Spontaneous Co-activation Patterns of the Brain Revealed by Selectively Averaging Resting-State fMRI Volumes

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Target Audience Neuroscientists, fMRI Researchers

Purpose Resting-state networks (RSNs) inferred from correlation or ICA analysis of fMRI data may reflect activity in only a fraction of the data [1], and in fact closely resemble the BOLD co-activation patterns of selected individual time frames [2]. Importantly, by grouping relevant time frames according to spatial similarity, a specific RSN can be temporally decomposed into multiple co-activation patterns (CAPs) with distinct features [2]. Here, we apply this temporal decomposition approach over the entire brain and to all time frames to extract 30 CAPs that occur most frequently and are interpreted as instantaneous network configurations that may provide information complementary to that available with conventional analysis methods.

Methods The resting-state data from 102 participants were selected from the "1000 functional connectomes project" (FCP) [3]. Typical preprocessing steps were applied, including motion correction, spatial (FWHM = 4 mm) and temporal (0.005 - 0.1 Hz) filtering, removal of linear and quadratic temporal trends, nuisance regression of 6 motion parameters and average signals from white matter, cerebrospinal fluid (CSF), and the whole brain, and spatial co-registration to the MNI template. Additionally, the fMRI voxel time series were demeaned and normalized by temporal standard deviation. After pre-processing, *k*-means clustering was applied to classify all fMRI volumes (time frames) into 30 groups based on their spatial similarity, and these volumes were then averaged within groups to extract 30 final CAPs.

Results Four CAPs show patterns resembling the default mode network (DMN) but with distinct differences (Fig. 1A). They differentially involve *hippocampus* (HC), *parahippocampal gyrus* (PHG), *caudate nucleus* (CN), *superior frontal gyrus* (SFG), or *retrosplenial cortex* (RSp), consistent with these regions' distinct functional roles. In contrast, another group of CAPs show spontaneous co-activation in different sets of "task-positive" regions together with co-deactivation in the DMN (Fig. 1B), suggesting that the "task-positive" and "task-negative" regions of the brain may actually have a multiple-to-one relationship instead of one-to-one relationship as suggested previously [4].

A portion of CAPs show very specific thalamocoritical co-activations. For example, CAPs 2, 3 and 26 cover visual-related cortical areas at different hierarchical levels, and correspondingly, their thalamic co-activations reside in different subdivisions of the *pulvinar* (CAP 2 & 3) and *lateral geniculate nucleus* (LGN, CAP 26) (Fig. 2A). In contrast, CAP 19 shows concurrent activation at the primary sensorimotor cortex and de-activation at *anterior and medial dorsal nuclei* (AN/MDN) (Fig. 2B), consistent with previously reported positive and negative correlations to simultaneously recorded alpha-band EEG power [5].

To examine whether certain CAPs may occur at different rates in different populations, the subjects were grouped by gender and the occurrence rates of each CAP were compared between groups. It was found that CAP 23, mainly covering the sensorimotor representation of the head and part of insular cortex, occurs much more frequently ($p < 0.01$, Bonferroni corrected, permutation test) in males than in females (Fig. 3).

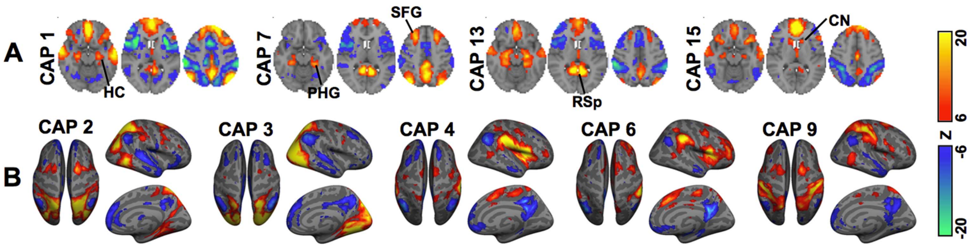

Fig. 1 Two groups of CAPs covering "task-negative" (A) and "task-positive" (B) regions of the brain.

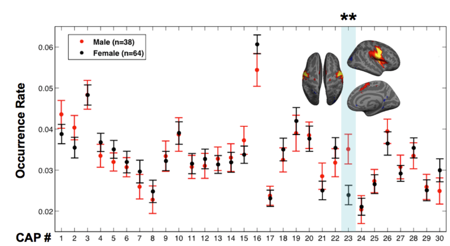

Fig. 3 Occurrence rates of CAPs in males and females.

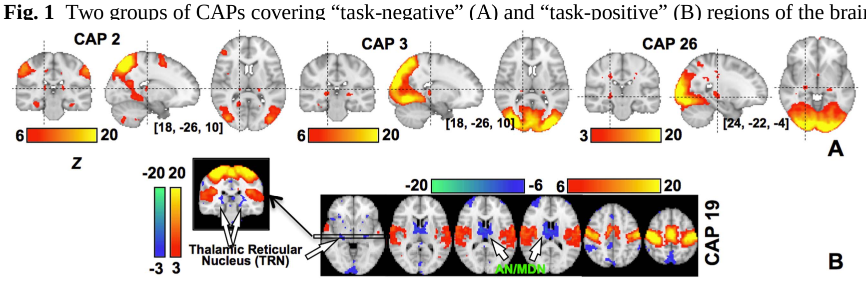

Fig. 2 CAPs showing thalamocortical co-activations in visual (A) and motor (B) systems. MNI coordinates in (A) are for cross points of dashed lines.

Discussion Selective averaging of fMRI volumes based on similarity of their activity patterns leads to CAPs that provide information supplementary to that obtained with conventional analysis methods. It allows for identifying patterns with significant spatial similarity and overlap (e.g., Fig. 1A), which may not be separated with correlation analysis or independent component analysis (ICA), due to constraints implied by their underlying assumptions. Depending on the neural origin of spontaneous fMRI activity, CAPs may represent the source signals in a more direct way since few assumptions and data transformations are involved in this method. The fact that distinct CAPs cover specific brain regions at different times is consistent with the previously reported non-stationary nature of functional connectivity [6]. The occurrence rate of CAPs might be a more sensitive index than correlation coefficients for differentiating populations or conditions through resting-state fMRI signals.

Conclusion A novel, data-driven technique is proposed for the analysis of resting-state fMRI signals, which may have advantages over conventional methods.

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