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Effects of Transcutaneous Electrical Nerve Stimulation and Therapeutic Exercise on Quadriceps Activation in People With Tibiofemoral Osteoarthritis

STUDY DESIGN: Blinded, randomized controlled trial.

OBJECTIVES: To determine if the combination of transcutaneous electrical nerve stimulation (TENS) set to a sensory level and therapeutic exercise would be more effective than the combination of placebo TENS and therapeutic exercises or therapeutic exercises only to increase quadriceps activation in individuals with tibiofemoral osteoarthritis.

BACKGROUND: Quadriceps activation deficits are common in those with tibiofemoral osteoarthritis, and TENS has been reported to immediately increase quadriceps activation. Yet the long-term benefits of TENS for motor neuron activation have yet to be determined.

METHODS: Thirty-six individuals with radiographically assessed tibiofemoral osteoarthritis were randomly assigned to the TENS and exercise, placebo and exercise, and exercise only groups. All participants completed a supervised 4-week lower extremity exercise program. TENS and placebo TENS were worn throughout the therapeutic exercise sessions, as well as during daily activities. Our primary outcome measures, quadriceps central activation ratio, and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were evaluated at baseline and at 2 weeks and 4 weeks of the intervention.

RESULTS: Quadriceps activation was significantly higher in the TENS with exercise group compared to the exercise only group at 2 weeks (0.94 ± 0.04 versus 0.82 ± 0.12, $P<.05$) and the placebo and exercise group at 4 weeks (0.94 ± 0.06 versus 0.81 ± 0.15, $P<.05$). WOMAC scores improved in all 3 groups over time, with no significant differences among groups.

CONCLUSION: This study provides evidence that TENS applied in conjunction with therapeutic exercise and daily activities increases quadriceps activation in patients with tibiofemoral osteoarthritis and, while function improved for all participants, effects were greatest in the group treated with a combination of TENS and therapeutic exercises.

LEVEL OF EVIDENCE: Therapy, level 1b–.
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Neuromuscular alterations, including decreased voluntary quadriceps activation, are commonly associated with tibiofemoral osteoarthritis (TFOA).[6,7,17,19,25,26] Quadriceps activation failure is a complex issue, due to the variety of factors and mechanisms that likely contribute to its existence. The inability to optimally activate the quadriceps muscle may be modulated by both cortical[8] and spinal reflex mechanisms.[21,22] While there is some evidence that motor recruitment may be altered cortically in reaction to chronic pain,[18] other models have suggested that spinal reflex circuits may also decrease quadriceps excitability, independent of pain reaction to a joint injury.[10,21,22] Although quadriceps activation deficits are likely a result of a combination of altered mechanisms arising from different areas of the central and peripheral nervous system, there is sufficient evidence that reflexive modulation of the quadriceps motor neuron pool is involved in altering muscle function following a knee injury.[23,21]

Arthrogenic muscle inhibition (AMI) is a clinical impairment characterized by a reflexive inhibition of the motor neuron pool in uninjured muscles surrounding an injured joint.[9,20-23] This reflex inhibition, modulated by both presynaptic and postsynaptic spinal mechanisms,[21,22] decreases the ability of the muscle to recruit motor neurons during a contraction,[11,12]

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thus limiting the potential force a muscle can generate. AMI is likely a protective mechanism aimed at decreasing excessive forces acting around an acutely injured joint. Unfortunately, prolonged quadriceps volitional activation deficits and muscle weakness may decrease shock attenuation at the knee, leading to increased joint surface breakdown.[23,33] For this reason, AMI has been referred to as a limiting factor in joint rehabilitation, which has led authors[9,24,28] to suggest that reflex inhibition affecting muscle activation must be considered prior to engaging in therapeutic exercise.

It has been suggested that specialized interventions need to be developed to target reflexive inhibitory circuits, which effectively decrease the ability to volitionally activate the quadriceps.[9] It has also been suggested that a modality capable of increasing quadriceps motor neuron pool excitability or disinhibiting the quadriceps prior to performing quadriceps strengthening would provide an optimal environment for treating reflex-modulated inhibition, which may provide a stimulus for regaining normal motor function.[28]

Sensory transcutaneous electrical nerve stimulation (TENS) applied to the knee joint has been reported to disinhibit the quadriceps motor neuron pool excitability in individuals with artificially effused knee joints.[10] Recently, increases in volitional quadriceps activation have been reported immediately following TENS application to the knee of patients with TFOA.[30] TENS may cause an immediate increase in stimuli interpreted as excitatory by interneurons, giving rise to increased motor output of otherwise inhibited musculature.[10,30] There is additional evidence that patients with knee osteoarthritis have increased muscle strength and beneficially altered gait following therapeutic exercise in conjunction with TENS.[1] Furthermore, previous increases in neural excitability due to TENS have been reported only in the presence of active stimulation.[10,30] Short-term use of TENS does not seem to elicit lasting improvements in quadriceps excitability,[10] yet it is undetermined if longer durations of TENS treatment during daily activities in addition to therapeutic exercise may provide a catalyst for sustainable improvements in neuromuscular function.

Therefore, more specifically, it is unknown if sensory TENS, applied to the knee in conjunction with therapeutic exercise and daily activities, will increase volitional quadriceps activation in patients with TFOA. In addition, it is uncertain how changes in muscle activation affect self-reported function. The primary purpose of the current study was to determine if the combination TENS set to a sensory level and therapeutic exercises would be more effective than the combination of placebo of TENS and therapeutic exercises, or therapeutic exercises only, to increase quadriceps activation in individuals with TFOA. We secondarily examined the effects of these therapies on quadriceps torque production and self-reported function scores, as well as the relationships between changes in central activation ratio (CAR) and torque production with changes in self-reported function.

METHODS

Participants

Potential participants were recruited through referrals from participating orthopaedic surgeons in the University Health System. Interested volunteers attended a screening session, in which investigators collected health history and quadriceps CAR. A fellowship-trained orthopaedic surgeon used bilateral radiographs, taken within 6 months prior to enrollment in the study, to assess and grade TFOA with the Kellgren-Lawrence grading system. Participants with a clinical diagnosis of TFOA, a quadriceps CAR of less than 0.90, and a Kellgren-Lawrence score between 1 and 4, were included in the study. A quadriceps CAR of less than 0.90 was adopted, based on the results from a recent meta-analysis[27] assessing those with TFOA and matched controls, reporting 0.90 as an average voluntary activation score for healthy participants. Therefore, we included participants who had a CAR less than the average value reported for healthy participants in this meta-analysis.[27] Participants with a diagnosed heart condition limiting exercise, altered sensation over the anterior knee region, and lower body surgery or knee trauma in the past 6 months were excluded. Participants with a history of a total knee arthroplasty were included in the study, but the side with the knee replacement was excluded from being classified as the involved knee. Therefore, only biological joints with TFOA were tested and treated. The involved knee used for the study was the knee with the greatest radiographic evidence of osteoarthritis. In cases where both knees were graded similarly, the knee that the participant reported to cause the most dysfunction was included in the study. A mandatory 2-week washout period, determined from previously published half-life data, was implemented for all participants who previously had a corticosteroid[2] or hyaluronic acid injection.[5] Participants were stratified into 1 of 4 categories, determined by baseline quadriceps CAR and radiographic evidence of TFOA, as assessed by the Kellgren-Lawrence grading system. Then they were randomly allocated, using a sealed-envelope technique, to 1 of 3 treatment groups (active sensory level TENS and exercise, placebo TENS and exercise, and exercise) (**FIGURE**). Forty-nine participants volunteered for this study and 36 participants were used in the final analysis (**FIGURE, TABLE 1**). The use of prescription and over-the-counter medications for pain relievers and anti-inflammatory drugs was monitored throughout the study, and participants were asked to discontinue the use of all nonessential pain medication 12 hours prior to therapy sessions and 24 hours prior to all testing sessions.

The protocol for this study was approved by The Institutional Review

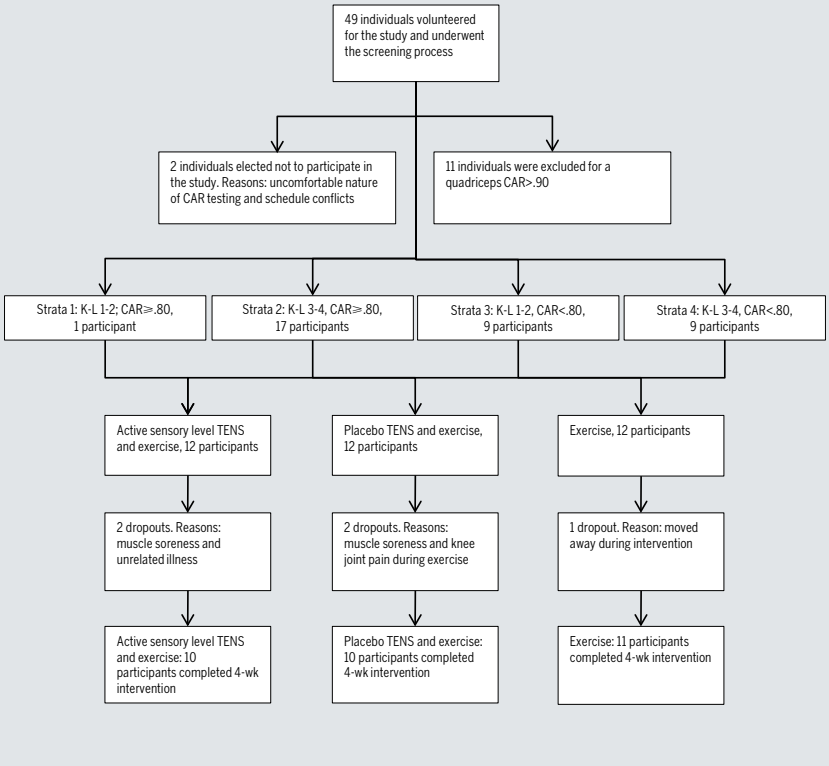

FIGURE. Diagram illustrating strata allocation and randomized group assignment, as well as retention of participants by group. Abbreviations: CAR, central activation ratio; K-L, Kellgren-Lawrence score.

Board at the University of Virginia prior to subject enrollment, and written informed consent was obtained prior to participation.

Interventions

Therapeutic Exercise Participants in all 3 groups performed quadriceps strengthening for their involved lower extremity 3 times per week for the 4-week treatment duration, for a total of 12 sessions. The therapeutic exercise sessions were supervised by either an experienced certified athletic trainer or licensed physical therapist. The clinical goal of the 4-week therapeutic exercise program was to increase lower extremity range of motion, strength, and function, as well as to decrease pain. Strengthening therapeutic exercises were systematically progressed using the daily adjustable progressive resistive exercise (DAPRE) system (**TABLE 2**).[16] All participants were challenged to increase weight, as directed by the DAPRE system, while maintaining no more than minimal discomfort throughout the therapeutic exercise session.

TENS and Placebo TENS The Select System TENS unit (EMPI, Inc, St Paul, MN) and 4 separate 2 × 2-in (5.08 × 5.08 cm) self-adhesive electrodes (Re-ply reusable electrodes; Uni-Patch, Wabasha, MN) were used to deliver the TENS stimulation to the knee joint of participants in both the active and placebo groups. The TENS electrodes were applied on the medial and lateral superior, as well as the medial and lateral inferior, borders of the patella, as previously reported.[30] Care was taken not to place TENS electrodes on the quadriceps muscles or muscles of the anterior leg. The 2 TENS currents (pairs of electrodes) were crossed to encompass the most surface area under stimulation. Participants in each group were instructed to utilize the TENS or placebo units during all therapeutic exercise sessions and at least 8 hours per day when they were the most active. Additionally, participants in the TENS and placebo groups were blinded to group assignment, while those in the control group were aware that they were receiving the standard of care. Participants in both the TENS and placebo group were told that this treatment might feel substantially different than previous electrical stimulation experiences because of differences in the electrical current parameters used in this study. Participants in the active TENS or placebo TENS group were educated on the respective TENS unit operation and electrode application. A daily log was utilized to track compliance of treatment duration, and any questions specifically regarding the TENS use were directed to the unblinded investigator responsible for group assignment.

The stimulators in the active TENS and exercise group were set to deliver a continuous TENS biphasic pulsatile current at 150 Hz, with a phase duration of 150 microseconds. Participants were instructed on how to increase and decrease amplitude, which could be adjusted between 1 and 60 mA. Amplitude was set at a strong, comfortable sensory stimulation intensity that was not strong enough to elicit muscle contraction. Participants were instructed to maintain this sensation throughout each treatment session by adjusting intensity as needed.

The participants using the placebo TENS received the same stimulators, and were instructed to increase the intensity until they felt a sensory stimulation. Following 30 seconds of stimulation, placebo TENS units were programmed to automatically gradually decrease the current over 10 seconds until no electricity was emitted. We provided 30 seconds of stimulation to provide the placebo group with the impression that they would receive an electrical stimulation treatment. Participants were told that the current parameters were set to a subsensory level, and the unit was delivering the treatments as long as the indicator light was on. This approach was used to keep this group blinded to receiving the placebo in-

tervention. Participants were instructed to maintain the intensity at a level above 5 out of 100 throughout the day.

Outcome Measures

Quadriceps CAR assessed with the burst superimposition method was the primary outcome measure. Secondarily, we examined peak knee extension torque with maximal voluntary isometric contractions (MVIC), and self-reported function, as measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). All outcome measures were evaluated for the involved lower extremity at baseline, 2 weeks, and 4 weeks. The investigator conducting all of the outcome measures was blinded to group assignment. On testing days, participants reported to a room separate from the investigator, where they removed any TENS units/electrodes and were reminded by an unblinded investigator not to provide any information to the investigator about any of the interventions that they received (therapeutic exercise or TENS), to ensure that blinding was achieved.

Instruments Isometric force signal was recorded from a dynamometer (Biodex System 3; Biodex, Shirley, NY) and the superimposed electrical stimulation was generated as previously reported.[30,31] Two 8 × 14-cm carbon-impregnated electrodes (Bloomex International, Inc, Elmwood Park, NJ) were secured to the quadriceps with an elastic bandage (Hartmann-Conco, Inc, Rock Hill, SC) to prevent movement of the electrodes during testing.[29-31] The WOMAC score was used to assess dysfunction, pain, and stiffness.[3]

CAR, MVIC, and Self-Reported Function Testing Prior to testing, participants pedaled a stationary bicycle at a self-selected speed for 5 minutes. Participants were then secured to the dynamometer unit, with hips flexed to 85° and 70° of knee flexion. All landmarks were properly aligned on the dynamometer, while the stimulating electrodes were positioned and secured over the distal vastus medialis and proximal vastus lateralis.[30,31] A graded warm-up was conducted on the dynamometer to assure that participants were able to exert maximal effort during the test and were accustomed to the electrical stimulus.[30] In addition to submaximal trials, participants performed 2 to 4 practice MVICs until the investigator was confident that each individual was able to exert maximal effort.

During CAR testing, an exogenous electrical stimulus was applied to the quadriceps when the test administrator observed that the maximal force plateau had been reached.[29-31] Two trials, separated by a 60-second rest, were performed to ensure that 2 acceptable trials could be averaged at each testing session.[30] The WOMAC was administered at each of the testing intervals, and participants were asked to reflect on pain, stiffness, and disability within the previous 48 hours.[3]

Data Analysis All raw torque data were

TABLE 1 Baseline Demographic*

	TENS and Exercise	Placebo TENS and Exercise	Exercise Only
Sex (males/females)	6/6	4/8	5/7
Body weight (kg)	82.4 ± 9.4	86.9 ± 25.7	83.6 ± 18.7
Height (cm)	170.6 ± 9.3	172.0 ± 7.5	170.0 ± 11.1
Body mass index (kg/m^2)	28.6 ± 4.8	29.5 ± 9.8	28.6 ± 5.6
Kellgren-Lawrence score, n (%)			
Grade 1	0	0	2 (16.7)
Grade 2	4 (25.0)	4 (25.0)	2 (16.7)
Grade 3	4 (25.0)	5 (41.7)	3 (25.0)
Grade 4	4 (25.0)	4 (25.0)	5 (41.7)
Previous history of knee injury or surgery (%)	66	50	58
Previous history of physical therapy for knee (%)	66	58	66
Previous history of TENS (%)	50	41	25

Abbreviation: TENS, transcutaneous electrical nerve stimulation.
**Values are means ± SD, except where otherwise indicated.*

TABLE 2 Therapeutic Exercise

	Week 1	Week 2	Week 3	Week 4
Stationary bicycle*	x	x	x	x
Unilateral stretching (involved lower extremity)†	x	x	x	x
Quadriceps sets and short arc quadriceps‡	x			
Flexion straight leg raises‡	x			
Abduction straight leg raises‡	x	x	x	x
Step-ups§	x	x	x	x
Seated knee extension and flexion with weight‡		x	x	x
Wall squats with physio ball assistance‖			x	x
Balance training¶	x	x	x	x
Cool-down walking*	x	x	x	x

**5 to 7 min comfortable speed.*
†3 × 30-s hold (quadriceps, hamstrings, hip rotators, gastrocnemius).
‡4 sets of daily adjustable progressive resistive exercise (DAPRE).
§3 sets of maximum 10 repetitions, progressed from a step height of 10.16 to 20.32 cm.
‖Maximum 10 repetitions, adjusting squat depth and hold time.
¶3 × 30 s adjusting footing and eyes open/closed.

low-pass filtered at 15 Hz. CAR was calculated by dividing the force measurements of the maximal voluntary contraction (F_{MVIC}) by that of the force produced by the superimposed burst (F_{SIB}) plus the MVIC (F_{MVIC}), as previously performed[30,31]: CAR = (F_{MVIC})/(F_{SIB} + F_{MVIC}).

The peak force (F_{SIB} + F_{MVIC}) value and the maximal voluntary contraction value (F_{MVIC}) were calculated from the mean of the 2 best separate trials at each time in the series, when the superimposed burst was applied. F_{MVIC} was calculated from a 0.15-second period immediately prior to the administration of the exogenous electrical stimulus. All MVICs were reported separately as Nm/kg of body weight.

Statistical Analysis

Sample size was determined for the primary aim (CAR), by using a related study[10] to estimate expected means and standard deviations. Although this study did not evaluate CAR, it did measure Hoffmann reflex voltages, which are measures of motor neuron pool excitability. A pooled mean difference of 2.26 and the pooled standard deviation of 1.5 were used to calculate sample size.[10] An alpha of .05 and a 1-beta level of .80 were used in the calculation. Our calculations estimated that 12 patients were needed per group for a total of 36 patients.

Means and 95% confidence intervals were calculated for all outcome measures prior to data analysis. Two separate, mixed-model analyses of variance (ANOVAs) of group (TENS and exercise, placebo TENS and exercise, and exercise) by time (baseline, 2 weeks, and 4 weeks), with the repeated measure on time, were used to evaluate differences in quadriceps CAR and quadriceps MVIC among treatment groups over time. Four additional individual, 3-by-3 mixed-model ANOVAs were used to calculate differences in total WOMAC score and WOMAC subsets (pain, stiffness, and function) among groups over time. A mixed-model ANOVA of group (TENS and exercise and placebo TENS and exercise) by week (week 1, week 2, week 3, and week 4), with the repeated measure on time, was used to assess differences in the reported hours of TENS and placebo use between groups over the 4 weeks. Also an independent *t* test was used to assess differences between the total hours of reported use between the TENS and placebo groups over the entire 4 weeks. Tukey post hoc analyses were utilized to evaluate multiple comparisons of significant interactions. Standardized Cohen *d* effect sizes, with 95% confidence intervals, were calculated using pooled standard deviations for all groups between baseline and 2 weeks and baseline and 4 weeks. Pearson product moments were calculated and squared to determine the amount of variance in percent change of CAR and MVIC, which explained variance in the change in WOMAC score and its subsets. Group means for each time point were imputed into the dataset to fill all missing data points due to attrition (**FIGURE**). In addition to the dropouts, we used the same mean imputation method for 1 participant in the placebo TENS and exercise group who completed the intervention but refused to perform the CAR follow-up measurements at 2 weeks and 4 weeks due to perceived discomfort during testing. All statistical analyses were performed with SPSS Version 16.0 (SPSS Inc, Chicago, IL).

RESULTS

Compliance

No adverse events were reported to the study personnel regarding TENS or placebo usage. Compliance data were not completed by 1 participant in the placebo group and, therefore, we treated these data as we did the other missing data points, by imputing group means at the time levels. There was no statistical difference in the total time of stimulator use reported by individuals in the TENS with exercise and the placebo TENS with exercise group over the 4-week period. There was a significant week-by-group interaction for reported time of use of the stimulator during specific weeks between the TENS with exercise and placebo TENS with exercise groups ($F_{1,32}$ = 5.38, *P* =.03). The TENS with exercise group reported significantly longer intervention usage during days 1 to 7 (*P* = .05) and days 22 to 28 (*P* = .008).

Central Activation Ratio

There was a significant group-by-time interaction ($F_{4,66}$ = 3.3, *P* = .02) for CAR. There were no statistical differences in quadriceps CAR ($F_{2,35}$ = 0.225, *P* = .8) at baseline among groups. Quadriceps CAR was significantly greater in the TENS with exercise group compared to the control group at 2 weeks (*P* = .02) and the placebo group at 4 weeks (*P* = .03) (**TABLE 3**). The CAR for TENS with exercise group were not significantly higher than the placebo with exercise group at 2 weeks (*P* = .08) (**TABLE 3**). CARs for the TENS with exercise group was significantly higher at 2 weeks (*P* = .001) and 4 weeks (*P* = .002), compared to baseline (**TABLE 3**). Additionally, CARs in the placebo TENS and exercise group were higher at 2 weeks (*P* = .001) but not at 4 weeks (*P* = .29), while no differences were found in the exercise group between baseline and 2 weeks (*P* = .57) and 4 weeks (*P* = .33) (**TABLE 3**). CAR effect sizes were large at 2 weeks (1.93) and 4 weeks (1.81) in the TENS and exercise group, as well as in the placebo TENS and exercise group at 2 weeks (0.88) (**TABLE 4**).

Maximal Voluntary Isometric Contraction There was a significant group-by-time interaction ($F_{4,66}$ = 6.75, *P* = .02) for MVIC. No significant differences in MVIC between groups were found at baseline ($F_{2,35}$ = 1.26, *P* = .30). MVIC for the TENS and exercise group was higher compared to the placebo and exercise group at 2 weeks (*P* = .005) and 4 weeks (*P* = .001), but not significantly higher compared to the control group at 4 weeks (*P* = .09) (**TABLE 3**). MVICs for the TENS with exercise group was significantly higher at 2 weeks (*P* = .001) and 4 weeks (*P*<.001) compared to baseline (**TABLE 3**). No differences were found in the placebo TENS and exercise group (*P* = .30, *P* =

TABLE 3 Self-Reported Function, CAR, MVIC*

	Exercise Only	Placebo TENS and Exercise	TENS and Exercise
Baseline			
WOMAC total (24-130 points)	53.8 (43.5, 64.0)	61.0 (49.5, 72.6)	57.7 (46.3, 69.0)
WOMAC pain (5-25 points)	14.3 (11.0, 17.0)	15.0 (11.7, 18.6)	14.7 (11.4, 18.1)
WOMAC stiffness (2-10 points)	5.3 (4.4, 6.1)	5.8 (4.4, 7.1)	5.3 (4.3, 6.3)
WOMAC function (17-85 points)	34.2 (27.3, 41.0)	40.2 (31.7, 48.7)	37.6 (30.0, 45.6)
CAR	0.80 (0.74, 0.86)	0.77 (0.72, 0.82)	0.78 (0.71, 0.86)
MVIC	1.89 (1.4, 2.4)	1.40 (1.0, 1.9)	1.80 (1.3, 2.3)
2 wk			
WOMAC total (24-130 points)	44.5 (37.6, 51.0)	50.0 (42.3, 57.7)	43. 9 (35.0, 52.5)
WOMAC pain (5-25 points)	11.8 (10.1, 13.5)	13.9 (12.1, 15.7)	11.6 (9.2, 14.0)
WOMAC stiffness (2-10 points)	4.2 (3.5, 4.8)	4.7 (3.8, 5.6)	3.4 (4.3, 5.0)
WOMAC function (17-85 points)	28.5 (23.1, 33.8)	31.4 (25.5, 37.3)	28.1 (22.4, 33.8)
CAR	0.82 (0.74, 0.89)	0.85 (0.78, 0.91)	0.94 (0.91, 0.96)†
MVIC	2.00 (1.6, 2.5)	1.60 (1.1, 2.0)	2.50 (2.2, 2.8)‡
4 wk			
WOMAC total (24-130 points)	40.7 (34.6, 46.7)	47.8 (40.6, 55.0)	35.7(30.9, 40.4)
WOMAC pain (5-25 points)	11.8 (8.9, 14.3)	12.3 (10.1, 14.5)	10.0 (8.3, 11.7)
WOMAC stiffness (2-10 points)	4.2 (3.4, 4.9)	4.4 (3.2, 5.6)	3.0 (2.4, 4.0)
WOMAC function (17-85 points)	24.9 (20.9, 28.9)	31.1 (26.2, 36.0)	22.5 (19.6, 25.4)
CAR	0.84 (0.75, 0.92)	0.81 (0.71, 0.91)	0.94 (0.90, 0.98)§
MVIC	2.10 (1.7, 2.5)	1.60 (1.1, 2.0)	2.80 (2.3, 3.2)§

Abbreviations: CAR, central activation ratio; MVIC, maximal voluntary isometric contraction; TENS, transcutaneous electrical nerve stimulation; WOMAC, Western Ontario and McMasters University Osteoarthritis Index (lower scores indicate improvement).
**Values are mean (95% confidence interval).*
†Significantly different than control at 2 weeks (P<.05).
‡Significantly different than placebo at 2 weeks (P<.05).
§Significantly different than placebo at 4 weeks (P<.05).

.35) and the exercise only group (P = .27, P = .14) (**TABLE 3**) for MVIC among baseline and 2 weeks and 4 weeks, respectively. Large effect sizes with 95% confidence intervals contained on the positive side of 0 were found for the TENS and exercise group at both 2 weeks (1.05) and 4 weeks (1.26) (**TABLE 4**).

Western Ontario and McMaster Universities Osteoarthritis Index There were no significant time-by-group interactions for total WOMAC score ($F_{4,66}$ = 1.01, P = .41) or any of the WOMAC subset scores (pain: $F_{4,66}$ = 0.7, P = .59; stiffness: $F_{4,66}$ = 1.3, P = .27; function: $F_{4,66}$ = 1.1, P = .37). There was a main effect for time, such that total WOMAC ($F_{2,66}$ = 30.6, P<.001) and all subset WOMAC scores (pain: $F_{2,66}$ = 13.4, P<.001; stiffness: $F_{2,66}$ = 25.3, P<.001; function: $F_{2,66}$ = 22.5, P<.001) significantly decreased over time in all treatment groups (**TABLE 3**). No differences were found between groups for total WOMAC score ($F_{2,33}$ = 1.51, P = .24) or any of the WOMAC subset scores (pain: $F_{2,33}$ = 0.79, P = .47; stiffness: $F_{2,33}$ = 0.90, P = .42; function: $F_{2,33}$ = 1.60, P = .22). Effect sizes were between –1.13 and –1.68 in the TENS and exercise group at 4 weeks for the total WOMAC scores and all WOMAC subsets (**TABLE 4**).

Relationships Among Outcome Measures Changes in CAR and MVIC were not correlated with changes in total WOMAC score. At 4 weeks, change in CAR predicted 17% of the change in WOMAC stiffness (r^2 = .17, P = .01). There were no significant correlations between change in WOMAC pain or function subset scores and change in CAR.

DISCUSSION

The primary aim of this study was to determine if the combination TENS set to a sensory level and therapeutic exercise would be more effective than the combination of placebo TENS and therapeutic exercises or therapeutic exercises alone to increase quadriceps activation over 4 weeks. We hypothesized that the group receiving TENS and exercise would have significantly higher CAR scores compared to the placebo TENS and exercise and exercise groups at both the 2-week and 4-week posttests. We found that the CARs in the group receiving a combination of TENS and exercise were significantly higher compared to the exercise only group at 2 weeks and placebo TENS and exercise group at 4 weeks. No significant differences were found between the TENS with exercise and placebo TENS with exercise groups at 2 weeks, or between the TENS with exercise and exercise only at 4 weeks. This being said, CAR effect sizes in the group receiving TENS and exercise were large at both posttests, with definitive 95% confidence intervals that did not cross zero (**TABLE 4**). These large definitive TENS with exercise effect sizes suggest that, although TENS with exercise was not statistically higher compared to both placebo and control groups at all posttests, the magnitude of the TENS CAR change from baseline may be substantially greater at 2 weeks and 4 weeks. Interestingly, large CAR effect sizes were evident for the placebo group at 2 weeks but not at 4 weeks, while controls had small CAR effect sizes at both posttests (**TABLE 4**). The statistically insignificant but strong placebo effect at 2 weeks may be due to minimal afferent excitation from merely having the adhesive electrodes on the skin or from the limited stimulation administered prior to the unit discontinuing treatment. This effect seemed to dissipate at 4 weeks, likely due to accommodation from the minimal stimulation.

We secondarily aimed to assess the effects of TENS with exercise on MVIC

and WOMAC. We hypothesized that MVIC would be higher and WOMAC scores would be lower in the TENS and exercise group following the intervention. MVIC torque was significantly higher in the TENS with exercise group compared to the placebo TENS with exercise group at 2 weeks and 4 weeks, and significantly higher at 4 weeks compared to the controls (**TABLE 3**). Large MVIC effect sizes with 95% confidence intervals that did not cross 0 in the TENS with exercise suggest that participants with TFOA were able to increase muscle strength in addition to activation (**TABLE 4**). Interestingly, small effect sizes in the placebo TENS with exercise and exercise only groups suggest that conventional therapeutic exercise in the absence of disinhibition may not provide an adequate stimulus for clinically relevant strength gains.

It has previously been suggested that strength gains in this population are somewhat meaningless unless paralleled with increased function.[13] We found that the total WOMAC score decreased over time for all groups, yet effect sizes were largest in the TENS with exercise group at 4 weeks (**TABLE 4**). Pain (**TABLE 3**), stiffness (**TABLE 3**), and function WOMAC subscales (**TABLE 3**) followed the same pattern of significantly decreasing in all groups over the 4 weeks, while having the largest effects in the TENS with exercise group at 4 weeks (**TABLE 4**). A change of 9.1 points on the function subscore of the WOMAC has been reported to be the minimally clinically important improvement.[34] Although all groups did reach improvements of 9.1 at 4 weeks (control, −9.3; placebo, −9.1; TENS, −15.1), only the TENS with exercise group reached this point at 2 weeks (control, −5.7; placebo, −8.8; TENS, −9.5). Interestingly, definitive large effects in CAR and MVIC occurred at 2 weeks, which seems to precede the large effects found for WOMAC scores in the TENS with exercise group. This may be evidence that, although significant disinhibition can occur as early as 2 weeks, the ability of patients to sense a difference may take longer.

TABLE 4 Effect Sizes and 95% Confidence Intervals*

	Exercise Only	Placebo TENS and Exercise	TENS and Exercise
At 2 wk compared to baseline			
WOMAC total	−0.69 (−1.46, 0.15)	−0.72 (−1.50, 0.12)	−0.87 (−1.67, −0.01)†
WOMAC pain	−0.62 (−1.41, 0.22)	−0.25 (−1.04, 0.56)	−0.68 (−1.47, 0.17)
WOMAC stiffness	−0.89 (−1.70, −0.03)†	−0.62 (−1.4, 0.22)	−0.78 (−1.58, 0.07)
WOMAC function	−0.59 (−1.38, 0.25)	−0.76 (−1.56, 0.09)	−0.87 (−1.67, −0.01)†
CAR	0.20 (−0.61, 0.99)	0.88 (0.02, 1.68)†	1.93 (0.91, 2.83)†
MVIC	0.20 (−0.61, 1.00)	0.19 (−0.62, 0.99)	1.05 (0.16, 1.86)†
At 4 wk compared to baseline			
WOMAC total	−0.99 (−1.80, −0.11)†	−0.88 (−1.69, −0.02)†	−1.60 (−2.46, −0.64)†
WOMAC pain	−0.58 (−1.37, 0.26)	0.59 (−1.38, 0.25)	−1.12 (−1.90, −0.22)†
WOMAC stiffness	−0.84 (−1.60, 0.02)	−0.69 (−1.49, 0.16)	−1.68 (−2.54, −0.70)†
WOMAC function	−1.05 (−1.86, −0.16)†	−0.85 (−1.65, 0.01)	−1.59 (−2.45, −0.63)†
CAR	0.39 (−0.43, 1.19)	0.33 (−0.48, 1.13)	1.81 (0.80, 2.68)†
MVIC	0.35 (−0.47, 1.14)	0.20 (−0.60, 1.00)	1.26 (0.35, 2.09)†

Abbreviations: CAR, central activation ratio; MVIC, maximal voluntary isometric contraction; TENS, transcutaneous electrical nerve stimulation; WOMAC, Western Ontario and McMasters University Osteoarthritis Index (lower scores indicate improvement).
**Negative scores for all WOMAC and WOMAC subsets, and positive scores for CAR and MVIC represent a beneficial effect.*
†95% confidence intervals that do not cross 0.

Previous authors[4] have found that volitional quadriceps activation may act as a moderator when relating strength and physical function; yet we found that changes in CAR did not explain changes in WOMAC score. Currently, the clinically significant change in CAR is unknown. Although promising beneficial effects in CAR and MVIC were found for the TENS with exercise group, these same participants did not exhibit changes in kinetic and kinematic variables during gait.[32] This additional information may suggest that specific training is needed to incorporate increased quadriceps voluntary activation and strength capabilities into changes in function. At this point it is unclear how changes in pain, muscle activation, and physical function relate, but our results suggest that the greatest effects for all 3 of these measures occurred in the TENS with exercise group. It should also be noted that changes in WOMAC pain scores did not significantly relate to changes in CAR, suggesting that alterations in muscle activation may be independent of changes in knee pain.

It has been suggested that the lack of relationship between changes in pain and changes in CAR following disinhibition indicates the existence of a unique disinhibitory neural pathway that may share little redundancy with pain modulation pathways.[30] Nevertheless, the causal nature between the changes in the pain-CAR relationship remains unknown. A case could be made to suggest that increased quadriceps CAR could assist in restoring proper movement patterns, thus decreasing pain associated with movement. Conversely, pain may be decreased by a different gating mechanism, which may give rise to increased motor output. Yet it can also be hypothesized that the relationship for both changes in pain and CAR are dependent upon each other, and a directional causal relationship is not appropriate. Unfortunately, this question cannot be answered from this data set.

Although the current study is the first to assess the disinhibitory effects of TENS in conjunction with a therapeutic exercise program, it is limited to a rela-

tively small sample of TFOA participants with quadriceps activation deficits (CAR, <.90). Although there were no statistical differences in the total amount of hours the TENS and placebo groups utilized the units, the TENS group used the devices more in the first and fourth week of the intervention compared to the placebo. Group means at all weeks indicated that both groups wore the devices for at least the suggested 8 hours per day. Future studies may set a specific amount of hours for patients to utilize the device, rather than only a minimum to decrease the risk of one group having more contact hours with the device. Additionally, future studies with larger sample sizes and which evaluate different populations may allow for more generalizable data. It is unknown if quadriceps CAR would continue to increase in any groups if treatments were continued beyond 4 weeks. It is possible that disinhibitory treatments may need to last longer than 4 weeks to gain the most optimal effects in patients with chronic joint injuries. Furthermore, while we chose a 4-week intervention, as it was the standard of care for TFOA at our institution, future studies might investigate the treatment duration to provide optimal therapeutic outcomes. We also only studied participants with baseline CARs of 0.90 or less, because we wanted to ensure that we included participants with the specific impairment (decreased quadriceps activation) that we were interested in improving with TENS and exercise. During screening, we excluded 11 participants (**FIGURE**) with CARs over 0.90. It remains unknown if people with TFOA and high quadriceps activation (CAR, >0.90) would benefit from TENS during therapeutic exercise therapy.

Authors of previous studies[10,21] have suggested that arthrogenic muscle inhibition is a clinical impairment that should be addressed in conjunction with therapeutic exercise. Data from previous studies[10,30] have indicated that quadriceps activation and motor neuron pool excitability increased while TENS was actively administered, and previous reports[10] have suggested that motor neuron pool excitability benefits from TENS were negated when the TENS was removed. For the present study, which assessed the possible clinical benefits of disinhibitory TENS, we felt that it was imperative to provide participants with TENS during both therapeutic exercise and normal daily activities, thus providing patients with greater exposure to the intervention. All testing in the current study was conducted following the removal of the TENS, suggesting that disinhibition performed over a period of weeks may allow for increased muscle activation in the absence of the disinhibitory modality. Although untested, previous hypotheses[10,30] suggest that TENS is interpreted by the central nervous system as excitatory, thus causing an increased excitation of the motor neurons. It is possible that continued excitatory stimulation over a 4-week period, in conjunction with progressive resistance training, may allow the neuromuscular system to access previously inhibited pathways. The underlying neural mechanism allowing for increased volitional activation to remain following the removal of the TENS is unclear. It is possible that altered afferent activity from the electrical stimulus may encourage synaptic plasticity within the motor system,[14] which may allow a patient to access previously inhibited motor neurons after the exogenous stimulus is removed. Hebbian synapse theories suggest that postsynaptic cells that continually depolarize in response to a presynaptic potential may renetwork to allow for multiple similar postsynaptic cells to depolarize together, even in the occasion that all of the postsynaptic neurons are not directly depolarized by afferent neurons.[15] It has been hypothesized that TENS may cause increased excitatory presynaptic potentials, which may increase motor output,[30] by allowing for recruitment of motor neurons that would otherwise not propagate excitatory postsynaptic potentials. Over weeks of multiple motor neurons depolarizing together, while the disinhibitory TENS was administered, neural networks might have been organized to depolarize this group of motor neurons simultaneously, regardless of whether only 1 or multiple motor neurons propagated an action potential. Thus, when the TENS was removed, a weaker excitatory presynaptic potential might have allowed for a similar postsynaptic effect (increased CAR).

CONCLUSION

The TENS with exercise group, compared to the control group, displayed significantly higher CARs and MVICs at various time points within the 4-week intervention, while no differences in WOMAC score were detected among groups. Large effect sizes for CAR, MVIC, and WOMAC, when using TENS in conjunction with therapeutic exercise, provide further evidence that TENS may be specifically used to target quadriceps inhibition in patients with TFOA.

KEY POINTS

FINDINGS: TENS in conjunction with exercise increased quadriceps CAR and MVIC compared to placebo TENS and exercise and exercise only in those with TFOA. TENS with exercise did not increase self-reported function more than placebo TENS and exercise and exercise alone.

IMPLICATION: Quadriceps activation failure is a common impairment in those with TFOA, which may be a modifier of physical function. TENS in conjunction with therapeutic exercise may provide a means of disinhibiting the quadriceps and activating motor neurons that were previously inhibited.

CAUTION: The sample size was relatively small (n = 36), and the participants with TFOA had fairly homogeneous signs and symptoms. Additionally, no outcome measures were performed beyond the intervention period.

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