Spontaneous BOLD Signal Fluctuations in the Young and Elderly Brain: a Non-Contrast Biomarker of Cerebral Vasomotor Reactivity?

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

Introduction: Spontaneous fluctuations in blood oxygenation level dependent (BOLD) signal have been observed in resting state time series measurements.[1] Although their precise physiological origin is not yet clear, they are likely to arise from oscillations in metabolic-linked brain physiology, arterial vasomotion and hemodynamics.[1,2] We hypothesized that these physiological fluctuations may reveal cerebrovascular autoregulatory mechanisms and consequently be associated with factors modulating the cerebrovasculature such as aging and hypertension. To test this hypothesis, we compared the magnitude of spontaneous BOLD fluctuations in two populations: 1) young healthy adults and 2) hypertensive elderly subjects with chronic kidney disease (CKD).

Methods: Nine healthy young volunteers (31±6 yrs; range 24-45) and nine older adults (73±9 yrs; range 59-86) were recruited for the study. Older adults were recruited as part of the SPRINT MIND the Kidneys trial, who were hypertensive and diagnosed with CKD defined as baseline estimated glomerular filtration rate (eGFR) <60 ml/min/1.73m^2. Subjects were scanned at 3T (MR750, GE Healthcare, Waukesha, WI) 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=20, TR=2 s, TE=25 ms, Number of time points = 120). A 3D T1-weighted image was also acquired using an IR-SPGR sequence covering the entire brain (TR/TE/TI = 8.18/3.2/900 ms, matrix = 256 × 206, in-plane resolution = 0.94 × 0.94 mm, slice thickness = 1 mm, 176 sagittal slices). EPI images were realigned using SPM8 software package (http://www.fil.ion.ucl.ac.uk/spm/). The 3D T1-weighted image was coregistered to the EPI images and segmented into gray matter (GM) and white matter (WM) using FSL software package (http://www.fmrib.ox.ac.uk/fsl). Baseline scanner drifts were estimated and removed from the EPI images by second-order polynomial detrending. The signal fluctuation (SF) for each voxel was then calculated as the temporal standard deviation of each voxel normalized by the mean signal intensity at that voxel.

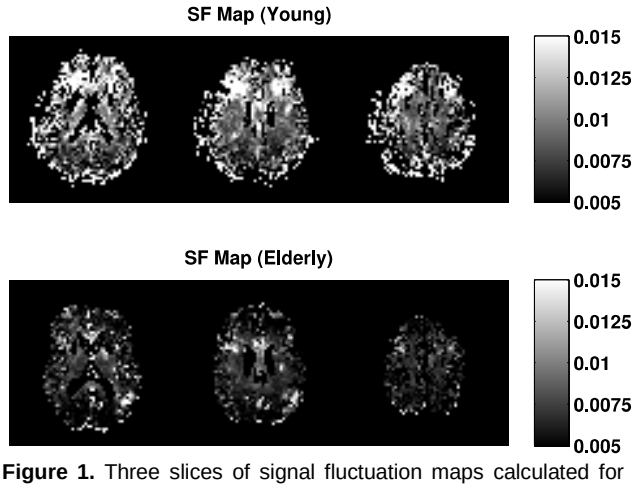

Figure 1. Three slices of signal fluctuation maps calculated for two representative subjects of hypertensive elderly (lower panel) and young healthy (upper panel) populations.

Results: Figures 1 and 2 show three slices of signal fluctuation (SF) maps and the histogram of the SF values obtained in representative young and elderly subjects. Mean SF values in GM and WM for all subjects are presented in figure 3. As can be seen, the signal fluctuations are higher in GM than WM in both populations. The difference between the mean SF values in GM and WM, however, is greater for the young adult population (Data not shown here). There is a statistically significant difference in SF values between the two populations in both GM and WM. The difference however is more significant in WM compared with GM (P value of 0.0067 vs 0.0445).

Discussions and Conclusions: Our preliminary results indicate a statistically significant difference in the BOLD signal fluctuations between the young and elderly cohorts. In this study however, we are not able to distinguish the effects of aging, hypertension, and CKD on the signal fluctuations. It is intriguing that WM fluctuations are particularly affected in the elderly group, many of whom also have significant WM hyperintensities on FLAIR imaging. Of note also is the ability to derive a marker of vascular reactivity without the use of contrast agents, which cannot be used in patients with CKD. Further studies with healthy elderly populations and those without CKD are required to assess the specificity of these findings. However, these initial results suggest that spontaneous signal fluctuations of BOLD signal can possibly be used to evaluate the cerebrovascular compensatory mechanisms and may provide valuable information about different cognitive disorders.

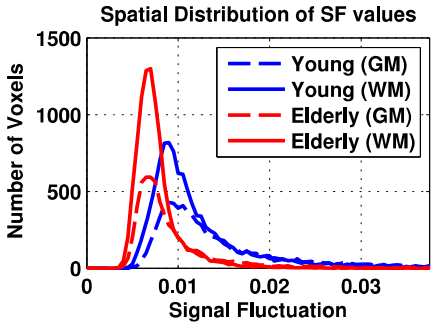

Figure 2. Histograms of the signal fluctuation (SF) values in GM (dotted lines) and WM (solid lines) for two representative subjects of hypertensive elderly (red) and young healthy (blue) populations.

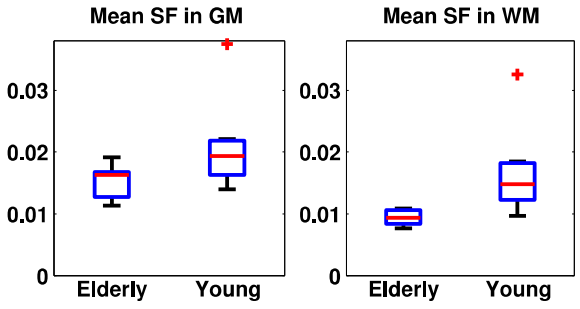

Figure 3. Boxplots of mean signal fluctuation (SF) in GM (left) and WM (right) for young healthy and hypertensive elderly populations.

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References:
[1] Kruger et al. MRM 46:631–637, 2001.
[2] Wise et al. NeuroImage 21:1652–1664, 2004.