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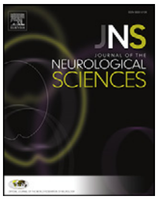

Review article

Computational models and motor learning paradigms: Could they provide insights for neuroplasticity after stroke? An overview

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ABSTRACT

Computational approaches for modelling the central nervous system (CNS) aim to develop theories on processes occurring in the brain that allow the transformation of all information needed for the execution of motor acts. Computational models have been proposed in several fields, to interpret not only the CNS functioning, but also its efferent behaviour. Computational model theories can provide insights into neuromuscular and brain function allowing us to reach a deeper understanding of neuroplasticity. Neuroplasticity is the process occurring in the CNS that is able to permanently change both structure and function due to interaction with the external environment. To understand such a complex process several paradigms related to motor learning and computational modeling have been put forward. These paradigms have been explained through several internal model concepts, and supported by neurophysiological and neuroimaging studies. Therefore, it has been possible to make theories about the basis of different learning paradigms according to known computational models.
Here we review the computational models and motor learning paradigms used to describe the CNS and neuromuscular functions, as well as their role in the recovery process. These theories have the potential to provide a way to rigorously explain all the potential of CNS learning, providing a basis for future clinical studies.

Contents

1. Introduction

Stroke is the third cause of death and the first cause of disability among adults regardless of ethnicity, worldwide [1]. At least half of the patients have neurological impairments limiting their independence and about 20% of patients are completely dependent on their care-givers [2].

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It is widely acknowledged that cortical reorganization of the motor areas occurs in patients recovering after stroke [3]. Passive movements of the hemiplegic side in stroke survivors have been shown to activate the same brain areas, as described for voluntary active movements in the contralateral side [4]. Changes of cerebral activation in the sensory and motor systems occur early after stroke and may be the first step toward recovery of motor functions. Functional re-organization of the motor system after focal stroke in primates depends on compensatory mechanisms supported by the intact motor cortex, as well as on the amount and intensity of motor training provided [5]. Recent research on motor control and learning provides emerging neurophysiological evidence that could be feasibly translated into rehabilitation practice. During motor activities, neurons from several areas are connected within the same hemisphere and across the contralateral one [6]. The existence and activity of these networks have been documented both in primates and humans [7]. The human motor system consists of several brain areas cooperating for the production of motor tasks. Among those, the most important are: the primary sensorimotor cortex in both hemispheres, the parietal and lateral premotor cortex, the cerebellum, and the basal ganglia (considered as secondary motor areas) [8,9]. The balance between the primary sensorimotor cortex and the secondary motor areas changes when part of the network is disrupted as a result of a stroke. Clinical studies with functional Magnetic Resonance Imaging (fMRI) have shown that after a stroke, there is a reorganization of the overall network the activity of which is higher depending on lesion extension, while activity decreases with the progression of brain reorganization [6]. Furthermore, many studies have shown that learning new motor skills stimulates brain plasticity and allows functional improvement. Plasticity in the central nervous system (CNS) is assumed to be preserved throughout the whole life of an individual, regardless of age [10]. Results from fMRI and Transcranial Magnetic Stimulation (TMS) studies have revealed that the cerebral cortex maintains the capacity for functional adaptation, both early and after a long time following a stroke [11–13]. Other results from studies in primates suggest that cortical reorganization is promoted by rehabilitation after injury of the M1 area (primary motor cortex), but reorganization only occurs when learning new motor abilities and not due to repetition of non-finalized movements [11,14,15].

The aim of this paper is to review the theoretical bases underpinning the organization and functioning of the brain after a lesion, while performing motor tasks.

2. Neuroplasticity and brain repair after stroke

Plasticity of the nervous system is the ability to create permanent structural and functional changes under the influence of external stimuli. Such stimuli can be understood also like information processed from the external environment. The plasticity of neuronal tissues (neuroplasticity) is intended as the biological substrate of learning and memory and is among the main factors influencing recovery after stroke. Neuroplasticity after brain lesion is due to spontaneous cortical reorganization. However, increasing evidence indicates that intensive stimulation provided with rehabilitation therapy is essential to increase improvement of motor function after stroke, thus potentially promoting neuroplasticity for learning new motor skills [4,16–18]. Many studies on both animals and humans have demonstrated that various changes occur in the CNS both at the molecular and synaptic level, when interacting with the external environment [17]. The plasticity properties of the CNS are preserved throughout the whole life in humans and are intensified in case of injury or adaptation to new environments. Such examples are the mechanisms of “self-repairing” and reorganization of neuronal connections exploiting new paths that are functionally consistent but anatomically different from those impaired [19]. Cortical plasticity can occur either as a result of training of different skills or of the same task at different levels of difficulty [20]. This plasticity can be assessed by means of non-invasive technologies (e.g. fMRI, Magnetoencephalography – MEG, TMS, High Density Electroencephalography – HD-EEG, Positron Emission Tomography – PET) [4,21,22]. Recently, several neurophysiological studies using neuroimaging techniques have provided insight on the mechanisms involved in neuroplasticity during recovery after stroke. Neuroplasticity refers to the brain's capacity to repair neural networks and its reorganization for information processing between neurons. Thus, neuroimaging techniques can help us to decipher brain connectivity patterns, which occur during motor task execution by means of network analysis approaches, such as structural, functional, and effective connectivity. Structural (anatomical) connectivity refers to a network of synaptic connections (fiber pathways) representing morphological change and plasticity. However, only invasive tracking studies are capable of revealing significant direct axonal connections. Functional connectivity is defined as a statistical dependency among remote neurophysiological events, and it is related to studies of patterns of functional connectivity among cortical regions and based on coherence or correlation. However, correlations can arise in a variety of ways. These studies have provided evidence for a fractal organization of functional brain networks [23]. The plasticity of intrinsic functional connectivity patterns was investigated in a clinical study and it revealed that the impact of rehabilitation can be measured on resting-state fMRI, and that the functional connectivity can provide prognostic insight for later motor recovery [24]. Effective connectivity describes networks of directional effects of neural elements i.e. providing significant differences between a given set of brain regions when estimated in different tasks, which is important for showing the time- and task- dependent nature of these patterns. Thus, effective connectivity could be seen as the union of both structural and functional connectivity [23]. The hypothesis that effective connectivity between cortical areas exists during execution of motor tasks has been tested by EEG and MEG. Thus, this activity might be used as biomarker to predict motor recovery in experimental paradigms. This connectivity can be measured observing two sources of signals (i.e. neuro-electrical and neuro-chemical) with the aim to study the relationship between cortical activity and movement [25,26]. However, some authors have reported that through these techniques, the neuro-electrical and neuro-chemical processes that mediate cerebral function cannot be measured directly [27]. For example, the brain activity that can be observed with fMRI techniques is inferred via measurements of focal hemodynamic changes in blood-oxygen-level dependent (BOLD) contrast imaging, whereas, in EEG or MEG measurements of the cortex, activity is inferred via measurements of extracranial electric or magnetic fields, respectively. Therefore, non-invasive and indirect measurement of activity occurring in the brain is a fundamental limitation.

An fMRI clinical study [4] carried out with stroke patients revealed that neuroplastic changes occur after motor rehabilitation and may be specifically fostered by the intervention provided. After specific rehabilitative treatment patients showed varied patterns of fMRI changes related to improvement of upper limb motor function [4]. Neurophysiological and neuroimaging studies suggest that neuroplasticity happens in the sensorimotor cortex of the affected hemisphere with task-specific training [28].

A large number of studies have considered repetitive TMS (rTMS) as a potential therapeutic technique for rehabilitation of neurological disorders, aimed to enhance the effect of conventional rehabilitative training [29]. This method has an impact on cortical activity and may be inhibitory or facilitatory depending on whether low (≤ 1 Hz) or high (≥ 1 Hz) frequency magnetic pulses are administered, and also depending on the length or intensity of stimulation. Generally, low frequency stimulation has an inhibitory impact while frequency higher than 1 Hz enhances cortical excitability [30]. Several pieces of evidence have reported that rTMS is effective for treatment of aphasia and visuospatial neglect after stroke. In the study by Martin et al., rTMS was used to stimulate Broca's area in patients with expressive aphasia [31]. The authors reported excessive activation of homologous structures to Broca's area in fMRI images [31]. Whereas, in the clinical study by Oliveri et al.,