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Transcranial Direct Current Stimulation: A Novel Approach to Control Hyperphagia in Prader-Willi Syndrome

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Prader-Willi syndrome is a genetically determined developmental disorder characterized at the second phase by overeating and obesity that are usually seen around the third year.[1] There are some hypotheses to explain hyperphagia in Prader-Willi syndrome such as a diminished inhibitory control.[2]Prader-Willi syndrome subjects when exposed to food have less inhibitory control resulting in hyperphagia, in other words, these subjects are not able to control craving associated with food exposure. In this context, it is not clear whether Prader-Willi syndrome leads to specific changes in neural circuits associated with food consumption or whether this symptom is a general deficit of inhibitory neural networks. Given that hyperphagia is not seen in other brain malfunction syndromes and this symptom is specifically seen in Prader-Willi syndrome, it is conceivable that Prader-Willi syndrome is associated with an impairment of food-control neural mechanisms. In this context, modulation of these neural circuits might bring benefits to these patients.

Several studies investigated the neural correlates of food craving. These studies have found hyperactivity on orbitofrontal cortex and anterior cingulate cortex and also an inhibitory dysfunction in lateral prefrontal circuitry[3]—perhaps them explaining the aberrant satiety regulation mechanisms observed in these patients. If cortical prefrontal activity is critically associated with food craving and consumption, it is plausible that modulation of prefrontal activity might lead to control of food craving and consumption.

One manner to modulate cortical activity is with the use of noninvasive and painless techniques of brain stimulation. In fact, a very simple, safe, and inexpensive technique of noninvasive brain stimulation, transcranial direct current stimulation, has shown to induce a powerful effect on cortical modulation.[4] Transcranial direct current stimulation is based on the application of low intensity direct current (0-2 mA) on the scalp via large electrodes (25-35 cm^2). Its effects are polarity dependents, that is anodal transcranial direct current stimulation is related with neuronal membrane depolarization and activity enhancement, and cathodal stimulation with hyperpolarization and activity inhibition. In the last decade, several studies have demonstrated that this technique induces significant behavioral changes on motor, visual, memory, and language performance[5] and mood changes in patients with major depression.[6]

Transcranial direct current stimulation has also been shown to modulate decision making and cue-induced craving. Fecteau et al[7] showed on healthy volunteers that transcranial direct current stimulation on right dorsolateral prefrontal cortex results in a decrease of risky-taking behavior. Boggio et al[8] and Fregni et al[9] found that transcranial direct current stimulation applied over dorsolateral prefrontal cortex reduces cue-induced craving related to alcohol and food exposition, respectively. In addition, a single session of active transcranial direct current stimulation reduces food consumption (as indexed by calorie intake) when compared to sham stimulation. We hypothesized that modulation of prefrontal cortex excitability inhibits increased subcortical activity (ie, amygdalae activity) associated with food craving and therefore reduce food consumption. Indeed, in this context, transcranial direct current stimulation might be a good tool to modulate other disorders associated with impulsive behavior such as compulsive gambling.

This evidence together with recent results showing that Prader-Willi syndrome subjects have altered prefrontal activity, led us to believe that (*a*) hyperphagia in Prader-Willi syndrome is associated with a dysfunction of prefrontal neural circuits; (*b*) transcranial direct current stimulation can modulate prefrontal neural circuits and therefore inhibit excessive activity in subcortical structures, such as amygdala; consequently, decreasing food consumption. A major concern regarding this hypothesis is how to investigate the proposed intervention on this group of patients. Fregni et al[9] measured the caloric intake after 1 transcranial direct current stimulation single session; considering that Prader-Willi syndrome patients are usually on restricted diets, an important issue is the main outcome to measure the effects of this treatment. One option would be to examine food-seeking behavior or number or episodes of binges as potential outcomes.

In summary, we propose that transcranial direct current stimulation, a nonexpensive, noninvasive and painless

technique, should be further explored to control food behavior in patients with Prader-Willi syndrome. The easy-of-use, low cost, and safe profile of this technique gives additional support for its use in this population of patients.

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References

1. Reddy LA, Pfeiffer SI. Behavioral and emotional symptoms of children and adolescents with Prader-Willi syndrome. *J Autism Dev Disord*. 2005;37:830-839.
2. Falkenstein M, Hoormann J, Hohnsbein J. ERP components in Go/Nogo tasks and their relation to inhibition. *Acta Psychologica*. 1999;101:267-291.
3. Uher R, Murphy T, Brammer MJ, et al. Medial prefrontal cortex activity associated with symptom provocation in eating disorders. *Am J Psychiatry*. 2004;161:1238-1246.
4. Priori A. Brain polarization in humans: a reappraisal of an old tool for prolonged non-invasive modulation of brain excitability. *Clin Neurophysiol*. 2003;114:589-595.
5. Wassermann EM, Grafman J. Recharging cognition with DC brain polarization. *Trends Cogn Sci*. 2005;9:503-535.
6. Boggio PS, Rigonatti SP, Ribeiro RB, et al. A randomized, double-blind clinical trial on the efficacy of cortical direct current stimulation for the treatment of major depression. *Int J Neuropsychopharmacol*. 249-254.
7. Fecteau S, Pascual-Leone A, Zald DH, et al. Activation of prefrontal cortex by transcranial direct current stimulation reduces appetite for risk during ambiguous decision making. *J Neurosci*. 2007;27:6212-6218.
8. Boggio PS, Sultani N, Fecteau S, et al. Prefrontal cortex modulation using transcranial DC stimulation reduces alcohol craving: a double-blind,sham-controlled study. *Drug Alcohol Depend*. 2008;92:55-60.
9. Fregni F, Orsati F, Pedrosa W, et al. Transcranial direct current stimulation of the prefrontal cortex modulates the desire for specific foods. *Appetite*. 2008;51:34-41.

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