

Functional Connectivity Differences to Ventral Putamen of Gulf War Syndrome II and Control Subjects

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Introduction: The basal ganglia (e.g., caudate, putamen, globus pallidus) are classically regarded as motor structures, but serve a wide range of functions including motor, motivational, cognitive and emotional processes. Dysfunction of basal ganglia has been implicated in numerous neurological and psychiatric disorders, including Parkinson's disease [1] and Gulf War syndrome [2]. Functional connectivity magnetic resonance imaging (fcMRI) has been used to investigate brain networks by analysis of temporal and spatial correlations in spontaneous resting state BOLD signal oscillations [3, 4]. The purpose of this study was to compare the connectivity of ventral putamen to other brain regions between two groups of Gulf War veterans (one with Haley Syndrome II and the other normal controls) with resting state fcMRI.

Data Acquisition: Twelve right-handed male Gulf War veterans (in two group exclusively consisting of either Gulf War Syndrome II patients or healthy deployed veterans: 5 members of Group A, mean age: 63.8 ± 7.5 years; 7 members of Group B, mean age: 58.8 ± 6.3 years) were studied. Signed informed consents were obtained prior to participation according to an IRB-approved protocol. A Siemens Trio TIM 3T MR scanner and a 12-channel array receive-only head coil were used for data acquisition. High-resolution T₁-weighted anatomical images were acquired using a MPRAGE sequence (TR/TE = 2250/3.02 ms, FA = 9°, 160 slices, 240 mm FOV). Resting-state functional images were acquired with 40 sagittal slices, TR/TE = 2000/24 ms, FA = 80°, in-plane resolution = 3 mm x 3 mm, FOV = 220 mm.

Processing and Analysis: Data processing was carried out using both FSL (www.fmrib.ox.ac.uk/fsl) and AFNI (<http://afni.nimh.nih.gov/afni>). Grey matter, white matter, CSF, and subcortical regions were segmented from T₁-weighted anatomical images using FSL's FAST (cortical) and FIRST (subcortical) programs. For seed region selection and group analysis, data were spatially transformed to Talairach space using AFNI's linear transformation based on manually defined landmarks. The preprocessing of EPI images using AFNI included slice-timing shifting, head motion correction, and spatial normalization to standard space. Data were then temporally band-pass filtered (0.01 < f < 0.1 Hz) and spatially smoothed with a 6-mm FWHM Gaussian kernel. A linear regression process was performed to remove the effects of head motion, global signal and ventricle signal. Spherical regions of interest with radii of 5 mm were roughly centered at (19, 12, -3) in Talairach space within the ventral right putamen following the prescription in [4]. For each subject, the mean time series within these ROIs were considered as the reference or seed time courses for voxel-wise cross correlations. Individual r-maps were normalized to Z-maps. All Z-maps were also entered into a two-sample t-test to determine the regions showing significant difference in functional connectivity ($p < 0.05$).

Results and Discussion: Examination of functional connectivity to right ventral putamen (Figure 1) during rest revealed the differences in brain function between subject Groups A and B. Significant differences between groups were found in ventral cuneus, medial precuneus (BA 7), thalamus, anterior cingulate (BA 24 and anterior BA 23) and dorsolateral prefrontal cortex regions and connections associated with stimulus-response learning, attention and cognitive flexibility [3-5]. Epidemiological studies [2] of Gulf War Illness have revealed behavioral deficits in these functions. The results suggest that functional connectivity MRI can be used to find biomarkers for subtle diseased states such as Gulf War Illness.

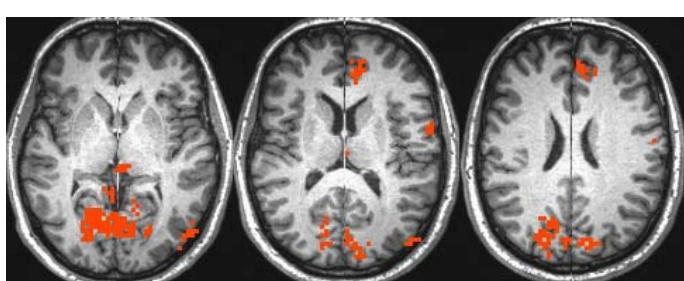


Figure 1. T-test maps of functional connectivity differences between Gulf War veteran Groups A & B (one Haley Syndrome II, the other healthy deployed veterans) thresholded at $t_8 > 2.3$, $p < 0.05$.

References:

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