

Transcutaneous Vagus and Trigeminal Nerve Stimulation: A New Perspective in the Treatment of Psychiatric Disorders

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Editorial

With the development of new tools to assess brain function and cerebrovascular health such as functional magnetic resonance imaging, new understanding of disrupted mechanisms underlying psychiatric conditions have been proposed. Findings regarding neuroplasticity-related pathways for the therapy of mental disorders such as depression and schizophrenia supports the hypothesis that abnormalities associated with psychiatric conditions go beyond neurochemical imbalances [1,2]. Specific impairments in brain circuitry are under growing evidence in psychiatric research. For instance, patients diagnosed with major depressive disorder (MDD) present with altered functioning of dorsolateral prefrontal cortex (DLPFC). In fact, in MDD there has been exhibit a reduction in neuronal activity in the dorsolateral pre-frontal cortex (DLPFC) [3,4]. For other diseases such as schizophrenia, similar impairments have been systematically reported [5]. The advances in the understanding of brain circuitry underlying mental disorders contributed to the development of new therapeutical strategies as Non-invasive brain stimulation techniques (NIBS). NIBS are techniques that might aid to overcome some of the current challenges related to pharmacotherapy. Ideally, NIBS should be not only as effective as pharmacotherapy but also present a low rate of adverse effects, thereby increasing treatment adherence. Neuromodulation techniques include novel techniques, such as trigeminal nerve stimulation (TNS) and transcutaneous vagus nerve stimulation (tVNS).

In fact, these cutting-edge neuromodulation interventions are driven by data from both neuro-functioning and experimental research, which help targeting specific brain areas related to psychiatric disorders. Different brain sites can be modulated throughout the use of electrical currents, what could restaure balance to impaired circuits leading to clinical amelioration of symptoms [6,7]. The rationale for using trigeminal or vagus nerves for delivering electric current toward specific brain areas is the anatomical correlation these nerves maintain with sites related to psychiatric symptoms such as the amygdala, insula, precentral gyrus, hippocampus, thalamus and prefrontal cortex (structures widely related to cognitive functioning and mood regulation). Therefore, both TNS and tVNS modulate brain structures throughout the “bottom-up” hypothesis, in which stimulation of these nerves would propagate to its cortical and subcortical projections [7]. Following this hypothesis, Cook et al. have initially proposed transcutaneous stimulation of the supraorbital branch of the trigeminal nerve (TNS) with interesting results for major depressive disorder [8,9]. Following the leading results of Cook et al., Shiozawa et al. proposed an innovative brief 10-day TNS protocol [10] that has been tested for depressive symptoms in a randomized sham-controlled clinical trial with positive results. The authors found significant interaction between the mean percentage change in depressive symptoms in the two groups over time with mean reduction of 6.32 points in the Hamilton Depression Rating Scale (HDRS17); $p=0.002$ [11]. The same protocol was further used for anxiety disorders with promising results for symptoms ameliorations in post-traumatic stress disorder [12] and generalized anxiety disorder [13]. Regarding tVNS, its use in clinical research is still scant. However, the rationale for stimulating a superficial branch of the X cranial nerve is

similar to the TNS given common pathways shared by both trigeminal and vagus nerves. Regarding depressive disorder, Hein and colleagues found transcutaneous vagus nerve stimulation to be an effective treatment. The authors evaluated a total of 37 patients suffering from major depression over a randomized sham controlled add-on study. Patients were stimulated five times a week on a daily basis over 2 weeks. Active treatment group presented markedly clinical amelioration of symptoms in comparison to sham stimulation [14]. Interestingly, once we observe potential clinical benefits of TNS and tVNS, it is reasonable to infer that stimulating other specific areas innervated by these nerves would also relate to hypothetical neuromodulatory effects. Considering those hypothetical areas of interest, different cranial sites would be under focus such as the skin over the mastoid process, a region innervated by the auricular branch of the vagus also called Alderman's nerve as proposed by Trevizol and colleagues [15].

Finally, the use of both TNS and tVNS protocols in clinical research are a safe strategy. In fact, no severe adverse effect has been reported hitherto. Regarding skin injury, the techniques have been innocuous in contrast to similar non-invasive neuromodulation strategies as tDCS (transcranial direct current stimulation), which markedly present safety concerns regarding skin integrity in different reports [16]. The results on the use of TNS and tVNS protocols for treating psychiatric disorders are pointing towards a relevant impact on the treatment of these diseases; however, there is a continuous need for translational research as to guarantee a more robust use of these promising results in daily clinical practice.

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