Long-lasting analgesic effect of transcranial direct current stimulation in treatment of chronic endometriosis pain

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Abstract

Approximately 10–20% of women of reproductive age suffer from endometriosis, with 70–90% of these women reporting chronic pain symptoms that persist during their menstrual cycle. We are presenting a case in which a novel form of noninvasive brain stimulation called transcranial direct current stimulation was used as an intervention in a 32-year-old woman with persistent, chronic pain symptoms caused by endometriosis for 20 years. Ten daily, 20-min sessions of 2-mA anodal transcranial direct current stimulation were applied over the left primary motor cortex. Acutely, visual analog scale pain symptoms were reduced by 60%. There were also significant decreases in modules of the Endometriosis Health Profile. At the 4-month follow-up, the patient still expressed an overall decrease in pain symptoms of 30%.

Key words: endometriosis, motor cortex, pain, transcranial direct current stimulation.

Introduction

Endometriosis is defined as the formation of endometrial glands and stroma outside the uterus and has been described as a disorder causing pain and infertility.1 The pain symptoms most commonly attributed to endometriosis are dysmenorrhea, dyspareunia, and chronic pelvic pain (non-cyclical, non-menstrual pelvic pain). Approximately 10–20% of women of reproductive age suffer from endometriosis,2 with 70–90% of these women reporting chronic pelvic pain (CPP), dysmenorrhea, dyspareunia, infertility and menstrual disturbances. CPP has numerous negative effects and is both physically and mentally debilitating. It can decrease the sufferer’s ability or inclination to pursue physical activities or sexual relations and may cause depression or anxiety, perhaps further impairing the patient’s health and level of functioning.3

Treatments for endometrial pain include ovariectomy, classic pain pharmacological treatments, and hormone substitution. The current treatment approaches may not always alleviate pain symptoms or result in temporary symptom palliation, after which relapses and repeated surgery are common. One hypothesis to explain this pain phenomenon is that CPP is related to a dysfunction in the pain-related neural networks, including the limbic system.4 This suggests that the perceived pain is a condition of the brain and direct treatment of pelvic organs alone may not be capable of exerting long-lasting analgesic effects occurring from limbic dysfunction.

Transcranial direct current stimulation (tDCS) is a form of noninvasive brain stimulation that has proven to be very promising in treating a variety of pain conditions.5 A low-dose direct electrical current delivered to the brain via electrodes placed directly on the scalp induces changes in the neuronal activity of the cortex by increasing excitability in the areas under the anode and decreasing it in the areas under the cathode.6 These facilitatory or inhibitory effects are not only seen acutely but can be long-lasting.7
Several studies have demonstrated the effectiveness of anodal tDCS applied over M1 in modulating motor cortex excitability and alleviating pain. The noninvasive and immediate effects to the targeted underlying cortical areas of tDCS make it a very promising option for neurological disorders. This study aims to investigate the effectiveness of tDCS treatment on chronic pain resulting from endometriosis.

Case Report

Patient M.R. is a 32-year-old woman (162 cm, 48 kg, body mass index = 18.3) who first expressed symptoms of endometriosis at age 12. The patient was diagnosed with endometriosis by a board-certified gynecologist and this was confirmed by a laparoscopy procedure. Her endometriosis was classified as stage 2 according to the American Society for Reproductive Medicine (deep endometriosis of the peritoneum and superficial endometriosis of both ovaries). She had been suffering from the resulting pain for nearly 20 years. During the first year, her pain, which only occurs around her menstrual cycle period, lasted approximately 2 h. In later years and most recently, her pain progressed to lasting continuously for 72 h during her menstrual cycle, accompanied by severe nausea and vomiting. To alleviate the pain, she took oral contraceptive pills for 4 months; however, she stopped due to unexpected weight loss. She also used cyproterone for 3 years and Drospirenone and ethinyl estradiol for 2 years, both of which were terminated because of hyperpigmentation on her nose. M.R. also received 10 sessions of acupuncture; this worsened the pain and became unbearable. She underwent an unsuccessful session of bloodletting which were terminated because of hyperpigmentation on her nose. M.R. also attempted drinking a holistic remedy mixture consisting of borage tea, oregano tea, vitagnus drop, ginger and cinnamon; however, this proved ineffective as well. A complete laboratory workup was carried out, investigating hematology, metabolic, and oncologic markers, including cancer antigen 125, all of which were normal or negative. The only treatment that proved successful in relieving pain was i.v. morphine, although due to consecutive injections, her forearms had bruises and she became self-conscious. She had exhausted all of the available conventional and holistic options over the past 20 years. Laparoscopy was performed to remove progressing endometriosis, but this was not effective. Her last viable treatment option was a hysterectomy, but the patient wanted to have children so refused this option.

M.R. was referred to Atieh Clinical Neuroscience Center (Iran, Tehran) in April 2012. After signing informed consent, she underwent 10 daily sessions of transcranial direct-current stimulation (tDCS) in which the clinicians used a Chattanooga Ionto device with 5×7 cm² electrodes for 20 min each session. During each session, 2-mA stimulation was delivered (anode centered over M1, cathode placed on right supraorbital region). The visual analog scale (VAS) was used to rate pain from 0 (no pain) to 10 (most intense pain) and the Endometriosis Health Profile (EHP-30) was employed to assess effectiveness of the tDCS intervention. VAS is a scale frequently used for pain evaluation and its validity and reliability is assessed and confirmed. The EHP is a health-related quality of life patient self-report patient reported outcome (PRO). It assesses various effects of endometriosis on different aspects of women’s lives. It is constructed from the patient’s perspective to evaluate health-related quality of life in endometriosis. Experimental evidence endorses the EHP’s reliability and validity in evaluating different areas of concern to women suffering from endometriosis.

M.R.’s baseline was recorded 5 days before, during and after her menstrual cycle. Then, 10 sessions of tDCS were implemented before and during the menstrual cycle. The EHP-30 was completed before, immediately after, and 4 months after the treatment course.

Results

M.R.’s perception of pain during the menstrual cycle was decreased by 60% after 10 sessions of anodal tDCS treatment. Although there was no longitudinal follow-up between 1 and 4 months post-stimulation, the patient did not report any major pain fluctuations during that time. At the 4-month follow-up, there was still a sizeable (30%) maintained analgesic effect. There were also significant decreases in most modules on the EHP-30, which persisted into the 4-month follow-up (See Table 1). Although there were no immediate decreases in the pain qualifier of the EHP-30, there was a gradual decrease over 4 months. Her emotional well-being and control ratings dropped by 50% and 67%, respectively, signifying her improved quality of life. The patient did not report any side-effects or adverse events.

As seen in Figure 1, there is a significant decrease in perceived pain immediately after the course of treatment. This trend continues to hold true at the 4-month follow-up.
Discussion

Pain syndromes, such as fibromyalgia, chronic back pain, and neuropathic pain, are accompanied by modulatory effects on neuroplasticity in pain-related neural circuits. This results in significant effects on the sensory and affective-emotional domains, such as hyperalgesia, allodynia, anxiety, and depression. M.R.’s decreases in EHP-30 modules relating to emotional aspects of pain represent not only a decrease in perceived pain but also a modulation in her emotional processing of the pain. A new way of approaching pain disorders may be suggested here by not only directly treating the pain symptoms but also attempting to increase the patient’s perceived control of their pain, which can make the perception decrease.

Ohara and colleagues have proposed that electrical stimulation of the cortex may implement its effects by: (i) preventing noxious stimuli from reaching the cortical level from the spinal cord; and (ii) by modulating excitability at the cortical level to induce changes in the emotional aspects of pain. This suggests that in a subset of patients, cortical stimulation may be the most effective form of pain management, as their neuronal excitability may be extremely sensitive to peripheral noxious stimuli. In the case of M.R., we noted that aside from opioids, only direct electrical stimulation of the cortex reduced pain sensation.

Another important finding of our current study is the long-lasting effect of a relatively short stimulation course. tDCS is thought to have short-lived effects, but the current study indicates more lasting effects than previously observed. In fact, 4 months after treatment, the patient still showed a significant and considerable reduction in pain. The durability of such an intervention method can be a key characteristic for clinical applications. This durability suggests that consecutive and intensive treatment might have a cumulative effect that contributes to long-lasting effects not seen in a single-session or sporadic sessions of stimulation.

tDCS is a safe, noninvasive, cost-effective technique that is easily administered. One problem related to tDCS (particularly in research) is that it is non-focal, making it difficult to draw conclusions about the cortical areas being stimulated and the effects created. Depending on the area of stimulation, tDCS modulation can take place in various neural circuits involved in sensory discriminative, cognitive, or emotional aspects of chronic pain. To amend this problem, more focal procedures, such as high-definition tDCS, can be employed. Another remedy could be using imaging techniques along with tDCS to measure the pre- and post-stimulation activity and relate the created changes within the neural circuit exerted by tDCS.

Table 1 Pre-treatment, post-treatment and 4-month follow-up evaluations of patient’s pain using VAS and EHP-30

<table>
<thead>
<tr>
<th>Scale</th>
<th>Domain</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>After 4 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS</td>
<td>Before pain period</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>During pain period</td>
<td>10</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>After pain period</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pain</td>
<td></td>
<td>61%</td>
<td>65%</td>
<td>47%</td>
</tr>
<tr>
<td>Control–powerlessness</td>
<td></td>
<td>100%</td>
<td>43%</td>
<td>33%</td>
</tr>
<tr>
<td>EHP-30</td>
<td>Emotional well-being</td>
<td>90%</td>
<td>46%</td>
<td>43%</td>
</tr>
<tr>
<td>Social support</td>
<td></td>
<td>90%</td>
<td>75%</td>
<td>65%</td>
</tr>
<tr>
<td>Self-image</td>
<td></td>
<td>40%</td>
<td>26%</td>
<td>40%</td>
</tr>
<tr>
<td>Work</td>
<td></td>
<td>60%</td>
<td>48%</td>
<td>64%</td>
</tr>
<tr>
<td>Medical attention</td>
<td></td>
<td>85%</td>
<td>55%</td>
<td>—</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td>86%</td>
<td>66%</td>
<td>53%</td>
</tr>
</tbody>
</table>

EHP-30, Endometriosis Health Profile; VAS, visual analog scale.
The results of this case may have significant implications in the area of pain management for patients suffering from intractable pain symptoms resulting from a variety of disorders. Additional research, including randomized, double-blind, sham-controlled studies with a larger population are merited.

Disclosure

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References