Validation of mouse traumatic brain injury model with behavioral and MRI endpoints

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BACKGROUND

Traumatic brain injury (TBI) is a leading cause of mortality and morbidity. There is a need for improved models to investigate pathophysiology and explore potential treatments. The aim of the current study was to validate cortical contusion injury in mice with behavioral assays for functional recovery and T2-MRI imaging. Validation of mouse model will also allow later combination of TBI with transgenic animals and creation of double hit models for TBI research.

MATERIALS AND METHODS

Animals

All animal experiments were carried out according to the NIH guidelines for the care and use of laboratory animals, and approved by the National Animal Experiment Board, Finland. Twenty-one C57BL/6J mice were purchased from Charles River, Germany, and weighing 20-25 g were used for the experiment. Animals were housed in a controlled environment (22 ± 1 °C) and in a 12 h light/dark cycle with free access to food and water.

TBI Procedure

Animals were anesthetized with isoflurane in 70% N2O and 30% O2; flow 300 ml/min, 2-3 min anesthesia induction with 5% isoflurane and maintenance with 1-2% isoflurane thereafter. The rectal temperature was monitored and maintained with a servo-controlled heating blanket. Following anesthesia induction, the animals were placed in a stereotaxic apparatus equipped with a gradient set capable of max. gradient strength 750 mT/m and interfaced to a Bruker Avance III console (Bruker Biospin GmbH, Ettlingen, Germany). Isoflurane-anesthetized mice (70% N2O and 30% O2; flow 300 ml/min, induction with 5%, maintenance 1.5%) were fixed to a head holder and positioned in the magnet bore in a standard orientation relative to gradient transmission and a two-element surface array coil for receiving (Rapid Biomedical GmbH, Rimpar, Germany). Each animal was placed in a stereotactic frame and a unilateral craniectomy of 3 mm in diameter was performed 2 mm craniectomy site epicenter) or other surgical complications were considered to be failed contusion (outside of the box). Presented as mean ± SEM.

RESULTS

MRI

Figure 1. Representative MRI images 24h post TBI. Coronal slices of 0.7 mm thickness were acquired using field-of-view 20x20 mm² and 256x128 imaging matrix.

Figure 2. MRI data on lesion volume (mm³) and tissue viability showing an 72 metabolic time (x) for the lesion and control side of the brain. Presented as mean ± SEM.

Figure 3. Suggested Study Schematic for TBI Studies.

Figure 4. Surgery lab at CR Discovery Services Finland

CONCLUSIONS

- Non-invasive imaging with T2-MRI provided information on the lesion size and tissue viability showing clear lesions as well as increased T2-relaxation time.
- The validated mouse TBI model can be a tool to study TBI in mice allowing combination with various transgenic lines and creating a valuable model for TBI research and drug discovery.
- Validation of mouse model will also allow later combination of TBI with transgenic animals and creation of double hit models for TBI research.

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