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Update article

Sites of electrical stimulation used in neurology

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ABSTRACT

Rehabilitation aims to decrease neurological impairments, in guiding plasticity. Electrical stimulation has been used for many years in rehabilitation treatment of neurological disabilities as a tool for neuromodulation inducing plasticity, although the mechanisms of its action are not well known. The applications vary, encompassing therapeutic and rehabilitative aims. The type and site of stimulation vary depending on the objectives. Some techniques are widely used in clinical practice; others are still in the research stage. They may be invasive, epidural or in direct contact with neurons; they may be noninvasive, applied transcutaneously or indirectly by current vectors. The indications vary: mobility, functionality, pain as well as pharyngeal, respiratory, and perineal function. This paper aims to summarize current data on electrical neuromodulation techniques used in neurorehabilitation, their effects and their mechanisms of action.

1. Introduction

Stroke and spinal cord injury (SCI) are 2 of the principal causes of morbidity and mortality in adults. They are responsible for neurological impairments that can have an important impact on patient life and represent considerable costs for health and social services.

Rehabilitation aims to decrease neurological impairments and restore independence in activities of daily living. It has to be intense, repeated and task-oriented to facilitate motor recovery for hemiplegic or incomplete quadriplegic patients, in guiding plasticity [1]. Indeed, brain plasticity is defined as all the mechanisms allowing the brain to adapt its own function to a new situation, such as a stroke. These mechanisms are a modification of the efficiency of existing synapses (long-term potentiation, long-term depression), global changes in post-synaptic excitability, and morphological changes (increase in number of dendrites or collateral axons). For example, changes in cortical maps have been widely reported after stroke [2]. Functional recovery is based on the recruitment of areas adjacent to the lesion or remote areas of the lesion, which could be in the healthy hemisphere [3]. Therefore, the opportunity to guide post-lesional plasticity is a key therapeutic goal for these patients [4]. Neuromodulation techniques can induce brain plasticity by increasing or decreasing the excitability of a neuron or a brain area.

Electrical stimulation (ES) has been used for many years for neuromodulation in rehabilitation programs for patients with neurological impairments, although the mechanisms of action are not well known. The applications vary; the choice of parameters depends on the objectives. ES is defined by its polarity, width, intensity, frequency of stimulation, transcutaneous or invasive application, and stimulation site (the nerve, muscle), for example. It can be coupled with other tools such as electromyography (EMG), robotic devices, brain–computer interface techniques, or transcranial magnetic stimulation (TMS). Some techniques are used in clinical practice; others are still in preclinical development.

This paper aims to summarize current data on electrical neuromodulation techniques used in neurorehabilitation, their effects and their mechanisms of action. The results are presented according to the stimulation sites. The list is not exhaustive.

2. Brain ES

2.1. Invasive brain ES

2.1.1. Movement disorders

Invasive brain ES has been developed for more than 25 years, with many clinical applications, including pharmacological resistance, reducing disability and improving quality of life [5]. Deep brain stimulation (DBS) involves intracerebral implantation

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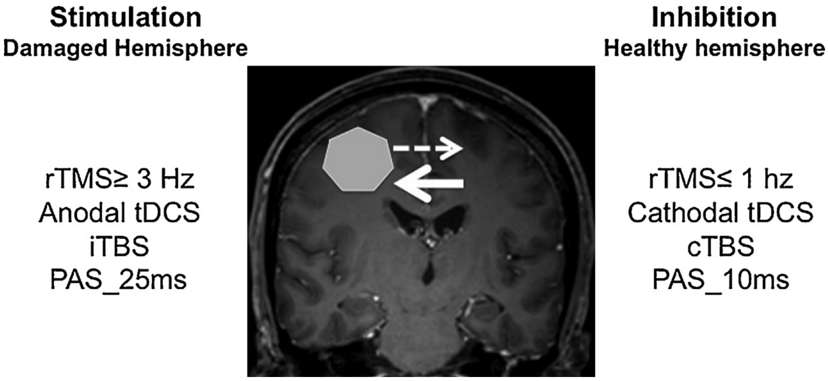

Fig. 1. Noninvasive electrical stimulation of the brain. Noninvasive brain stimulation is based on the concept of restoring interhemispheric balance after brain injury, stimulating the damaged cortex or inhibiting the healthy cortex. Techniques used to stimulate the damaged cortex include high-frequency repetitive transcranial magnetic stimulation (rTMS; ≥ 3 Hz), anodal transcranial direct current stimulation (tDCS), intermittent theta burst stimulation (iTBS) or paired associative stimulation (PAS–25 ms) (applied on the upper limb, with interstimuli interval [ISI] about 25 ms). To inhibit the healthy cortex, techniques include low-frequency rTMS (≤ 1 Hz), cathodal tDCS, continuous TBS (cTBS) or PAS–10 ms (applied to the upper limb, with ISI about 10 ms).

of stimulation electrodes that are connected to a subcutaneous generator. The technique involves continuously delivering small electrical pulses to modulate the activity of the targeted brain area and related brain networks. The precise site of stimulation depends on the indication. The most frequent targets are the subthalamic nucleus, a key structure within the basal ganglia circuit in Parkinson's disease [6,7], the ventral intermediate nucleus of the thalamus in severe tremor secondary to Parkinson's disease or in essential tremor [8,9], and the globus pallidus internus in primary dystonia [10,11]. For complex tremors, the DBS targets the ventral oralis posterior thalamus or the zona incerta. The clinical results vary [5].

2.1.2. Epilepsy

ES has been developed for drug-resistant epilepsy. Vagal nerve stimulation by microelectrodes may result in long-term seizure reduction. In cases of no benefit with vagal nerve stimulation, different sites of DBS have been proposed: the anterior nucleus and centromedian nucleus of the thalamus and mesiotemporal structures [5,12,13].

2.1.3. Psychiatric disorders

DBS is used clinically for depression by targeting the subgenual cingulate region, the ventral caudate nucleus and the ventral striatum and for obsessive–compulsive disorder by targeting the caudate nucleus, anterior limb of the internal capsule and nucleus accumbens [5].

2.1.4. Central neuropathic pain

Tsubokawa et al. introduced epidural motor cortex stimulation as an alternative treatment for the central neuropathic brain [14,15]. Literature results are discordant, except for deafferentation facial pain, which responds positively to this ES [16].

2.1.5. Stroke

Epidural stimulation was investigated by Brown et al., who applied ES at 50 Hz through epidural electrodes implanted in relation to the cortical motor area of the wrist in 6 chronic hemiplegic patients for 3 weeks, coupled with rehabilitation [17]. The results were promising, but tests have not been continued.

2.2. Noninvasive brain ES

Noninvasive brain stimulation (NIBS) (Fig. 1) has been developed for more than 10 years and includes transcranial direct current stimulation (tDCS), repetitive TMS (rTMS) and paired associative stimulation (PAS), which couples peripheral ES and cortical magnetic stimulation [18,19]. These techniques are based on the concept of restoring interhemispheric balance after brain injury to modulate and promote functional recovery. Indeed, after stroke, functional imaging studies have shown hypoactivation of the ipsilesional cortical areas, followed over time by activation of ipsi- and contralesional sensorimotor areas and finally, a return to a more conventional circuit, so ipsilesional, which allows for better quality of recovery [3]. The larger the interhemispheric asymmetry, the more limited the motor recovery. NIBS aims to stimulate the damaged cortex or inhibit the healthy cortex to restore interhemispheric balance.

2.2.1. tDCS

The technique consists of applying a galvanic, constant, continuous current at low intensity (1–2 mA) via 2 large non-metallic electrodes (5 × 7 cm) wetted by a saline solution. One of the electrodes is positioned in relation to the target area. Stimulation can involve the anode or cathode, called anodal or cathodal stimulation, respectively. The second electrode is usually positioned on the skin on the side of the contralateral fronto-orbital region [20]. When applied for more than 3 min at 1 mA or 5 min at 0.6 mA, the stimulation induces excitatory after-effects if anodal or inhibitory after-effects if cathodal. Effects lasting beyond the duration of the stimulation define after-effects.

On the basis of the concept of restoring interhemispheric balance, to enhance motor recovery, tDCS is applied to the damaged primary motor area with anodal stimulation to stimulate it or with cathodal stimulation on the healthy side to inhibit it [21]. Its impact on motor recovery was first assessed by Hummel et al., who showed that tDCS improved hand motor function as assessed by the Jebsen-Taylor Hand Function Test [22]. In a recent Cochrane meta-analysis, Elsner et al. found some evidence of the effectiveness of tDCS for improving activities of daily living and function after stroke [23].

Similarly, the effects of tDCS have been studied in aphasia, with anodal stimulation applied to Broca's area or cathodal stimulation of the right part of Wernicke's area [24,25]. Elsner et al. did not find any evidence of the effectiveness of tDCS for improving functional communication or language impairment [26].

More recently, some studies explored the effect of tDCS on spatial neglect by anodal stimulation of the injured posterior parietal cortex [27] and in disorders of consciousness after head injury or cerebral anoxia by anodal stimulation of the left primary sensorimotor cortex or the left dorsolateral prefrontal cortex [28].