IFESS 2011 Abstract

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Non-invasive Brain Stimulation to improve arm an hand function following central nervous system (CNS) lesions

A primary aim for rehabilitation following lesions of the CNS is to drive useful neuroplastic changes with the aim of improving recovery of function. Neuroplasticity occurs as a result of regeneration, such as axonal and dendritic sprouting and /or re-organization, such as strength and number of synapses or re-mapping of functional projections to undamaged areas, either adjacent to the lesion or to the ipsilateral cortex. Exercise and functional activities have been the core approaches, but there is emerging evidence for other modalities such as pharmacological treatments, stem cell therapy and non-invasive brain stimulation (NIBS) that can augment physical therapy. Changes in cortical activity observed through fMRI have been shown to correlate with change in function (Ward et al Brain 2003, 126: 1430-1448)

The focus of this talk is NIBS – Transcranial direct current stimulation tDCS, Transcranial Magnetic Stimulation (rTMS) both alone and in combination with other therapies.

Following a subcortical stroke in onehemisphere that causes a sensorimotor deficit of the contralateral arm and hand, the primary motor cortex of the unaffected (contralesional) hemisphere is disinhibited and exerts enhanced transcallosal inhibition of the primary motor cortex (PMC) of the affected (ipsilesional). This affect hinders motor performance and recovery of the affected hand. (Nowak D.A. et al. Neurorehabilitation and Neural Repair 23: 641-656, 2009). NIBS can be used to modulate inter-cortical excitability either through inhibition of the unaffected PMC or facilitation of the damaged PMC (Figure 1.).

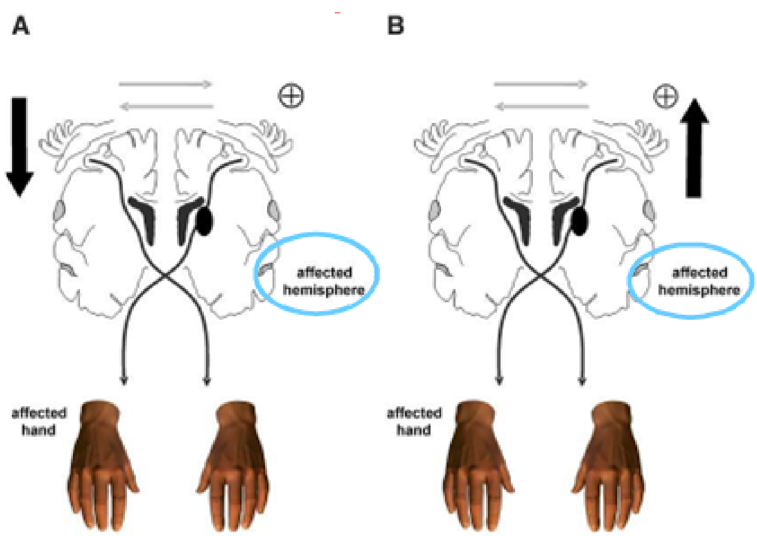


Figure 1. illustrates the potential for modulation of cortical excitability following stroke, through NIBS.

High frequency repetitive rTMS or anodal tDCS to the affected PMC increases cortical activity, whereas low frequency rTMS or cathodal tDCS inhibits the unaffected cortex. Currently, research evidence does not favour one over the other.

tDCS is applied via the scalp using electrodes measuring approximately 10cm x5cm and a current of between 1mA and 1.5mA. Most studies have used about 20 minutes stimulation period and only minor adverse effects have been reported, usually a slight tingling as the stimulation starts and occasionally slight itching or reddening of the skin under the electrodes. (Fregni&Pascual Leone 2007).

In a study with unimpaired subjects (n=16) Vines et al (BMC Neuroscience 2008) compared sham stimulation with unilateral and bilateral stimulation and demonstrated improvement in finger sequence performance on a keyboard immediately following stimulation which was greatest in the bilateral stimulation group.

A recent review of studies that have used either tDCS or repetitive TMS for recovery of arm and hand function (Nowak 2009) identified 22 studies and a total of 277 patients. They found converging evidence that both rTMS and tDCS are effective in enhancing recovery of function. There appeared to be no difference between rTMS and tDCS or whether stimulation was aimed at increasing (applied to the lesioned cortex) or inhibiting (applied to the unaffected cortex) cortical activity. They concluded that future studies should examine the effect of combining NIMS with other treatment modalities. This would seem a reasonable development as NIBS may influence potential for neuroplasticity, but for the changes to be driven towards improvement in function may also require training of those movements during the period in which excitability modulated. Examples are robot therapy and peripheral stimulation.

Edwards et al. (2009) examined the effect of anodal tDCS combined with robotic wrist therapy in chronic stroke (n=6) on cortical excitability; measured as changes in the EMG evoked potential in the flexor carpi radialis muscle in response to single pulse TMS before and after tDCS and after one hour robot training. They noted significant changes both following tDCS and robot training suggesting that the two can co-exist and that the effect is probably due to reduced intra-cortical inhibition.

Figure 2. Bi-Manu-Track

Hesse et al. (2007), evaluated a six-week training programme combining tDCS with robot-assisted hand training (Bi-manu-Track) (Figure 2) with people 4-6 weeks post stroke (n=10). Each session comprised 20 minutes training during which 1.5mA anodal stimulation was applied for the first 7 minutes to the non-lesioned PMC (Cathode over the contralateral orbit). This uncontrolled pilot study reported improvement in Fugl Meyer score (range 0-66) in 3 patients: 6 -28; 10-49 and 11-48 and changes in <5 points in the remaining 7 patients. Interestingly aphasia improved in 4 patients. There were no adverse events.

Both these studies used wrist robots, but arguably a greater functional effect could be obtained using combined arm and hand training in 3D.

Celnik (Stroke 2009) reported the effect of single applications of peripheral nerve stimulation (PNS) via the median and ulnar nerve at the wrist and tDCS in combination and singly, using sham tDCS and PNS (stimulation applied to the deep peroneal and posterior tibial nerve at the knee), with chronic post-stroke patients (n=9) who had severe post-stroke deficit (MRC muscle strength score of 2 or less) but had since regained sufficient function to perform a finger tapping test. Each subject received each combination of stimulation in random sequence preceded by a familiarisation session; i.e. 5 session in all. Stimulation was followed in each case by a motor practice session. Performance on a key-pressing test was measured before and after. The experimental design is shown in Figure 3.

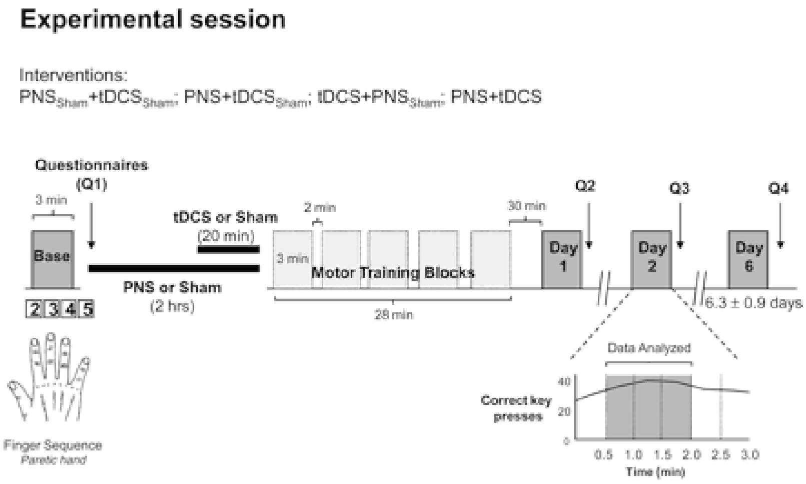
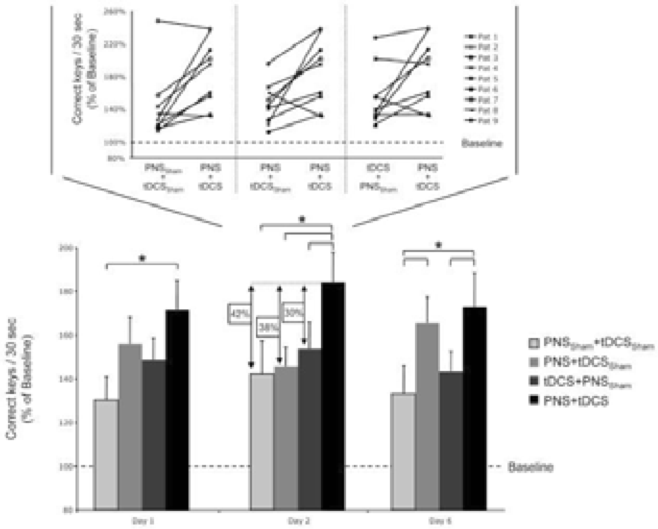


Figure 3. Experimental design



Their results showed an improvement in all cases when before and after performance was compared, but greatest improvement was shown in following PNS and tDCS.

Figure 4. Effects of the for different intervention on % change in correct key presses per 30s

In summary, beneficial effects of NIBS have been shown in healthy people and people with stroke; both in the subacute and chronic phases. Effects have been shown to last beyond the treatment period and influence motor function and well as changes in cortical excitability. NIBS has the potential to be used in combination with other therapy modalities. Currently there are no well-powered randomized controlled trials and studies have mainly explored effects with small groups of patients.