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Motor cortex reorganization across the lifespan

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Abstract

The brain is a highly dynamic structure with the capacity for profound structural and functional change. Such neural plasticity has been well characterized within motor cortex and is believed to represent one of the neural mechanisms for acquiring and modifying motor behaviors. A number of behavioral and neural signals have been identified that modulate motor cortex plasticity throughout the lifespan in both the intact and damaged brain. Specific signals discussed in this review include: motor learning in the intact brain, motor relearning in the damaged brain, cortical stimulation, stage of development and genotype. Clinicians are encouraged to harness these signals in the development and implementation of treatment so as to maximally drive neural plasticity and functional improvements in speech, language and swallowing.

Learning outcomes: Readers will be able to: (1) describe a set of behavioral and neural signals that modulate motor cortex plasticity in the intact and damaged brain; (2) describe the influence of stage of development on plasticity and functional outcomes; and (3) identify a known genotype that alters the capacity for motor learning and brain plasticity.

1. Introduction

The brain is a highly dynamic structure with the capacity for profound structural and functional adaptation. Such neural plasticity can be defined as any observable change in neuron structure or function and is the neurobiological mechanism by which the central nervous system (CNS) encodes novel behavior (Kleim, 2010). The continuous advent of more sophisticated molecular techniques and methods for measuring neuron structure and function have allowed neuroscientists to make very specific statements about both the nature of neural plasticity and the cellular mechanisms that orchestrate it.

The motor cortex has been used extensively to identify the key behavioral and neural signals that drive different forms of plasticity within the intact and damaged CNS. These signals can be classified as either extrinsic or intrinsic modulators of neural plasticity. Extrinsic factors include: Motor learning, motor relearning, electrical stimulation, pharmacological stimulation and behavior. Intrinsic factors include: stage of development, age, sex, genotype and prior experience as well as injury related factors such as the location and severity of injury as well as time post injury. Though the interactions of these signals is complex and not completely understood, it is important to recognize that

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they can influence the capacity for neural plasticity and therefore the efficacy of any rehabilitation intervention. Furthermore, there appear to be a common set of neural and behavioral signals that drive plasticity across sensory, motor and cognitive functional domains (Kleim & Jones, 2008). Thus, we can gain insight into the neural mechanisms underlying improvements in function after CNS injury or disease by studying the experience-dependent plasticity within motor cortex. Clinicians are therefore met with the challenge to develop novel and neurobiologically informed therapies that incorporate behavioral and neural modulators of plasticity to maximize outcomes in the treatments of speech, language and swallowing.

2. Extrinsic modulators of motor cortex plasticity

2.1. Motor learning in the intact brain

Cortical stimulation techniques that provide measures of changes in corticospinal function have been used to demonstrate motor learning-dependent plasticity within motor cortex. Transcranial magnetic stimulation (TMS) has been used to demonstrate plasticity in the healthy human motor cortex with skill training of the hand and tongue. For example, individuals trained on a one handed, five finger piano playing task demonstrated larger motor evoked potential (MEP) amplitudes and increased motor map area for the muscles controlling the trained hand (Pascual-Leone et al., 1995). Similarly, following a skilled tongue training task, healthy subjects demonstrated increased tongue motor map area, MEP amplitudes and a reduction in the threshold for evoking MEP's of the tongue (Svensson, Romaniello, Wang, Arendt-Nielsen, & Sessle, 2006).

Similar changes have been observed in animal models of motor skill learning. Kleim, Barbay, and Nudo (1998) investigated the effects of a skilled versus unskilled reaching task on rodent forelimb motor cortex representation using intracortical microstimulation (ICMS). Rats in the skilled reaching condition were trained to reach through a slot for a food pellet located outside the training cage (a task requiring the development of coordinated of wrist and digit movements), while those in the unskilled reaching task were trained to press a lever inside the cage for a food pellet reward with either their tongue or mouth. Following 10 days of training, animals in the skilled reaching condition exhibited a greater area of wrist and digit representations as compared to the unskilled reaching animals. This study and others (Conner, Culberson, Packowski, Chiba, & Tuszynski, 2003; Nudo, Milliken, Jenkins, & Merzenich, 1996; Remple, Bruneau, VandenBerg, Goertzen, & Kleim, 2001) reveal some important principles of motor map topography, namely: (1) motor maps are highly dynamic; (2) greater dexterity equates to greater cortical representation; and (3) motor map topography reflects motor experience.

What are the underlying neural mechanisms facilitating reorganization of cortical movement representations? Motor maps are highly dependent on the strength of synaptic connections onto corticomotor neurons within motor cortex (Monfils, Plautz, & Kleim, 2005). Therefore, any change in the topography of movement representations observed during skill learning should be associated with changes in synapse number and/or strength. Indeed, dendritic growth (Allred & Jones, 2004; Bury & Jones, 2002; Greenough, Larson, & Withers, 1985; Withers & Greenough, 1989), synaptogenesis (Kleim et al., 2002, 2004) and enhanced synaptic responses (Monfils & Teskey, 2004; Rioult-Pedotti, Friedman, Hess, & Donoghue, 1998) within the forelimb motor cortex have all been documented in animal models following skilled training and likely represent the underlying structural changes that support learning-dependent reorganization of cortical movement representations.

Kleim et al. (2004) investigated temporal relationship between synaptogenesis and motor map reorganization associated with motor skill learning in rats trained for 3, 7 or 10 days. Although significant improvements were observed after 3 days of training, a significant increase in number of synapses per neuron were not observed until day 7 of training. A significant expansion of wrist and digit movement representations was not observed until 10 days of training. Thus behavioral performance was followed by synaptogenesis and then expansion in the amount of cortex involved in controlling distal movements. This and other studies have revealed a number of important principles of motor cortex plasticity: (1) skill learning is associated with synapse formation and reorganization; (2) these changes are not linearly related to improvements in motor performance and occur during the late slow phase of motor learning; (3) synaptogenesis precedes motor map reorganization but follows motor skill acquisition; (4) learning-dependent plasticity is temporally dynamic in nature and (5) different forms of plasticity support different phases of learning. Therefore, there appears to be a specific cascade of neural events associated with motor learning in motor cortex (Fig. 1).