

# Case Report is Transcutaneous Vagus Nerve Stimulation Helpful in the Treatment of Treatment-Resistant Depression? A Case Presentation and Discussion of Clinical Efficacy



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## Abstract

Depression is a highly prevalent disorder, which is characterized by over-reaction, rumination, and cognitive decline. Less than 40% of depressed patients in clinical practice can be relieved after the first treatment with antidepressants [1], and about 35% of patients have a lack of response to treatment and become treatment-resistant depression (TRD) [2]. Considerable effort has been devoted to trying to find effective treatments for TRD. Studies to date have found that long-term vagus nerve stimulation (VNS) can effectively reduce the degree of depression in some patients [3]. In 2005, the United States Food and Drug Administration (FDA) approved VNS as an adjunctive treatment for patients with TRD. However, invasive VNS not only has high surgical costs but also has the risk of postoperative infection. The transcutaneous vagus nerve stimulation (tVNS) in recent years, although still in its early stages, has shown potential for mild and moderate major depressive disorder (MDD) patients, and its efficacies are similar to those of vagus nerve stimulation (VNS) [4,5]. From this point we used tVNS to preliminarily explore its therapeutic effect on TRD and be eager to improve the new treatments for TRD. This case is the first exploration of tVNS on the treatment of TRD.

**Abbreviations:** TRD: Treatment-Resistant Depression; VNS: Vagus Nerve Stimulation; FDA: Food and Drug Administration; TVNS: Transcutaneous Vagus Nerve Stimulation; MDD: Major Depressive Disorder; SDS: Self-Rating Depression Scale; HT: Hydroxy Tryptamine; NE: Norepinephrine; DA: do-pamine; SSRI: Selective 5-Ht Reuptake Inhibitors; ZDF: Zucker Diabetic Fatty; DN: Default Network; FC: Functional Connectivity

## Case Report

We report here a case of a 55-year-old male patient with a history of depression for almost 20 years. In November 2001, he was diagnosed with depression at Xuanwu Hospital, Capital Medical University in Beijing, China. The patient was prescribed to receive Paroxetine Hydrochloride 20 mg/day until 2006. The drug has improved depressive symptoms, but the side effects were sexual dysfunction. Physicians recommend dressing changes. Between 2007 and 2012, the patient was prescribed to receive antidepressant Cipramil 40 mg/day. However, the side effect of this drug is that it causes significant sweating. As a result, doctors recommend changing medicines again. Since 2013, he was received sustained oral antidepressant Lexapro 20 mg/day until April 2018 which has the same

side effect with Ciprom. After all, none of these drugs can effectively relieve his depressive symptoms without side effects. The patient presented himself in April 2th, 2018 with a severe depressive episode with depressed mood, loss of activity, feelings of hopelessness, sleep disturbances, and loss of appetite and energy. The 17-item Hamilton Depression Rating Scale (17-HAMD) scores greater than 17 points and met Diagnostic and Statistical Manual of Mental Disorders, 4th Edition criteria for major depressive disorder.

After a professional physician assessment, it meets TRD's diagnostic criteria. The patient began to use tVNS combined with medicine Sertraline (50mg/day, qd) to treat TRD in April 9th, 2018. Sertraline is taken before bedtime every day. The tVNS treatments

were self-administered by the patients at home after he received training from the hospitals. After stimulation points were disinfected according to standard practice, ear clips were attached to the auricular concha. Stimulation parameters included: (1) a 20 Hz continuous dilatational wave and (2) stimulation intensity increased gradually (starting from 0) to the highest point that the patients could tolerate (typically between 4 and 6 mA). Each treatment lasted for 30 min and was carried out twice a day (once in the morning after getting up in bed, once before going to bed) The primary outcome measurement was the 17-HAMD、14-item Hamilton Anxiety Scale (HAMA)、self-rating depression scale(SDS)、self-Rating Anxiety Scale (SAS) measured at weeks 0, 2, 4. The patients successfully completed 4 weeks of anti depression treatment. At the end of week 2, the antidepressive treatment decreased the severity of depressive symptoms (17-HAMD score: 18 (0 week) versus 7 (2weeks) / HAMA score: 20 versus 8/ SDS score:46 versus 42/ SAS score:55 versus 38). After 4 weeks, the relief of depressive symptoms with insomnia, dizziness in the morning are even more pronounced (17-HAMD score: 18 (0 week) versus 1 (4weeks) / HAMA score: 20 versus 1/ SDS score:46 versus 25/ SAS score:55 versus 20).

## Discussion

In conclusion, we believe that tVNS might be potentially useful as an anti depressive method and adjunctive treatment therapy in patients with TRD. So far, the research and development of new drugs for the treatment of TRD have achieved certain results. Triple reuptake inhibitors is a novel drug in monoamine antidepressants which block the reuptake of 5-hydroxytryptamine (5-HT), norepinephrine (NE), and do-pamine (DA) and can be used as a second-line treatment for depression patients who are not responsive to selective 5-HT reuptake inhibitors (SSRI) antidepressants. Because sertraline acts as an antidepressant similar to Lexapro and Cipramil, it may not work for this patient alone. Therefore, in this case, the role of tVNS is even more pronounced. But after all, it is a combination therapy that cannot deny the efficacy of Sertraline. Since 2005, almost 3000 clinical and preclinical papers dealing with VNS have been published, with many concerning its use in ep-

ilepsy or depression. Basic research studies in Zucker diabetic fatty rats (ZDF, fa/fa) with depression-like behaviors are suggesting that 30 min-tVNS procedures per day is antidepressive [6]. The study of Rong found the effectiveness of stimulating the superficial branches of the vagus nerve as a solo treatment for MDD [4]. Although there are few studies on the antidepressive mechanism of tVNS, preliminary studies have suggested that tVNS treatment can regulate the functional connectivity (FC) of the default network (DMN), amygdala and other regions. All these FC increases are also associated with 24-item Hamilton Depression Rating Scale reduction. In our clinical case, we found that the first intervention of tVNS played a pivotal role in the course of TRD patients. Based on our clinical observation, we propose that tVNS might be a useful option in therapeutic refractory situations or as maintenance treatment in TRD. Our observation of an decrease of depressive symptoms in this patient possibly linked to tVNS treatment might suggest tVNS also in off label use in patients suffering from other diseases, including insomnia, diabetes and epilepsy, which has been suggested at least by the other studies.

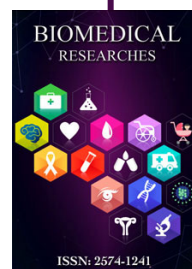
## References

- Holtzheimer, Paul E, Mayberg (2011) Stuck in a rut: rethinking depression and its treatment. *Trends Neurosci* 34(1): 1-9.
- Carreno FR, Frazer A (2017) Vagal Nerve Stimulation for Treatment-Resistant Depression. *Neurotherapeutics* 14(3): 716-727.
- Aaronson ST, Carpenter LL, Conway CR, Reimherr FW, Lisanby SH, et al. (2013) Vagus Nerve Stimulation Therapy Randomized to Different Amounts of Electrical Charge for Treatment-Resistant Depression: Acute and Chronic Effects. *B M J* 6(4): 631-640.
- Rong P, Liu J, Wang L, Liu R, Fang J, et al. (2016) Effect of transcutaneous auricular vagus nerve stimulation on major depressive disorder: A nonrandomized controlled pilot study. *J Affect Disord* 195: 172-179.
- Li S, Zhai X, Rong P, Michael F. McCabe, Jingjun Zhao, et al. (2014) Transcutaneous Auricular Vagus Nerve Stimulation Triggers Melatonin Secretion and Is Antidepressive in Zucker Diabetic Fatty Rats. *Plos One* 9(10): e111100.
- Fang J, Rong P, Hong Y, Fan Y3, Liu J, et al. (2016) Transcutaneous Vagus Nerve Stimulation Modulates Default Mode Network in Major Depressive Disorder. *Biol Psychiatry* 79(4): 266-273.



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