Susceptibility artefacts in experiments involving changes in inspired oxygen level

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INTRODUCTION – A hyperoxic challenge has been shown to provide a method for the measurement of venous blood volume (1) and calibrated BOLD (2). The administration of a hyperoxic gas mixture (F_IO_2>0.21) increases venous haemoglobin saturation causing an increase in the BOLD weighted signal. However, increasing oxygen concentration in the nasal cavity may itself lead to artefactual signal changes. In this study we used a sinusoidally modulated hyperoxic challenge with Fourier analysis techniques to detect changes correlated with increased oxygen saturation and to investigate artefactual effects using the phase of associated signal changes. This is of particular relevance for hyperoxia studies performed at ultra-high field.

METHOD – *Challenge Presentation:* End-tidal CO_2 ($P_{ET}CO_2$) was maintained at 40mmHg and end-tidal O_2 ($P_{ET}O_2$) was sinusoidally modulated between 100mmHg and 500mmHg using a computer-controlled gas blender and a modified sequential gas delivery breathing circuit (3) (RespirAct™, Thornhill Research Inc., Toronto, Can.). $P_{ET}O_2$ and $P_{ET}CO_2$ were monitored throughout.

MR Acquisition: Three healthy subjects were scanned with local ethical approval, using a Philips Achieva 7.0 T equipped with a volume transmit and 16-ch receive coil. GE-EPI images were acquired with 2×2×3mm^3 resolution and SENSE 2. Transverse slices were acquired parallel to the corpus callosum from the base of the frontal lobe in the superior direction. A pilot experiment (TE=20ms, TR=4s, slices=30) was repeated in 2 further subjects (TE=25ms, TR=2s, slices=20).

Analysis: Images were realigned in SPM5 and the time-courses normalised to the mean signal and detrended (4th order polynomial). A pixel-by-pixel FFT was applied allowing the phase and the magnitude of MR signal to be analysed at the challenge frequency.

RESULTS –The phase information presented in Fig. 1 (left: inferior slice, right: superior slice) shows a dipole pattern of phase (ϕ) values consistent with a sinusoidally changing susceptibility artefact at the tissue-air interface in the nasal cavity. The large variation in oxygen concentration in this region is associated with a large variation in susceptibility in the nasal sinuses due to the paramagnetic properties of oxygen. The artefact is most prominent in the inferior slices but is still visible in superior slices, superimposed on the expected changes in BOLD signal in the GM. Fig. 2 shows the mean time-course of two regions in the inferior slice of Fig. 1 (ϕ<π and ϕ>π) confirming a π phase difference. Also of note was the lack of a time delay between presentation of the hyperoxic gas and the signal change. A local tissue effect would be delayed by the time taken for freshly oxygenated blood to reach the brain. Fig. 3 shows the magnitude of the BOLD signal derived from the Fourier analysis. Fig. 4 is the result of a more conventional analysis of this data, subtracting the images at minimum $P_{ET}O_2$ from those at maximum $P_{ET}O_2$, and reveals the same pattern as Fig. 4, but with negative signal changes reflecting differences in phase.

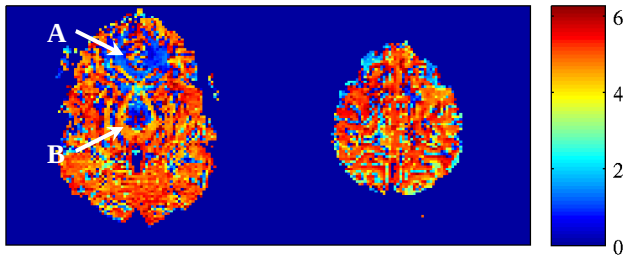

Fig. 1 – Phase (ϕ) of MR signal at challenge frequency.

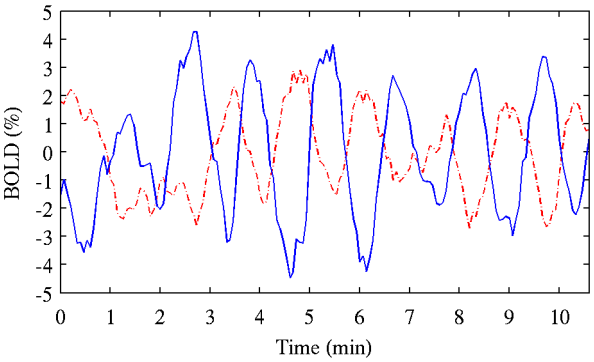

Fig. 2 – Mean time-course over region of interest for region A (ϕ<π, solid) and region B (ϕ>π, dashed).

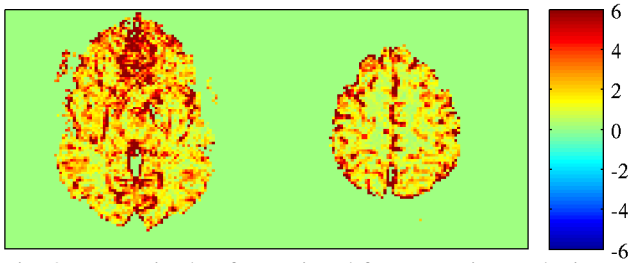

Fig. 3 – Magnitude of MR signal from Fourier analysis.

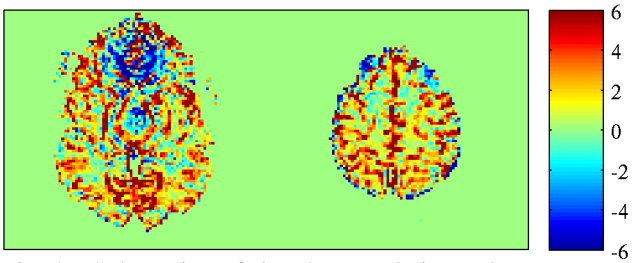

Fig. 4 – Subtraction of signal at max/min $P_{ET}O_2$.

DISCUSSION – This experiment illustrates that MR signal changes due to a hyperoxic challenge are confounded by the changes in oxygen concentration in the nasal cavity. The combination of ultra-high field, a sinusoidal hyperoxic challenge and Fourier Analysis made the effect particularly obvious in this experiment. However it will be present in any experiment that involves modulating the concentration of inspired oxygen, and so care is required when interpreting such data particularly in regions of the brain close to the nasal cavity. There is a ~40mmHg variation in $P_{ET}O_2$ during the respiratory cycle; this paradigm could be useful for investigating the resulting contribution to physiological noise.

REFERENCES – (1) Bulte *et al*., JMRI, 26:894, 2007, (2) Chiarelli et al., NeuroImage, 37:808, 2007, (3) Slessarev *et al*., J. Physiol., 581:1207, 2007