Mapping autoregulatory capacity through manipulation of pCO2 with BOLD MRI - a reproducibility study

A. Kassner[1], J. Poublanc[2], D. Mikulis[2], A. Crawley[2]

[1]Medical Imaging, University of Toronto (UHN), Toronto, Ontario, Canada, [2]Medical Imaging, The Toronto Western Hospital of the UHN, Toronto, Ontario, Canada

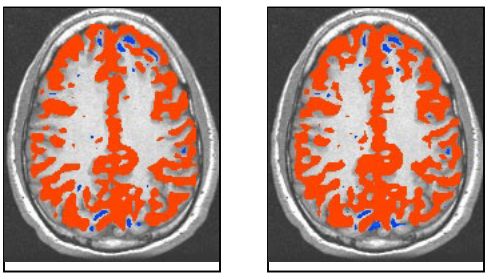
Introduction: Combining inhaled CO_2 manipulation with BOLD MRI is a promising method for assessing regional differences in cerebrovascular reactivity (CVR) which is a measurement of the brains autoregulatory capacity. This becomes important for the assessment of vascular disorders in which autoregulation is compromised or exhausted such as in moyamoya disease or carotid stenosis/occlusions. Since this technique is beginning to be used pre-operatively to guide surgical decision making and to assess efficacy of revascularization, knowledge concerning reproducibility is essential in establishing the accuracy of this method. This study provides quantitative CVR measurements by correlating BOLD MR signal intensity with square wave changes in end-tidal pressure of CO2 ($p_{ET}CO_2$).

Materials and Methods: Ten healthy male volunteers (age range 25 - 42 years) were imaged on a 1.5T GE Signa MR system 4 times (2 sequential runs on day1 and 2 sequential runs on a separate day 1-2 weeks later) using a rebreathing circuit as previously described by Vesely et al. [1]. The subject was placed inside the scanner and the rebreathing device was applied. Scanning was performed using a standard single shot BOLD protocol with a spiral read out (TE=40ms, TR=2240ms, FA=85°, FOV=20mm). Scanning duration for each run was 12 minutes for an acquisition of 320 volumes. Each volume contained 28 slices and spatial resolution of the BOLD data was approx 3 x 3 mm with a slice thickness of 4.5mm. In addition, high resolution T1 weighted images were acquired for co-registration purposes. Changes in $p_{ET}CO_2$ were achieved by controlling the subjects inspired gases with the aid of a nose clip, a mouthpiece, the rebreathing circuit, and a gas sequencer. To ensure that end-tidal gases are representative of lung gas concentrations, subjects were instructed to breathe deeply during the test. The test itself consisted of eight cycles of hypercapnia (45sec at ~ 50mmHg) interspersed with eight cycles of hypocapnia (45sec at ~ 30mmHg) all of which was regulated by an automated sequencer. Hypercapnia was induced by administering a gas mixture of 8% CO_2/92% O_2 at 14L/min for 15 sec and maintained at plateau for a subsequent 30 sec by reducing gas flow to 1.5-2 L/min of O_2. During the plateau phase, the decreased inflow of fresh gases resulted in rebreathing of previously exhaled gases contained in the expiratory reservoir tube. Intervals of low CO_2 were achieved by supplying subjects with 15sec of high flow (16-18 L/min) of 100% O_2 and maintained by O_2 flow at a rate of 12-14 L/min. Partial pressures of end-tidal CO_2 ($p_{ET}CO_2$) and O_2 ($p_{ET}O_2$) were monitored continuously using a commercially available capnograph and recorded digitally at a sampling rate of 60Hz/channel. After completion of the measurement, the collected $p_{ET}CO_2$ data was reduced to one measure of $p_{ET}CO_2$ per breath and correlation analysis with the BOLD data was performed. Prior to this, the BOLD data was co-registered to compensate for motion artifacts. Signal of the whole brain was used as a reference to determine the shift needed to bring the CO_2 and the MR data sets in phase. Once in phase, CVR maps were calculated on a pixel by pixel basis from the slope of the regression of the percentage change of MR signal on the $p_{ET}CO_2$. This leads to a measure of reactivity expressed in units of % Δ MR signal/mmHg $p_{ET}CO_2$. A variance components analysis was used to estimate variability between runs, different days and subjects. Reproducibility was quantified using the interclass correlation coefficient (ICC).

Results: BOLD signal changes were on average 0.16 %Δ MR signal/mmHg $p_{ET}CO_2$ which was in good agreement with other activation studies. Results for the day to day variation of runs show excellent reproducibility with an ICC=0.86 (95%CI:0.62-0.96) for the entire brain and an ICC=0.90 (95%CI:0.70-0.97) for correlated values above r=0.3. Images from a typical experiment are shown in figure 1. Within a session, there is approximately a 95% chance that repeated measures for entire brain values on a subject would lie within ±0.017 %Δ MR signal/mmHg $p_{ET}CO_2$ of each other. For values above r=0.3, the measurement error is slightly higher in the absolute sense. Here, 95% of repeated reads should lie within ±0.029 %Δ MR signal/mmHg $p_{ET}CO_2$ of each other.

Discussion: This study demonstrates excellent reproducibility of a controllable physiological stimulus (CO_2) for the quantitation of CVR measurements using BOLD MRI. This will allow the application of this technique as a useful tool for guiding treatment decisions in cases where autoregulatory capacity is either compromised or exhausted.

References: 1. Vesely et al. MRM 2002



Day 1 Day 14

Figure 1: CVR maps (r=0.3) of a normal volunteer acquired on 2 different days; red indicated normal reacitivty