

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (TMS) AS TREATMENT OF CHRONIC DRUG-RESISTANT NEUROPATHIC PAIN IN BLADDER PAIN SYNDROME: PRELIMINARY DATA

Hypothesis / aims of study

Chronic pelvic pain associated to the Bladder Pain Syndrome (BPS) is a typical example of neuropathic pain, involving peripheral and central mechanisms of sensitization. Cortical stimulation has emerged as a novel approaches for pain relief. Specifically, a non-surgical technique modulating cortical excitability and inhibiting pain perception is repetitive transcranial magnetic stimulation (rTMS) applied to the motor cortical areas. The H-coil can therefore be used to stimulate the motor cortex concerning the pelvic area, a region that lied deep in medial motor area sections folding into the brain medial longitudinal fissure. To date, no studies have used rTMS with an H-coil to stimulate the motor cortex as therapy for resistant neuropathic pain in BPS patients. In the present pilot study, we investigated whether modulation of excitability of the motor cortex with rTMS in patients with BPS could result in modifications of neuropathic pain and urinary disturbances.

Study design, materials and methods

Eight patients with BPS were enrolled. All patients were resistant to standard therapies for neuropathic pain taken for at least six months. The patients received two weeks of rTMS sessions, with three week-break between the two weeks of treatment. Standard TMS coils (such as the figure-of-8 coil) permit to stimulate only superficial cortical regions of the human brain. A newer cooled coil, the Hersed (H)-coil allows deep brain stimulation without significantly increasing fields induced in superficial cortical regions.

In each patient, the rTMS sessions were delivered with a H-coil for 5 consecutive days, lasting 20 minutes and consisting of 30 consecutive trains of 50 stimuli delivered at 20 Hz, at 100% of resting motor threshold, separated by intertrain intervals lasting 30 s. The patient's clinical condition was evaluated before treatment began, immediately after it ended, 3 weeks later, and every 3 weeks in a follow up lasting 126 days (18 weeks). At baseline patients was submitted to DN4 and sensitization scale. At various time-points, all patients underwent to the following assessments: Visual Analogue Scale (VAS) for pain and Neuropathic Pain Symptom Inventory (NPSI) to assess changes in *pain*; Overactive Bladder Questionnaire (OABq), O'Leary Sant questionnaire and post-voiding bladder ultrasound to assess changes in *urinary disturbances*; Short Form-36 Health Survey (SF-36) and Beck depression inventory (BDI) to evaluate changes in the *quality of life*. The *Minnesota Multiphasic Personality Inventory* (MMPI) and a urodynamic examination with cystoscopy were performed at baseline, at the end of the two rTMS sessions and three months later. Data were analyzed using the one way ANOVA and Fisher post hoc test.

Results

Eight women were enrolled (mean±SD: 55.5±10 years). The delay between the onset of symptoms and the inclusion in the study was 18±9.5 years. At the enrollment, the DN4 was 5.28±1.38 and the sensitization scale score was 66.4±20. The bladder residue significantly improved after the rTMS (F=2.43; p=0.02). The OABq score reduced significantly after the rTMS (F=1.36; p=0.05). Also the NPSI score reduced after the rTMS (F=1.62; p=0.05). The BDI score did not change significantly. The effect on the OABq and the NPSI tests persisted at least for 3 weeks.

Interpretation of results

The preliminary results of this pilot study show that the rTMS of the brain motor cortex related to the pelvic area changes both the subjective perception of the pain and the objective measurement of bladder voiding. In a previous study the efficacy of rTMS on chronic drug-resistant neuropathic pain associated to other syndromes was already demonstrated (Onesti E et al, 2013, Khedr EM et al 2005). Our results are consistent with recent characterization of brain white matter micro structural abnormalities in women with BPS, suggesting a brain neuropathological contribution to chronic pelvic pain "1-2". In our research, a placebo effect could be ruled out because a long latency between the treatment and the effects was demonstrated, such as previously evidenced "3". Also the frequency, urgency and incontinence symptoms, such as reported in OABq, improved. Moreover, the depression did not improved before the changes in painful and urinary parameters, meaning that the change of psychic disease did not cause the clinical improvement reported.

Concluding message

Deep H-coil rTMS applied to the motor cortex could be provide pain and urinary disturbances relief in patients with BPS. The interpretation of this results is limited by the small sample size, and more data are certainly need to confirm this preliminary report and to better understand the mechanisms by which rTMS may modulate pain and urinary disturbances in BPS patients.

References

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Disclosures

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