Applied & Educational Psychology (2025)
Clausius Scientific Press, Canada

DOI: 10.23977/appep.2025.060405
ISSN 2523-5842 Vol. 6 Num. 4

The Regulation of Negative Emotion by Transcutaneous Auricular Vagus Nerve Stimulation and Its Mechanism

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Keywords: Transcutaneous auricular vagus nerve stimulation, negative emotions, emotional regulation, regulatory mechanisms, clinical applications

Abstract: Transcutaneous Vagus Nerve Stimulation (taVNS), as an emerging neuromodulation technique, has garnered significant attention in the field of emotional regulation in recent years. Negative emotions such as anxiety and depression have become increasingly prevalent in modern society, gradually emerging as major psychological issues affecting the quality of life in contemporary individuals. To explore effective emotional regulation methods, the medical and psychological communities have been continuously seeking novel therapeutic approaches. The rise of taVNS has brought new hope to this field. By stimulating the auricular vagus nerve, taVNS exerts positive effects on the regulation of negative emotions, with its mechanisms involving multiple neurobiological processes, including neurotransmitter release, neural circuit remodeling, and autonomic nervous system modulation. Although preliminary studies have revealed the potential mechanisms of taVNS, systematic research on its clinical applications remains insufficient. This article aims to review the regulatory effects of taVNS on negative emotions and its underlying mechanisms, explore its significance in the treatment of mood disorders, and discuss future research directions to provide theoretical support for clinical applications.

1. Preface

Transcutaneous Vagus Nerve Stimulation (taVNS) is a non-invasive neuromodulation technique that modulates brain function by stimulating the auricular vagus nerve. In recent years, taVNS has garnered significant attention in the fields of emotional regulation and mental health. Negative emotions typically refer to adverse responses to stress, loss, or threats, encompassing emotional states such as anxiety, depression, and anger. These emotions not only impact an individual's mental health but may also lead to physiological health issues, including cardiovascular diseases and compromised immune function [1]. Studies indicate that the persistent presence of negative emotions significantly affects quality of life and is closely associated with various psychological disorders[2]. Therefore, exploring effective methods for emotional regulation is of paramount importance.

Against this backdrop, taVNS emerges as a novel emotional regulation tool with diverse potential applications. Research demonstrates that taVNS can help individuals better manage negative emotions and enhance psychological resilience through mechanisms such as regulating neurotransmitter levels in the brain, improving autonomic nervous system function, and strengthening emotional recognition capabilities [3][4]. Literature reports indicate that taVNS has been proven effective in improving emotional states in patients with depression and showing certain therapeutic efficacy in alleviating symptoms related to anxiety disorders and insomnia [5][6]. As researchers conduct more in-depth and systematic investigations into taVNS, its application prospects in the field of emotional regulation will become even more promising.

2. Main Body

2.1. Basic Principles of taVNS

2.1.1. Anatomy and Function of the Vagus Nerve

The vagus nerve, the tenth cranial nerve and a key component of the parasympathetic nervous system, primarily transmits signals between the brain and various organs to maintain homeostasis and stability[7]. Its complex anatomy originates from the brainstem, extending through the neck, chest, and abdomen, and branches into multiple pathways that innervate distinct organs and tissues. Key functions include regulating heart rate, promoting digestion, and modulating airway smooth muscle tone[8]. Furthermore, the vagus nerve plays vital roles in emotional regulation, stress response, and immune system control, with studies indicating its close association with mood disorders such as depression and anxiety[1]. Stimulating the vagus nerve can influence the brain's emotional processing regions, thereby mitigating negative emotions and offering novel therapeutic approaches.

2.1.2. Development and Fundamental Principles of taVNS

Given the critical regulatory role of the vagus nerve in individual physical and mental health, invasive vagus nerve stimulation (iVNS) has been widely applied since the mid-1980s for the treatment and intervention of various conditions such as epilepsy, depression, and primary headache, achieving favorable outcomes [9]. However, iVNS requires invasive surgical implantation of therapeutic devices in patients, which not only incurs high surgical costs but also often entails adverse effects, thereby limiting its large-scale application to some extent [10]. In response, Ventureyra proposed taVNS in 2000, a novel, safe, and non-invasive brain neural stimulation modulation technique [11]. Its fundamental principle involves applying intermittent pulse electrical stimulation to branches of the vagus nerve in the external ear, allowing electrical signals to be transmitted non-invasively via the vagus nerve pathway to the brain, thereby inducing cortical activity and alterations in related neurobiomarkers, achieving neural modulation [12]. This technology eliminates the need for craniotomy to implant electrodes, significantly reducing surgical risks and complication rates, making it more acceptable to patients. Studies have demonstrated that, compared to iVNS, taVNS not only activates the same neural pathways [13] but also offers advantages such as simpler operation, greater cost-effectiveness, and enhanced safety and reliability[14].

The stimulation method of taVNS typically involves applying weak electrical currents through electrodes at specific anatomical locations in the ear (e.g., the external auditory canal portion of the auricle) to activate the vagus nerve [15], thereby influencing cerebral neural activity. The stimulation signal travels along the vagus nerve to regions such as the solitary tract nucleus in the brain, further projecting to brain structures associated with emotion and cognition, including the amygdala, hippocampus, and prefrontal cortex. This modulates neurotransmitter release and neural activity patterns in these regions, ultimately achieving emotional regulation. Studies have shown that taVNS can induce a series of physiological responses, including increased heart rate variability and changes in skin electrical responses, which are closely related to autonomic nervous system regulation [16]. Additionally, taVNS has been found to improve emotional states, enhance affective memory, and reduce symptoms of anxiety and depression, demonstrating its potential application value in emotional regulation [17]. Research on the mechanisms of taVNS can provide deeper insights into its role in negative emotion regulation and offer new strategies for the treatment of related disorders.

2.2. Regulatory Effect of taVNS on Negative Emotions

2.2.1. Regulatory Effects on Anxiety Symptoms

Transcranial electrical nerve stimulation (taVNS) has demonstrated positive effects in modulating anxiety symptoms. Studies indicate that taVNS can alleviate anxiety symptoms by stimulating the vagus nerve and regulating the balance of the autonomic nervous system. A randomized controlled trial found that taVNS significantly reduced participants 'anxiety scores and improved their mood [18]. Another study revealed that patients with anxiety disorders who received taVNS reported a significant decrease in self-reported anxiety levels, along with improvements in physiological indicators such as cortisol levels [17]. Additionally, research has shown that taVNS can significantly reduce the intrusion of negative thoughts in individuals with high anxiety, suggesting its potential clinical value in the intervention of anxiety symptoms [19]. Furthermore, taVNS promotes relaxation responses by enhancing heart rate variability, which is closely associated with the reduction of anxiety[20]. In clinical practice, taVNS is recognized as a safe and well-tolerated non-invasive treatment for anxiety disorders, particularly for patients who respond poorly to conventional pharmacotherapy [17]. Further research suggests that the effects of taVNS on anxiety symptoms may be related to its influence on the brain's emotional regulation networks. taVNS enhances activity in the prefrontal cortex, a brain region closely associated with emotional regulation, thereby potentially improving mood states and reducing anxiety manifestations [21]. Therefore, as an emerging therapeutic approach, taVNS offers a promising direction, especially in the management of anxiety disorders.

2.2.2. Modulatory Effects on Depressive Symptoms

Transcranial electrical nerve stimulation (taVNS) has demonstrated significant regulatory effects in the treatment of depression. Multiple studies have shown that taVNS can effectively reduce symptom scores in patients with depression and improve their overall psychological status. A study involving patients with major depressive disorder (MDD) found that after taVNS treatment, the patients' depressive scores were significantly reduced, and this improvement persisted for a period of time post-treatment[20].

Another study on adolescent patients with depression demonstrated that transcranial vagus nerve stimulation (taVNS) significantly enhances the ability to recognize negative emotions during emotional recognition tasks, indicating its positive impact on emotional processing[21]. Additionally, taVNS has been found to modulate depression-related biomarkers, such as reducing the levels of tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), which play crucial roles in the pathogenesis of depression[22]. The mechanism of taVNS may be related to its stimulation of the vagus nerve, which plays a key role in regulating emotions and stress responses. By enhancing vagal activity, taVNS can promote the release of neurotransmitters associated with emotional regulation in the brain, such as norepinephrine and 5-hydroxytryptamine (5-HT), thereby alleviating depressive symptoms[5]. taVNS is also believed to exert antidepressant effects by enhancing the activity of the dopaminergic system, as supported by animal studies, which show that taVNS can reduce depression-like behaviors and that this effect is associated with the activation of dopaminergic neurons[23]. Furthermore, taVNS may help patients better cope with negative emotions and stress by influencing the brain's self-regulatory capacity[24]. In conclusion, taVNS, as a non-invasive therapeutic approach, demonstrates multifaceted therapeutic potential, offering novel perspectives and possibilities for the management of depression.

2.2.3. Regulatory effects on other negative emotions

In addition to anxiety and depressive emotions, taVNS has demonstrated positive effects in regulating other negative emotions. Studies indicate that taVNS can effectively alleviate multiple symptoms in patients with post-traumatic stress disorder (PTSD), particularly in improving emotional regulation and reducing stress responses. A study involving responders to the 9/11 attacks found that taVNS could reduce hyperarousal associated with PTSD and improve patients' mood and quality of life[25]. Furthermore, taVNS alleviates emotional distress and anxiety levels in PTSD patients by modulating neural networks in the brain related to emotion and memory[26]. Another study showed that taVNS was applied to treat negative emotions associated with eating disorders, finding that it helped patients reduce emotional fluctuations and thereby decrease the occurrence of eating disorder behaviors[27]. Simultaneously, taVNS was also used to treat patients with borderline personality disorder, with results indicating a significant reduction in emotional vulnerability and improvement in emotional regulation[1]. In improving negative emotions in patients with insomnia, taVNS also exhibited positive effects, primarily by enhancing sleep quality, which indirectly alleviated anxiety and depressive symptoms[17]. These studies suggest that taVNS may influence the regulation of various negative emotions by modulating the autonomic nervous system and brain neural networks, providing new directions for future clinical applications.

2.3. Regulatory Mechanism of taVNS

2.3.1. Changes in Neurotransmitters

taVNS modulates negative emotions by influencing neurotransmitter release. Studies have demonstrated that taVNS significantly increases the levels of norepinephrine (NE), dopamine (DA), and serotonin (5-HT), which are involved in various physiological processes such as mood regulation, motivation, and behavioral control. Specifically, taVNS improves mood states by enhancing the release of 5-HT and DA. For instance, taVNS can stimulate the vagus nerve to activate the hypothalamic-pituitary-adrenal axis, thereby promoting the synthesis and release of 5-HT, which is of significant importance in alleviating anxiety and depressive symptoms[5]. Additionally, taVNS may improve attention and executive function by modulating the dopamine pathway, a finding that has been validated in patients with attention deficit hyperactivity disorder (ADHD) [28]. taVNS can also enhance mood memory performance by stimulating the vagus nerve to promote the release of norepinephrine in the brain[5]. Furthermore, studies suggest that taVNS may influence the cognitive and regulatory mechanisms of emotions by modulating other neurotransmitters such as gamma-aminobutyric acid (GABA) and glutamate[29]. Furthermore, taVNS has been found to reduce levels of inflammatory markers such as TNF-α and IL-6, which are closely associated with the onset of negative emotions like depression and anxiety[20]. Through these mechanisms, taVNS not only improves negative emotions but may also play a significant role in broader mental health domains.

2.3.2. Activation of the Endogenous Opioid System

The vagus nerve is not only involved in neurotransmitter regulation but also closely associated with the endogenous opioid system. Endogenous opioid peptides such as enkephalins and endorphins play crucial roles in regulating mood and pain perception. Studies have found that transcranial vagus nerve stimulation (taVNS) can enhance analgesic effects and improve mood states by activating the vagus nerve, thereby increasing the activity of the endogenous opioid system[21]. Specifically, taVNS may stimulate the vagus nerve to increase the release of opioid peptides, which subsequently influences brain regions related to mood and pain perception. This mechanism not only helps understand the role of taVNS in mood regulation but may also provide new intervention strategies for treating chronic pain and mood disorders[17]. Therefore, the interaction between the vagus nerve and the endogenous opioid system provides an important biological basis for the clinical application of taVNS.

2.3.3. Interaction between the cerebral cortex and limbic system and the influence of brain functional networks

Transcranial electrical nerve stimulation (taVNS) is believed to influence emotional states by modulating interactions between the cerebral cortex and the limbic system. The limbic system, particularly the amygdala and anterior cingulate cortex, is involved in the generation and regulation of emotions, while the cerebral cortex handles higher-order cognitive functions. Studies indicate that taVNS can enhance limbic system activity, thereby affecting the perception and expression of emotions. For instance, taVNS stimulation may improve the performance of emotional memory, especially in processing negative emotions, likely through enhanced amygdala responses[5]. Additionally, taVNS may promote cognitive regulation of emotions by influencing the function of the prefrontal cortex, thereby improving emotional states. Specifically, increased activity in the prefrontal cortex is associated with enhanced emotional regulation capacity, suggesting that taVNS may strengthen emotional regulation by facilitating effective communication between the cerebral cortex and the limbic system[21]. Furthermore, taVNS has been found to alter functional connectivity patterns in the brain, promoting integration within the emotional regulation network and further enhancing cognitive and reactive abilities related to emotions[24]. For example, taVNS can strengthen connections between the prefrontal cortex and other emotion-related regions, which is crucial for emotional regulation and inhibiting impulsive responses[2]. In one study, taVNS was demonstrated to improve performance in emotional inhibition tasks, indicating its potential to enhance emotional control by increasing functional connectivity in the prefrontal cortex[30]. Furthermore, transcranial audiovisual neurostimulation (taVNS) may modulate individual self-reflection and emotional experiences by influencing the interaction between the default mode network (DMN) and the task-positive network (TPN)[31]. These findings indicate that taVNS not only affects neurotransmitter release at the physiological level but also influences emotional and cognitive processes by reshaping functional brain networks.

2.3.4. Effects on the Autonomic Nervous System

The autonomic nervous system (ANS) consists of the sympathetic and parasympathetic nerves, which interact in numerous bodily functions. Transcranial autonomic nervous stimulation (taVNS) primarily enhances vagal activity by activating the parasympathetic nervous system, thereby promoting heart rate variability (HRV) and reducing sympathetic excitability. Studies demonstrate that taVNS significantly lowers heart rate and blood pressure while increasing HRV, both of which are markers of parasympathetic activity[32]. This parasympathetic enhancement helps alleviate negative emotions such as anxiety and depression, thereby improving overall emotional well-being. Such regulation of the ANS not only facilitates immediate emotional improvement but may also promote long-term emotional health, further supporting the efficacy of taVNS as a potential therapeutic approach for mood disorders [24].

2.3.5. Psychological Mechanism: Cognitive Process of Emotional Regulation

In terms of psychological mechanisms, transcranial audiovisual neurostimulation (taVNS) exerts its effects by influencing cognitive processes of emotional regulation. Studies have demonstrated that taVNS enhances individuals' emotional recognition and regulation abilities, particularly in managing negative emotions[21]. Specifically, taVNS facilitates cognitive reappraisal of emotions, enabling more effective management of negative affect. For instance, after receiving taVNS stimulation, individuals can more rapidly employ cognitive reappraisal strategies when facing negative emotions, thereby reducing their intensity and duration[33]. Additionally, taVNS may improve emotional regulation by enhancing self-awareness and attention, allowing individuals to better understand and cope with their emotional states[17]. These psychological mechanisms provide critical evidence for the clinical efficacy of taVNS, especially in the treatment of mood disorders.

3. Conclusion

After a comprehensive review of the application of transcranial electrical stimulation (taVNS) in the regulation of negative emotions, it is evident that this therapy demonstrates significant potential in the treatment of mood disorders. Current research indicates that taVNS not only effectively reduces the level of negative emotions but may also achieve its effects through mechanisms such as modulating the autonomic nervous system and influencing the brain's emotional processing regions. This discovery provides a new direction for non-pharmacological treatment of mood disorders, holding important clinical application value.

Although transcranial electrical nerve stimulation (taVNS) holds broad application prospects in emotional regulation, it currently faces several challenges. For instance, the mechanism of taVNS has not been fully elucidated, requiring further in-depth research on its neural pathways and molecular mechanisms in the brain. The optimization of stimulation parameters remains a critical issue, as no unified standards have been established, leading to significant variations in the parameters used across different studies, which compromises the comparability of research findings and the generalizability of clinical applications. Additionally, the safety and efficacy of long-term use necessitate further evaluation.

However, with the continuous advancement of research and technological progress, it is believed that these challenges will be gradually resolved. As an innovative non-invasive brain stimulation technique, taVNS (transcranial audiovisual neurostimulation) holds promise for exploring its synergistic effects with other therapeutic approaches (such as psychotherapy and pharmacotherapy), potentially leading to novel breakthroughs in the treatment and prevention of mood disorders and making significant contributions to improving human emotional health. In the future, we anticipate more high-quality research outcomes to propel the widespread application and ongoing development of taVNS in the field of mood regulation.

In conclusion, taVNS, as an emerging emotion regulation modality, demonstrates promising potential. However, more rigorous studies are required to confirm its broad applicability and safety in clinical practice, with the goal of providing more effective treatment options for patients with mood disorders.

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