Translating tDCS into the field of obesity: mechanism-driven approaches

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Translating tDCS into the field of obesity: mechanism-driven approaches

Miguel Alonso-Alonso1,2*

1 Berenson-Allen Center for Noninvasive Brain Stimulation, Division of Cognitive Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA
2 Center for the Study of Nutrition Medicine, Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

Obesity is an unmet global medical need. Modification of lifestyle behaviors, i.e., limiting food intake and increasing physical activity, remains the cornerstone treatment in the vast majority of cases, but it is often ineffective (Fabricatore and Wadden, 2006). There is need for innovative approaches to facilitate behavioral changes leading to a successful weight loss.

Recent data from obesity neuroimaging studies point to an imbalance in prefrontal and limbic brain circuits that support cognition- and reward-related aspects of eating behavior (Carnell et al., 2012; Brooks et al., 2013; Vainik et al., 2013). Manipulating brain activity could help rebalance these circuits and translate into beneficial behavioral changes. Three small proof-of-concept studies have reported an acute decrease in food craving following one session of transcranial direct current stimulation (tDCS) aimed at enhancing the activity of the dorsolateral prefrontal cortex (Fregni et al., 2008; Goldman et al., 2011; Montenegro et al., 2012). The gap between the effects reported in these studies and the efficacy standards expected for clinical trials related to weight management (FDA, 2007) seems large at this time. How can we start closing this gap and rationally guide the translation of tDCS into the field of obesity? In this mini-review I summarize some of the challenges and questions ahead, related to basic science and technical aspects, and suggest future directions.

Keywords: transcranial direct current stimulation, obesity, weight loss, inhibitory control, prefrontal cortex
cognitive target in obesity is inhibitory control, a core component of executive functions that supports self-regulatory processes and goal-oriented eating behavior (Appelhans, 2009; Houben, 2011; Yokum et al., 2012; Vainik et al., 2013). Prior studies have mapped inhibitory control capacity (indexed by performance in response inhibition tasks) to a basic set of brain regions that include inferior frontal gyrus, pre-supplementary motor area, and subthalamic nucleus (Chambers et al., 2009). tDCS is well suited to reach this target according to preliminary computational models (Truong et al., 2013) and experimental data (Juan and Muggleton, 2012). Given that tDCS enhances synaptic plasticity processes related to learning (Stagg and Nitsche, 2011), the combination of tDCS with computerized training of inhibitory control is a good strategy. This can narrow down tDCS-induced plasticity effects to the cognitive process and brain circuit being targeted. A recent study supports the feasibility and efficacy of pairing tDCS with inhibitory control training (Ditye et al., 2012) and two preliminary clinical trials are underway in obesity based on this approach (Clinical trials.gov website; study numbers: NCT01632280, NCT01793766).

Most of what has been learned to date about tDCS as a technique can be extended into obesity, but there are largely unexplored factors that could modify the impact of tDCS on the brain, particularly in obese subjects. First, the potential influence of metabolic/physiological state: being in a weight-reduced or weight-stable state as well as prandial status (fasting/fed) are associated with different underlying brain activity (Tataranni et al., 1999; Rosenbaum et al., 2008). This source of variability may change the predicted effect of tDCS on obesity-related brain networks, as initial brain activation state has an important role in determining the behavioral outcome of brain stimulation (state-dependency; Silvanto et al., 2008). Additionally, weight-loss diets may influence tDCS-induced plasticity mechanisms. Intake of high-fat, low-carbohydrate, ketogenic diets (e.g., Atkins) enhances GABA-A-receptor-mediated intracortical inhibition and Obesity Research Center, 5 P30 DK046200, and the Nutrition Obesity Research Center at Harvard, P30 DK040561. Dr. Alonso-Alonso thanks Rita Buckley for her help in editing the manuscript.

REFERENCES

In conclusion, the translation of tDCS into the field of obesity is still at a very early stage, with many challenges and open questions ahead. There is need for foundational studies that generate an adequate knowledge base and principles to guide the development of this emerging field.

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