A Functional MRI Study of Motor Activation During Inhaled Oxygen Challenges

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Introduction: Positive BOLD, a robust expression of haemodynamic response (HDR), is by far the most commonly used MRI means in brain activation studies. Positive BOLD results from reduced deoxyHb in capillary and venous compartments due to disproportionate increase in cerebral blood flow (CBF) in relation to the needs of brain oxygen metabolism ($CMRO_2$). Since the blood oxygenation changes are determined by a mismatch between CBF and $CMRO_2$, i.e. oxygen extraction ratio (OER), it can be anticipated that variation in baseline CBF would influence amplitude of positive BOLD-response. O_2 is a well-known affector of CBF, so that in hyperoxia CBF declines and in hypoxia it increases (1). In the present study we have altered inspired O_2 (FIO_2) between 15 and 100 % and determined CBF and BOLD in healthy volunteers performing self-paced finger tapping.

Methods: Experiments were performed on a clinical Philips Intera 1.5 T MRI scanner (Philips Medical Systems, Best, The Netherlands) using standard body coil transmission and SENSE head coil reception. Nine healthy volunteers (four women, five men, age range 25-48 years) gave informed written consent before participation. The volunteers inhaled either 100% O_2 (open circuitry), room air or 15/85% O_2/N_2 (a non-rebreathing circuitry). Oxygen saturation and pulse rate were monitored with a 4500-series Pulse Oximeter (In vivo Research, Inc). The protocol was approved by the Ethical Committee of the University of Manchester. For motor stimulation, subjects performed self-paced finger tapping with right hand according to guidance projected on a screen. In EPI fMRI-trials, eight oblique contiguous transverse slices (thickness 3.5 mm) were imaged with GRE-EPI (FOV 240 mm, matrix 128x128, TR=1 s, TE=40 ms, flip angle 54º). EPI-series consisted of 140 scans, with three periods of 20-s tapping beginning and ending with an OFF-period. Arterial Spin Labeling (ASL) was performed with Transfer Insensitive Labeling Technique (TILT)-sequence using three delay-times: 800, 1000 and 1200 ms (FOV 240 mm, matrix 64x64, slice thickness 8 mm, TE=12 ms, TR=3 s) (2). In oxygen challenge experiments, only one delay-time (1000 ms) was used. TILT-series consisted of 70 scans, with three periods of 10-scan tapping beginning and ending with an OFF-period. CBF was computed in baseline condition according to kinetic perfusion model (3). Cerebral T_2 was quantified using an EPI CPMG-sequence (FOV 240 mm, matrix 256x256, ten echoes, inter echo spacing=20 ms, TR=3 s). Functional EPI-data was analyzed off-line using the FMRIB Software Library (FSL). All other data analysis was carried out using Matlab™ routines. EPI time-series statistical analysis was carried out using FILM (FMRIB's Improved Linear Model) with local autocorrelation correction. Z (Gaussianised T/F) statistic images were thresholded using GRF-theory-based maximum height thresholding with a (corrected) significance threshold of P=0.01. For TILT time-series, r-value maps derived from box-car analysis were thresholded with $r>0.4$ ($P<0.0008$, not corrected for multiple comparisons), and at least one neighboring pixel was required.

Results: Exposure to FIO_2 = 15 % resulted in decline of oxygen saturation down to 95±2 % and increase in heart rate by ~5 % ($p<0.01$, two-sided *t*-test). Blood transverse relaxation is not affected by this small decline in Y_a at 1.5 T (4). Neither gray nor white matter T_2 changed upon altered FIO_2 (Table 1). The BOLD-response amplitude was not significantly influenced by oxygen challenges, although mean response showed a tendency towards higher values in subjects breathing 100 % O_2. Largest number of activated pixels was determined at room air, though the number of pixels in 100 % and 15 % FIO_2 were not significantly different from room air. Increase in CBF during finger tapping was not affected by FIO_2. In room air, the mean CBF in a large ROI containing both gray and white matter was 75±20 ml/100g/min over all subjects.

Conclusions: These data suggest that BOLD and ASL –determined CBF-responses are remarkably insensitive to large variation in FIO_2. This is particularly intriguing, since blood oxygen saturation regulates cerebral perfusion. Our observations indicate that modest variation in blood oxygenation does not influence fMRI characteristics demonstrating the robust nature of HDR to neuronal activation.

FIO_2	BOLD-response (%)	No. of Pixels	CBF-response (%)	Gray Matter T_2 (ms)	White Matter T_2 (ms)	Y_a (%)
100 %	1.8±0.3	260±80	70±40	108±3	88±3	100
21 %	1.4±0.6	420±230	90±30	107±3	87±4	99±1
15 %	1.5±0.2	270±160	90±50	107±2	86±7	95±2

Table 1. BOLD-response, number of activated pixels, CBF-response, gray and white matter T_2 and arterial oxygen saturation as a function of FIO_2.

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