A Novel Technique for Improving the Accuracy of Head Kinematics Measurements in Mice Using High-Speed Videography

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I. INTRODUCTION

Experimental animal models are instrumental to understanding the biological mechanisms of traumatic brain injury (TBI) because they allow collection of pre-injury and longitudinal data, including characterisation of the biological aspects of the injury cascade, as well as preparation of biospecimens under controlled conditions. Given their wide availability, cost-effectiveness and utility for assessing behaviour, physiology and in drug discovery, rodent models are the most widely used in preclinical TBI studies [1]. CHIMERA (Closed Head Injury Model of Engineered Rotational Acceleration) is an efficient and reliable model for producing mild TBI (mTBI) in rodents using an impact-acceleration mechanism [2-4], but the lack of an effective head kinematics measurement system has limited researchers' ability to accurately characterise the mechanical insult during these impacts. Measuring head accelerations directly in mice with head-mounted accelerometers is not possible due to constraints inherent to the injury model and the size/mass restrictions imposed by the mouse head. As such, using high-speed videography is the only viable option for kinematics measurements, but highly accurate position measurements are necessary to compute the associated head accelerations as their fidelity degrades tremendously with measurement errors. A novel head motion tracking system was developed with the goal of improving the accuracy, reliability, repeatability and efficiency of head kinematics measurements using high-speed video.

II. METHODS

Fig. 1. Tooth-mounted, 3D-printed motion tracking head-marker (A). Head-marker model with mouse skull to show strapped attachment. The upper incisors fit tightly within the slot (B), and the elastic strap around the snout (C) maintains firm pressure between the teeth and head-marker.

We developed a head-marker structure (Fig. 1(A)), 3D-printed with polylactic acid, that mates to the upper jaw of the mouse using a tooth slot for the incisors. The head-marker was designed to fit tightly around the teeth and head to minimise relative motion (Fig. 1(B)).The head-marker can be temporarily secured to the head with a band over the snout (Fig. 1(C)) for live animal experiments or glued directly to the teeth for terminal experiments. Two tracking markers are attached to one side to enable planar motion tracking.

The head-marker system performance was evaluated and compared against the previous skin-tracking technique by impacting cadaver mice according to the established CHIMERA protocol [2] (Fig. 2), using an impact energy of 0.7 joules. These tests were performed on wild-type C57Bl/6 male mice (age: 8 months, mass: 37.4 ± 3.3 grams).

Impact videos were recorded using a Phantom V12 high-speed camera at 15000 fps, and image analysis was performed using ProAnalyst Motion Analysis Software. The resultant linear velocities and accelerations were computed for a point midway between the eye and ear that approximates the brain centre of mass. Angular parameters were calculated using two points (either the head-marker targets or the cheek paint mark and anterior head-marker target) to determine the rigid body rotation of the skull. All data were passed through a 500 Hz 5th order low-pass Butterworth filter.

The head-markers were either strapped to the mouse's snout or glued to the upper incisors. We assumed the glued head-marker system to be the gold standard for comparison because the glue ensured that no relative

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motion between the head and markers would occur. The strapped version is required for live experiments due to ethical and practical limitations of gluing materials to the teeth.

Three experiments were performed to evaluate the improvements in repeatability, accuracy and tracking time realised by the strapped head-marker system over the skin-tracking method. The repeatability test involved three different operators, repeating the tracking and analysis of the same video three times using both methods. The accuracy of the skin tracking technique was determined by comparing its kinematic outputs to those of the glued head-marker in five mice. The accuracy of strapped head-marker was evaluated by comparing the mean kinematic outputs from it and the glued head-marker from five repeated impacts with each method for three mice.

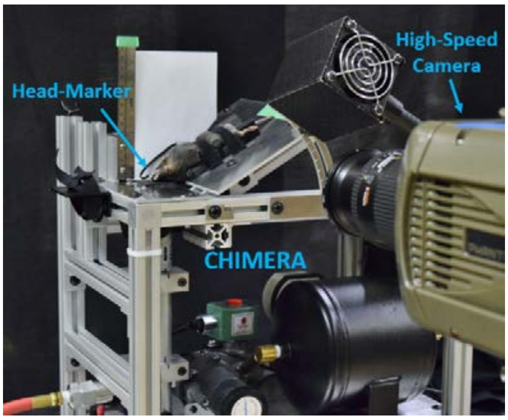

Fig. 2. Experimental set-up for head kinematics tracking using the CHIMERA device.

III. INITIAL FINDINGS

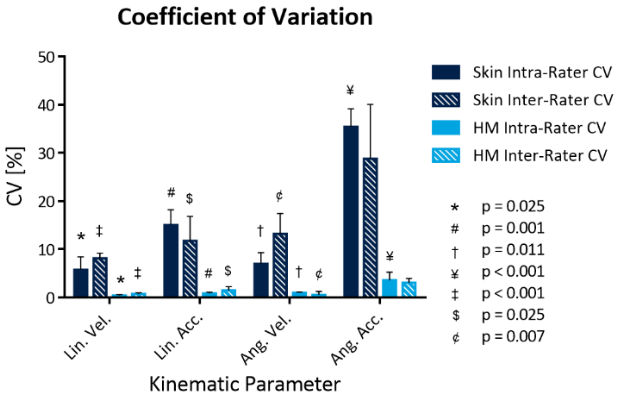

Fig. 3. Coefficient of variation between and within raters for the kinematic parameters derived from skin and head-marker tracking methods. Error bars represent one standard deviation.

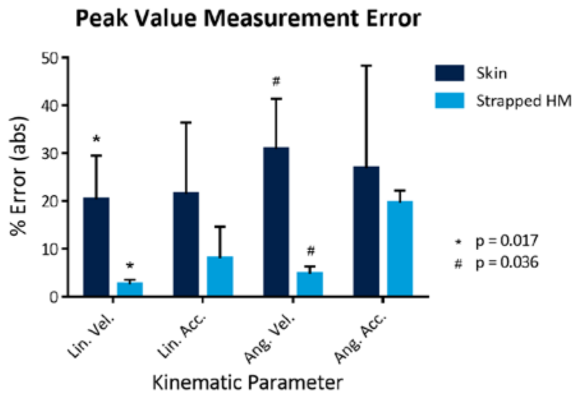

Fig. 4. Percent error of peak kinematic values from skin and strapped head-marker methods compared to corresponding glued head-marker measurements. Error bars represent one standard deviation.

We saw dramatic improvements in the reliability of kinematic measurements both between and within operators across all parameters when using the head-marker system (Fig. 3). Measurement error was significantly decreased for all parameters except angular acceleration (Fig. 4), agreement of the temporal kinematic curves were vastly improved, and the video analysis time was decreased by 74%.

IV. DISCUSSION

The challenges associated with rigidly attaching a marker carrier to such a small and delicate structure that is subjected to massive accelerations without affecting critical physiological functions make the application of tracking markers in a mouse TBI model a substantial accomplishment. Compared to the previous method, which relied on manually tracked reference points on the skin, the head-marker increased measurement accuracy through better coupling of the markers to the skull, minimised inter-operator variability by reducing the amount of subjective user input required during digitisation, and greatly decreased the time required for video analysis by automating the tracking. Despite these marked improvements, imperfect skull mating when using the strap for fixation resulted in errors that overestimate the angular acceleration far more than the errors associated with the other parameters, and caution should be taken in its interpretation.

V. REFERENCES

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