Estimation of blood transit time differences through pCO2 manipulation with BOLD MRI in different cerebral vascular territories

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Introduction: Cerebrovascular reactivity (CVR) is a measure of the brain's autoregulatory capacity and can be measured using BOLD MRI combined with inhaled CO_2 manipulation. Although the magnitude of the BOLD signal is primarily employed to assess the reactivity of the cerebral vasculature, the temporal delay of the BOLD response may contain useful information concerning blood transit times. Since the CO_2 can be considered as a blood flow contrast agent, it is possible to extract relative transit time maps similar to those obtained with dynamic susceptibility contrast (DSC) MRI. In this study, we calculated the time delay differences between vascular territories of the anterior, middle, and posterior cerebral arteries as well as white compared to overall grey matter.

Material and Methods: Ten healthy male volunteers (age range 25-42 years) were imaged on a 1.5T MRI system (GE Medical Systems, Milwaukee, WI). The functional sequence was a BOLD MRI protocol with the following parameters: 28 slices, slice thickness = 4.5mm, 64x64 matrix size, FOV=200mm, TR=2240ms, TE=40ms, 320 frames, flip angle = 85°, and a spiral readout. The gas mixture was administered to the subject in the MRI scanner using a re-breathing device described previously by Vesley al [1]. Hypercapnia was induced by delivering 8% CO_2 balanced with 92% O_2 for 15 sec at a flow rate of 14 L/min, followed by 30 seconds of 100% O_2 at 1.5 L/min during which the subjects re-breathed their expired gases. Subsequent to this state, hypocapnia was induced by using 12 to16 L/min of 100% O_2 for a period of 45 seconds. The total length per cycle was 90 seconds, which was repeated 8 times resulting in a total scan duration of 12min for one experiment. The BOLD sequence was always started in synchrony with the flow sequencer and end tidal pCO_2 was recorded. Each subject underwent a series of 4 experiments (2 on the same day, 2 others 1-2 weeks later). In addition, anatomical T1-weighted images were acquired for co-registration purposes. All data was transferred to an independent workstation for further analysis. Each dataset was transformed into Talairach space using AFNI software. Spatially averaged data from grey matter were obtained using a standard magnitude CVR map representing the correlation between BOLD signal and end tidal pCO_2 (time-adjusted for maximum correlation to average BOLD signal) thresholded at r=0.3. Grey matter was subdivided into middle, anterior and posterior cerebral artery territories using vascular territory maps previously defined in our laboratory. Deep white matter ROIs were drawn manually. All ROIs were selected over the same volume (15 mm in thickness) above the corpus callosum (Talairach coordinate z=24.5-39.5mm). The average time-courses were Fourier transformed, and the phase at the CO_2 frequency (1/90 Hz) was used to calculate the time delay (with phase-unwrapping where appropriate to ensure all delays fall within a physiologically meaningful window ±45sec around the average brain response). Statistical analysis was performed using a 2 tailed t-test.

Results: A difference was observed between the posterior and anterior circulation of 1.3sec ±0.25 ($p<0.005$) and a difference between grey and white matter transit time of 5.8sec ± 1.4 ($p<0.005$). The overall within-subject reproducibility error was 0.8 sec for posterior-anterior difference measurements.

Discussion: The observed transit time differences are in line with values reported previously for DSC imaging [2]. The transit time differences for the different vascular territories show quite good reproducibility, which is mandatory for using this technique in patients with cerebrovascular diseases where autoragulatory capacity is compromised. Since there is very tight coupling between blood CO2 and blood flow, a time varying change in CO2 causes a similar time varying change in blood flow that leads to the same temporal variation in dHb concentration (in the setting of constant oxygen utilization by the tissue) measurable directly with BOLD MRI. The relative time at which the BOLD signal changes yields information about perfusion delay. We believe that the use of CO_2 inhalation combined with BOLD MRI may provide a less invasive alternative to DSC which is currently under investigation in our laboratory.

References: [1]Vesely et al. (2001) MRM 45(6): 1011-3
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