

Can't sleep? You might need some stimulation

Scientists discover the therapeutic potential of electrical vagus nerve stimulation in the treatment of primary insomnia

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The therapeutic effects of transcutaneous auricular vagus nerve stimulation (taVNS) have only recently been explored in the last few years. TaVNS involves the application of electrical stimulation to the external portion of the ear to activate an essential cranial nerve called the vagus nerve.¹ In a recent article published in Frontiers in Neuroscience, researchers from the China Academy of Chinese Medical Sciences revealed the immediate effects of taVNS on the brains of patients with primary insomnia (PI).² They found that patients with primary insomnia showed higher resting-state neural activity than healthy patients, particularly in areas in the cerebral cortex. Interestingly, the application of taVNS to PI patients caused a significant decrease in neuronal activity in these abnormally hyperactive areas. These results provide a promising non-invasive treatment for patients with primary insomnia.

Primary insomnia is becoming an increasingly common issue, with as high as 10% to 15% of the world adult population classifying for a PI diagnosis.³ PI is classified as sleep disturbances that are unrelated to other medical disorders, substance use, or prescription use and must persist for three nights per week for at least three months.³ While most patients are treated using pharmacologic drugs, including benzodiazepines, non-pharmacological methods are being explored as alternatives, such as cognitive-behavioral therapy and taVNS. The therapeutic effects of taVNS have been primarily studied in the context of treatment-resistant depression.⁷ Clinical studies have shown that taVNS can alleviate many adverse symptoms associated with depression, including anxiety, hopelessness, and sleep disturbance.^{4,6,8} If taVNS can reduce depressive symptoms, one of which includes insomnia, taVNS can be a viable method for treating PI. While the exact mechanism for PI is not entirely understood, many scientists believe that "hyperarousal" is to blame. This theory suggests that patients with insomnia express abnormally high amounts of neurological activity. TaVNS induces a regulatory effect on patients with hyperactive symptotic activity through stimulation of the vagus nerve.

The experiment

The study observed twenty-two participants with primary insomnia and twenty healthy patients without insomnia. Bilateral electrodes were placed on the auricular concha area for both ears.² The stimulus frequency was set at 20 Hz, and stimulus intensity varied from patient to patient (4 mA to 6 mA).² Stimulation was applied for 30 minutes.² Then, fMRI scans were taken of the PI patients before and directly after taVNS treatment.² The brains of healthy participants were also imaged once using fMRI.² The researchers performed two sets of analyses on the brain image: amplitude of low-frequency fluctuations (ALFF) and resting- state functional connectivity (RSFC) analysis. ² These tests aimed to identify any statistically significant differences between brain activity between healthy controls and PI patients.



A proposed schematic for the hyperarousal theory (created in bioRender). Bilateral electrodes are placed on the ear's Auricular Branch of the vagus nerve (ABVN). The signal travels to the peripheral jugular ganglion, and then to

the peripheral jugular ganglion, and then to the nucleus tractus solitarius (NTS). Projections are made to various medullary structures, including the dorsal vagal nucleus (DVN), nucleus ambiguus (NA), the rostral ventrolateral Medulla (RVLM), and the caudal ventrolateral medulla (CVLM). The DVN, NA, and RVLM can then send neuronal projections to the spinal cord and heart, causing a regulatory effect on sympathetic activity.¹ Vagal afferent projections are denoted by the red line, while vagal efferent projections are denoted by the green lines.

What they found

Significance was measured using a t-test, incorporating voxel quantification from the fMRI scans. Patients with PI had significantly increased ALFF in the right precuneus when compared to the control subjects.². Following taVNS treatment, ALFF was remarkably decreased in the right precuneus and raised in the left middle occipital gyrus.² These findings implicated the right precuneus and the right cerebral cortex as regions of interest (ROI). After taVNS, RSFC analysis showed significant decreases in connectivity between the right precuneus and the right middle frontal gyrus, and the right angular gyrus. These results indicate that taVNS may have an unarousing effect on the brain.

Future directions

The exact mechanism by which taVNS operates in patients with primary insomnia is unknown. Studies have uncovered a general mechanism for the pathway of taVNS and how signals project from the ear to the medulla. However, the number of brain areas and pathways activated are far too numerous to attribute one mechanism to insomnia with our current body of knowledge. Further studies will need to explore the functions of the right precuneus and cerebral cortex in sleeplessness and hyperarousal. Additionally, studies will need to identify what medullary structures project to neurons in these ROIs to understand better why taVNS decreases (or increases) frequency fluctuations in these areas. While vagal nerve afferents (to the brain) are known to project to the medulla, vagal nerve efferents (away from the brain) are known to project to the medulla, and other vital organs. Studying how these projections might regulate autonomic function may give insight into its therapeutic effects on primary insomnia.

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