Quantification of reproducible spatiotemporal dynamic patterns using bootstrapping from randomized phase data in the rodent model

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Target audience- This work is intended for groups analyzing and interpreting the dynamic properties of BOLD resting state data.

Purpose- In 2009 Majeed et al. published a manuscript detailing the visualization of spatiotemporal patterns of activity in the rodent cortex [1]. A second dynamic analysis paper [2] was published which delivered an algorithm for automatically detecting the most prominent and repeatable patterns of spatiotemporal activity, which in the rodent propagated from the secondary somatosensory cortex bilaterally towards the primary motor cortex and midline (potentially homologous dynamic patterns have also been seen in humans [2,3]). A limitation of both of our previous studies was the inability to quantify the results based on the continuous nature of the dynamics, providing a value for every voxel in the image regardless of its role in the dynamic pattern. In the work presented here we have overcome this limitation using a bootstrapping algorithm to pinpoint only the significant voxels passing multiple comparison testing, followed by averaging of voxel amplitudes allowing for quantification and inter-subject analysis.

Methods- Single slice, 500 ms TR resting state data was collected from 7 rats. Eleven 8 minute scans from collected from each rat. Preprocessing included whole brain signal regression (dynamics are present with or without GS removal), linear detrending, band-pass filtering (0.01 – 0.3 Hz), normalization to unit variance, and spatial smoothing. Spatiotemporal dynamic templates were generated for each data set according to Majeed et al., 2011. Using the same data set each voxel's timecourse was randomly circularly permuted, and spatiotemporal dynamic patterns were generated from this randomized phase data. This was done 1,000 times for each scan and rat to form a 2-tailed null distribution. P-values were calculated by comparing the actual voxel template value to the cumulative distribution function of the generated null distribution. Strict Bonferroni correction was implemented followed by rejection of spatial clusters less than 25 voxels (based on smallest anatomical component in rodent cortex; secondary somatosensory cortex).

Results- Figure 1 (top) shows the formation of a spatiotemporal dynamic template using the original algorithm. Quantification is difficult due to the continuous nature of template values. Figure 1 (bottom) illustrates the statistically limited amplitude values from the template, overlayed on the mean EPI image, allowing for quantification. Comparing static bilateral functional connectivity to mean amplitude values from statistically thresholded spatiotemporal dynamics reveals a statistically significant linear relationship between the two measures (p = 0.005) (Figure 2).

Discussion/Conclusion- Spatiotemporal dynamic analysis is a novel approach for exploring functional activity, providing a more complete and information dense representation of the complex processes occurring over the duration of a functional scan. Quantification is necessary for inter-subject comparisons. The tight coupling between the quantified dynamics and the static measure of functional connectivity suggests they are directly influencing one another or a product of the same source.
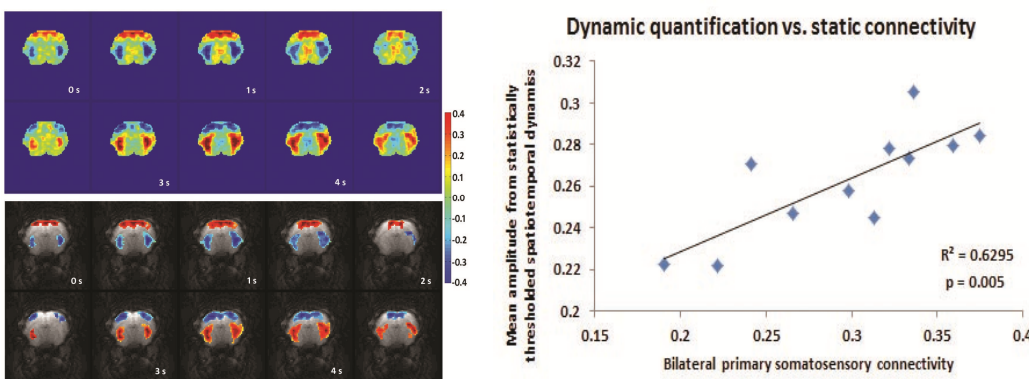

Figure 1 (L): Original spatiotemporal dynamic template (top), statistically thresholded spatiotemporal dynamics overlayed on EPI image for quantification (bottom).

Figure 2 (R): Mean amplitude from statistically thresholded spatiotemporal data vs. static functional connectivity from 7 rats.

References- [1] Majeed W, et al. J Magn Reson Imaging. 2009; 30(2):384-93. [2] Majeed W, et al. Neuroimage. 2011. 54(2):1140-50. [3] Grigg O and Grady C. PLoS One. 2010. 5(10):e13311.