VENOUS SUPPRESSION IN RESTING STATE FMRI: IMPLICATIONS FOR CORRELATION ANALYSIS

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Introduction:

Resting state functional MRI (RS-fMRI) is a popular technique for studying functional connectivity in the brain. However, the spatial specificity of the connectivity maps is limited by the strong biasing of the BOLD signal to macroscopic veins[1], which can shift the detected signal away from the site of true activation and influence connectivity measures through coherent oscillations. Macroscopic veins, in addition to producing magnitude BOLD-related signal changes also exhibit a strong MR signal phase response. This knowledge can be used to identify and remove venous signals from datasets[2]. In this work, a phase regressor technique is employed to remove venous contributions from RS-fMRI datasets, resulting in substantial changes in the spatial organization and correlation values of resting state signal correlation maps.

Methods: *Phase regressor***:** Correlated magnitude and phase changes are removed on a per voxel basis via a modification of the phase regressor technique as introduced in [2]. Briefly: on a per voxel basis, given a magnitude signal timecourse S, and a phase timecourse Φ, each with standard deviation σ_S and σ_Φ respectively, one can find the best linear estimate $S_{est} = A\Phi + B$ via minimizing the chi-square:

$$\chi^2(\Phi, S) = \Sigma_i \left(S_i - B - A\Phi_i \right)^2 / \left(\sigma_S^2 + (A^2 \sigma_\Phi)^2\right).$$

Magnitude time-courses are then filtered by removing the signal component explainable by the phase: $S_{filt} = S - S_{est}$. Originally applied to task-based fMRI investigations, it was suggested to estimate the voxel-wise non-BOLD signal standard deviations by filtering the timecourses at the paradigm frequency. In RS-fMRI there are no constrained events as subjects are free to cycle through mental processes, thereby requiring a novel approach. Since RS-fMRI is typically analyzed in a band-pass frequency region of 0.01 to 0.1 Hz, where physiologically relevant correlations are measurable, σ_S and σ_Φ are instead estimated from the high-pass filtered timecourses at frequencies greater than 0.2 Hz.

*Imaging***:** Sample data from a consenting, healthy volunteer were acquired on a 7T MRI scanner. Five minutes of resting state EPI data were acquired at a 1.5mm isotropic resolution with a 220mm x 180mm FOV and 70 oblique-axial slices to cover the brain. EPI data were accelerated with a GRAPPA factor of 3 in-plane, and a slice-multiplexing acceleration of 2. TR=2s, TE=20ms.

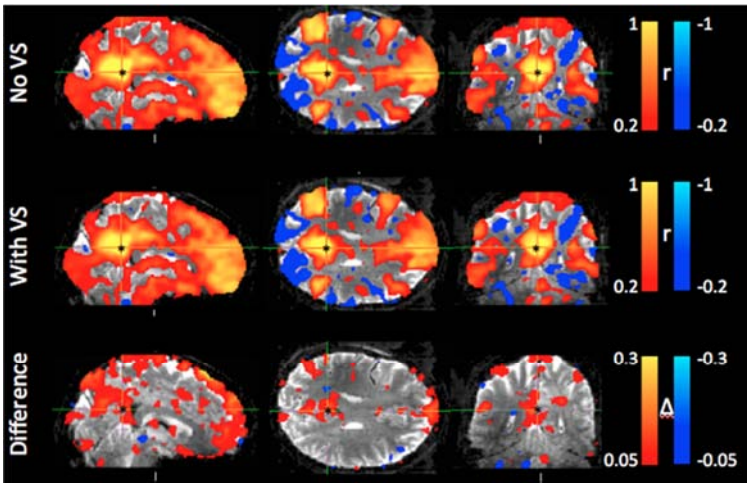
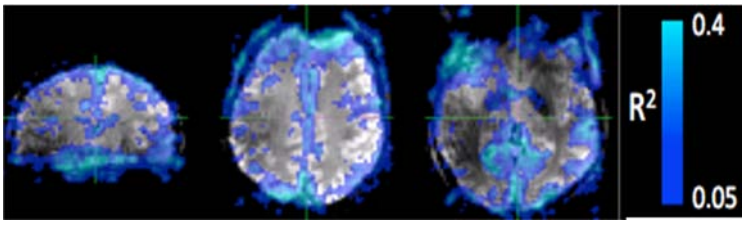


Figure 1 (top): Seed based correlation maps (see text) of DMN. Seed region is identified by the crosshairs and asterisk. Maps generated from the original *(top row)* and filtered *(mid)* data are shown, as well as a difference map *(bottom).* Differences in correlations are most pronounced in areas that are potentially vascular in nature.

Figure 2 (below): Coronal and two axial slices from a map of R^2 quality-of-fit of phase to magnitude data. Higher values respresent regions where more of the signal was explainible by the phase componenet and thus filtered out. Larger values are present around the periphery of the brain as well as throughout the midline and sagittal sinus areas.



Results:

Figures 1 and 2 demonstrate the results of applying the phase regressor to the sample dataset.

*Seed based analysis***:** For demonstration of the effect of the phase-regressor on resting state data, seed based correlation analysis was performed after motion correction, low pass filtering, and blurring with a 3mm gaussian kernel. A seed was placed in the posterior cingulate (PCC), generating maps of the default motor network (DMN). Differences in correlations (filtered - original) were then generated (see Figure 1).

Conclusion and Discussion:

Use of the phase regressor technique as modified for RS-fMRI has the potential to reduce venous signal contribution, as evidenced by differences in measured spatial correlation maps of resting state networks. Regions that showed strong correlations between the magnitude and phase timecourses (Figure 2) suggest that mostly vascular sources are being identified and filtered. Our results demonstrate a very strong vascular contribution to both the spatial pattern and correlation values of conventional resting state maps. However, the phase signal can also be strongly affected by residual motion, and as such, future work will attempt to identify the source of these phase changes and implement methods for their removal.

References: [1] RM Hutchison *et al. J Neurophysiol* 107:2463 (2012). [2] RS Menon, *Mag. Reson. Med.* 47:1 (2002).