Scientific Research Publishing

Pain Studies and Treatment, 2023, 11, 27-42
https://www.scirp.org/journal/pst
ISSN Online: 2329-3276
ISSN Print: 2329-3268

Clinical Trial Demonstrates Efficacy of Transcranial Direct Current Stimulation (tDCS) in Improving Pain Management from Post-Laminectomy Syndrome

Marilia Capuço Oliveira, Fernanda Menezes de Faria, Gerardo Maria de Araújo Filho, Ana Carolina Gonçalves Olmos, Demosthenes Santana Silva Junior, Camila Souza Alves Cosmo

Department of Neurological Sciences, Psyquiatry and Medical Psychology, Faculdade de Medicina de São José do Rio Preto, São Paulo, Brazil
Email: marilia.capuco@edu.famerp.br

How to cite this paper: Oliveira, M.C., de Faria, F.M., de Araújo Filho, G.M., Olmos, A.C.G., Silva Jr., D.S. and Cosmo, C.S.A. (2023) Clinical Trial Demonstrates Efficacy of Transcranial Direct Current Stimulation (tDCS) in Improving Pain Management from Post-Laminectomy Syndrome. *Pain Studies and Treatment*, **11**, 27-42.
https://doi.org/10.4236/pst.2023.114004

Received: September 14, 2023
Accepted: October 24, 2023
Published: October 27, 2023

Abstract

Chronic pain, a multidimensional experience affecting individuals' sensory, cognitive, and emotional aspects, significantly impacts their quality of life. Post-laminectomy syndrome, a condition characterized by persistent back pain following spinal surgery, often leads to disability and increased healthcare utilization. Methods: This randomized, controlled, blind clinical trial aimed to investigate the efficacy of Transcranial Direct Current Stimulation (tDCS) in managing pain from post-laminectomy syndrome in patients. Twenty-four participants were assigned to three groups: sham stimulation, active stimulation over primary motor cortex (M1), or stimulation over dorsolateral prefrontal cortex (DLPFC). Stimulation was administered for five consecutive days, 20 minutes per session, using a current of 1.5 mA through 25 cm^2 electrodes. Pain intensity was assessed using Visual Analog Scale (VAS) before, during, and after intervention. Results: An ANOVA model demonstrates significant reduction in pain intensity compared to baseline in VAS, ($F(7, 285) = 12.292$; $p < 0.001$; Power = 1.000; $\eta 2p = 0.534$), in tDCS applied to M1, after five days of intervention. After stimulation, a significant improvement was observed in WHOQoL-Bref Quality of life item 1 ($p = 0.04$), considering statistical significant difference $p < 0.05$. Correlation between the variables: quality of life, depression, anxiety and pain also demonstrates reduction in depression and anxiety according to Beck's Depression and Anxiety Inventories (BDI and BAI), $p < 0.05$. This effect was not observed in DLPFC stimulation group. Patients who believed they received active stimulation, in sham group, demonstrated potential for effective blinding.

Conclusion: The tDCS applied to primary motor cortex effectively improved pain management and psychiatry symptoms in post-laminectomy syndrome patients. The technique's low cost, ease of use, and high tolerability make it a promising adjuvant therapy for chronic pain conditions like post-laminectomy syndrome.

Keywords

Non-Invasive Neuromodulation, Transcranial Direct Current Stimulation, Post-Laminectomy Syndrome, Chronic Pain

1. Introduction

Pain is defined as a multifaceted experience that affects not only sensory perception but also cognition and emotional well-being [1]. It exerts direct influences on quality of life whose individuals experiencing it [2]. According to International Association Study of Pain (IASP), chronic pain is characterized by continuous and recurrent symptoms persisting for a minimum of three months [3] [4], often associated with central sensitization [5]. Post-laminectomy syndrome, also referred as surgical failure syndrome, which is defined as "low back spinal pain of undetermined origin persisting in the same location as original pain despite surgical interventions or developing after surgeries" [6] [7]. Several clinical presentations of post-laminectomy syndrome frequently overlap, with low back pain being the predominant manifestation [7] [8]. When it persists, it leads to significant physical disability, increased use of analgesics, and heightened utilization of emergency services [8].

Also, disability resulting from chronic pain is a matter of great societal concern [9], with physiological, emotional, behavioral, and socio-cultural factors significantly influencing the progression, severity, and persistence of pain. In this regard, chronic pain is considered multidimensional [3] [10] [11].

Despite substantial advancements in pain management over recent decades, including pharmaceutical interventions and incorporation of patients into multidisciplinary therapies, chronic pain remains a formidable therapeutic challenge [2]. In this context, therapies directly modulating cortical activity, such as non-invasive brain stimulation, have gained increasing attention in treatments [2] [12].

Some researches appointed the efficacy of Transcrananial Direct Current Stimulation (tDCS) in chronic pain treatment [1] [2] [9] [13], such as the Pain Management Program at The Menninger Clinic in Houston, Texas. Eighty-four participants were randomized (1:1) into a single-blind, 2 × 12 (group × time) controlled trial. A battery-powered direct and constant current stimulator (Soterix Medical Inc. 2014) delivered anodal stimulation over the left dorsolateral prefrontal cortex (DLPFC) and cathodal stimulation over the right DLPFC. Active tDCS is applied by supplying a 2 mA current for 20 min/session over 10 ses-

sions. This study proves the efficacy of a minimally invasive neuromodulation technique as an adjunctive treatment for chronic pain among individuals with significant psychiatric comorbidity. A meta-analyses [13] included from 2 to 16 clinical trials demonstrates positive and larger effects on pain relief, quality of life, depression and anxiety by combining tDCS with aerobic exercise or even in intervention alone.

Despite several studies involving tDCS in chronic pain, to our knowledge, there is limited literature supporting the potential benefits of adjunctive tDCS a in pain management in post-laminectomy syndrome patients. This study aims to provide that (tDCS) shall improve as a efficacy treatment in this cases. Furthermore, this technique's low cost, ease of use, and high tolerability make it a promising adjuvant therapy for chronic pain conditions like post-laminectomy syndrome.

2. Methods

2.1. Design

This is a randomized, controlled, double-blind clinical trial. Approval for this study was granted by Research Ethics Committee of Faculdade de Medicina de São José do Rio Preto (FAMERP) under opinion number 1.291.038, in 2019.

Twenty-four individuals suffering from chronic pain due to post-laminectomy syndrome were enrolled in this study. Participants were recruited from Chronic Pain Clinic of Faculdade de Medicina de São José do Rio Preto and Centro Traumatológico Ortopédico de São José do Rio Preto. The patients completed a form for selection or exclusion, attached in **Appendix 1**. As a limitation of the study, a small sample size was chosen due to difficulties in patient transportation (most of them came from other cities) and their refusal to participate in the study due to worsened pain and discomfort during transportation. To standardize the study, the maximum number of patients that could be selected was divided into three groups with an equal number of individuals.

Transcranial direct current stimulation instrument used was TCT (Trans Cranial Technologies (TCT) Research Limited) (28). Participants were divided into three distinct groups. Group 1 underwent sham stimulation, while active stimulation was administered over primary motor cortex (M1) for Group 2 (M1) and dorsolateral prefrontal cortex (CDLPF) for Group 3.

Stimulation occurred over five consecutive days, with each session lasting 20 minutes, delivering a current of 1.5 mA via 25 cm^2 electrodes. Electrodes soaked in a saline solution facilitated passage of electric current. Cathode electrode was positioned in extraball region, over deltoid muscle. Choice of hemisphere for stimulation was determined by lateralization of pain. For patients with asymmetric pain, contralateral hemisphere was stimulated, whereas for those with symmetric pain, right-handed patients received stimulation in left hemisphere, and left-handed patients received it in right hemisphere. Regarding sham stimulation, electrodes were placed in the same position as the anodic stimulation in

M1. Sham stimulation consisted of a 30-second application followed by discontinuation. The 30-second ramp-up period allowed patients in control group to experience initial sensations of current passage, such as local discomfort and itching.

Each group comprised eight individuals. Randomization of patients involved pre-determining a specific type of stimulation in week. Thus, patients in each week received the same type of stimulation, considering possibility that these patients shared the same environment while awaiting treatment.

In the end of each session, patients were asked which type of stimulation they believed had received to evaluate blinding. Adverse events were also assessed through open-ended questions, with sleep quality also being evaluated.

Pain assessment employed by Brief Pain Inventory (33) (BPI) and Visual Analog Scale (VAS) Additionally, World Health Organization Brief Quality of Life Questionnaire (WHOQoL-Bref) (29), Short Form Health Survey (SF-12) (30), Beck's Depression and Anxiety Inventories (BDI and BAI) (31, 32), and Clinical Global Impression Scale (34) (CGI) were applied. All instruments were administered in initial evaluation before intervention, except for CGI (disease improvement) and VAS. CGI was applied after five days of stimulation, while VAS was used at eight different time points: 1) before stimulation (baseline VAS); 2) after fifth day stimulation (post-intervention); 3) in the first; 4) second; 5) third; 6) and fourth weeks after the end of stimulation (VAS 1, 2, 3, 4 weeks); 7) in the second month; and 8) in the third month after sessions (VAS 1 and 2 months). Clinical improvement was defined as a reduction at least 1 point on post-intervention VAS compared to baseline VAS.

Exclusion criteria encompassed: a) individuals taking carbamazepine, based on previous studies suggesting attenuation of tDCS effects in individuals using this medication; b) patients with metallic objects above neck, as they could interfere with electrical current direction.

2.2. Statistical Analysis

Data normality distribution and homoscedasticity were assessed using Shapiro-Wilk and Levene tests, respectively. Comparisons between groups were conducted using the following methods: ANOVA-one way (for normally distributed and homoscedastic data), ANOVA-Welch (for heteroscedastic data), Kruskal-Wallis (for data with no assumed normal distribution, comparing three groups), and Mann-Whitney (for data with no assumed normal distribution, comparing two groups). Fisher's test was employed for qualitative variables. The threshold for statistical significance was set at 5%.

3. Results

The sample comprised 24 subjects, evenly distributed between three groups with 8 subjects in each group (n = 8). Table 1 presents the sample characterization based on clinical intervention groups, with no statistically significant differences observed between them ($p > 0.05$).

Table 1. Sample description.

Variable N	Group				
	Sham	M1	CDLFP	Total	p
Sex	8	8	8	24	0.87
Female	5	3	4	12	
Male	3	5	4	12	
Age					0.37
average ± dp	52 ± 11.33	58 ± 6.20	52 ± 8.80	54 ± 9.04	
Education					0.47
Illiterate	-	-	-	-	
Incomplete secondary education	3	4	1	8	
Complete secondary education	4	4	5	13	
Complete higher education	1	-	2	3	
Marital Status					1.00
Single	1	1	-	2	
Married	6	6	6	18	
Divorced	1	1	2	4	
Widowed	-	-	-	-	
Religion	-	-	-	-	1.00
No	2	1	2	5	
Yes	6	7	6	19	
Housing					0.62
Same city as the research	5	5	7	17	
Other city	3	3	1	7	
Belief Stimulation					1.00
No	1	-	1	2	
Yes	7	8	7	22	

Overall, participants provided positive evaluations for items related to their quality of life, as average scores for most items exceeded 2.5. The items that received lowest ratings were satisfaction with health (WHOQoL: 2), ability to perform daily activities without pain (WHOQoL: 3), need for treatment to lead a normal life (WHOQoL: 4), availability of leisure opportunities (WHOQoL: 14), and ability to work (WHOQoL: 18).

The sample had a mean total score (standard deviation) of 16.42 (10.39) on Beck Depression Inventory (BDI). None of items received a high average re-

sponse, *i.e.*, above midpoint of response scale (1.50). Concerning the distribution of individuals based on severity of depression, 14 had no depression, 3 had mild depression, 4 had moderate depression, and 3 had severe depression.

For the Beck Anxiety Inventory (BAI), the sample had a mean total score (standard deviation) of 16.58 (13.28). Notably, the mean responses for items BAI 4 (inability to relax) and BAI 10 (feeling nervous) exceeded midpoint of response scale (1.5). Regarding distribution of individuals according to severity of anxiety, 8 had no anxiety, 5 had mild anxiety, 8 had moderate anxiety, and 3 had severe anxiety.

Participants reported experiencing moderate to severe pain levels, with pain affecting general activities, mood, walking, and work the most.

Most individuals (n = 15, 62.5%) were undergoing some form of pain treatment (BPI 7), with an average pain relief percentage of 39.0% (sd = 23.1) (BPI 8).

The distribution of variables such as quality of life, degree of depression and anxiety, pain intensity, pain interference with activities and mood, and overall clinical impression of severity and improvement among individuals is presented in Table 2, broken down by intervention groups.

Concerning characteristics detailed in Table 2, the distribution of individuals across the groups remained uniform. There was a notable positive association between improvement of individuals, as assessed by Clinical Global Impression scale, and intervention group, with a significant improvement observed in individuals allocated to Group M1.

Additionally, regarding the effects after clinical intervention, presence of side effects and improvements in sleep were documented.

Reported side effects included headache (n = 8), pruritus (n = 5), and tingling (n = 1). Headaches were exclusively reported in active stimulation groups (M1 and CDLFP). In contrast, the sham group only reported pruritus.

Regarding improvements in sleep, there were more subjects who reported enhanced sleep quality in Group M1. However, these differences between groups did not achieve statistical significance.

Correlation study examining relationships between variables such as quality of life, depression, anxiety, and pain is presented in Table 3.

It is noted that patient's initial report of intensity of their pain is positively correlated to severity of their depression. The states of depression and anxiety are inversely correlated to all aspects of quality of life. Quality of life shows a higher correlation (inversely proportional) with interference of pain in individual's daily life than with reported pain intensity. The effect of tDCS on the assessment of pain intensity, based on VAS, is shown in Table 4. The minimum pain reported on VAS by participants at beginning of study was 6.38 ± 0.92.

As it is notable in Table 4, there was improvement in pain intensity following tDCS in Group M1, mainly after a week intervention (3.88 ± 1.55), with statistically significant improvement ($F(7, 285) = 12.292$; $p < 0.001$; Power = 1.000; $\eta 2p = 0.534$). However, the degree of improvement among individuals depends on the interaction between time and the stimulation group. This improvement

Table 2. Comparison of variables according to intervention groups.

Variable	Group				
	Sham	M1	CDLFP	Total	P
WHOQoL					
Life quality (item 1)	2.75 ± 1.28	3.38 ± 0.92	2.88 ± 1.02	3.00 ± 1.02	0.45†
Health satisfaction (item 2)	2.38 ± 1.06	2.75 ± 1.16	2.50 ± 1.07	2.54 ± 1.06	0.88†††
Physical	42.25 ± 27.26	42.88 ± 1.71	43.00 ± 16.18	42.71 ± 19.05	0.94†††
Psychological	61.13 ± 23.87	62.63 ± 21.41	63.38 ± 15.67	62.38 ± 19.71	0.98†
Social relations	64.13 ± 23.74	61.75 ± 20.89	61.63 ± 24.12	62.50 ± 21.97	0.92†††
Environment	61.75 ± 14.24	61.88 ± 14.95	68.75 ± 10.96	64.13 ± 13.32	0.51†
SF-12					
Physical Component	33.24 ± 7.42	30.23 ± 4.51	31.92 ± 6.16	31.80 ± 6.01	0.62†
Mental Component	49.75 ± 12.29	42.03 ± 12.86	49.65 ± 12.86	47.15 ± 12.66	0.39†
BDI Depression Rating					
None	5	3	6	14	0.86
Slight	1	2	-	3	
Moderate	1	2	1	4	
Severe	1	1	1	3	
BAI Anxiety rating					
None	2	3	3	8	1.00
WHOQoL					
Life quality (item 1)	2.75 ± 1.28	3.38 ± 0.92	2.88 ± 1.02	3.00 ± 1.02	0.45†
Health satisfaction (item 2)	2.38 ± 1.06	2.75 ± 1.16	2.50 ± 1.07	2.54 ± 1.06	0.88†††
Physical	42.25 ± 27.26	42.88 ± 13.71	43.00 ± 16.18	42.71 ± 19.05	0.94†††
Absent	7	4	8	19	0.08
Present	1	4	-	5	

*statistically significant (= 5%) difference; †ANOVA-one way; ††ANOVA-Welch; ††††Kruskal-Wallis.

Table 3. Correlation between the variables quality of life, depression, anxiety and pain.

	1	2	3	4	5	6	7	8	9	10	11	12
1) Physical	1.00	0.61**	0.59**	0.44*	0.70**	0.53**	−0.75**	−0.73**	−0.26	−0.70**	−0.63**	−0.66**
2) Psychological	-	1.00	0.84**	0.55**	0.32	0.74**	−0.79**	−0.64**	−0.37	−0.63**	−0.37	−0.74**
3) Social Relations	-	-	1.00	0.44*	0.35	0.65**	−0.79**	−0.56**	−0.54**	−0.70**	−0.57**	−0.72**
4) Environment	-	-	-	1.00	0.34	0.52**	−0.55**	−0.64**	−0.41*	−0.52**	−0.47*	−0.50*
5) Physical Compenent	-	-	-	-	1.00	0.24	−0.60**	−0.63**	-0.14	−0.50*	−0.51*	−0.43*
6) Mental Component	-	-	-	-	-	1.00	−0.71**	−0.67**	−0.23	−0.64**	−0.46*	−0.69**
7) BDI_sum	-	-	-	-	-	-	1.00	0.80**	0.46*	0.75**	0.62**	0.75**
8) BAI_sum	-	-	-	-	-	-	-	1.00	0.30	0.65**	0.54**	0.65**

Continued

9) Pain intensity	-	-	-	-	-	-	-	-	1.00	0.62**	0.67**	0.51*
10) Pain Interference Total	-	-	-	-	-	-	-	-	-	1.00	0.91**	0.95**
11) Pain Interference Activity	-	-	-	-	-	-	-	-	-	-	1.00	0.73**
12) Pain Interference Affectivity	-	-	-	-	-	-	-	-	-	-	-	1.00

*statistically significant difference ($p < 0.05$); **statistically significant difference ($p < 0.001$).

Table 4. Effect of intervention on pain intensity assessment using VAS.

VAS (time)	Group			
	Sham	M1	DLPFC	Total
Baseline	6.38 ± 0.92[a]/A	7.25 ± 1.58[a]/A	6.63 ± 1.30[a]/A	6.75 ± 1.29
After intervention	6.63 ± 0.92[a]/A	3.75 ± 1.49b/D	6.13 ± 1.46[a]/A	5.50 ± 1.79
1 week	6.50 ± 0.53[a]/A	3.88 ± 1.55b/D	6.13 ± 1.46[a]/A	5.50 ± 1.69
2 week	6.63 ± 1.06[a]/A	4.38 ± 1.41b/D	6.50 ± 1.51[a]/A	5.83 ± 1.66
3 week	6.38 ± 1.06[a]/A	5.25 ± 1.83[a]/C	6.75 ± 1.39[a]/A	6.13 ± 1.54
4 week	6.63 ± 0.52 [a]/A	5.88 ± 1.89[a]/C,B	6.50 ± 1.07[a]/A	6.33 ± 1.27
2 months	6.50 ± 0.93[a]/A	6.25 ± 1.91[a]/A,B	6.13 ± 1.46[a]/A	6.29 ± 1.43
3 months	6.50 ± 0.93[a]/A	6.00 ± 1.69[a]/B	6.63 ± 1.41[a]/A	6.38 ± 1.35
Total	6.52 ± 0.87	5.33 ± 2.01	6.42 ± 1.17	6.09 ± 1.54

A, b Different letters indicate statistically significant differences, capital letters indicate differences between lines, lower case letters indicate differences between row.

persisted for four weeks after conclusion of care protocol. However, beginning the third week, the average pain intensity reported by participants in this group started to resemble reports of individuals in other groups (6.00 ± 1.69).

Regarding improvement of participants, Table 5 provides the profile of individuals who experienced either improvement or not in pain intensity following clinical intervention.

As it is mentioned in Table 5, there was a statistically significant difference in how individuals assess their quality of life WHOQoL-item 1 ($p = 0.04$), considering statistical significant difference $p < 0.05$. Those who reported improvement in pain intensity tended to rate their quality of life higher than those who did not experience improvement. However, it's important to note that these differences, while clinically meaningful, did not achieve statistical significance. For instance, among individuals who reported improvement (n = 14), 86% (n = 12) had no or mild depression. It is worth mentioning that the relatively small sample size may have limited statistical power of these findings.

Among individuals who exhibited some degree of anxiety and/or depression (n = 17), we investigated whether there was an association between pain

Table 5. Profile of individuals according to improvement or not in pain intensity (baseline VAS-after intervention).

Variable	Improvement VAS (Baseline-After)			
	No	Yes	Total	P
N	10	14	24	
Gender				
Female	5	7	12	1.00
Male	5	7	12	
Age				0.75†
Average ± dp	53.40 ± 8.91	54.54 ± 9.43	54.13 ± 9.04	
Education				
Illiterate	-	-	-	1.00
Incomplete secondary education	3	5	8	
Complete higher education	7	6	13	
	-	3	3	
Marital Status				
Single	1	1	2	1.00
Married	8	10	18	
Divorced	1	3	4	
Widowed	-	-	-	
Religion				
No	3	2	5	1.00
Yes	7	12	19	
Housing				
Same city as the research	6	11	17	0.39
Other city	4	3	7	
Belief stimulation				
No	1	-	2	0.42
Yes	7	8	22	
WHOQoL				
Quality of Life (item 1)	2.50 ± 0.97	3.36 ± 0.93	3.00 ± 1.02	0.04†*
Health satisfaction (item 2)	2.20 ± 1.03	2.79 ± 1.05	2.54 ± 1.06	0.23††
Physical	34.50 ± 22.20	48.7 ± 14.58	42.71 ± 19.05	0.07†
Psychological	56.30 ± 21.18	66.71 ± 18.12	62.38 ± 19.71	0.21†
Social Relations	52.50 ± 24.04	69.64 ± 17.95	62.50 ± 21.97	0.09††
Environment	60.60 ± 12.79	66.64 ± 13.58	64.13 ± 13.32	0.28†

Continued

SF-12				
Physical Component	30.26 ± 7.75	32.90 ± 4.37	31.80 ± 6.01	0.30†
Mental Component	43.08 ± 14.72	50.05 ± 10.57	47.15 ± 12.66	0.19†
BDI Depression Rating				
None	4	10	14	0.08
Slight	1	2	3	
Moderate	3	1	4	
Severe/extremely severe	6	6	12	
Improvement				
Improvement	1	5	6	0.34
No changes	8	9	17	
Worsens	1	-	1	
Side Effects				
Absent	3	8	11	0.24
Present	7	6	13	
Sleep Improvement				
Absent	9	10	19	0.36
Present	1	4	5	

*statistical significant difference (= 5%); †ANOVA-one way; †††Man-Whitney.

improvement (baseline VAS - after intervention) and the intervention group (Table 6).

4. Discussion

Transcranial Direct Current Stimulation (tDCS) is a promising neuromodulation technique that has garnered extensive attention as a therapeutic option for various neuropsychiatric disorders as well as cognitive and physical rehabilitation [10]. Recent clinical trials have yielded satisfactory responses in treatment of a wide range of pain disorders, including headache, fibromyalgia, chronic pelvic pain, neuropathic pain, and chronic low back pain [2] [5] [14]-[20]. To our knowledge, this clinical trial represents one of few investigations into application of tDCS in post-laminectomy syndrome as an adjunctive treatment for pain control.

Post-laminectomy syndrome is a condition that arises subsequent to surgeries that did not meet the initial expectations of both patient and surgeon, affecting approximately 10% to 40% of individuals undergoing such procedures [18]. Pain constitutes one of primary consequences, leading to patient dissatisfaction, often being reported as more severe following surgical intervention [18] [21].

As noted by Teixeira *et al.* [21] the evaluation and treatment of this syndrome pose a challenge for medical team, given low success rate of reoperations. Consequently, complementary therapies have emerged as alternatives for pain

Table 6. Association study between improvement in pain intensity (VAS) and intervention group in patients with some degree of depression and anxiety.

	Group			
EVA Improvement (Baseline-After)	Sham	M1	CDLFP	Total
No	4	1	2	7
Yes	2	5	3	10
TOTAL	6	6	5	17

management in this patient population. Among these therapeutic approaches for pain modulation, non-invasive techniques like tDCS have gained prominence. This clinical trial has demonstrated the effectiveness of tDCS in reducing pain intensity in Group M1, mainly after a week intervention (3.88 ± 1.55), with statistically significant ($F(7, 285) = 12.292$; $p < 0.001$; Power = 1.000; $\eta 2p = 0.534$).

The analgesic effects of Transcranial Direct Current Stimulation (tDCS) are believed to originate from modulation of excitability in brain regions associated with medial system and descending inhibitory pain system [10] [11]. Valle *et al.* [22] propose that anodic stimulation in the primary motor cortex (M1) produces analgesic effects through modulation of thalamic inhibitory pathways, among other cortico-cortical and cortico-subcortical projections involved in pain processing. In a study investigating the application of transcranial magnetic stimulation, de Andrade *et al.* [22] demonstrated that stimulation of M1 induces analgesic effects and involves opioid system as one of the circuits modulated.

Regarding various targets for pain modulation through stimulation, the existing literature suggests that stimulating M1 is effective in pain control. Some studies have also shown pain improvement after dorsolateral prefrontal cortex (DLPFC) stimulation, with these effects often accompanied by enhancements in cognition and emotional symptoms. Consequently, this region has been identified as a promising target for modulating emotional aspects of pain, as well as for addressing depressive and anxious symptoms [18] [20] [23]. Interestingly, in our study, the application of tDCS to CPFDL did not lead to significant improvements in pain control.

It is important to highlight that post-laminectomy syndrome is a chronic pain condition. Individuals dealing with chronic pain often present with psychiatric comorbidities, such as depression and anxiety [20] [24] [25]. Approximately 30% to 45% of chronic pain patients receive a diagnosis of these psychiatric conditions.

This study provides valuable insights into potential application of Transcranial Direct Current Stimulation (tDCS) as a neuromodulation technique in management of post-laminectomy syndrome. It is clear from literature that this condition, which develops after surgeries that do not meet initial expectations, is associated with chronic pain and often presents with comorbidities such as depression and anxiety, making it a complex challenge for medical teams [6] [20]

[24] [25].

The study results reveal several positive aspects:

4.1. Association between Depression and Pain

There is a significant association between depression and pain intensity and improvement. The relationship between depression and chronic pain is complex, with both conditions possibly contributing to each other due to shared biological substrates. Chronic pain can increase substances like P-substance and cytokines while decreasing catecholamine action, potentially predisposing individuals to depression. Conversely, depression can impact pain perception and sensitivity by affecting substance P levels and inhibitory mechanisms [5]. This study demonstrates reduction in depression and anxiety according to Beck's Depression and Anxiety Inventories (BDI and BAI), $p < 0.05$ in M1 group.

4.2. Safety Profile

tDCS appears to have a generally safe profile, with reported adverse events such as tingling, headache, pruritus, and nausea being of minor severity [6] [26] [27] [28].

Blinding: The study's sham technique effectively blinded participants, with some believing they were receiving active stimulation despite being in the sham group. This blinding technique, which provides initial sensations of active stimulation through a brief (30 seconds) period, contributes to maintaining the double-blind design. The study underscores the feasibility of tDCS in clinical practice, given its significant impact on pain control, safety, and device accessibility.

4.3. Quality of Life

A substantial proportion of the patients reported impaired quality of life, consistent with existing literature [5] [6] [29] [30]. There was a clear association between patients' assessment of their quality of life and their pain improvement. Quality of life also inversely correlated with pain intensity, underlining the multidimensional nature of pain. After stimulation in M1 group, a significant improvement was observed in WHOQoL-Bref Quality of life item 1 ($p = 0.04$), considering statistical significant difference $p < 0.05$. It highlights the importance of evaluating pain from multiple aspects beyond just intensity, considering factors like pain interference with daily activities and affectivity.

Despite these valuable findings, the study has some limitations. The sample size, while sufficient to demonstrate the efficacy of tDCS with high power and effect size, may not have allowed for an in-depth examination of the impact of various patient characteristics on treatment outcomes. Additionally, the study focused solely on pain intensity measured by the VAS, while future research should explore tDCS's effects on other dimensions of pain and related aspects such as quality of life and psychiatric comorbidities. Further clinical trials with

comprehensive protocols are recommended to investigate the broader impact of tDCS in individuals with post-laminectomy syndrome.

5. Conclusions

The application of Transcranial Direct Current Stimulation (tDCS) to the primary motor cortex has demonstrated its effectiveness in pain management for patients with post-laminectomy syndrome. Interestingly, the comorbidities present in the patients did not appear to have a significant association with the observed pain improvement. This suggests that tDCS may be a promising adjuvant therapy for modulating chronic pain in conditions like post-laminectomy syndrome.

Furthermore, tDCS appears to offer several advantages, including its cost-effectiveness, high tolerability, and ease of management. These characteristics make it a feasible and attractive option for inclusion in the treatment regimen for individuals dealing with chronic pain.

The study's findings highlight the potential of tDCS as a valuable addition to the therapeutic toolkit for managing chronic pain, particularly in cases like post-laminectomy syndrome. Further research and clinical trials are encouraged to explore and validate the broader applications of tDCS in pain management and its potential benefits for patients with various chronic pain disorders.

Acknowledgements

We would like to extend our gratitude to all patients who participated and consented to the publication of this report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] DosSantos, M.F., Love, T.M., Martikainen, I.K., Nascimento, T.D., Fregni, F., Cummifor, C., Deboer, M.D., Zubieta, J.K. and DaSilva, A.F.M. (2012) Immediate Effects of tDCS on the Opioide System of a Cronic Pain Patient. *Frontiers in Psychiatry*, **3**, Article 31714. https://doi.org/10.3389/fpsyt.2012.00093

[2] Fregni, F., Freedman, S. and Pascual-Leone, A. (2007) Recent Advances in the Treatment of Chronic Pain with Non-Invasive Brain Stimulation Techniques. *The Lancet Neurology*, **6**, 188-191. https://doi.org/10.1016/S1474-4422(07)70032-7

[3] Marques Filho, P.R. (2014) Impacto da Estimulação Transcraniana por Corrente Contínua (ETCC) na resposta comportamental e neuroquímica de ratos submetidos a um modelo de dor neuropática. Master's Thesis, Universidade Federal do Rio Grande do sul, Porto Alegre.

[4] Dellaroza, M.S.G., Furuya, R.K., Cabrera, M.A.S., Matsuo, T., Trelha, C., Yamada, K.N. and Pachola, L. (2008) Caracterização da dor crônica e métodos analgésicos utilizados por idosos da comunidade. *Revista da Associação Médica Brasileira*, **54**,

36-41. https://doi.org/10.1590/S0104-42302008000100018

[5] David, M.C.M.M. and Franco, C.I.F. (2017) Estimulação transcraniana por corrente contínua na modulação da dor neuropática: Uma revisão sistemática. Universidade Estadual da Paraíba.

[6] Ferreira, K.A.S.L., Siqueira, S.R.D.T. and Teixeira, M.J. (2008) Características demográficas, da dor e do tratamento dos pacientes atendidos em Centro Multidisciplinar de Dor. *Cadernos Saúde Coletiva*, **16**, 449-470.

[7] Von Roenn, J.H., Paice, J.A. and Preodor, M.E. (2008) Current Diagnóstico e Tratamento—Dor. McGrawHill, New York.

[8] Boggio, O.S., Zaghi, S. and Fregni, F. (2009) Modulation of Emotions Associated with Images of Human Pain Using Anodal Transcranial Direct Current Stimulation. *Neuropsychologia*, **47**, 212-217. https://doi.org/10.1016/j.neuropsychologia.2008.07.022

[9] Radu, A.S. (2000) Síndrome pós-laminectomia e fibrose epidural. *Revista Brasileira de Reumatologia*, **40**, 137-148.

[10] Fregni, F., Boggio, P.S. and Brunoni, A.R. (1994) Neuromodulação Terapêutica—Princípios e avanços da estimulação cerebral não invasiva em neurologia, reabilitação, psiquiatria e neuropsicologia. Sarvier, São Paulo, 2012.

[11] Guyton, A.C., Hall, M.E. and Hall, J.E. (2021) Tratado de fisiologiamédica. 14. Ed., Grupo GEN, Rio De Janeiro, 1121.

[12] Pinto, C.B., Teixeira Costa, B., Duarte, D. and Fregni, F. (2018) Transcranial Direct Current Stimulation as a Therapeutic Tool for Chronic Pain. *The Journal of ECT*, **34**, e36-e50. https://doi.org/10.1097/YCT.0000000000000518

[13] Boggio, P.S., Zaghi, S., Lopes, M. and Fregni, F. (2008) Modulatory Effects os Anodal Transcranial Direct Current Stimulation on Perception and Pain Thresholds in Healthy Volunteers. *European Journal of Neurology*, **15**, 1124-1130. https://doi.org/10.1111/j.1468-1331.2008.02270.x

[14] Fenton, B.W., Palmieri, P.A., Boggio, P., Fanning, J. and Fregni, F. (2009) A Preliminaty Study of Transcranial Direct Current Stimulation for the Treatment of Refractory Chronic Pelvic Pain. *Brain Stimulation*, **2**, 103-107. https://doi.org/10.1016/j.brs.2008.09.009

[15] Okano, A.H., Montenegro, R.A., Farinatti, P.T.V., Li, L.M., Brunoni, A.R. and Fontes, E.B. (2013) Estimulação cerebral na promoção da saúde e melhoria do desempenho físico. *Revista Brasileira de Educação Física e Esporte*, **27**, 315-332. https://doi.org/10.1590/S1807-55092013005000009

[16] Krause, B., Marquez-Ruiz, J. and Kadosh, R.C. (2013) The Effect of Transcranial Currente Stimulation: A Role for Cortical Excitation/Inhibition Balance? *Frontiers in Human Neuroscience*, **7**, Article 59351. https://doi.org/10.3389/fnhum.2013.00602

[17] Shansis, F. (2012) Tratado de PsiquiatriaClínica 5. Ed: Hales, Yudofsky e Gabbard. *Brazilian Journal of Psychiatry*, **34**, 122-122. https://doi.org/10.1590/S1516-44462012000100024

[18] Teixeira, M.J., Yeng, L.T., Garcia, O.G., Fonoff, E.T., Paiva, W.S. and Araujo, J.O. (2011) Síndrome dolorosa pós-laminectomia: Estudo descritivo da abordagem terapêutica em 56 pacientes. *Revista da Associação Médica Brasileira*, **57**, 286-291. https://doi.org/10.1590/S0104-42302011000300010

[19] Cavenaghi, V.B., Serafim, V., Devido-Santos, M., Simis, M., Fregni, F. and Gagliardi, R.J. (2013) Estimulação cerebral não-invasiva na prática clínica: Atualização. *Arquivos*

Médicos dos Hospitais e da Faculdade de Ciências Médicas da Santa Casa de São Paulo, **58**, 29-33.

[20] Rosa, M.A. and Rosa, M.O. (2013) Estimulação Magnética Transcraniana em Psiquiatria: Guia básico. 2ª edição, Sarvier, São Paulo.

[21] Fregni, F., Boggio, P.S., Lima, M.C., Ferreira, M.J.L., Wagner, T., Rigonatti, S.P., Castro, A.W., Souza, D.R., Riberto, M., Freedman, S.D., Nitsche, M.A. and Pascual-Leone, A. (2006) A Sham-Controlled, Phase II Trial os Transcranial Direct Current Stimulation for the Treatment of Central Pain in Traumatic Spinal Cord Injury. *Pain*, **122**, 197-209. https://doi.org/10.1590/S0104-42302011000300010

[22] Warner, T., Fregni, F., Fecteau, S., Grodzinsky, A., Zahn, M. and Pascual-Leone, A. (2007) Transcranial Direct Current Stimulation: A Computer-Based Human Model Study. *NeuroImage*, **35**, 1113-1124. https://doi.org/10.1016/j.neuroimage.2007.01.027

[23] Castro, M.M.C., Quarantini, L.C., Daltro, C., Pires-Caldas, M., Koenen, K.C., Kraychete, D.C. and Oliveira, I.R. (2011) Comorbidade de sintomas ansiosos e depressivos em pacientes com dor crônica e o impacto sobre a qualidade de vida. *Archives of Clinical Psychiatry* (*São Paulo*), **38**, 126-129. https://doi.org/10.1590/S0101-60832011000400002

[24] DaSilva, A.F., Mendonça, M., Zaghi, S., Lopes, M., Santos, M.F., Spierings, E.L., *et al.* (2014) sTCD-Indulced Analgesia and Electrical Fields in Pain Related Neural Networks in Chronic Migraine. *Headache*, **52**, 1283-1295. https://doi.org/10.1111/j.1526-4610.2012.02141.x

[25] Mori, F., Codeca, C., Kusayanagi, H., Moteleone, F., Buttari, F., Fiore, S., *et al.* (2010) Effects of Anodal Transcranial Direct Current Stimulation on Chronic Neurophatic Pain in Patients with Multiple Sclerosis. *The Journal of Pain*, **11**, 436-442. https://doi.org/10.1016/j.jpain.2009.08.011

[26] http://www.trans-cranial.com/

[27] Power, M., Kuyken, W., Orley, J., Herrman, H., Schofield, H., Murphy, B., *et al.* (1998) The World Health Organization Quality of Life Assessment (WHOQOL): Development and General Psychometric Properties. *Social Science & Medicine*, **46**, 1569-1585. https://doi.org/10.1016/S0277-9536(98)00009-4

[28] Ware, J.E., Kosinski, M. and Keller, S.D. (1995) SF-12: How to Score the SF-12 Physical and Mental Health Summary Scales. 2nd Edition, The Health Institute, New England Medical Center, Boston.

[29] Janice Jimenez-Torres, G., Weinstein, B.L., Walker, C.R., Christopher Fowler, J., Ashford, P., Borckardt, J.J. and Madan, A. (2017) A Study Protocol for a Single-Blind, Randomized Controlled Trial of Adjunctive Transcranial Direct Current Stimulation (tDCS) for Chronic Pain among Patients Receiving Specialized, Inpatient Multimodal Pain Management. *Contemporary Clinical Trials*, **54**, 36-47. https://doi.org/10.1016/j.cct.2016.12.024

[30] Antal, A., Terney, D., Kühnl, S. and Paulus, W. (2010) Anodal Transcranial Direct Current Stimulation of the Motor Córtex Ameliorates Chronic Pain and Reduces Short Intracortical Inhibition. *Journal of Pain and Symptom Management*, **39**, 890-903. https://doi.org/10.1016/j.jpainsymman.2009.09.023

Appendix 1

Pre-screening form

Do I have your permission to proceed? Yes _____	No _____	
Please answer yes or no to respond the following pre-screening questions	Include	Exclude
Are you 18 years old or older?		
Were you admitted to Chronic Pain Clinic or Centro Traumatológico Ortopédico?		
Where are you right now? Could you say your name?		
Do you have chronic pain diagnosis?		
Are you pregnant or suspect you may be pregnant?		
Do you have any skin disease or noticeable skin irritations or cuts?		
Have you ever been diagnosed with Raynauld Syndrome?		
Do you suspect you are experiencing any delusions, hallucinations or difficulty speaking?		
Have you ever been diagnosed with epilepsy? Have you ever had a seizure?		
Do you have a metallic intracranial implant?		
Have you ever had severe cranial trauma?		
Do you have any clinic comorbidity? Are unstable at the present?		
If you are elegible to participate in this study, please ask for the monitor to receive the instructions		