Novel Technique Localizes fMRI Dynamic Functional Connectivity State Transitions

Spencer Brown, OMS-II; Daniel Selski, PhD

Pacific Northwest University of Health Sciences College of Osteopathic Medicine, Department of Anatomy

Introduction/Background

Functional Magnetic Resonance Imaging (**fMRI**) is a neuroimaging modality which measures neural activity level at regions of interest (**ROIs**) in the brain.[1] This modality relies on the Blood Oxygen Level Dependent (**BOLD**) signal, which notes that regions of the brain with increased blood flow demonstrate **elevated neural activity.**

Dynamic functional connectivity (**DFC**) studies how the brain changes over time.[2] It has been well documented that the brain undergoes **discrete state transitions** which are of particular interest in the fields of computational and cognitive neuroscience.[3] These transitions may be perturbed in both **psychiatric** and **neurodegenerative** conditions.[4-6] Existing but imperfect methods for evaluating state transitions include Sliding Windows (which do not precisely localize state transitions), and Hidden Markov Models (which are non-deterministic)[7,8].

Previous work has utilized graph theory to consider pairwise distances between ROIs which allow for unique fMRI analyses.[9] The Euclidean ***(L2)*** distance can be used to compare two distance matrices, each representing a brain state. Given two states A and B, and their linear combinations, it is readily proven that:

$$\|A - B\|_2 \geq \|(nA + (1-n)B) - B\|_2 \text{ for } 0 \leq n \leq 1 \quad (1)$$

This provides a basis for the proposed method of assessing peaks to identify state transitions.

The primary aim of this research is to develop a method which has the potential to improve the localization of brain state transitions that will create a framework for understanding the topology of dynamic brain networks and their biologic relevance.

Materials

3 Tesla fMRIs (n = 18) were obtained from the Human Connectome Project motor task dataset that had previously undergone preprocessing.[10-14] Participants (ages 22-35) included 7 males and 11 females. Each underwent two 204-second scans. **3 seconds** following an anticipatory task change **cue**, participants were instructed to **switch** to one of 6 tasks: movement of the hand (left vs right), foot (left vs right), tongue, or were instructed to rest. Task blocks lasted **15 seconds.**

Analysis was completed in python. Code is available below on GitHub.

Acknowledgements/Citations:

Methods

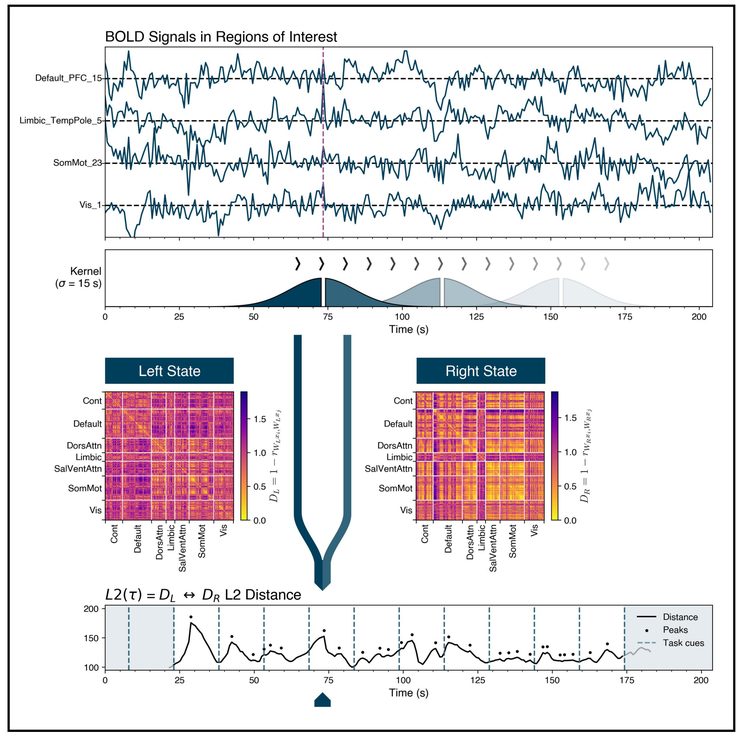

Figure 1. Depiction of methodology for assessing state transitions.

The obtained task fMRI data had previously been preprocessed using robust protocols into a time series of BOLD signals (***x(t)***) for each voxel.[15-21] The Schaeffer 2018 7-network atlas was chosen due to support for multiple parcellation options.[22] These 7 networks are: executive control, default mode, dorsal attention, limbic, ventral attention, sensorimotor, and visual networks. To balance spatial resolution and noise, the data was parceled into **300 ROIs.** The signal was averaged for all voxels within each ROI to obtain 300 separate time series.

2 kernels for each left ***(W_L)*** and right ***(W_R)*** brain state were defined and centered around a time point ***τ:***

$$W_L(t,\tau) = \begin{cases} \frac{2}{\sigma\sqrt{2\pi}} e^{-\frac{(t-\tau)^2}{2\sigma^2}} & \text{if } t < \tau \\ 0 & \text{if } t \geq \tau \end{cases} \qquad W_R(t,\tau) = \begin{cases} 0 & \text{if } t \leq \tau \\ \frac{2}{\sigma\sqrt{2\pi}} e^{-\frac{(t-\tau)^2}{2\sigma^2}} & \text{if } t > \tau \end{cases} \quad (2)$$

A distance ***(D)*** was then estimated between BOLD signals for ROIs ***($x_i(t)$, $x_j(t)$)*** using the **Pearson correlation** ***(r)***, such that a high r gives a low distance between ROIs:[23]

$$D_L(\tau) = 1 - r_{W_L(t,\tau)x_i(t), W_L(t)x_j(t)} \quad D_R(\tau) = 1 - r_{W_R(t,\tau)x_i(t), W_R(t)x_j(t)} \quad (3)$$

Determining the ***L2*** distance between ***D_L*** and ***D_R*** subsequently yields:

$$L_2(\tau) = \|D_L - D_R\|_2 \quad (4)$$

A buffer of ***2σ*** was used on either end of L_2, from which data was excluded. In addition, regions where there was not a complete 15 second *cue to cue* period available for analysis were also excluded.

Peaks were determined from $L2(\tau)$. These were hypothesized to be representative of brain state transitions. The offset of peak time to most recent task cue was assessed, then aggregated for all runs and subjects. Analysis was completed via χ^2-test and visualized on a histogram.

Results

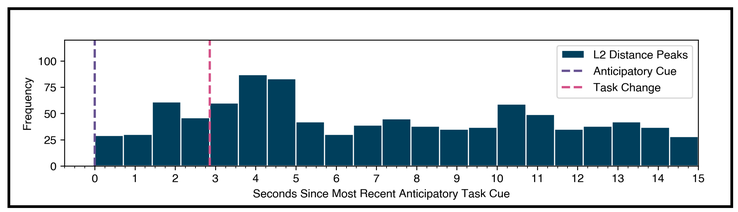

Figure 2. Histogram of frequency of timing of peaks.

- χ^2-test of peak offsets suggests that the distribution is non-uniform and statistically significant ($p=10^{-287}$). This indicates that the proposed method captures task-relevant changes in brain state.
- Qualitatively, the peaks seem to preferentially occur 4 seconds after the anticipatory cue and 1 second after the task change cue. Notably, many of the peaks seem to be the result of noise rather than signal. The development of a robust metric for de-noising these peaks is left to future work.

Discussion/Conclusions

- A technique for identifying brain state transitions has herein been introduced with the ability to successfully identify state transitions with temporal precision.
- L2 peaks preferentially occurred with changes in motor task more than the anticipatory visual cue. This may be suggestive that brain state transitions are more associated with a motor task change than the anticipation for that task. Direct testing of this is needed.
- State transitions seem to occur **4 seconds** after a cue. This has the potential to allow for a more refined analysis of this task motor dataset. Future work will assess the topology of discrete brain states to improve understanding of the mechanics of the human brain and related pathophysiology.