High temporal resolution quantification of global $CMRO_2$ during apneic challenge

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INTRODUCTION: $CMRO_2$ (cerebral metabolic rate of oxygen consumption) is an important index of cerebral oxygen metabolism found to be altered in many neurological diseases [1,2]. Although recently developed MR-based methods achieve $CMRO_2$ quantification with 25 s temporal resolution [3,4], improving this temporal resolution further is needed to quantify $CMRO_2$ changes in response to short term physiologic stressors, such as breath hold apnea. While the normal physiologic response to apnea involves central vasodilation to maintain cerebral oxygen delivery [5], it is hypothesized that this response becomes blunted in patients with obstructive sleep apnea (OSA) [6,7], potentially contributing to the neurological complications associated with the disease. We present a $CMRO_2$ quantification method with 5-second temporal resolution and apply it to a breath hold paradigm, illustrating the potential of the method to investigate changes in cerebral metabolism and cerebrovascular reactivity during dynamic stressors.

METHODS: An interleaved, multi-slice GRE pulse sequence (**Fig. 1**) was developed to simultaneously measure total cerebral blood flow (tCBF) in the carotid and vertebral arteries of the neck and venous oxygen saturation (S_vO_2) in the superior sagittal sinus (SSS) of the head. The sequence alternates between two interleaves: 1) a neck-level non-phase encoded single-echo acquisition (TE1) with toggled first gradient moment to generate 1D projection velocity images to quantify total cerebral blood flow (tCBF) [8] and 2) an identical head-level single-echo acquisition (TE2) to quantify SSS blood flow (SSSBF) followed by a phase-encoded multi-echo acquisition (TE3&4) in the same TR to generate 2D phase difference maps to quantify SSS S_vO_2 [9]. Venous signal in the neck is suppressed by a saturation band inserted before each neck interleave.

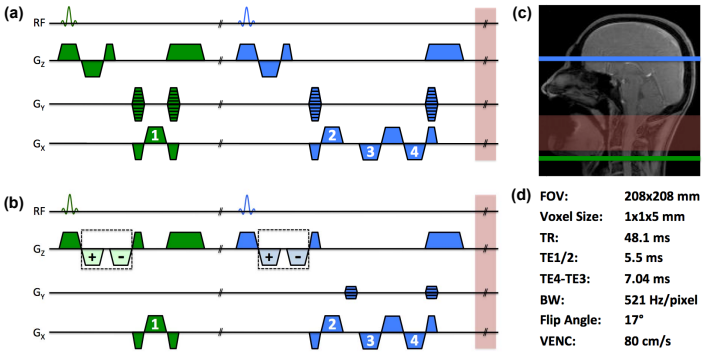

Figure 1: Pulse sequence diagram: **(a)** reference image with full phase encoding before TE2; **(b)** main loop with projection velocity encoding (alternating positive and negative first gradient moment indicated by dashed boxes) followed by keyhole phase encoding after TE2; **(c)** sagittal image indicating locations of head slice (blue), neck slice (green), and venous suppression band (red); **(d)** imaging parameters.

Prior to running the main sequence loop, a 2D flow-compensated reference image (**Fig. 1a**) is generated by inserting phase encoding lobes before TE1&2. The central k-space line of this reference image, with vessels masked prior to k-space transformation, is subtracted from the velocity-encoded projections to eliminate signal contribution from static tissue [8]. tCBF in the neck vessels is then determined by taking the phase difference between consecutive projections with alternating positive and negative first gradient moment. S_vO_2 is quantified by measuring the phase accumulation in the SSS between TE3&4, a result of the paramagnetic properties of deoxyhemoglobin [10-12]. During the main loop (**Fig. 1b**), the number of phase encodes is reduced by four fold to 52, and 2D phase maps are reconstructed using keyhole with outer k-space filled from the fully sampled reference image. $CMRO_2$ is quantified by Fick's principle as the product of tCBF and the arterio-venous difference, normalized to brain volume and hematocrit (Hct): $CMRO_2=C_a \bullet tCBF \bullet (S_aO_2-S_vO_2)$. tCBF and S_vO_2 are determined from phase images, S_aO_2 measured with pulse oximetry, brain volume measured with a 3D MPRAGE image set [13], and hematocrit assumed as 0.4.

Two healthy subjects (24 y.o. F, 26 y.o. M) were scanned during a breath-hold paradigm involving an initial 90 s baseline followed by two end-expiratory breath holds of 40 s and 30 s with 90 s recovery after each. Projection velocity data were time averaged to match the 5 s temporal resolution of the susceptometry acquisition. All experiments were performed on a 3T Siemens Trio scanner using a 12-channel head and 2-channel neck coil.

RESUTLS AND DISCUSSION: S_vO_2, tCBF, SSSBF, and $CMRO_2$ are plotted for a healthy 26 y.o. subject during a breath-hold paradigm (**Fig. 2a**). Pulse oximetry derived S_aO_2 did not change and therefore was assumed to remain constant at 98%. $CMRO_2$ averaged over the initial 90 s baseline was 118±6 $\mu molO_2/100g/min$, in agreement with literature [3]. Flow and S_vO_2 are observed to increase during breath hold and drop during recovery, undershooting before returning to baseline, while $CMRO_2$ remains relatively constant during breath-hold, dropping during recovery before returning to baseline. The transient $CMRO_2$ drop post-apnea results from the ≈5-10 s delay in S_vO_2 recovery relative to tCBF recovery after cessation of breath hold. This delay may result from the time needed for blood measured in the neck slice to reach the head slice, but, surprisingly, it becomes more pronounced (≈15 s) when considering flow in the SSS. Furthermore, SSSBF increases about twice as much relative to baseline than tCBF (105% vs. 48%). For this reason, calculating $CMRO_2$ with SSSBF substituted for tCBF (**Fig. 2b**) changes the observed $CMRO_2$ response significantly, causing a marked increase during breath-hold with return to baseline during recovery. The lack of drop in pulse oximetry derived S_aO_2 values during breath hold is questionable given the demands of the paradigm. In the future, we will attempt to measure S_aO_2 in addition to S_vO_2 in cerebral arteries to eliminate the need for pulse oximetry.

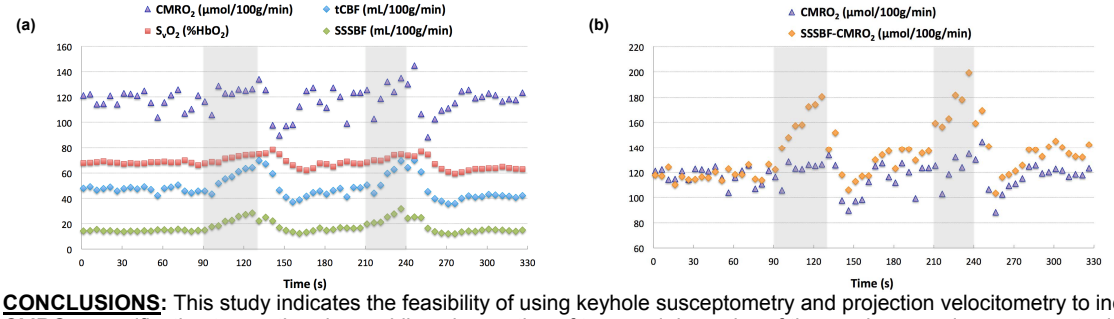

Figure 2: (a) plots of S_vO_2, tCBF, SSSBF, and $CMRO_2$ vs. time with breath hold periods indicated by shaded boxes; **(b)** effect of calculating $CMRO_2$ with SSSBF substituted for tCBF (baseline values are normalized between data sets for comparison).

CONCLUSIONS: This study indicates the feasibility of using keyhole susceptometry and projection velocitometry to increase the temporal resolution of $CMRO_2$ quantification to 5 s, thereby enabling observation of temporal dynamics of the cerebrovascular response to dynamic stressors. This technique will be applied to answer questions such as how $CMRO_2$ responds to apnea and whether this response is altered in diseases such as OSA.

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