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Chapter 23

Plasticity in somatic receptive fields after nerve injury

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Paper: Devor, M., and Wall, P. D. (1981). Plasticity in the spinal cord sensory map following peripheral nerve injury in rats. *The Journal of Neuroscience*, 1(7), 679–84.

Review

At the time that Devor and Wall's (1981) paper was published, it was already well established that the skin surface was mapped in an orderly fashion onto second-order sensory neurons in the dorsal horn of the spinal cord. For example, the receptive fields of neurons within the dorsal horn correspond to the legs and the feet. If the relevant peripheral nerve was cut, the neurons within that area of the dorsal horn would be left without a receptive field. Previous work by the authors in cats revealed that these deafferented spinal neurons could acquire new different receptive fields in other areas of skin.

This paper uncovers evidence of neuroplasticity in the spinal cord as a response to peripheral nerve injury. It is very much of its time with respect to the brevity of the methodology section and the relatively low numbers of experimental animals used. Experiments were performed on live adult rats acutely after nerve injury and at various intervals after that. The rats were anaesthetised with pentobarbital and then received specific peripheral nerve injuries to the saphenous and sciatic nerves. Subsequently, in vivo electrical recordings were taken from the dorsal horn of the spinal cord by using micropipettes while, separately, various stimuli were applied to the skin of the lower limb. The tips of the micropipette electrodes were cut off to facilitate mapping within the dorsal horn.

The medial sides of the rat L4 and L5 dorsal horn were found to have receptive fields devoted to the toes and foot. In the acute phase after neurectomy, there was a low density of neurons with active receptive fields in this area, and the ones encountered corresponded to the calf, the thigh, the lower back, or the perineum. The domination of the medial dorsal horn by toe–foot afferents changed drastically 4 days after peripheral nerve section. In addition, substantial numbers of cells with receptive fields that were located in the medial part of the dorsal horn and usually extended medially as far as the border of the dorsal column were found. These receptive fields were all located proximal to the ankle, within the distribution of the lateral cutaneous nerve of the thigh. Transection of this nerve eliminated these novel receptive fields. In contrast, after crush injury to the

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nerve, no reorganization of the dorsal horn neurons was observed, either acutely or in the chronic phase after peripheral neural regeneration had occurred. In the rats that had received peripheral nerve section, three survived for more than 140 days. In these, many sensory fibres had re-established connections to the periphery, and mapping of the dorsal horn neurons of these rats revealed that the spinal reorganization had reversed towards normality.

Thus, the peripheral receptive fields of medial dorsal horn neurons change 4–5 days after peripheral nerve transection, leading to novel receptive fields, via an unknown spinal mechanism. This change may be reversed if the transected peripheral nerve regenerates. Reassuringly, the spinal synaptic reorganization in rats was the same as what had been observed in cats.

Reflection

In this landmark paper, Devor and Wall investigated the pathophysiological changes occurring within the spinal cord after peripheral nerve injury in rats. This approach alone set them apart from many of their contemporaries, who were focused solely on physiological function. This is of particular relevance to clinical practice because of the pain and disability associated with neural injury and the limited therapeutic options (even in the present day). Indeed, this paper may be considered an early example of translational research by pioneers in the field.

This paper raised the question of what was the underlying mechanism responsible for the spinal plasticity observed. The authors discussed various hypotheses, discounting a purely peripheral mechanism through the methodology employed in their experiments. They postulated that there may be a trophic signal at the site of the injury and that this molecular signal was picked up peripherally and then transported retrogradely to the spinal cord. A great deal of research exploring this question was to follow, and this paper continues to be cited, right up to the present day, with close to 300 citations at present. It has cemented the concept of neuroplasticity at multiple levels of the nervous system in response to a peripheral insult. It provided key insights into the adaptive changes that can occur in the CNS in response to peripheral nerve injury. The nervous system could no longer be considered to be a passive hard-wired structure, but something that was much more fluid and malleable. Through this research, some of the underlying pathophysiological mechanisms involved in the initiation of chronic neuropathic pain became clearer, paving the way for subsequent groundbreaking research into neuroplasticity. Of particular relevance was the link between synaptic plasticity and reorganization of the cortical map in response to changes in the peripheral nervous system (Buonomano et al., 1998). Indeed Lotze and colleagues later used functional MRI to reveal how cortical remapping correlated specifically with phantom limb pain (Lotze et al., 2001).

Despite being from a basic science paper, the findings also reinforced the theoretical rationale for the biopsychosocial approach to the assessment and management of chronic pain (Gatchel et al., 2007). The adaptive neuroplasticity observed in the spinal cord,

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combined with that seen later in the cortex, illustrated the inherent dynamism of the nervous system. Indeed, by combining this basic neuroscience research with that from the field of psychology, it became clear how psychological and social factors can interact with neurological processes to impact on health and illness.

Prior to this paper, it was accepted knowledge that sensory maps were formed during embryogenesis and that they were essentially fixed and unchangeable. The data from this paper demolished that concept by demonstrating that massive and rapid synaptic rearrangement of the mammalian sensory map may occur and that it is a dynamic process involving both the peripheral nervous system and the CNS.

References

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