

Effect of Task/Condition-Related Signal Variance on Functional Connectivity: An fMRI Simulation Study

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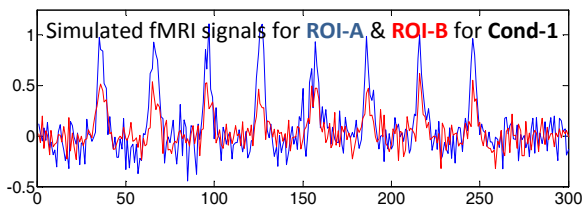
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Target Audience: Researchers who are doing functional connectivity analysis of fMRI data will benefit from this work.

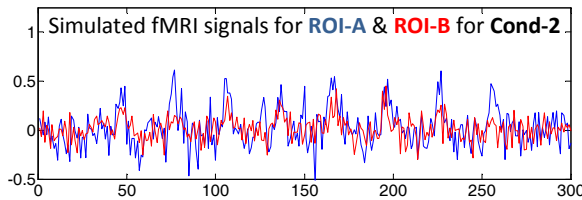
Introduction and Purpose: In fMRI, temporal blood-oxygenation dynamics of different brain regions, which is an indirect measure of collective neural activity, are captured while the subjects rest, engage different tasks and/or undergo different stimulus conditions. Interaction between the dynamics of different brain regions are commonly quantified by correlation-based techniques, which are simply referred to as functional connectivity (FC) analyses. If the two time signals from two different brain regions are significantly correlated, these brain regions are considered to exhibit significant FC. This can also be probed under different tasks or conditions to see how FC is modulated by task. In these studies, if a particular task or condition is found to be associated with greater FC between certain brain regions when compared with another task, then the study concludes that these brain regions are engaged more under this particular task or condition. However, certain tasks, conditions or stimuli can simply cause the fMRI signal to fluctuate more, thereby causing greater signal variance. In these analyses, the possible effect of task/condition-related variance differences to FC differences has been often ignored or understudied. In this work, we study the effects of task/condition-related signal variance to FC using simulated fMRI signals.

Methods: We simulated two tasks/conditions, Cond-1 and Cond-2, and two region-of-interest (ROI) time-courses, ROI-A and ROI-B. We studied the scenario under which the time-course of the noise-free signal from Cond-1 were constructed so as to have twice the standard deviation (std) of that of Cond-2 for both ROIs. We also let ROI-A noise-free signal have twice the std of that of ROI-B for both conditions. Simulated time-courses were generated in MATLAB [1] as vectors with length of 300 “volumes”, with repetition time (TR) of 1s, with 8 blocks of length-10 stimulus delta functions (inter-block interval was 30 seconds) for each task convolved with a standard hemodynamic response function of the SPM Toolbox [2]. Zero-mean Gaussian noise were added to ROI-A and ROI-B signals, with std of 0.15 and 0.10, respectively, to simulate different noise levels for different ROIs. One hundred realizations/cases were simulated (n=100). Standard deviation of the simulated signal for each ROI and condition, FC between ROIs for each condition, and the correlation across realizations between these two measures for each ROI and each condition were calculated.

Results: Figures on the left depict the simulated fMRI signals for the two ROIs under the two conditions. By design, the FC under the high-variance task condition was higher (top-middle table). Considerable correlation was found across realizations between the FC and the standard deviations of the ROI signals (bottom-middle table). More importantly, very significant correlation across realizations was found (bottom-right table) between the condition-related FC difference (Cond-1 minus Cond-2) and the condition-related standard deviation difference (Cond-1 minus Cond-2).



Mean Std of the Simulated fMRI signal (n=100)				Mean±Std Functional Connectivity (FC)	
ROI-A		ROI-B			
Cond-1	Cond-1	Cond-2	Cond-2	Cond-1	Cond-2
0.29±0.009	0.20±0.006	0.16±0.005	0.12±0.005	0.67±0.023	0.35±0.042



Correlation between FC & Std (n=100)				Correlation between ΔFC & ΔStd (n=100)	
ROI-A		ROI-B			
Cond-1	Cond-1	Cond-2	Cond-2	ROI-A	ROI-B
0.11	0.12	0.26	0.25	0.66	0.79

FC: Functional Conn., ΔStd = Std Cond1 - Std Cond2, ΔFC=FC Cond1-FC Cond2

Discussions and Conclusions: Correlation between the condition-related FC difference and the condition-related fMRI signal standard deviation difference shows that FC differences are associated with systematic differences in the variance of the fMRI signal in the different experimental tasks/conditions. This result highlights the need for caution in interpreting task/condition-dependent differences in functional connectivity analyses; one cannot rule out the possibility that the observed differences were merely a consequence of differences in the variance of the respective signal time-courses.

References: [1] <http://www.mathworks.com/matlab> [2] <http://www.fil.ion.ucl.ac.uk/spm/software/spm8>