

# ROLE OF CORTICAL EXCITABILITY IN CHRONIC MIGRAINE PREVENTION: A STUDY DESIGN FOR A RANDOMIZED OPEN-LABEL TRIAL



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**Introduction and Objectives:** Chronic migraine (CM) is a disabling disorder with daily or almost daily severe headaches. Cortical hyperexcitability and dysmodulation of the brainstem with further development of central sensitization are considered to be the pathophysiological basis of CM. Currently, the most informative, noninvasive, and safe method to study cortical excitability and intracortical inhibition processes in patients with CM during the migraine attack and in the interictal period is transcranial magnetic stimulation (TMS).

The ability to reduce the frequency of headaches in CM is proven (Level A evidence) for topiramate, an anticonvulsant, and onabotulinumtoxin A (Botox). The effect on cortical excitability has only been studied for topiramate. Currently the beneficial effect of onabotulinumtoxinA in chronic migraine is attributed to its peripheral effect on the transmission of inflammatory neuropeptides, but possible central effects have not been studied. The aim of this study will be to assess the dynamics of cortical excitability under the influence of migraine-preventive drugs topiramate and onabotulinumtoxinA using the TMS. The design for this study is briefly described here.

**Methods/Design:** This open-label, prospective, randomized study will enroll approximately 80 adult CM patients in the Moscow University Neurological Clinic. The basic group will include 40 patients before and after one cycle of treatment with onabotulinumtoxinA (dosed according to the PREEMPT [Phase III Research Evaluating Migraine Prophylaxis Therapy 1] trial dosing paradigm), and a comparison group of 40 patients before and after treatment with topiramate (100 mg/day for 3 months). We will study motor cortex thresholds, phosphene thresholds, and the silent period, using TMS and the change in the number of headache days based on headache diaries.

**Conclusion/Discussion:** The study will enable clarification of the role of cortical excitability in the preventive effect of drugs with proven clinical efficacy in CM patients and broaden the understanding of the pathophysiology of this disabling form of primary headache.

