

THE EFFECTS OF NONINVASIVE BRAIN STIMULATION ON HEART RATE AND HEART RATE VARIABILITY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Noninvasive brain stimulation (NIBS) techniques such as transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are widely used to test the involvement of specific cortical regions in cognitive, affective and (sensori-)motor processing. Despite NIBS being capable of testing causal directions, current models on cortical regulation of autonomic nervous system (ANS) functions such as heart rate (HR) and heart rate variability (HRV) rely primarily on brain imaging studies or animal models. In a systematic review and meta-analysis, we explored whether NIBS represents an effective method for modulating HR and HRV and to examine whether the ANS is modulated by cortical mechanisms that can be targeted by NIBS. In a series of four meta-analyses, 131 effect sizes from 35 sham-controlled trials were analyzed using meta-regression models. Robust variance estimation (RVE) was employed to account for dependencies between multiple outcomes from individual studies. NIBS was found to effectively modulate HR and HRV with small to medium effect sizes. Moderator analyses yielded significant differences in effects between stimulation of distinct cortical areas, particularly for HRV. In primarily vagally mediated HRV measures, stimulation of the dorsolateral prefrontal cortex (dlPFC) produced higher effect sizes than stimulation of temporal/insular areas. Although the motor cortex is rarely if ever mentioned in current models of cortical ANS regulation, stimulation of the motor cortex resulted in effect sizes comparable to stimulation of the dlPFC. Our results show that NIBS is a promising tool to investigate the cortical regulation of ANS, whereby future research is needed to identify further factors modulating the size of effects. To advance research in this area, we recommend the use of high methodological standards (e.g., use of neuronavigation), the use of newly developed TMS and tDCS devices that allow more focal or deeper stimulation, as well as the combined use of NIBS and neuroimaging.

Key words: *transcranial magnetic stimulation (TMS) - transcranial direct current stimulation (tDCS) - autonomic nervous system - heart rate variability - meta-analysis*

EFFECTS OF TRANSCUTANEOUS AURICULAR VAGUS NERVE STIMULATION (taVNS) ON AUTONOMIC AND COGNITIVE RIGIDITY DURING PERSEVERATIVE COGNITION

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Perseverative cognitions can provoke psychophysiological stress in the absence of an actual stressor and are considered important transdiagnostic vulnerability factors for several (mental) health issues. These stress-related cognitive processes are reflected by both cognitive and autonomic inflexibility (assessed by heart rate variability; HRV), with a key role attributed to the vagus nerve. Interestingly, modulation of vagal activity can be achieved with transcutaneous auricular vagus nerve stimulation (taVNS), a non-invasive technique that employs a low-intensity electrical current applied to the ear. In a sample of healthy subjects, we investigated the effects of taVNS of the left concha, compared to sham (earlobe) stimulation, on the cognitive and autonomic correlates of perseverative cognition following a

psychosocial stress task. Interestingly, taVNS significantly reduced cognitive rigidity, reflected by reduced subjective perseverative thinking after psychosocial stress. Although there were no direct effects on autonomic correlates of perseverative cognition, stimulation intensity significantly moderated the effects of taVNS on HRV, with higher taVNS intensities being associated with higher levels of HRV. Contrarily, the results indicated that individuals who engaged more in perseverative thinking showed more autonomic flexibility during stress recovery following taVNS, suggesting a possible dissociation between the physiological and psychological changes following taVNS. Again, this effect was moderated by stimulation intensity. Overall, the study findings endorse the causal link between perseverative cognitions and the vagus nerve and, although replication is pivotal, hint towards a linear relationship between taVNS intensity and HRV.

Key words: *transcutaneous auricular vagus nerve stimulation (taVNS) - perseverative cognition - heart rate variability - cognitive rigidity - psychosocial stress*

REDUCING DISGUST AND MORAL RIGIDITY THROUGH TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS): CLINICAL IMPLICATIONS FOR OBSESSIVE-COMPULSIVE DISORDER

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The experience of deontological guilt has been found to selectively activate the brain region of the insula, a well-known structure implicated in the processing of disgust. Moreover, previous studies showed a hyperactivity of the insula in persons with obsessive-compulsive disorder (OCD), in which deontological guilt and disgust play a pivotal role in pathogenesis and maintenance of symptoms. The present study tested the hypothesis that indirect inhibition of the insula via cathodal transcranial direct current stimulation (tDCS) would decrease disgust and moral rigidity. By using a randomized, sham-controlled, within-subject design, 36 healthy individuals (18 women) underwent 15-min anodal, cathodal, and sham tDCS over T3 in three different days. Levels of OC tendencies as well as pre and post-stimulation momentary emotional states were assessed. Subjects' heart rate (HR) was recorded to derive measures of parasympathetic nervous system activity (Heart Rate Variability, HRV). After the first 10 minutes of tDCS stimulation, participants were asked to complete a computerized moral task and a word-stem completion task with either disgust-related words or neutral alternatives. Compared to sham condition, anodal and cathodal stimulation of T3 respectively enhanced and decreased self-reported disgust, severity of moral judgements in the deontological domain, and HRV. A positive correlation emerged in the anodal condition between scores on the Obsessive-Compulsive Inventory-Revised (OCI-R) and self-reported disgust, between deontological guilt and the Fear-of-Sin (FoS) subscale of the Pennsylvania Inventory of Scrupolosity (PIOS), and between deontological guilt and the washing and obsessing subscales of the OCI-R; in the cathodal condition, disgust inversely correlated with the FoS and the washing and obsessing subscales of the OCI-R. To conclude, results showed a decrease in self-reported and physiological disgust, and deontological moral rigidity following cathodal tDCS on T3, with stronger effects in individuals with higher levels of OC traits, thereby suggesting potential implications for OCD treatment.

Key words: *transcranial direct current stimulation (tDCS) – disgust - moral rigidity - heart rate variability - obsessive-compulsive disorder (OCD)*

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