A novel multiphase scheme for simultaneous ASL and BOLD acquisition

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Purpose: To improve the accuracy of simultaneous blood oxygenation level dependent (BOLD) signal and cerebral blood flow (CBF) measures under the situation of increased flow (e.g. hypercapnia) where transit time changes must be considered [1]. The Double Acquisition Background Suppressed (DABS) scheme [2] provides a solution to simultaneous background suppressed arterial spin labelling (ASL) and BOLD acquisitions. However, a single post-label delay is typically used, with a constant transit time assumed. Here we present a multiphase variant of the pulse sequence termed Lock-Locker Double Acquisition Background Suppressed (LL-DABS) ASL (Fig. 1), and demonstrate its increased sensitivity for CBF measurements under hypercapnia and for assessment of $CMRO_2$. BOLD-weighted images are collected by increasing the signal recovery time (TA2) prior to the last LL-readout pulse and setting the final readout flip angle to 90°.

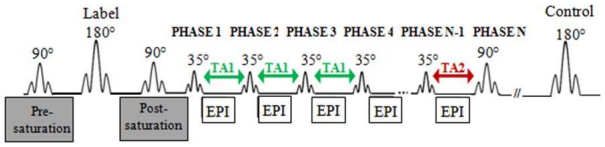

Figure 1) Schematic of LL-DABS pulse sequence. The time TA between the (N-1)th and Nth readout is increased to maximise BOLD sensitivity.

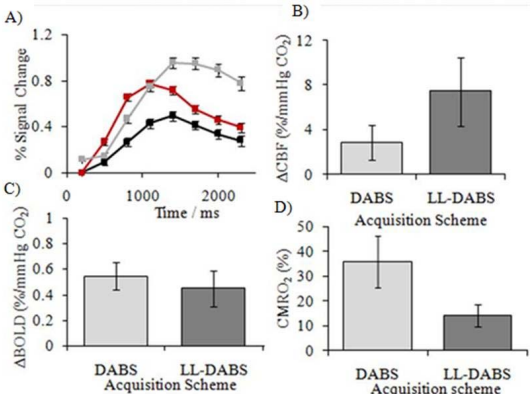

Figure 2: A) Representative LL-DABS timecourse for normocapnia (black), hypercapnia (red) and motor task (grey). Change in B) CBF and C) BOLD to hypercapnia measured using DABS and LL-DABS. D) $CMRO_2$ change to the motor task. Mean (± SEM) across subjects.

Methods: 5 male subjects (24± 1yr) were scanned using a Philips Achieva 7T system with a head volume transmit coil and 32-ch SENSE receive coil.

Respiratory paradigm: 3 min of normocapnia (subject specific $P_{ET}CO_2$ and $P_{ET}O_2$), were followed by a 6 min iso-oxic hypercapnic challenge (+ 8 mmHg CO_2) and a final 3 min of normocapnia (RespirAct^{TM}, Thornhill Research Inc., Ca).

Data acquisition: CBF and BOLD data were collected with both DABS and LL-DABS schemes during the respiratory challenge. DABS data were collected with background suppression pulses at TI_{BGS1}=402 and TI_{BGS2}=632ms and a 1550 ms post-label delay. LL-DABS parameters were $TI/TA_1/TA_2/TR$ = 200/300/1300/4000ms with 9 readout times per TR, FA = 35° and TE = 16ms for phases 1-8, and FA = 90° and TE = 25 ms for phase 9. IR data (10 TI's: 100-2500ms) were collected to form a T_1 map from which to create GM masks ($1.7<T_1<2.1$ s). M_0 was estimated for each scheme from a corresponding base image.

Motor task: CBF and BOLD data were acquired with LL-DABS (parameters as above) in response to a motor task (bilateral fingertap: 24s on, 40s off, 7 cycles).

Analysis: For DABS and LL-DABS, label and control images were subtracted to produce perfusion-weighted (PW) images. BOLD-weighted data were motion corrected using MCFLIRT (FSL, Oxford) and parameters applied to ASL data. A motor ROI was formed by GLM analysis (FEAT, FSL) on the LL-DABS fingertap PW data and used for both CBF and BOLD analysis. Data were divided into active (hypercapnia/fingertap) and baseline (normocapnia/rest) periods and mean BOLD change calculated across the GM and the motor ROI. LL-DABS signal curves were fitted to a multi-compartment kinetic model [3] for CBF and tissue transit time. DABS images were converted to CBF using a single compartment kinetic model [4]. T_1 was assumed to be 2.2 s and 2.0 s for blood and tissue respectively, and M_0 scaled for changes in T_2^* under hypercapnia/motor activation. The relative changes in CBF and BOLD were used to calculate the calibration constant *M* [5] for the GM ROI (assuming α=0.2, β=1) and subsequently used to estimate relative $CMRO_2$ in response to the motor task. Statistical comparisons were made using Wilcoxon Signed Rank Tests in SPSSv16.

	CBF (ml/100g/min)	Tissue transit time (ms)
DABS	NC 42 ± 5	--
	HC 47 ± 6	--
LL-DABS	NC 49 ± 12	520 ± 67
	HC 61 ± 9	442 ± 52

Table 1) Absolute CBF and tissue arrival time for normocapnia (NC) and hypercapnia (HC). Results averaged across subjects (mean ±SEM)

Results: There was no significant difference in normocapnic CBF between schemes, but the LL-DABS measurement of CBF under hypercapnia was significantly higher than for DABS (Fig. 2B, P=0.04, Table 1), attributed to the transit time change in response to hypercapnia. There was no significant difference in BOLD reactivity between the schemes (Fig. 2C). Significantly higher *M* values were estimated using DABS (88±46%) compared to LL-DABS (15±7%) (P=0.04). Motor activation increased BOLD signal by 2.6±0.2%, CBF by 51±7% and reduced tissue transit time from 650 ± 89 ms to 346 ± 13ms, averaged across the motor ROI. Combining these measurements resulted in a significantly greater $CMRO_2$ estimation with DABS (36±11%) in comparison to LL-DABS (14±45%) (Fig. 2D, P=0.03).

Conclusion: Simultaneous CBF/BOLD acquisition is important for the calibration of the BOLD signal and to investigate cerebrovascular reactivity. Our novel LL-DABS sequence allows quantification of both CBF and transit time, whilst maintaining high BOLD sensitivity. We demonstrate that single phase ASL may lead to overestimation of CBF and subsequently hypercapnia calibrated BOLD measures of $CMRO_2$, due to individual variability in transit time in response to hypercapnia. The LL-DABS scheme will provide the sensitivity required for simultaneous acquisition of CBF, BOLD and cerebral blood volume (CBV) [6] using a combined hyperoxia/hypercapnia paradigm.

References:[1] Tancredi et al. *JMRI* (2012) [2] Wesolowski et al. *Proc. ISMRM* (2009) [3] Francis et al. *MRM* (2008) [4] Buxton et al. *MRM* (1998) [5] Davis et al. *PNAS* (1998) [6] Driver et al. *Neuroimage* (2012).