Psychiatria Danubina, 2012; Vol. 24, No. 1, pp 102-103 *Letter to Editor*

EMOTIONAL SIDE EFFECTS AFTER HIGH-FREQUENCY RTMS OF THE RIGHT DORSOLATERAL PREFRONTAL CORTEX IN AN ADULT PATIENT WITH ADHD AND COMORBID DEPRESSION

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Dear Editors,

an article by Michael Rösler on attention deficit in adult patients suffering from attention deficit hyper-activity disorder (ADHD) and an article by Yuval Bloch on the possibility of alleviating these problems using high-frequency repetitive transcranial magnetic stimulation (rTMS) of the right dorsolateral prefrontal cortex (DLPFC) awakened our interest (Rösler et al. 2010, Bloch et al. 2010). Although using rTMS in other indications than in depression remains controversial (George et al. 2009), it is important to evaluate its effectivity in other disorders too.

So we decided to try this method in ADHD at our site too. Our patient was a man (36 years old), who had been diagnosed with ADHD in childhood (according to ICD-9 314.0 Attention deficit disorder, later changed to F90.0 Disturbance of activity and attention according to new ICD-10). He has especially long-lasting problems with attention. During childhood he remained without medication, but in adulthood he was unsuccessfully treated with atomoxetine. In adulthood he was also diagnosed with comorbid depressive disorder (F33 according to ICD-10), he had three depressive episodes treated with antidepressants (venlafaxine, milnacipran, mirtazapine and tianeptine). The last depressive episode was in 2009. Symptoms during these episodes were different from his "usual" problems with attention. The patient came to our Department to ask for some treatment of his attention deficit at the beginning of 2011, not for problems with depression.

Stimulation treatment was divided into three parts. During the first part, the patient underwent five sessions of sham rTMS. In the second part there were five sessions using 10 Hz stimulation of the left DLPFC with intensity 120% of individual resting motor threshold (RMT; RMT was measured using EMG) with 1500 stimuli per session (every train lasted 10 seconds, every intertrain lasted 30 seconds). In the third part there were five sessions using 10 Hz stimulation of the right DLPFC with intensity 120% of individual RMT with 1500 stimuli per session (every train lasted 10 seconds, every intertrain lasted 30 seconds). We used Magstim Super Rapid stimulator from The Magstim Company with an eight coil. For the start, end and changes between individual rTMS settings, a total of four check-ups were evaluated (V_0 – V_3), during which depression using Montgomery and Asberg Depression Rating Scale (MADRS; due to patient's comorbidity) and attention using an neuropsychological examination with the d2 Test of Attention by Rolf Brickenkamp and Eric Zillmer (Brickenkamp & Zillmer 1998), were assessed.

Before treatment the patient subjectively complained of impaired attention (his results in d2 test were quite good, he reached 86.4 percentile, but he complained of impaired attention during longer time periods than necessary for testing, for example during 8 hours lasting shift) and mild residual depression was present (MADRS=14). Firstly the patient underwent sham stimulation (MADRS=12, with an improvement of attention from the 86.4 to the 98.2 percentile); then the patient underwent high-frequency stimulation of the left DLPFC (MADRS=7, further improvement of attention to the 98.9 percentile). This type of rTMS was well tolerated and without any side-effects. Lastly, the high-frequency rTMS of the right DLPFC was started (similarly as described in the Bloch's study). However, after the first session the patient reported substantial side-effect, in particular dysphoria, inability to response emotionally, hypobulia, tension and also impaired attention. This negative effect started to develop immediately after stimulation, culminated about two hours later and persisted in a milder form into the next day; as for the MADRS, worsening went from 7 to 21 points (V_X). No other reason for this worsening than high-frequency stimulation of the right DLPFC was found. The patient refused resumption of right-sided stimulation and instead asked for left-sided rTMS (see Table 1). As early as after the first session of the left-sided rTMS the patient felt better and improvement continued during the other four sessions. At the end of the treatment (V_3) he reached 9 points on the MADRS and improved in attention to the 99.2 percentile.

Such a considerable negative effect on the emotivity, due to a single right-sided high-frequency stimulation of DLPFC, is noteworthy but not fully unexpected. It is known that low-frequency rTMS of the right DLPFC is used in the treatment of depressive disorder (Fitzgerald et al. 2003) and, on the contrary, high-frequency rTMS of this area has been used in patients with mania (Grisaru et al. 1998). Therefore, we would like to warn against its use in patients with ADHD and comorbid affective disorder, and to recommend consideration of high-frequency rTMS of the left DLPFC.

Table 1. Design of therapy – expected and real

Design therapy - expected	V_0	5 sessions of sham rTMS	V_1	5 sessions of HF rTMS of left DLPFC	V_2	5 sessions of HF rTMS of right DLPFC	V_3		
Design therapy - real	V_0	5 sessions of sham rTMS	V_1	5 sessions of HF rTMS of left DLPFC	V_2	1 session of HF rTMS of right DLPFC	V_X	5 sessions of HF rTMS of left DLPFC	V_3

Legend: DLPFC – dorsolateral prefrontal cortex; HF rTMS – high-frequency repetitive transcranial magnetic stimulation;
V_0 - V_3, V_X – visit 0 to visit 3, visit X

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