Diffusion tensor imaging measures of white matter integrity dissociate damage to memory versus attention networks in mild traumatic brain injury

S. N. Niogi[1], P. Mukherjee[2], R. Kolster[1], R. Sarkar[3], J. Ghajar[3], and B. D. McCandliss[1]

[1]Sackler Institute for Developmental Psychobiology, Weill Cornell Medical College, New York, NY, United States, [2]Department of Neuroradiology, University of California, San Francisco, San Francisco, CA, United States, [3]Brain Trauma Foundation, New York, NY, United States

Introduction

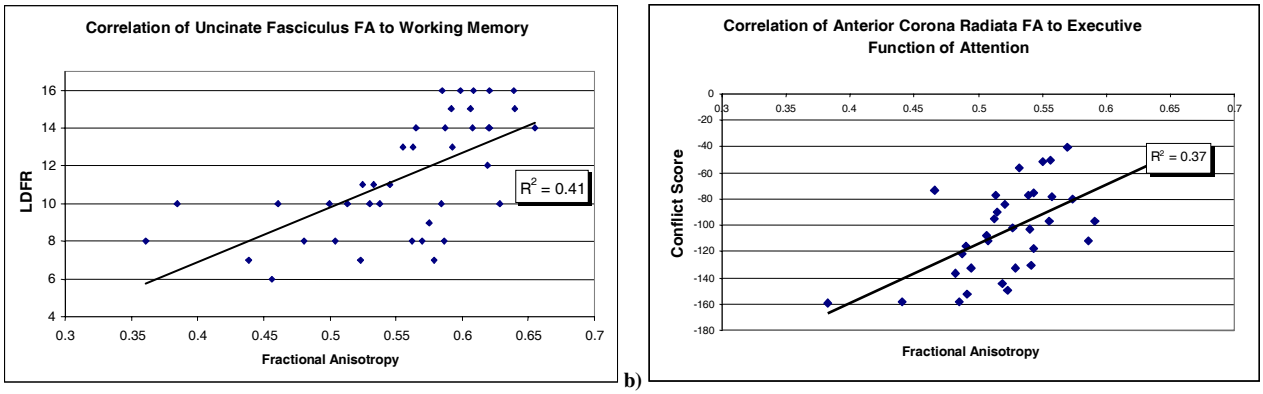
Mild Traumatic Brain Injury (TBI) most commonly causes nonspecific axonal disruption and shearing of large nerve fibers, termed diffuse axonal injury (DAI), in over 1.5 million cases reported annually in the United States[1]. While MRI is generally accepted as the neuroradiological test of choice for the diagnosis of head trauma over CT, both CT and MRI underestimate the severity of damage following a TBI[2,3]. This results in mild TBI subjects often having undiagnosed physical injuries that may be associated with known cognitive and psychological dysfunction, most commonly attention and/or short term memory deficits. In order to effectively assess damage following a TBI, one needs to probe the microstructural white matter changes as a result of the injury. One available technique is magnetic resonance diffusion tensor imaging (DTI) which uses the characteristics of water diffusion in the brain to assess the integrity of white matter pathways. In the current study, we use DTI to evaluate the extent of DAI due to closed head injury which may account for transient pathologic conditions and, as shown in this study, residual cognitive deficits that persist in the chronic phase.

Methods

Subjects included 20 mild TBI patients (11 male, 9 female, 17-61 years old) and 26 health control subjects (14 male, 12 female, 17-58 years old). All patients were examined at least 1 month post-injury, had chronic post-concussive symptoms, and were amnestic near time of injury with a Glasgow Coma Score between 13 and15. In addition, 26 healthy control subjects (14 male) were examined for comparison. DTI was acquired with a 3.0 T GE Scanner (GE Healthcare, Milwaukee, WI) using 55 gradient directions at b=1000 s/mm^2, 1 image with b=0 s/mm^2, 72 contiguous slices (1.8mm thickness) with 128x128 resolution that is zero-filled during reconstruction to 256x256, and a field of view of 230mm resulting in a pixel size of 0.898mm. A region of interest (ROI) approach was adopted to test specific regions throughout the brain selected in an *a priori* fashion. The ROI procedure was applied on a subject-by-subject basis to non-normalized DTI data and consisted of using standard ellipse shaped ROIs with the size and dimensions kept constant for each tract across subjects. Mean and standard deviation (SD) of FA values for each ROI was recorded. Structures with FA values less than 2.5 SD from the normal control mean for that ROI was considered damaged. Participants completed a battery of cognitive and behavioral tests including the California Verbal Learning Test [4] for long delay free recall (LDFR) memory and the Attention Network Task (ANT). [5] In addition, all subjects completed the Head Injury Symptom Checklist (HISC) survey and patients were evaluated with the Glasgow Outcome Scale-Extended (GOS-E) and Wechsler Abbreviated Scale of Intelligence (WASI). In an effort to demonstrate that a relationship between loci of damage and domains of cognitive impairment exist, a series of correlations were calculated between the cognitive performance measures and FA of the inferior longitudinal fasciculus (ILF), anterior corona radiata (ACR), uncinate fasciculus (UNC), superior longitudinal fasciculus, and forceps minor.

Results

Predominant areas of damage detected by DTI include the ILF, damaged in 45% of patients, UNC, damaged in 40% of patients, ACR, damaged in 40% of patients, and the genu of the corpus callosum, damaged in 35% of patients. Despite the tendencies for certain tracts to be damaged over others, it is clear that distribution of damage due to TBI is heterogeneous. Significant correlations exist between LDFR memory and the UNC (Right UNC r=0.640, p<0.05; Left UNC r=0.388, p<0.05; bilateral average r=0.538, p<0.05) but no other structure (Figure 1a). Similarly, a significant relationship exists between attention measured by mean RT of the ANT and the FA in the ACR (right ACR, r = -0.453, p<0.05; bilateral average r = -0.417, p<0.05). Interestingly, only the executive function component of attention, not alerting or orienting, correlated significantly with the ACR (right ACR, r = 0.606, p<0.05; bilateral average, r = 0.484, p<0.05, Figure 1b). All mild TBI subjects demonstrated damage to at least one white matter pathway evaluated by DTI.



a) b)

Figure 1. Structure-function relationships demonstrate dissociable white matter pathways of memory and attention.

Discussion

Conventional MRI and CT techniques cannot adequately detect the extent of DAI in the brain nor quantify the severity of damage to a particular tract. 3T DTI is sensitive to microstructural changes in white matter following even a mild TBI incident. As shown in this study, the most predominant areas of damage are frontal association fibers, the ILF, and the corpus callosum. Moreover, specific relationships exist between loci of damage and the most prevalent post-concussive symptoms associated with memory and executive function. The data suggests white matter integrity in the UNC specifically modulates memory while white matter integrity in the ACR specifically modulates the executive function.

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1. Bazarian JJ, McClung J, Shah MN, Cheng YT, Flesher W, Kraus J. Mild traumatic brain injury in the United States, 1998--2000. Brain Inj 2005;19(2):85-91.
2. Hammoud DA, Wasserman BA. Diffuse axonal injuries: pathophysiology and imaging. Neuroimaging Clin N Am 2002;12(2):205-216.
3. Inglese M, Makani S, Johnson G, et al. Diffuse axonal injury in mild traumatic brain injury: a diffusion tensor imaging study. J Neurosurg 2005;103(2):298-303.
4. Delis DC, Freeland J, Kramer JH, Kaplan E. Integrating clinical assessment with cognitive neuroscience: construct validation of the California Verbal Learning Test. Journal of Consulting & Clinical Psychology 1988;56(1):123-130.
5. Fan J, McCandliss BD, Fossella J, Flombaum JI, Posner MI. The activation of attentional networks. Neuroimage 2005;26(2):471-479.