Journal of Hand Therapy 26 (2013) 87–93

Contents lists available at SciVerse ScienceDirect

Journal of Hand Therapy

journal homepage: www.jhandtherapy.org

JHT Read for Credit Article #266.
Scientific/Clinical Article

Neural plasticity and implications for hand rehabilitation after neurological insult

Kelly P. Westlake PhD, PT[a,*], Nancy N. Byl MPH, PhD, PT, FAPTA[b]

[a] Department of Physical Therapy & Rehabilitation Science, University of Maryland School of Medicine, Baltimore, MD 21201, USA
[b] Department of Physical Therapy and Rehabilitation Sciences, University of California San Francisco, San Francisco, CA

ARTICLE INFO

Article history:
Received 9 November 2012
Received in revised form
24 December 2012
Accepted 26 December 2012
Available online 4 February 2013

Keywords:
Plasticity
Brain
Motor learning
Rehabilitation

ABSTRACT

Experience dependent plasticity refers to ability of the brain to adapt to new experiences by changing its structure and function. The purpose of this paper is to provide a brief review the neurophysiological and structural correlates of neural plasticity that occur during and following motor learning. We also consider that the extent of plastic reorganization is dependent upon several key principals and that the resulting behavioral consequences can be adaptive or maladaptive. In light of this research, we conclude that an increased understanding of the complexities of brain plasticity will translate into enhanced treatment opportunities for the clinician to optimize hand function.

Introduction

Neural plasticity is the phenomenon by which the healthy and the damaged brain can adapt to new experiences by changing its function and structure. In contrast to the long-held dogma that brain plasticity occurs only during critical phases of development, it is now well established that the brain maintains a capacity for functional and structural changes throughout life.[1] Neuroplastic changes occur along the entire neural axis and have been associated with altered motor function, such as that which occurs following a peripheral, spinal, or cortical injury, or after the acquisition of novel motor and sensory skills.[2–8] This discovery has enormous implications for rehabilitation. More than ever, the concept of plasticity has brought together the fields of neurophysiology, neuroscience, and rehabilitation in an exciting transference of knowledge from cell to behavior. Although the clinical link between the processes of brain reorganization and specific rehabilitative approaches and outcomes is still in its infancy, the combined effort of these scientific fields has the exciting potential to help guide and improve future treatment protocols. The purpose of this paper is to review the neurophysiological and anatomical correlates of neural plasticity that occur during and following motor learning. We first describe the neurophysiological mechanisms and neuroanatomical substrates of plasticity in the brain and spinal cord. We then consider that the extent of plastic reorganization is based upon several key principles and that resulting behavioral consequences can be either beneficial or maladaptive.[1] As a clinician, it is important to understand the potential to enhance plasticity and behavioral relevance, but also the limits by which plasticity leading to successful outcomes may be induced.

Mechanisms of plasticity

Neural change in structure and function

At the cellular level, several mechanisms have been implicated to explain plasticity induced by novel experience or motor skill learning. Some of the earliest investigations reported plastic changes with respect to increased strength of synaptic connections, synaptogenesis, and dendritic branching. Changes in the strength of synaptic connections induced by environment and experience were first observed by Donald Hebb.[9] In what became known as *Hebbian plasticity*, he postulated that, "When an axon of cell A is near enough to excite cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficacy, as one of the cells firing B, is increased."[9] In other words, when a presynaptic cell is repeatedly active with a postsynaptic cell, an increase in synaptic efficacy arises in a manner that is very much activity dependent. The most widely studied processes of synaptic efficacy are known

* Corresponding author. Tel.: +1 410 706 5919; fax: +1 410 706 6387.
E-mail address: kwestlake@som.umaryland.edu (K.P. Westlake).

0894-1130/$ – see front matter © 2013 Hanley & Belfus, an imprint of Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jht.2012.12.009

as long-term potentiation (LTP) and long-term depression (LTD). When somatosensory input is decreased, such as with the loss of peripheral nerve function, there is a reduction in the amount of GABA-ergic inhibition. An increased number of excitatory synapses are therefore "unmasked" in somatosensory brain regions adjacent to the sensory deprived areas such that the efficiency of these connections increases.[10] This process of enhanced synaptic strength and sensitivity is a demonstration of LTP, which is classified as one type of *Hebbian plasticity*. Although LTP and LTD contribute to motor learning,[11] these changes in effectiveness are not necessarily long lasting. Rather, they are considered an intermediate process followed by structural changes of new synapse growth and dendritic branching.[12]

Synaptogenesis, or the creation of new synapses, is a well-documented process shown to be dependent on the type of motor practice. Motor tasks that involve a complex motor learning task appear to enhance synaptogenesis beyond what can be achieved using simple movements,[13] thereby highlighting the importance of enriched skill training for hand rehabilitation.[14] Black et al,[15] identified the differential effects of a repetitive motor activity versus motor skill acquisition on synaptogenesis in the cerebellum. An increased number of cerebellar synapses was observed in rats trained on challenging acrobatic tasks compared to an increased vascularization without new synapses in rats trained using repetitive exercises. Numerous investigations have since supported these findings and together, suggest that without motor skill learning, increased synaptic activity through repetition of well-practiced movements is insufficient to induce the formation of new synapses in the cerebellum,[15–17] and motor cortex.[13,18,19]

Learning dependent synaptogenesis is thought to have a role in the functional reorganization of motor circuits. Support for this notion arises from studies of adult rats trained on specific forelimb reaching tasks. Following training, the rats demonstrated increased functional representation of the forelimb regions of the motor cortex in a manner that was paralleled by synaptogenesis, yet not found in motor regions of the untrained limbs.[20] Although the relationship of synaptogenesis to functional outcomes remains unclear, this process does appear to mediate the development of learned behavior through persistent changes in cortical and cerebellar circuitry.[18] Although most evidence is in support of synaptogenesis at the level of the cerebellum and motor cortex, the spinal cord is emerging as another possible site. However, synaptic changes at the level of the spinal cord appear to be in response to increased strength as opposed to motor skill learning.[21] Therefore, depending on the nature of motor training (i.e. skill versus strength), synaptogenesis may be induced at suprapinal or spinal cord level.

Dendritic branching has also been implicated as one of the mechanisms underlying plasticity. Since dendrites are the site of most postsynaptic contacts, further branching essentially enables an increased number of synapses received by each neuron.[22] This effect has been demonstrated in rats in an enriched environment[22] and with specific reach training of the affected limb following an experimentally induced lesion.[13] In rats with good functional outcomes, increases in dendritic branching were found in the contralesional hemisphere,[22] suggesting that plasticity may be involved as part of a distributed network of change (Fig. 1).

Neurogenesis, the process by which new neurons are produced, is a more recently discovered mechanism of plasticity. In 1998, naturally occurring neurogenesis was observed in the hippocampus.[23] Since that time, the potential to induce neurogenesis using growth factor in spatial skill learning has been investigated.[24] However, it should be noted that the potential to enhance neurogenesis within and beyond the hippocampus is still remote at this stage.

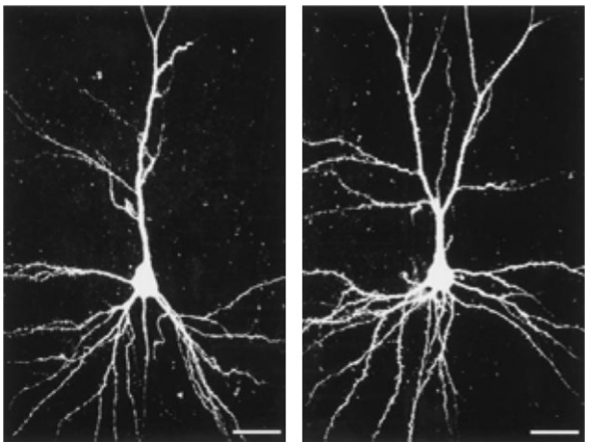

Fig. 1. Dendritic morphology of pyramidal neurons in layer III of the somatosensory cortex in a rat housed in standard (left) and enriched (right) environments, as viewed in confocal imaging. Reprinted by permission from Macmillan Publishers Ltd: J Cereb Blood Flow Metab, copyright 2002.[22]

Because behavior is the result of the activity of the nervous system, the success of hand rehabilitation may be intricately related to these neuroplastic processes. For example, the process of synaptogenesis and dendritic branching is enhanced in the lesioned brain compared to the healthy brain, highlighting the potential for tap into these processes to promote plasticity.[25] Nevertheless, interpretation of these cellular processes in relation to motor behavior must also account for the fact that a cause and effect association has not been established. Although plasticity plays a role in motor learning, the underlying mechanisms at both a neural and system level are still under investigation.

Patterns of motor map reorganization

Neural plasticity can also be described at a systems level by reorganized cortical patterns of activation associated with motor control. 'Use it or lose it' is a principle that has derived extensive anatomical evidence from both animal and human studies. The most prevalent example is when a peripheral nerve is lesioned or when a limb is amputated. In each condition, cortical remapping occurs such that the somatotopic boundaries of intact sensory afferents expand into cortical regions previously representing the affected limb or digits.[26] One early demonstration was in the primate somatosensory cortex following transection of the median nerve. Over the course of a few weeks, a progressive expansion of cortical representations of adjacent skin regions occurred to occupy portions of the former median nerve cortical representational zone (Fig. 2).[28] In a related study, somatosensory cortical representations of the hand were examined before and after the amputation of a digit.[29] Two to eight months after amputation, most of the cortex that originally responded only to the skin surfaces on the amputated digit now responded to inputs from adjacent digits or the palm. While these changes pertained to the representation of the intact, immediately adjacent digits, there was not a significant increase of the representation of more distant digits. The reverse arrangement has been shown in patients with corrected syndactyly. Following surgical correction, two distinct regions of primary motor cortex (M1) emerged to activate each digit in contrast to a single region of cortical representation.[30]

Shifts in cortical representation are generally described in terms of regional representation, such as the hand or fingers, but individual muscle responses are also of interest. In a recent study, Vallence et al,[31] used transcranial magnetic stimulation (TMS) to