Available online at www.sciencedirect.com

SCIENCE DIRECT

Brain Research 1050 (2005) 180 – 189

BRAIN RESEARCH

www.elsevier.com/locate/brainres

Research Report

Hindlimb loading determines stepping quantity and quality following spinal cord transection

Wojciech K. Timoszyk[a], Jeff A. Nessler[a], Cynthia Acosta[b], Roland R. Roy[c], V. Reggie Edgerton[c], David J. Reinkensmeyer[a,*], Ray de Leon[b]

[a]Department of Mechanical and Aerospace Engineering, 4200 Engineering Gateway (EG3225), University of California, Irvine, CA 92697-3975, USA
[b]Department of Kinesiology and Nutritional Science, California State University, Los Angeles, CA 90032, USA
[c]Department of Physiological Sciences and Brain Research Institute, University of California, Los Angeles, CA 90095-1761, USA

Accepted 18 May 2005
Available online 24 June 2005

Abstract

We compared the bipedal hindlimb stepping ability of untrained and trained (step-trained 6 min/day) spinal rats (mid-thoracic spinal cord transection at post-natal day 5) at different levels of body weight support on a treadmill over a 40-day period, starting at 69 days of age. A robotic device provided precise levels of body weight support and recorded hindlimb movement. We assessed stepping ability using: (1) step quantity determined from the measured hindlimb movement, (2) ordinal scales of paw placement, weight-bearing, and limb flexion, and (3) the lowest level of body weight support at which stepping was maintained. Stepping quantity and quality depended strongly on the level of support provided. Stepping ability improved with time, but only at the higher levels of weight-bearing, and independently of training. Increasing limb loading by gradually decreasing body weight support altered the spatiotemporal properties of the steps, resulting in an increase in step length and stance duration and a decrease in swing and step cycle duration. The rats progressively improved their ability to support more load before collapsing from a maximum of about 42 g (~25% of body weight) at Day 1 to 73 g (~35% of body weight) at Day 40. We conclude that the level of hindlimb loading provided to a spinally transected rat strongly influences the quantity and quality of stepping. Furthermore, the relationship between stepping ability and loading conditions changes with time after spinal cord transection and is unaltered by small amounts of step training. Finally, load-bearing failure point can be a quantitative measure of locomotor recovery following spinal cord injury, especially for severely impaired animals that cannot step unassisted.

Theme: Motor systems and sensorimotor integration
Topic: Spinal cord and brainstem

Keywords: Locomotion; Spinal cord injury; Pattern generation; Sensory information; Motor control

1. Introduction

Assessment and training of locomotion after spinal cord injury are fundamentally constrained by residual load-bearing ability. For example, assessments of locomotor function suffer from a floor effect, in which severely impaired animals cannot be accurately evaluated because they are unable to generate sufficient locomotor activity for measurement [9,11,14,15]. Training of locomotor function benefits from the provision of appropriate levels of body weight support so that proper patterns of sensorimotor activity are generated to stimulate neural plasticity [2,3].

Despite its importance, studies of locomotion after spinal cord injury have generally suffered from an inability to precisely control limb loading. Investigators have addressed this problem by studying stepping-like behavior in reduced-gravity conditions (e.g., swimming and air-stepping) or by using static frames to support the body.

* Corresponding author. Fax: +1 949 824 8585.
E-mail address: dreinken@uci.edu (D.J. Reinkensmeyer).

0006-8993/$ - see front matter
doi:10.1016/j.brainres.2005.05.041

However, these techniques provide only limited resolution for varying the loading forces created by gravity. This gap in knowledge has recently begun to be addressed in studies of humans with spinal cord injury using force-controllable body weight support systems. A primary finding is that leg muscle activity varies with the level of body weight support, even following a complete spinal cord injury [5,10,12]. These results are consistent with the viewpoint that the human lumbosacral spinal cord interprets load-related afferent information in creating motor output.

Investigators have yet to carefully examine the relationship between locomotion and weight support for rodents, even though the rodent is the primary model for the study of spinal cord injury and regeneration. To address this issue, we recently developed a novel body weight support (BWS) device that can precisely vary the level of loading delivered to the hindlimbs of rats during bipedal treadmill stepping [20] (Fig. 1). The device holds the rat in a harness at the end of a lever and permits the level of support to be controlled to within a few percent of the animal's body weight. The device is incorporated into a robotic system that also has a pair of small, lightweight robot arms that attach to the hindlimbs and can accurately measure limb motion.

The goal of the present study was to use this device to rigorously assess the effects of load on stepping ability following a complete spinal cord transection. We chose to study rats that were transected as neonates because such rats typically show a more robust recovery of stepping ability than rats transected as adults. We sought to assess the effects of load on stepping ability with two different protocols. We measured the stepping ability of spinally transected rats at several fixed levels of weight support and as the level of weight support was gradually decreased from a high level (i.e., increasing weight-bearing during stepping). In addition, we assessed the effects of short sessions of step training (6 min/day) with either fixed or continuously decreasing BWS on stepping ability. Our results confirm that limb loading plays a major factor in determining the quantity and quality of stepping following spinal cord injury in rats. Portions of this work have been published in conference abstract format [17].

2. Materials and methods

2.1. Animals

Thirty-five Sprague–Dawley rat pups received a spinal cord transection as neonates (post-natal day 5). The rats were anesthetized via hyperthermia, a laminectomy was performed at the mid-thoracic level, the dura was incised, and the spinal cord completely transected in the mid-thoracic region using microscissors. Two surgeons verified the completeness of the transection. Gel foam was inserted at the transection site and the wound closed. All surgical procedures were done under aseptic conditions. The pups were allowed to recover in a warm incubator until fully mobile and then returned to their mothers until weaned at 25 days of age. Thereafter, the rats were housed singly in standard cages. Training on the robot was initiated when the rats were 69 days old. All procedures were approved by the Animal Use Committee at the University of California, Los Angeles, where the surgery and recovery took place, and by the California State University at Los Angeles, where the testing and training took place.

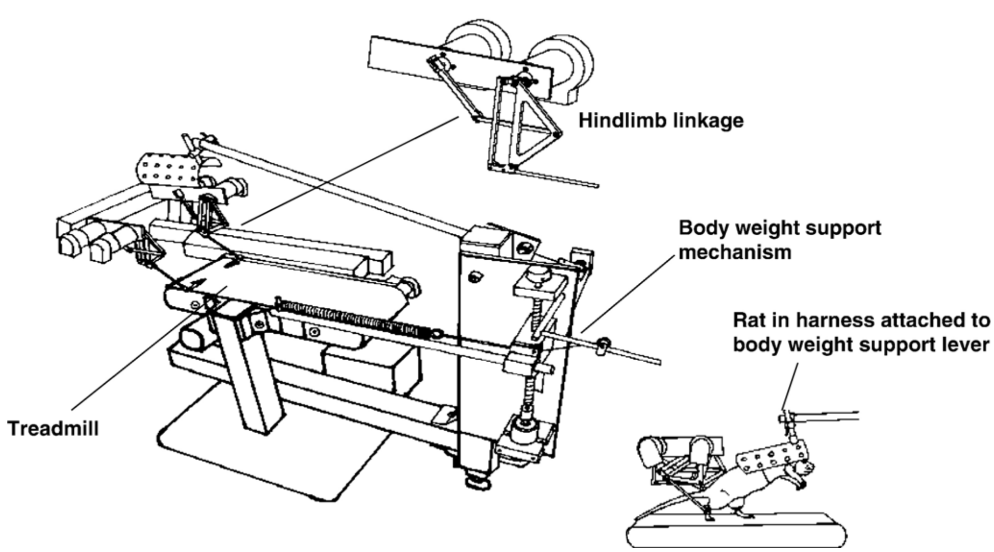

Fig. 1. Prototype version of the "rat stepper". The rat is placed in a cloth harness and attached to the end of the body weight support (BWS) lever. The orientation of the rat's torso is adjustable, and the amount of weight support delivered to the animal is precisely controlled. The rat steps bipedally in the device, and the small, lightweight, robotic arms attach to the lower shanks of the hindlimbs, just above the ankle, with plastic cable ties that rotate in the parasagittal planes. These robotic arms can impart forces to the animal or simply record the trajectories of each ankle (as used in the present study), similar to optical motion capture.