Journal of Clinical Neuroscience 93 (2021) 54–60

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Clinical study

Transcranial direct current stimulation for provoked vestibulodynia: What roles do psychosexual factors play in treatment response?

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ARTICLE INFO

Article history:
Received 24 August 2020
Accepted 1 August 2021

Keywords:
Transcranial direct current stimulation (tDCS)
Vulvodynia
Predictive factors
Dyspareunia
Depression
Vaginal penetration cognition

ABSTRACT

There is growing evidence that provoked vestibulodynia (PVD), a frequent and debilitating condition, is characterized by central sensitization. This study aimed to examine predictive factors of transcranial direct current stimulation (tDCS) efficacy in this chronic pain population. Exploratory analysis derived from a randomized controlled trial was performed to assess predictors of pain reduction among 39 women with PVD who received 10 daily sessions of either active or sham tDCS. Clinical characteristics (e.g. pain intensity, duration and pain sensitivity) and psychosexual factors (e.g. pain catastrophizing, pain-related fear, anxiety, depressive symptoms and vaginal penetration cognitions) were assessed at baseline and used to predict tDCS response at 3-month follow-up. Analysis revealed that higher depressive symptoms and lower negative self-image cognitions were significant predictors of pain reduction at follow-up and accounted for 62.3% of the variance in the active tDCS group. Higher genital incompatibility cognitions were related to poorer response, regardless of treatment group. These findings suggest that women with PVD presenting higher depressive symptoms and lower levels of negative self-image cognitions could derive greater benefits from tDCS. These results suggest that tDCS could be effective in a subgroup of women with PVD - a possibility worth exploring with future prospective larger studies.

1. Introduction

Affecting 8–16% of women, vulvodynia, defined as chronic vulvar pain with no identifiable cause, is a neglected and poorly understood condition [29,28]. Considered to be the foremost cause of pre-menopausal vulvodynia, provoked vestibulodynia (PVD) is characterized by a recurrent sharp pain at the vulvar vestibule (i.e., vaginal introitus) in response to pressure application or attempt of sexual intercourse [17]. Women with PVD appear to have functional abnormalities related to pain perception which are not limited to the vulvar vestibule [22]. They also tend to have a lower thermal and mechanical pain threshold and lower pain tolerance [5,25,53,60,24]. These alterations are present in the vestibule area [5,53,60], but also in distant areas such as the thumb, forearm, deltoid and shin [25,53,22]. Growing evidence suggests that peripheral and central sensitization are involved in PVD, and that the central nervous system would play a role in the pathophysiology of this chronic pain condition [54].

Past studies have shown that non-invasive brain stimulation techniques, such as transcranial direct current stimulation (tDCS), can modulate the activity of the central nervous system and relieve chronic pain [62]. Interestingly, results coming from a case study suggest that tDCS could be an effective modality to relieve chronic vulvar pain [8]. Unfortunately, the positive results observed in this patient could not be replicated in a recent double-blind randomized controlled trial, performed on 40 women suffering from PVD [45]. Even though anodal tDCS did not significantly reduce pain during intercourse over sham, more than half of the women

Abbreviations: BDI, Beck Depression Inventory-II; DLPFC, dorsolateral prefrontal cortex; FSDS, Female Sexual Distress Scale; FSFI, Female Sexual Function Index; GMSS, Global Measure of Sexual Satisfaction; M1, motor cortex; MPQ-PRI, McGill Pain Questionnaire – Pain Rating Index; NRS, numeric pain rating scale; PASS-20, Pain Anxiety Symptom Scale (20 items); PCS, Pain Catastrophizing Scale; PT, thermal pain threshold; PTol, thermal pain tolerance; PVD, provoked vestibulodynia; tDCS, transcranial direct current stimulation; VPCQ, Vaginal Penetration Cognition Questionnaire.

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https://doi.org/10.1016/j.jocn.2021.08.003
0967-5868/

assigned to the active group reported pain reduction at their 3-month follow-up, suggesting that some women with PVD might respond more favorably than others to tDCS.

Past studies have shown that clinical characteristics (e.g., PVD subtype, duration of symptoms) and psychosexual factors (e.g., pain catastrophizing, fear of pain) could help predict treatment response in women with PVD [27,9]. These observations are in line with the fear avoidance model of Vlayen & Linton [63], which suggests an interrelationship between the pain experience and the negative affect of patients suffering from chronic pain. Supporting this are the results of Desrochers et al. [11] showing that women with PVD with high pain catastrophizing and fear of pain respond less favorably to topical cortisone and cognitive behavioral therapy. Based on these findings, it is likely that clinical characteristics and psychosexual factors could be associated with tDCS outcomes in women suffering from PVD. However, no study has formally tested this hypothesis.

The objective of this study was to examine predictive factors of tDCS efficacy in women suffering from PVD. More specifically, we sought to determine if baseline clinical characteristics (pain intensity and quality, PVD subtype, duration of symptoms and pain sensitivity [thermal pain threshold and tolerance]) and psychosexual factors (pain catastrophizing, pain-related fear, anxiety, depressive symptoms, vaginal penetration cognitions, as well as sexual function, distress, and satisfaction) were related to the tDCS response.

2. Methods

2.1. Study design

This study was an exploratory analysis of data from a previous randomized clinical trial comparing active and sham tDCS in PVD women [45,46] . Detailed study design and procedures have been described in these companion papers [45,46] . For this study, only data pertaining to pre-treatment (at baseline) and follow-up assessments (3 months after treatment) in both intervention groups were considered. Ethical approval was obtained from the ethics committee of the CIUSSS de l'Estrie-CHUSeth and all participants gave written informed consent prior to participating in the study.

2.2. Participants

Forty women suffering from PVD were assigned to either active or sham tDCS treatment group (1:1). Participants were eligible if, in the last six months, they experienced moderate to severe pain ($\geq$5/10) in at least 90% of attempted sexual intercourse. PVD diagnosis was confirmed by a gynecologist of the research team (GW, YB or IG) following a standardized protocol [17,4]. The exclusion criteria were the following: (1) pregnant or breastfeeding women; (2) women suffering from other urogynecological conditions (e.g. urinary tract or vaginal infection), pelvic pathology associated with pelvic pain (e.g. deep dyspareunia); (3) having contraindications to tDCS.

2.3. Study procedures

A structured interview was conducted at baseline by a trained research assistant blinded to treatment allocation, during which the participants' sociodemographic information (age, nationality, culture, education, marital status, religious affiliation), relationship duration with current partner, and gynecological and vulvovaginal pain history were collected. Clinical characteristics and psychosexual factors were also collected at baseline and at 3-month follow-up using validated procedures/questionnaires (see below).

2.4. tDCS treatment

Participants assigned to the active tDCS treatment received 10 daily sessions of anodal tDCS (NeuroConn DC stimulator, Model 0008, Ilmenau, Germany) over a period of 14 days (once a day on weekdays). Two electrodes were applied to the subject's scalp; the anode was placed over the motor cortex (M1) [48] and the cathode over the contralateral supraorbital area [48,16,59,34,58]. The location of M1 was estimated by positioning the centre of the electrode pad at 1 cm anterior and 4 cm lateral from the vertex [50]. A saline solution (77 mM NaCl) was used to soak the synthetic sponge electrode covers (5 cm $\times$ 7 cm; 35 cm^2). For the active group, the intensity of the stimulation was set at 2 mA for the entire treatment duration (20 min) [16,59,55,34,58] whereas the stimulation was gradually shut down after 30 s in the sham group.

2.5. Dependent variable: Percentage of pain reduction

Participants were asked to verbally rate the intensity of pain during intercourse on a numeric pain rating scale (NRS) ranging from "0" (no pain) to "10" (worst pain ever experienced). NRS is recommended for assessing adult pain intensity in most settings [33,13]. The percentage of pain reduction in NRS scores from baseline to follow-up assessment was calculated using the following formula: (Baseline - Follow-up) / Baseline $\times$ 100 [49,32].

2.6. Independent variables

2.6.1. Clinical characteristics

Baseline pain intensity and quality were evaluated with the NRS and the McGill Pain Questionnaire, respectively [12,49,15,32]. PVD subtype (primary [affecting women from their first sexual intercourse] *vs* secondary [which appears after a period of pain-free sexual intercourse]) and duration of symptoms were also collected. Regarding pain sensitivity, thermal pain threshold (PT) and thermal pain tolerance (PTol) were measured using a 9-cm^2 Peltier-type thermode (Medoc Thermal Sensory Analyser, Model TSA-2001, Medoc, Advanced Medical Systems, Ramat Yishai, Israel) on the volar surface of the right forearm. This body area was selected because of its sensitivity and accessibility. The thermode temperature was initially set at 32 °C and gradually increased at a rate of 0.3 °C per second until it reached the participant's PTol (up to a maximum of 51 °C). Subjects were asked to verbally report when their perception changed from heat sensation to pain perception (corresponding to PT) and when their pain became intolerable (i.e. PTol). For each participant, the procedure was repeated three times to ensure the stability of PT and PTol measurements. In order to avoid skin sensitization, the position of the thermode was shifted slightly on the volar surface of the same forearm each time the procedure was repeated [61,40,52].

2.6.2. Psychosexual factors

Standardized and validated questionnaires measuring pain catastrophizing (13-item Pain Catastrophizing Scale; PCS) [23], pain-related fear (20-item Pain Anxiety Symptoms Scale; PASS-20) [43], state and trait anxiety (40-item State-Trait Anxiety Inventory of Spielberger; STAI-Y) [21], depressive symptoms (21-item Beck Depression Inventory-II; BDI) [3]and cognitions related to vaginal penetration (40-item Vaginal Penetration Cognition Questionnaire; VPCQ) [35] were completed. The latest, developed to assess women's intercourse-specific cognitions, is divided into five subscales, which were all used as clinical predictors: 1) control cognitions composed of four items (e.g., "I am afraid that I will

panic during penetration."), 2) catastrophic and pain cognitions including five items (e.g., "Penetration surely will not succeed."), 3) self-image cognitions assessed in six items (e.g., "I am a poor partner when penetration fails."), 4) positive cognitions which entailed five items (e.g., "Penetration will feel good."), and 5) genital incompatibility cognitions composed of two items (e.g., "I am afraid that my vagina is too narrow for penetration."). Finally, sexual function (19-item Female Sexual Function Index; FSFI) [56], sexual distress (13-item Female Sexual Distress Scale; FSDS) [10] and sexual satisfaction (5-item Global Measure of Sexual Satisfaction; GMSS) [37]were also collected.

2.6.3. Statistical analyses

All statistical analyses were carried out using SPSS Statistics for Windows, version 22.0 (SPSS Inc., Chicago, IL, USA). Regression analyses were used to evaluate the relative contribution of each baseline independent variable (clinical characteristics and psychosexual factors) and group assignment to predict percentage of pain reduction at follow-up assessment (dependent variable). Considering the small sample size and the exploratory nature of this study, separate regression analyses were conducted to examine the predictive relationship between each baseline potential predictors and the dependent variable (percentage of pain reduction from baseline to 3-month follow-up). For each regression model, the interaction term between the treatment group and the independent variable was entered to examine moderation using the PROCESS macro developed by Hayes [30]. This program computes 95% CI around the estimates on 5000 bootstrapping samples, centers variables to avoid multicolinearity [1], and computes simple slopes. When an interaction term reached $p \leq 0.10$, the predicting variable was included in a subsequent multivariate regression analysis for each group. This threshold was selected to prevent type II errors considering the small sample size and the exploratory nature of the analysis [14]. Findings from the multiple regression model, computed separately for each group, were considered to be statistically significant at $\alpha \leq 0.05$.

3. Results

3.1. Baseline sample characteristics

Of the 40 women assigned to either active or sham tDCS treatment in the original study, 39 were considered for these secondary analyses (see 45 for original randomized controlled trial flowchart). One woman was not considered in the analysis because she did not attempt any intercourse after the tDCS treatment. Sample's sociodemographic characteristics are detailed in Table 1.

The data pertaining to all 39 women's clinical (i.e., pain intensity and quality, PVD subtype, duration of symptoms and pain sensitivity [thermal pain threshold and tolerance]) and psychosexual (i.e. pain catastrophizing, pain-related fear, anxiety, depressive symptoms, vaginal penetration cognitions, and sexual function, distress and satisfaction,) variables at pre-treatment assessment are presented in Table 2. The mean pain intensity during intercourse on the 0 to 10 NRS was 7.2 (95% CI 6.8–7.6; range 5–10) at pre-treatment and 5.6 (95% CI 4.7–6.3; range 1.0–9.5), at follow-up assessment. The mean percentage of reduction of pain observed from pre-treatment to follow-up was 22.2% (95% CI 11.1–33.4; range −54.0–100.0).

3.2. Predictive factors

As depicted in Table 3, genital incompatibility cognitions showed a significant main effect (b = −9.01; se = 2.82; p = 0.003; 95%CI [−14.73, −3.23]), suggesting that higher baseline genital incompatibility was associated with lower percentage of pain reduction at 3-months follow-up for both groups. Regarding the interaction terms, the analysis revealed that both the depressive symptoms X group (b = 3.49; se = 1.73; p = 0.05; 95%CI [−0.01, 6.99]) and the self-image cognitions X group (b = −15.94; se = 7.56; p = 0.04; 95%CI [−31.28, −0.60]) were associated with pain reduction at 3-months follow-up, suggesting that depressive symptoms and self-image cognitions predicted treatment response differently in the two groups.

Multiple regression analyses were then conducted separately for the active and sham tDCS treatment groups. Results showed that depressive symptoms and self-image cognitions were significant predictors of pain reduction and accounted for 62.3% of the variance in the active tDCS group ($F(2,16) = 13.236$, $p < 0.001$; see Table 4). In contrast, the same multiple regression model was non-significant in the sham tDCS group $F(2.17) = 1.525$, $p = 0.246$). Hence, baseline higher depressive symptoms and lower self-image cognition score (corresponding to better self-image thoughts) were associated with better treatment outcomes in the active tDCS group, but not in the sham tDCS group.

Table 1
Participants' characteristics.

	Median (IQR)
Age (yr)	22.0 (20.0–24.0)
Age at first intercourse attempt (yr)	16.0 (15.0–18.0)
Lifetime number of sexual partners	3.0 (1.0–5.0)
Relationship duration with current partner (yr)	2.5 (1.5–4.0)
Intercourse frequency (wk)	1.0 (0.2–2.4)
	n (%)
Education	
Elementary school	1 (2.5)
High school	9 (22.5)
Professional study diploma	2 (5.0)
College	21 (52.5)
University	7 (17.5)
Marital status	
Regular partner	22 (55)
Cohabiting	16 (40)
Married	2 (5)
Birth control method	
Oral contraceptive	39 (97.5)
Previously attempted interventions	
Topical lidocaine	13 (35.0)
Topical oestrogen	4 (10)
Lubricant	1 (2.5)
Pelvic floor physical therapy	10 (25)
Antifungal	4 (10)
Natural products	2 (5)
None	19 (47.5)
More than one treatment	11 (27.5)

N = 40. Continuous variables are expressed as median and interquartile range (IQR). Categorial variables are presented as absolute numbers (percentage). Yr, year; wk, week.

4. Discussion

The present exploratory study examined the associations between clinical characteristics/ psychosexual factors and treatment response in women with PVD who received tDCS interventions. We found that women suffering from PVD having higher genital incompatibility cognitions had poorer outcomes, regardless of the treatment group. This suggests that genital incompatibility is associated with lower pain reduction in both the active and the sham group. Most importantly, women presenting higher depressive symptoms and better self-image thoughts had a better response to tDCS treatment. This association was

Table 2
Baseline potential predictors.

Variables	Pre-treatment	
	Mean or n (%)	95% CI
Clinical characteristics		
Pain intensity (NRS)	7.2	[6.8, 7.6]
Pain quality (MPQ-PRI)	23.9	[20.7, 27.1]
PVD subtype	–	–
Primary	10 (25)	
Secondary	30 (75)	
Duration of symptoms (yr)	3.4	[2.5, 4.3]
Pain sensitivity		
Thermal pain threshold (PT [°C])	39.7	[38.8, 40.7]
Thermal pain tolerance (PTol [°C])	47.0	[46.4, 47.5]
Psychosexual factors		
Pain catastrophizing (PCS)	26.4	[22.7, 30.0]
Pain related fear (PASS-20)	38.2	[32.4, 44.0]
State anxiety (STAI-S)	36.7	[33.2, 40.2]
Trait anxiety (STAI-T)	41.3	[37.5, 45.1]
Depressive symptoms (BDI)	7.7	[5.8, 9.6]
Vaginal Penetration and Cognition (VPCQ)		
Control cognitions (VPCQ_ctrl)	4.7	[4.3, 5.1]
Catastrophic and pain cognitions (VPCQ_catpain)	2.7	[2.2, 3.1]
Self-image cognitions (VPCQ_selfim)	2.3	[1.9, 2.8]
Positive cognitions (VPCQ_pos)	2.7	[2.3, 3.1]
Genital incompatibility cognitions (VPCQ_genincom)	1.8	[1.3, 2.4]
Sexual function (FSFI)	20.2	[18.5, 22.0]
Sexual distress (FSDS)	28.5	[24.7, 32.4]
Sexual satisfaction (GMSS)	21.5	[19.2, 23.9]

found in the active tDCS group but not in the sham group, and accounted for 62.3% of the variance for pain reduction. As these findings were found in the active group only, this emphasizes their relevance for potentially predicting tDCS outcome and identifying possible responders.

Of note, many clinical and psychosexual factors measured during this study, of which several were previously identified to contribute to treatment response in PVD women, did not emerge as significant predictors for successful outcome. For instance, past studies have shown that women with secondary PVD respond better to multidisciplinary treatment [31]and vestibulectomy surgery [6,36] than women with primary PVD. Lower levels of pain avoidance have also been associated with better treatment outcome for topical treatment interventions in PVD women, whereas a lesser fear of pain, lower catastrophizing, and greater pain self-efficacy at baseline have been identified as predictors of a better treatment outcome in both topical treatment and cognitive-behavioral therapy [11]. All psychological factors mentioned above, except self-efficacy, were assessed in the present study. Although we could have expected that the onset of pain, pain catastrophizing, pain-related fear, and pain avoidance levels would be associated with the tDCS response, none of the studied factors were associated with pain improvement. One possible explanation is that most of these studies looked at the effect of interventions acting on vulvo-vaginal structures whereas tDCS targets structures of the central nervous system.

4.1. Depressive symptoms

We observed that women who benefited the most from active tDCS were those presenting higher depressive symptoms. The contribution of psychological variables to predict experimental and clinical pain, as well as pain-associated disability, and treatment response in chronic-pain patients is well documented in both musculoskeletal disorders and PVD [18,19,20,51,38,64,41,42,24,26]. Our results extend these observations by suggesting that depressive symptoms can modulate treatment response in women receiving tDCS. Surprisingly, whereas high depression at baseline generally predicts poor treatment response [41,7], the opposite was observed in our study for tDCS treatment. The role of depression on treatment success might differ for tDCS interventions. In a study investigating the effect of tDCS in patients with fibromyalgia, Mendonca et al. showed that higher initial depressive symptoms were associated with better outcomes [44]. The underlying mechanism of action of tDCS and its effect on the neurocircuitry of mood regulation may explain these results [39,47]. In the present study, cathodal stimulation of the supraorbital area could have improved the mood in women presenting higher depressive scores and diffusely improve their pain perception.

4.2. Self-image and genital incompatibility cognitions

Lower negative self-image at baseline was also associated with higher pain relief at 3-month follow-up for women in the active tDCS group. Negative self-image relates to the conception that women do not perceive themselves as an adequate partner when penetration is unsuccessful [35]. Klaassen & Ter Kuile have shown that women with dyspareunia show higher levels of negative self-image cognitions compared to asymptomatic controls [35]. To the best of our knowledge, no previous study has looked into self-image cognition as a predictor of treatment success.

We also noticed that women with higher levels of genital incompatibility cognitions (negative genital thoughts – impression that vagina is too narrow or that the penis of partner is too big for penetration) conveyed a lower percentage of pain reduction, regardless of the treatment received. Indeed, this effect was not specific to the experimental group, suggesting that women with strong genital-incompatibility thoughts do not respond well to real or sham non-invasive brain stimulation. For many PVD patients, emotional responses related to pain might be more afflictive than the pain sensation itself [57]. PVD women presenting negative penetration cognitions have lower sexual satisfaction and function, and greater pain intensity during intercourse [2]. Treatments specifically addressing self-image and genital-incompatibility thoughts, such as CBT and other psychosexual interventions, could be relevant for women with negative cognitions.

5. Limitations

To our knowledge, this is the first study to identify psychosexual factors as predictors of tDCS response. Although this study was not initially designed to explore these predictive factors, interesting associations have been made between women's outcome and their psychosexual state. Nevertheless, the reader must bear in mind that these results are exploratory and need to be further validated by sufficiently powered trials specifically investigating clinical prediction rules, using more stringent methodological and statistical criteria. Also, considering the relative proximity of M1 and DLPFC, the dimension of the electrodes (35 cm^2) and the fact that their position was not confirmed by neuronavigation techniques, multiple cortical structures might all have been diffusely modulated by the tDCS [65]. Neuroimaging studies aiming to eval-

Table 3
Clinical and psychosexual factors predicting percentage of pain reduction at follow-up assessment in all women.

	Main effect				Interaction with treatment			
Predictors	b	SE	95% CI	P-*value*	b	SE	95% CI	P-*value*
Clinical characteristics								
Pain intensity (NRS)	3.45	4.66	[-6.01, 12.93]	0.46	9.84	9.34	[-9.12, 28.81]	0.30
Pain quality (MPQ-PRI)	−0.15	0.56	[-1.28, 0.97]	0.79	−1.37	1.10	[-3.61, 0.87]	0.22
PVD subtype	−10.69	11.65	[-34.32, 12.95]	0.36	−37.30	23.28	[-84.57, 9.96]	0.12
Duration of symptoms	2.29	1.94	[-1.66, 6.25]	0.25	1.23	3.93	[-6.74, 9.20]	0.76
PT	−1.39	2.02	[-5.59, 2.71]	0.50	−5.37	4.06	[-13.62, 2.88]	0.20
PTol	3.61	3.15	[-2.78, 9.99]	0.26	−3.79	6.28	[-16.56, 8.96]	0.55
Psychosexual factors								
Pain catastrophizing (PCS)	0.68	0.50	[-0.34, 1.71]	0.18	0.14	1.00	[-1.89, 2.18]	0.89
Pain related fear (PASS-20)	0.34	0.36	[-0.38, 1.08]	0.34	−0.11	0.71	[-1.56, 1.33]	0.88
State anxiety (STAI-S)	0.53	0.55	[-0.59, 1.65]	0.34	0.79	1.09	[-1.43, 3.01]	0.48
Trait anxiety (STAI-T)	0.62	0.48	[-0.34, 1.58]	0.20	0.38	0.94	[-1.53, 2.30]	0.69
Depressive symptoms (BDI)[†]	1.18	0.87	[-0.58, 2.95]	0.18	3.49	1.73	[-0.01, 6.99]	0.05
Vaginal Penetration and Cognition (VPCQ)								
Control cognitions (VPCQ_ctrl)	−7.40	4.26	[-16.05, 1.25]	0.09	4.68	8.48	[-12.53, 21.89]	0.58
Catastrophizing and pain cognitions (VPCQ_catpain)	−0.14	4.63	[-9.55, 9.26]	0.98	−2.64	9.15	[-21.22, 15.95]	0.77
Self-image cognitions (VPCQ_selfim)[†]	1.76	3.78	[-5.92, 9.44]	0.64	−15.94	7.56	[-31.28, −0.60]	0.04
Positive cognitions (VPCQ_pos)	−1.72	4.40	[-10.66, 7.21]	0.70	12.41	8.78	[-5.42, 30.23]	0.17
Genital incompatibility cognitions (VPCQ_genincom)	−9.01	2.82	[-14.73, −3.23]	0.003	6.83	5.67	[-18.34, 4.67]	0.24
Sexual function (FSFI)	−0.85	0.98	[-2.85, 1.14]	0.39	−0.33	1.96	[-4.31, 3.65]	0.87
Sexual distress (FSDS)	0.67	0.44	[-0.23, 1.56]	0.14	−1.10	0.88	[-2.89, 0.69]	0.22
Sexual satisfaction (GMSS)	−1.05	0.71	[-2.50, 0.40]	0.15	0.57	1.43	[-2.32, 3.46]	0.69

N = 39. NRS = Numeric Pain Rating Scale (range 0–10); MPQ-PRI = McGill-Melzack Pain Questionnaire total score; PVD = Provoked vestibulodynia; PT = Thermal Pain Thresholds; PTol = Thermal Pain Tolerance; PCS = Pain Catastrophizing Scale; PASS-20 = Pain Anxiety Symptoms Scale; STAI-S = State Anxiety Inventory of Spielberger; STAI-T = Trait Anxiety Inventory of Spielberger; ; BDI = Beck Depression Inventory-II; VPCQ = Vaginal Penetration and Cognition Questionnaire; ctrl = Control Cognitions subscale; catpain = Catastrophic and Pain Cognitions subscale; selfim = Self-Image Cognitions subscale; pos = Positive Cognitions subscale; genincom = Genital Incompatibility Cognitions subscale; FSFI = Female Sexual Function Index; FSDS = Female Sexual Distress Scale; GMSS = Global Measure of Sexual Satisfaction; b = unstandardized regression coefficient; SE = standard error; 95% CI indicates 95% confidence interval.
[†] Significant predictor ($P \leq 0.15$).

uate changes in brain structures or brain activation/deactivation patterns in women with PVD prior and after tDCS treatment are also needed.

In conclusion, our findings suggest that PVD women presenting higher depressive symptoms and lower negative self-image cognitions at baseline might derive greater benefits from tDCS. These results shed light on potential predictors of tDCS response, which could hopefully guide the design of future studies investigating at the efficacy of tDCS in women with PVD. The possibility that tDCS intervention would be effective in a subgroup only of women with PVD, such as women with higher depressive symptoms and lower negative self-image cognitions, is appealing, but needs to be confirmed in further investigation.

Funding

This research was funded by an operating grant from the Research Center of the CHUS. Drs. Morin and Léonard are supported by research salary award from the Fonds de la recherche du Québec – Santé (FRQ–S).

Trial registration

Clinicaltrials.gov, NCT02543593; clinicaltrials.gov/ct2/show/NCT02543593; registration date: September 4, 2015.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This research was funded by an operating grant from the Research Center of the CHUS. Drs. Morin and Léonard are supported by research salary award from the Fonds de la recherche du Québec – Santé (FRQ–S). The authors thank all the women who agreed to participate in the study.

Table 4
Multivariate regression analyses of the variables associated with percentage of intercourse pain reduction at follow-up assessment for women in the active and sham tDCS treatment.

	Active tDCS treatment				Sham tDCS treatment			
	b	SE	Standardized β	*P-value*	b	SE	Standardized β	*P-value*
Depressive symptoms (BDI)	3.928	0.815	0.788	<0.001	−0.058	1.418	−0.009	0.968
Self-image cognition (VPCQ_selfim)	−12.736	3.780	−0.551	0.004	9.482	5.557	0.388	0.106
	R^2 = 0.623, F(2,16) = 13.236, P < 0.001, Adjusted R^2 = 0.576				R^2 = 0.152, F(2,17) = 1.525, P = 0.246, Adjusted R^2 = 0.052			

tDCS = transcranial direct-current stimulation; N = 39. BDI = Beck Depression Inventory-II; VPCQ = Vaginal Penetration and Cognition Questionnaire; selfim = Self-Image Cognitions subscale; b = unstandardized regression coefficient; SE = standard error; R^2 = percentage of variance explained by the model; 95% CI indicates 95% confidence interval.

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