available at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

BRAIN RESEARCH

Research Report

Differential motor and electrophysiological outcome in rats with mid-thoracic or high lumbar incomplete spinal cord injuries

Guillermo García-Alías[a,*], *Antoni Valero-Cabré*[b], *Rubén López-Vales*[a], *Joaquim Forés*[a,c], *Enrique Verdú*[a], *Xavier Navarro*[a]

[a]*Neuroplasticity and Regeneration Group, Institute of Neurosciences and Department of Cell Biology, Physiology and Immunology, Universitat Autònoma de Barcelona, E-08193, Bellaterra, Spain*
[b]*Department of Anatomy and Neurobiology, Boston University School of Medicine, 700 Albany Street, Boston, MA 02118, USA*
[c]*Hand Unit, Hospital Clínic i Provincial de Barcelona, Barcelona, Spain*

ARTICLE INFO

Article history:
Accepted 10 June 2006
Available online 21 July 2006

Keywords:
Motoneuron
Motor-evoked potential
Nerve conduction
Spinal cord injury
Spinal reflex

ABSTRACT

We have investigated the motor changes in rats subjected to a moderate photochemical injury on mid-thoracic (T8) or high lumbar (L2) spinal cord segments. Fourteen days after surgery, L2 injured animals presented gross locomotor deficits (scored 10±2.8 in the BBB scale), decreased amplitude of motor-evoked potentials (MEPs) recorded on tibialis anterior (TA) and plantar (PL) muscles (24% and 6% of the preoperative mean values, respectively), reduced M wave amplitudes (75%, 62%), and also facilitated monosynaptic reflexes evidenced by an increase of the *H/M* amplitude ratio (158% and 563%). On the other hand, T8 injured animals had only slight deficits in locomotion (18±0.6 in the BBB scale), a minimal reduction in MEP amplitudes (78% and 71% in TA and PL muscles), normal M wave amplitudes, and a milder increase of the *H/M* ratio in the TA muscle (191%) but less pronounced in the PL muscle (172%). The percentage of spared tissue at the site of injury was similar in both experimental groups (L2: 79% and T8: 82%). Taken together, these results indicate that lumbar spinal injuries have more severe consequences on hindlimb motor output than injuries exerted on thoracic segments. The causes of this anatomical difference may be attributed to damage inflicted on the central pattern generator of locomotion resulting in dysfunction of lumbar motoneurons and altered spinal reflexes modulation.

1. Introduction

Trauma to the spinal cord results in the damage of gray and white matter, with death of neurons and disruption of spinal pathways at the site of injury. As a result, patients lose motor, sensory and autonomic control of the segments of the body below the injury. These deficits persist throughout their whole lifespan. Cell grafting (Ramón-Cueto et al., 2000; Takami et al., 2002; García-Alías et al., 2004), neurotrophic factor delivery (Schnell et al., 1994; Kobayashi et al., 1997; Blesch and Tuszynski, 2003), growth inhibitor blockade (Brosamle et al., 2000; Bradbury et al., 2002; Li and Strittmatter, 2003) and

* *Corresponding author*. Present address: Centre for Brain Repair, Department of Clinical Neuroscience, University of Cambridge, Cambridge CB2 2PY, UK. Fax: +44 1223 331174.
E-mail address: gg284@cam.ac.uk (G. García-Alías).

0006-8993/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.brainres.2006.06.029

intracellular signaling manipulation (Qiu et al., 2002; Dergham et al., 2002) have proven limited success in restoring function after spinal cord injuries in experimental models. Alternatively, rehabilitative therapies based on treadmill training (Hutchinson et al., 2004; Timoszyk et al., 2005) or on electrical stimulation of muscles, peripheral nerves and spinal cord (Stein et al., 2002) might represent useful complementary strategies for improving motor function in daily life activities, particularly for hand use in tetraplegics and standing and walking in paraplegics (Stein and Mushahwar, 2005). Notwithstanding, their final efficiency will strongly depend on the volume and functional relevance of the preserved neural tissue and its ability to accurately respond to stimulation devices.

The degree of neurological deficits caused by a spinal cord injury depends on various parameters, including the area of preserved parenchyma, the primitive function of the spinal tracts impacted by the lesion, and the contribution and plasticity of circuitry spared by the primary and secondary damage (Fehlings and Tator, 1995). In this study, we hypothesize that under conditions of identical mechanisms and extent of spinal cord damage, the localization of the injury per se plays a crucial role in the final outcome. This is particularly relevant if the local circuitry in the damaged segments is in charge of highly specific sensory-motor regulation. The upper lumbar segments of the spinal cord have special functional relevance since it is the location of the hindlimbs central pattern generator (CPG) of locomotion (Cazalets et al., 1995; Cazalets, 2000). This specialized network of neurons generates both the rhythm and the correct pattern of hindlimb sensory-motor activity. Thus, damaging the CPG should reduce the efficiency of restoring therapies. On the other hand, if the amount and extent of damage inflicted to the motoneuron pool at the mid- and low lumbar spinal segments is limited, the use of external electrical devices may still be able to elicit alternate flexion and extension movements of the hindlimb muscles, which by mimicking some behavioral aspects of locomotion will help patients to become more independent (Stein and Mushahwar, 2005).

In order to address this issue, we studied two groups of rats submitted to photochemical injury at the mid-thoracic (T8) or high lumbar (L2) spinal cord, both located above the bulk of the spinal representation of hindlimb muscles, but the latter level involving the CPG network. The anatomical extent of the lesion was evaluated to ascertain the similarity of the injury in both groups, whereas walking scores and electrophysiological evaluation of descending spinal tracts, spinal motor reflexes and peripheral nerves were used to assess differences in the pattern of deficits.

2. Results

2.1. *Behavioral evaluation*

All the control rats displayed normal locomotion during the 14 days follow-up (scored 21 on the BBB scale), whereas rats with spinal cord injuries showed locomotor deficits of different severity depending upon the site of injury. At 3 days postoperation (dpo), iT8 animals presented only mild deficits in locomotion (BBB score 17.0±1.1; $p<0.01$ vs. CNT), characterized by slight rotation of the paws during the initiation of the swing phase, whereas iL2 animals displayed complete abolition of hindlimb function and developed paraplegia (0.0±0.1; $p<0.01$ vs. CNT and iT8). Over the 2-week follow-up, animals of both injury groups partially improved their locomotor abilities, yielding significantly higher scores after T8 (18±0.6; $p<0.01$ vs. CNT) than L2 injuries (10.0±2.8; $p<0.01$ vs. CNT and iT8) (Fig. 1). At 14 dpo, iT8 rats showed only mild deficits, with coordinated and balanced stepping but irregularity of fine details of locomotion, whereas iL2 rats displayed gross locomotor deficits, characterized by uncoordinated stepping. None of the rats presented muscular atrophy or weight loss during the time they were followed when compared to their own presurgery values or to the control rats.

2.2. *Electrophysiological results*

MEP baseline recordings of the TA muscle consisted of a single biphasic wave, with an amplitude of about 20–28 mV and an onset latency of ~6 ms (Fig. 2). Fourteen days after the injury, the mean amplitude value of group iT8 was slightly smaller than in the CNT group, whereas it was markedly decreased in group iL2. Significant differences were found in iL2 and iT8 groups in comparison to the controls (Table 1). The latency of MEPs was significantly longer in group iL2 than in groups iT8 and CNT. MEPs recorded in the plantar muscles of normal rats were of small amplitude, averaging 0.4 mV. After spinal cord injury the amplitude decreased significantly in both injured groups with respect to controls, but again more markedly in group iL2 than in group iT8 (Table 1).

Electrical stimulation of the sciatic nerve evoked in all the animals two consecutive muscle responses, the M and the H waves (Fig. 3). Prior to injury, the mean latency and amplitude of the M wave were about 1.6 ms and 47 mV respectively for the TA muscle and 3.0 ms and 9 mV for the PL muscle. The mean peak latency of the H wave of the TA muscle was ~6.5 ms with a mean amplitude of ~2.6 mV and a corresponding *H/M* ratio of

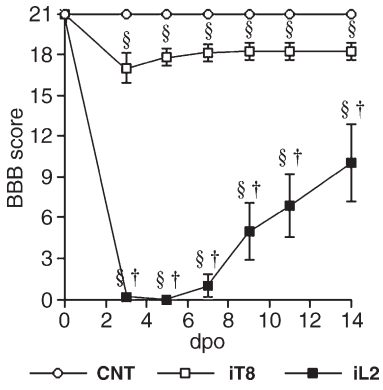

Fig. 1 – Open field walking results. BBB scores achieved during the 14 days follow-up in the control (CNT) and spinal cord injured groups (iT8 and IL2) in the open field walking evaluation. Note the mild decrease in BBB scores as a result of the lesion at T8 that plateaud around a score of 18 by 7 days. In contrast, injury at L2 resulted in a dramatic decline in locomotor performance that recovered partially by 14 days. ($^{§}p<0.01$ vs. CNT; $^{†}p<0.01$ vs. iT8).