Brain Advance Access originally published online on September 14, 2007
Brain 2007 130(10):2508-2519;
doi:10.1093/brain/awm216

White matter integrity and cognition in chronic traumatic brain injury: a diffusion tensor imaging study

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Traumatic brain injury (TBI) is a serious public health problem. Even injuries classified as mild, the most common, can result in persistent neurobehavioural impairment. Diffuse axonal injury is a common finding after TBI, and is presumed to contribute to outcomes, but may not always be apparent using standard neuroimaging. Diffusion tensor imaging (DTI) is a more recent method of assessing axonal integrity *in vivo*. The primary objective of the current investigation was to characterize white matter integrity utilizing DTI across the spectrum of chronic TBI of all severities. A secondary objective was to examine the relationship between white matter integrity and cognition. Twenty mild, 17 moderate to severe TBI and 18 controls underwent DTI and neuropsychological testing. Fractional anisotropy, axial diffusivity and radial diffusivity were calculated from the DTI data. Fractional anisotropy was the primary measure of white matter integrity. Region of interest analysis included anterior and posterior corona radiata, cortico-spinal tracts, cingulum fibre bundles, external capsule, forceps minor and major, genu, body and splenium of the corpus callosum, inferior fronto-occipital fasciculus, superior longitudinal

fasciculus and sagittal stratum. Cognitive domain scores were calculated from executive, attention and memory testing. Decreased fractional anisotropy was found in all 13 regions of interest for the moderate to severe TBI group, but only in the cortico-spinal tract, sagittal stratum and superior longitudinal fasciculus for the mild TBI group. White Matter Load (a measure of the total number of regions with reduced FA) was negatively correlated with all cognitive domains. Analysis of radial and axial diffusivity values suggested that all severities of TBI can result in a degree of axonal damage, while irreversible myelin damage was only apparent for moderate to severe TBI. The present data emphasize that white matter changes exist on a spectrum, including mild TBI. An index of global white matter neuropathology (White Matter Load) was related to cognitive function, such that greater white matter pathology predicted greater cognitive deficits. Mechanistically, mild TBI white matter changes may be primarily due to axonal damage as opposed to myelin damage. The more severe injuries impact both. DTI provides an objective means for determining the relationship of cognitive deficits to TBI, even in cases where the injury was sustained years prior to the evaluation.

Key Words: traumatic brain injury; diffusion tensor imaging; white matter fibre tracts; fractional anisotropy; diffuse axonal injury; MRI

Abbreviations: DTI, diffusion tensor imaging; FA, fractional anisotropy; TBI, traumatic brain injury; MTBI, mild traumatic brain injury; M/STBI, moderate to severe traumatic brain injury; DAI, diffuse axonal injury; $\lambda\|$, axial diffusivity; $\lambda\perp$, radial diffusivity; λ, eigenvalues; ACR, anterior corona radiata; PCR, posterior corona radiata; CST, corticospinal tracts; Cing, cingulum fibres; fMin, forceps minor; fMaj, forceps major; bCC, body of the corpus callosum; gCC, genu of the corpus callosum; sCC, splenium of the corpus callosum; IFO, inferior fronto-occipital fasciculus; SLF, superior longitudinal fasciculus; ExCap, external capsule; SS, sagittal stratum

Received June 28, 2007. Revised August 14, 2007. Accepted August 16, 2007.