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**Rutherford, D. J.,** Hubley-Kozey, C. L., Stanish, W. D., Dunbar, M. J. (2011). Neuromuscular alterations exist with knee osteoarthritis presence and severity despite gait velocity similarities. Clinical Biomechanics. 26 377-383.

## Abstract

***Background***: Neuromuscular strategies during walking in individuals with knee osteoarthritis are being explored for diagnostic information; however, isolating differences to disease progression is difficult given walking velocity decreases with osteoarthritis severity. This study investigated lower extremity electromyograms during walking in asymptomatic individuals and individuals with different severities of knee osteoarthritis who walked with similar self-selected velocities.

***Methods****:* Muscle activity in lateral and medial gastrocnemius, vastus lateralis and medialis, rectus femoris and the lateral and medial hamstrings was monitored during self-selected walking in 230 subjects with asymptomatic knees, moderate and severe knee osteoarthritis. Sixteen asymptomatic individuals, 16 individuals with moderate and 15 individuals with severe knee osteoarthritis were identified based on similarities in average walking velocity. Principal component analysis was employed to derive amplitude and temporal characteristics of the EMG waveforms. Analysis of variance models tested for group and muscle differences in principal pattern scores ($\alpha$=0.05). Bonferroni post hoc testing was utilized on all significant findings.

***Findings****:* Despite similar walking velocities, individuals with moderate knee OA had elevated and prolonged quadriceps and elevated lateral hamstring activity compared to asymptomatic individuals ($P<0.05$). A diminished phase shift between medial and lateral gastrocnemius muscle activation, greater and prolonged lateral compared to medial

hamstring activation were found in the severe group compared to asymptomatic and moderate knee OA groups ($P<0.05$).

***Interpretation***: Lower extremity neuromuscular function during walking is altered with the presence and severity of knee osteoarthritis and not simply a direct function of walking velocity.

Key Words: Knee Osteoarthritis; Gait; Velocity; EMG; Electromyography; Lower Extremity Musculature; Walking

## Introduction

Knee osteoarthritis (OA) impairs lower extremity function, influencing ambulatory ability in older adults (Guccione et al., 1994). Reduced muscle strength (Hurley et al., 1997; Slemenda et al., 1997) and endurance (Fisher and Pendergast 1997), reports of giving-way (Fitzgerald et al., 2004), and stiffness (Hubley-Kozey et al., 2006) suggest that neuromuscular function may be impaired. Studies have begun to explore lower extremity neuromuscular characteristics of the knee OA disease process during walking through surface electromyography however, isolating differences to disease presence or severity is difficult given factors that affect neuromuscular characteristics may differ between groups such as walking velocity.

Lower extremity neuromuscular characteristics are altered with walking speed in asymptomatic individuals. Amplitude changes are the most prominent alteration (Hof et al., 2002; Shiavi et al., 1987; Yang and Winter 1985), although minor changes in shape have also been shown (Shiavi et al., 1981). Determining what changes are associated with the disease process can be a challenge since slower walking velocities have been reported for those with knee OA compared to asymptomatic controls (Hubley-Kozey et al., 2009; Rutherford et al., 2010; Zeni et al., 2010). Attempts have been made to account for walking velocity and include setting a threshold, (Childs et al., 2004; Hortobagyi et al., 2005; Zeni et al., 2010), entering velocity as a covariate when making statistical comparisons (Lewek et al., 2004; Rudolph et al., 2007; Zeni et al., 2010) or describing velocity as self-selected and reporting the differences among groups (Hubley-Kozey et al., 2009). All three approaches have merits and limitations when attempting to

differentiate the effect of walking velocity that accompanies OA progression from changes associated with structural and symptomatic differences among groups at different stages of OA progression.

A predetermined walking velocity may unknowingly alter habitual walking patterns influencing intra-subject variability (Shiavi et al., 1987), as individuals will have to modify their walking velocity to meet the required threshold. While appealing, employing analysis of covariance (ANCOVA) models to study walking in individuals with knee OA has the potential to mask group differences. Astephen et al. (2008) argued that critical assumptions are violated since walking velocity is not independent of treatment/group (knee OA). When a variable co-varies with a disease process, the use of an ANCOVA model will adjust disease effects for differences caused by the disease (i.e. slower walking velocity) (Cox and McCullagh 1982) and may remove part of the disease signal. Reporting results without considering walking velocity is also problematic.

In asymptomatic individuals, reduced walking velocity is associated with decreased muscle activation amplitudes (Hof et al., 2002; Yang and Winter 1985). However, for those with knee OA, despite reduced walking velocities, muscle activation amplitudes of the quadriceps and hamstrings were higher and more prolonged than faster walking asymptomatic controls (Hubley-Kozey et al., 2009; Rutherford et al., 2010). Providing a mechanism for these neuromuscular alterations is still at an early stage in our understanding of OA and may include a response to nociceptive inputs and reflex activity (Courtney et al., 2009), muscle inhibition during maximal normalization testing (Fahrer et al., 1988), joint loading (Hubley-Kozey et al., 2006), laxity (Lewek et al., 2004) and walking velocity (Zeni et al., 2010) . Given walking velocities in individuals with knee

OA are typically reduced in comparison to asymptomatic cohorts, understanding neuromuscular function driven by the OA disease process rather than confounded by group differences in walking velocity may provide further information on disease mechanisms.

This study investigated amplitude and temporal characteristics using principal component analysis from surface electromyograms of seven lower limb muscles during walking in asymptomatic individuals and individuals with different severities of knee OA. To address the question of whether neuromuscular alterations are apparent in the electromyogram despite similarities in average self-selected walking velocity, three groups separated by their clinical status were selected based on matching average self-selected walking velocity. We hypothesized that increased amplitudes, medial and lateral site imbalances and temporal alterations would be found between asymptomatic controls and patients with knee OA and between knee OA severities.

## Methodology

### Subjects

Surface electromyographic (EMG) data were collected from a large sample of individuals with asymptomatic knees and a clinical population with knee OA during self-selected, level-ground walking (N=230). Subjects over age 35 with no history of cardiovascular disease or neurological disorders were included. Subjects with knee OA were recruited from the practice of two orthopedic surgeons (WDS, MJD). Standard anterior/posterior radiographs confirmed predominant medial compartment radiographic disease presence and were scored using the Kellgren-Lawrence global scoring algorithm (Kellgren and Lawrence 1957). Fair to good reliability for this assessment has been previously reported (McKean et al., 2007), but for these two surgeons, substantial reliability was found (Weighted Kappa statistic = 0.6). Asymptomatic subjects were recruited from the general community using website and poster board advertisements. Written informed consent approved by the local institutional ethics review committee was attained. All subjects were tested between 2001 and 2009 at the Dynamics of Human Motion Laboratory, Dalhousie University, Halifax, Nova Scotia.

Three groups, matched for walking velocity were identified from the sample including i) asymptomatic, ii) moderate knee OA and iii) severe knee OA. First, 15/62 individuals with severe OA were identified from the sample who walked at an average walking velocity greater than 1m/s. Their clinical prognosis was poor and they received a total knee arthroplasty within one-week after testing. Asymptomatic individuals

presented with no lower extremity injuries within six months prior to data collection and no symptoms of lower extremity degenerative joint disease including knee pain, morning stiffness, prior knee surgery or fracture. Of the 77 asymptomatic individuals, those with the slowest walking velocities who were the best match based on demographic factors to the severe knee OA group were identified (16). Of the 91 patients with moderate knee OA, 16 were matched to both the asymptomatic and severe knee OA groups based on self-selected velocity and demographics. These individuals self-reported their ability to perform three functional tasks; i) jog five meters, ii) walk one city block and iii) reciprocally ascend and descend 10 stairs and were being managed with conservative approaches.

Procedures

The Western Ontario McMaster Osteoarthritis Index (WOMAC-LK3.1) was completed by all participants. For individuals with knee OA, the most affected lower extremity was tested. For asymptomatic individuals, the tested lower extremity was randomly assigned. Surface electrode locations were identified as previously reported (Hubley-Kozey et al., 2006) and standard procedures consistent with recommended guidelines (SENIAM 1999) were employed. Skin was shaved and cleaned with alcohol wipes (70% alcohol) and 10 mm bipolar electrodes (Ag/AgCl, interelectrode distance 20 mm) were affixed to the lateral (LG) and medial (MG) gastrocnemius, vastus lateralis (VL) and medialis (VM), rectus femoris (RF), biceps femoris (LH) and semitendinosis/membranosis (MH). A reference electrode was affixed to the mid-

anterior tibial shaft. Following electrode placement, muscle palpation and a series of isometric contractions for specific muscle groups (Kendall et al., 1993) were used for EMG signal validation (Winter et al., 1994) and gain adjustment. In addition, active Infrared Emitting Diode (IRED) triangular sets of markers were affixed to the lower extremity segments, individual IRED markers were secured on the lateral malleolus, lateral epicondyle of the femur, greater trochanter and lateral aspect of the shoulder then virtual points were digitized as previously reported (Landry et al., 2007; Rutherford et al., 2008).

After three to five familiarization walking trials, subjects were instructed to walk along a six-meter walkway at their self-selected velocity. At least five walking trials with a consistent walking velocity (+/- 10%) and correct force plate contact were collected. Following the walking trials, baseline muscle activity was recorded in supine lying. Then subjects performed a series of eight maximal voluntary isometric contractions (MVIC) (seven against a Cybex™ dynamometer (Lumex, NY, USA)) to elicit maximal activation amplitudes for normalization purposes and to provide a measure of muscle strength for the ankle plantarflexors, knee extensors and flexors (Hubley-Kozey et al., 2006). Following at least one practice and warm-up contraction, two maximal isometric contractions were completed for each exercise. Standard feedback was given to ensure a consistent maximum effort (Johansson et al., 1983; McNair et al., 1996). Exercises included; 1) knee extension in sitting (knee position 45 degrees flexion) 2) knee extension/hip flexion in sitting (knee position 45 degrees flexion) 3) knee flexion in sitting (knee position 55 degrees flexion) 4) knee extension in supine lying (knee position

15 degrees flexion) 5) knee flexion in supine lying (knee position 15 degrees flexion) 6) Ankle plantar flexion in long sitting (neutral ankle position) 7) standing unilateral heel raise and 8) knee flexion in prone lying (knee position 55 degrees flexion). The torque from exercises one, three and six were used to quantify quadriceps, hamstrings and plantarflexion muscle strength.

Data acquisition

Lower extremity motion was captured at 100Hz using two optoelectronic motion analysis sensors (Optotrak 3020™, Northern Digital Inc., Waterloo, ON, Canada). A single force plate (AMTI™, Advanced Mechanical Technology Incorporation, Newton, MA, USA), aligned to the global coordinates of the motion capture system recorded the three-dimensional ground reaction forces. Motion and ground reaction forces combined to demarcate heel strike and toe off events for electromyogram time normalization. EMG signals were amplified using an AMT-8 (Bortec, Inc., Calgary, AB, Canada), eight-channel EMG measurement system (CMRR: 115dB at 60 Hz, Input Impedance: ~10GΩ, Band-pass filter (10-1000 Hz)). A Cybex II™ Isokinetic dynamometer (Lumex, NY, USA) was utilized to record the torque associated with the maximal isometric contraction series. EMG, ground reaction force and dynamometer signals were analogue to digital converted (16bit, +/- 2V) at 1000Hz and stored for offline processing.

Data Processing

EMG signals were processed through custom software, written in MatLab™ version 7.0 (The Mathworks Inc., Massachusetts, USA). Raw EMG signals were corrected for subject bias, converted to micro-volts, full wave rectified and low pass filtered (Butterworth 6-Hz low pass filter). Maximal amplitudes recorded from a 100-ms moving-average window across the eight MVIC exercises were identified for each muscle for amplitude normalization (Hubley-Kozey et al., 2006). The EMG waveforms (%MVIC) were time normalized to 101 data points, representing one complete gait cycle (0-100 percent). Muscle torque was determined using a static model that included the gravity correction torque and the torque recorded by the dynamometer during the three MVIC conditions. The maximum torque calculated over a 500-ms moving window from the three-second steady state contraction was averaged for the two trials of each exercise and recorded as muscle strength.

Analysis

Ensemble average EMG waveforms were calculated for each subject for each muscle (Winter and Yack 1987). Principal component analysis (PCA) was used to capture amplitude and temporal features in the asymptomatic, moderate and severe knee OA EMG waveforms using custom MatLab™ Ver.7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA). This multivariate statistical technique has been utilized previously (Hubley-Kozey et al., 2006; Rutherford et al., 2010). Three separate PCA were performed, one for each muscle grouping (gastrocnemius, hamstrings, quadriceps). Three matrices (X) were formed from the time-normalized waveforms (101 points). An

eigenvector decomposition of the cross product matrix ([S] = [$X^T$]*[X]) was performed, yielding the predominant orthonormal patterns called eigenvectors (Jackson 1991). Eigenvectors are referred to as principal patterns (PP). Principal patterns explaining the greatest percent of variation, estimated by the percent trace were retained and referred to as PP1, PP2 etc. (Hubley-Kozey et al., 2006). Principal pattern scores (*PP-Scores*) were computed for individual gait waveforms (*PP-Score* = [X]*[PP]) to provide a weighting coefficient for how each principal pattern related to each measured EMG waveform. *PP-scores* were utilized for statistical hypothesis testing.

Statistical Analysis

One-way analysis of variance (ANOVA) models tested group main effects for age, body mass index (BMI), self-selected walking velocity, stride length and strength measures. Independent student t-tests were employed to test for significant knee OA group differences in WOMAC sub-scores. A Mann-Whitney U-test tested for significant differences in Kellgren-Lawrence radiographic scores. Normality and equal variance of the *PP-scores* were determined from Kolmogorov-Smirnov and Levene's tests respectively. Two-factor mixed model ANOVA tested for significant group (between) and muscle (within) main effects and interactions ($\alpha$=0.05). Significant findings were post hoc tested using a Bonferroni adjusted alpha level to determine pair-wise significant differences. Statistical procedures were completed on Minitab™ Ver.15 (Minitab Inc. State College, PA, USA).

**Results**

Subject demographics, WOMAC scores, strength measures and stride characteristics are shown in table 1. Significant differences are indicated on the table. Asymptomatic individuals had a lower BMI ($P<0.05$) and greater ($P<0.05$) relative knee extensor and knee flexor strength (Nm/kg) compared to individuals with knee OA ($P<0.05$). Relative plantar flexor strength was greater in asymptomatic individuals compared to individuals with severe knee OA only ($P<0.05$). Significantly higher Kellgren-Lawrence radiographic scores and WOMAC physical function sub-scores were found for the severe knee OA compared to moderate knee OA group ($P<0.05$).

**Table 1:** Mean and standard deviation (SD) subject demographics, gait characteristics and knee joint muscle strength.

| | Group | | |
|---|---|---|---|
| | Asymptomatic | Moderate OA | Severe OA |
| Sample Size | 16 | 16 | 15 |
| Gender (M/F) | 8/8 | 8/8 | 10/5 |
| Age (years) | 56 (6) | 61 (6) | 61 (9) |
| BMI (kg/m$^2$) | 24.6 (3.9) * | 31.3 (3.6) | 30.7 (5.4) |
| Velocity (m/s) | 1.23 (0.09) | 1.22 (0.10) | 1.20 (0.14) |
| Stride Length (m) | 1.36 (0.09) | 1.35 (0.12) | 1.36 (0.12) |
| KL Scores | --- | 2.4 (0.9) # | 3.1 (0.7) |
| WOMAC Pain | --- | 6.6 (3.7) | 8.3 (3.3) |
| WOMAC Stiffness | --- | 3.8 (1.6) | 4.1 (1.3) |
| WOMAC Physical Function | --- | 21.2 (13.9) # | 30.9 (9.2) |
| Knee Extension Strength (Nm)^ | 102.7 (35.7) | 93.9 (36.7) | 94.2 (18.4) |
| Knee Extension Strength (Nm/kg)^ | 1.4 (0.4) * | 1.0 (0.3) | 1.0 (0.3) |
| Knee Flexion Strength (Nm)^ | 47.2 (21.7) | 45.6 (18.1) | 43.5 (15.6) |
| Knee Flexion Strength (Nm/kg)^ | 0.7 (0.2) * | 0.5 (0.2) | 0.5 (0.2) |
| Ankle Plantarflexion Strength (Nm)^ | 73.9 (32.3) | 74.7 (28.7) | 59.7 (17.7) |
| Ankle Plantarflexion Strength (Nm/kg)^ | 1.1 (0.3)$^{\&}$ | 0.8 (0.2) | 0.7 (0.3) |

- * - indicates asymptomatic significantly different from knee OA groups
- $^{\&}$ - indicates asymptomatic significantly different from severe OA group
- # - indicates difference between OA groups
- ^ Knee Extension Strength (1 - Asymptomatic and 1- SOA), Knee Flexion Strength (1-Asymptomatic) and Ankle Plantarflexion Strength (1-Asymptomatic and 2-SOA) patients removed due to data errors.

EMG waveform characteristics

Ensemble average profiles for each muscle and each group are illustrated in Figure 1. Differences among groups are apparent, but differences are not systematic throughout the gait cycle or among the muscles. A description of the characteristic captured by the principal patterns and the statistical results are found in Table 2 along with the *PP-scores* in Table 3.

**Table 2**: P-values for *PP-score* main effects and interactions

| | Principal Pattern Description | Group | Muscle | Group x Muscle |
|---|---|---|---|---|
| **Gastrocnemius** | | | | |
| PP1 - scores | Greater scores = Greater magnitude | 0.427 | 0.192 | 0.070 |
| PP2 - scores | Greater scores = Earlier activity | 0.040 | 0.000 | **0.020** |
| PP3 - scores | Greater scores = larger difference between early and late stance activity levels | **0.002** | 0.353 | 0.178 |
| **Quadriceps** | | | | |
| PP1 - scores | Greater scores = Greater magnitude | **0.015** | **0.000** | 0.409 |
| PP2 - scores | Greater scores = larger difference between early and mid-late stance activity levels | **0.045** | **0.000** | 0.940 |
| PP3 - scores | Greater scores = higher activity during late stance compared to mid stance and swing phase | **0.032** | **0.000** | 0.887 |
| **Hamstring** | | | | |
| PP1 - scores | Greater scores = Greater magnitude | 0.028 | 0.006 | **0.035** |
| PP2 - scores | Greater scores = greater activity during mid-stance and late swing burst of activity attenuation | 0.007 | 0.001 | **0.023** |
| PP3 - scores | Greater scores = greater differences between early and late gait cycle compared to mid gait cycle | 0.299 | 0.914 | 0.950 |

*Significant findings that were post hoc tested are in **bold.**

Gastrocnemius

A significant group by muscle interaction was found for *PP2-scores* ($P<0.05$). Post hoc analysis ($\alpha=0.05/15$ pair wise comparisons) revealed significantly lower *PP2-scores* for LG compared to MG in the asymptomatic and moderate knee OA groups only ($P<0.003$). Medial gastrocnemius *PP2-scores* in the severe knee OA group were significantly lower than scores found for MG in the asymptomatic and moderate knee OA groups ($P<0.003$). A group main effect was found for *PP3-scores* ($P<0.05$). Post hoc analysis ($\alpha=0.05/3$ pair wise comparisons) revealed that individuals with severe knee OA had significantly lower *PP3-scores* compared to asymptomatic and moderate knee OA groups ($P<0.017$).

Quadriceps

Non-normality and unequal variance were found for quadricep *PP-Scores* ($P<0.05$) and they were transformed. Significant group and muscle main effects were found for all three *PP-scores* ($P<0.05$). There were three pair wise comparisons for each main effect ($\alpha=0.05/3$). *PP1-scores* were greater in individuals with knee OA compared to individuals with asymptomatic knees ($P<0.017$), indicating higher overall amplitudes. VL and VM *PP1-scores* were greater than RF *PP1-scores.* Lower *PP2-scores* were found in the severe knee OA group compared to asymptomatic and moderate knee OA groups ($P<0.017$) and in the moderate knee OA group compared to those with asymptomatic knees ($P<0.017$). *PP2-scores* for VM and VL were significantly greater than RF ($P<0.017$). Lower *PP3-scores* were found for the severe knee OA group

compared to asymptomatic and moderate knee OA groups (P<0.017). Greater *PP3-scores* were found for VM and RF compared to VL (P<0.017).

Hamstrings

Non-normality and unequal variance were found in the hamstring *PP-scores* (P<0.05). A significant group by muscle interaction was found for the transformed *PP1 and PP2-scores* (P<0.05). Post hoc analysis required 15 pair wise comparisons for each interaction ($\alpha$=0.05/15). In the severe knee OA group, post hoc analysis revealed greater *PP1-scores* for LH compared to MH (P<0.003). Lateral hamstring *PP1-scores* were lower in the asymptomatic group, compared to those with knee OA (P<0.003) where no differences were found between individuals with moderate and severe knee OA (P>0.003). In the severe knee OA group, greater *PP2-scores* were found for lateral hamstrings compared to medial hamstrings (P<0.003). Lateral hamstring *PP2-scores* were also greater in the severe knee OA group compared to LH *PP2-scores* in the asymptomatic and moderate knee OA groups (P<0.003). No differences were found for MH *PP1-scores* and *PP2-scores* among all three groups (P>0.003).

Table 3: Mean and Standard Deviation (SD) *PP-scores* for each group and muscle

| | | Group | | |
|---|---|---|---|---|
| | | Asymptomatic | Moderate OA | Severe OA |
| **Gastrocnemius** | | | | |
| PP1-scores | LG | 214.2 (74.9) | 200.3 (71.6) | 208.7 (101.7) |
| | MG | 245.0 (117.4) | 253.0 (90.0) | 181.6 (96.9) |
| PP2-scores | LG | -18.3 (42.5) | -15.9 (31.1) | -30.3 (61.0) |
| | MG | 28.1 (47.3) | 34.2 (49.3) | -22.0 (41) |
| PP3-scores | LG | 25.1 (24.1) | -0.4 (33.8) | -18.0 (43.3) |
| | MG | 9.0 (25.7) | 6.7 (37.9) | -23.3 (24.1) |
| **Quadriceps** | | | | |
| PP1-scores | VL | 107.5 (43.5) | 172.8 (51.6) | 174.8 (51.6) |
| | VM | 124.8 (74.6) | 162.3 (89.9) | 159.4 (87.1) |
| | RF | 62.2 (27.8) | 106.1 (63.1) | 138.8 (92.2) |
| PP2-scores | VL | 21.5 (13.5) | 8.5 (35.5) | 5.2 (39.0) |
| | VM | 23.0 (22.1) | 8.1 (24.4) | 2.6 (37.2) |
| | RF | 0.5 (10.4) | -9.9 (30.0) | -25.9 (40.1) |
| PP3-scores | VL | -4.7 (16.7) | -0.9 (25.8) | -24.3 (28.9) |
| | VM | 11.3 (25.4) | 9.7 (27.2) | -5.9 (24.3) |
| | RF | 10.8 (9.3) | 11.8 (17.8) | -1.9 (19.3) |
| **Hamstrings** | | | | |
| PP1-scores | LH | 98.8 (41.7) | 159.5 (75.1) | 195.9 (109.3) |
| | MH | 99.9 (38.2) | 126.4 (51.0) | 116.6 (62.9) |
| PP2-scores | LH | -25.8 (24.7) | -0.8 (43.0) | 35.3 (52.6) |
| | MH | -30.8 (19.8) | -12.4 (26.1) | -10 (44.3) |
| PP3-scores | LH | -4.5 (27.0) | 2.02 (37.7) | -2.5 (36.0) |
| | MH | -2.6 (28.2) | 8.5 (17.6) | -3.2 (19.2) |

**Gastrocnemius** – PP1 explained 90%, PP2 explained 4% and PP3 explained 2% of the overall waveform variability. **Quadriceps** – PP1 explained 89%, PP2 explained 4% and PP3 explained 2% of the overall waveform variability. **Hamstrings** – PP1 explained 85%, PP2 explained 7% and PP3 explained 3% of the overall waveform variability.

## Discussion

This study confirmed that altered neuromuscular patterns during walking exist with knee OA presence and severity providing evidence that specific differences are found despite similarities in self-selected walking velocity. Individuals with severe OA were considered clinically appropriate for total knee arthroplasty in comparison to individuals with moderate disease who were being managed conservatively. The moderate knee OA group reported their ability to walk a city block, reciprocally ascend and decent stairs and jog 5-meters would not be encumbered by their knee OA. These clinical entities were previously used to determine group assignment (Hubley-Kozey et al., 2009), and while some classification methods have focused on radiographic evidence (Zeni et al., 2010), the present approach identified two distinct groups as evidenced by the significant WOMAC function (symptoms) and KL-score (structural) differences between the two OA groups.

### Gastrocnemius

Overall amplitude differences (*PP1-scores*) were not found among groups with the elevated activity in the OA groups during early stance and to a lesser extent swing phase accounting for this finding. The asymptomatic and moderate knee OA groups however; displayed an earlier increase (phase shift- *PP2-scores*) in MG activation compared to LG consistent with findings reported when walking velocities were different between groups (Hubley-Kozey et al., 2006) whereas the severe group did not display

this shift. This latter finding is consistent with reports from a severe OA group that walked at a slower walking velocity (Hubley-Kozey et al., 2008). Shiavi et al, (1981) found a trend for earlier gastrocnemius activity with increased walking velocity, but the current result suggests that this phase shift is also related to disease severity. Furthermore, individuals with severe knee OA had a reduced late stance to early stance activity differential (*PP3-scores*) compared to the other groups. While higher early stance activity was apparent in both gastrocnemius sites, only the MG had decreased activity in late stance. This decrease in activity may reflect an inhibition of the MG in late stance (figure 1), a strategy thought to reduce medial joint loading (Hubley-Kozey et al., 2006). Increased gastrocnemius activity during early stance may provide active stiffness, potentially improving joint stability during weight acceptance and single leg stance consistent with higher vastus medialis-medial gastrocnemius co-contraction indices reported during early stance in those with medial joint instability (Lewek et al., 2004). While a mechanism is not established by this study, it is evident that severe knee OA disease processes influence MG strategies, more so than the moderate knee OA disease severity despite similar walking velocity.

Quadriceps

Quadriceps activity was greater in individuals with knee OA compared to asymptomatic knees, consistent with reports in which self-selected walking velocity was lower for OA groups (Hubley-Kozey et al., 2009). Since decreased quadriceps activity with reduced walking velocities have been reported for asymptomatic controls (Yang and

Winter 1985), the higher quadriceps activity in this present study, despite the similar average walking velocities among groups supports an OA related alteration. Increased activity during early to mid-stance may be necessary to counter external moments of force in the frontal plane (Shelburne et al., 2006) and internal flexion moments produced by knee flexor coactivity during early stance (Figure 1). Overall magnitudes were similar for those with moderate and severe knee OA contrasting previous findings (Hubley-Kozey et al., 2009). The lack of significant differences in quadriceps strength between the OA groups in the present study may partially explain differences from previous findings in which group differences in average walking velocity were found and the severe group had lower strength values (Hubley-Kozey et al., 2006; Hubley-Kozey et al., 2009). While overall magnitude differences were apparent, waveforms in Figure 1 illustrate a prolonged elevated activity in the OA waveforms, most notably in RF during mid-stance phase. *PP2-scores* captured this mid-stance activity, consistent with previous reports (Hubley-Kozey et al., 2006; Rutherford et al., 2010), supporting the finding of prolonged quadriceps activation in knee OA subjects by others (Childs et al., 2004). This feature showed progressive traits, where all three groups were different and individuals with severe knee OA having the greatest mid-stance magnitude and asymptomatic individuals having the lowest mid-stance activity. The lower *PP3-scores* in individuals with severe knee OA also exemplifies the greater stance phase activity required by this group compared to asymptomatic and moderate knee OA individuals. Mid-stance increases in quadriceps activity were specific to disease severity. Since walking velocities and muscle strength were similar between the OA groups, an alternate explanation for the higher mid-stance quadriceps activity for the severe group may be

related to the need for active joint stiffness to prevent pain or giving away (Fitzgerald et al., 2004) as the severe group had greater joint changes based on higher KL scores. In summary, these results corroborate previous cross-sectional studies that show higher quadriceps activity for individuals with knee OA compared to controls despite slower self-selected walking velocity (Hubley-Kozey et al., 2009; Rudolph et al., 2007; Zeni et al., 2010) and are not consistent with the reductions in early stance quadriceps amplitudes with reduced walking speeds found in asymptomatic subjects (Yang and Winter 1985).

Hamstrings

Recent studies found that activation levels and patterns of activity differ between medial and lateral sites during walking in the presence of both moderate and severe knee OA (Hubley-Kozey et al., 2009; Lynn and Costigan 2008; Rutherford et al., 2010). While overall magnitude of LH activity in those with knee OA was greater than asymptomatic individuals supporting previous work (Hubley-Kozey et al., 2006), differential levels of activation between LH and MH were only significant in the severe knee OA group despite the 10% higher LH compared to MH amplitudes in early stance in the moderate OA group (Figure 1). Differential recruitment patterns included both overall magnitude (*PP1-scores*) and prolonged activity during stance (*PP2-scores*). Asymmetric co-activity between LH and MH was expected given medial compartment dominated disease and the possible presence of a varus perturbations (Buchanan et al., 1996) along with greater knee adduction moments (Heiden et al., 2009). These characteristics may be more prevalent in individuals with progressing knee OA (Chang et al., 2004; Miyazaki et al., 2002). This

lack of differential LH versus MH activity in moderate knee OA contrasts previous literature using PCA (Hubley-Kozey et al., 2006; Rutherford et al., 2010), where higher overall magnitude and prolonged LH compared to MH activations were found. Alterations in LH activity were related to disease severity however, no differences were reported for MH. This contrasts previous reports of higher overall MH amplitude in severe OA individuals compared to asymptomatic and moderate OA (Hubley-Kozey et al., 2009). In asymptomatic individuals, increased hamstring amplitude and prolonged activation during stance were related to increased walking speed (Ivanenko et al., 2004; Yang and Winter 1985) but the current study illustrates an association with disease severity for the LH site. In summary, activation characteristics in the hamstring musculature are sensitive to presence and severity of medial compartment dominant knee OA despite similar walking velocity, strength and self-reported function.

In this study, self-selected walking velocity, WOMAC pain and stiffness sub-scores, lower extremity muscle strength, age and BMI were not different between individuals with a clinical diagnosis of moderate and severe knee OA. In contrast, neuromuscular patterns were sensitive to both the presence and severity of knee OA. This implies that objective neuromuscular function measures provides unique information for monitoring the disease process that addresses both symptomatic and structural progression with a particular emphasis on functional ability in individuals with knee OA.

Limitations

Amplitude normalization to MVIC has its limitations, however the procedures employed were consistent with previous studies aiming to produce maximal activations

(Hubley-Kozey et al., 2006; Lewek et al., 2004; Zeni et al., 2010) providing a standard for comparison (Knutson et al., 1994). Arthrogenic muscle inhibition may (Fahrer et al., 1988) or may not (Jones et al., 1987) significantly impair the quadriceps muscles during maximal testing for individuals with joint arthropathy. The present study sought to minimize this effect as much as possible by utilizing a normalization protocol that provided feedback and positioned the leg differently from early studies of quadriceps inhibition (Fahrer et al., 1988). In addition, this inhibition has not been reported for the hamstrings and gastrocnemius muscles. Never the less, the potential that inhibition can lower both the force-generating properties of the quadriceps muscle and amplitude of the EMG signal during normalization exercises can partially explain why individuals with knee OA present with elevated quadriceps magnitude (*PP1-scores*) compared to asymptomatic individuals during walking. It is less clear as to how inhibition could alter the hamstrings and gastrocnemius activity or features other than magnitude (*PP1-scores*) that were found in the present study.

Although many consistencies were found between this study and previous studies that examined similar diagnostic groups walking at different self-selected velocities (Hubley-Kozey et al., 2006; Hubley-Kozey et al., 2009), there were notable differences. The smaller sample size in the present study resulted in lower statistical power than previous work, thus the results provide a conservative estimate of these differences. Difference detection, given the small sample and overlap of the groups (low functioning asymptomatic and high functioning severe OA group), speaks to the strength of the findings. The present study found that despite the reported similarities in measures of symptoms (i.e. pain and stiffness) and function (i.e. muscle strength, self-selected

walking velocity), neuromuscular patterns were different with OA presence, and some were progressive.

## Conclusion

Walking velocity decreases are part of the disease process yet individuals with varying clinical presentations of knee OA who chose to walk at the same velocity still present with altered neuromuscular patterns during walking. In particular, selective delay in medial gastrocnemius activity with severe knee OA, temporal synchrony of lateral and medial gastrocnemius, the increased and prolonged activation of the quadriceps muscles and the selective and prolonged activation of the lateral hamstring were all a function of the disease classification. This supports that differences are not the result of walking velocity only.

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**Conflict of Interest**

The authors acknowledge that there are no conflicts of interest pertaining to this manuscript.

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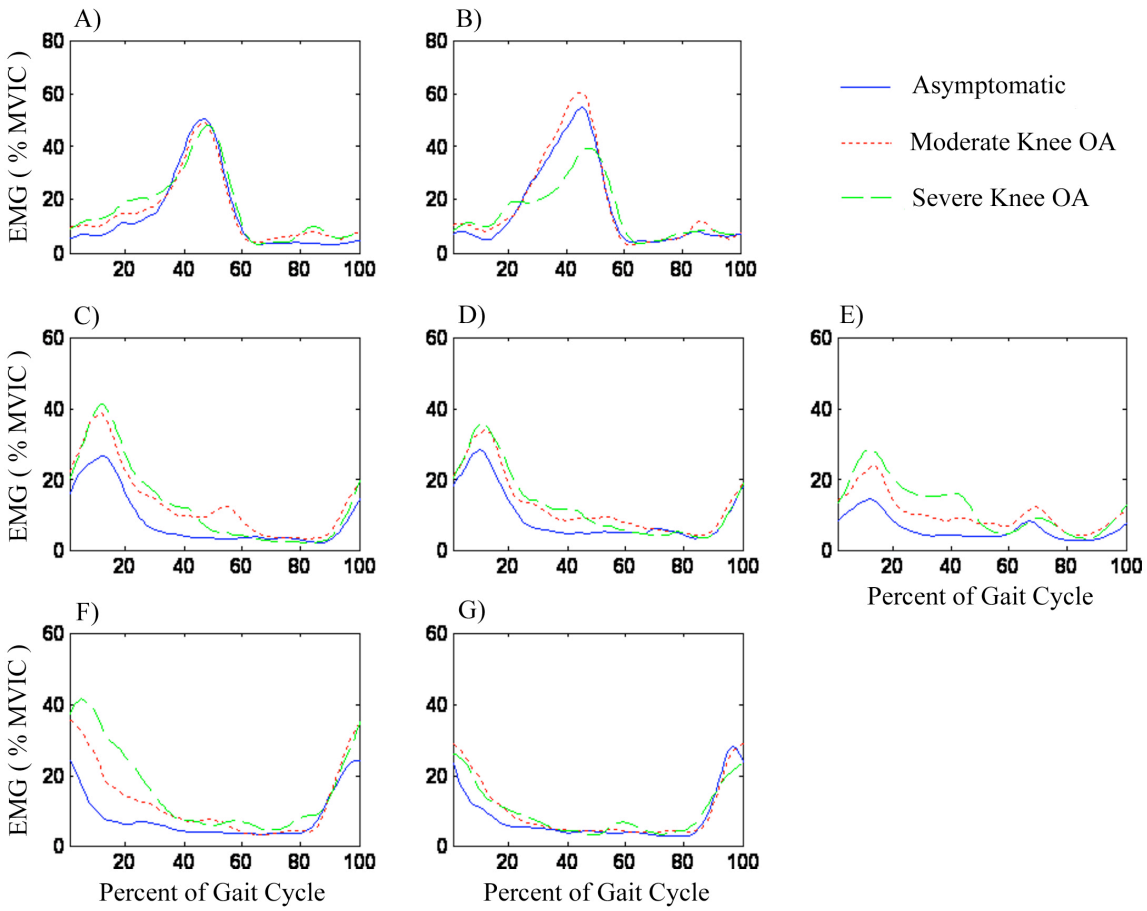


Figure 1: Group (asymptomatic - solid, moderate knee OA - dotted and severe knee OA - dashed) and muscle ensemble-average waveforms. A) lateral gastrocnemius B) medial gastrocnemius C) vastus lateralis D) vastus medialis E) rectus femoris F) biceps femoris (lateral hamstrings) and G) semitendinosis/membranosis (medial hamstrings). Percent MVIC is on the y-axis and percent gait cycle on the x-axis.

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