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Repetitive transcranial magnetic stimulation (rTMS) in the double-blind treatment of a depressed patient suffering from bulimia nervosa: a case report

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In the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV; APA, 1994), bulimia nervosa (BN) is classified as an eating disorder. The disease is characterized by discrete periods of binge eating during which, large amounts of food are consumed and a sense of control over eating is absent, followed by differing types of purging behaviour to prevent weight gain. Since the first descriptions of the diagnosis, little is known about the aetiological background of the disease. BN is accompanied by, or due to, alterations of serotonin and/or norepinephrine activity. These changes may possibly be involved in the pathological eating behaviour and in causing associated depression.

The affective spectrum disorder model (ASD) is based on the hypothesis that certain psychiatric disorders such as major depressive disorder; panic disorder; obsessive-compulsive disorder; BN, etc., share a common link in their aetiology which is critical for their pathogenesis. In a large family study the objective was to prove this model, and preliminary results showed a familial aggregation of depression and eating disorders within families (Mangweth et al., 2003).

Functional imaging techniques have shown that left prefrontal hypo-metabolism in patients with bulimia varies with depressive symptomatology (Nozoe et al., 1995). Compared to controls, blood flow was high before eating and lower after eating in the bilateral inferior frontal areas. Therefore Nozoe and co-workers (1995) proposed that the frontal area changes might affect eating control. Frontal damage would lead to hyperphagia, indicating that the frontal lobe may contain a feeding suppression area and that reduced activity after eating may result in bulimic hyperphagia. In analogy, depressed patients without any

symptoms of an eating disorder exhibit similar signs of prefrontal hypo-metabolism (Ketter et al., 1996).

Transcranial magnetic stimulation (TMS) is a novel tool in psychiatry with mild side-effects. As demonstrated by positron emission tomography, repetitive application of high frequency TMS can locally up-regulate metabolism as well as in remote, functionally linked areas (Paus et al., 1997).

Controlled studies over the left dorsolateral prefrontal cortex (LDLPFC) have shown antidepressive effects in humans (Fitzgerald et al., 2003). Animal models have demonstrated that TMS releases biogenic amines and modulates serotonergic neural transmission (Hausmann et al., 2002). Both mechanisms are considered to be critical for the aetiology of depression. In addition, data from randomized, placebo-controlled studies suggest that BN may respond to treatment with antidepressants (Fluoxetine Bulimia Nervosa Collaborative Group, 1992).

Based on the evidence reviewed above, we sought to study the effects of rTMS in the treatment of a depressed patient suffering from BN.

The 28-yr-old patient was recruited by newspaper advertisement. The patient fulfilled the DSM-IV criteria for BN and suffered from a major depressive episode as defined by DSM-IV. After extensive information about potential risks of the treatment, she signed the informed consent form, approved by the Ethics Committee of the University of Innsbruck.

The patient's disease began at the age of 19 yr. When she was an au pair in France she started to suffer from anorexia nervosa and switched to bulimia at the age of 25 yr. Three years ago she developed a first depressive episode. A year ago an antidepressant therapy with 30 mg/d mirtazapine was started. This medication neither brought relief of her depressive symptoms, nor did it improve her bulimic symptoms. She sporadically underwent professional psychotherapy for one year, which was terminated half a year before the trial. Three weeks before starting the trial her current antidepressant medication was tapered. Prior to treatment, contra-indications to rTMS were ruled out.

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At baseline, after 1 wk, and at the end of treatment (day 14), the Hamilton Depression Scale (HDRS; Hamilton, 1960), the Beck Depression Inventory (BDI; Beck and Beamesderfer, 1974), the Yale–Brown Obsessive Compulsive Scale (YBOCS; Goodman et al., 1989), as well as the Binge–Purge Diary were assessed. The rating clinician was blind to treatment conditions.

While the HDRS, the BDI and the YBOCS are well known tools, the Binge–Purge Diary is designed to record the number of binge-eating episodes and purge compensations which occur daily for a 7-d period of time. Additional psychiatric disorders other than bulimia, or personality disorder, which might interfere with a diagnostic assessment, treatment, or compliance, were ruled out using SCID (Wittchen et al., 1997).

Stimulation was performed by an air-cooled 70-mm double loop coil (focal coil) attached to a rapid Magstim Stimulator (Magstim Company Ltd, Whitland, Carmarthenshire, UK) placed over the LDLPFC. Stimulation was delivered for 2 wk (2 × 5 d) (10 trains × 10 s, 20 Hz, 80% motor threshold 60-s train interval). Stimulation was performed as described previously (Hausmann et al., 2004).

At baseline the patient exerted an average of two binge attacks and vomited twice a day. Another purge mechanism consisted of excessive sports activities. At entry she had a body mass index (BMI) of 18. On the HDRS she was rated 20. After 10 sessions of rTMS over 10 d with a break at weekends the patient recovered completely from binge and purge symptoms as assessed by the Binge–Purge Diary. The changes of the HDRS baseline until end of treatment almost reached a 50% decrease, reflecting the response to treatment.

This positive outcome may, however, be attributable to a strong placebo effect, or to the reassurance of treatment due to frequent visits. In addition a spontaneous remission of depression with a subsequent behavioural change of her eating habits might have been a plausible explanation. The fact is that the patient, for the first time within a year, experienced a solid improvement of her bulimic behaviour as well as her depressive symptoms.

To our knowledge, except for Brewerton et al. (personal communication) this is the first published case of rTMS treatment in comorbid depression and bulimia that has been reported. It demonstrates a positive outcome in depression as indicated by a nearby response of depressive symptoms and a complete absence of bulimic binge and purge behaviour. Further controlled studies appear warranted to evaluate rTMS treatment in BN. This case-report may shed light on the mechanism of action of left prefrontal rTMS and its

role in modulating the serotonergic system underlying the aetiology of depression and BN, thus insinuating that both BN and depression share a common link in their aetiology, as theorized by the concept of ASD.

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None.

Statement of Interest

None.

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