BRAIN RESEARCH 1591 (2014) 86–92

Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

Brain Research

Research Report

White matter integrity and cognition in mild traumatic brain injury following motor vehicle accident

Kunlin Xiong[a], *Yongshan Zhu*[a], *Yulong Zhang*[a], *Zhiyong Yin*[b], *Jingna Zhang*[c], *Mingguo Qiu*[c,*], *Weiguo Zhang*[a,*]

[a]*Department of Radiology, Daping Hospital, Third Military Medical University, Chongqing 400042, China*
[b]*Department 4th, Research Institute of Surgery, Third Military Medical University, Chongqing 400042, China*
[c]*Department of Medical Image, College of Biomedical Engineering, Third Military Medical University, Chongqing 400038, China*

ARTICLE INFO

Article history:
Accepted 15 October 2014
Available online 23 October 2014

Keywords:
Mild traumatic brain injury
Diffuse axonal injury
Cognitive impairment
Diffusion tensor imaging
Tract-based spatial statistics
Fractional anisotropy
Mean diffusivity

ABSTRACT

The aim of this study is to explore the white matter structure integrity in patients with mild traumatic brain injury (mTBI) using diffusion tensor imaging (DTI), and to analyze the relationship between the white matter structure integrity and cognitive impairment of patients with mTBI. Twenty-five patients with mTBI and 25 healthy control subjects were studied with conventional MR imaging and diffusion tensor imaging. Fractional anisotropy (FA) and mean diffusivity (MD) maps of patients with mTBI were calculated and compared, with these control maps using tract-based spatial statistics (TBSS). Significantly lower fractional anisotropy was found in patients in the uncinate fasciculus, superior longitudinal fasciculus, inferior longitudinal fasciculus, and internal capsule. Mean diffusivity was significantly elevated in the body of corpus callosum, uncinate fasciculus, superior longitudinal fasciculus, and internal capsule in the mTBI group compared with the control group ($P<0.05$). The mTBI group showed a significant negative correlation between the elevated mean diffusivity of the uncinate fasciculus and the working memory index (WMI) ($R^2=0.51$, $P<0.05$), and the internal capsule of MD values was significantly negatively related to processing speed index (PSI) ($R^2=0.45$, $P<0.05$). There was a positive correlation between the FA value of the uncinate fasciculus and Mini Mental State Examination (MMSE) in the mTBI patient group ($R^2=0.36$, $P<0.05$). TBSS analysis of DTI suggests that patients with mTBI have focal axonal injury, and the pathophysiology is significantly related to the MMSE and IQ of mTBI patients. Diffusion tensor imaging can be a powerful technique for in vivo detection of mTBI, and can help in the diagnosis of patients with mTBI.

*Corresponding authors.
E-mail address: jellyhuangsci2@163.com (W. Zhang).

http://dx.doi.org/10.1016/j.brainres.2014.10.030
0006-8993/

1. Introduction

Mild traumatic brain injury (mTBI) accounts for 80% to 90% of TBI cases, in which loss of consciousness and/or confusion and disorientation is shorter than 30 min. Although this type of TBI is called "mild" and conventional MRI and CT scans are often normal, the effects on the family and the injured person can be devastating. Approximately 30% of mTBI patients experience some degree of residual neurologic or cognitive deficit (Whitnall et al., 2006). The cognitive domains of memory, executive function and processing speed are commonly affected (Scheid et al., 2006; Draper and Ponsford, 2008). Until now, the underlying pathophysiology of these cognitive impairments remains poorly understood (Lowenstein, 2009). This is likely because damage to brain connectivity is a critical factor in the development of cognitive impairment after traumatic brain injury. Diffuse axonal injury (DAI) is widely believed to account for these persistent problems. DAI is a consequence of sustained acceleration and deceleration forces that can shear axons and produce microscopic changes in the brain. A component of DAI is present in all motor vehicle crashes where the patient has lost consciousness.

White matter disruption is an important determinant of cognitive impairment after traumatic brain injury, but conventional CT and standard MRI underestimate the extent of white matter damage—(Arfanakis et al., 2002; Rugg-Gunn et al., 2001). A more recent noninvasive imaging technique, diffusion tensor imaging (DTI), as implemented in MR imaging (Arfanakis et al., 2002; Assaf and Pasternak, 2008), can be used to probe, in vivo, the intrinsic diffusion properties of deep tissues. In the tensor model, DTI data are used to estimate the amount of water diffusion in a number of directions at each point (voxel) in the image. From this, metrics such as fractional anisotropy can be derived to quantify the degree of white matter disruption (Basser and Pierpaoli, 1998). Greater anisotropy, as indicated by a higher fractional anisotropy value, is believed to reflect more coherent tissue structure, while increased diffusivity suggests tissue damage (Arfanakis et al., 2002). Changes in fractional anisotropy persist after traumatic brain injury and predict a functional outcome over and above patients' initial clinical state or focal lesion load (Sidaros et al., 2008).

Previous work in patients with traumatic brain injury has typically focused on a limited number of brain locations defined as regions of interest (Kraus et al., 2007; Kennedy et al., 2009). This approach is a sensitive way of identifying white matter damage, but because it is restricted to assessment of the a priori defined regions, only a small amount of the total white matter is usually investigated (Niogi et al., 2008). This is problematic for a number of reasons. Traumatic brain injury produces a complex pattern of diffuse axonal injury at variable locations across individuals and so it is difficult to define the location of white matter disruption. The investigation of a small number of regions is likely to result in a failure to identify significant white matter damage elsewhere in the brain. As the cognitive functions commonly affected by traumatic brain injury depend on a distributed network function, such an approach limits analysis of the structural causes of cognitive impairment. These issues are compounded by our limited knowledge of how tract structure relates to cognitive function in the normal brain, making it important to assess white matter structure after traumatic brain injury as comprehensively as possible.

Tract-based spatial statistics (TBSS) is a new voxel-based technique for analyzing white matter structure across the whole brain (Smith et al., 2006). TBSS allows complex patterns of white matter disruption to be identified and their relationships with cognitive function to be studied in a data-driven way. Statistical calculations are performed at each point within an individual's white matter 'skeleton', which has been registered to a standard space using a two-stage process involving non-linear warping and subsequent alignment of individual white matter tracts across subjects. This allows a comprehensive analysis of tract structure to be performed in a way that has a strong effect on brain injury, such as brain atrophy. TBSS has been used to show a relationship between white matter structure and cognitive function in other neurological conditions (Ceccarelli et al., 2009; Dineen et al., 2009). Kinnunen et al. (2011) also used TBSS to analyze the white matter damage and cognitive impairment in traumatic brain injury patients.

The relationship between cognitive impairment after traumatic brain injury and white matter damage is likely to be complex. Diffusion tensor imaging provides a valid and sensitive way of identifying the impact of axonal injury. The purpose of this study is to detect white matter damage in patients with mild traumatic brain injury using DTI that appears normal on conventional CT and standard MR images, and to investigate whether there are differences in white matter structure in a group of chronic patients with mild traumatic brain injury and an age-matched control group using TBSS. The secondary objective is to examine the relationship between white matter integrity and cognitive impairment following mild traumatic brain injury. We hypothesize that increased white matter disruption following mild traumatic brain injury will be associated with greater cognitive impairment.

2. Results

For all patients, the T1 and T2-weighted structure MR images exhibited no abnormalities. In our study, 19 patients were associated with soft tissue-injuries, and 6 patients were associated with limb fractures. The average years of education of the mTBI group was 12.84 ± 3.05, while the average years of education of the control subjects was 13.89 ± 3.22, hence no notable difference between the two groups. Comparing mTBI patients with the control subjects, the total IQ, VCI, WMI, PRI, PSI and MMSE scores of the mTBI patients showed a decreased tendency, but only the WMI and PSI significantly decreased (Table 1).

TBSS approaches detected differences in FA between control and TBI participants. Comparing mTBI patients with the control subjects, significantly lower fractional anisotropy was found in the uncinate fasciculus, superior longitudinal fasciculus, inferior longitudinal fasciculus, and internal capsule (Fig. 1). Mean diffusivity was significantly elevated in