Trumatic brain injury (TBI) is one of the most prevalent risks of death and disability in young people, with about 1.6 million reported per year in the US. Mild TBI (mTBI) is characterized as a negligible loss of consciousness with minimal neuropathology, and is estimated to account for 70-90% of all TBI cases. Some of the most devastating injuries from brain trauma are the rupturing of arteries between the dura and the skull in an epidural hematoma, as well as tears in emissary veins, resulting in hemorrhagic contusions seen in subdural hematomas. This accumulation of blood can squeeze and increase pressure on the brain. Microvessel disruption plays substantial role in primary, secondary and chronic effects of TBI, and understanding the response of the vascular system following traumatic brain injury is critical to our ability to effectively treat brain trauma. Here, we introduce a novel application of our previously developed imaging modality, quantitative ultra-short time-to-echo contrast-enhanced (QUTE-CE) MRI using FDA-approved superparamagnetic iron oxide nanoparticle (SPION) ferumoxytol to image blood accumulation and to detect microbleeds in mild TBI animals.

Materials and Methods

Sprague Dawley rats were divided into two groups: control group and TBI group which received 3 mild hits for 3 continuous days. Rats in TBI group underwent QUTE-CE MRI before and immediately after ferumoxytol administration (for a 200μg/ml iron concentration in the blood) for 1.5 hours while control group underwent the same imaging sessions without traumatic brain injury. Quantitative global percentage of signal intensity change map based on baseline (pre-contrast imaging) and regional percentage of signal intensity change were calculated from QUTE-CE MRI and a 174-region rat brain atlas.

We replicated the pneumatic pressure drive. 50g compactor described by Viano at. el. reproduced consistently, the 7.4, 9.3 and 11.2 m/s impact velocities described for mild, medium and severe rat head injury, respectively. The data reported here all came from the 7 m/s impact velocities as determined using high-speed video recordings. Rats were impacted once, twice, and three times with a one-day interval between each impact.

Summary

- Rats underwent 1 mild hit barely showed significant difference in QUTE-CE MRI measure of ferumoxytol accumulation, indicating blood brain barrier was not disrupted after 1 mild concussion
- Rats underwent 3 hits showed significant difference in QUTE-CE MRI measures of ferumoxytol accumulation extravascular space
- These differences were primarily in cortex, hypothalamus, basal ganglia, cerebellum and brainstem
- Ferumoxyt continue to leak out from vasculature and to accumulate in brain tissues after mTBI
- QUTE-CE MRI can be used to detect microbleeds early following mTBI