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Trigeminal Nerve Stimulation (TNS) for Generalized Anxiety Disorder: A Case Study

Dear Editor,

Generalized anxiety disorder (GAD) [1] presents with an overall prevalence of 4–7%. Although available treatment is effective in many patients, treatment-resistance and low adherence due to adverse effects are some issues that compromise optimal treatment. In fact about 25% of patients reportedly fail to respond to treatment [2,3]. Brain stimulation techniques have shown promising results for anxiety symptoms [4,5]. Following previous results of different neuromodulation strategies, Trigeminal Nerve Stimulation (TNS) may also be able to exert anxiolytic effects in the clinical scenario. TNS is a non-invasive strategy based on the application of an low-energy electric signal to stimulate branches of the trigeminal nerve with further propagation of the stimuli toward brain areas related to mood and anxiety symptoms [6]. TNS has been reported to reduce anxiety symptoms in patients with a primary diagnosis of major depression [7] but has not been previously examined as a treatment for primary GAD.

Here, we describe the management of a 39-year-old female patient diagnosed with GAD accordingly to DSM-V criteria. The patient did not present with any psychiatric comorbidity at clinical evaluation. Moreover, no other psychiatric history was reported rather than the development of anxiety symptoms over the last three years. During this period the patient failed to respond to different adequate pharmacological protocols (such as venlafaxine, sertraline, fluoxetine and escitalopram). Considering the severity of her symptoms and lack of clinical response to pharmacotherapy, a experimental TNS protocol was started after written informed consent was provided utilizing IRB-approved materials and procedures. The patient was not under any pharmacological approach at the time she underwent the experimental protocol.

Ten consecutive daily TNS sessions (except for weekends) were performed. Electric stimulation was performed at 120 Hz with a pulse wave duration of 250 μs for 30 min per day. The 25 cm² conductive rubber electrodes were wrapped in cotton material, which was moistened with saline so as to reduce impedance. For assessment of anxiety symptoms we used the Generalized Anxiety Disorder 7-item scale (GAD-7) and the Hamilton Anxiety Rating Scale (HARS). We also assessed cognitive functions with the Montreal Cognitive Assessment (MoCA). At the end of the experimental protocol, Ms. E presented with symptomatic remission of her symptoms. Cognitive function exhibited a minor improvement (from 25 at baseline to 27 at final outcome) as assessed by MoCA. Anxiety symptoms substantially improved during the 10-day treatment course (reduction of 93.7% and 88.3% according to GAD-7 and HARS, respectively) and remained stable during one-month follow-up (Fig. 1).

Zwanzger et al. and Pallanti et al. reviewed the use of transcranial magnetic stimulation (TMS) to treat anxiety symptoms, with interesting positive results. Improvements were observed on anxiety symptoms in panic disorder with depression and treatment-resistant depression [4,5]. Trigeminal nerve stimulation may modulate brain activity through bottom-up mechanisms by stimulating a cranial nerve whose nuclei lie in the brain stem, and which, in turn, make extensive connections to the limbic cortex and monoaminergic nuclei. There are a growing number of publications on the use of TNS for psychiatric disorders [6–8].

![Figure 1](Image)

**Figure 1.** Clinical assessment at baseline, 10 days and 40 days follow up. GAD-7: Generalized Anxiety Disorder clinical scale; HARS Hamilton Anxiety Rating Scale. Treatment was administered during the period from Day 0 to Day 10; Day 45 measurements show continued remission one month after the last treatment administration.

References:
[1] Connor KP. Neurocognitive changes following tic disorder: A Case Study
We present this first report of the use of TNS for GAD. Some study limitations, however, should be acknowledged. Our findings are based on a single case study, and thus have limited generalizability. As well, there was no control condition. Nonetheless, these encouraging results should be seen as hypothesis-driving for further controlled, randomized trials exploring the impact of TNS in the treatment of anxiety disorders.

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