Comparing Behavioral and Region of Interest Driven Effective Connectivity Analyses of Motor Learning

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Introduction: Effective connectivity analyses have vastly improved our understanding of the human brain (Buchel *et al.*, 1999; He *et al.*, 2003; Toni *et al.*, 2002). Although novel, these approaches may be compromised by their dependence upon regions of interest (ROIs), as they typically require *a priori* hypotheses of ROI connectivity and may not account for task-independent correlations across regions with strong anatomical connections. A previously described connectivity analysis based upon behavioral data (James, 2004) was contrasted against a ROI-based analysis to assess the relative merits of both approaches.

Participants/Materials: Fifteen graduate students (nine female) participated in a motor learning study in accordance with Institutional Review Board policy. Participants underwent functional imaging in a 3T Siemens Allegra head dedicated scanner (Siemens). Anatomical images (matrix=256x256, TR=5.24s, TE=13ms, FA=150^{o}, FOV=240mm, 36 slices, slice thickness= 3.8mm without gaps) were obtained for co-registration with gradient echo EPI images sensitive to BOLD signal (matrix=64x64, TR=3s, TE=25ms, FA=90^{o}, FOV=240mm, 36 slices, slice thickness=3.8 mm without gaps) obtained while participants performed a serial reaction time (SRT; Nissen and Bullemer, 1997) explicit motor learning task. Stimuli presentation was coded in E-Prime (Psychology Software Tools) and displayed to participants by LCD screen (MRI Devices). Participant behavioral responses were recorded in E-Prime with a response button glove (MRI Devices).

Data Processing: Functional data underwent motion correction and linear detrending (Brain Voyager, Brain Innovations) with all subsequent analyses performed in Matlab (MathWorks). Seeding analyses were conducted for one participant whose behavioral data demonstrated significant learning of a motor sequence. For the seeding analyses, every brain voxel's timecourse was correlated against a) participant reaction time (RT) and b) the average timecourse of a cluster of cerebellar voxels that were significantly active ($p<.001$) during motor learning. Seeding maps (where each voxel intensity represents its correlation value **r**) were produced for varying minimum correlational and cluster thresholds.

Results: The behavioral (**RT**) seeding method produced stronger correlations than the traditional (**ROI**) seeding approach. To test for false positives, voxels active at high **r** thresholds were checked for occurrence at lower **r** thresholds with larger minimum cluster sizes. For the RT seed, 69% of voxels correlating at |**r**| > .8 were also present at |**r**| > .5 and cluster size > 3. In contrast, only 60% of voxels correlating with the ROI seed at |**r**| > .7 were also present at |**r**| > .4 and cluster size > 3. Figure 1 provides a qualitative comparison of brain regions correlating with both seeds during motor learning.

Discussion: The RT seeding approach produced fewer false positives then the ROI seeding approach, but this difference was not significant. Voxel correlations were stronger for the RT seed than the ROI seed, presumably due to the lesser variance of behavioral measures. Figure 1 (top right) demonstrates the RT seed's greater capacity for detecting ROIs previously established as involved in motor learning, including the supplementary motor area, anterior cingulate, caudate, and frontal cortices. Note that these regions are negatively correlated with RT, indicating increasing activity as reaction times decrease (i.e. performance improves). In contrast, the cerebellar ROI seed demonstrated more widespread (positive) correlation with other cerebellar regions. Using behavioral measures as a seed better differentiates regions involved with a functional task, while the ROI seeding approach better illustrates both task-dependent and –independent connectivity. Together, these techniques stand to significantly improve our understanding of brain connectivity and function than either technique alone.

References:

Buchel C, Coull JT & Friston KJ. (1999). Science, 283, 1538-1541.
He G, Tan L-H, Tang Y, James GA, Wright P, Eckert M, Fox PT & Liu Y. (2003). Human Brain Mapping, 18, 222-232.
James GA, He G & Liu Y. (2003). 12th Scientific Meeting of ISMRM.
Nissen MJ & Bullemer, P. (1987). Cognitive Psychology, 19, 1-32.

Figure 1: Comparison of Correlational Seeding Techniques

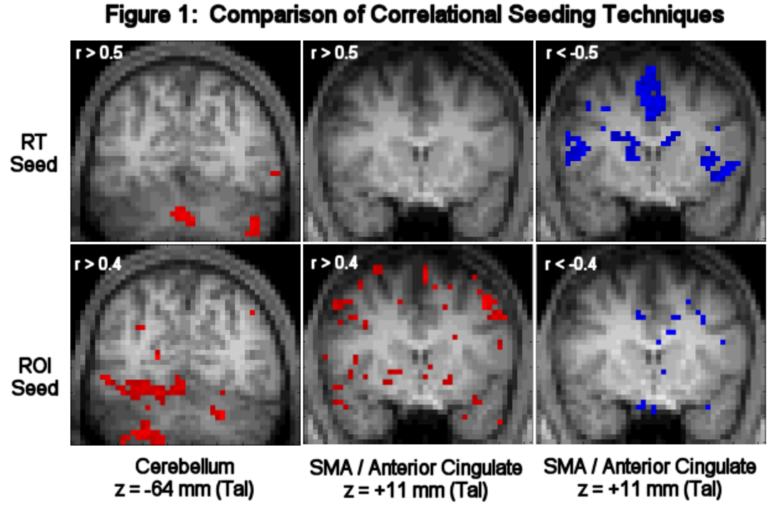

Figure 1: Comparison of Correlational Seeding Techniques. Brain voxel activities' during a motor learning task were correlated with (a) reaction time, a behavioral measures of learning (**RT seed**) and (b) a cerebellar cluster demonstrating significant activation during learning (**ROI seed**). Seeding maps (see Data Processing) were constructed for |r| > .5 (RT seed) and |r| > .4 (ROI seed) with minimum cluster sizes >3.