Presence of AVA in High Frequency Oscillations of the Perfusion fMRI Resting State Signal

Domenico Zacà[1], Uri Hasson[1,2], Ben Davis[1], Nicola De Pisapia[2], and Jorge Jovicich[1,2]
[1]*Center for Mind/Brain Sciences, University of Trento, Mattarello, TN, Italy,* [2]*Department of Psychology and Cognitive Sciences, University of Trento, TN, Italy*

Target audience: Researchers and clinicians interested in understanding and potentially using information extracted from brain resting state activity, in particular high frequency dynamics.

Purpose: The main aim of this study was to investigate the presence of nonrandom transient patterns in the high frequency oscillations of the cerebral blood flow (CBF) resting state signal as recently demonstrated for Blood Oxygen Level Dependent (BOLD) resting state signal (1). To this purpose we measured and compared the amplitude variance asymmetry (AVA) in BOLD and CBF time series generated by MR perfusion imaging resting state data.

Methods: Thirty five participants (mean age = 25.0±5.3, 20 males) with no history of neurological disease gave informed consent to participate in the study, approved by the ethical committee of The University of Trento. Images were acquired with a 4T Bruker Medspec MRI scanner using a birdcage transmit 8 channel receive head coil. Structural images were acquired using a 3D MP-RAGE sequence. Functional images were acquired using a Q2TIPS pulse arterial spin labeling sequence (TR/TE/TI1/TI2/T1s=2000/17/700/1400/1050 ms, FA=72°, in plane resolution 3.0x3.0 mm, slice thickness 7 mm, 9 oblique axial slices parallel to the AC-PC line). A total of 150 EPI volumes were acquired during the functional run. Data analysis was performed using AFNI and FSL software. Structural and functional images were coregistered and normalized to MNI space. Preprocessing included removal of the first 4 volumes to allow for T1 stabilization effects, motion correction, despiking, spatial smoothing (10 mm FWHM) and regression out of the mean CSF time series and the 6 motion parameters. BOLD time series was generated by averaging two consecutive label and control images. The perfusion image series was generated by sinc subtraction of the label and control images, followed by conversion to CBF image series based on the kinetic model (2). For each subject and for each voxel BOLD and CBF time series, AVA was calculated using the following equation: $AVA = log\frac{\sigma^2 peaks}{\sigma^2 pits}$ as reported in (1) where peaks are the local maxima and pits are the local minima in the time series as illustrated in Figure 1.

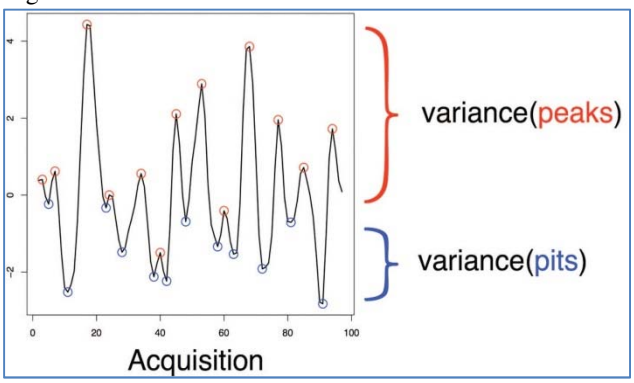

Figure 1: Schematic of AVA calculation in a single-voxel resting-state fMRI time series. For each voxel, deflection points corresponding to local-maxima (peaks, in red) and local-minima (pits, in blue) are identified. The variance of the identified peaks' amplitude is compared with the variance of the identified pits' amplitude.

Group level analysis was performed by applying a T-test to determine whether AVA departed significantly from 0. Both BOLD and CBF AVA maps were thresholded at an alpha level of $p < 0.001$ single-voxel uncorrected, with family wise error controlled using cluster-based thresholding. We then compared the extent of significant AVA for the BOLD and CBF signal by identifying, for each participant, voxels where AVA was statistically significant (p<0.05 using Levene's test). In these voxels we compared also the BOLD and CBF time series characteristics.

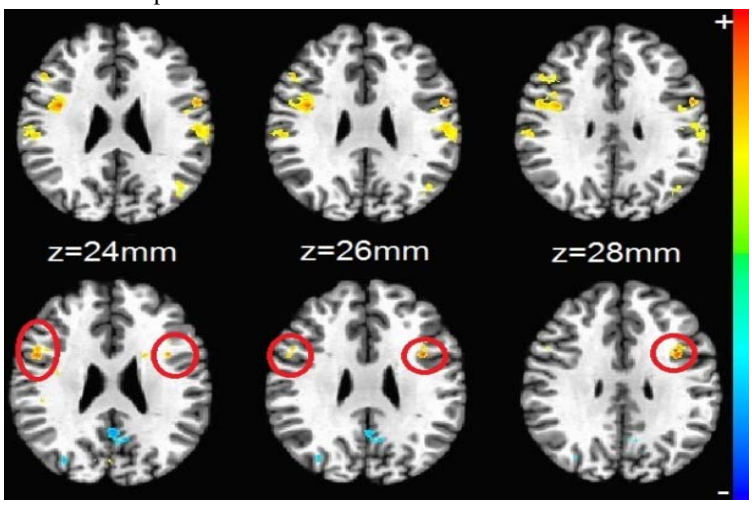

Figure 2: Region showing significant (p<0.001) AVA for the BOLD (top row) and CBF (bottom row).

Results: Figure 2 shows sample slices in the MNI space for BOLD (top) and CBF group-level AVA (bottom). The perfusion-derived BOLD AVA replicated pure BOLD results reported by Davis et al. (1). We detected CBF AVA with similar bilateral patterns as in the BOLD in addition to clusters where the variance of pits was significantly higher than the variance of peaks (blue clusters in Fig.2). The number of voxels where AVA significantly departed from chance was significantly larger for BOLD than CBF (794±434 vs. 540±323, p=0.003). The number of peaks in the CBF time series was significantly higher than the number of peaks in the BOLD time series (21.03±0.56 vs. 19.03±0.67. p<0.0001). The spatial overlap between the two maps was 10.7% (Dice coefficient).

Discussion and Conclusion: This study demonstrates the existence of an AVA pattern in resting state CBF signal, suggesting a neuronal origin of these transients as CBF measurements are more coupled with metabolism than BOLD measurements. The smaller extent of significant AVA in CBF time series may be due in part to a more spatially specific CBF pattern (less affected by venous artifacts) and/or due the lower signal to noise ratio of perfusion signal (3). The higher number of transitions in CBF time series could be explained by the lower intrinsic temporal autocorrelation of the CBF compared to the BOLD time series due to the image subtraction step needed to construct the CBF time course. Improvement on the acquisition data protocol and more investigations on the time series characteristics may clarify these issues.

References: 1) Davis B. et al. *Cereb Cortex* 2013 in press 2) Buxton R. et al. *MRM* 1998;40:383 3)Aguirre GK et al. *Neuroimage* 2002:15:488