Journal of Hand Therapy 31 (2018) 184–194

Contents lists available at ScienceDirect

Journal of Hand Therapy

journal homepage: www.jhandtherapy.org

JHT Read for Credit Article #536.
Scientific/Clinical Article

Peripheral nerve injuries, pain, and neuroplasticity

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ARTICLE INFO

Article history:
Received 18 October 2017
Received in revised form
15 January 2018
Accepted 20 January 2018

Keywords:
Peripheral nerve injury
Neuroplasticity
Neuropathic pain
Rehabilitation

ABSTRACT

Introduction: Peripheral nerve injuries (PNIs) cause both structural and functional brain changes that may be associated with significant sensorimotor abnormalities and pain.
Purpose of the Study: The aim of this narrative review is to provide hand therapists an overview of PNI-induced neuroplasticity and to explain how the brain changes following PNI, repair, and during rehabilitation.
Methods: Toward this goal, we review key aspects of neuroplasticity and neuroimaging and discuss sensory testing techniques used to study neuroplasticity in PNI patients.
Results: We describe the specific brain changes that occur during the repair and recovery process of both traumatic (eg, transection) and nontraumatic (eg, compression) nerve injuries. We also explain how these changes contribute to common symptoms including hypoesthesia, hyperalgesia, cold sensitivity, and chronic neurogenic pain. In addition, we describe how maladaptive neuroplasticity as well as psychological and personality characteristics impacts treatment outcome.
Discussion and Conclusion: Greater understanding of the brain's contribution to symptoms in recovering PNI patients could help guide rehabilitation strategies and inform the development of novel techniques to counteract these maladaptive brain changes and ultimately improve outcomes.

Introduction

Peripheral nerve injuries (PNIs) can be the result of traumatic or nontraumatic causes. Traumatic PNIs are a source of disability worldwide[1] causing significant sensorimotor impairment and neurogenic pain (also classified as neuropathic pain).[2,3] Traumatic PNIs are commonly the result of motor vehicle accidents and less commonly from penetrating trauma, falls, and work-related injuries. Nontraumatic causes of PNI (eg, compression neuropathies, diabetic neuropathy, vasculopathies) are also a significant burden to both patients and the health care system. Unfortunately, there is a paucity of studies reporting on the prevalence of PNI, and as such, the rate of PNI in the general population is difficult to define with accuracy.

Studies estimate that approximately 2%-3% of all patients admitted to a Level I trauma center have PNI.[4,5] In 2008, Taylor et al examined the incidence of PNI within 3 months of a limb trauma diagnosis in patients who had presented to the hospital or outpatient clinic. The authors found a total incidence of PNI within 3 months of upper or lower limb trauma was 1.64%.[6] The prevalence of traumatic upper limb PNI appears to be relatively small compared to other traumatic injuries. Compression neuropathies (eg, carpal tunnel syndrome [CTS]) are a major health care burden. For example, CTS can affect 3%-4% of the population.[7,8] Though there have been important surgical innovations (eg, nerve transfers) over the last decade, we have not seen significant improvements in the management or rehabilitation of patients with PNI. Clinicians continue to face the challenges of significant sensorimotor deficits,[9-11] disabling neuropathic pain,[11-14] allodynia, hyperalgesia, referred pain, and other somatosensory abnormalities.[14-16] Adding to this burden, Jaquet et al[17] confirmed that 25% of patients with upper limb PNI had not returned to work 1.5 years after surgery. In addition, 57% of patients with PNI are between 16 and 35 years of age; thus, a long life of disability and economic

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https://doi.org/10.1016/j.jht.2018.01.011

difficulties are associated with upper limb PNI.[18] Chronic neurogenic pain following PNI is common and the cost of upper limb PNI to patients, their families, and society may be substantial.[19-21]

Neuroplasticity research has confirmed and continues to unravel the interplay between the central nervous system (CNS) and peripheral nervous system (PNS). Several studies[22,23] (eg, Taylor et al, 2009; Goswami et al, 2016) confirmed that injury to the peripheral nerve causes measurable functional and structural changes in the brain.[22,23] Understanding the interplay between the CNS and PNS following PNI is important to develop strategies for treatment and rehabilitation. In the future, the hand therapist could use this insight to serve an even greater role to manipulate the interplay between PNS and CNS in an effort to improve patient motor and sensory outcomes following PNI.

Studying neuroplasticity

The term "plasticity" simply refers to the ability to change. The classical view of the brain was that it was a fixed entity with hard-wired circuitry that did not change. Modern neuroscience proved this old belief to be incorrect, and we now know that the brain can and does undergo change throughout the lifespan. In the field of neuroscience, studies of plasticity examine changes in the structure or function of the nervous system at the molecular/cellular (eg, channels, receptors, synapses, neurons) and the system levels (eg, networks, connections)—both in the periphery (peripheral neuroplasticity) and in the CNS (central neuroplasticity). Such studies have found that the adult brain undergoes tremendous plasticity as we learn, age, are exposed and respond to our environment, as well as in response to injury and disease.[24] Thus plasticity can be an adaptive mechanism ("good or adaptive neuroplasticity"), but in some cases, maladaptive brain changes ("bad or maladaptive neuroplasticity") do occur.[25]

A variety of experimental techniques can be used to identify and study neuroplasticity in both animal models and in humans. An overview of the indicators of neuroplasticity has been previously described and summarized in Figure 1 and Table 1.[25,26] In this article, we focus on those techniques that are applicable to studying neuroplasticity in PNI patients and healthy human subjects as related to the somatosensory and pain systems. Human neuroplasticity is typically assessed using psychophysical measures and objective modern neuroimaging measures. Some examples are summarized in the following sections.

Psychophysical measures for neuroplasticity

While nerve conduction studies (NCSs) provide an objective measure of peripheral large diameter sensory and motor fiber function, psychophysical testing measures the perceived sensations reported by the subject in response to the application of physical stimuli. Psychophysical testing captures the integrated response of the entire somatosensory system, including the influence of psychological factors such as attention and anxiety. Quantitative sensory testing[27] (QST) refers to a collection of psychophysical measures that assess the function of both large- and small-diameter fibers; for a review of the strengths and limitations of QST, see the studies by Yarnitsky 1997; Siao & Cros, 2003; Rolke et al, 2006a; 2006b; Pfau et al, 2012.[27-31] QST protocols can be used

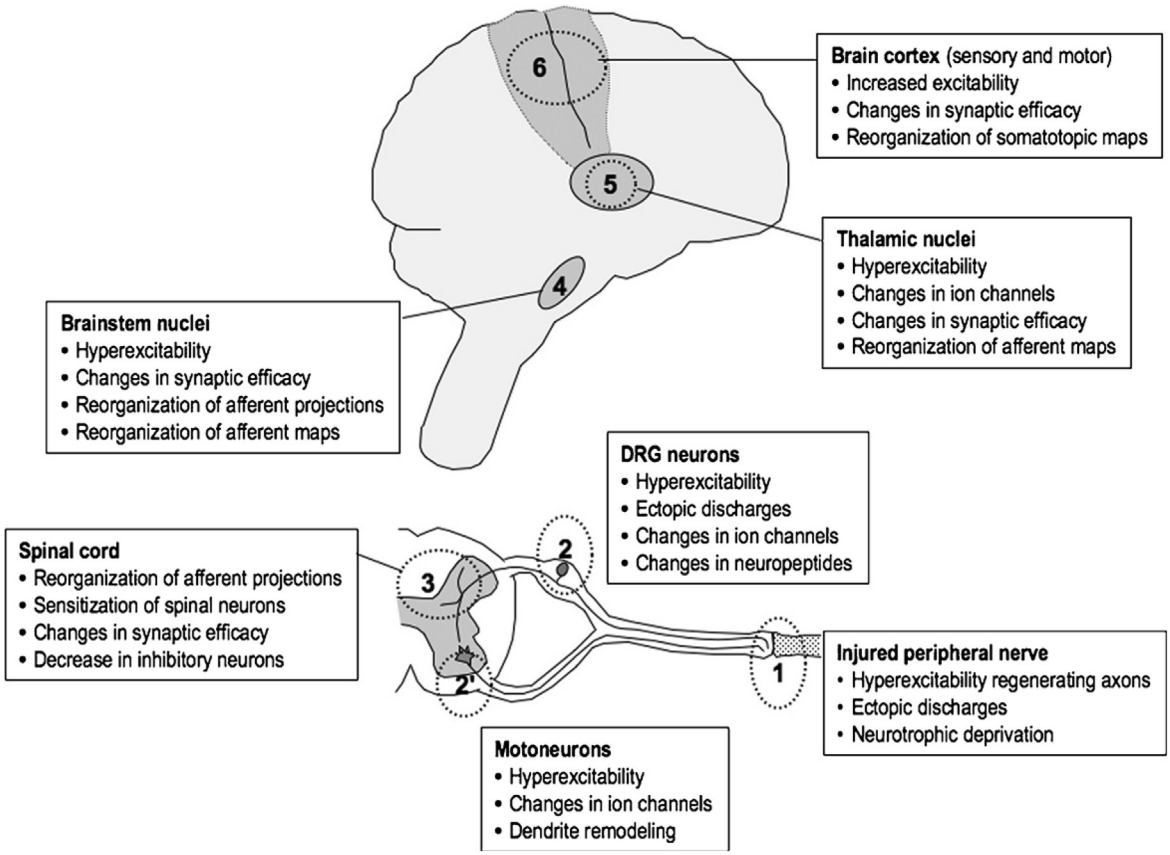

Fig. 1. A summary of the types of neuroplasticity that can occur in the peripheral and central nervous systems after injury to a peripheral nerve. Examples are shown for mechanisms occurring (1) in peripheral nerves, (2) in cell bodies of sensory primary afferents in the dorsal root ganglia and ventral horn motor neuron cell bodies, (3) in the spinal cord, and (4–6) supraspinal sites including the cortex. Used with permission from Navarro et al, 2007.[26]