The ladder rung walking task as a technique to quantify traumatic cerebellar injury in rats
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Introduction: Traumatic brain injury (TBI) affects 1.7 million people annually in the United States, leading to death in 3% of the cases and various cognitive, psychological, motor, and sensory deficits in non-fatal cases.¹ The cerebellum is often affected by trauma to other parts of the cranium even though direct cerebellar injury is uncommon.² Previous studies have used fluid percussion injury (FPI) in rats as a model for TBI² and have documented both the electrophysiological and histological effects of TBI on the rat cerebellum³; however, less is known about the behavioral changes caused by direct cerebellar insult. The goal of this research is to develop a method to quantify the behavioral changes in rats following cerebellar TBI in order to find a relationship between motor impairments and previously documented changes observed in the cerebellum. This would lead to a better understanding of the progression of behavioral symptoms in TBI patients. The ladder rung walking task, used in previous studies to quantify motor deficits in rats, is used here to analyze impairments to cerebellar function.

Materials and Methods: The subjects used in this research were four experimentally naïve, male, Sprague-Dawley rats, each initially weighing between 210 and 275 grams. Each rat was food-restricted during the week, but had unlimited access to food on weekends. The ladder apparatus we designed was constructed using Plexiglas side walls, each 3 feet long, and 3 mm diameter stainless steel rungs, which were spaced 2 cm apart. Prior to injury, the rats were trained to cross the ladder for a period of 10 to 14 days. A sucrose pellet was placed at the opposite end of the ladder to serve as a reward for each successful crossing. After the training period, each rat was tested on the ladder for ten trials with video recording done for future analysis. Fluid percussion injury was then performed on each rat. The FPI apparatus (built previously) consists of a voice coil actuator, controlled by a Matlab program, which applies a pressure pulse through a column of deionized water onto the surface of the cerebellum. Pulses varying from 15 psi to 30 psi were administered to different rats in order to determine the minimum injury intensity required to induce behavioral change. After injury, the rats were tested again on the ladder. The videos of the pre- and post-injury tests were analyzed using the forepaw placement scoring system developed by Metz and Whishaw.⁴ The average forelimb step duration and step distance for each rat were also calculated from the video recordings.

Results and Discussion: Step duration of post-injury trials (Fig. 1) for each rat increased compared to pre-injury values (n= 4 rats, paired t-test, p=0.0024). The post-injury step distance (not shown) was shorter than pre-injury step distance (p=0.11). This test did not provide a significant result, which may be due to the small sample size. The pre- and post-injury forepaw placement scores (not shown) did not yield any significant difference (p=0.98). It is likely that the longer step duration post-injury allowed for greater accuracy in forepaw placement, leading to post-injury scores that were similar to pre-injury scores.

Conclusions: We have shown that the ladder rung walking task can be used as a method for assessing cerebellar traumatic brain injury. The average step duration, rather than the forepaw placement score, proved to be a better measure for quantifying cerebellar injury due to the slower post-injury walking pace. Future studies comparing results from the ladder rung walking task with electrophysiological changes in the cerebellum can confirm this task as a viable behavioral paradigm for assessing cerebellar damage.

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