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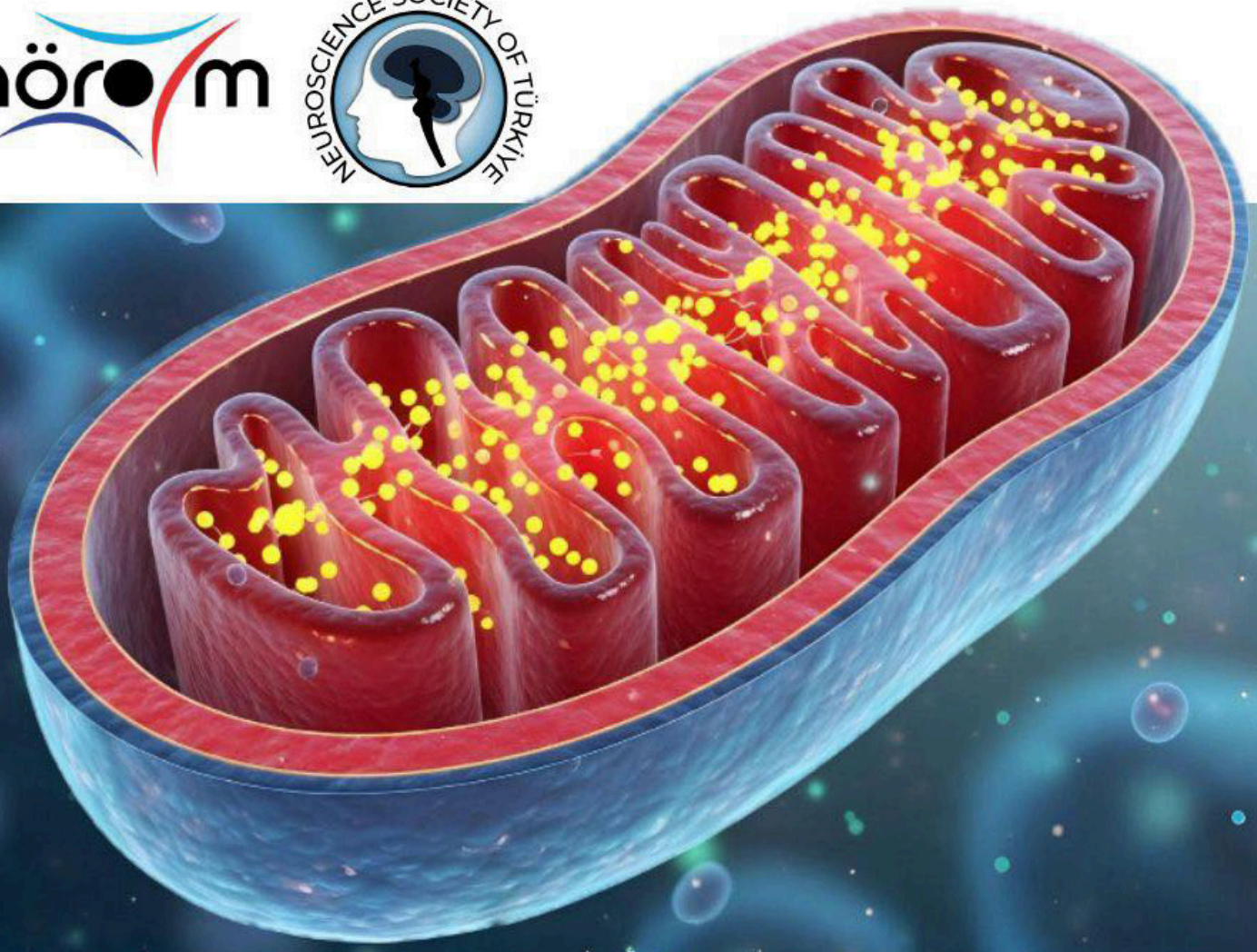

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SPEECH TEXTS

The Impact of Transcranial Magnetic Stimulation on Brain Morphometry in Early Stroke Rehabilitation Using the Bobath Approach: A Pilot Study

Furkan Karakoç[1], Bernis Sütçübaşı[2], İpek Erdoğan[3], Yakup Krespi[4]

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Objective: This pilot study aimed to compare the effects of inhibitory and excitatory repetitive Transcranial Magnetic Stimulation (rTMS) protocols, applied in addition to the Bobath approach, on early rehabilitation of hemiparetic stroke patients with upper extremity motor deficits due to subcortical lesions.

Method: Eight patients diagnosed with early-stage subcortical stroke in the neurology clinic were included in the study. The study consisted of three groups: (1) sham rTMS, (2) ipsilateral excitatory rTMS, and (3) contralateral inhibitory rTMS. Each patient received 15 sessions of rTMS applied to the primary motor cortex. Immediately after the rTMS sessions, all groups underwent physiotherapy techniques based on the Bobath approach, which is founded on neurodevelopmental principles aiming to improve postural control, reduce abnormal movement patterns, and promote functional movements. Pre- and post-treatment clinical motor assessment scales were used to evaluate the patients' upper extremity motor functions, and structural brain images were recorded on the same day. Pre- and post-treatment gray matter volume changes were assessed for the whole brain using voxel-based morphometry (VBM) and region-of-interest -based analyses. VBM analyses were performed using Computational Anatomy Toolbox-12 and Statistical Parametric Mapping-12 software implemented in MATLAB. Additionally, correlations between brain regions showing significant changes and demographic variables were calculated.

Results: Although the clinical evaluation results were not statistically significant when comparing pre- and post-treatment outcomes, it was demonstrated that all rTMS groups (placebo, excitatory, and inhibitory) applied combined with Bobath therapy supported post-stroke recovery and induced positive changes in mobility and upper extremity motor functions. In the VBM analyses, although not statistically significant, a trend toward decreased gray matter volume in the ipsilesional superior frontal gyrus was observed in the inhibitory rTMS group after treatment compared to before treatment, whereas the placebo and excitatory rTMS groups showed a trend toward increased volume ($p = 0.09$). The results obtained from other investigated motor regions were also not statistically significant.

Conclusion: As a result of the combined application of the Bobath approach and rTMS, an improvement in clinical outcomes and a trend toward opposite-direction volumetric changes in structural brain measures were observed during early-stage stroke rehabilitation depending on the mode of rTMS, inhibitory vs excitatory; however, in this pilot study, no statistically significant differences were found between the excitatory and inhibitory rTMS protocols. Larger-scale studies conducted during the acute and early subacute phases - when post-stroke neuroplasticity is at its peak-will better elucidate the morphometric effects of such multifaceted interventions. This study provides important preliminary findings that highlight the potential contributions of rTMS in early stroke rehabilitation and may serve as a foundation for future research.

Keywords: Stroke, early rehabilitation, bobath concept, transcranial magnetic stimulation, motor function

Mitochondrial Myopathy Due To Thymidine Kinase 2 Deficiency: Clinical Spectrum and Therapeutic Implications From A Case Series

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Objective: Thymidine kinase-2 deficiency (TK2d) is a rare autosomal recessive mitochondrial myopathy caused by impaired phosphorylation of deoxythymidine and deoxycytidine, leading to mitochondrial DNA (mtDNA) depletion/deletions, defective oxidative phosphorylation, and cellular energy failure. While no approved therapies currently exist, recent evidence suggests that oral pyrimidine nucleoside supplementation may restore mtDNA and improve outcomes. We aimed to describe the clinical, biochemical, genetic characteristics of five patients with TK2d, treated under an international early access program, and to discuss mechanisms of potential therapeutic strategies.

Methods: We retrospectively reviewed clinical and follow-up data, laboratory findings, genetic results of five patients with TK2d.

Results: Four early-onset patients, all diagnosed genetically with TK2d, presented between 12-20 months with hypotonia, motor regression, bulbar/respiratory dysfunction. Three infants required invasive ventilation. Within 3-8 weeks of oral nucleoside therapy, respiratory symptoms resolved, tracheostomies were closed. Over a follow-up period of 18 months-6 years, all achieved independent ambulation. In the fourth patient, who had lost ambulation by 17 months, nucleoside therapy was recently initiated, clinical response is under follow-up. The fifth case, a 22-year-old woman with gradual proximal weakness since infancy, developed dysphagia and hypoventilation requiring gastrostomy and nocturnal non-invasive ventilation during adolescence. Genetic testing confirmed homozygous pathogenic variant in TK2. After six years of nucleoside therapy, her disease course has slowed and shows relative stabilization.

Conclusion: TK2d demonstrates how impaired mitochondrial nucleotide salvage results in energy failure with heterogeneous clinical outcomes. Early recognition is essential, as pyrimidine nucleoside therapy offers a promising therapeutic strategy together with multidisciplinary supportive care.

Keywords: TK2 deficiency, mitochondrial myopathy, pediatric neurology, nucleoside therapy