



Effects of transcranial direct current stimulation on the gut microbiome: A case report



The imbalance of the gut microbiome or dysbiosis has been implicated as a cause of obesity [1] and brain disorders [2]. Eat well is one of the most effective tools to relief metabolic or brain disorders. However, this practice is difficult to be followed by health agents and patients. Transcranial direct current stimulation (tDCS) is a non-invasive neuromodulation method that has been widely investigated in recent years [3]. The method consists of applying a low intensity continuous electric current over the scalp. When applied for 20–30 minutes it is able to alter significantly the cortical excitability. For this reason, this method has been used in the treatment of food craving and overweight [4]. On the other hand, none of the studies evaluated the impact of tDCS on the gut microbiome. Considering the bidirectional mechanisms of the brain-gut axis, it is conceivable to think that tDCS could also induce a significant change in the composition of the gut microbiome and, therefore, induce therapeutic effects.

A 38-year-old woman diagnosed with overweight and cravings for sugary foods ten years ago, according to the WHO specification, presented herself in October 2019 at the Neuromodulation Clinic in Porto Alegre-RS. According to her unsuccessful weight loss attempts history, a 10-week treatment of transcranial direct current stimulation (tDCS) was provided. Therefore, the patient filled out the free and informed consent form, agreeing with the use of the tDCS and microbiome analysis using the 16S molecular technique. The tDCS involved the application of weak direct electric current (2 mA) through two electrodes (5×5 cm) embedded in saline solution and placed on the scalp, with the anode on the right dorsolateral prefrontal cortex and the cathode on the contralateral supraorbital region, for 20 minutes a day, twice a week [5]. This montage was based on previous studies for the treatment of cravings by drugs and food [4]. Three stool samples were also collected by swab for intestinal microbiome analysis in the pre-intervention moments, after a session of tDCS (acute effect) and after 20 sessions of tDCS (chronic effect), through the sequencing of the human fecal 16S ribosomal RNA gene. No dietary intervention was performed during treatment.

It was observed a decrease in the bacteroidetes/firmicutes ratio from 8.5 to 5.2 after a single session of tDCS and from 5.7 after 20 sessions, represent an improvement of 38.8% and 33% for acute and chronic effects respectively. The patient showed a quick and significant decrease in the *firmicutes* proportions which were most prevalent, with an increase in *Roseburia intestinalis* and *Faecalibacterium prausnitzii*, a gradual and sustained effect until the 10th week. There was also an increasing number in the *bacteroidetes*

proportion, with an acute beneficial effect, predominantly sustained, in the main bacterial species found, *Bacteroides vulgatus* and *Bacteroides uniformis*.

The influence of the gut on the brain is vastly reported in the literature [2,6,7]. Studies have shown that the gut microbiome influences reactivity to stress and anxiety [8]. There are several papers evaluating the effects of the brain on the intestine [2], but none of them used microbiome analysis as a parameter.

We observed changes in intestinal microbiome after tDCS, measured by the ratio of bacteroidetes and firmicutes. This finding supports the hypothesis of the existence of bidirectional mechanisms of the brain-gut axis. The evidences indicate that microbiota communication with the brain involves the vagus nerve, which transmits information from the luminal environment to the central nervous system (CNS), and classifies it as the main modulatory constitutive communication path between the microbiota and the brain [9]. One possibility that could explain our discovery is that tDCS has induced species-specific central effects that are associated with restoring the integrity of narrow junctions and protecting the intestinal barrier. In addition, the effects of the CNS on the microbiota composition are likely to be mediated by a disturbance of the luminal habitat/normal mucous that can also be restored using probiotics and fermented foods and, therefore, influencing behavior [8]. Ray and colleagues (2019) claimed that neurotransmitters alteration and the cortical reorganization of the prefrontal regions related to compulsion is the main mechanism of food craving reduction. We believe that our findings may add as one possible mechanism to improve the microbiome in addition to those already mentioned. It is possible that microbial composition changes may reduce intestinal permeability and consequently the systemic inflammation, as well as to contribute to the neurotransmitters synthesis promoted by the intestinal ecosystem [10].

In conclusion, our data suggest that the application of anodal tDCS from the right dorsolateral prefrontal cortex induces changes in the intestinal microbiome that, in turn, could assist in the treatment of obesity and other relevant chronic diseases. If this discovery is confirmed by studies with a larger samples and more adequate designs, the microbiome analysis might be incorporated as a diagnostic and follow-up tool in future studies involving patients with metabolic syndrome.

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