Keywords: temporal interference stimulation, noninvasive subcortical stimulation, NHP electrophysiology, animal model

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P3.054

INTERMITTENT STIMULATION OF THE NUCLEUS BASALIS OF MEYNERT IN SENILE MACAQUE MONKEYS IMPROVES WORKING MEMORY BEHAVIOR

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Abstract

Degeneration of the basal forebrain cholinergic system is a key component in Alzheimer's disease (AD) and age-related cognitive decline. Using Deep Brain Stimulation to target the nucleus basalis of Meynert (NB) presents an alternative means of increasing cholinergic activity and hence improving cognitive functions. Here we tested whether NB stimulation improves working memory in aged monkeys. Rhesus monkeys (Macaca mulatta) 25-30 years of age were trained on a delayed match-to-sample task and tested after reaching reach asymptotic performance. Adaptive control of delay durations allowed tracking of threshold delay periods for which the animals could achieve 79% correct choices in each session. Monkeys were implanted with electrodes targeting the NB and an Implantable Pulse Generator (IPG) under the skin. A micro-welded pigtail connected the IPG device and stimulation electrodes. In experiment one, animals received unilateral 60-Hz stimulation, lasting 20 seconds every minute, for one hour. Across a 12 week period, four animals (2M, 2F) showed robust, 2-3-fold increases in working memory delays, two females showed modest 1-2 fold increases in working memory delays, and three animals (1M, 2F) showed no improvements. Subsequently, three of the animals that showed robust improvements were tracked for another 12 weeks without further stimulation, and improvements in cognition were sustained. In two animals, unilateral stimulation was followed by bilateral stimulation, and working memory delays improved in both. Four other, non-implanted animals, were given high doses of Donepezil daily for 12 weeks, and working memory did not improve in any of them. Known modes of failure of the method include lost connectivity to the electrode, missed implant targets, and behavioral intractability. Our results show that NB stimulation improves working memory functions in an aged non-human primate model of age-related memory decline.

Research Category and Technology and Methods

Translational Research: 1. Deep Brain Stimulation (DBS)

Keywords: nucleus basalis of Meynert, acetylcholine, monkey, working memory

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MODELLING NOVEL TDCS SETTINGS FOR INTERFERING WITH THE BRAINSTEM ACTIVITY

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Abstract

Background and aims: Transcranial direct current stimulation (tDCS) seems to affect the excitability of trigemino-facial reflexes, although the changes might be due to sensitization through cutaneous trigeminal afferents, rather than be a direct effect of polarization. To explore tDCS effects on brainstem, we assessed blink reflex (BR) and masseter inhibitory reflex (MIR) in healthy subjects undergone a tDCS protocol derived from realistic computational models, and a control protocol.

Methods: In this randomized, assessor-blinded, crossover study, eight healthy subjects (mean age: 30.88 ± 10.52, 4 women) underwent anodal tDCS (2 mA for 20 min) with an experimental (anode: left and right motor cortex, reference: right deltoid) and control (anode: left motor cortex, reference: right supraorbital area) montage in two different single sessions separated by a ≥ 1-week washout period. Experimental protocol was chosen from realistic computational models predicting the current density along the brainstem. Stimulation was delivered via rubber pads (25 cm2 for active electrodes, 35 cm2 for reference electrodes). BR was bilaterally assessed from orbicularis oculi muscle after the stimulation of each supraorbital nerve, while MIR were recorded from the left masseter muscle after stimulation of the inferior alveolar branch of the mental nerve. For BR, we considered reflex threshold (RT) and latencies of RI, RII ipsilateral and RII contralateral as outcomes; for MIR, RT, onset latencies and duration of two silent periods (SP1, SP2). Assessments were recorded before (T0) and after (T1) each stimulation.

Results: For experimental stimulation, paired samples T-Test revealed a significant decrease in RI latencies [ms, right BR: $t(7) = 4.98$, $p = 0.002$; left BR: $t(7) = 2.88$, $p = 0.023$] and a trend in increasing the duration of SP1 [ms, MIR: $t(7) = -2.33$, $p = 0.052$]. No significant results were found for control condition.

Conclusions: Our results suggest that, for our experimental protocol, tDCS might modulate brainstem circuitries.

Research Category and Technology and Methods

Clinical Research: 9. Transcranial Direct Current Stimulation (tDCS)

Keywords: tDCS, neuromodulation, non-invasive deep brain stimulation, brainstem

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SPECIFIC EFFECT OF HIGH FREQUENCY TRNS OVER PARIETAL CORTEX COMBINED WITH COGNITIVE TRAINING ON NUMERICAL COGNITION IN CHILDREN AND ADOLESCENTS WITH DYSCALCULIA

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Abstract

Established therapeutic options are still scarce for youths with dyscalculia, with little evidence of efficacy. In recent years, the advancement of knowledge about the neurobiology of dyscalculia has paved new avenues for brain-directed interventions. Accordingly, the present study aims to explore the effect of tRNS over dorsolateral prefrontal cortex (dlPFC) or posterior parietal cortex (PPC) plus cognitive training in improving numerical cognition. Twenty-three youths with dyscalculia (9-14 years) were randomly allocated to Parietal Group (active tRNS over PPC), to Frontal Group (active tRNS over dlPFC), or to Sham Group (sham tRNS over PPC or dlPFC). The groups were matched for age ($p = 0.92$), IQ ($p = 0.41$), and mathematical performance ($p = 0.98$). In the active conditions, tRNS was