfusion at FiO2=1.0 is comparable to that found in other studies [2] using different measurement techniques. However; the apparent decrease in perfusion at even mild levels of hyperoxia in grey matter regions has not previously been reported. Studies which have measured MCAFV or employed magnetic resonance phase-contrast angiography are generally insensitive to changes in CBF beyond the arteries and thus inappropriate for detecting regional changes within grey matter. Methods of measuring changes in CBF using injected paramagnetic contrast agents have produced lower relative changes at FiO2=1, but are not readily comparable to ASL methods such as used in this study. There are thus reasonable grounds to have confidence that the reduction in perfusion seen at the moderate levels of hyperoxia is genuine.

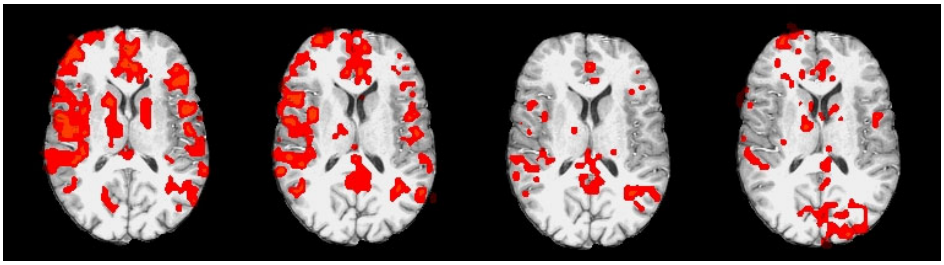

Figure 2: Regions of decreased perfusion at FiO2=1.0, 0.8, 0.6, and 0.4.

Conclusions

Contrary to much published literature claiming otherwise, grey matter perfusion was shown to begin decreasing even at very low levels of hyperoxia. The regional nature of the change is supported by other studies as is the level of change seen at FiO2=1.0. As the Haldane effect is not significant at low levels of hyperoxia it is unlikely that the drop in perfusion is due to changes in PCO2, but is rather a direct result of the increase in PaO2. For administered oxygen to be practical as a contrast agent in studies where grey matter perfusion is of interest this effect must be taken into account.

References
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