

## fMRI of Working Memory in Military Traumatic Brain Injury

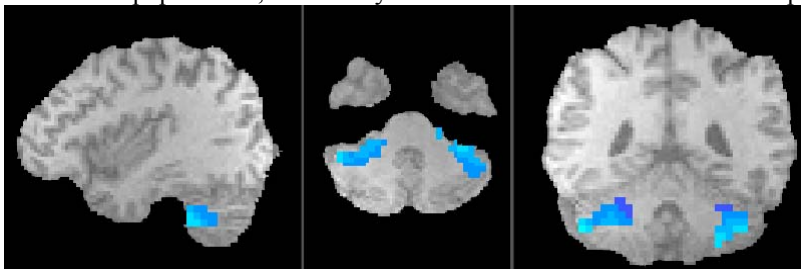
J. Graner<sup>1</sup>, H. Pan<sup>1</sup>, P-H. Yeh<sup>1</sup>, B. Wang<sup>1</sup>, T. R. Oakes<sup>1,2</sup>, W. Liu<sup>1,2</sup>, L. M. French<sup>3</sup>, F. Munter<sup>2</sup>, and G. Riedy<sup>2,4</sup>

<sup>1</sup>TBI Image Analysis Lab, Uniformed Services University of the Health Sciences / HJF, Bethesda, MD, United States, <sup>2</sup>National Capital Neuroimaging Consortium, Walter Reed Army Medical Center, Washington, DC, United States, <sup>3</sup>Defense and Veterans Brain Injury Center, Walter Reed Army Medical Center, Washington, DC, United States, <sup>4</sup>National Intrepid Center of Excellence, Bethesda, MD, United States

**Introduction:** Traumatic brain injury (TBI) has become increasingly prevalent in recent military conflicts. Lack of injury findings with anatomical diagnostic imaging techniques often cause difficulty in accurate diagnosis, subsequently leading to difficulty developing suitable rehabilitation plans for affected individuals. Functional neuroimaging techniques, such as fMRI, may provide additional insight into the neurophysiological causes of the common functional deficits seen in TBI victims. Here we present a comparison of fMRI results from injured USA military personnel and results from a control group of active, but not previously deployed, USA military personnel as they performed an N-back working memory task.

**Methods:** *Participants:* Sixteen (16) participants were recruited from USA military personnel at Walter Reed Army Medical Center (WRAMC) who had been recently injured in combat and categorized as having TBI. The average number of days between injury and scan acquisition was 88 (s.d.=70). All but one of the patients suffered blast-related injuries due to exposure to an explosive device or weapon. Thirteen (13) control subjects were also recruited from military personnel at WRAMC who were on active duty but had not previously been deployed. *fMRI acquisition:* Imaging was carried out on a 3T Signa MRI scanner (General Electric, Milwaukee, WI) with a 32-channel head coil. The images were obtained using an echo-planar imaging (EPI) sequence. *Task:* A visual facial N-back task was presented to the subjects using a goggle system (Nordic NeuroLab Inc., Milwaukee, WI). The N-back series consisted of twelve blocks, with each block asking the subject to perform either a 1-, 2- or 3-back task. Each block contained 15 human face stimuli (Minear and Park, 2004) and was 30 seconds long. Blocks were separated by a resting period of 18 seconds. *Image analysis:* The EPI data were preprocessed and analyzed using AFNI (Cox, 1996). Using a general linear model approach and a block design analysis, contrasts were calculated on a voxel-wise basis between the three task levels (1-, 2- and 3-back) for each subject. A 2x2 factorial analysis was then applied using a linear mixed-effects modeling approach to determine group differences for these contrasts. Separate group maps were also created for each contrast between task levels. Data from 2 of the TBI patients and 2 of the controls had to be excluded due to excessive head motion during the scan, leaving a patient group of 14 and a control group of 11.

**Results/Discussion:** The 2x2 factorial analysis showed significant (corrected  $p < .05$ ) differences in the 3-back versus 1-back activation between the two groups in the cerebellum (Figure 1). The patient group had less increase in activation between the 1-back and 3-back tasks than did the control group. The cerebellum has been indicated in several cognitive tasks, including working memory (Cabeza and Nyberg, 2000; Durisko and Fiez, 2009). Decreased relative activation in this region may signify damage to the cerebellum itself or damage to the frontal thalamic cerebellar circuitry, hindering communication between the cerebellum and cortical regions of the brain. Such damage could be associated with diffuse axonal injury. The 2-back-to-1-back (2-1) contrast maps for the two groups contained some statistically significant regions that were in similar locations but slightly smaller (contained fewer significant voxels) in the patient results. This may reflect the heterogeneity inherent in blast-related TBI. As a means of preliminary investigation, a region in the left lateral PFC that showed significant activation in both the patient and control 2-1 contrasts was chosen. Each subject's individual 2-1 contrast map was then searched for a similar significant region and the center-of-mass for each was recorded. For each group, the average distance between the center-of-mass of the group-level activation region and each individual's activation region was calculated. This preliminary analysis revealed that 8 of the 11 control subjects had regions near the location of the significant group contrast that also showed a significant 2-1 contrast. One additional control subject had a region that was present but did not meet the cutoff for significance. The average distance between the individual regions of contrast and the control group region was 8.9 mm (s.d.=6.0). Only 7 of the 14 patients had significant 2-1 contrast regions near the location of the patient group contrast region. The average distance between the centers-of-mass of the individual regions of contrast and that of the group region was 15.5 mm (s.d.=12.7). Although additional quantitative analysis is warranted, this suggests that the spatially variable and potentially diffuse injury due to blast-related trauma may lead to greater heterogeneity in statistical contrast results within blast-related TBI populations, which may need to be accounted for when attempting traditional voxel-wise group analysis.



**Figure 1:** Statistically significant regions in the cerebellum showing less relative activation in patients than in controls for the 3-back vs. the 1-back task.

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