Longitudinal changes in surface-based morphometry of U.S. military personnel following mild blast-related traumatic brain injury: A preliminary study

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Introduction: Blast-related traumatic brain injury (TBI) has been one of the 'signature' injuries in the war of Iran and Afghanistan. Neuroimaging studies in concussive 'mild' blast-related TBI (bTBI) have been challenging due to absence of abnormalities in conventional MRI and heterogeneity of the blast-related injury mechanisms. Here, we performed a longitudinal, morphological study on U.S. military personnel following concussive bTBI to overcome these challenges and to identify subtle structural changes occurring over time.

Methods: High resolution T_1-weighted MPRAGE images (TR/TE=2000/2.92msec; FA=8°; FOV=25.6×25.6cm; matrix=256×256; 176 slices, 1mm thick) of 27 (18 controls and 9 TBI patients) active duty U.S. military personnel were analyzed for this morphometry study. All subjects were exposed to blasts with 9 patients diagnosed with concussive, uncomplicated traumatic brain injury. The initial scans were acquired using a Siemens Magnetom Avanto 1.5T MRI scanner (Siemens, Erlangen, Germany) within 1-90 days after the blast exposures. After 6-12 months from the initial scans, the follow-up scans were performed using a second 1.5T Avanto MR scanner. Cortical surfaces of the cohorts were reconstructed using the Freesurfer image analysis suite[1–3]. Following the longitudinal pipeline[4] in Freesurfer, an unbiased within-subject template from MR images of the two scans for each subject was created and the two cross-sectional images were registered to the template to increase reliability and statistical power[4]. Five surface morphometric measures[1–3] (cortical thickness, mean curvature, average convexity, metric distortion and pial surface area) per vertex were obtained from the each registered MR image. Symmetrized percentage change[4] (SPC) with respect to the average measure across two time points was subsequently obtained. Group comparisons of vertex-specific SPC were made using the Mann-Whitney U test as the distributions of these measures did not pass the normality test at vertex level.

Results: Cortical thickness (the left anterior middle cingulate cortex (L aMCC)), metric distortion (the left calcarine sulcus (L CAL S) and precuneus gyrus (L PCN G)) and pial surface area (the right MCC and rostral anterior cingulate cortex (rACC)) had statistically significant differences between the two groups at $p_{\text{uncorr}} < 0.01$ (Fig. 1). Group comparisons of mean curvature and average convexity were not statistically significant at $p_{\text{uncorr}} < 0.01$. Scatter plots for the average measures within L aMCC and R MCC (Fig. 2) show TBI patients with greater surface morphometric changes over time than the controls at single-subject level.

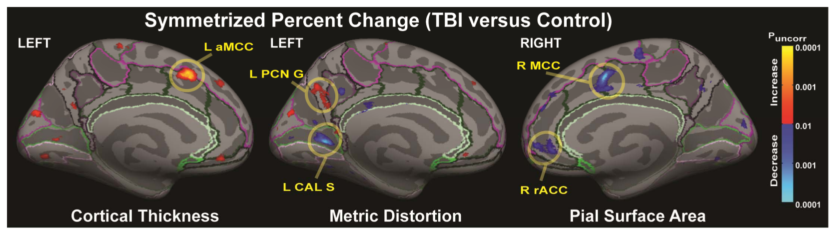

Fig. 1: Group comparison maps.

Discussion: Greater longitudinal changes in morphometry of the TBI patients relative to the controls indicate that blast exposure may affect brain morphology in concussive bTBI patients. However, the underlying biological mechanisms and consequences of these phenomena observed in the structural MRI are not clear and further studies with more subjects are required to validate these findings. Statistical significance from the group comparisons did not survive after correction for multiple comparisons at $q_{\text{FDR}} < 0.05$. Therefore, an additional, independent dataset is also needed to confirm that these phenomena did not occur by chance.

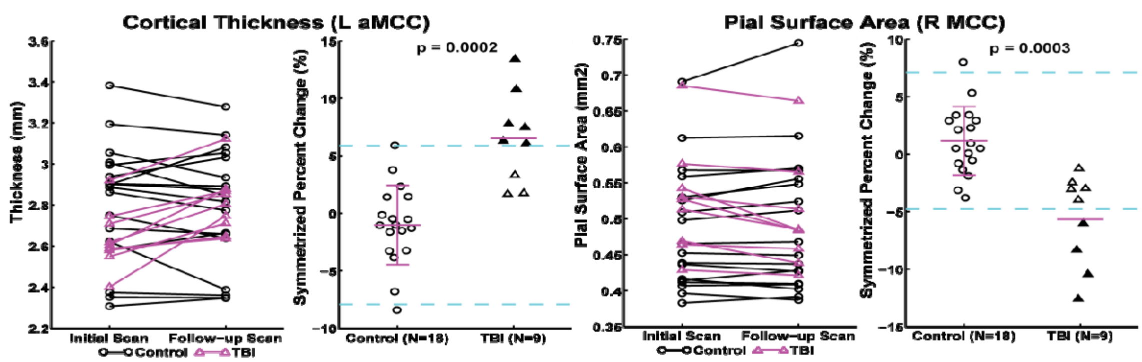

Fig. 2: Scatter plots for longitudinal changes of measures within L aMCC and R MCC.

Funding: Department of Defense CDMRP Grants PT075299 and PT090444.

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