Spinal Cord Injury Reveals Unexpected Function of Cutaneous Receptors

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INTRODUCTION

A major challenge for clinical neuroscience is to develop procedures for enhancing functional recovery after damage or disease of the CNS. The advent of powerful molecular and cellular techniques for promoting growth and regeneration of nerve cells, and for the production of engineered cells for incorporation into the nervous system, has yielded a sense of optimism that procedures for routine use will be developed in the near future (Horner and Gage 2000; Schwab 2002). In the meantime, the conventional approaches of drug therapy and rehabilitation therapy will continue to provide the main avenues for treatment combined in some instances with functional electrical stimulation of nerves and muscles. Therefore it is comforting that a number of significant advances have been made over the past decade in the rehabilitation of some groups of patients with damage of the CNS. One is the use of constraint-induced movement therapy to enhance arm and hand movement in stroke patients (Taub and Vaadia 2003; Wolf et al. 2002) and another is the use of treadmill training for improving walking in incomplete spinal cord injured patients (Dietz et al. 1998; Harkema 2001; Ladouceur et al. 1997; Wernig et al. 2000). The development of both of these procedures was based soundly on animal research in monkeys and cats.

With the efficacy of intense training procedures now established (although see van der Lee 2001), attention has turned to gaining an understanding of underlying mechanisms with the hope that knowledge of these mechanisms will lead to further enhancement of therapeutic effectiveness. Two papers appearing in this issue (Bouyer and Rossignol 2003a, b), pages 3625–3653, make a significant contribution to our knowledge of sensory signals that are necessary for the recovery of stepping in cats after a complete transection of the spinal cord.

One of the most useful animals models for examining the effects of training on functional recovery after spinal cord injury is the spinal cat. After complete transection of the spinal cord at the thoracic level, adult animals can be trained to step with their hind legs on a moving treadmill belt (Barbeau and Rossignol 1987; Lovely et al. 1986). With daily training sessions over a period of a few weeks, spinal animals regain the ability to produce weight-bearing stepping of the hind legs. The kinematics of leg movements and underlying patterns of muscle activity closely resemble those in normal walking animals. Currently we have very little knowledge about how training enhances stepping, although we do know that it involves a reduction in inhibition of the pattern generating networks within the spinal cord (De Leon et al. 1999; Tillakaratne et al. 2002). The fact that movements of the hind legs are required indicates that the adaptive changes within the spinal cord are driven by sensory signals from the stepping legs. An important issue, therefore, is to identify those sensory signals that are especially important in regulating stepping in spinal animals because these may provide the necessary information for modifying the locomotor pattern-generating networks.

The fundamental new finding of the studies of Bouyer and Rossignol is that feedback from cutaneous receptors in the hind paws is essential for stepping in spinal cats. After complete removal of cutaneous signals from the paws, spinal cats could not be trained to produce weight-bearing steps with plantar support on the treadmill belt. Electromyographic analysis of the motor patterns after cutaneous denervation of the paws revealed that the inability to step correctly was associated with a major restructuring of the motor pattern in the ankle flexor muscles. Instead of the normal reciprocal pattern of activity in ankle flexors and extensors, the ankle flexors were coactivated with extensors during the stance phase and silent during the swing phase. This is an unexpected finding because we know that reciprocity of activity in flexors and extensors is preserved after complete deafferentation. Why selectively removing cutaneous input from the paws drastically alters this basic motor pattern cannot be explained by modifications in known spinal pathways. It would be of some interest to know which groups of afferents are functioning to produce the coactivation of flexors and extensors in the partially deafferented spinal animals.

Another important finding was that spinal animals have the capacity for functional improvement after partial deafferentation of the paws. By progressively sectioning the five different nerves to the paws, Bouyer and Rossignol found that deficits produced by sectioning a nerve were rapidly overcome, and it was only after removal of all cutaneous input from the paws that normal stepping was permanently abolished. Thus minimal cutaneous input is sufficient to guide re-learning of stepping. This finding adds to the growing list of demonstrations of adaptive plasticity in the spinal cord (Pearson 2000; Wolpaw and Tennissen 2001).

The finding that cutaneous signals from the hind paws are essential for stepping in spinal cats comes as a surprise because it has been known for almost a century that deafferentation of the paws of otherwise intact cats has no obvious influence on the ability to walk on flat horizontal terrains (Sherrington 1910). The first paper by Bouyer and Rossignol confirms this early observation, although their careful analysis of leg movements and motor patterns revealed subtle alterations in the regulation of flexion movements of the knee. Much more dramatic deficits were observed when animals deprived of cutaneous input from the paws walked up and down slopes, and especially when they walked across the rungs of a hori-
horizontal ladder. In the latter situation, these animals often required considerable coaxing to walk on the ladder and, when they did, they were unable to place their paws correctly on the rungs. These observations demonstrate an important function of feedback from cutaneous receptors in the ongoing regulation of locomotor activity even in situations in which the environment is reasonably predictable.

By demonstrating the importance of cutaneous feedback in walking in normal and spinal cats, the authors have broadened our outlook about which sensory modalities might be manipulated to enhance stepping in spinal-cord-injured patients. Until now most of the focus has been on manipulating feedback from load-sensitive receptors in muscles by using body-support devices (Harkema 2001). Thus a question for future research is whether increasing cutaneous feedback from the feet (perhaps using a vibrating shoe insert) can enhance the rate of improvement in walking of spinal-cord-injured patients when combined with weight-supported treadmill training. Apart from this practical point, these reports also raise a number of important issues related to basic mechanisms generating the motor pattern for stepping. First, the finding of co-activation of ankle flexors and extensors after paw deafferentation highlights the long-standing issue of which features of the normal motor pattern are normally established by feedback from peripheral receptors. Second, none of the known influences of cutaneous signals can explain the radical reorganization of the motor pattern after deafferentation. And signals can explain the radical reorganization of the motor receptors. Second, none of the known influences of cutaneous pattern are normally established by feedback from peripheral long-standing issue of which features of the normal motor exors and extensors after paw deafferention highlights the Barbeau H and Rossignol S. Recovery of locomotion after chronic spinal-

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