Title: Reverse Translating Magnetic Resonance Spectroscopy to a Rodent Concussion Model

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Structured Abstract:

Introduction: A concussion is a brain injury caused by forces applied to the head or another part of the body, causing the brain to experience rapid rotational and translational accelerations. Athletes participating in contact sports have a high risk of sustaining a concussion, which can lead to structural and metabolic changes in the brain. Our group has previously measured changes in prefrontal white matter metabolite levels using magnetic resonance spectroscopy. Previous work presented reduced choline levels in male adolescent hockey players [Manning et al. 2017, Neurology], and reduced glutamine levels in female varsity rugby players [Schranz et al. 2017, Human Brain Mapping, in revisions]. Development of a rodent concussion model will allow assessment of the reproducibility of metabolite changes post-concussion and longitudinally, to aid in the development of therapeutics. The purpose of this current study was to demonstrate the feasibility of measuring metabolite changes in mice post-concussion.

Methods: Twenty-Four C57 Black 6 male mice (in collaboration with the Brown lab at Robarts Research Institute) were used in the current study. Mice were divided into two groups, Control (n=12) and Concussed (n=12). Concussed mice were anaesthetized and positioned under a traumatic brain injury device (TBI 0310, Precision Systems and Instrumentation, LLC). Following a midline incision, the animal received a mild controlled cortical impact centred at the midline bregma, with a custom-made silicone tip. Mice received 5 impacts at 24-hour intervals. The concussed mice were then imaged 48 hours after the final impact. Control mice solely underwent imaging. All imaging was performed on the 9.4 Tesla small-bore MRI scanner at the Robarts Research Institute. Magnetic resonance spectroscopy was acquired using Localization by adiabatic selective refocusing (LASER; TR/TE=3250/20ms, 128 Averages). Acquisition of the full spectrum was interleaved with a macromolecule only spectrum using a single-inversion recovery technique. Spectra were lineshape corrected by combined QUALITY and eddy current correction (QUECC), macromolecule subtracted, then fitted in the time domain using a Levenberg-Marquardt minimization routine. The analysis software (fitMAN) created in our laboratory in the IDL programming language was used to model the in vivo spectra using prior knowledge of metabolite lineshapes.

Results and Discussion: A significant decrease in glutamine ($p=0.03$) was observed in the concussed group in comparison to the control group. The decrease in Glutamine in the current study is consistent with our previous human studies and studies of rodent models using 13C spectroscopy that have found reduced Glutamine levels up to 24-hours post-injury, suggesting the reduction in Gln is the result of reduced glucose metabolism. Future work includes assessing the reproducibility of this glutamine change in male and female mice.