Trigeminal nerve stimulation for the treatment of major depressive disorder and obsessive-compulsive disorder: a case study

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Abstract

Neuromodulation techniques have been proposed as add-on strategies for modulating brain areas involved in obsessive-compulsive disorder symptoms. Trigeminal nerve stimulation is a novel neuromodulation technique, which, to date, has not yet been explored for obsessive-compulsive disorder treatment. In this report, we describe a 52-year-old female patient suffering from major depressive disorder and obsessive-compulsive disorder for 18 and 32 years, respectively and successfully undergoing a trigeminal nerve stimulation intervention protocol (10 consecutive daily trigeminal nerve stimulation sessions), with amelioration of symptoms. Cognitive function was not obviously altered as assessed by the Montreal Cognitive Assessment. Major depressive disorder and obsessive-compulsive disorder symptoms assessed using the Yale-Brown Obsessive-Compulsive Scale and the 17-item Hamilton Depression Rating Scale substantially improved after the 10-day treatment course and remained stable after 1-month follow-up (30 days after final trigeminal nerve stimulation). The patient reported significant global clinical gains and mild diurnal sleepiness without severe adverse effects. Trigeminal nerve stimulation has been studied for the treatment of various neuropsychiatric disorders that share common functional alterations at the frontal cortex and subcortical areas, usually altered in obsessive-compulsive disorder. We present the first case report on trigeminal nerve stimulation for co-morbid obsessive-compulsive disorder and major depressive disorder. These encouraging results should be seen as hypothesis-driving for further controlled randomized trials exploring the impact of trigeminal nerve stimulation in the treatment of obsessive-compulsive disorder.

Key words: obsessive-compulsive disorder; non-pharmacological therapies; brain stimulation; trigeminal nerve stimulation; trigeminal nerve; neuromodulation

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INTRODUCTION

Excessive activities in orbitofrontal-striatal regions, medial and lateral frontal areas, such as the supplementary motor area, anterior cingulate, dorsolateral prefrontal cortex and parietal regions (Trevizol et al., 2016b) in the brain are associated with the inability of obsessive-compulsive disorder (OCD) patients to suppress intrusive thoughts, impulses, or images and repetitive motor responses. Neuromodulation techniques have been proposed as add-on strategies for modulating brain areas involved in OCD symptoms (Trevizol et al., 2016e). Trigeminal nerve stimulation (TNS) is a novel neuromodulation technique based on the hypothesis that through the stimulation of a cranial nerve, activities in cortical and subcortical cerebral areas could be modulated. To date, effects of TNS on OCD have not yet been reported.

CASE REPORT

In this report, we describe a 52-year-old female patient...
suffering from major depressive disorder (MDD) and OCD for 18 and 32 years, respectively, who met the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) for MDD and OCD, and successfully underwent a TNS intervention protocol, with amelioration of symptoms. The patient experienced intrusive thoughts that lead to time-consuming rituals for more than 3 hours a day, with significant distress and occupational impairment that led her to quit her job. The patient presented fair insight of her condition, which did not diminish the involvement in checking rituals. She did not present a tic disorder associated. She was also diagnosed with severe depressive symptoms with anxious distress, without psychotic features. Prior to the TNS stimulation protocol, the patient received pharmacological therapy with sertraline 300 mg per day, risperidone 6 mg per day and mirtazapine 60 mg per day for 4 months, with poor response for OCD and MDD. Dose escalation had been prescribed based on tolerability. The patient had previously taken amitriptyline and clomipramine, which were discontinued due to unbearable side effects and poor clinical response. Her medical presentation was unremarkable. Considering the severity of her symptoms and lack of clinical improvement with pharmacotherapy, experimental TNS was proposed and written informed consent was provided with the approval of an Institutional Review Board.

Ten consecutive daily TNS sessions were performed. Electric stimulation was performed at 120 Hz with pulse wave duration of 250 µs, continuously, for 30 minutes per day. Square auto-adhesive rubber electrodes of 25 cm² were placed over supraorbital trigeminal branches (V1) bilaterally according to our previous protocol (Trevizol et al., 2016a). To assess OCD and MDD symptoms, we used the Yale-Brown Obsessive-Compulsive Scale and the 17-item Hamilton Depression Rating Scale. We also assessed cognitive functions with the Montreal Cognitive Assessment (MoCA). Cognitive function was not obviously altered as assessed by MoCA (24 at baseline and 29 at final outcome). MDD and OCD symptoms substantially improved after the 10-day treatment course and remained stable after 1-month follow-up (30 days after final TNS) (Figure 1). The patient reported significant global clinical gains and mild diurnal sleepiness without severe adverse effects.

**Discussion**

TNS is based on the rationale that through the stimulation of the supraorbital branch of the trigeminal nerve of brain stem centers would lead to modulation of activity in central brain structures, such as the amygdala and the hippocampus, with further propagation to the prefrontal cortex and its correlated areas, such as the supplementary motor area, anterior cingulate, dorsolateral prefrontal cortex and parietal regions. Transcranial magnetic stimulation has been previously studied in OCD to alter the cortical activity that could be involved with the symptomatology (Trevizol et al., 2016e). Trevizol et al. (2016e) reported in a thrilling robust result on transcranial magnetic stimulation for OCD via systematic review and meta-analysis. TNS was recently studied for the treatment in various neuropsychiatric disorders with interesting results for MDD (Trevizol et al., 2015b, 2016f), panic disorder (Trevizol et al., 2016d), posttraumatic stress disorder (Trevizol et al., 2015d, 2016c), generalized anxiety disorder (Trevizol et al., 2015c) and irritable bowel syndrome (Trevizol et al., 2015a). These disorders and OCD share common frontal cortex and subcortical areas alterations and are commonly co-morbid.

We present the first case report on TNS for co-morbid OCD and MDD. Limitations of this study, however, should be addressed. The principal limitation is that our findings are based on a case study, and thus have limited generalizability. Nonetheless, these encouraging results should be seen as hypothesis-driving for further controlled randomized trials exploring the impact of TNS in the treatment of OCD.

**Declaration of patient consent**

The authors certify that they will obtain all appropriate patient consent forms. In the form the patients will give their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Conflicts of interest**

None declared.

**Author contributions**

APT was responsible for patient clinical evaluation and manuscript...
elaboration. IAS was responsible for the clinical evaluation and for stimulation protocol execution. QC was responsible for designing the stimulation protocol and manuscript review. All authors approved the final version of this paper for publication.

Plagiarism check
This paper was screened twice using CrossCheck to verify originality before publication.

Peer review
This paper was double-blinded and stringently reviewed by international expert reviewers.

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