CHIMERA (Closed Head Injury Model of Engineered Rotational Acceleration) Is a Novel and Clinically Relevant Traumatic Brain Injury Model in Rodents

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Abstract

Background: Traumatic brain injury (TBI) is a leading cause of death and disabilities in developed countries. A major challenge in TBI research is that many common experimental models do not faithfully replicate the biomechanical aspects of TBI in real-life. To address this issue, we have recently developed a novel rodent TBI model with high precision, reliability and translatability, called CHIMERA (Closed-Head Impact Model of Engineered Rotational Acceleration). It is distinct from existing TBI models in that it delivers precise impact to the intact head in a non-surgical procedure, and allows unrestrained head movement, which facilitates integration of functional and histological outcomes to biomechanical analysis.

Objectives: (1) To use CHIMERA to perform mild repetitive TBI in wildtype mice at a single energy level, and characterize the biomechanical, histological and function outcomes. (2) To subject wildtype mice to single TBI at increasing energy levels, and correlate the head kinematic parameters to the behavioral and histological outcomes.

Methods: In part (1), adult C57Bl/6 mice received two TBI each of 0.5J impact energy, 24 hr apart. In part (2), a single TBI of 0.1J to 0.7J impact energy was induced. Head kinematics were assessed using high-speed videography (5000 fps). Post-injury neurological outcomes were

assessed by loss of righting reflex duration (immediately post-injury) and neurological severity score (1h). Axonal injury was assessed by Neurosilver staining (2d).

Results and Discussions: In part (1), head kinematic analysis of repetitive 0.5J impacts showed that CHIMERA induced a peak linear head displacement of 49.6 ± 3.5 mm, and a peak angular deflection of 2.6 ± 0.28 rad. Peak linear and angular velocities were 6.6 ± 0.8 m/s and 305.8 ± 73.7 rad/s, respectively. The head experienced peak linear and angular accelerations of 385.1 ± 52 *g* and 253.6 ± 69.0 krad/s^2, respectively. Injured mice showed significantly prolonged loss of righting reflex, and displayed neurological deficits. Histological analysis revealed diffuse axonal injury at various white matter areas including the optic tract. In part (2), head kinematics of 0.1J to 0.7J impacts were analyzed, and a significant correlation is observed between linear head kinematic parameters (displacement, velocity, and acceleration) vs behavior (loss of righting reflex ($R^2 > 0.41$ and $p < 0.02$)), as well as vs histology (axonal injury ($R^2 > 0.46$ and $p < 0.02$)).

Conclusion: CHIMERA is a simple, reliable model of TBI that offers integration of biomechanics with histological and functional assessments.

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