

## TRANSCRANIAL MAGNETIC STIMULATION THERAPY IN OBSESSIVE COMPULSIVE DISORDER: A CASE SERIES

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### ABSTRACT

The effectiveness of repetitive transcranial magnetic stimulation therapy in obsessive compulsive disorder is indefinite, although it has been shown to be helpful in depression in many studies. Six cases of obsessive compulsive disorder who received repetitive transcranial magnetic stimulation therapy are presented. Afterwards, the literature about the effectiveness of transcranial magnetic stimulation in obsessive compulsive disorder is reviewed.

**Key words:** transcranial magnetic stimulation, obsessive compulsive disorder.

NPAKADEMİ. 2012; 1(1):45-49

## OBSESİF KOMPULSİF BOZUKLUKTA TRANSKRANİYAL MANYETİK UYARIM TEDAVİSİ: BİR OLGU SERİSİ

### ÖZET

Repetitif transkraniyal manyetik uyarım tedavisinin depresyonda faydalı olduğu pek çok çalışmada gösterilmiştir, ancak obsesif kompulsif bozuklukta etkinliği açık değildir. Burada repetitif transkraniyal manyetik uyarım tedavisi uygulanmış altı olgu bildirilmektedir. Ardından, obsesif kompulsif bozuklukta transkraniyal manyetik uyarımın etkinliği hakkındaki literatür gözden geçirilmektedir.

**Anahtar sözcükler:** Obsesif kompulsif bozukluk, transkraniyal manyetik uyarım tedavisi

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### INTRODUCTION

Six cases of obsessive compulsive disorder (OCD) are presented. All diagnoses were made according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). Repetitive transcranial magnetic

stimulation (rTMS) was applied with Magstim Superrapid magnetic stimulator (The Magstim Company Ltd.; Spring Gardens, Whitland/ Carmarthenshire, Wales, U.K.).

### CASE 1

She was 34 years-old female with OCD for eight years and depression. Predominant symptoms were obsessions of contamination. She was unresponsive to many trials of medication and seven sessions of electroconvulsive therapy (ECT) one year before.

She was applied repetitive 30 sessions (six sessions a week) of low-frequency (1 Hz) transcranial magnetic stimulation over the left dorsolateral prefrontal cortex (DLPFC) at 110% of the motor threshold (MT) for 5 seconds. One hundred

trains and 500 pulses were applied at each session. She began simultaneously taking fluoxetine 80 mg daily and trazodone 100 mg daily.

OCD did not show any improvement at all while depression improved significantly: Yale-Brown Obsessive Compulsive Scale (Y-BOCS) was 40 both at beginning and at the end of the treatment; on the other hand Hamilton Depression Rating Scale-17 Items (HDRS-17) decreased from 23 to 11.

### CASE 2

She was a 48 years-old female having OCD (predominantly obsessions of being harmed) for 20 years plus depression. She was unresponsive to many trials of medication and seven sessions of electroconvulsive therapy (ECT) 18 years before.

She was applied 30 sessions of rTMS (six sessions a week, over the left DLPFC, 1 Hz, 110% of MT, 5 seconds, 100 trains, 500 pulses) in addition to paroxetine 60 mg daily. Y-BOCS decreased from 20 to 7, HDRS-17 from 25 to 10.

### CASE 3

She was a 59 years-old female having OCD (predominantly obsessions of contamination) for nearly 30 years. She was unresponsive to three trials of selective serotonin reuptake inhibitors (SSRIs), two of which she had used for at least one year and in high doses. Besides, she had two generalized tonic-clonic seizures during SSRIs use.

She was applied 30 sessions of rTMS (six sessions a week, over the left DLPFC, 1 Hz, 110% of MT, 5 seconds, 100 trains, 500 pulses). She was prescribed valproic acid, not SSRI or clomipramine because of seizure history. Y-BOCS decreased from 40 to 25, HDRS-17 from 6 to 4.

### CASE 4

He was 26 years-old male with OCD (obsessions of blasphemy and contamination) and depression. He was partially responsive to medications.

He was applied 30 sessions of rTMS (six sessions a week, over the left DLPFC, 1 Hz,

110% of MT, 5 seconds, 100 trains, 500 pulses). He was prescribed fluoxetine 80 mg, trazodone 100 mg, ziprasidone 80 mg and clonazepam 1 mg. Y-BOCS decreased from 40 to 13, HDRS-17 from 18 to 8.

### CASE 5

He was 26 year-old male with OCD (obsessions of contamination). He was unresponsive to six-month use of fluoxetine 60 mg daily.

He was applied 30 sessions of rTMS (six sessions a week, over the left DLPFC, 1 Hz,

110% of MT, 5 seconds, 100 trains, 500 pulses). He was prescribed citalopram 60 mg daily. Y-BOCS decreased from 29 to 10, HDRS-17 from 8 to 2.

## CASE 6

He was a 45 years-old male, had severe OCD. He had no other medical problem, no personality disorder, and no psychosocial stressor and had never used substances or alcohol. There was no significant feature in his family history.

He had OCD for 25 years. He had had diagnoses such as schizo-obsessive disorder or psychotic disorder not otherwise specified because of severity of the clinical table. He has been using antidepressants and antipsychotics of high doses for 25 years. He was hospitalized for ten times because of intractable and devastating anxiety and depression. He had not applied ECT.

He had graduated the law faculty. He had obsessions of having AIDS at first, when he was a student of law. When he was a young judge; a different kind of obsessions occurred: 'If someone offers bribe to me, and if I am slandered even though I refuse the bribe, I may be put in prison.' This obsession got so severe that, he was hospitalized the first time in his life. He resigned his job as a judge. He was not able to work in the area of law. He began to work as a government employee in a much lower level.

The major obsession for nearly 20 years has been the fear of making a mistake concerning official documents and being put in prison His functioning was always very low.

Y-BOCS was 40 although he had been using clomipramine 300 mg/day, escitalopram 40 mg/day, clozapine 600 mg/day, valproic acid 1000 mg/day, clonazepam 2 mg/day. He began to apply rTMS in 2008, without cessation of drugs.

rTMS was applied over the left DLPFC. The intensity was 110% of the motor threshold, the frequency 1 Hz, 100 trains per session, 500 pulses per each train; the duration of each train was 5 seconds.

Y-BOCS was 25 after 30 sessions (six sessions a week) of rTMS. Additional cures each of which was approximately 30 sessions were applied at intervals of 4-6 months. Two years after the first session, 112 sessions had been applied and Y-BOCS was 10. In December 2011, Y-BOCS was 6 after 152 sessions had been applied.

## DISCUSSION

In this case series, five out of six patients benefited rTMS significantly. Although all patients also took medications, the improvement can be attributed to rTMS since response to medications in OCD takes longer time (five patients were applied 30 sessions of rTMS, six sessions in a week, therefore the total duration of the therapy was five weeks, except the sixth case).

Results of studies investigating the effectiveness of rTMS on OCD are equivocal. Sarkhel et al. designed a sham-controlled study and did not find any significant effect of 10 sessions of high-frequency (rapid) rTMS on the right DLPFC in the treatment of OCD in 42 patients.<sup>1</sup> Kang et al. found no therapeutic effect in a 10-day, open-label, sham-controlled study on 20 treatment-resistant patients with OCD employing low frequency (1 Hz) rTMS over the right DLPFC and sequentially the supplementary motor area (SMA).<sup>2</sup> Prasko et al. showed that 10 sessions of low frequency (1 Hz) rTMS over the right DLPFC in double-blind

design did not differ from sham rTMS in a sample of 33 patients.<sup>3</sup> Alonso et al. found that 18 sessions of low frequency rTMS over the right DLPFC in a sham-controlled double-blind study failed to produce significant improvement of OCD.<sup>4</sup>

Sachdev et al. found that two weeks of high frequency rTMS over the left DLPFC was ineffective for treatment-resistant OCD, however over 20 sessions, there was a significant reduction in total Y-BOCS scores.<sup>5</sup> Ruffini et al. found that 15 sessions of low frequency rTMS over the left orbitofrontal cortex produced significant but time-limited improvement in 23 drug-resistant OCD patients.<sup>6</sup> Reduction of Y-BOCS scores were significant comparing active versus sham treatment for 10 weeks after the end of rTMS, with loss of significance after 12 weeks.

Mantovani et al. conducted a sham-controlled, double-blind study and found that bilateral application of low frequency rTMS for four weeks over the SMA produced significant im-

provement in a study on 21 medication-resistant patients.<sup>7</sup> However, there were no significant differences between the active and sham group. Mantovani et al. showed in an open-label study that 10 sessions of low frequency rTMS over the SMA resulted in a significant clinical improvement and a normalization of the right hemisphere hyperexcitability and improvement in symptoms was stable at three months follow-up.<sup>8</sup>

Sachdev et al. applied 10 sessions of rTMS randomly over the right or left DLPFC in an open fashion in 12 patients.<sup>9</sup> The study had a four weeks follow-up phase. They found that about one quarter of patients with resistant OCD appear to respond to rTMS to either prefrontal lobe, although the possibility of this being a placebo response could not be ruled out because of the absence of a sham treatment group.

Greenberg et al. observed that compulsive urges decreased significantly for 8 hours after a single session of high frequency (20 Hz) rTMS over right DLPFC in an open fashion.<sup>10</sup> However, there were nonsignificant increases in compulsive urges after repetitive transcranial magnetic stimulation of the midoccipital site. A shorter-lasting (30 minutes), modest, and nonsignificant reduction in compulsive urges occurred after left DLPFC.

Mansur et al. conducted a double-blind randomized trial involving 30 treatment-resistant OCD outpatients, allocated to have either sham or active high-frequency rTMS (over the rDLPFC) added to their treatment regimens for 6 weeks, with 6 weeks of follow-up.<sup>11</sup> Active rTMS consisted of 30 applications (10 Hz at 110% of motor threshold; 1 session/d; 40 trains/session; 5 s/train; 25-s intertrain interval). In treatment-resistant OCD, active rTMS over the rDLPFC does not appear to be superior to sham rTMS in relieving obsessive-compulsive symptoms, reducing clinical severity, or improving treatment response, although there is evidence of a placebo effect.

Kumar et al. administered 10 sessions of rTMS on 12 persons with medication-resistant OCD as an add-on treatment.<sup>12</sup> Stimulation was applied at 1 Hz for 10 seconds followed by 15 seconds pause and 100 trains of stimulus over the SMA per session. The subjects showed significant improvement.

Although lack of statistical analysis and control group makes any conclusion difficult, the

fact that five of six OCD patients improved significantly after rTMS may be promising. It seems that our results are more encouraging in comparison to other studies.

The reasons for that may be:

1) longer duration of treatment (30 sessions in five patients, 152 sessions in the sixth case) in comparison to other studies (10 sessions in five studies, 14 sessions in one study, 15 sessions in one study, 18 sessions in one study, 20 sessions in one study),

2) employment of low-frequency (1 Hz) rTMS. In some studies in the literature high frequency (10 Hz) were applied. rTMS of low frequency may be effective in anxiety disorders, in contrary to depression.

3) application over the left DLPC. The site of application was the right DLPC in four studies, SMA in two studies, orbitofrontal cortex in one study. Left prefrontal application may be more effective than other applications.

In a recent review, it was reported that in open-label studies, high-frequency rTMS of the right and/or left DLPFC appears to be effective in reducing obsessive-compulsive symptoms.<sup>13</sup> However, this could not be replicated in double-blind, sham-controlled studies.

In contrary, a very recent review states that although available data about the use of rTMS in OCD treatment are quite heterogeneous in terms of sample size, study design, stimulus parameters used and stimulation areas targeted, promising findings regarding rTMS efficacy appeared for two structures based on recent controlled studies: the supplementary motor area and the orbitofrontal cortex.<sup>14</sup>

Finally, it worths mentioning another study: Wu et al. recently designed a novel stimulation paradigm: theta-burst stimulation, a low-intensity burst of rTMS at 50 Hz as a safer, more consistent, and longer lasting rTMS.<sup>15</sup> The results of the first case study with this paradigm in OCD and depression are promising and warrant further exploration.

In conclusion, because of the lack of studies with comparable stimulation or treatment parameters and with reliable designs, it is difficult to draw clear conclusions about the effectiveness of rTMS in OCD. To generalize the results of these studies, further research is necessary. Careful consideration of target regions and stimulation parameters, longer follow-up, and

the use of a double-blind, sham-controlled design may allow us to draw founded conclusions in the future.

The following shortcomings have prevented the drawing of definitive conclusions about the clinical efficacy of rTMS:

- the small sample size in the clinical studies,
- a considerable variability in the stimulation site,
- variability of parameters used:
  - \* low or high frequency?
  - \* number of sessions?

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