Connectivity patterns produced without neuronal activity

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Introduction: Since its inception more then a decade ago, functional connectivity studies using fMRI remain a topic of great interest to neuroscience researchers[1,2]. In particular, resting state scans showing connections between regions that are not actively engaged in a task have been used to study an ever-widening array of brain states and disorders. The underlying assumption for these connectivity studies is that groups of interconnected neurons will produce similar time courses of activation when at rest based on a default mode of interaction. However, it is important to remember that, since these BOLD signals are based on underlying hemodynamic activities, the observed connectivity may not all be associated with neuronal activity. In order to explore whether the basic vascular hemodynamic activity, outside of neuronal activity, is sufficient to create patterns of functional connectivity, we imaged human legs at rest where the vascular signal is predominant. In this study, we aim to determine whether the traditional analysis of functional connectivity has a significant vascular component, which will help design optimal acquisition and analysis strategies for applications in the brain with minimal vascular influences.

Methods: Images were acquired on a GE 3T Excite system using a quadrature coil. The subject placed both calves into the coil, and functional images were acquired using an EPI sequence with TR=2sec, TE=30msec, FOV=25.6cm, with 30 slices each 4mm thick. A total of 150 time points were acquired for a total acquisition time of 5 minutes. Data was corrected for slice-timing differences. The first 5 time points were removed from the data to allow for signal stabilization, and linear trends in the data were removed. A low-pass filter was applied to the data, cutting off frequencies > 0.08Hz.
ICA was applied to the image data using the GIFT program (http://icatb.sourceforge.net). ICA was used rather than an ROI reference time course and correlation since we did not have an *a priori* hypothesis on the connectivity between regions. The algorithm was run to estimate 50 components. The components were inspected to determine potential widespread connectivity patterns.

Results and Discussion: For a representative subject, one component stood out with a great deal of structured activation. This is shown in Fig 1 for five slices. Other components displayed connectivity across the legs as well, but with much smaller spatial extents.

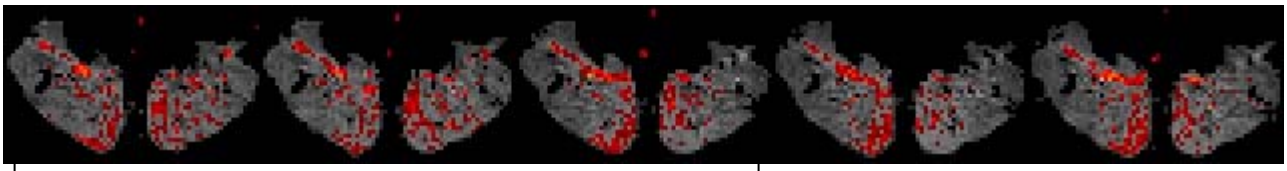

Fig 1: ICA based results showing connectivity in the human leg

The analysis clearly shows what appears to be functional connectivity both within and between legs in a human subject. These patterns extend through multiple slices, as well, and are not limited to single slice planes in individual legs. Given the lack of neuronal activity, the observed connectivity is likely of vascular origin.
In the human brain, the neuronal activation will certainly contribute to hemodynamic changes to create added connectivity. However, as this study shows, the vasculature by itself is sufficient to create patterns of connectivity. Therefore, functional connectivity studies within the brain must be careful to account for the added baseline vasomotion. Alternative approaches which aim to eliminate the vascular signal should also be considered, such as the use of diffusion weighting strategies and ASL techniques with long transit time to acquire signal after capillary exchange.

Conclusion: We demonstrate that basic vascular fluctuations in the absence of neuronal activity are sufficient to produce "connectivity" patterns across large and separate regions. This result suggests that studies of functional connectivity in the brain must carefully consider the input of vascular signals when determining connectivity between brain regions.

References: 1: Biswal et al, MRM, 1995; 2: Lowe et al, NeuroImage 1998