activation, leading to functional deficits. Facilitation of the activation of residual cortico-spinal axons could reestablish the missing excitation, restoring voluntary muscle control. We hypothesized that facilitation could be achieved by increasing the excitability of cortical motoneurons in the motor cortex, thereby increasing CST and CBT output. While noninvasive neuromodulation methods have shown promising results in increasing cortical excitability, effects are often moderate and short-lived in patients with severe impairments. Therefore, we proposed that deep brain stimulation (DBS) could be a viable approach to modulate cortical excitability by targeting thalamo-cortical connections in motor thalamus. To test our hypothesis, we aimed to increase muscle activation in the upper limb and face with continuous motor thalamus DBS (mThal-DBS). We observed significantly larger motor evoked potentials (MEPs) in upper limb and orofacial muscles, generated by internal capsule stimulation in nonhuman primates or direct cortical stimulation in intact human patients, with concurrent mThal-DBS. We then tested whether the increase in MEPs with mThal-DBS persisted in patients with CST and CBT lesions and, importantly, whether this increase would produce functional improvements in voluntary motor control. We demonstrated that mThal-DBS enhanced respiratory, phonatory, resonatory, and articulatory control, resulting in clinically significant improvements in speech intelligibility in patients with dysarthria. We also observed a clinical improvement in swallowing function, arm and hand strength, and force control. Here, for the first time, we have shown that mThal-DBS can simultaneously ameliorate dysarthria, dysphagia, and upper-limb paralysis in individuals with cerebral lesions.

Research Category and Technology and Methods

Translational Research: 1. Deep Brain Stimulation (DBS)

Keywords

Deep brain stimulation, Motor control, Neuromodulation, Speech

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FS4F.7

IMPLEMENTATION OF RTMS TREATMENT IN POST-STROKE CLINICAL REHABILITATION

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Symposium title

Novel brain stimulation therapies to promote recovery after stroke - clinical implementation, treatment personalization, mechanistic explanation and scientific exploration

Abstract

Despite acute stroke treatment, many stroke survivors experience upper limb impairment. In recent years, non-invasive brain stimulation techniques, such as repetitive transcranial magnetic stimulation (rTMS), and continuous theta burst stimulation (cTBS) in particular, have shown promise as a therapeutic means to promote upper limb recovery after stroke. However, phase III trials are required before rTMS treatment can be recommended as standard of care. Therefore, we aim to assess effectiveness and cost effectiveness of cTBS treatment in promoting upper limb recovery after stroke in a phase III randomized clinical trial, called B-STARS2.

B-STARS2 is a multicentre double-blind randomized sham-controlled trial. Patients with an ischemic stroke or intracerebral haemorrhage and a unilateral upper limb paresis are assigned to receive ten daily sessions of active or sham cTBS (1:1), delivered over the contralesional primary motor cortex, combined with regular care upper limb therapy and started within three weeks after stroke onset.

The primary outcome is the Fugl-Meyer Upper Extremity Assessment (FM-UE) at 90 days post-stroke. Secondary outcomes are the FM-UE at 12 months post-stroke and the Action Research Arm Test, Nine Hole Peg Test, modified Rankin Scale, Barthel Index, hand and participation sections of the Stroke Impact Scale, the EuroQol-5D-5L at 90 days and 12 months post-stroke. Additional secondary outcomes are cost effectiveness, length of stay and ipsilesional and contralesional excitability.

We aim to recruit 454 participants across 16 rehabilitation centres in the Netherlands, with a sample size based on a minimal detectable effect of 6.6 points on the FM-UE scale. The first inclusion is scheduled for September 2024.

If cTBS treatment leads to a cost-effective and clinically meaningful additional recovery of 6.6 points on the FM-UE at 90 days post-stroke, cTBS treatment will be approved as standard of care by the National Health Care Institute of The Netherlands.

Research Category and Technology and Methods

Clinical Research: 21. Neurorehabilitation

Keywords

Stroke, Upper limb recovery, Repetitive transcranial magnetic stimulation, Rehabilitation

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FS4F.8

ABNORMAL PREMOVEMENT INTERHEMISPHERIC INTERACTIONS ARE PRESENT IN THE CHRONIC BUT NOT IN THE ACUTE OR SUBACUTE POST-STROKE PERIODS

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Symposium title

Novel brain stimulation therapies to promote recovery after stroke - clinical implementation, treatment personalization, mechanistic explanation and scientific exploration

Abstract

A long-standing model of stroke recovery is that the contralesional hemisphere exerts increased inhibition to the ipsilesional hemisphere, causing an imbalanced inhibitory interaction between the two hemispheres. A seminal study by Murase et al. (2004) showed that chronic stroke patients presented persistent interhemispheric inhibition (IHI) immediately before movement onset. However, outcomes of clinical trials attempting to rebalance IHI are mixed. One reason could be the lack of knowledge of the time course of the emergence of this imbalance. Here, in a longitudinal study, we investigated the evolution of premovement IHI over the first year after stroke and relate it to motor recovery of the hand. Patients with first-time acute ischemic stroke (N=22) and healthy age-matched controls (N=11) were tested at 5 time-points (week 1, 4, 12, 24, and 52 after stroke, or since recruitment for controls). Participants performed a simple reaction time task with voluntary index finger abduction using their paretic hands (controls' dominant hands), while paired-pulse TMS was applied at four timings during movement preparation (20, 50, 80, and 95% of estimated RT), with conditioning stimulus over the contralesional M1 (right M1 for controls) and test stimulus over the ipsilesional M1. Hand function was also accessed using a finger individuation paradigm and clinical assessments.

Contrary to previous beliefs, we found that in the acute/subacute stages (weeks 1-12) patients showed normal release of pre-movement IHI ($t(21)=0.50$; $p=0.62$); it becomes abnormal from week 24 onward ($t(31)=3.30$, $p=0.0025$). Interestingly, premovement IHI was not correlated with behavioral measures cross-sectionally; instead, the emergence of the abnormality was negatively correlated with the improvement of finger individuation ($r=-0.73$, $p=0.003$). These findings suggest that the emergence of abnormal premovement IHI and poor finger-individuation recovery may share a latent cause, which could be a maladaptive process not present early after stroke.

Research Category and Technology and Methods

Clinical Research: 10. Transcranial Magnetic Stimulation (TMS)

Keywords

Interhemispheric imbalance, Stroke, Rehabilitation, TMS

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