Neurophysiologie Clinique 36 (2006) 105–115

available at www.sciencedirect.com

ScienceDirect

journal homepage: http://france.elsevier.com/direct/neucli

ORIGINAL ARTICLE / ARTICLE ORIGINAL

Stroke recovery can be enhanced by using repetitive transcranial magnetic stimulation (rTMS)

Intérêt de la stimulation magnétique transcrânienne répétitive (SMTr) pour améliorer la récupération fonctionnelle des accidents vasculaires cérébraux

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Available online 30 August 2006

KEYWORDS
Aphasia;
Cortical reorganization;
Motor cortex;
Stroke;
Transcranial magnetic stimulation;
Visual neglect

Abstract Post-stroke recovery is based on plastic changes in the central nervous system that can compensate the loss of activity in affected brain regions. In particular, monohemispheric stroke is thought to result in disinhibition of the contralesional unaffected hemisphere. Neurorehabilitation programs improve function partly by enhancing cortical reorganization. Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive way of producing potent changes in cortical excitability. Therefore, the application of rTMS was recently proposed to promote functional recovery in stroke patients, owing to the induced neuroplasticity. This review discusses the first clinical results that were obtained by rTMS in patients with post-stroke motor deficit, visuospatial neglect, or aphasia. These results are promising and depend on the site and frequency of stimulation. In summary, functional recovery might be obtained either when rTMS is applied at low-frequency (around 1 Hz) over the disinhibited, unaffected hemisphere in order to restore defective inhibition or when rTMS is applied at high-frequency (5 Hz or more) over the affected hemisphere in order to reactivate hypoactive regions. The overall procedure remains to be optimized, in particular regarding the number of rTMS sessions and the time of rTMS application after stroke. Cortical stimulation is an exciting perspective for improving functional recovery from stroke. Transient application of non-invasive transcranial stimulation during the time of the rehabilitation process will be preferable to the temporary implantation of epidural cortical electrodes, as recently proposed. Therefore, in the future, acute or recent stroke might be a major indication of rTMS in neurological practice.

MOTS CLÉS
Accident vasculaire cérébral ;

Résumé La récupération fonctionnelle après un accident vasculaire cérébral (AVC) est liée à la plasticité du système nerveux central qui permet de compenser la perte d'activité des zones lésées. En particulier, un AVC monohémisphérique peut se traduire par la désinhibition de l'hémisphère sain controlatéral. Les techniques de rééducation fonctionnelle entraînent une

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0987-7053/$ - see front matter
doi:10.1016/j.neucli.2006.08.011

Aphasie ;
Cortex moteur ;
Négligence visuelle ;
Réorganisation corticale ;
Stimulation magnétique transcrânienne

amélioration clinique qui passe notamment par une réorganisation des activités corticales. La stimulation magnétique transcrânienne répétitive (SMTr) produit de façon non-invasive des modifications significatives de l'excitabilité du cortex cérébral. De ce fait, l'utilisation de la SMTr a été récemment proposée pour promouvoir la récupération des AVC en générant des phénomènes de neuroplasticité. Cette revue a pour objet de faire le point sur les premiers résultats cliniques obtenus par SMTr chez des patients présentant un déficit moteur, une négligence visiospatiale ou une aphasie post-AVC. Ces résultats sont prometteurs et se fondent sur des mécanismes d'action dépendant du site et de la fréquence des stimulations. En résumé, une amélioration fonctionnelle peut être observée après SMTr appliquée à basse fréquence (autour de 1 Hz) sur l'hémisphère sain désinhibé dans le but d'y restaurer les processus inhibiteurs, ou bien après SMTr appliquée à haute fréquence (5 Hz ou plus) sur l'hémisphère lésé pour réactiver des zones hypoactives. Cette nouvelle approche thérapeutique doit encore être optimisée, notamment en ce qui concerne le nombre et la chronologie des séances de SMTr par rapport à la survenue de l'AVC. La stimulation corticale offre de réelles perspectives en vue d'améliorer les chances de récupération fonctionnelle après un AVC. Dans ce domaine, l'application transitoire de stimulations transcrâniennes non-invasives, de façon concomitante aux techniques de réadaptation fonctionnelle, est préférable à l'implantation temporaire d'électrodes corticales épidurales. Ainsi, la prise en charge des AVC en phase aiguë ou post-aiguë pourrait constituer dans le futur proche l'une des indications thérapeutiques majeures de la SMTr en pratique neurologique.

Introduction

Post-stroke functional recovery is related to various plastic processes leading to central nervous system reorganization. This was particularly well demonstrated for motor strokes [104]. Adaptive plasticity includes changes in synaptic connectivity and excitability in surviving neural cell population in the perilesional zone, in remote structures, and in the contralateral unaffected hemisphere in case of a monohemispheric lesion. Based on single- and paired-pulse paradigms, transcranial magnetic stimulation (TMS) can serve as a tool to study post-stroke cortical reorganization. TMS techniques allow assessing inhibitory and facilitatory networks in each hemisphere, as well as evaluating interhemispheric connections. Various changes in excitability of both affected and unaffected hemispheres were shown by TMS in stroke patients, according to the extent of the stroke and to the time that has elapsed after stroke [56]. Thus, TMS was applied to characterize the mechanisms of adaptive cortical reorganization in response to neurorehabilitation protocols. The recent development of machines, which are now able to deliver repetitive trains of TMS (rTMS), opens new perspectives to use magnetic stimulation not only for assessment but also for treatment. This paper will review the first reports of rTMS-enhanced stroke recovery. Three types of stroke were concerned so far by rTMS studies: motor stroke with limb weakness, visuospatial neglect, and aphasia.

Cortical excitability changes after motor stroke

Before considering the capacity of rTMS to enhance stroke recovery, we will summarize the changes in cortical excitability that can be revealed by TMS technique at various times after stroke, together with their clinical correlates (Table 1).

In the first week after stroke, the presence of motor evoked potentials (MEPs) in the paretic limb in response to the stimulation of the affected hemisphere was found to be a predictive factor of good recovery [13,17,18,24,37]. Conversely, the absence of MEPs at initial examination was associated with subsequent poor recovery [78]. However, in this latter case, a poor prognosis could only be expected in case of a marked increase in amplitude and a decrease in motor threshold of the contralateral normal MEPs to stimulation of the unaffected hemisphere. This is because hyperexcitability of the unaffected hemisphere correlates with more severe cortical lesions at the affected side [98]. Neuroimaging studies also revealed that patients with poor recovery have higher levels of activation in the unaffected hemisphere during motor tasks [104]. This imbalance of excitability between both hemispheres decreases in parallel with functional improvement in the first months after stroke [15,17,97].

Ipsilateral motor responses to cortical stimulation must be also considered for a more reliable prediction of stroke recovery. Indeed, if MEP amplitude at the paretic limb is greater following ipsilateral stimulation of the unaffected hemisphere than contralateral stimulation of the affected hemisphere, a rather poor recovery can be expected [69, 100], unless premotor areas were stimulated [12]; conversely, a good recovery may usually be expected in the absence of any significant contribution of ipsilateral pathways from the primary motor cortex (M1) of the unaffected hemisphere in a simple motor task or in MEPs from the paretic limb [31]. Indeed, stroke recovery is better when it relies predominantly on cortical reorganization within the affected hemisphere [106].

The involvement of bilateral premotor areas in post-stroke motor function needs also to be determined. Ipsilateral contribution of the premotor cortex of the unaffected hemisphere in motor performance of the paretic limb was observed in chronically impaired stroke patients [43]. This