The impact of auricular transcutaneous vagus nerve stimulation on cognitive control, aging and its potential adjunctive role in alcohol use disorder

Abstract

Cognitive neuroscience aims to understand the neural mechanisms underlying cognition. Until recent times, most evidence has been correlational. However, the development of non-invasive brain stimulation techniques opens up new research horizons for exploration. These techniques enable researchers to directly influence brain function, allowing for the validation of correlational theories and provide mechanistical evidence for causal relationships between brain and behavior. In this work, the focus is on auricular transcutaneous vagus nerve stimulation (atVNS), an electrical non-invasive brain stimulation technique that stimulates the auricular branch of the vagus nerve, which is directly connected to key nuclei in the brain stem such as the locus coeruleus and the nucleus solitary. These nuclei, through their projections to the cortex, play an important role in regulating cognitive functions. atVNS device usually contains small electrodes that are placed on the ear to stimulate the auricular branch and provides a safer and simpler alternative with minimal side effects compared to invasive procedures, making it more accessible for broader use in both research and clinical settings. The aim of the current work was to provide insights into the effects of atVNS on cognitive functions such as working memory gating mechanisms and conflict monitoring, including the neurophysiological mechanisms and the neuroanatomical regions involved. Moreover, to investigate how atVNS affects cognitive functions, particularly working memory functions, across different age groups, in the context of healthy aging. Secondly, its aim was to examine the potential impact of atVNS in clinical settings, particularly in substance disorders like alcohol use disorder. In terms of conflict monitoring, using a randomized cross-over design it was revealed that atVNS reduces task performance, particularly when applied after prior exposure to the task. This suggests that atVNS in combination with learning, may disrupt conflict resolution processes possibly by overstimulating noradrenergic levels, leading to a reduction in alpha band activity in the frontal cortex. In regards to working memory gating mechanisms, we show that atVNS enhanced working memory gate closing in young adults, supporting maintenance of information via the modulation of alpha band activity in fronto-polar, orbital and inferior parietal regions. This modulation seems to be mediated through the GABAergic system, due to the lack of effects on noradrenaline proxies (salivary alpha amylase and pupil dilation), thereby enabling atVNS to stabilize information and reduce distraction in the neural circuits. When investigating the effects of atVNS on WM gating in healthy older adults compared with younger ones, we also found that atVNS modulated WM maintenance, leading to reduced efficiency, while alpha and theta band activity was lower. Overall, the findings of the current work suggest that atVNS exerts a modulatory influence on cognitive functions via its impact on mainly alpha frequency band, consistently affecting neural processes in key regions associated with cognitive control and information processing, particularly in the prefrontal and parietal cortices. While atVNS appears to be a promising technique for modulating cognitive control processes, its effects seem to be impacted by the complex interaction of internal factors like brain states, neurotransmitter levels as well as external factors such as the stimulation parameters. Since atVNS modulates GABA and catecholamines-

neurotransmitters that play a key role in alcohol use disorder (AUD), we suggest atVNS as a potentially valuable add-on tool in treating AUD. Further, we indicate that atVNS might aid in improving cognitive control in AUD by promoting a better balance between top-down cognitive processes and habitual behaviors. As a result, atVNS presents a promising technique for future research and clinical practice.