



Basic Science

Analysis of equivalent parameters of two spinal cord injury devices: the New York University impactor versus the Infinite Horizon impactor

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Abstract

BACKGROUND CONTEXT: The New York University (NYU) impactor and the Infinite Horizon (IH) impactor are used to create spinal cord injury (SCI) models. However, the parameters of these two devices that yield equivalent SCI severity remain unclear.

PURPOSE: To identify equivalent parameters, rats with SCIs induced by either device set at various parameters were subjected to behavioral and histologic analyses.

STUDY DESIGN: This is an animal laboratory study.

METHODS: Groups of eight rats acquired SCIs by dropping a 10 g rod from a height of 25 mm or 50 mm by using the NYU device or by delivering a force of 150 kdyn, 175 kdyn, 200 kdyn, or 250 kdyn by using the IH impactor. All injured rats were tested weekly for 8 weeks by using the Basso, Beattie, and Bresnahan (BBB) test and the ladder rung test. On the 10th week, the lesion volume of each group was measured by using a 9.4 Tesla magnetic resonance imaging (MRI), and the spinal cords were subjected to histologic analysis using anterograde biotinylated dextran amine (BDA) tracing and immunofluorescence staining with an anti-protein kinase C-gamma (PKC- γ) antibody.

RESULTS: Basso, Beattie, and Bresnahan test scores between the 25 mm and the 200 kdyn groups as well as between the 50 mm and 250 kdyn groups were very similar. Although it was not statistically significant, the mean scores of the ladder rung test in the 200 kdyn group were higher than the 25 mm group at all assessment time points. There was a significantly different cavity volume only between the 50 mm and the 200 kdyn groups. Midline sagittal images of the spinal cord on the MRI revealed that the 25 mm group predominantly had dorsal injuries, whereas the 200 kdyn group had deeper injuries. Anterograde tracing with BDA showed that in the 200 kdyn group, the dorsal corticospinal tract of the caudal area of the lesion was labeled. Similar labeling was not observed in the 25 mm group. Immunofluorescence staining of PKC- γ also revealed strong staining of the dorsal corticospinal tract in the 200 kdyn group but not in the 25 mm group.

FDA device/drug status: Not applicable.

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CONCLUSIONS: The 25 mm injuries generated by the NYU impactor are generally equivalent to the 200 kdyn injuries generated by using the IH impactor. However, differences in the ladder rung test scores, MRI images, BDA traces, and PKC- γ staining demonstrate that the two devices exert qualitatively different impacts on the spinal cord. © 2016 Elsevier Inc. All rights reserved.

Keywords: Anterograde tracing; BBB test; IH impactor; Ladder rung test; NYU impactor; Spinal cord injury

Introduction

Various experimental animal models are needed to understand spinal cord injury (SCI) pathophysiology and to develop optimal treatment strategies for injuries to the central nervous system [1,2]. In the current SCI models, SCI is induced by three methods, namely compression, contusion, and transection [3]. Compression and contusion are used particularly frequently to induce SCI in animal models [4] because these injuries more closely resemble the most common clinical cord injuries seen in humans. With regard to spinal contusion, it is known to disrupt a variety of spinal tracts located in the white matter as well as in the central gray matter [5,6]. Depending on the spinal cord area, contusion injuries can affect numerous descending motor tracts that mainly control limb movements. The area or amount of the loss of these tracts may result in different behavioral deficits or motor scores [7].

Most contusion SCI models are generated by two different instruments, namely the New York University (NYU) impactor and Infinite Horizon (IH) impactor. The NYU impactor has been widely used since it was created in 1991 and requires user skill because a weight must be dropped manually [8–10]. The IH impactor was developed in 2003 and has sensors, a mechanical servo control, and a micro-processor control [11]. It is a user-friendly device that creates various contusion injuries by applying the desired force using computer software [11]. Although both instruments offer useful information, such as height, force, velocity, and tissue compression depth [12], problems arise when the data obtained from these devices are compared with each other. This is because the devices involve different impact parameters, and the equivalence of these parameters, in terms of lesion severity, has not yet been precisely and systematically assessed.

Therefore, the purpose of this study is to identify the parameters of the two devices that yield equivalent SCI severity in rats. For this, the functional locomotor outcomes and the histologic and magnetic resonance imaging (MRI) characteristics of the SCIs produced by the two devices were compared.

Materials and methods

Experimental animals

The study involved 48 female Sprague-Dawley rats (Orient Bio Inc., Seongnam, Korea) for behavior tests, MRI, and

the histologic analysis, and an additional six rats for the biotinylated dextran amine (BDA) staining. The animals were aged 8 weeks (250–300 g), were housed three to a cage, were exposed to a 12 h light-dark cycle, and were provided with sufficient food and water. All procedures adhered to the Institute for Laboratory Animal Research standards and were approved by the Institutional Animal Care and Use Committee of the Asan Institute for Life Science (Seoul, Korea).

Preparation of the spinal cord contusion models

All experimental rats were anesthetized with 2% isoflurane (Piramal Critical Care, Inc., Bethlehem, PA, USA), and the vertebral column was exposed between T7 and T8. A total laminectomy was performed at T7 without rupturing the dura. After the laminectomy, all animals were randomized and classified into six groups, with eight rats in each group. The exposed vertebral column was stabilized by clamping the rostral T6 and caudal T10 vertebral bodies with forceps. The exposed dorsal surface of the cord was then subjected to a contusion injury by using either the NYU impactor (New York University, New York, NY, USA; Fig. 1) or the IH impactor (Precision Systems & Instrumentation, Lexington, KY, USA; Fig. 2). Two NYU impactor parameters were tested: 10 g with 25 mm height (25 mm group) and 10 g with 50 mm height (50 mm group). Four IH impactor parameters were tested, namely 150 kdyn (150 kdyn group), 175 kdyn (175 kdyn group), 200 kdyn (200 kdyn group), and 250 kdyn (250 kdyn group) [2,13–16]. After inducing the SCI, the surgical site was sutured in layers and the rats were injected subcutaneously with sterile saline, cefazolin (10 mg/kg), and ketoprofen (5 mg/kg) to inhibit secondary infection and pain. Postoperative care involved the daily manual expression of the bladder until spontaneous urination returned. Before day 7, four of the 48 rats died so we supplemented them with animals that had undergone the same preparation.

The Basso, Beattie, and Bresnahan (BBB) test

The BBB test was used to assess hind limb function in the rats [9]. Briefly, the injured rats were adapted to a treadmill (Jeung Do Bio & Plant Co., Seoul, Korea) that was set to a rate of 8 m/min for 3 minutes, after which the hind limb movements were recorded with a video camera for 1 minute. The scores were calculated by using the BBB locomotor rating scale, which is a 22-point scale that yields scores ranging from

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