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Activating the somatosensory system enhances net quadriceps moment during gait

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ABSTRACT

Quadriceps muscle rehabilitation following knee injury or disease is often hampered by pain, proprioception deficits or instability associated with inhibition of quadriceps activation during walking. The cross-modal plasticity of the somatosensory system with common sensory pathways including pain, pressure and vibration offers a novel opportunity to enhance quadriceps function during walking. This study explores the effectiveness of an active knee brace that used intermittent cutaneous vibration during walking to enhance the peak knee flexion moment (KFM) during early stance phase as a surrogate for net quadriceps moment (balance between knee extensor and flexor muscle moments). The stimulus was turned on prior to heel strike and turned off at mid-stance of the gait cycle. Twenty-one subjects with knee pathologies known to inhibit quadriceps function were tested walking under three conditions: control (no brace), a passive brace, and an active brace. Findings show that compared to the control, subjects wearing an active brace during gait exhibited a significant ($p < 0.001$) increase in peak KFM and no significant difference when wearing a passive brace ($p = 0.17$). Furthermore, subjects with low KFM and knee flexion angle (KFA) in control exhibited the greatest increase in KFA at loading response in the active brace condition ($R = 0.47$, $p < 0.05$). Intermittent cutaneous stimulation during gait, therefore, provides an efficient method for increasing the KFM in patients with knee pathologies. This study's results suggest that intermittent vibration stimulus can activate the cross-modalities of the somatosensory system in a manner that gates pain stimulus and possibly restores quadriceps function in patients with knee pain.

1. Introduction

Knee injuries and pathologies, such as anterior cruciate ligament (ACL) tears, meniscus tears, and knee osteoarthritis (OA), are commonly associated with neuromuscular dysfunction, leading to significant alterations in the activation and strength of the quadriceps (Lewek et al., 2002; Slemenda et al., 1997; Thomas et al., 2016). Quadriceps weakness and activation inhibition due to knee pathology often result in kinematic and kinetic gait alterations that compromise the capacity of the quadriceps muscles (Torry et al., 2000). The net quadriceps moment has been previously defined as the net balance between the extensor moment and the knee flexor moment (Nagura et al., 2002; Scanlan and Andriacchi, 2016). A reduction in the net quadriceps moment during walking has been frequently related to a reduction in the external net knee flexion moment (KFM) (Bulgheroni et al., 2007; Childs et al., 2004; Lewek et al., 2004; Schipplein and Andriacchi, 1991) and by a reduction in knee flexion angle (KFA) at loading response(Farrokhi et al., 2015, 2013; Mizner and Snyder-Mackler, 2005). The reduction of the KFM during walking is clinically important since it is reported as a significant predictor of knee OA (Baliunas et al., 2002; Chen et al., 2003; Creaby et al., 2013), OA progression (Chehab et al., 2014) and related to knee pain (Henriksen et al., 2010). Patients with knee OA (Farrokhi et al., 2015, 2013) or post ACL (Di Stasi et al., 2013; Gao and Zheng, 2010; Lewek et al., 2002; Palmieri-Smith and Thomas, 2009) reconstruction exhibit a significant quadriceps weakness with reduced KFA during the loading response of gait, which occurs near the peak KFM. It is, therefore, likely that gait changes associated with a long-term impairment in quadriceps muscle activation may be related to the onset and progression of knee OA symptoms with consequent alterations in gait patterns.

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Rehabilitation programs achieving quadriceps strengthening have been shown to have short-term benefits to reduce pain and disability in subjects with knee OA (Anwer and Alghadir, 2014; Norden et al., 1994). However, these programs often require complex clinic-based regimens and/or machinery not readily available to patients, and thus, can be limited by poor adherence rates (Bhatia et al., 2013; Marks and Allegrante, 2005; Pisters et al., 2010). Similarly, aggressive rehabilitative approaches following ACL and/or meniscus injury have been used to mitigate the risk for re-injury and development of knee OA (Chaudhari et al., 2008; Daniel et al., 1994; Kannus and Järvinen, 1989; Lohmander et al., 2004), yet no treatment approach has so far been generally approved for its effectiveness to treat this type of muscle weakness. Given the long-term risk of developing knee OA after injury (Lohmander et al., 2007), there remains a need for alternative novel approaches to restore the muscle function of the quadriceps during gait while overcoming the above mentioned limitations.

The properties of the somatosensory system offer a novel approach to restore muscle function. Specifically, the cross-modal plasticity of the somatosensory system controls common sensory pathways including pain, pressure and vibration, and responds to mechanical stimuli in such a manner that over stimulation in one mode of the system (e.g. vibration) can gate response in other modalities (e.g. pain) (Melzack and Wall, 1965) (Fig. 1). This cross-modal plasticity of the somatosensory system could, therefore, be exploited to induce desired changes in patterns of muscle contraction via mechanical stimulation of cutaneous mechanoreceptors that respond to stimuli such as compressive pressure and vibration (Bolanowski, 1996; Johnson, 2001). Additionally, an intermittent stimulus may produce an optimal response since a constant stimulus can have a diminished response (Pubols, 1982; Ribot-Ciscar et al., 1989). Muscle activation in response to cutaneous receptor stimulation can be modulated by a variety of factors (Zehr et al., 1997) including the phase of the gait cycle, the intensity of stimulation and the nature of the task being performed, i.e. rhythmic movements such as walking.

It has also been suggested (Melzack and Wall, 1965) that the gating potential of the somatosensory system (Fig. 1) can be used to mitigate pain. Further, it has been shown that interventions to decrease pain (Boyer et al., 2012; Hurwitz et al., 2000) result in an increase in the KFM (net quadriceps moment) during walking, where interventions to increase pain result in lower KFM (Henriksen et al., 2010). Thus, the KFM can provide a convenient and objective surrogate measure of changes in pain as well as net quadriceps moment resulting from an intervention, while overcoming some of the limitations of self-reported pain that occur with the influence of a placebo effect.

Thus, the purpose of this study was to explore the potential that an intermittent cutaneous vibration stimulation applied at a specific phase of the gait cycle will have an immediate effect by increasing quadriceps function during walking in patients with knee pain during activities of daily living. Assuming the KFM is a surrogate measure for assessing change in pain (Boyer et al., 2012; Hurwitz et al., 2000) and quadriceps function (Scanlan and Andriacchi, 2016; Schipplein and Andriacchi, 1991), the following hypotheses were tested; (H1) Patients wearing a brace that applied an intermittent stimulus (active brace) to the thigh and shank will have a significant increase in peak KFM and peak KFA at loading response during gait relative to control (no brace condition), while no significant increase in peak KFM or peak KFA during loading would be seen in the passive brace condition relative to control; (H2) Patients with the lowest KFM in control condition (linked to more severe quadriceps deficits) will have a greater increase in KFM with the active brace; and (H3) the changes in knee flexion angle during loading response of the gait cycle with the active brace will be correlated to knee flexion angle during loading in the control condition.

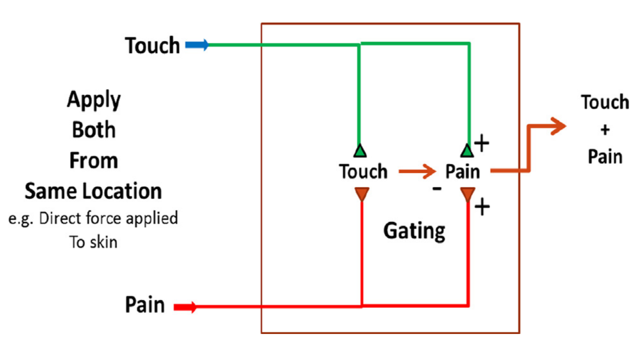


Fig. 1. A mechanical cutaneous stimulus can reduce the pain response by gating through the somatosensory system.

2. Methods

2.1. Subjects

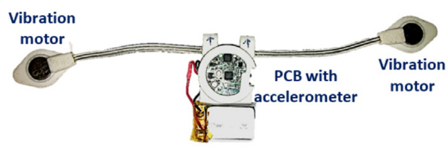
The study population included 21 subjects (14 females, 7 males, age: 53.2 ± 14 yrs., height: 167.7 ± 10.2 cm, mass: 74.6 ± 15.5 kg, BMI: 26.3 ± 3.6 kg/m^2) selected on the basis of having knee pain associated with a knee pathology commonly linked with reduced quadriceps function during walking. Specifically, the primary inclusion criterion was self-reported symptomatic knee pain ≥3/10 for most of the 30 days prior to testing using a single 11-point numeric scale with 0 representing "no pain" and 10 representing "worst pain imaginable"; it was also required that the pain was associated with ACL, and/or meniscus injuries and/or physician-diagnosed medial compartment knee OA. This project was approved by the university's Institutional Review Board, and signed informed consents were obtained for all subjects prior to study participation.

2.2. Instruments: cutaneous stimulation active knee brace

The knee brace consisted of two elastic straps with strategically placed stimulus modules, positioned on each patient to elicit the greatest response based on his/her specific anatomy and nerve ending locations. These straps were tightly attached around the lower part of the thigh and the upper-shank so that the stimulus modules could apply static compressive pressure and active vibration to the surface of the skin, that is, cutaneous stimulus (Fig. 2). The timing of the vibration was synchronized to the movement of the limb using an accelerometer to detect the limb movement, turning on the stimulus prior to heel strike (for development of optimal KFM) and turning off the stimulus at mid-stance of the gait cycle.

2.3. Gait test procedure

Unilateral gait tests were performed on the subjects' index knee, determined by the subject-identified greatest knee pathology/pain. Subjects were asked to walk along a level 10-m walkway at a self-selected comfortable walking speed under three conditions: control (no brace), active knee brace (vibration on, contact pressure), and passive knee brace (no vibration, contact pressure), where active and passive brace conditions were randomized. Subjects were instructed to walk at their normal walking speed and no attempt was made to control walking speed. Subjects started walking at the same location for the trials and made the same number of footsteps to yield a steady state speed before



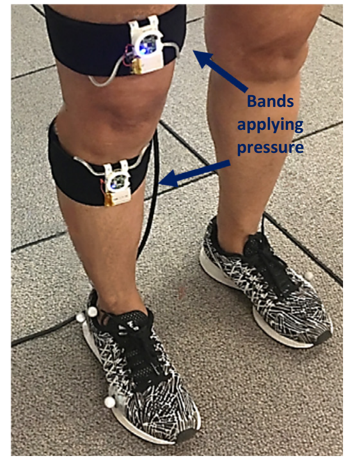


Fig. 2. (a) Device for mechanical cutaneous stimulation including stimulus modules and PCB with the ability to detect movement and position. (b) Knee brace placement on a subject applying pressure and vibration to the thigh and shank.

entering the measurement volume. After an adaptation period consisting of numerous practice trials for each condition, subjects performed five successful trials per condition, with a trial being considered successful when the foot of the index limb fully stepped within the force plate's boundaries. Speed and kinematic data were recorded for each condition using a multi-camera motion capture system (Qualisys Medical, Gothenburg, SE) and the point cluster technique (Andriacchi et al., 1998). Ground reaction forces were collected using a floor-embedded multicomponent force plate (Bertec Corporation, Columbus, OH). Both systems were synchronized, and data were sampled at 120 Hz. A standing reference pose was captured before the walking trials by means of markers placed on bony landmarks throughout the lower limb that defined an anatomical reference frame for each segment according to a previously-described protocol (Dyrby and Andriacchi, 2004). The knee moments, operationally defined by external moments in the tibial anatomical frame, were calculated with the software BioMove (Stanford University, Stanford, CA) as detailed in prior work and normalized to percent of body weight and height (%Bw*Ht) (Zabala et al., 2013). The peak knee flexion moment (KFM) was defined as the maximum value during the first half of stance phase and the peak knee flexion angle (KFA) during loading was defined as the maximum knee flexion angle during the first half of stance. These parameters were averaged over five walking trials for each subject in each condition.

2.4. Statistical analysis

Paired Student's t-tests comparisons between (1) control (no brace) and passive brace (passive contact pressure), (2) control and active brace (contact pressure + intermittent vibration), and (3) passive and active brace assessed differences in gait variables (peak KFM, peak KFA at loading response, and walking speed) among conditions. Additionally, Pearson correlation coefficients were used to determine associations between percent change in peak KFA at loading response and KFA in the control condition and between percent change in peak KFM and peak KFM in the control condition. A significance level of $\alpha = 0.017$ was used for paired t-tests analyses to account for multiple comparisons using Bonferroni adjustment, and $\alpha = 0.05$ was used for Pearson correlations. Calculations were performed to estimate the necessary sample size for paired two-tailed t-tests using data from preliminary testing in a healthy population. Eighteen subjects are required to detect a change in KFM of 5.5% with a standard deviation of 6.6% and power of 80%.

3. Results

3.1. Participant characteristics

The common finding among the twenty-one subjects enrolled in this study was increased knee pain prior to entering the study with an average score of 4.2 (sd. 1.5) on a scale from 0 (no pain) to 10 (worst pain). Eight of the twenty-one subjects had a history of ACL tears and six had undergone reconstructive ACL surgery, twelve had meniscus tears with nine of them undergoing meniscal surgery, and eight subjects reported having been physician-diagnosed with knee OA.

3.2. Knee motion and loading

The active condition with the cutaneous intermittent vibrating knee brace was found to cause a significant increase in the magnitude of the peak KFM during walking ($p = 0.0002$) and a trend towards an increase in KFA during loading response ($p = 0.047$) (Table 1) relative to the control condition (with no brace). In contrast, no significant differences were observed in the peak KFM magnitude or KFA during loading when comparing subjects' gait in the passive brace condition (no vibration) relative to the control condition (KFM: $p = 0.24$, KFA: $p = 0.69$) and relative to the active condition (KFM: $p = 0.07$, KFA: $p = 0.21$). No significant change in average gait speed was observed when comparing subjects' gait

Table 1
Mean values (SD) of the peak KFM, KFA at loading response, speed, cadence and stride length under control, passive and active knee brace conditions.

	Control	Passive Brace	Active Brace
KFM (%Bw*Ht)	2.66 (1.12)	2.73 (1.15)	2.82 (1.14)*
KFA loading response (deg)	16.48 (5.54)	16.59 (5.87)	16.9 (5.32)**
Speed (m/s)	1.24 (0.17)	1.24 (0.17)	1.24 (0.17)
Cadence (steps/min)	0.92 (0.07)	0.92 (0.08)	0.92 (0.06)
Stride length (m)	1.36 (0.17)	1.35 (0.15)	1.34 (0.12)

* Significant difference ($p = 0.0002$) from control.
** Trend ($p < 0.047$) from control.

in the control versus the active brace conditions (p = 0.87) or the control versus the passive brace conditions (p = 0.99) or passive versus the active brace conditions (p = 0.81). Additionally, no significant changes were observed in average cadence and stride length when comparing subjects' spatiotemporal measures between the different conditions (Table 1, P > 0.28).

Almost all subjects (20 of 21) responded to the active brace condition with an increase in KFM relative to control (Fig. 3b) yet there was substantial variability in the KFM increase (0–20% increase) among individual subjects. No significant correlation was found between KFM percentage change and KFM in the control condition (R(21) = 0.33, p = 0.15). To explore factors that influence the variable response, the subjects were group based on whether their KFM at control was less (low KFM group) or greater (high KFM group) than 2.5 %Bw*Ht (Fig. 3a). The results showed that patients with the lowest initial KFM had the greatest response to the brace, as analysis of the low KFM group showed a strong significant negative correlation (R(11) = 0.85, p = 0.002) (Fig. 4a) between the control KFA and percent KFA change with the brace. As such, patients with the lowest initial KFM had the greatest response to the brace. There was also a significant negative correlation between KFA at loading response in the control condition and the percent change in KFA at loading response (active-control) for all subjects. However, the correlation for all subjects was weaker (R(21) = 0.47, p = 0.03) (Fig. 4b) and appeared to be dominated by the strong correlation in the Low KFM group as the correlation for the High KFM group was not significant (p = 0.173). Similarly, the Low KFM group showed a trend in the negative correlation between the peak KFM in the control condition and percent change in KFM (R(11) = 0.52, p = 0.10) whereas no trend was apparent for the high KFM group (R(10) = 0.31, p = 0.39) or for all subjects (R(21) = 0.33, p = 0.15). However, when excluding the subject with the smallest KFM prior to intervention, the negative correlation between the peak KFM in the control condition and the percent change in KFM in the low KFM group no longer holds (R(11) = 0.19, p = 0.59).

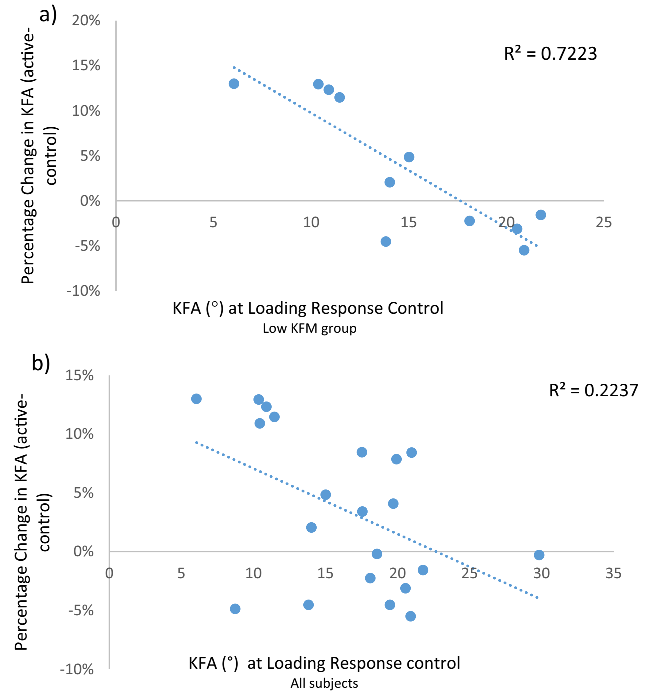


Fig. 4. Percent change in KFA at loading response (active – control) vs. KFA at loading response in control condition for (a) N = 11, low KFM group (p = 0.002) and (b) N = 21, all subjects (p = 0.03).

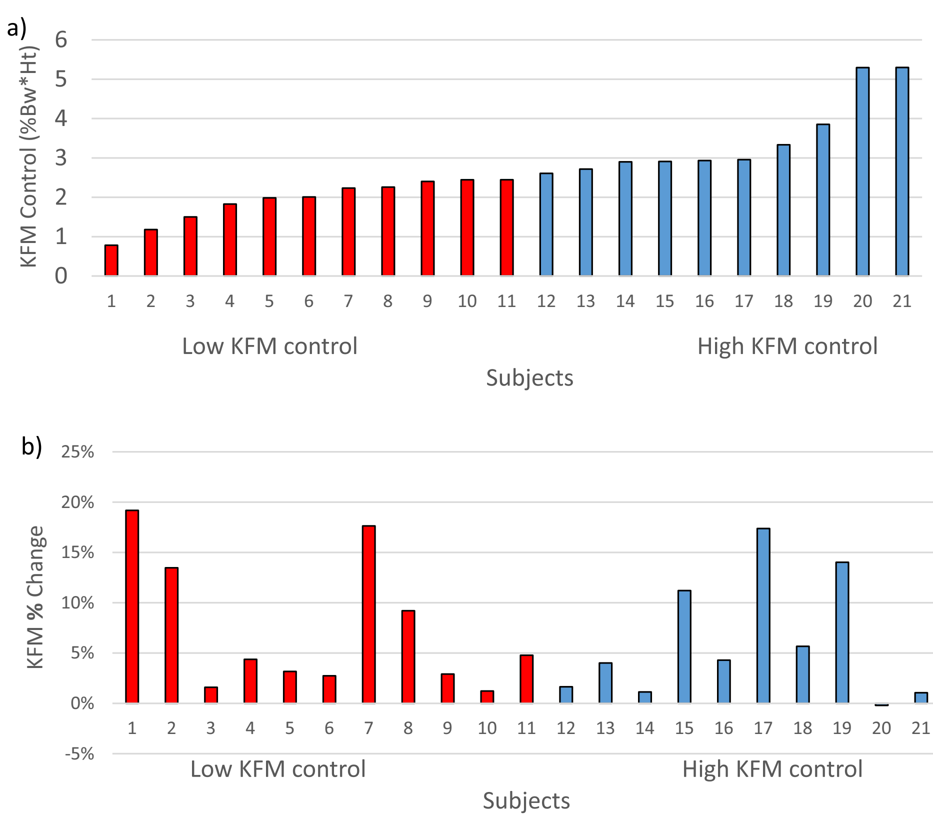


Fig. 3. Distribution of individual subjects' KFM (a) under control condition and (b) percentage changes in peak KFM with the active knee brace relative to control. 20 out of 21 subjects exhibited an increase in KFM and responded positively to the active knee brace.

4. Discussion

The results of this study (H1) showed that the knee flexion moment (KFM) increased significantly and there was a trend towards increased KFA when a mechanical stimulus incorporating intermittent vibration (active brace) was applied. These results suggest that the intermittent vibrational stimulus can activate the somatosensory in a manner that increases the KFM during walking. Given the mechanical linkage (Schipplein and Andriacchi, 1991) to quadriceps function, these results can be interpreted to indicate increased quadriceps function during walking, as a reduction in net quadriceps moment has been shown to be exhibited by a reduction in the balancing KFM (Childs et al., 2004; Lewek et al., 2004; Schipplein and Andriacchi, 1991) and reduced KFA (Farrokhi et al., 2015, 2013; Mizner and Snyder-Mackler, 2005) at loading response. The negative trend (partially confirming H2) between the increase in KFM in the active brace condition versus the baseline KFM prior to intervention in the low KFM group suggests that the patients with the lowest KFM (quadriceps activation) benefitted the most by activating a response from the somatosensory system. Nevertheless, when the subject with the smallest KFM prior to intervention was excluded from the analysis H2 no longer holds. Even though this subject was not a statistical outlier, they did drive the correlation and therefore removing from the analysis negates our findings. The results (H3) further showed that there is an association between percent change in KFA and KFA during loading in the control condition. These results are important since current rehabilitation methods have emphasized the urgency of treating quadriceps function as a method to address knee OA (Astephen et al., 2008; Huang et al., 2008). In addition, previous studies (Boyer et al., 2012; Hurwitz et al., 2000) have reported an association between reduced KFM peak and knee pain, with patients progressively reducing KFM and KFA at mid-stance as the disease develops, in an effort to reduce the pain they experience, similar to how a healthy cohort responds to pain by reducing KFM (Henriksen et al., 2010).

The previously reported (Boyer et al., 2012; Henriksen et al., 2010; Hurwitz et al., 2000) relationship between KFM and pain provides a potential basis for understanding how an intermittent cutaneous mechanical stimulus may increase KFM during gait in patients with painful knees. Specifically, as pain was the one common clinical symptom to all the subjects entered into this study, vibratory stimulation (Lundeberg et al., 1984) may gate pain in a manner to restore quadriceps function during walking. It is important to note that the gait changes identified in this study were influenced by the intermittent vibrational stimulus as application of the passive brace (e.g. pressure) without intermittent vibration did not result in an increase in KFM. The results of this study are consistent with the concept that over stimulation in one mode of the somatosensory system pathways (e.g. vibration and pressure) can gate the response in other modalities (e.g. pain) and is supported by a previously described gate control theory (Guieu et al., 1991; Melzack and Wall, 1965). Further, the finding that the patients starting with the lowest KFM prior to intervention (control) had the greatest response to the active brace suggests a potential graded response that is dependent on the severity of quadriceps dysfunction.

Alternative interpretations of these results should consider the fact that the timing of the stimulus was synced to a specific phase of the gait cycle which is important since vibration can also activate sensory receptors (tendons) (Vedel and Roll, 1982) and thus contribute to muscle control and movement (Ribot-Ciscar et al., 1989). It should also be noted that the subjects with soft-tissue injury (meniscus and/or ACL) might have a loss of joint stability or proprioception. Therefore enhanced sensory feedback could be an alternative or a complementary mechanism to gating pain which would explain the increase in KFM since vibration can produce the appropriate kinesthetic cues to activate the supplementary motor area of the brain that is usually activated during self-initiated movements (Naito et al., 2000). Vibration influences the excitation of the peripheral and central structures that facilitate subsequent voluntary movements (Cardinale and Bosco, 2003). Thus, the intermittent vibration applied in this study likely enabled some level of increasing KFM in all patients in this study through both a gated stimulus of pain as well as through excitation of peripheral and central structures, while application of the passive brace did not. Thus, the gated pain response and the enhanced sensory feedback appear to have a similar and perhaps complementary therapeutic benefit.

The application of an intermittent as opposed to constant vibration stimulus is an important consideration since there is evidence that cutaneous sensory receptors adapt to constant vibration/stimulation in a manner that diminishes the response of sensory receptors to the point where vibration no longer activates the mechanoreceptors (Pubols, 1982; Ribot-Ciscar et al., 1989). In the present study, we hypothesized that an active knee brace with intermittent vibration in conjunction with constant pressure as opposed to only constant cutaneous pressure (passive brace) would be more efficient in producing optimal stimulation of sensory receptors with consequent response of afferent muscles. The findings of the present study support this assumption by showing that wearing a knee brace with intermittent cutaneous vibration significantly increased the peak KFM, while a passive knee brace did not.

In evaluating the results of this study, it is important to consider the exploratory nature of this study using intermittent cutaneous vibration in knee pathologies. As in previous studies, KFM was interpreted as a surrogate for net quadriceps moment (net quadriceps and net knee flexor muscle moment) (Scanlan and Andriacchi, 2016; Schipplein and Andriacchi, 1991). While the altered KFM has been shown in numerous studies (Chehab et al., 2014; Mündermann et al., 2005; Scanlan and Andriacchi, 2016; Schipplein and Andriacchi, 1991) to be indicative of a knee pathology, it is, nevertheless, an indirect measure of net quadriceps moment and future studies could use more direct measures of muscle activation, such as electromyography, that might provide additional insight into efficacy of the active brace. An additional limitation of the present study is related to the small and heterogeneous nature of the sample and the short time period subjects were observed wearing an active brace, as is often the case in exploratory studies. Nevertheless, all subjects entered the study with a common symptom of knee pain and they responded to the intermittent vibrating knee brace with an increase in KFM and a trend towards an increase in KFA at loading response during gait. Self-reported pain was not examined in this study due to the short time period during which the subjects were wearing an active brace, as well as the need for a valid placebo control when assessing self-reported pain. However, as previous noted the increase in KFM does suggest that pain was mitigated with the active brace (Henriksen et al., 2010). As such, the results of this study provide motivation for larger placebo-controlled studies to examine changes in self-reported pain levels when walking with an active knee brace.

5. Conclusion

The results of this study support the conclusion that quadriceps muscle rehabilitation following knee injury or disease can be enhanced by exploiting a pathway that engages the cross-modal plasticity of the somatosensory system with common sensory pathways including pain, pressure, and vibration. The practical application of this pathway was established by applying intermittent cutaneous vibration stimulation applied at a specific phase of the gait cycle designed to activate the cross-modalities of the somatosensory system in a manner that increases the KFM during walking and by inference gates the pain response. This cutting-edge exploratory research has great potential for an effective method to help patients progressively regain quadriceps muscle function during daily walking in addition to physical therapy, independent strengthening, and exercise rehabilitation.

Author' contribution

Dr. Fischer participated in the design and conception of the research study, acquisition, analysis, and interpretation of the data, and drafting of the manuscript. Dr. Erhart-Hledik and Dr. Andriacchi each participated in conceptualization of the research study, interpretation of the data, and drafting of the manuscript. Dr. Chu participated in interpretation of the data and drafting of the manuscript. Ms. Asay and Dr. Erhart-Hledik participated in acquisition and analysis of the data and drafting of the manuscript. Dr. Fischer takes responsibility for the manuscript content. All authors have read and approved the final submitted manuscript.

Conflict of interest statement

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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