Assessing vascular reactivity with resting-state BOLD signal fluctuations: a clinically practical alternative to the breath-hold challenge

Hesamoddin Jahanian[1], Wendy W Ni[1], Thomas Christen[1], Michael E Moseley[1], Manjula K Tamura[2], and Greg Zaharchuk[1]
[1]*Stanford University, Department of Radiology, Stanford, California, United States,* [2]*Stanford University, Division of Nephrology, Stanford, California, United States*

Purpose: Measuring vascular reactivity (VR) may provide insights into vascular health and assist in the diagnosis and treatment planning of cerebrovascular diseases such as stroke and Moyamoya[1]. It can also be used in fMRI studies to account for vascular variability between different populations[2]. VR studies measure the ability of vessels to respond to a vasodilatory stimulus such as a change in CO_2 levels. Currently MR based VR experiments are carried out using breath-holding tasks, administration of CO_2 enriched gas, or use of Acetazolamide injection. These methods however, may not be suitable or feasible for all research and patient scenarios. In this study we propose an alternative approach for obtaining VR information using the resting-state blood oxygenation level-dependent (rsBOLD) signal. Spontaneous fluctuations in the rsBOLD time series signal have been observed and used for resting-state fMRI studies[3]. We view the spontaneous rsBOLD signal fluctuations as the response of the brain to the internal challenges to the cerebrovascular system, including heartbeat, inhalation, and baseline neuronal activity. We hypothesize that the response of the brain to these tiny stimuli, as expressed by the normalized amplitude of the rsBOLD fluctuations, may provide information about cerebrovascular autoregulatory and reactivity mechanisms. To test this hypothesis, we compared the magnitude of rsBOLD signal fluctuations to the VR measured as percentage signal change during a breath-holding (BH) challenge in a population of older adults. We chose this population because they are expected to have a more diverse vasculature compared to healthy young population[4].

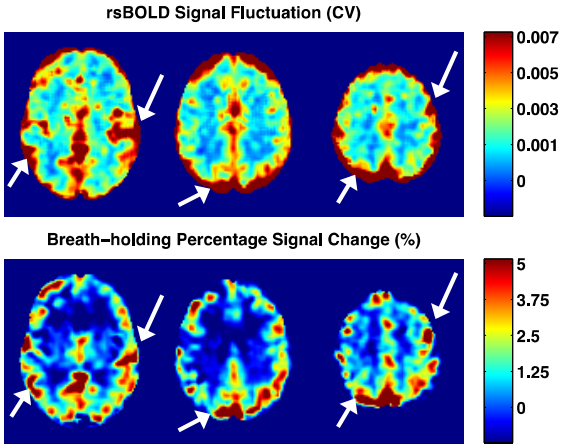

Figure 1. Three slices of an example rsBOLD signal fluctuation and BH percentage signal change maps.

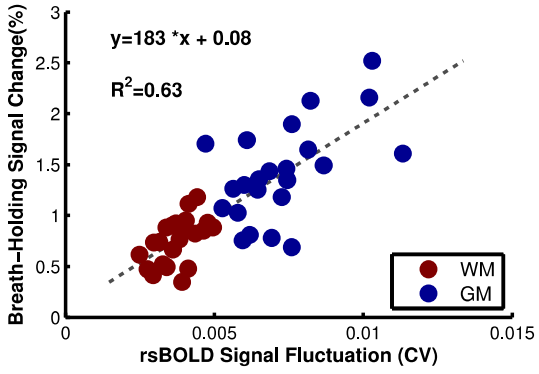

Figure 2. Mean percent signal change in the BH experiment vs. the mean coefficient of variation (CV) of the rsBOLD time series for all subjects within GM (blue) and WM (Red).

Methods: 30 older adults (70±8 years; range 56-83; 12 females) were recruited for this study. 21 of these volunteers were hypertensive and diagnosed with chronic kidney disease. Subjects were scanned at 3T (GE MR750) using an 8-channel head coil. BOLD signals were measured using a 2D gradient echo EPI sequence (FOV=22 cm, matrix= 64×64, slice thickness=3.5 mm, number of slices=35, TR=2 s, TE=25 ms, Number of time points = 120 for rsBOLD and 105 for BH). A 3D T1-weighted image was also acquired using an IR-SPGR sequence covering the entire brain. For each scan, EPI images were realigned, coregistered to MNI atlas, and segmented into grey matter (GM) and white matter (WM) using FSL (http://www.fmrib.ox.ac.uk/fsl). Baseline scanner drifts were estimated and removed from the EPI images by first-order polynomial detrending. The coefficient of variation (CV) of the rsBOLD time series (defined as the temporal standard deviation of the time series divided by the mean signal intensity) for each voxel was calculated. The breath-holding paradigm consisted of 4 cycles of 26 s of normal breathing followed by 4 s of exhalation and 16 s of breath-hold. The breath-hold paradigms were cued using textual instructions. BH data were analyzed using FSL employing a 16 s ramp regressor delayed by 8 s and convolved with gamma variate hemodynamic response function[5]. The temporal derivative of the regressor was also included in the model to allow for temporal shifts between the model and the BH data. Obtained BH results were then converted to percentage signal change. Seven subjects could not adequately comply with the BH task and were eliminated from the study.

Results: Figure 1 shows three slices of rsBOLD signal fluctuation and BH percentage signal change maps in a representative subject. Of note are the common areas of hyper-reactivity detected using both methods (white arrows). Figure 2 plots the mean rsBOLD signal fluctuation and BH percentage signal changes for all subjects calculated within GM and WM masks. As expected the VR was lower in WM compared to GM in both methods.

Discussions and Conclusions: Our results indicate a strong linear relation between the mean CV of rsBOLD signal time series and mean BH percentage signal change in GM and WM across subjects (R^2=0.63). Good spatial correlation was also noted. These results suggest that rsBOLD signal can possibly be used to evaluate VR and cerebrovascular compensatory mechanisms without the need for a breath-holding challenge, which may not always be appropriate or feasible for all experiments. For example, in this study of older adults, although they did not have any acute problems, 7 of 30 (23%) could not perform the BH task. Similar to our experience, others have suggested that the degree of cooperation for breath holding varies too much in patients with neurologic diseases to be considered routinely useful[6]. The proposed approach however, by eliminating the need for cooperation from the subjects can circumvent this problem. This technique may offer a new attractive feature to the rsBOLD fMRI sequence and allow the evaluation of VR in a wider range of conditions (clinical or research) where it may have otherwise been impractical.

Acknowledgements: This work is supported by NIH grants 1R01NS066506, 2R01NS047607, R01 DK092241.
References: [1] Gupta et al, Stroke 43:2884–2891 (2012). [2] Handwerker et al, HBM, 28:846–859 (2007). [3] Wise et al. Neuroimage 21:1652–1664 (2004). [4] Chang et al, J Clin Ultrasound 39, 383-9 (2011). [5] Bright et al, Neuroimage 83:559–68 (2013). [6] Spano et al. Radiology 266:592-8 (2013).