

Functional Connectivity to Dorsal and Ventral Striatum Exhibit Different Dependencies on fMRI Baseline Conditions

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Introduction: Resting state fluctuations in BOLD fMRI time-series have been increasingly employed to study functional connectivity networks in the brain [1,2]. FcMRI studies have employed different baseline conditions, e.g. resting with eyes open/closed [1], visual fixation [2], and finger tapping [3] to assess brain connectivity. Basal ganglia are an integral part of a number of networks studied with FcMRI [1,2]. The dorsal and ventral striatum (DS and VS, respectively) are thought to engage functionally distinct networks in the brain [4-6]. DS has been associated with connections from dorsolateral prefrontal cortex such as Brodmann (BA) Area 6, 9, 32, 45, 46, and is involved in stimulus-response learning, attention and cognitive flexibility. VS is connected from ventromedial prefrontal cortex (i.e., ventral portions of BA 10, 11, 12, as well as 24, 25, 38, 47) and is associated with basic drive states, internal motivation and classically conditioned learning. In this study, resting state fMRI networks were examined under 3 baseline conditions: resting eyes open, resting visual fixation and resting eyes open with concurrent sub-threshold transcutaneous electrical stimulation, to examine the effects of study environment on the networks identified as associated with dorsal and ventral striatum resting fluctuations.

Methods: Thirteen healthy subjects (5 F, 8 M, mean age 32 yrs, all R-handed, mean education 17 yrs) participated. Written informed consent was obtained for all subjects. FcMRI was acquired under 3 baseline conditions: 1) eyes open resting (Rest); 2) eyes open resting with visual fixation on a red cross with grey background presented on a screen (VisFix); 3) eyes open resting with concurrent sub-pain threshold (minimally perceptible) transcutaneous electrical nerve stimulation (TENS) provided with a custom-built device. FcMRI images were acquired on a 3T Siemens Trio scanner with a 12-channel receiver array head coil with an EPI sequence: TR/TE 2000/28 msec, 74 x 74 matrix size; 37 3-3.5 mm axial slices. Each baseline condition FcMRI scan had 326 volumes. Foam padding was provided to minimize head motion. A Biopac (*Goleta, CA*) respiration belt and finger pulse-oximeter was provided to acquire time-locked physiological waveforms. The FcMRI time-series were detrended of cardiac and respiration signals using RETROICOR [7], registered, and detrended of: linear trends, signal related to motion parameters, whole-brain averaged EPI time-series and whole-brain averaged non-ventricular CSF time-series. The resultant time-series data was further wavelet filtered (Daubechies 'db4' wavelet order 1) to isolate low frequency fluctuations and smoothed with a FWHM = 5mm isotropic gaussian filter. ROI-averaged time-series were obtained for the left dorsal striatum and left ventral striatum segmented using established practices [8]. Separate voxelwise cross-correlation analyses were performed to assess the connectivity of the left dorsal and ventral striatum with other brain regions. The least squares fit coefficient from cross-correlation analysis [9] from each subject was warped to Talairach space and analysis of variance was performed to assess group-level functional connectivity to each of the two striata during each of the 3 baseline conditions. Data analysis was performed with AFNI, FSL and Matlab.

Results & Discussion: The functional connectivity patterns of the VisFix condition were similar to the Rest and are therefore not reported in this paper. Figure 1 (a, b) shows the group functional connectivity map (thresholded at $|t_{72}| > 3.9$; FDR $q < 0.001$) for the Rest condition (1a) and TENS condition (1b) using left DS seed ROI. Compared to Rest, the TENS baseline appears to reveal accentuated DS connectivity along a dorsal prefrontal network, including bilateral cingulate gyrus (primarily BA 32), posterior cingulate, primary sensory cortex, superior parietal lobe (BA 7), and extensive occipital lobe (BA 18, 19). In addition, compared to Rest, TENS shows a greater spatial extent and magnitude of DS connectivity ($|t_{72}| > 2.6$; FDR $q < 0.05$) in other areas involved in attention (not shown) such as bilateral BA 10, 44, 45, and 46. Figure 1 (c, d) depicts the group functional connectivity map (thresholded at $|t_{72}| > 3.9$; FDR $q < 0.001$) for the left VS seed ROI. The Rest condition (1c) exhibited functional connectivity with VS along a ventral anterior network including the bilateral subcallosal gyrus, anterior medial frontal cortex and BA 25 as well as bilateral amygdala and hippocampus (not shown). In contrast, the TENS condition (1d) evoked a lower magnitude of VS connectivity activation in BA 24 and 25, no anterior medial prefrontal activation and additional activation in more dorsal structures such as in dorsal anterior cingulate BA 32 and BA24. Thus the TENS condition seems to engage more connectivity of dorsal attentional networks for both DS and VS compared to Rest, and to potentially suppress the expression of VS connectivity in ventroanterior prefrontal systems. Thus, the choice of baseline appears to have profound effects on FcMRI results, and these effects may be exquisitely network-specific. These results indicate that care must be taken when choosing baseline conditions for FcMRI studies. Although some networks particularly those involved in attention and cognitive control may be accentuated by more active baseline conditions like TENS, our results suggest that other networks in the limbic system may be suppressed.

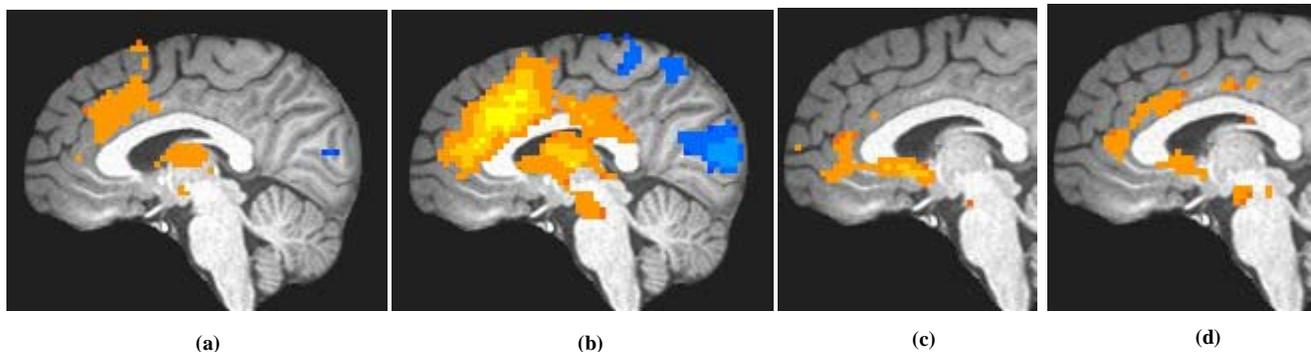


Figure 1: Functional connectivity maps (thresholded at $|t_{72}| > 3.9$; FDR $q < 0.001$) for (a) dorsal striatum during "Rest", (b) dorsal striatum during TENS, (c) ventral striatum during "Rest" and (d) ventral striatum during TENS, showing differential dependence of the dorsal attention network and the ventral emotional network on baseline conditions.

References

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