Resting state BOLD fluctuations in large draining veins are highly correlated with the global mean signal

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Introduction: The removal of a global mean signal has been widely adopted in the processing of resting-state fMRI studies [1]. However, there has been recent controversy regarding its usage, since negative correlations with a seed ROI are mathematically mandated after regressing out the whole brain global mean signal (denoted as 'whole-gs') [2]. Here we introduce an alternative "global" signal based on the BOLD signal in the large draining veins. The basic idea is that fluctuations in these draining veins will represent the sum of fluctuations from smaller venules that are upstream. For example, the BOLD signal from the sagittal sinus ('sinus-gs') will average the fluctuations from venules in the cerebral cortex, while that from the great vein of galen ('galen-gs') averages the signals from the basal ganglia region. In this pilot study, we compared the relationship between the 'whole-gs', the 'sinus-gs', and the 'galen-gs' signals.

Methods: The data were collected on a GE Signa HDx 3T scanner with an 8-channel head coil from one healthy male subjects. The scan protocol included a susceptibility weighted imaging (SWI) scan, a sagittal T1 weighted 3D anatomical scan, field maps, and two resting state BOLD scans. The resting scans were acquired with an echo-planar imaging sequence (TR = 2s, TE = 30ms, flip angle = 90°, slice thickness = 4mm with gap = 1mm, FOV = 24cm, matrix size = 64×64, reps = 185). All images were coregistered in AFNI. The SWI scan used the parameters for 3T described in [3]. The region of interest (ROI) masks for the sagittal sinus and the great vein of galen were defined based on the SWI minimum intensity projection (mIP) map. A whole brain mask was also generated from the anatomical data. All these masks were then resampled to the resolution of functional data. Preprocessing for the functional images included field map, slice-timing and head-motion corrections. The first 10 volumes of both functional runs were discarded due to T1 equilibration. The resultant data were low-pass (<0.1Hz) filtered after regressing out nuisance terms, which included constant and linear trends and head-motion parameters. These corrected data were further normalized on voxel-wise basis by the standard deviation of the voxel time course. The global signals were calculated by averaging the corrected data over the voxels in the whole brain mask for the 'whole-gs' (excluding the sagittal sinus and galen vein regions), in the sagittal sinus mask for the 'sinus-gs', and in the galen vein mask for the 'galen-gs' respectively. Cross correlations were calculated between the 'whole-gs' and the 'galen-gs', as well as the 'sinus-gs'. For comparison, we also showed the correlation maps with PCC after regressing out different global terms.

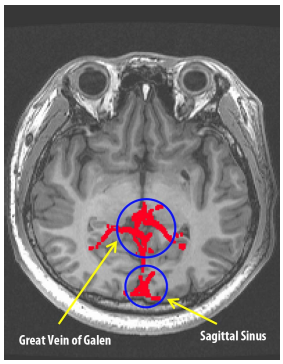

Fig. 1. The high-resolution vein ROI masks overlaid on its anatomical slice.

Results: Fig. 1 shows two high-resolution vein masks (in red) from a single slice overlaid over a high-resolution structure image. As labeled in red, the upper ROI is for the great vein of galen, whereas the lower one is the sagittal sinus. The ROIs were down-sampled into the same size as functional data for global signal calculation. The averaged signal of each ROI is compared with the 'whole-gs' for both runs (Fig. 2). Both 'galen-gs' and 'sinus-gs' are well correlated with 'whole-gs' in both runs ($p<0.005$ for 'sinus-gs' in run1, and $p<0.0001$ for the other three conditions in Table 1). The correlation maps with PCC with different combination of global signals are shown in Fig 3.

	'galen-gs'	'sinus-gs'
Run1	0.5430	0.2172*
Run2	0.8210	0.4955

Table 1. Correlation between 'whole-gs' and 'galen-gs', as well as 'sinus-gs'. *: $p<0.005$, $p<0.0001$ for other correlation values.

Discussion: Our results suggest that resting-state BOLD signals from the major veins, such as the 'galen-gs' and 'sinus-gs', could be used as global signal estimators. Physiologically, the vein signal fluctuation in the sagittal sinus reflects the average of deoxyhemoglobin fluctuations from cortical cortex; while that in the galen contains overall information from basal ganglia region. The high resolution mIPs provide a good opportunity to locate the vein regions. As the regions of sagittal sinus and galen are defined based on anatomy, the mathematical problem of forcing negative correlations between brain networks by averaging method with the 'whole-gs' [2] is avoided. However, a potential drawback of the venous global signal estimators is that phase information in the time signals may be lost due to variable hemodynamic delays.

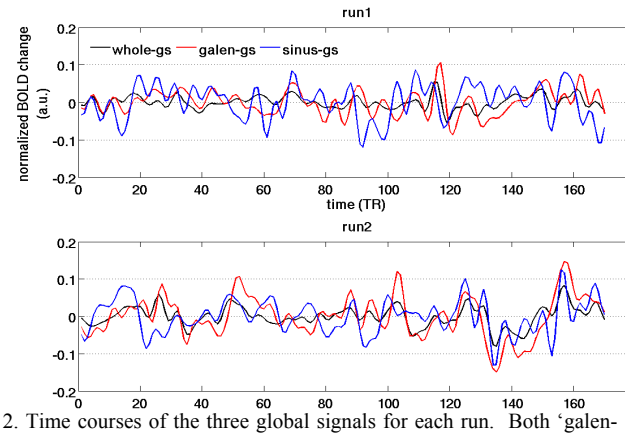

Fig. 2. Time courses of the three global signals for each run. Both 'galen-gs' (in red) and 'sinus-gs' (in blue) are correlated with 'whole-gs' (in black).

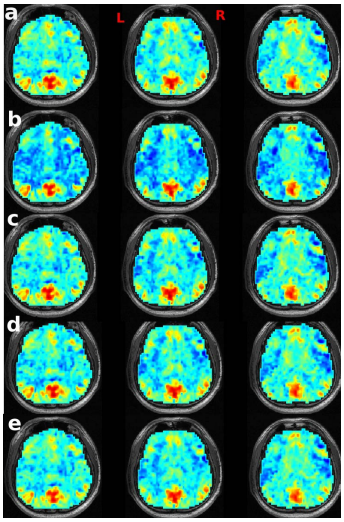

Fig. 3. Correlation maps with PCC after regressing out a) none; b) whole-gs; c) both galen-gs and sinus-gs d) galen-gs; e)sinus-gs

References

[1] Fox et al., J Neurophysiol 101:3270-3283, 2009. [2] Murphy et al., Neuroimage,44:893-905, 2009. [3] Haacke et al., AJNR 20:19-30, 2009.