Study protocol

„Repetitive Transcranial Magnetic Stimulation as Therapy in Hereditary Spastic Paraplegia and Adrenomyeloneuropathy”

NCT03627416

Document date: 06.01.2017

Study objective: to compare the effectiveness of 10 hertz (Hz) rTMS over the primary motor cortices in improving the gait and strength and spasticity of lower extremities with sham stimulation in HSP and AMN patients.

Study design: prospective, randomized, controlled, single blinded clinical trial in cross-over design

Patients: 16 subjects with HSP and AMN

Inclusion Criteria:

- Diagnosis of HSP - confirmed genetically, on the basis of family history or on exclusion or diagnosis of AMN - confirmed genetically or by the elevated plasma very long chain fatty acid or on family history
- Gait disturbances affecting daily activities
- Ability to walk 10 meters without assistance or with crutches or with rollator walker

Exclusion Criteria:

- Presence of signs or symptoms indicating other than HSP or AMN etiology of gait disturbances
- Contraindications for rTMS as listed by the Guidelines of the International Federation of Clinical Neurophysiology (IFCN 2009) i.e. seizure in the past, epilepsy, presence of magnetic material in the reach of magnetic field, pregnancy, likelihood to get pregnant, intracranial electrodes, cardiac pacemaker or intracardiac lines, frequent syncopes

Intervention:

Experimental:

active rTMS 10 hertz (Hz) rTMS was administered over bilateral primary motor areas for the muscles of lower extremities. Therapy included five daily sessions (on consecutive weekdays). In every session 3000 magnetic pulses of 90% of the resting motor threshold intensity was elicited.

Sham Comparator:

Sham rTMS Sham stimulation mimicked the active one except that the stimulating coil was being held perpendicularly to the scalp, which assures similar impression as the active stimulation but prevents that significant magnetic field will reach brain tissue.

Every included participant underwent real and sham stimulations in random order. The randomization list contained blocks of random size of two or four. Information about assignment of every patient was kept in sealed envelopes. Eight patients received the active treatment first.

Outcome Measures

Primary Outcome Measure(s):

Change from baseline Walking Time in 10 Meter Walk Test to the measurement taken directly after rTMS

Secondary Outcome Measure(s):

Change in Timed up and go Test from baseline to the measurement taken directly after rTMS and to the measurement taken two weeks after rTMS

Change in Medical Research Council Scale (MRC) from baseline to the measurement taken directly after rTMS and to the measurement taken two weeks after rTMS

Change in Modified Ashworth Scale from baseline to the measurement taken directly after rTMS and to the measurement taken two weeks after rTMS

Change from baseline Walking Time in 10 Meter Walk Test to the measurement taken two weeks after rTMS

Statistical analysis

The measurements of spasticity were averaged for both extremities in each movement tested, and then, the scores for movements of the proximal segments of lower extremities, i.e., hip flexion, knee extension, and knee flexion, as well as of the distal segments, i.e., ankle flexion and extension, were summarized. The times of performing 10MWT and TUG, as well as the spasticity of proximal and distal segments measured before active rTMS, were compared with respective measurements done after active rTMS and during follow-up. For sham rTMS, the same comparisons were done. Owing to the small number of subjects and the presence of ordinal data, the nonparametric Wilcoxon signed rank test was used. The significance level was set to $p < 0.05$. Power analysis was conducted in G∗Power v.3.2 software [30], for large (dz = 0.8), medium (dz = 0.5), and small (dz = 0.2) effect sizes, assuming a sample size of 15 subjects. The power for the three effect sizes was 80%, 56%, and 18%, respectively. The rest of calculations was done with the Statistica data analysis software system, version 12.0 (StatSoft, 2008; Palo Alto, CA, USA). Considering our interest in all symptoms tested (gait performance, weakness, and spasticity), which might respond to rTMS differently, as well as our intention to avoid excessive type II errors, which may occur in such a limited number of subjects, we decided not to conduct a correction for multiple comparisons.