IS TRANSCRANIAL MAGNETIC BRAIN STIMULATION EFFECTIVE IN IMPROVING RECOVERY AFTER STROKE? – YES!

Wolf-Dieter Heiss
Max Planck Institute for Neurological Research, Cologne, Germany

Aphasia, the most disabling functional defect after ischemic stroke, affects more than a third of all stroke victims. It improves during the first 4 weeks in one-third of patients and during the first 6 months in approximately half of them. Early and intensive speech and language therapy (SLT) is the only effective treatment to date but usually is limited in duration and intensity. Therefore, improved and additional treatment strategies are required to improve recovery of language functions.
Poststroke aphasia results from the lesion of cortical areas involved in the motor production of speech (Broca´s aphasia) or in the semantic aspects of language comprehension (Wernicke´s aphasia). Such lesions induce an important reorganization of speech/language-specific brain networks due to an imbalance between cortical facilitation and inhibition. In fact, functional recovery is associated with changes in the excitability of the damaged neural structures and their connections. Two main mechanisms are involved in poststroke recovery: the recruitment of perilesional regions of the left hemisphere in case of small lesions and the acquisition of language processing ability in homotopic areas of the nondominant right hemisphere when left hemispheric language abilities are severely impaired.

The purpose of NICS application in the neurorehabilitation of aphasic patients is to act on specific networks involved in the pathophysiology of language processing and to promote adaptative cortical reorganization after stroke. The rehabilitation of poststroke aphasia refers to two different strategies: the recruitment of perilesional cortical regions in the dominant (left) hemisphere on one hand and the development of language ability in the nondominant (right) hemisphere on the other hand using either rTMS or tDCS. The compensatory potential of the nondominant hemisphere is probably limited and the recovery from poststroke aphasia seems to be more effective in patients who recover left hemisphere networks and left IFG function.
Therefore, the majority of NICS trials in poststroke aphasia aimed to reinforce the activity of brain regions in the left hemisphere. This goal can be achieved by using an excitatory NICS protocol (either intermittent TBS [iTBS] or anodal tDCS) to reactivate the lesioned area or an inhibitory NICS protocol (either low-frequency rTMS or cathodal tDCS) to reduce activities in the contralesional homologous area.

Most conventional rTMS studies employed an inhibitory paradigm (low-frequency stimulation) for the stimulation of the contralesional right IFG (pars triangularis, BA 45) aiming to reduce right hemisphere hyperactivity and transcallosal inhibition exerted on the left Broca’s area. However, most studies concerned isolated clinical cases without any control condition. Improvement of speech performance mainly consists of enhanced fluency in various naming test. A recent controlled rTMS trials gave further evidence of potential therapeutic benefit of low-frequency rTMS delivered to the right IFG in chronic aphasic patients, but only one pilot study enrolled patients in the postacute phas and combined rTMS with speech and language therapy and followed the activation patterns by PET.

In our controlled proof-of-principle study 30 patients with subacute post-stroke aphasia were randomized to a 10 day protocol of 20 minutes inhibitory 1Hz rTMS over the right triangular part of the posterior inferior frontal gyrus (pIFG) or sham stimulation followed by 45 minutes of speech and language therapy (SLT). Activity in language networks was measured with O-15-water positron emission tomography during verb generation before and after treatment. Language performance was assessed using the Aachen Aphasia Test battery (AAT).
The primary outcome measure, global AAT score change, was significantly higher in the rTMS group (t-test, $P=0.003$). Increases were largest for subtest naming ($P=0.002$) and tended to be higher for comprehension, token-test and writing ($P<0.1$). Patients in the rTMS group activated proportionally more voxels in the left-hemisphere after treatment than before (difference in activation volume index, AVI) compared to sham treated patients (t-test, $P=0.002$).There was a moderate but significant linear relationship between AVI change and global AAT score change ($r2 = 0.25$, $P=0.015$).
<u>Conclusions</u>: 10 sessions of inhibitory rTMS over the right pIFG in combination with SLT significantly improves language recovery in subacute ischemic stroke and favors recruitment of left hemispheric language networks. The results of this study indicate that inhibitory 1Hz rTMS over the right pIFG in combination with SLT improves recovery from post-stroke aphasia and favors recruitment of left hemisphere language networks. The proposed protocol sets the stage for larger multicenter trials to further confirm the effectiveness of NBS and to specifically address the influence of lesion location, stimulation site, activation pattern and possibly timing of NBS therapies. Finally, studies directly comparing different NBS modalities are required to determine the most effective and economical treatment strategy under clinical conditions.