

Multi-parametric MRI characterization of methylene blue treatment of mild Traumatic Brain Injury

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Introduction: The goal of this study was to investigate the spatiotemporal dynamics of multi-parametric MRI associated with mild traumatic brain injury (TBI) following methylene blue (MB) treatment.

Methods: Anesthetized rats were placed in a stereotaxic frame and a 6mm craniotomy over the left primary motor/somatosensory cortex region exposed the intact dura matter. The dura was impacted directly using a pneumatic cortical impactor with an impact velocity of 5.0m/s, a 250 μ s dwell time, and 1mm depth to mimic a moderate TBI. A double-blinded randomized design was utilized. Vehicle (n=6) or MB (n=6) was administered (1mg/kg at 1 hr and 0.5mg/kg at 3 hrs post TBI). Longitudinal MRI was performed on the day of the TBI, and again on days 1, 2, 7 and 14 after TBI onset. Comparison of MRI scans was made with the evolution of lesion volume, behavioral analysis (cylinder test and foot fault test).

Results & Discussion: Figure 1 shows representative T2, ADC and FA maps from a vehicle- and MB-treated animal 2 days after TBI. In the vehicle animal, the lesion was larger, showing hyper-intense T2 and ADC and hypo-intense FA. In the MB animal, ADC was hypo-intense and there was an apparent FA change in contrast to the vehicle animal. Figure 2 shows the temporal evolution of T2, ADC, and FA of the S1 and CC for the group data.

S1 cortex: Compared to contralesional T2, the ipsilesional T2 was elevated at 3 hrs, day 1 and day 2 but reduced toward normal values at day 7 and 14. Compared to contralesional T2, the ipsilesional ADC was elevated slightly at 3 hrs, peaked at day 2 but returned normal value at day 14. Compared to contralesional T2, the ipsilesional ADC was elevated slightly at 3 hrs, peaked at day 2, but returned to normal value at day 14.

CC: In contrast to S1 cortex, ipsilesional T2 and ADC were not significantly different from contralesional values except the ADC at 3hrs. However, ipsilesional FA values were significantly different from contralesional FA at 3 hrs, day 1 and day, and ipsilesional FA values but not on day 7 and 14.

Conclusion: TBI-induced edema peaked at day 2 and resolved substantially by day 7 and 14. The reduction in edema by day 14 is in general agreement with improvement in behavioral scores. Lesion volume and behavioral scores also correlated well with the improvement by MB treatment. However, despite the presence of lesions at day 7 and 14, forepaw asymmetry scores returned to normal for both groups, suggesting functional reorganization and compensation. Multi-parametric MRI offers a range of biomarkers that are sensitive to changes in different tissue types (e.g., white and gray matter) and to different stages of mild TBI.

REFERENCE: 1) Nair G, et. al. (2005) NeuroImage 28:165-174.

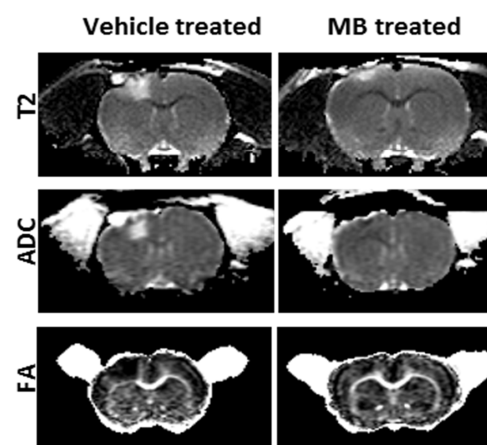


Figure 1. T2, ADC and FA of TBI animals treated with vehicle or methylene blue (MB).

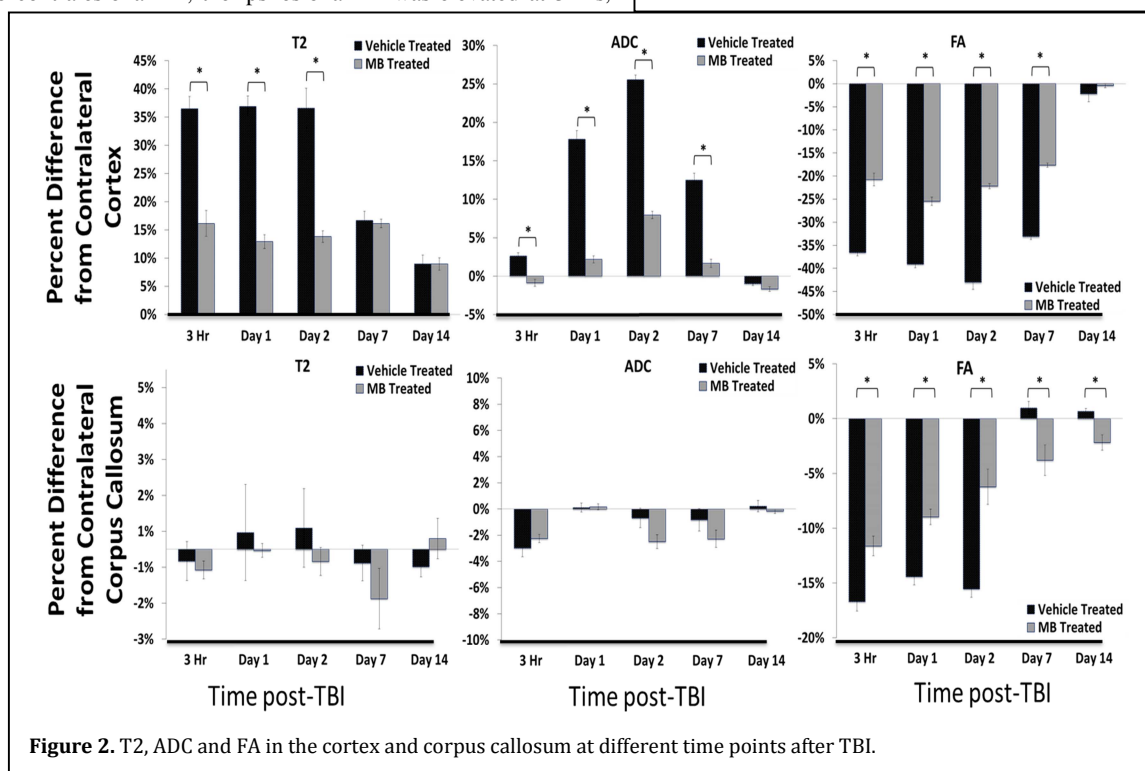


Figure 2. T2, ADC and FA in the cortex and corpus callosum at different time points after TBI.