# Altered magnetic susceptibility in white matter after mild traumatic brain injury

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**Audience:** Researchers interested in white matter damage after traumatic brain injury (TBI).

**Introduction:** Traumatic brain injury (TBI) is a complex injury with a broad spectrum of symptoms and disabilities**.** Although focal brain damage is common in TBI, the TBI patient's cognitive impairment is often inadequately explained by the location and extent of the injury. Recent studies suggested that white matter damage and its related alterations in brain structural connectivity can also play an important role. While diffusion tensor imaging (DTI) is the most widely used method in studying brain white matter, recent studies showed that magnetic susceptibility, a novel contrast calculated from gradient echo signal phase using quantitative susceptibility mapping (QSM), may provide a different, but potentially more sensitive marker of white matter damage [1]. In this study, we explored the application of QSM in delineating the white matter changes after TBI, and compared it with DTI.

**Materials and Methods**

Animals: Seven male Sprague Dawley rats (250-350g) were studied. A Ø6mm craniotomy was created over the left forelimb somatosensory cortex (S1: 0.25mm anterior and 3.5mm lateral to bregma), exposing the dura matter. The intact dura matter was impacted with a Ø3mm tip (5.0m/s, 250μs dwell time, 1mm depth). The cranial opening was sealed with bone wax following the impact.

Brain imaging and analysis**:** The rats were scanned using a Bruker 7T scanner 1hr, 3hrs, 2, 7 and 14 days after TBI under the anesthesia with 1.5% isoflurane. 3D multi-gradient echo (MGE) images were acquired with the following parameters: FOV=2.56x2.56x2.56cm$^3$, data matrix=256x192x128, TE1=4.4ms, Echo spacing=6.1ms, 4 echoes, and TR=28ms. QSM was performed as described by Li et al [2]. The resulting magnetic susceptibility values were directly used for comparison, similar to a previous study [3]. DTI was performed on seven 1-mm thick coronal positions with FOV=2.56x2.56cm and data matrix=96x96. Standard T2 weighed images were also acquired for measuring lesion size. Magnetic susceptibility, fractional anisotropy (FA), and mean diffusivity in ipsilesional and contralateral segments of corpus callosum were measured.

**Results:** Fig. 1A and B shows the magnetic susceptibility and DTI FA of brain tissue after TBI. While magnetic susceptibility showed a clear focal change in white matter at day 2, DTI FA shows no visually apparent changes in white matter. At day 14, both magnetic susceptibility and DTI FA shows no significant differences between ipsilesional and contralateral sides of corpus callosum.

Quantitatively, the ipsilesional side of corpus callus shows an initial increase in magnetic susceptibility comparing to the contralateral, with a significant difference at day 2 ($P<0.05$), followed by a decrease (Fig. 4C). At day 14, magnetic susceptibility is similar between the two sides. Similarly, DTI FA also shows a significant decrease at day 2, followed by an increase with similar FA at day 14. In contrast, the ipsilesional side of corpus callosum shows no significant changes in mean diffusivity and T2 (data not shown).

**Discussion:** Our results revealed a reversible changes in white matter following mild TBI, which can be detected using both magnetic susceptibility and diffusion FA, but not mean diffusivity and T2. Comparing with FA, magnetic susceptibility offers a larger dynamic range, higher signal and contrast to noise ratios, and higher spatial resolution. A previous study suggested that the magnetic susceptibility contrast between gray and white matter is linearly related to the myelin lipid fraction and the sine square of the fiber angle with respect to the main field [4]. With the typical prone positioning, the majority of the corpus callosum is perpendicular to the field with a narrow distribution of fiber orientation. Therefore, our findings are likely indicative of the white matter fiber disruption, loss of myelin and remyelination processes following TBI.

**Conclusion:** QSM is sensitive to the reversible white matter injury in this rat model of mild TBI. Complementary to DTI, QSM may provide novel opportunities for sensitive detection of white matter damage and alterations in vivo.

**References:** [1] Liu et al, NeuroImage, 2011; 56: 930. [2] Li et al, NeuroImage 2011; 55, 1645. [3] Li et al, Human Brain Mapp 2013, doi:10.1002/hbm.22360. [4] Li et al, NeuroImage, 2012; 59: 2088.

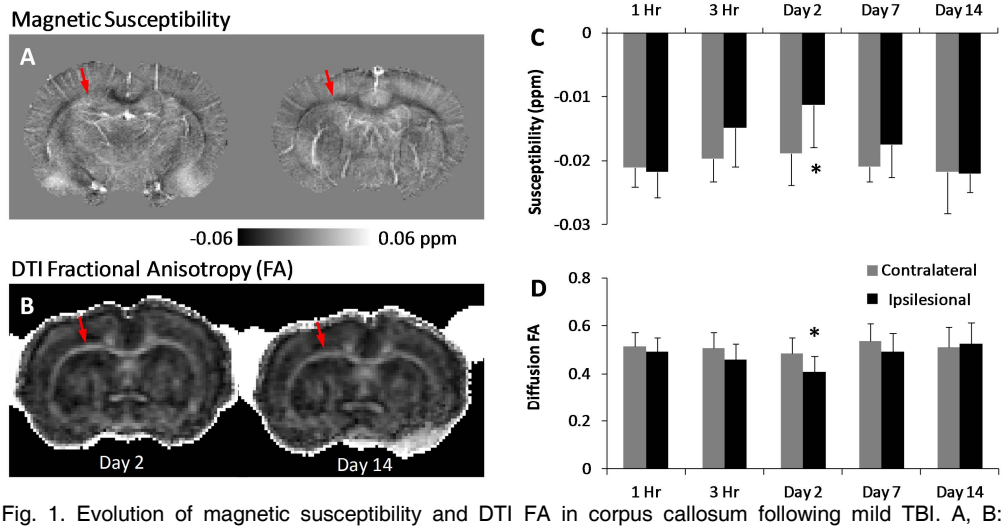


Fig. 1. Evolution of magnetic susceptibility and DTI FA in corpus callosum following mild TBI. A, B: Magnetic susceptibility and DTI FA at day 2 and day 14. The arrows pointed to the ipsilesional side. C, D: magnetic susceptibility and DTI FA of ipsilesional and contralateral sides of corpus callosum.