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Effect of transcranial direct current stimulation (tDCS) and transcutaneous electrical nerve stimulation (TENS) in knee osteoarthritis

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Abstract

Introduction. To compare the effectiveness of transcranial direct current stimulation (tDCS) and transcutaneous electrical nerve stimulation (TENS) when used in combination or in isolation on pain, function, and quality of life in primary knee osteoarthritis.

Methods. A 4-arm parallel group, participant-blinded, placebo-controlled randomized trial was performed. Patients with chronic knee osteoarthritis as per the American College of Rheumatology criteria were eligible. The lottery method was used for randomization and blocked randomization served to ensure an equal number of patients in each group. The participants were allocated to 4 groups and received tDCS and TENS either in combination or in isolation. Pain, function, and quality of life were measured with a visual analogue scale, 6-minute walk test, and Knee Injury and Osteoarthritis Outcome Score, respectively. The subjects were blinded to group allocation. The outcome measures were evaluated at baseline and day 5, 8, and 20 after the intervention. Data were analysed with the SPSS (version 21.0) software.

Results. On implementing the inclusion and exclusion criteria, 72 participants were enrolled in this trial; 69 of them completed the protocol. There was a significant reduction in pain in all the 3 experimental groups as compared with the control group. The maximum reduction in pain was seen in the group receiving active tDCS and active TENS at week 6.

Conclusions. The combination of tDCS and TENS along with strengthening exercises is effective in reducing pain in knee osteoarthritis.

Key words: visual analogue scale, 6-minute walk test, Knee Injury and Osteoarthritis Outcome Score

Introduction

Osteoarthritis (OA) was found to be the second most common condition by the Global Burden of Disease study, with a prevalence of 29% in India and an overall prevalence of 20–28% [1, 2]. It was earlier conceptualized as a condition producing symptoms which are driven by the peripheral pathology resulting from the destruction of joint and the cartilage but the recent research has shown the role of central sensitization in knee OA [3]. It has been reported that the persistent nociceptive inputs generated by the pathology in the joint in knee OA can escalate the synaptic excitability and efficiency in the central pain pathway. This results in central sensitization, which causes local and widespread hyperalgesia, impaired pain and sensory processing in the central nervous system similar to that observed in other chronic pain conditions [4–6]. Persistent pain is a common problem associated with knee OA. It causes maladaptive changes in the brain and spinal cord [7, 8]. The persistent inflammatory process in the joint and the anatomic lesions lead to significant atrophy in the grey matter of OA patients [5].

Various pharmacological treatments are available and have shown effectiveness in retarding the symptoms of OA, but these are usually associated with side effects. Non-pharmacological treatments like yoga, exercises, acupuncture are also known to be effective but to a limited extent. Therefore, a treatment intervention targeting the central sensitization and pain processing is a potential approach to treat this condition. Non-invasive brain stimulation techniques are researched extensively for treating various chronic pain disorders. All these findings reinforce the need of using treatment that has the potential to modulate the central pain processing system.

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that has the potential to modulate the central sensitization and pain processing. It involves the application of low current on the scalp through the electrodes and thereby increases the firing of neurons underneath the electrodes, producing changes in the local and distant interconnected areas of the cortex. The method has recently been used to treat musculoskeletal conditions like fibromyalgia, low back pain, and knee OA [9–13]. The application of anodal stimulation over the primary motor cortex (M1) has been reported to increase motor learning when administered along with exercises in normal and stroke patients, as well as to decrease pain when used in conjunction with electrical stimulation by the mechanism known as the priming effect [14, 15]. There are studies which combined tDCS and exercise therapy and reported a significant reduction of pain in knee OA and fibromyalgia patients [11, 16].

Pain management with transcutaneous electrical nerve stimulation (TENS) in knee OA patients is a conventional approach. The application of low-amplitude currents by tDCS induces changes in the neuronal membrane potential and releases endogenous opioids in the mid anterior cingulate cortex and periaqueductal grey matter [17, 18]. High-frequency TENS manages pain by segmental inhibition in the pain gate along with descending pain suppression via the opioid mechanisms. Thus, the cortical effects produced by tDCS and the spinal and peripheral effects obtained by TENS may result in a superior reduction in pain when both methods are used in combination. Various studies have investigated the com-

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bined effects of these modalities and have reported a superior pain reduction in various conditions [19, 20]. Similarly, exercise following tDCS has also shown to increase the overall benefit by the priming and motor learning effect [11, 12].

Taking into account these encouraging results, it was hypothesized that the combined application of tDCS and TENS along with strengthening exercises would upsurge the effect of the interventions and produce a superior result to overcome the 2 major symptoms of pain and muscle weakness encountered in knee OA, enhancing the clinical and mechanistic outcomes in knee OA.

Subjects and methods

Study design

The present study was an experimental study, a 4-arm parallel group, participant-blinded, placebo-controlled, randomized trial.

With regard to sample size determination, data gathered from the pilot study suggested a minimum of 15 patients per intervention arm at 90% power and 5% significance level to find the minimal clinically important difference of our primary outcome variable (VAS). Assuming a dropout rate of 25%, 18 patients per arm were recruited (a total of 72 patients).

The patients were divided into group 1 (active tDCS/active TENS), group 2 (active tDCS/sham TENS), group 3 (sham tDCS/active TENS), and group 4 (sham tDCS/sham TENS). A CONSORT flow diagram of the study is presented in Figure 1.

Randomization and allocation concealment

Blocked randomization was used for assigning the patients in the different arms. After evaluating the eligibility and collecting the informed consent, the outcome variables were recorded. The patients were randomly allocated to the groups by simple random sampling with the use of the lottery method, applied by a person independent from the study. The allocation was recorded in the central register and remained concealed from the patients until the end of the study. The assessment and the treatment were carried out by the principle investigator of the study.

Study groups

The patients were divided into 4 equal groups. They were given a common physiotherapy intervention that included hot packs and stretching of hamstring and quadriceps, followed by the interventions as per the respective groups. Group 1 received active tDCS and active TENS, group 2 received active tDCS and sham TENS, group 3 received sham tDCS and active TENS, and group 4 received sham tDCS and sham TENS, followed by strengthening exercises for 5 consecutive days in the first week and hot packs and strengthening exercises thrice a week for the remaining 5 weeks. The overall duration of the study was 6 weeks, with a total of 20 sessions. A minimum of 12 sessions of supervised exercise sessions were kept mandatory for eligible completion of the study. The details of the procedure are published in the pro-

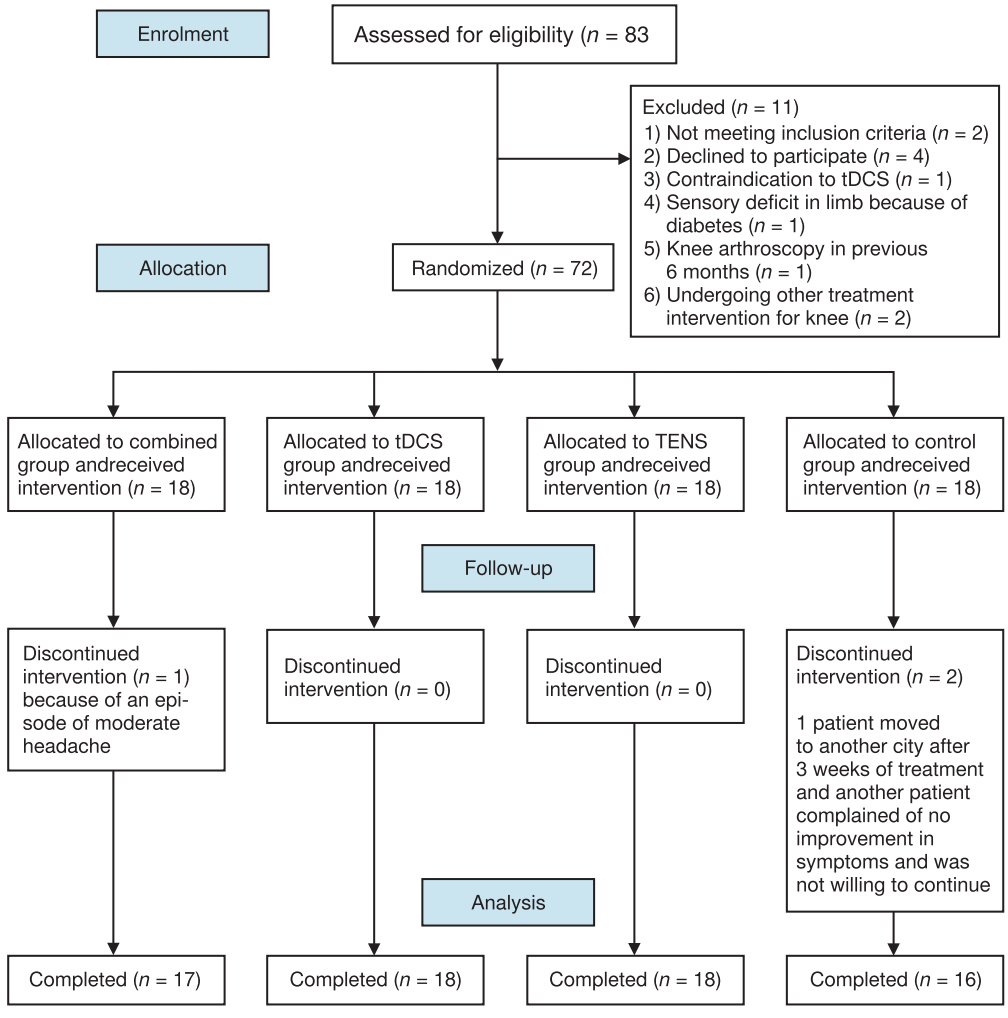

Figure 1. CONSORT flow diagram of the study

tocol paper for the study [21]. The outcomes were measured before the treatment or at the baseline visit, as well as at week 1, 2, and 6 after the treatment.

The number of participants screened and recruited in the study, the percentage of attendance in the treatment sessions, the number of dropouts, and the participants' safety determined by the number of reported adverse effects in each group were noted.

Transcranial direct current stimulation

The tDCS was applied through Medicaid (serial No.: TD 216209, India). Constant current of 2 mA was delivered for 20 minutes, by using a circular sponge soaked in normal saline, on the primary motor cortex once a day for 5 consecutive days. The anode was placed on the primary motor cortex (M1, C3, or C4), as per the International 10–20 Electroencephalogram System, contralateral to the more painful knee, and the cathode on the opposite supraorbital region, ipsilateral to the affected knee. The same electrode placement was used for the sham applications; the equipment was turned on for 30 seconds and then turned off. The particular stimulation regime (M1-SO montage) was chosen on the basis of the proven effectiveness for chronic pain conditions showing a widespread stimulatory effect on the motor, frontal, and somatosensory cortices, modulating pain sensitivity [11–13, 16].

Transcutaneous electrical nerve stimulation

TENS was applied through Enraf Nonius (USA). High-frequency TENS at 100 Hz was administered with a pair of surface electrodes 5 × 5 cm, placed at the medial and lateral side of the knee joint, for 20 minutes for 5 consecutive days, on the more painful side. The same electrode placement was used for sham stimulation, with the stimulator turned on for 30 seconds and then turned off [22].

Patients

Primary knee OA clinical criteria defined by the American College of Rheumatology were used to recruit the participants. Patients with the following conditions were excluded: secondary knee OA, knee flexion deformity, crepitus during sitting to standing, any surgical intervention in a knee, any inflammatory arthritis, inability to walk for 6 minutes, use of an external appliance, already undertaking structured exercise, intra-articular injection, epilepsy, loss of sensation. The study was conducted at the Department of Physiotherapy, out-patient clinic, Guru Jambheshwar University of Science and Technology, Hisar. The data were collected between March 2018 and September 2019.

Main outcome variables

Pain was assessed with a visual analogue scale (VAS), which consists of a 10-cm scale. The left end indicates 0, meaning 'no pain,' and the right end indicates 10, meaning 'extreme pain'. The patient was asked to mark a point to indicate the pain.

Function was measured with the 6-minute walk test. The patient was asked to walk at their own pace in a 20-m corridor marked with cones. No feedback was given. The 6-minute walk test is a reliable tool for an objective measurement of function in knee OA [23].

Other variables

Disability was assessed with the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire, which is an extension of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and contains the following components: Symptoms, Pain, Function, Sport and Recreation, Quality of Life. The score ranges from 0 to 100, where 100 indicates a minimum problem.

All the outcome variables were measured before treatment and at weeks 1, 2, and 6 after the treatment.

Statistical analysis

Data were presented as mean and standard deviation. The normality of the data was checked with the Kolmogorov-Smirnov test. If there were any missing data, the principle of intention to treat was followed. One-way ANOVA was used to estimate between-group differences in the outcome variables. If significant, the Scheffe correction was applied for post-hoc analysis. The paired *t*-test served to estimate the changes in the outcome variables in each of the individual groups at each time point. Repeated-measures ANOVA indicated within-group effects and the overall effect of the interventions. The *F* value, *p* value, and effect size for each outcome variable is presented. The effect size was classified as small, medium, large, and very large for the values of 0.2–0.5, 0.51–0.8, 0.81–1.2, and > 1.2, respectively. Mean differences (MD) along with 95% confidence intervals (95% CI) were reported if the values were found significant. The IBM SPSS software (version 21.0) was used for statistical analysis.

Ethical approval

The research related to human use has complied with all the relevant national regulations and institutional policies, has followed the tenets of the Declaration of Helsinki, and has been approved by the authors' institutional ethics committee in December 2017. The trial was prospectively registered in the Clinical Trials Registry – India (CTRI/2018/02/012027) on February 21, 2018.

Informed consent

Informed consent has been obtained from all individuals included in this study.

Results

A total of 83 patients were screened on the basis of the inclusion and exclusion criteria and were assessed at the baseline visit. After the screening, 11 individuals were excluded: 2 did not meet the inclusion criteria, 1 had a history of epilepsy (which is a contraindication for the use of tDCS), 4 declined to participate, 2 were undergoing other treatment interventions (acupuncture, intraarticular injection), 1 had undergone knee arthroscopy within the previous 6 months, and 1 had a diabetic sensory deficit. A total of 72 participants were then randomized into 4 groups; 69 of them completed the treatment and assessment. The dropout rate was 4.12% (n = 2 in the control group, n = 1 in the combined group) (Figure 1). The baseline characteristics of the participants are presented in Table 1. The data are freely available in the Mendeley Data repository [24].

Pain

The between-group analysis showed a statistically significant improvement in pain at week 1, 2, and 6. The post-hoc

Table 1. Baseline characteristics of included participants

Variable	Combined group	tDCS group	TENS group	Control group
Age (years)	54.88 ± 6.78	52.78 ± 5.37	54.78 ± 5.91	51.75 ± 5.79
Height (cm)	158.92 ± 6.47	157.07 ± 7.44	161.28 ± 9.01	158.75 ± 5.96
Weight (kg)	72.75 ± 9.13	72.75 ± 10.91	73.66 ± 9.55	69.15 ± 8.28
BMI (kg · m^{-2})	28.87 ± 3.74	29.57 ± 4.75	28.43 ± 3.85	27.48 ± 3.41
Sex				
Male	6	7	6	4
Female	12	11	12	14
Marital status				
Single	–	–	–	–
Married	18	16	17	16
Widowed	2	2	1	2
Medication				
Yes	9	7	8	7
No	9	11	10	11
X-ray Kellgren-Lawrence grade				
1	–	3	–	–
2	4	6	8	10
3	14	9	10	8

BMI – body mass index, tDCS – transcranial direct current stimulation, TENS – transcutaneous electrical nerve stimulation

analysis revealed a significant reduction in pain only in group 2 as compared with group 4 at week 1: MD = –1.32, 95% CI (–2.41, –0.22), $p = 0.011$. At week 2, there was a significant reduction in pain in group 1 as compared with group 4: MD = –1.35, 95% CI (–2.40, –0.31), $p = 0.006$, as well as a significant improvement in group 2 as compared with group 4: MD = –1.42, 95% CI (–2.46, –0.39), $p = 0.003$. Group 3 presented a significant reduction in pain as compared with group 4: MD = –1.20, 95% CI (–2.24, –0.17), $p = 0.015$. At week 6, the improvement in pain was significantly maintained in group 1, 2, and 3 as compared with group 4: MD = –2.04, 95% CI (–3.03, –1.04), $p = 0.015$; MD = –1.64, 95% CI (–2.62, –0.66), $p = 0.0001$; MD = –1.34, 95% CI (–2.32, –0.36), $p = 0.003$, respectively.

Function

There were no significant between-group differences in the 6-minute walk test results in any of the 4 groups at any time point ($F = 0.973$, $p = 0.411$ at week 1; $F = 1.45$, $p = 0.236$ at week 2; $F = 1.964$, $p = 0.128$ at week 6).

Other variables

As can be seen in Table 2, in the KOOS Symptoms subvariable, between-group differences were found to be significant at week 1, 2, and 6 ($F = 3.160$, $p = 0.030$ at week 1; $F = 3.11$, $p = 0.032$ at week 2; $F = 5.512$, $p = 0.003$ at week 6). The post-hoc comparisons showed a significant improvement in KOOS Symptoms in group 1 as compared with group 4 at week 2: MD = 10.36, 95% CI (0.63, 20.08), $p = 0.032$, as well as at week 6: MD = 10.96, 95% CI (0.14, 21.78), $p = 0.046$. At week 2, the improvement was also significant in group 2 as compared with group 4: MD = 13.98, 95% CI (3.31, 24.65), $p = 0.005$.

The KOOS Pain, Function, and Sport and Recreation subvariables indicated no significant between-group differences at any time points. The KOOS Quality of Life subvariable showed statistically significant between-group differences at week 6 ($F = 2.94$, $p = 0.040$). However, the post-hoc multiple comparison determined no significant differences between the groups.

The paired *t*-test showed a significant improvement in all the outcome variables at each time point compared with the baseline values in each group except for KOOS Sport and Recreation, Function, and Quality of Life at week 1 in group 2, as well as KOOS Pain at week 1 and KOOS Sport and Recreation at weeks 1 and 6 in group 4.

Effects and interactions

The result of repeated-measures ANOVA within-subject analysis showed a significant overall effect of the intervention and a VAS*group interaction. The between-subject effect for VAS was also found to be significant. In the 6-minute walk test, the within-subject analysis presented a significant overall effect and a 6-minute walk test*group interaction. However, the between-subject analysis result was found to be insignificant. The within-subject analysis estimating the overall effect and the variable*group interaction for all the KOOS subvariables brought about statistically significant results. However, between-subject comparisons implied no significant effect in any of the KOOS subvariables. Thus, the within-subject analysis of the overall effect of the interventions and the variable*group interaction revealed significant results for all the variables. However, the between-subject

Table 2. Between-group comparisons with one-way ANOVA and repeated-measures ANOVA

Items	Variables	Combination group (n = 17)	tDCS group (n = 17)	TENS group (n = 18)	Control group (n = 16)	Between-group F and p	Within-group F and p
1.1	VAS-BS	6.06 ± 0.82	5.51 ± 1.13	6.01 ± 1.39	5.55 ± 1.12	F = 1.129 p = 0.344	F = 400.645 p = 0.0001**
1.2	VAS-W1	2.91 ± 0.95	2.63 ± 1.25	2.97 ± 1.05	3.95 ± 1.14	F = 4.485 p = 0.006*	
1.3	VAS-W2	2.54 ± 0.84	2.47 ± 1.18	2.70 ± 1.00	3.90 ± 1.12	F = 6.728 p = 0.001**	
1.4	VAS-W6	1.97 ± 0.67	2.37 ± 1.21	2.67 ± 0.94	4.01 ± 1.04	F = 13.09 p = 0.0001**	
2.1	WT6M-BS	338.65 ± 59.20	348.94 ± 42.36	340.61 ± 24.96	327.81 ± 46.38	F = 0.640 p = 0.592	F = 60.263 p = 0.0001**
2.2	WT6M-W1	352.82 ± 58.32	351.39 ± 42.87	343.39 ± 24.90	329.38 ± 45.71	F = 0.973 p = 0.411	
2.3	WT6M-W2	360.41 ± 56.98	353.89 ± 43.68	346.61 ± 24.07	330.06 ± 45.78	F = 1.453 p = 0.236	
2.4	WT6M-W6	366.69 ± 54.83	356.17 ± 44.18	351.22 ± 24.07	330.81 ± 45.76	F = 1.964 p = 0.128	
3.1	KS-SYM-BS	40.88 ± 6.48	49.61 ± 15.32	46.56 ± 11.85	49.06 ± 11.57	F = 1.950 p = 0.130	F = 184.38 p = 0.0001**
3.2	KS-SYM-W1	52.00 ± 8.46	60.89 ± 12.91	56.72 ± 7.46	51.56 ± 11.45	F = 3.160 p = 0.030*	
3.3	KS-SYM-W2	61.59 ± 6.09	66.61 ± 11.64	61.61 ± 9.17	56.25 ± 11.52	F = 3.118 p = 0.032*	
3.4	KS-SYM-W6	70.59 ± 7.97	73.61 ± 11.39	69.06 ± 12.08	59.63 ± 11.26	F = 5.15 p = 0.003*	
4.1	KS-PAIN-BS	44.76 ± 8.48	52.61 ± 17.64	53.72 ± 17.96	50.38 ± 6.05	F = 1.435 p = 0.241	F = 106.296 p = 0.0001**
4.2	KS-PAIN-W1	53.59 ± 7.78	59.39 ± 16.04	58.11 ± 15.40	50.94 ± 6.39	F = 1.709 p = 0.174	
4.3	KS-PAIN-W2	61.82 ± 10.78	66.00 ± 14.04	62.89 ± 12.78	57.25 ± 7.86	F = 1.609 p = 0.196	
4.4	KS-PAIN-W6	68.41 ± 9.53	71.61 ± 14.12	68.67 ± 14.05	61.69 ± 10.78	F = 1.914 p = 0.136	
5.1	KS-FUNC-BS	40.59 ± 8.00	49.89 ± 13.25	47.28 ± 16.03	47.69 ± 14.07	F = 1.591 p = 0.200	F = 149.10 p = 0.0001**
5.2	KS-FUNC-W1	52.00 ± 7.02	58.22 ± 10.85	53.78 ± 15.11	52.75 ± 12.15	F = 0.999 p = 0.399	
5.3	KS-FUNC-W2	61.06 ± 5.90	63.72 ± 11.59	57.33 ± 15.81	59.44 ± 9.22	F = 1.016 p = 0.394	
5.4	KS-FUNC-W6	70.29 ± 8.94	70.17 ± 12.04	63.67 ± 15.24	63.44 ± 11.78	F = 1.700 p = 0.176	
6.1	KS-SR-BS	17.94 ± 7.81	22.28 ± 16.90	24.11 ± 15.47	30.69 ± 12.91	F = 2.417 p = 0.074	F = 68.81 p = 0.0001**
6.2	KS-SR-W1	24.00 ± 8.54	24.67 ± 15.13	36.56 ± 17.84	31.81 ± 14.04	F = 0.995 p = 0.401	
6.3	KS-SR-W2	29.94 ± 10.65	32.11 ± 17.73	30.89 ± 18.12	35.31 ± 12.19	F = 0.472 p = 0.703	
6.4	KS-SR-W6	35.59 ± 11.30	38.56 ± 20.72	35.17 ± 16.03	34.75 ± 12.21	F = 0.214 p = 0.886	
7.1	KS-QOL-BS	33.88 ± 5.56	31.28 ± 10.43	35.67 ± 6.20	35.94 ± 8.20	F = 1.309 p = 0.279	F = 113.15 p = 0.0001**
7.2	KS-QOL-W1	39.24 ± 5.49	34.72 ± 12.57	38.61 ± 5.65	39.31 ± 9.42	F = 1.086 p = 0.361	
7.3	KS-QOL-W2	46.24 ± 4.32	43.83 ± 11.75	40.11 ± 6.20	42.00 ± 7.31	F = 1.883 p = 0.141	
7.4	KS-QOL-W6	53.88 ± 5.11	47.11 ± 12.79	47.06 ± 7.51	45.13 ± 9.38	F = 2.942 p = 0.040*	

VAS – visual analogue scale, BS – baseline, W1 – week 1, W2 – week 2, W6 – week 6, WT6M – 6-minute walk test, KS – Knee Injury and Osteoarthritis Outcome Score, SYM – Symptoms, PAIN – Pain, FUNC – Function, SR – Sport and Recreation, QOL – Quality of Life, tDCS – transcranial direct current stimulation, TENS – transcutaneous electrical nerve stimulation
* significant at $p < 0.05$, ** significant at $p < 0.0001$

Table 3. Repeated-measures ANOVA *F* and *p* values for overall, within-group, and between-group effects

Outcome variable	Overall effect		Variable*group effect		Between-subject interaction	
	F	*p*	*F*	*p*	*F*	*p*
Visual Analogue Scale	400.64	0.0001*	10.327	0.0001*	4.569	0.006*
6-minute walk test	60.263	0.0001*	12.506	0.0001*	1.111	0.351
KOOS Symptoms	184.387	0.0001*	6.219	0.0001*	2.525	0.065
KOOS Pain	106.296	0.0001*	2.585	0.008*	1.460	0.234
KOOS Function	149.106	0.0001*	3.769	0.0001*	0.825	0.485
KOOS Sport and Recreation	68.81	0.0001*	4.106	0.0001*	0.591	0.623
KOOS Quality of Life	113.150	0.0001*	4.740	0.0001*	0.947	0.423

KOOS – Knee Injury and Osteoarthritis Outcome Score
* significant at $p < 0.0001$

analysis the overall effect of the intervention demonstrated a significant outcome only for the pain (VAS) variable. Table 3 presents the *F* and *p* values for overall, within-group, and between-group effects.

Discussion

The objective of this study was to verify whether the combination of tDCS and TENS or the application of these interventions alone was more effective in the areas of pain, function, and quality of life in knee OA patients. The study revealed a significant improvement in pain in group 1 (active tDCS/active TENS), group 2 (active tDCS/sham TENS), and group 3 (sham tDCS/active TENS). A reduction in pain was observed in group 2 at week 1 and the improvement remained consistent up to week 6. The reduction in pain at week 2 was significant in all the 3 experimental groups but a greater reduction in pain was seen in group 2 as compared with groups 1 and 3. At week 6, the reduction in pain was consistently maintained in all the 3 experimental groups but the improvement was maximal in group 1. Therefore, a condescending effect of the combined application of tDCS and TENS in group 1 over the isolated application of the interventions can be established. The superior reduction in pain in the combination group can be because of the 'top down bottom up mechanism,' i.e. the cortical modulation by tDCS (top down) and the pain modulation via segmental inhibition in the descending pain system caused by the application of TENS (bottom up). Moreover, there is a well-documented anti-nociceptive effect produced by exercises, and the priming effect might have collectively led to significant improvements in pain in this group. The pain modulation by the 'top down bottom up mechanism' and the analgesic effect brought about by exercises are well documented in some studies [25, 26]. The priming effect of tDCS, i.e. increasing the effect of the subsequent intervention, has also been demonstrated in various studies [11–13, 19, 20]. In consistence, the present study also suggests a significant reduction in pain with the combined application of tDCS and TENS.

Function, measured with the 6-minute walk test, exhibited no significant improvement in any of the groups at any time point of the assessment.

In KOOS, a significant improvement was observed in the Symptoms and Quality of Life subvariables. KOOS Symptoms showed significant between-group differences for group 1 at week 2 and 6 and for group 2 at week 6 as compared with the control group.

The effectiveness of tDCS in psychological and neurological conditions is well explored and now various researchers are investigating its use in chronic musculoskeletal pain disorders. To our knowledge, only 3 studies have focused on the effect of tDCS in knee OA to date and have reported a significant improvement in pain [11–13]. Therefore, the result of the study suggests that the application of tDCS effectively manages pain in knee OA patients. The early analgesic effect observed in group 2 can be because of the application of tDCS for 5 consecutive sessions. The effectiveness of tDCS for 5 consecutive sessions has also been shown significant in various conditions. Da Graca-Tarragó et al. [27] displayed that 5 consecutive tDCS sessions per week at 2 mA significantly reduced pain in knee OA patients. The application of 5 consecutive sessions of tDCS was reported to significantly decrease pain in fibromyalgia and low back pain patients [16, 28]. Sakrajai et al. [29] determined a significant reduction in pain with 5 consecutive sessions of tDCS in patients with myofascial pain syndrome.

The effect of the combination of tDCS and TENS was prominent at week 2 and significantly maintained at week 6 at a larger extent as compared with isolated application of the interventions. As the role of central sensitization is prominent in knee OA, strategies that modulate pain by the 'top down bottom up mechanism' can be of utmost importance. Therefore, it can be inferred that the combination of tDCS with TENS along with strengthening exercises is a propitious approach in treating knee OA patients.

Limitations

The limitation encountered in the study was a lack of a larger sample size, long-term follow up of the patients, follow-up for medication intake, and double blinding.

Conclusions

It can be concluded that the application of tDCS in combination with TENS is a promising tool for treating knee OA patients.

Implication in physiotherapy

The combination of tDCS and TENS can be considered as a potential tool for persuasive management of knee OA. Although the use of tDCS is not yet approved to be practised in clinical settings, its easy portability, inexpensiveness, and few side effects make it a potent future tool.

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Disclosure statement

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Conflict of interest

The authors state no conflict of interest.

References

1. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis. 2014;73(7):1323–1330; doi: 10.1136/annrheumdis-2013-204763.
2. Pal CP, Singh P, Chaturvedi S, Pruthi KK, Vij A. Epidemiology of knee osteoarthritis in India and related factors. Indian J Orthop. 2016;50(5):518–522; doi: 10.4103/0019-5413.189608.
3. Finan PH, Buenaver LF, Bounds SC, Hussain S, Park RJ, Haque UJ, et al. Discordance between pain and radiographic severity in knee osteoarthritis: findings from quantitative sensory testing of central sensitization. Arthritis Rheum. 2013;65(2):363–372; doi: 10.1002/art.34646.
4. Woolf CJ. Central sensitization: implications for the diagnosis and treatment of pain. Pain. 2011;152(3 Suppl.): 2–15; doi: 10.1016/j.pain.2010.09.030.
5. Lluch E, Torres R, Nijs J, Van Oosterwijck J. Evidence for central sensitization in patients with osteoarthritis pain: a systematic literature review. Eur J Pain. 2014;18(10): 1367–1375; doi: 10.1002/j.1532-2149.2014.499.x.
6. Davis KD, Moayedi M. Central mechanisms of pain revealed through functional and structural MRI. J Neuroimmune Pharmacol. 2013;8(3):518–534; doi: 10.1007/s11481-012-9386-8.
7. Schaible H-G. Mechanisms of chronic pain in osteoarthritis. Curr Rheumatol Rep. 2012;14(6):549–556; doi: 10.1007/s11926-012-0279-x.
8. Howard MA, Sanders D, Krause K, O'Muircheartaigh J, Fotopoulou A, Zelaya F, et al. Alterations in resting-state regional cerebral blood flow demonstrates ongoing pain in osteoarthritis: an arterial spin-labeled magnetic resonance imaging study. Arthritis Rheum. 2012;64(12): 3936–3946; doi: 10.1002/art.37685.
9. Marlow NM, Bonilha HS, Short EB. Efficacy of transcranial direct current stimulation and repetitive transcranial magnetic stimulation for treating fibromyalgia syndrome: a systematic review. Pain Pract. 2013;13(2):131–145; doi: 10.1111/j.1533-2500.2012.00562.x.
10. O'Connell NE, Cossar J, Marston L, Wand BM, Bunce D, De Souza LH, et al. Transcranial direct current stimulation of the motor cortex in the treatment of chronic nonspecific low back pain: a randomized, double-blind exploratory study. Clin J Pain. 2013;29(1):26–34; doi: 10.1097/AJP.0b013e318247ec09.
11. Chang W-J, Bennell KL, Hodges PW, Hinman RS, Young CL, Buscemi V, et al. Addition of transcranial direct current stimulation to quadriceps strengthening exercise in knee osteoarthritis: a pilot randomised controlled trial. PLoS One. 2017;12(6):e0180328; doi: 10.1371/journal.pone.0180328.
12. Ahn H, Zhong C, Miao H, Chaoul A, Park L, Yen IH, et al. Efficacy of combining home-based transcranial direct current stimulation with mindfulness-based meditation for pain in older adults with knee osteoarthritis: a randomized controlled pilot study. J Clin Neurosci. 2019;70: 140–145; doi: 10.1016/j.jocn.2019.08.047.
13. Ahn H, Woods AJ, Kunik ME, Bhattacharjee A, Chen Z, Choi E, et al. Efficacy of transcranial direct current stimulation over primary motor cortex (anode) and contralateral supraorbital area (cathode) on clinical pain severity and mobility performance in persons with knee osteoarthritis: an experimenter- and participant-blinded, randomized, sham-controlled pilot clinical study. Brain Stimul. 2017;10(5):902–909; doi: 10.1016/j.brs.2017.05.007.
14. Reis J, Fritsch B. Modulation of motor performance and motor learning by transcranial direct current stimulation. Curr Opin Neurol. 2011;24(6):590–596; doi: 10.1097/WCO.0b013e32834c3db0.
15. Schabrun SM, Chipchase LS. Priming the brain to learn: the future of therapy? Man Ther. 2012;17(2):184–186; doi: 10.1016/j.math.2011.12.001.
16. Mendonca ME, Simis M, Grecco LC, Battistella LR, Baptista AF, Fregni F. Transcranial direct current stimulation combined with aerobic exercise to optimize analgesic responses in fibromyalgia: a randomized placebo-controlled clinical trial. Front Hum Neurosci. 2016;10:68; doi: 10.3389/fnhum.2016.00068.
17. Nitsche MA, Paulus W. Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. Neurology. 2001;57(10):1899–1901; doi: 10.1212/wnl.57.10.1899.
18. Nitsche MA, Seeber A, Frommann K, Klein CC, Rochford C, Nitsche MS, et al. Modulating parameters of excitability during and after transcranial direct current stimulation of the human motor cortex. J Physiol. 2005; 568(Pt 1):291–303; doi: 10.1113/jphysiol.2005.092429.
19. Hazime FA, Baptista AF, de Freitas DG, Monteiro RL, Maretto RL, Hasue RH, et al. Treating low back pain with combined cerebral and peripheral electrical stimulation: a randomized, double-blind, factorial clinical trial. Eur J Pain. 2017;21(7):1132–1143; doi: 10.1002/ejp.1037.
20. Boggio PS, Amancio EJ, Correa CF, Cecilio S, Valasek C, Bajwa Z, et al. Transcranial DC stimulation coupled with TENS for the treatment of chronic pain: a preliminary study. Clin J Pain. 2009;25(8):691–695; doi: 10.1097/AJP.0b013e3181af1414.
21. Chaturvedi R, Kulandaivelan S, Malik M, Joshi S. Transcranial direct current stimulation in combination with TENS: effectiveness on pain and functional outcomes in knee OA patients – a study protocol. Indian J Public Health Res Dev. 2019;10(4):337–341; doi: 10.5958/0976-5506.2019.00714.9.
22. Vance CGT, Rakel BA, Blodgett NP, DeSantana JM, Amendola A, Zimmerman MB, et al. Effects of transcutaneous electrical nerve stimulation on pain, pain sensitivity, and function in people with knee osteoarthritis: a randomized controlled trial. Phys. Ther. 2012;92(7): 898–910; doi: 10.2522/ptj.20110183.
23. Ateef M, Kulandaivelan S, Tahseen S. Test-retest reliability and correlates of 6-minute walk test in patients with primary osteoarthritis of knees. Indian J Rheumatol, 2016;11(4):192–196; doi: 10.4103/0973-3698.192668.
24. Chaturvedi R, Kulandaivelan S. Combination of transcranial direct current stimulation (tDCS) and transcutaneous electrical nerve stimulation (TENS) on pain, function and quality of life: single blind, placebo controlled randomized trial. 2020. Mendeley Data. Version 1.

25. Schabrun SM, Jones E, Elgueta Cancino EL, Hodges PW. Targeting chronic recurrent low back pain from the top-down and the bottom-up: a combined transcranial direct current stimulation and peripheral electrical stimulation intervention. Brain Stimul. 2014;7(3):451–459; doi: 10.1016/j.brs.2014.01.058.
26. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage. 2010;18(4):476–499; doi: 10.1016/j.joca.2010.01.013.
27. Da Graca-Tarragó M, Lech M, Moro Angoleri LD, Silva Santos D, Deitos A, Brietzke AP, et al. Intramuscular electrical stimulus potentiates motor cortex modulation effects on pain and descending inhibitory systems in knee osteoarthritis: a randomized, factorial, sham-controlled study. J Pain Res. 2019;12:209–221; doi: 10.2147/JPR.S181019.
28. Straudi S, Buja S, Baroni A, Pavarelli C, Pranovi G, Fregni F, et al. The effects of transcranial direct current stimulation (tDCS) combined with group exercise treatment in subjects with chronic low back pain: a pilot randomized control trial. Clin Rehabil. 2018;32(10):1348–1356; doi: 10.1177/0269215518777881.
29. Sakrajai P, Janyacharoen T, Jensen MP, Sawanyawisuth K, Auvichayapat N, Tunkamnerdthai O, et al. Pain reduction in myofascial pain syndrome by anodal transcranial direct current stimulation combined with standard treatment: a randomized controlled study. Clin J Pain. 2014;30(12):1076–1083; doi: 10.1097/AJP.0000000000000069.