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NEUROMODULATORY APPROACH IN PAROXYSMAL NEUROLOGICAL DISORDERS.

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Introduction

Nowadays, neuromodulation offers different devices and techniques in the treatment of neurological patients suffering from paroxysmal disorders such as epilepsy and migraine. Among non-pharmacologic therapies rTMS shows good results. At the moment, rTMS is considered a useful tool in the management and treatment of several disorders originating in the cerebral cortex. The small intensity currents induced by the magnetic field have an impact on various mechanisms at cellular level being able to change the expression of neurotransmitters thus in result modulating pathophysiological pathway of migraine.

The primary mechanisms causing migraine attacks still remain largely unrecognized due to the complex and dynamic organization of processes in the brain neuronal networks. Cortical excitability has been suggested to be dysfunctional in patients with migraine. The ability to modulate cortical activity and induce persistent, plastic effects renders repetitive transcranial magnetic stimulation (rTMS) as a potential therapeutic approach.

We hypothesized that multifocal rTMS reduces the frequency and intensity of migraine attacks in comparison to a baseline period, and that this effect exceeds a possible placebo effect. Furthermore, we hypothesized that this stimulation protocol can induce improvements in quality of life scores: Headache disability index 6 (HIT-6), Migraine disability index score (MIDAS), and Headache disability index (HDI).

Material and methods

We conducted a longitudinal, double-blinded, rTMS-intervention study including subjects with episodic migraine (both with and without aura). After a 4-week baseline period, participants attended 6 intervention sessions within 2 weeks to receive either multifocal rTMS- or a placebo-treatment. The blinding was performed by means of a specific active/placebo coil. Quality of life questionnaires were conducted on follow-up dates. Table 1 shows the demographic characteristics of the study lot and Fig.1 shows a schematic of the study design.

Table 1.

Variables	Total (n=42)	Real (n=22)	Sham (n=20)
Female, n (%)		19 (86.3%)	20 (100%)
Age in years (M ± SD)		38.4 ± 10.2	41 ± 12.6
Range		20 – 58	22 - 62
Frequency of headache per month (M ± SD)		7.5 ± 3.7	7.3 ± 3.6
Range		2 – 14	3 – 14
Pain intensity (M ± SD)		6.7 ± 1.5	6.2 ± 1.2
*HIT-6 (M ± SD)		63.4 ± 6.3	64.2 ± 4.4
•HDI (M ± SD)		64.2 ± 17.4	55.4 ± 22
†MIDAS (M ± SD)		36.5 ± 22.9	35.9 ± 23.9

*Headache Impact Test, •Headache Disability Index, †Migraine Disability Assessment Score.

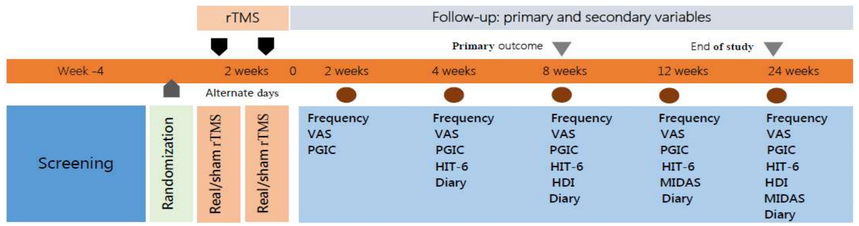

Figure 1. Study design. Participants were asked to fill out a headache diary for 4 weeks and complete the HDI, HIT-6, and MIDAS questionnaire before the first stimulation session. Frequency and severity of migraine attacks within the 8 weeks following the intervention serve as primary outcome variables. Quality of life questionnaires were conducted on several other follow-up dates.

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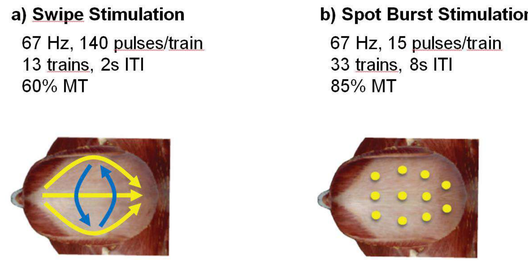

Figure 2. Stimulation protocol. a) during swipe stimulation the coil is pulled across 3 anterior-posterior and 2 lateral-lateral tracks. b) during spot burst stimulation each of 11 spots are stimulated three times.

The stimulation protocol consisted of 2 steps, a swipe-stimulation and a spot burst stimulation. High frequency rTMS comprised 140 pulses/train in trains at 60% of motor threshold, followed by 5 pulses/train in trains at 85% of motor threshold applied over cortex within a predefined multifocal delivery scheme consisting of 11 points marked on individual caps according to the 10-20 EEG system during the first session (Fig. 2). Stimulation procedures had been performed respecting the IFCN committee safety protocols and re-commendations (Groppa et al., 2012).

To assess the efficacy of multifocal rTMS we analyzed frequency and intensity of attacks in a 6-month follow-up period in comparison to the 4-week baseline period as primary outcomes on the basis of a headache diary.

To evaluate the impact on every day life, questionnaires about the quality of life were conducted as secondary variables. Student-test was applied to process the statistical mean values, repeated measures ANOVAs were performed separately for both groups. To determine the statistical significance, the P value should have been less than 0.05

Results

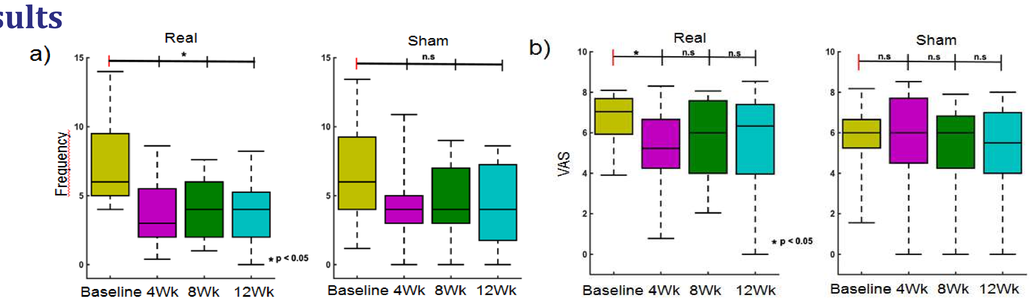

Figure 3. Primary outcomes. a) The number of migraine attacks b) The severity of the attacks.

Figure 3 shows the results for frequency and intensity of the attacks from the baseline period until 3 month after the stimulation. In the stimulation group, the number of attacks was significantly reduced following stimulation ($p<0.05$). This effect lasts for at least three months. The number of attacks was also reduced in the placebo group. However, this was not statistically significant. The severity of attacks was significantly reduced 4 weeks after the treatment exclusively in the treatment group ($p<0.05$). The assessment of secondary outcomes in both rTMS groups revealed a positive impact on quality of life and functional outcome in both groups, more prominent in the real rTMS group but with no statistical inter-group difference ($p>0.05$).

Conclusions

We showed that the rTMS paradigm reduces the number and severity of migraine attacks to a lager extent than the placebo treatment. Multifocal rTMS it is a novel and effective treatment approach for episodic migraine prophylaxis in adults. Importantly, the experimental protocol is well tolerated, showing no serious adverse events.

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