

Reduced Hippocampal Body Functional Connectivity in Gulf War Illness

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Introduction: Memory loss is a common complaint among veterans with Gulf War Illness (GWI) [1], and preliminary studies have documented hippocampal dysfunction in GWI [2,3]. Abnormal functional connectivity to hippocampus has also been observed in various other diseased populations [4,5]. This study used resting state or functional connectivity MRI (fcMRI) to examine functional connectivity of the hippocampus in GWI subjects.

Methods: Fourteen right-handed subjects with GWI Syndrome 2 (Syn2)[6] (ages 53-73 yrs; mean 62.8 yrs) and 15 right-handed age-matched veteran controls were scanned in a Siemens 3T Tim Trio scanner using a 12-channel array receive-only head coil. Written informed consent was obtained from all participants. In the fcMRI paradigm subjects lay quietly in the scanner with eyes open (“Rest”) during an 11-minute run, followed by another run with simple visual fixation (“Fix”). FcMRI scans were acquired with a sagittal whole-brain gradient echo EPI (TR/TE = 2000/24 ms, FA = 90°, in-plane resolution = 3 mm x 3 mm; slice thickness 3-4mm).

Left and right hippocampal head, body and tail masks were traced on each subject’s T1W high-resolution anatomic image using established procedures [7] and resampled to EPI space to construct seed ROIs. The fcMRI data were slice-time corrected, volume registered, and band-pass filtered (0.03 Hz – 0.1Hz). Functional connectivity of each of hippocampal left and right head, body and tail was obtained by voxel-wise cross-correlation of the pre-processed fcMRI data with corresponding seed ROIs. The regression coefficient map from cross-correlation analysis [8] from each subject was warped to Talairach space and analysis of variance was performed to assess between-group differences in functional connectivity for each of the six hippocampal regions.

Results and Discussion: Figures 1 and 2 show the between-group differences in connectivity to the left and right hippocampal body, respectively (collapsed across the “Fix” and “Rest” conditions). In the Syn2 group the functional connectivity of the hippocampal body was significantly ($p < 0.03$) reduced compared to controls in a number of contralateral areas: anterior insula and ventrolateral prefrontal cortex (1a, 2b) and premotor cortex (1c, 2e), potentially indicating dysfunction of inter-hemispheric connectivity in Syn2. Further, the Syn2 group exhibited significantly ($p < 0.03$) decreased functional connectivity between the hippocampal body and bilateral ventral striatum (1b, 2c), amygdala (1d, 2e), superior temporal gyrus and right hemisphere pulvinar and parahippocampal cortex (1e, 1f, 2f). The right hippocampal body in Syn2 also exhibited much reduced ($p < 0.01$) functional connectivity, compared to controls, with bilateral dorsal striatum (2b) and medial and lateral prefrontal cortex (2a). In sum, the Syn2 group exhibits strongly reduced functional connectivity between bilateral hippocampus body and many other brain regions. Further investigations will focus on determining the contributions of both hippocampal dysfunction and disruption of white matter in GWI patients

References: [1] Binns J., et al., GWVI-RAC report, 2004; [2] Haley R., et al., Psych. Res. Neuroimag., 171:207-220, 2009; [3] Menon P., et al., Brain Res. 1009:189-194, 2004; [4] Bai et al., Biol. Psych 65:951-958, 2009; [5] Zhou et al., Schizo. Res., 100:120-132, 2008; [6] Haley R. et al., JAMA, 277:215-222, 1997; [7] Pruessner et al., Cereb.Cortex, 12: 1342-1353, 2002; [8] <http://afni.nimh.nih.gov/afni/doc/manual/3dfimplus>

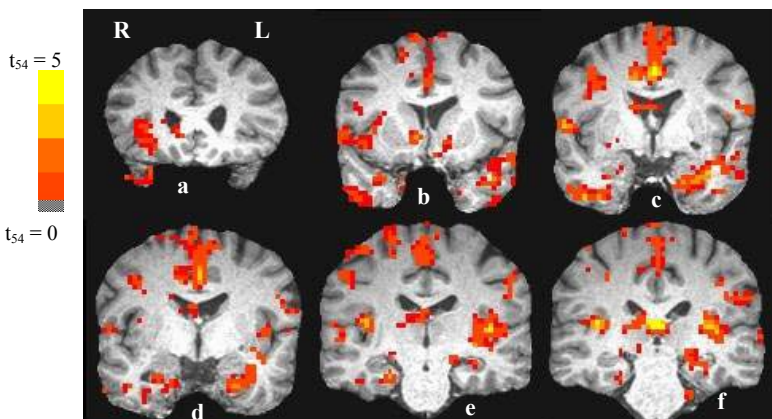


Figure 1: Functional connectivity differences (Controls – Syn2) to left hippocampus body; corrected $p < 0.03$.

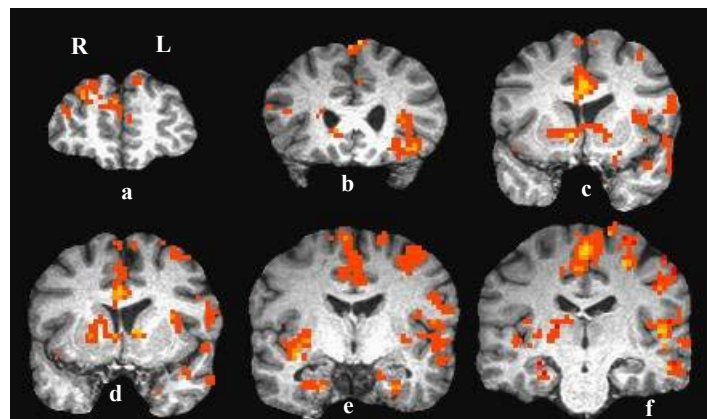


Figure 2: Functional connectivity differences (Controls – Syn2) to right hippocampus body; corrected $p < 0.01$.

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