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Effects of TENS on Voluntary Quadriceps Activation and Vertical Ground Reaction Force During Walking in Subjects with Experimental Knee Pain

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Effects of Transcutaneous Electrical Nerve Stimulation on Voluntary

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ABSTRACT

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Context: Knee pain is a common symptom in knee pathology and is associated with alterations in quadriceps activation and movement patterns. Reducing pain through intervention may help reestablish neuromuscular function. The independent effects of knee pain are difficult to examine and unclear. **Objective**: To investigate the effects of transcutaneous electrical nerve stimulation (TENS) on quadriceps activation and vertical ground reaction force (VGRF) during walking. **Design**: Crossover. **Setting**: Laboratory. **Subjects**: 15 in the TENS group (10M and 5F, 23.5 ± 2.8 yrs, 70.5 ± 12.5 kg, 178.1 ± 7.4 cm), and 15 in the sham group (10M and 5F, 22.5 ± 2.0 yrs, 72.1 ± 13.7 kg, 177.5 ± 9.3 cm). **Interventions**: Subjects underwent three experimental conditions (pain, sham, and control). Measurements were recorded across four time points (preinfusion, infusion, treatment, and posttreatment). Hypertonic or isotonic saline, respectively, was infused into the infrapatellar fat pad for 48 minutes (total 7.7 mL). The TENS group received a 20-minute treatment. A sham treatment was administered to the sham group. **Main Outcome Measures**: Perceived knee pain on a 10-cm visual analog scale, knee extension maximum voluntary isometric contraction (MVIC) normalized to body mass, knee extension central activation ratio (CAR), and VGRF. **Results**: Knee pain peaked at 4 cm during infusion and remained consistent across time in the sham group ($F_{2,28} = 49.90$, $P < 0.0001$), while knee pain gradually decreased to 1.5 cm following TENS treatment ($F_{2,28} = 23.11$, $P < 0.0001$). A group x condition x time interaction was detected for both the MVIC ($F_{6,168} = 2.92$, $P < 0.01$) and CAR ($F_{6,168} = 3.03$, $P < 0.008$) measurements. Post hoc analysis revealed that the infusion of hypertonic saline reduced knee extension MVIC by 29% in the TENS group, and by 26% in the sham group ($P < 0.05$). However, while the MVIC remained depressed by 26% following sham treatment, the MVIC was found to improve by 12% following TENS treatment ($P < 0.05$). Similarly, a 10% decrease in CAR was detected in both sham and TENS groups prior to treatment. This 10% deficit held, with a 9% deficit following sham treatment, while the deficit of CAR was improved by 4% following TENS treatment ($P < 0.05$). For the TENS group, infusion of hypertonic saline changed VGRF at initial loading, midstance, and push-off phase. VGRF was only different at initial loading and push-off phase following TENS treatment. For the sham group however, sham treatment did not restore VGRF, showing alterations in initial loading, midstance, and push-off phase ($\alpha = 0.05$). **Conclusions**: Infusion of hypertonic saline increased perceived knee pain, reduced knee extension MVIC, reduced CAR, and altered VGRF over some of stance phase. TENS lessened the deficits in MVIC, CAR, and VGRF, suggesting decreased muscle inhibition and improved movement function.

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Introduction

Knee pain is a common symptom in knee pathology exhibited frequently in athletes and nonathletes.[1,2] Among all knee complaints, knee pain accounts for 40% of symptoms reported in sports medicine clinics.[3,4] Knee osteoarthritis (OA), which is a possible result of long-term knee pain,[5] affected nearly 27 million adults (12.1%) in the U.S. in 2008.[6] Acutely, knee pain decreases quadriceps motor function[7,8] and alters movement biomechanics.[9] It also changes movement biomechanics over the long-term, including climbing stairs and walking.[1,10,11] Although etiologies and diagnoses vary, it is obvious that knee pain causes short- and long-term changes in lower extremity neuromuscular function.[1,5,7-9,12]

The acute effects of knee pain include alterations in quadriceps activation.[7,8] Among other lower extremity muscle groups, the quadriceps contribute to the stability of the knee joint. The quadriceps could play an important role in absorbing impact shock and distributing load across the knee joint.[13-15] The quadriceps work eccentrically during initial stance to help proper knee joint loading, and to decelerate the limbs in terminal swing before heel strike, thereby decreasing knee load during initial stance.[16] However, quadriceps function is reduced due to knee pain.[8,1,7,17] Quadriceps inhibition is an immediate effect of knee pain, and eventually gives rise to chronic quadriceps muscle weakness and atrophy,[18] which in turn is likely associated with altered knee joint loading.[15] Since decreased quadriceps function due to experimental knee pain (EKP) is likely to cause a reduction of internal knee extension moments during walking,[9] reduced quadriceps activity can lead to alterations in vertical ground reaction force (VGRF). It is for these reasons that we and others[1,5,17] speculate that the quadriceps may play a critical role in prevention of degenerative knee joint disease.

Chronic knee pain likely contributes to knee OA genesis and progression and other long-term pathologies because it results in abnormal knee joint load during gait.[5,19] Pain-avoidance gait patterns are the first stage of the pathogenesis of medial knee OA.[20-22] Since VGRF is a primary contributor to knee load, knee joint muscle function,[23] and joint loading rate,[24] the observation of VGRF during painful walking can help us better understand the effects of knee pain on knee joint muscle function and corresponding knee joint load.

To alleviate acute and chronic effects of knee pain, a disinhibitory intervention is likely necessary. Among all disinhibitory interventions, including cryotherapy, thermotherapy, electrotherapy, and manual therapy, transcutaneous electrical nerve stimulation (TENS) could offer the most potential for reducing knee pain[25,26] and increasing quadriceps activation.[27,28] It is thought that TENS stimulates large-diameter sensory nerves, increasing inhibition of T cells and decreasing the ability of pain signals to reach the brain.[29] Sensory signals created by TENS are considered to be an excitatory stimulus which supersedes inhibitory sensory signals, and improves motor output.[27] As a result, early TENS could prevent the consequences of knee pain, including perceived knee pain, quadriceps muscle inhibition, altered VGRF, and altered knee joint loading.

Recent studies found that subjects with experimental knee pain (EKP) showed a 34% reduction of knee extension maximal voluntary isometric contraction (MVIC),[8] a 5% reduction of central activation ratio (CAR),[8] and a decrease in peak VGRF during gait.[9] However, no study has looked at the effects of TENS on quadriceps activation and VGRF during gait in subjects with EKP.

The purpose of this study was to investigate the effects of TENS on quadriceps activation and VGRF during gait in subjects with EKP. We hypothesized that EKP could reduce quadriceps activation and VGRF, and TENS could improve deficits of the quadriceps activation and VGRF.

Methods

Experimental Design

This study was conducted as a crossover, controlled laboratory trial. Independent variables were: four time intervals (preinfusion, infusion, treatment, and posttreatment), three conditions (pain, sham, and control), and two treatment groups (TENS and sham). Dependent variables were: perceived knee pain, knee extension MVIC, knee extension CAR, and VGRF during walking.

Subjects

Thirty volunteer subjects were recruited from a college population: 15 subjects in the TENS group (23.5 ± 2.8 yrs, 70.5 ± 12.5 kg, 178.1 ± 7.4 cm), and 15 subjects in the sham group (22.5 ± 2.0 yrs, 72.1 ± 13.7 kg, 177.5 ± 9.3 cm). To participate, each subject had to be physically active (exercising at least three times a week for 30 min), with no history of neurological disorders, no history of lower extremity orthopedic surgery, and no lower extremity injury in the past six months. Moreover, no pain medication was allowed 12 hours before data collection. Each subject was randomly assigned to either the TENS or sham treatment group. Each subject was required to come three times and each visit was separated by at least a 48-hour washout interval between each data collection. We asked each subject to maintain his or her physical activity prior to and between the data collection sessions. Prior to participation, an informed consent form was signed by each subject.

Instruments

Knee extension MVIC was measured using a Biodex dynamometer (system Pro 4, Biodex, Shirley, NY) with a sampling rate of 100 Hz. After shaving and cleaning electrode locations, 2 electrodes (Dura-Stick II, Chattanooga, Hixson, TN; 70x127mm) were placed on the proximal-lateral aspect of the thigh and the distal-medial aspect of the thigh. When knee extension MVIC reached a plateau, a supramaximal electrical stimulus (100 pps, 600 μsec, 10 trains in 100 ms duration, and 125 V with peak output current 450mA) was manually transmitted to the quadriceps via two electrodes. To measure CAR, the S88 grass stimulator with the SIU8T transformer stimulus isolation unit (Grass-Telefactor, West Warwick, RI) was used to produce a supramaximal electrical stimulus.

VGRF was recorded using a force-sensing tandem treadmill (AMTI, Watertown, MA) with a sampling rate of 1200 Hz. VGRF data was smoothed by a fourth-order Butterworth filter with cutoff frequency of 25 Hz.[30] The unfiltered signal showed noise and 25 Hz cutoff frequency eliminated the noise effectively from the original data.

Perceived knee pain was measured using a 10-cm visual analog scale (VAS).[31] Every 2 minutes, each subject was asked to rate their perceived knee pain level.

Procedures

Each subject performed a 5-minute walking warm-up on the treadmill. After warm-up, electrode placement points on the anterior thigh were shaved and cleaned with alcohol wipes. Two electrodes were placed on the anterior thigh, one at the proximal-lateral aspect of the thigh and the other at the distal-medial aspect of the thigh (Figure 1).

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Measure Knee Extension MVIC and CAR

Each subject was positioned on the Biodex with the knee and hip secured at 90° and 85° flexion using a goniometer (Figure 2). The subject was requested to execute knee extension MVIC. When the MVIC reached a plateau approximately 1.5 to 2 s after each bout of MVIC, a supramaximal electrical stimulus was manually transmitted to two electrodes on the anterior thigh. The CAR was calculated by dividing knee extension MVIC by the force generated by the superimposed burst (SIB) plus knee extension MVIC: CAR = (knee extension MVIC) / (SIB + knee extension MVIC).[8,32]

Measure VGRF

VGRF was recorded (1200 Hz) during 30 s of walking at a self-selected speed. To minimize influence of speed on VGRF, the preinfusion walking speed was used as a covariate in the statistical analyses.

Pain Infusion

After preinfusion measurements, EKP was induced in each subject's dominant leg. A 20-gauge flexible catheter (Becton Dickinson Medical System, Sandy, UT) was inserted into the lateral infrapatellar fat pad. The angle of the catheter insertion was 45° in an inferior-medial direction to the middle of the infrapatellar fat pad with a depth of 1 cm (Figure 3). Using a 100-cm extension tube (B. Braun, Bethlehem, PA), the catheter was connected to a 30 mL syringe, which was attached to a portable infusion pump (Graseby Medical, Hertfordshire, UK). This portable pump created a continuous saline flow of 0.16 mL·min for 48 minutes (total 7.7 mL).

For the pain condition, 5% hypertonic saline (B. Braun, Irvine, CA) was infused. After the initiation of infusion, each subject assumed three different positions (supine for 3 min, sit upright for 3 min, and stand for 2 min), to help with familiarization to the effects of the infusion

(Figure 4, 5, and 6). For the sham condition, 0.9% isotonic saline (Hospira, Inc., Lake Forest, IL) was infused. For the control condition, measurements were recorded at each of the time intervals. The control condition was identical to the other sessions, except that no infusion was administered.

TENS Treatment

TENS treatment was given to each subject in the TENS group 14 min after initial infusion. The skin around the knee joint was shaved and cleaned with alcohol wipes to ensure the adherence of electrodes. Four self-adhesive square electrodes were placed on the superior-medial and superior-lateral, and the inferior-medial and inferior-lateral borders of the patella (Figure 7).[27] Two TENS currents covered the entire knee joint. The TENS protocol was set at a continuous asymmetric biphasic square-pulse wave with a pulse width of 120 and a pulse rate of 180.[33] The intensity of TENS was increased until a visible contraction of the vastus medialis was seen. Then, the intensity of stimulus was reduced until no contraction was seen or felt by investigators.[27] The duration of treatment was set for 20 min.

Sham Treatment

Sham treatment was given to the sham group. Each subject was told that an electrical stimulation was set to subsensory level and the indicator light was on during treatment (Figure 8). This approach allowed us to keep the sham group blinded to receiving placebo treatment. The preparation for electrodes was the same with the TENS group as previously described.

Data Reduction

We recorded the MVIC and CAR at four time intervals (preinfusion, infusion, treatment, and posttreatment). Each measurement consisted of three trials. Between each of the MVIC and

CAR, there was a 30-second resting period. Means of the MVIC and CAR were calculated from three trials.

We measured walking VGRF for 30 s at the four time intervals. The smoothed VGRF corresponding to the first five stance phases of each 30-s collection were imported into MATLAB and normalized to weight (amplitude) and stance (time). Then we averaged the VGRF trace across the five observed stance phases.

Statistical Analysis

Means of the MVIC and CAR were calculated from three trials at each of the four time intervals. To detect difference in infusion, treatment, and posttreatment measurements compared to preinfusion (baseline) measurements, 2 x 3 x 4 mixed model ANOVAs with repeated measures were used for: perceived knee pain, knee extension MVIC, and knee extension CAR. A functional analysis of variance (FANOVA) was used to determine differences between groups and times for VGRF ($\alpha = 0.05$) over the entire stance phase. A FANOVA allows for a comparison of treatment effects as functional effects (polynomial functions) over the entire stance phase, rather than univariate or multivariate (discrete values) effects. In other words, we can detect whether there is a difference between the factors, and where in the stance phase those differences exist. As the means for inference, any difference between factors (effect) that is not equal to zero (no effect) at 95% confidence level is deemed statistically and clinically significant.

<div align="center">Results</div>

Perceived Knee Pain

Perceived knee pain peaked at 4 cm ($F_{2,28} = 49.90$, *P* < 0.0001) on a 10-cm VAS during infusion in both the sham and TENS groups. While perceived knee pain remained consistent

across time intervals following sham treatment, perceived knee pain was gradually decreased to 1.5 cm (F2,28 = 23.11, $P < 0.0001$) following TENS treatment (Figure 9).

Knee Extension MVIC

A group x condition x time interaction was detected for MVIC (F6,168 = 2.92, $P < 0.01$) and CAR (F6,168 = 3.03, $P < 0.008$) measurements. Post hoc analysis revealed that EKP acutely reduced knee extension MVIC by 29% (preinfusion = 3.20±0.66 Nm/kg, infusion = 2.28 ± 0.98 Nm/kg) in the TENS group, and by 26% (preinfusion = 3.34 ± 0.80 Nm/kg, infusion = 2.47 ± 0.77 Nm/kg) in the sham group ($P < 0.05$). However, while the MVIC remained depressed by 26% following sham treatment (treatment = 2.48 ± 0.69 Nm/kg, posttreatment = 2.49 ± 0.61 Nm/kg), reduced MVIC was improved by 12% following TENS treatment, which was statistically no different from preinfusion values (Figure 10).

Knee Extension CAR

Similarly, a 10% decrease in CAR was detected in both sham (preinfusion = 99 ± 1%, infusion = 89 ± 7%) and TENS groups (preinfusion = 98 ± 1%, infusion = 88 ± 12%) prior to treatment. While a 9% deficit remained following sham treatment (treatment = 89 ± 6%, posttreatment = 90 ± 6%), decreased MVIC was improved from 9% to 4% following TENS treatment, which was statistically no different from preinfusion values ($P < 0.05$) (Figure 11).

VGRF

Means of VGRF over five stance phases during 30 seconds of walking were calculated in both TENS and sham groups with three conditions in four time intervals. The stance phase of walking is divided into 4 phases, including 0%–17% (loading response), 17%–50% (midstance), 50%–83% (terminal stance), and 83%–100% (preswing).[34] Figures 12–17 show differences of VGRF between factors. The shaded areas represent 95% confidence intervals for the population

mean effect size. When the shaded area crosses the dotted line, clinically and statistically

significant differences exist. The functional analysis showed that VGRF was altered during

infusion measurements compared to preinfusion measurements in the TENS group (Figure 12).

After TENS treatment, the difference of VGRF areas was reduced (Figure 13). During 6-min

posttreatment measurements, the difference of VGRF areas was even more reduced (Figure 14).

For the sham group, the functional analysis revealed that VGRF was also changed following

infusion compared to preinfusion measurements (Figure 15). After sham treatment, there still

existed some differences of VGRF (Figure 16). During posttreatment measurements, altered

VGRF was consistently revealed (Figure 17). No difference was shown in sham and control

conditions in both TENS and sham groups.

<div align="center">Discussion</div>

The primary purpose of this study was to examine the acute effects of TENS on voluntary

quadriceps activation and walking biomechanics in subjects with EKP. We hypothesized that

TENS treatment would decrease perceived pain intensity and mitigate associated alterations for

MVIC, CAR, and VGRF. The present data generally support our hypotheses. The present EKP

model acutely produced knee pain for 48 min while being infused, and caused a reduction of

quadriceps activation and alterations in walking VGRF. After TENS treatment, quadriceps

inhibition was somewhat disinhibited, as shown by the mitigation of the altered MVIC and CAR

due to EKP. The TENS treatment also caused walking VGRF to move in a return direction

toward normal relative to the altered VGRF, due to EKP throughout stance. Due to confounding

variables such as inflammation, effusion, joint degeneration, and/or receptor damage, it is

difficult to investigate the independent effects of knee pain on alterations in lower extremity

neuromechanics. However, our EKP model allowed us to examine the effects of EKP as an independent variable by eliminating the aforementioned confounding variables.

Perceived Knee Pain

Many studies[1,3,7-9,35] have investigated the effects of EKP on lower extremity neuromuscular alterations. Bennell et al.[35] suggested that the quality, regions, and patterns of pain caused by EKP are similar to those in patients with clinical knee pain. Hypertonic saline, placed in the infrapatellar fat pad, is a safe and efficient method to produce anterior knee pain through release of substance P, a substance that is released through the c-fiber pathways in the dorsal horn, which is commonly seen in musculoskeletal pain.[36] Several anatomic structures and regions may produce anterior knee pain such as the infrapatellar fat pad, patellar tendon, joint capsule, medial and lateral retinaculum, and anterior synovium.[35] Among those aforementioned regions, the infrapatellar fat pad has a good blood supply from the synovial membrane[35] and is innervated by a posterior articular nerve.[37] Investigators reported perceived knee pain via arthroscopic palpation of the interior knee without intra-articular anesthesia.[38] They noted that the fat pad is highly sensitive to pain.[38]

We infused 7.7 mL (0.16 mL·min for 48 min) of hypertonic saline into the infrapatellar fat pad to induce the EKP condition. An average of perceived knee pain level at 4 cm in the present study was consistent with previous research, which reported 4.29 cm by infusing 6.6 mL (0.3 mL·min for 22 min).[9] The present study examined the effects of EKP for 48 min. While the previous single-injection model provides a very short window of time of significant pain (approximately 5 min), the current model allowed us a longer duration to examine the effects of EKP on lower extremity neuromuscular alterations.

Knee Extension MVIC

Multiple researchers have attributed muscle inhibition to pain.[23,39-41] After knee injuries, quadriceps inhibition is commonly observed in previous studies.[42-46] The muscle inhibition has been investigated in clinical anterior knee pain,[42,44,45,47,48] experimentally induced knee pain,[1,7,8] and postoperative knee pain.[25,49,50] One study reported that patients with unilateral anterior knee pain showed bilateral quadriceps inhibition,[44] which suggests that knee pain contributes to negative sensorimotor function in the contralateral limb. Since the present study only calculated knee extension MVIC in the involved limb, we can only speculate that EKP could decrease force output in the uninvolved limb.

Our results show that EKP acutely reduced knee extension MVIC by 29% in the TENS group and by 26% in the sham group compared to preinfusion measurements. The results are consistent with previous research that showed that EKP (a 1 mL single injection of hypertonic saline) decreased knee extension MVIC.[7,8] When EKP is administered, afferent activity from nociceptor may give rise to alterations in the excitability of spinal reflex pathways, which contributes to a reduction of quadriceps alpha motoneuron excitability.[51]

Previous authors supported the idea that TENS treatment plays a critical role in a decrease in perceived pain in musculoskeletal injuries.[24,26] Nociceptors in the patella fat pad are stimulated by hypertonic saline through the group III and IV afferent fibers.[52] Afferent sensory stimuli (knee pain signals) are transmitted to the brain through both large- and small-diameter nerve fibers.[29] Both sensory stimuli meet at the T cell, where the gate is located.[29] The substantia gelatinosa, which transmits inhibitory signals to the T cell, obtains different stimuli from both large- and small-diameter fibers. TENS treatment aims to stimulate large-diameter sensory nerves, resulting in an increase in inhibitory effects on the T cell which closes the gate, where

sensory pain signals are unable to transmit to the brain.[29] In the present study, perceived knee pain was reduced from 4 cm (peak) to 1.2 cm following TENS treatment. Our findings are consistent with previous studies.[25,26] However, we do not know how a reduction of pain intensity affects an increase in quadriceps activation.

Many research studies have reported the disinhibitory effects of TENS on quadriceps activation in knee pathologies.[27,28,32] A 20-min TENS treatment effectively reduced the amount of quadriceps inhibition arising from EKP, and it seems to be more effective 6-min posttreatment in the present study. The disinhibitory mechanism of TENS on quadriceps function is not fully understood. However, we can speculate that TENS may stimulate inhibitory reflex mechanisms, which lead to the excitation of inhibited motor neurons.[27] Sensory stimulation created by TENS is considered as the excitatory stimulus, which supersedes inhibitory sensory signals, thereby improving motor output.[27] We speculate that TENS may diminish quadriceps muscle inhibition by: inhibiting the activity of the Ib inhibitory interneuron, creating excitation of the Ia excitatory interneuron leading to an excitatory potential at the motoneuron pool, and/or activating supraspinal centers to abate the effects of muscle inhibition via descending inhibitory fibers, which connect to the Ib interneuron (an integrative station for sensory signals).[27]

Knee Extension CAR

Even though central activation failure possibly can result from decreased voluntary force production,[8] altered central neural reflex pathways,[53] or reduced maximum firing rate,[54] the main cause of a reduction of CAR is poorly understood. A CAR of 1.0 represents a complete muscle contraction, and a CAR ≥ 0.95 is considered full muscle activation.[55] Previous research showed that the relationship between CAR and MVIC is commonly curvilinear, showing a CAR of 0.8 is equivalent to a MVIC of 60% ($R^2 = 0.98$; 98% of accurate prediction).[55] In the present study, a

CAR of 0.9 is proportionate to a MVIC of 75% under pain condition. As knee extension MVIC improved from 71% to 88% following TENS treatment, CAR increased from 0.9 to 0.96. We speculate that TENS possibly contributes to increasing excitation of the motor neurons and firing rate, suggesting increased force production and decreased muscle inhibition. Due to the nature of curvilinear shape (the flat portion of the curve at the end), CAR is not a sensitive measure at greater than 90% of MVIC.[55] Healthcare professionals should consider the curvilinear nature of the relationship as they interpret CAR values relative to MVIC values.[55]

VGRF

Presently, EKP altered VGRF. Infusion of hypertonic saline in the TENS group resulted in a reduction of VGRF at initial loading response (0%–4%), early midstance (16%–32%), and terminal stance (69%–91%), and an increase of VGRF at midstance (44%–67%) (Figure 12). Similarly, a reduction of VGRF is also observed in the sham group at slightly different stance phases (Figure 15). This fits with previous findings that showed decreased peak VGRF due to knee pain in patients with knee OA.[12,56] In addition, our findings are consistent with previous data published by Seeley et al., showing a reduction of peak VGRF in subjects with EKP.[9] Decreased VGRF during the loading response and push-off phases of walking are likely associated with quadriceps inhibition resulting from EKP as knee extensors contribute to vertical acceleration of the center of mass during loading response and push-off phase.[9,16] Normal quadriceps function likely plays a critical role in knee joint loading during walking.[5,7-9]

The present study has three important key points: how EKP affects quadriceps function, how altered muscle function affects articular cartilage health, and how TENS appears to mitigate the effects of EKP on quadriceps activation.

EKP significantly results in a decrease in knee extensors function and changes in knee joint load through an unloading strategy, which may cause altered VGRF in certain parts of the stance phase. Quadriceps strength contributes to proper knee joint load during initial loading response and push-off phase of gait.[9,23] However, since EKP gives rise to a reduction of quadriceps strength, knee joint load is consequently changed in the present study. Altered VGRF in the present study can be explained by two possible perspectives: poor quadriceps activation and an unloading strategy. A reduction of quadriceps activation may likely be associated with a subconscious alteration in voluntary effort, resulting in fear of damaging or increasing knee pain from the involved limb.[57,58] Inhibited quadriceps function due to knee pain consequently contributes to a reduction of internal knee extension moments in the involved limb, which ultimately results in altered knee joint load.[9] In addition, altered VGRF is possibly related to an unloading strategy due to perceived knee pain. The unloading strategy might also be related to perception of pain, which makes subjects feel fear for damaging or provoking pain more during movement from the involved limb.[57,58]

Previous studies reported that participants with clinical knee pain showed a greater knee joint load response in the uninvolved limb rather than the involved limb.[59] This unloading motor strategy can result from perceived pain and/or quadriceps dysfunction. The abnormal shape of the VGRF is often observed, showing an absence of two distinguishable peaks at initial loading response and push-off, and an increase in VGRF at midstance. Since we did not calculate VGRF in the uninvolved limb, we can only speculate that both an intentional unloading motor strategy and poor quadriceps coordination may contribute to alterations in VGRF. Importantly, we observed an increase in VGRF at only midstance while a decrease in VGRF was shown in initial loading response and terminal stance phase. We speculate that altered neuromuscular strategies

in both unloading and poor muscle control might change the characteristic of knee joint load responses in both limbs. For example, during gait cycle transitions from heel-strike to midstance, subjects may be able to rely on knee joint load in the uninvolved limb at initial heel-strike since heel-strike is supported by double-leg. However, once double-leg support is passed, subjects are only able to rely on their knee joint load in the involved limb. Therefore, unsmooth gait transitions from heel-strike to midstance may likely contribute to an increase in VGRF at midstance.

Articular cartilage health is highly associated with surrounding knee joint muscle function and load.[5,7,60] Quadriceps activation failure is a critical issue in knee joint loading since it may influence all aspects of lower extremity movement biomechanics. This impairment begins with altered motor recruitment patterns, which lead to abnormal joint loading, and eventually may accelerate the long-term effects of joint disease progression. Altered gait patterns or motor strategy are likely associated with articular cartilage health in the knee joint.[9,19] Many studies showed that altered gait patterns due to knee pain are severely harmful for articular cartilage in the knee joint because it may accelerate the rate of progression of articular cartilage.[5,9,19,23,59] Previous research using a knee OA population reported that knee pain resulted in a greater loading response in the uninvolved limb rather than the involved limb.[59] This altered loading strategy may result in chronic asymmetric joint load and muscle function.[9,60] If this is consistent over the long-term, the progression of degenerative joint disease may not be avoidable. Therefore, restoring altered gait patterns and reducing quadriceps dysfunction could be a primary goal for healthcare professionals because those factors are highly related to cartilage health condition.

TENS mitigated the effects of EKP on quadriceps activation and walking VGRF in the present study. TENS treatment not only decreased perceived pain, but also improved motor strategy. We speculate that the effects of TENS on both perceived pain and quadriceps function are likely related to an increase in internal knee extension moments which contribute to walking VGRF. However, we are not sure which factor (decreased pain or increased quadriceps activation) influence VGRF more. Presently, VGRF improvement appeared to be related to quadriceps function and played a pivotal role in gait patterns by absorbing impact shock and distributing load across the knee joint.[16]

Conclusion

There were three main findings in this study. First, our EKP model produced consistent knee pain for 48 min while being infused. Second, EKP altered lower extremity muscle function (knee extension MVIC and CAR) and neuromechanics during walking (VGRF). Last, TENS treatment mitigated the aforementioned alterations. This was the first study to investigate effects of TENS on lower extremity neuromechanics.

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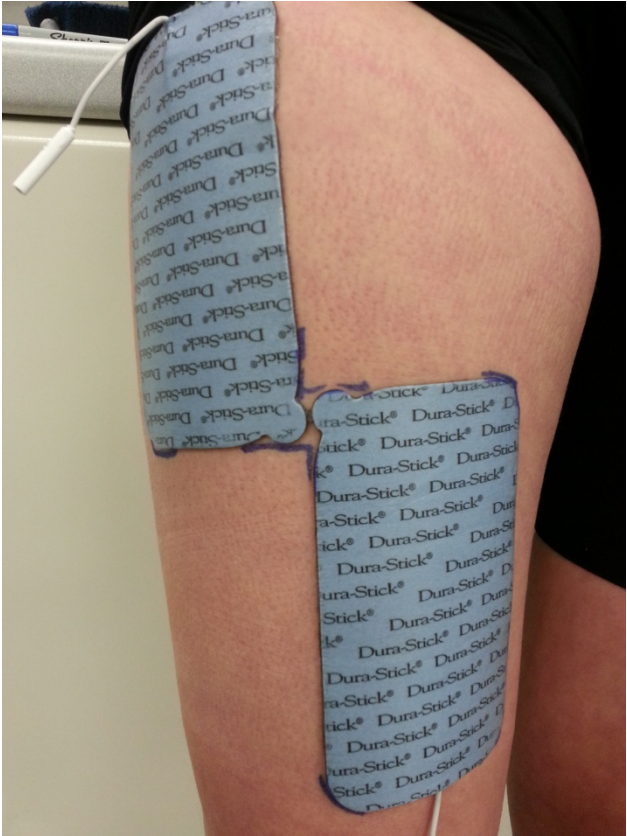
Figure 1. CAR electrodes placement

Figure 2. Biodex seated position

Figure 3. Infusion placement

Figure 4. Supine position
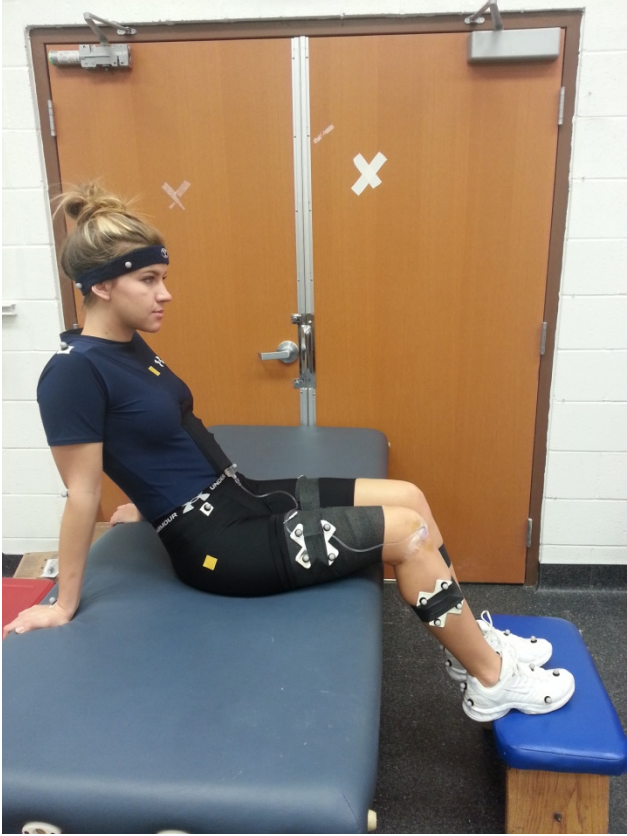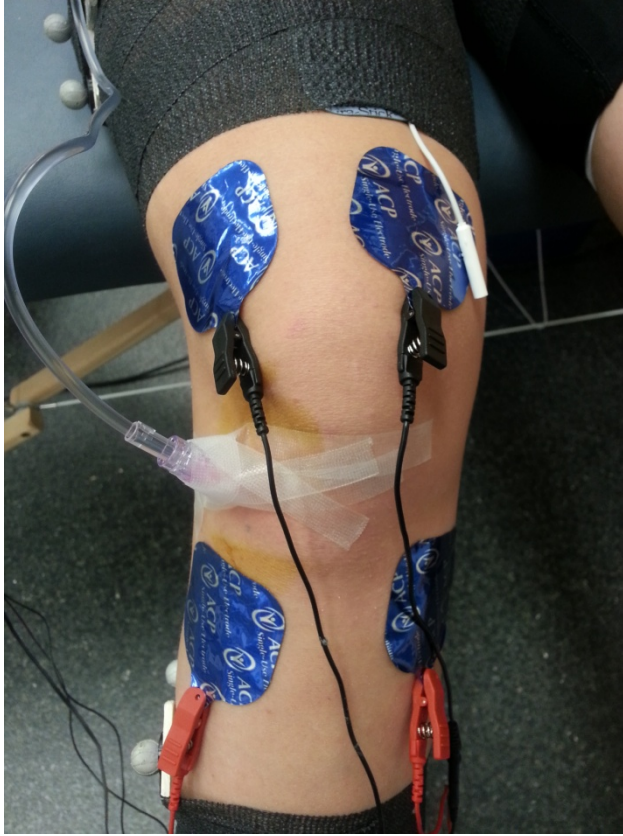
Figure 5. Seated position

Figure 6. Standing position

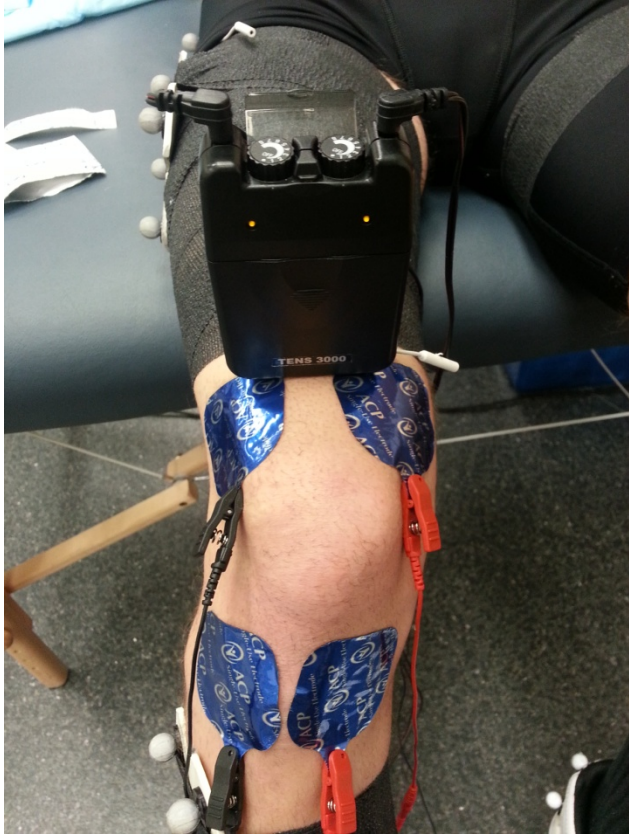Figure 7. TENS electrodes placement
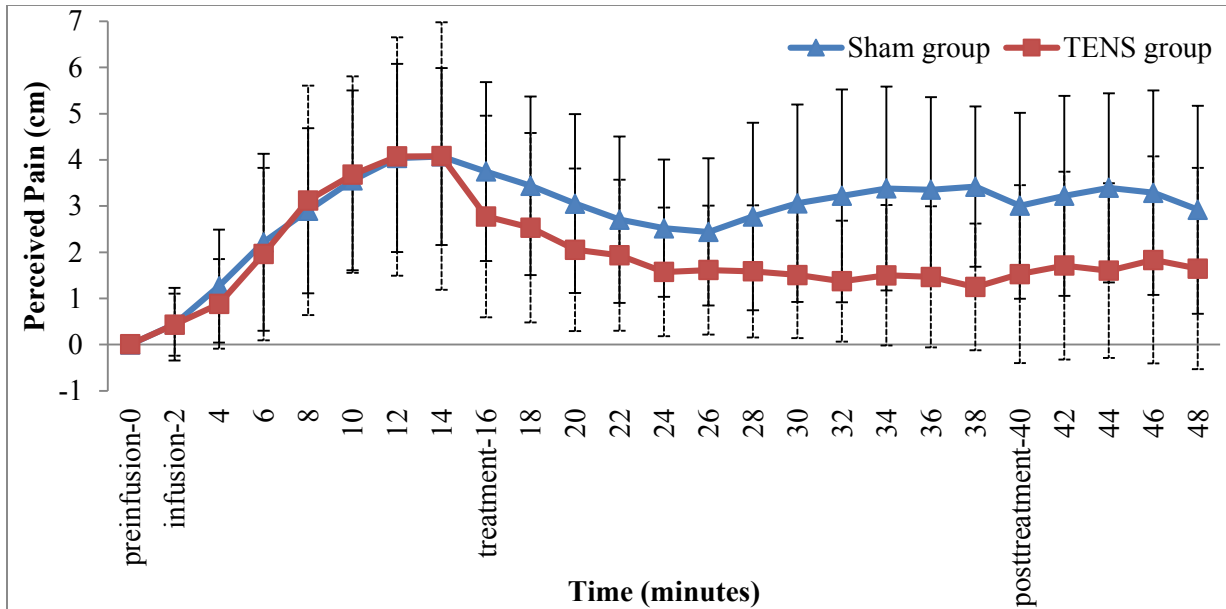
Figure 8. Sham treatment (indicator light is on)

Figure 9. Peceived knee pain normalized to the preinfusion (baseline) measurement. Knee pain peaked at 4 cm in both groups ($P < 0.0001$). While perceived pain gradually decreased to 1.25 cm follwing TENS treatment, knee pain remained consistent across time at 3.42 cm following sham treatment. Perceived pain was different from 6 min to 48 min, the only exception was at 38 min in the TENS group. Perceived pain was different from 6 min to 48 min in the sham group relative to the preinfusion measurement.
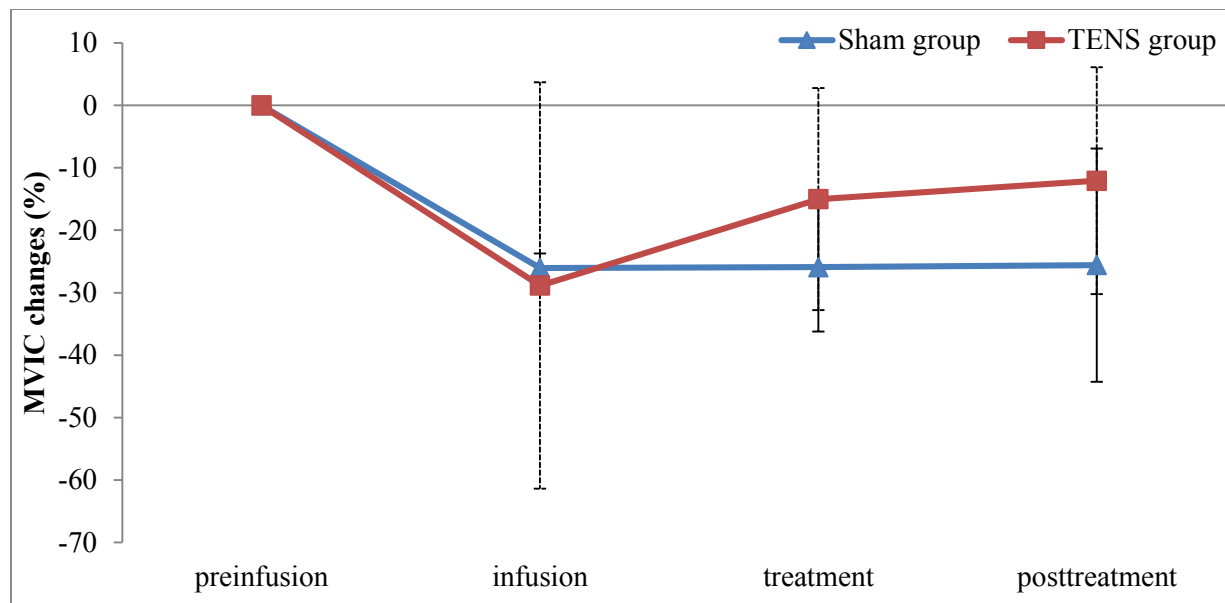
Figure 10. Knee extension MVIC normalized to the preinfusion (baseline) measurement. The MVIC under knee pain in the TENS group was only different during infusion ($P < 0.05$). However, the MVIC under knee pain in the sham group was different during infusion, treatment, and posttreatment ($P < 0.05$).
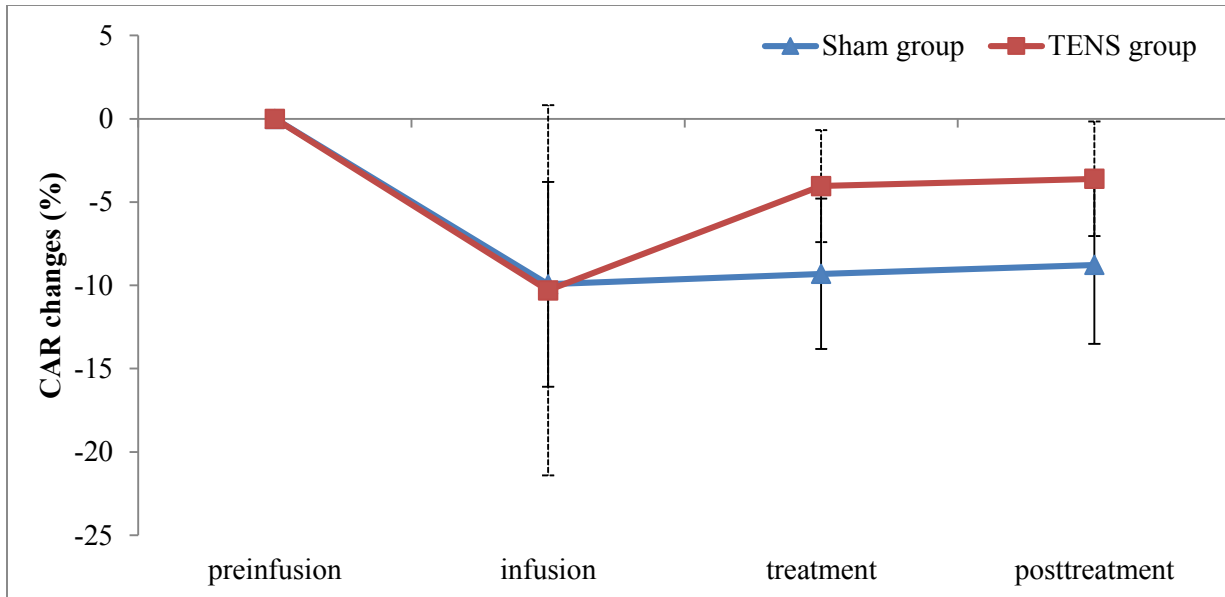
Figure 11. Knee extension CAR normalized to the preinfusion (baseline) measurement. The CAR under knee pain in the TENS group was only different during infusion ($P < 0.05$). However, the CAR under knee pain in the sham group was different during infusion, treatment, and posttreatment ($P < 0.05$).
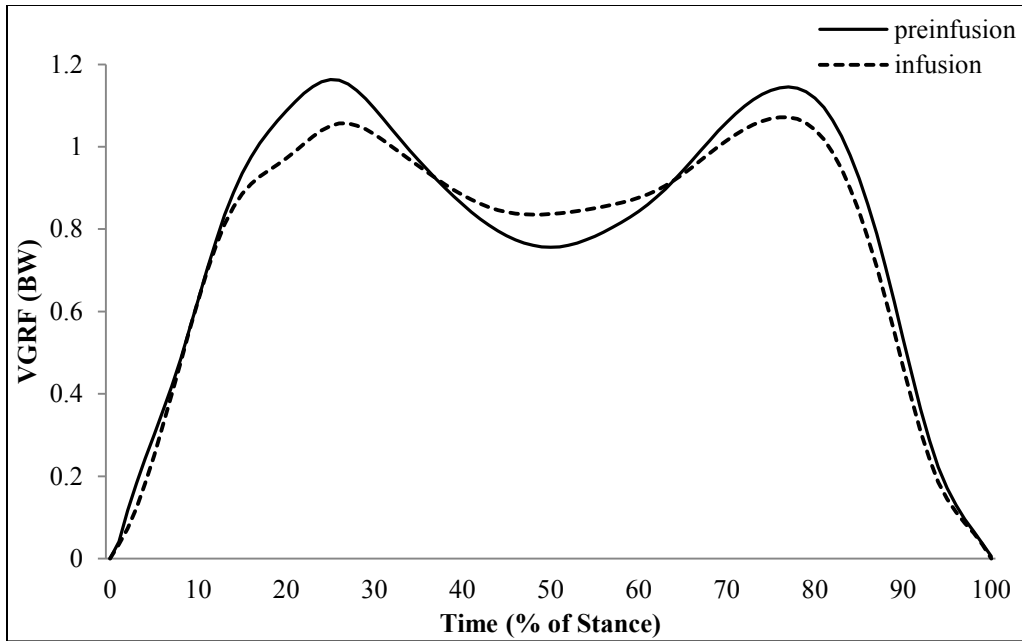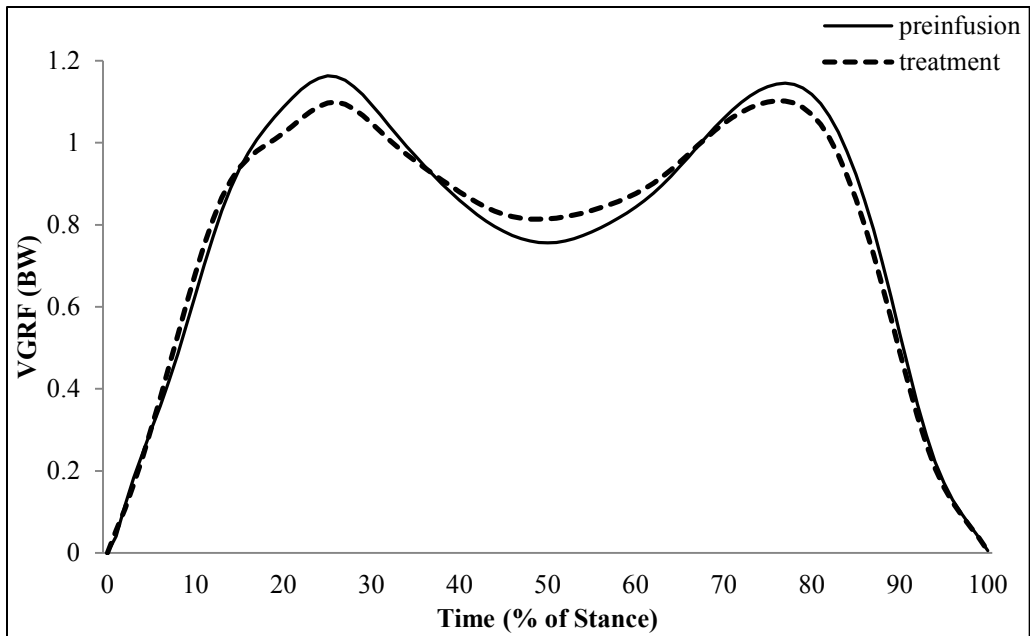
Figure 12a. Difference between preinfusion and infusion VGRF in the TENS group
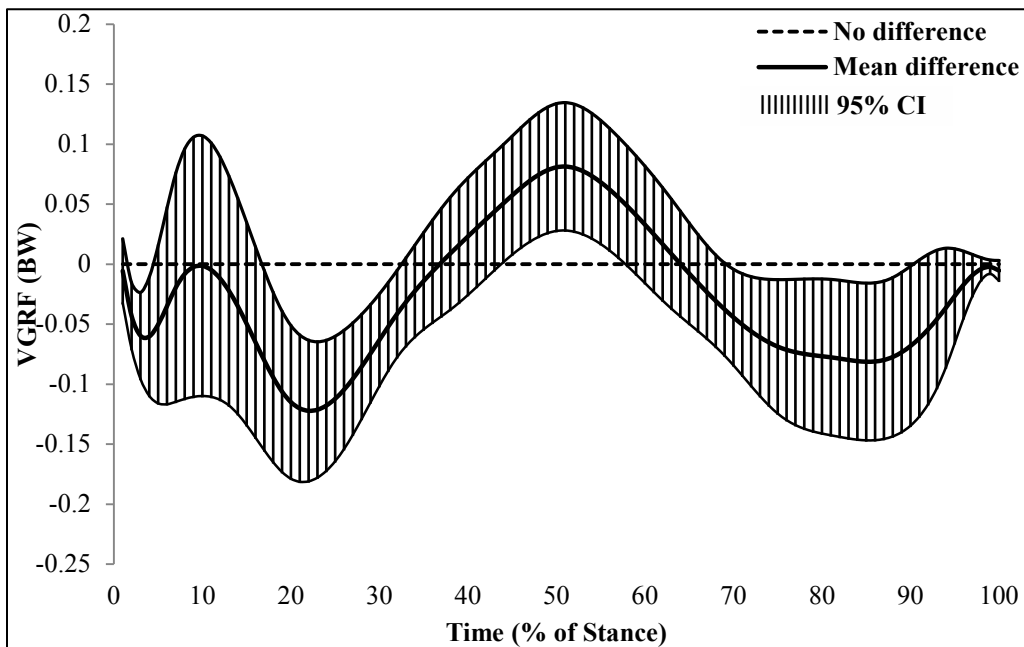
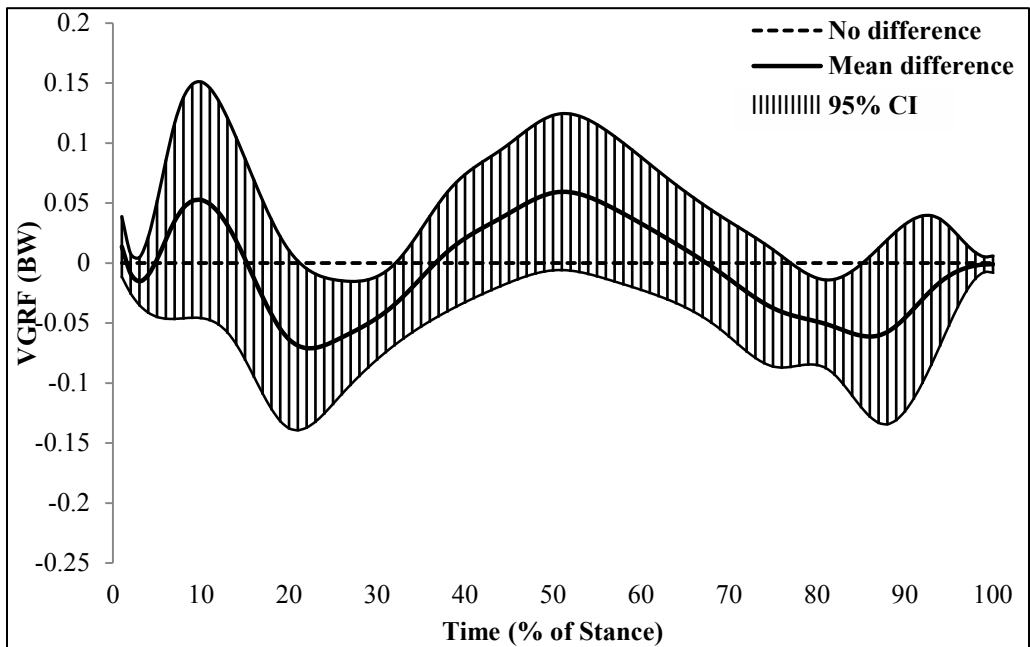

Figure 12b. Infusion VGRF–preinfusion VGRF in the TENS group

Figure 12. Functional analysis of VGRF under knee pain between preinfusion and infusion factors in the TENS group. Shaded areas represent 95% confidence intervals. Significant differences are defined by any area where the edges of the confidence intervals are separated from the dotted line. Less deviation represents decreased VGRF, while greater deviation represents increased VGRF between factors. VGRF was decreased at heel-strike (0% to 4%), initial loading response (16% to 32%), and terminal stance phase (69% to 91%). VGRF was increased at midstance phase (44% to 58%), compared to the preinfusion measurement ($\alpha = 0.05$).

Figure 13a. Difference between preinfusion and treatment VGRF in the TENS group

Figure 13b. Treatment VGRF–preinfusion VGRF in the TENS group

Figure 13. Functional analysis of VGRF under knee pain between preinfusion and treatment factors in the TENS group. VGRF was only decreased at loading response (20% to 32%) and terminal stance phase (76% to 86%) following TENS treatment, compared to the preinfusion measurement.
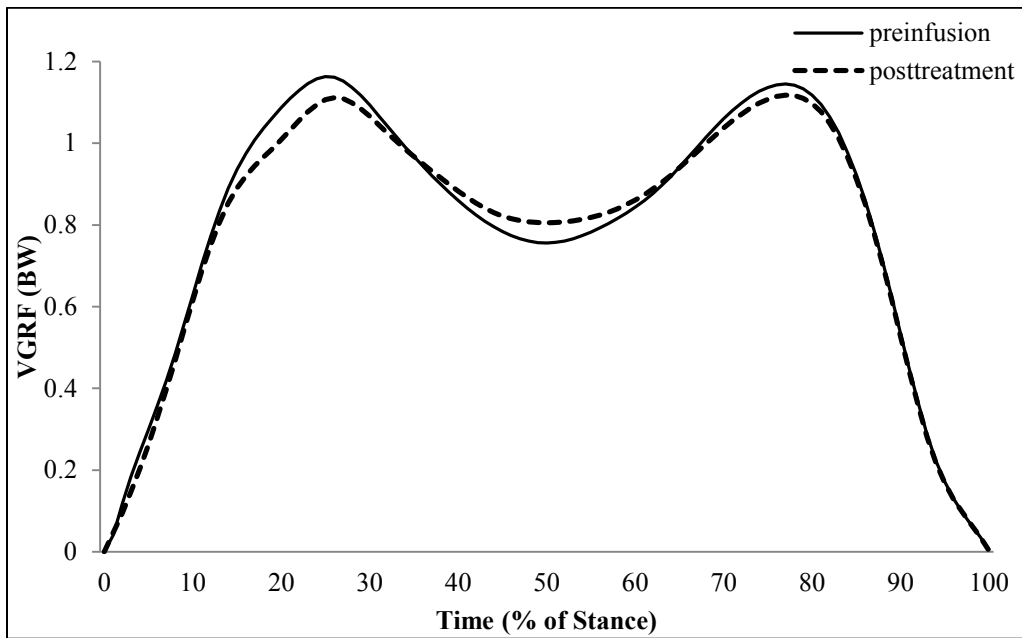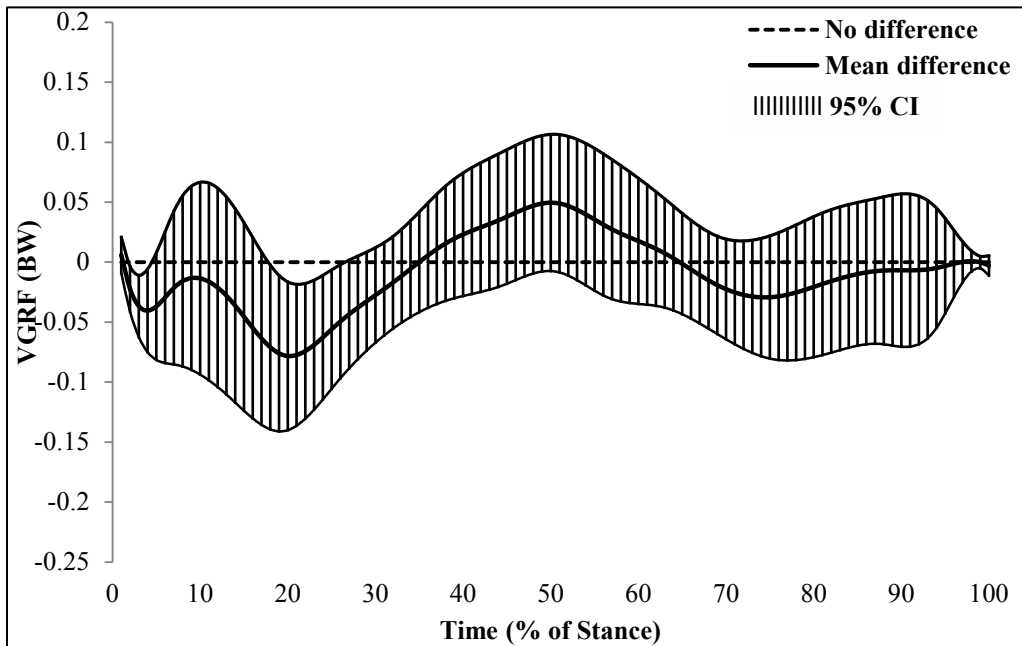
Figure 14a. Difference between preinfusion and posttreatment VGRF in the TENS group

Figure 14b. Posttreatment VGRF–preinfusion VGRF in the TENS group

Figure 14. Functional analysis of VGRF under knee pain between preinfusion and posttreatment factors in the TENS group. VGRF was decreased at initial heel-strike (1% to 4%) and loading response phase (16% to 26%), compared to the preinfusion measurement.
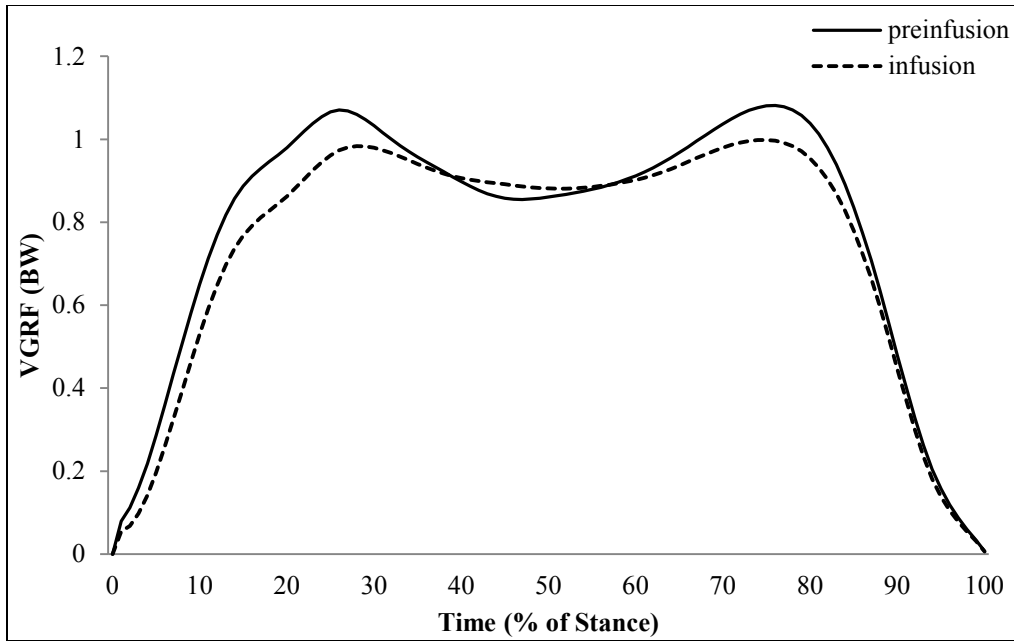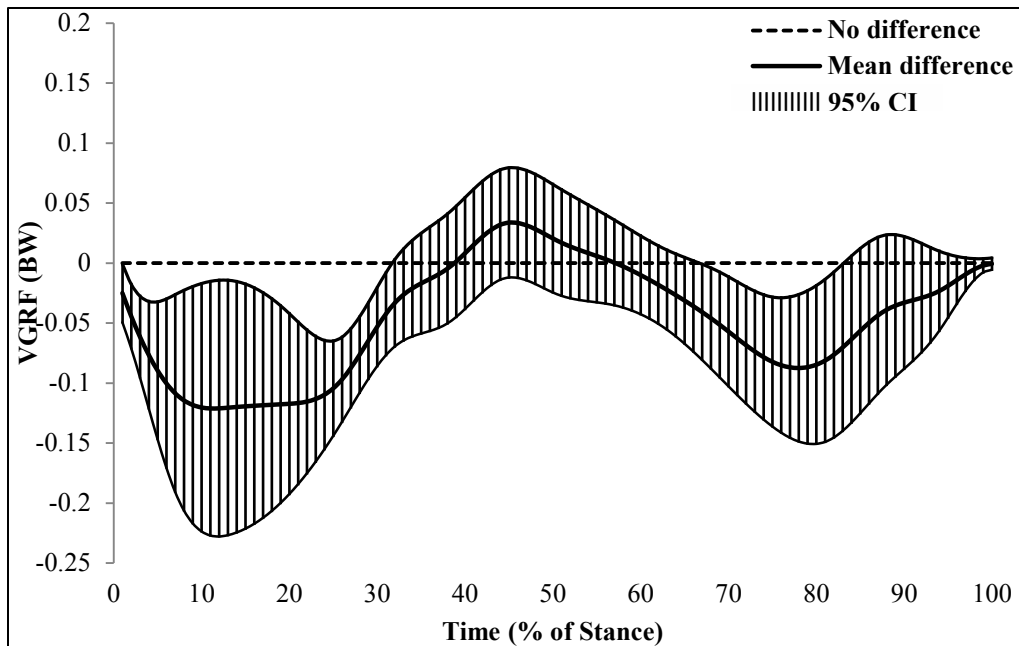
Figure 15a. Difference between preinfusion and infusion VGRF in the sham group

Figure 15b. Infusion VGRF–preinfusion VGRF in the sham group

Figure 15. Functional analysis of VGRF under knee pain between preinfusion and infusion factors in the sham group. VGRF was decreased at initial loading response (0% to 31%) and terminal stance phase (66% to 84%), compared to the preinfusion measurement.
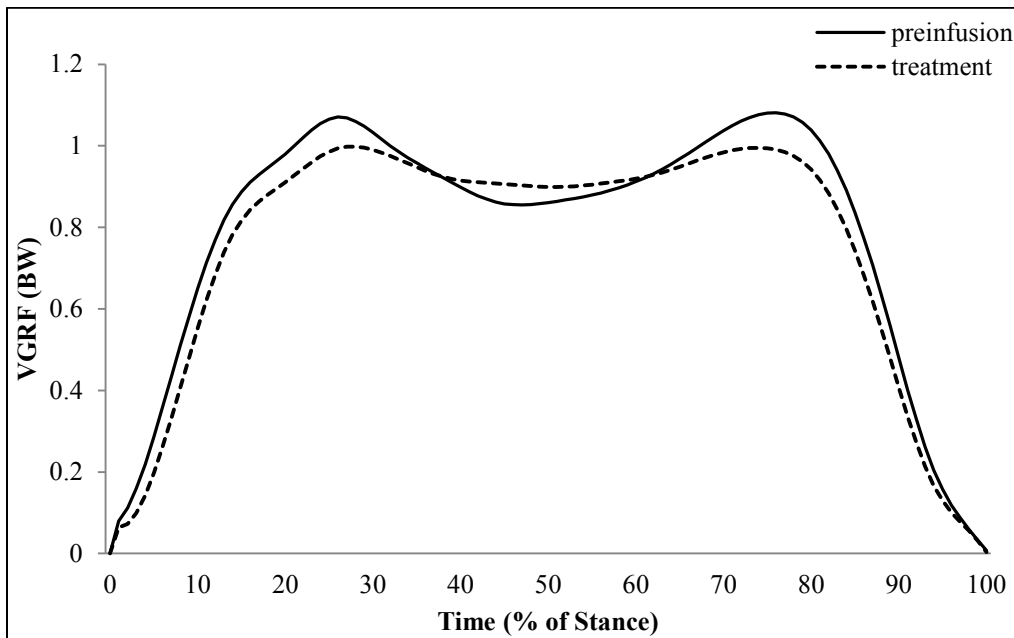
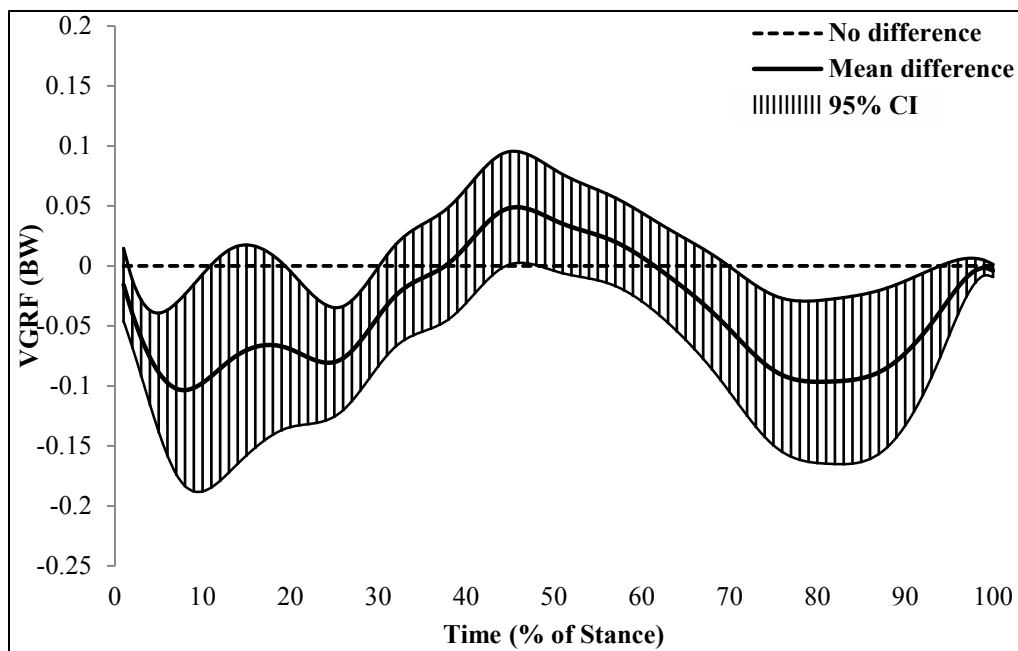Figure 16a. Difference between preinfusion VGRF and treatment VGRF in the sham group

Figure 16b. Treatment VGRF–preinfusion VGRF in the sham group

Figure 16. Functional analysis of VGRF in the sham group under knee pain between preinfusion and treatment factors. VGRF was decreased at initial heel-strike (1% to 10%), loading response (18% to 30%), and terminal stance phase (70% to 94%). VGRF was increased at midstance phase (42% to 45%) following sham treatment, compared to the preinfusion measurement.
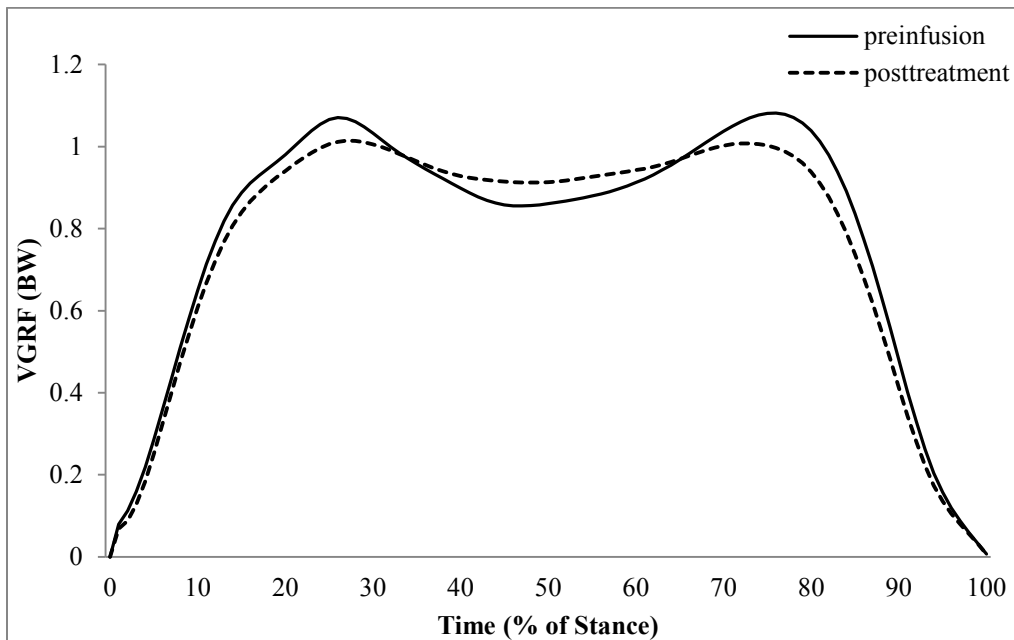
Figure 17a. Difference between preinfusion VGRF and posttreatment VGRF in the sham group
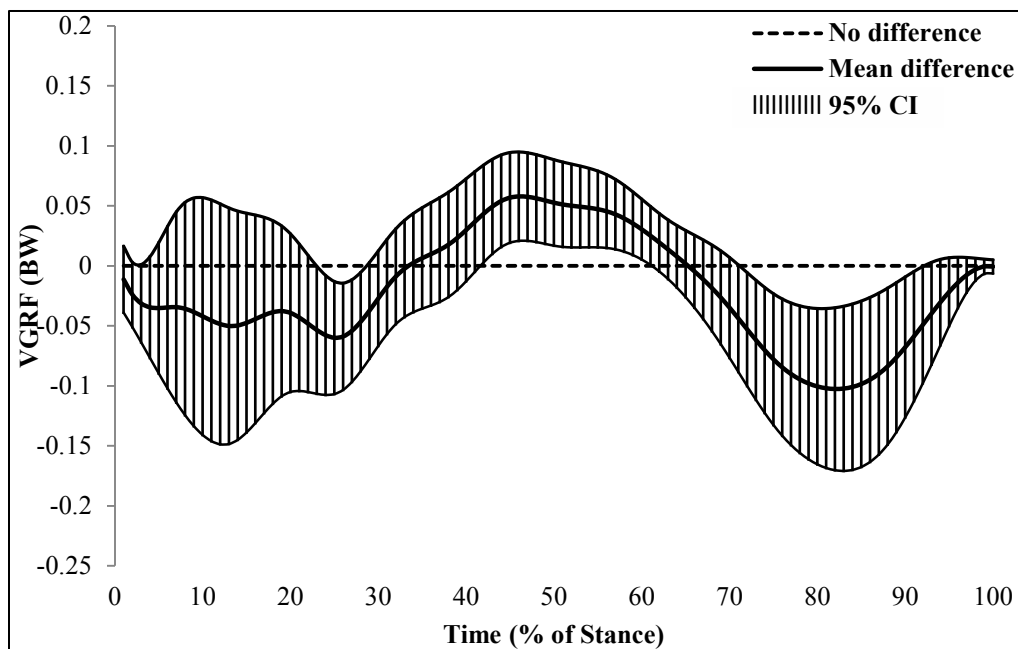

Figure 17b. Posttreatment VGRF – preinfusion VGRF in the sham group

Figure 17. Functional analysis of VGRF under knee pain between preinfusion and posttreatment factors in the sham group. VGRF was decreased at loading response (22% to 28%) and terminal stance phase (70% to 92%). VGRF was increased at midstance phase (41% to 61%), compared to the preinfusion measurement.