Regionally-Specific Atrophy Following Traumatic Brain Injury Revealed by Deformation Morphometry of Serial 3 Tesla Volumetric MRI

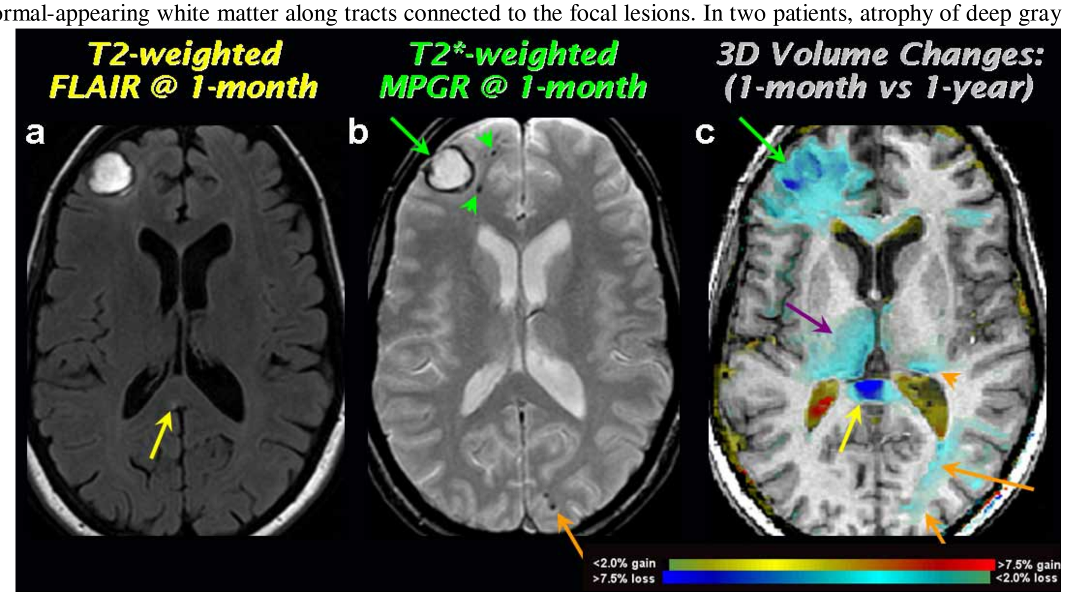
P. Mukherjee[1], H. Lee[2], S. Veerarhagavan[1], D. Xu[1], M. Meeker[2], J. Ghajar[3], G. T. Manley[2], and C. Studholme[1]

[1]Radiology, University of California, San Francisco, CA, United States, [2]Neurosurgery, University of California, San Francisco, CA, United States, [3]Brain Trauma Foundation, New York, NY, United States

Introduction: Diffuse brain atrophy is known to occur as a consequence of traumatic brain injury (TBI), but post-traumatic neurodegeneration is often not spatially homogeneous. Prior studies of regionally-specific atrophy following TBI have been limited to manual region-of-interest (ROI) analysis or voxel-based morphometry (VBM), as reviewed by Levine et al. [*J Neurotrauma* 2006; 23:1396-1411]. ROI analysis is laborious, operator-dependent, and does not usually cover the entire brain. VBM does not account for the alterations in shape and contour that accompany volume changes [Gitelman et al., NeuroImage 2001; 13:623-31], and also usually requires pooling of data from multiple subjects, which is problematic given the spatial heterogeneity of injury across different TBI patients. Deformation morphometry overcomes all of these limitations by generating quantitative whole-brain maps of 3D volume and shape changes across serial MRI scans of individual subjects in a fully automated fashion [Studholme et al., IEEE Trans Med Imaging 2006; 25:626-39]. In this study, we use deformation morphometry of 3T volumetric T1-weighted imaging in mild to moderate TBI to characterize the local patterns of volume loss that occur between 1 month and 1 year after head injury.

Methods: Four patients with mild TBI (Glasgow Coma Scale 13-15 in the Emergency Dept.), two patients with moderate TBI (GCS 9-12), and one trauma control subject who suffered leg injury but not head injury underwent volumetric MRI at 1 month and again at 1 year after trauma on a 3T GE Signa EXCITE scanner with an 8-channel head coil. The whole-brain volumetric T1-weighted acquisition was performed at 1-mm isotropic voxel resolution using a 3D inversion recovery fast spoiled gradient echo pulse sequence (TR=6.3 ms, TE=1.5 ms, TI=400 ms, FA=20 degrees, NEX=1). Robust fluid registration driven by regional mutual information was used to estimate a spatial transformation capturing shape changes between scans at 1 month after injury and follow-up scans at 1 year after injury. The Jacobian determinant of this transformation gives the fractional volume expansion or contraction of each voxel of the first scan required to match the second scan anatomy. The voxel-level percentage volume changes above a minimum threshold of 2% are displayed in color overlaid on each subject's first time point image.

Results: No regional volume changes > 2% were found during the 1-month to 1-year interval in the leg injury control subject. In the TBI patients, local volume loss was seen associated with small cortical contusions. With large contusions and with axonal shearing injuries, more extensive atrophy was identified that included normal-appearing white matter along tracts connected to the focal lesions. In two patients, atrophy of deep gray matter nuclei (1 caudate, 1 thalamus) was revealed ipsilateral to the focal cortical and/or white matter lesions. The Figure illustrates these findings in a moderate TBI patient. Non-hemorrhagic axonal shearing injury of the splenium of the corpus callosum is barely perceptible on the FLAIR image at 1-month after trauma (a, *yellow arrow*), yet it is associated with severe localized atrophy on deformation morphometry (c, *yellow arrow*). A large area of right frontal lobe volume loss (c, *green arrow*) crossing into the genu of the corpus callosum is the sequelae of a large hemorrhagic contusion (b, *green arrow*) and adjacent hemorrhagic shearing injuries (b, *green arrowheads*). Extensive volume loss is seen in the normal-appearing ipsilateral thalamus (c, *purple arrow*). Punctate foci of hemorrhagic axonal shearing injury in the left occipital lobe (b, *orange arrow*) are associated with atrophy along the left optic radiations (c, *orange arrows*) and the left lateral geniculate nucleus (c, *orange arrowhead*).



Discussion: To our knowledge, this is the first study to apply deformation morphometry for measuring 3D volume changes after TBI. This new computational neuroanatomy technique reveals more widespread regions of post-traumatic neurodegeneration than has been previously recognized. Beyond the localized atrophy around focal contusions and shearing injuries, volume loss was also identified along normal-appearing white matter projections and ipsilateral deep gray matter nuclei, presumably the result of Wallerian degeneration. Deformation morphometry is a powerful new tool for better visualizing the extent of brain injury following head trauma, to be used for diagnosis, prognosis, and treatment monitoring.

Acknowledgements: The Cognitive and Neurobiological Research Consortium in Traumatic Brain Injury is supported by the James S. McDonnell Foundation through a collaborative grant to the Brain Trauma Foundation. Methodology developed with support from NIH MH65392 and the Whitaker Foundation R-01-0115.