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Running Head: Muscle co-activation across ADL in KOA

Muscle co-activation across activities of daily living in individuals with knee osteoarthritis

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Abstract

Objective: Muscle co-activation has been shown to be elevated in individuals with knee osteoarthritis (KOA) during gait. Comparisons of muscle co-activation across different activities of daily living such as stair negotiation has yet to be explored. The aim of the study was to explore muscle co-activation across different activities of daily living in patients with KOA.

Methods: Muscle co-activation was assessed in 77 symptomatic KOA participants (age 62.5±8.1years; bodymass index 29.4±9.0kg/m^2; gender 48/29 female/male) using electromyography (EMG), during a series of walking, stair negotiation (ascent, descent) and sit-to-walk activities. EMG was recorded from 7 sites, medial/lateral gastrocnemius, biceps femoris, semitendinosus, vastus lateralis/medialis and rectus femoris and normalised to maximal voluntary isometric contraction. Correlation was used to assess the consistency of co-activation across activities. Repeated measures ANOVA assessed the muscle combination by activity differences.

Results: Muscle co-activation was highest during stair ascent. When comparing muscle combinations within the same activity correlations ranged from r=0.003-0.897 of which 80% of combinations were significant. Between activities muscle co-activation was significantly different (P<0.05). Medial:lateral muscle co-activation was higher than hamstrings:quadriceps across activities.

Conclusion: Two muscle co-activation strategies were observed during activities of daily living in patients with KOA to maintain stability. Muscle co-activation was higher during more challenging activities, particularly when the joint is accepting load. Medial:lateral muscle co-activation was higher than hamstrings:quadriceps whereby medial:lateral co-activation is thought to be a stabilisation mechanism whilst hamstrings:quadriceps responds to knee flexion moments, suggesting different muscle combinations may have different roles in responding to joint demand.

Keywords: osteoarthritis; co-activation; muscle; gait; stairs; activities of daily living;

Significance and Innovations

- The same patients demonstrated consistently high or low muscle co-activity across all muscle combinations.
- Muscle co-activation was significantly different across activities, whereby muscle co-activation was higher during more challenging activities e.g. stair negotiation than less challenging activities e.g. gait.
- Neither overall nor selective muscle co-activation strategies were prominent, whereby it appears both muscle co-activation strategies modulate in unison to promote joint stability.

Introduction

Individuals with knee osteoarthritis (KOA) exhibit altered movement patterns (i.e. reduced knee flexion; altered knee stiffening) compared to healthy controls (1–6), as a result of structural changes, pain, muscle weakness and a loss of proprioception (7). Muscle activation is controlled by two mechanisms: feedforward based on cognitive control; and feedback responding to changes detected by joint receptors (mechanoreceptors; proprioceptors) (8). These altered movement patterns have been associated with high joint loads; loss of joint stability; and the inability of the musculature to provide stability (9–11).

Muscle co-activation (simultaneous coordinated agonist and antagonist muscle activity) is thought to be a major mechanism for joint stabilisation, load distribution and movement control during gait in KOA (1–3,5–7,11–17). Baratta et al (9) suggested muscle co-activation is necessary to aid the ligaments in maintaining joint stability; distributing joint surface pressure and regulating joint mechanical impedance. In healthy young individuals and KOA, two muscle co-activation strategies have been identified. Overall muscle co-activation, is considered as high muscle co-activation across all muscle combinations surrounding the joint (18). Selective muscle co-activation involves high muscle co-activation in specific, but not all muscle combinations, (e.g. agonist:antagonist (2,3,18), or medial:lateral (3,19) combinations, but not both). In KOA high levels of muscle co-activation are thought to stabilise the knee in the absence of sufficient stabilisation from the passive-restraints system (20). This strategy has been associated with increased joint contact pressures and maybe a risk factor for cartilage degeneration and KOA disease progression (1–3,5,6,11–14,20,21).

It is well established that during walking, individuals with KOA demonstrate higher muscle co-activation than controls (1,2,4,12,14–17,21) in anterior-posterior (1,2,12,14–17,21) and medio-lateral (1,17) muscle combinations. This has been reported during specific phases of gait (1,2,4,13,14,17,21) and the entire gait cycle (3–6,12,15,19,22). Schmitt and Rudolph (1) found that as the knee prepares to accept and accepts weight, high anterior-posterior co-activation stabilised the joint. During progression from double-limb to single-limb-support, the knee becomes increasingly unstable and high muscle co-activation across all muscle combinations is needed as a stabilisation mechanism (1). DeMont (23,24) also suggested control of the knee position during dynamic movement may be dependent on muscle activation prior to a stress occurring, emphasising the importance of exploring muscle co-activation prior to heel strike during dynamic activities. For other activities of daily living (ADL) very little evidence of muscle co-activation in individuals with KOA exists. Two studies looking at stair negotiation found conflicting results. Childs et al. (2) found high tibialis anterior:gastrocnemius co-activation in individuals with KOA, whilst Hortobágyi, et al. (14) found there was no difference between KOA and controls. When activities were grouped, individuals with KOA had higher biceps femoris:vastus lateralis co-activation. Patsika et al. (25) found higher biceps femoris muscle activity and no difference in the vastus lateralis between individuals with KOA and controls during sit-to-stand. Bouchouras et al. (4) also found significantly higher biceps femoris:vastus lateralis co-activation during sit-to-stand compared to controls. In healthy individuals, it would be expected that during more challenging activities (i.e. stair negotiation) requiring higher muscle activation, muscle co-activation would be higher. In individuals with neuromuscular deficits such as those with KOA, this may not be true. This may have implications for rehabilitation (i.e. limit tasks

which can be undertaken). It is therefore important to understand muscle co-activation strategies across different ADL and across different muscle combinations.

It has been suggested that agonist:antagonist, especially hamstrings:quadriceps co-activation increases joint stiffness, where it's primary role is to influence anterior tibial shear force and internal rotation (1,2,26–28). The vastii muscles have however been suggested to be general joint stabilisers (26,27), whereby medial:lateral co-activation is thought to respond to joint space narrowing, and instability, increasing joint stiffness and joint load (2,3,26,27). This raises questions about co-activation in KOA. Specifically, do the same people consistently demonstrate the highest muscle co-activation across different activities and muscle groups (e.g. high positive correlation between agonist:antagonist and medial:lateral muscle co-activation across all activities)? Alternatively, do different individuals exhibit high muscle co-activation during different activities or muscle combinations (e.g. high medial:lateral and low agonist:antagonist muscle co-activation during stair negotiation, and low medial:lateral and high agonist:antagonist muscle co-activation during gait).

The purpose of this study was to explore muscle co-activation patterns across different ADL and investigate specific areas of muscle co-activation during different phases of gait. It was hypothesised that 1) for a specific activity, patients will demonstrate high muscle co-activity across all muscle combinations; 2) muscle co-activation will be higher in the medial:lateral than agonist:antagonist muscle combinations in patients with KOA; 3) muscle co-activation will be higher during more challenging activities (e.g. stair descent) compared to less challenging activities (e.g. gait).

Methods

Participants

Data analysis presented here is part of the NEKO study (NCT02314715, www.clinicaltrials.gov). A convenience sample of adults (40 years or over), with doctor-diagnosed unilateral/bilateral KOA, with self-reported knee pain, stiffness lasting <30minutes and confirmed by ultrasound and/or magnetic resonance imaging (data not presented), were recruited through rheumatology clinics; general practitioner practices; and a local newspaper advert. Participants were excluded if they had any current neuromuscular skeletal injury or disease, knee replacement, knee surgery in the past year, steroid injections in the past 3 months or severe co-morbidity which would limit participation in the study.

All participants gave written informed consent to participate in the study. The assessment protocol was approved by the West of Scotland Research Ethics Committee (ref 13/WS/0146) and Glasgow Caledonian University (ref HLS12/86) and carried out in compliance with the Declaration of Helsinki.

Electromyography and muscle co-activation

Wireless surface electrodes (99% silver, 4 5x1mm bar 'Trigno' sensors, fixed inter-electrode distance 10mm, Delsys, Boston, USA) were placed over the belly of the vastus medialis (VM); rectus femoris (RF); vastus lateralis (VL); semitendinous (ST); biceps femoris (BF); medial and lateral gastrocnemius (MG; LG) muscles of the test leg (6,12,29). The test leg was

defined as the most symptomatic knee based on self-report. The electrode placement was in accordance with surface electromyography for the non-invasive assessment of muscles (SENIAM) recommendations (30,31). The area was shaved, lightly abraded and cleaned with alcohol. Isolated contractions assessed electromyography (EMG) recordings. The raw signal was passed through a Trigno differential amplifier, input impedance 10,000MΩ, CMRR >80dB, gain 1,000 with a bandwidth of 20Hz-450Hz. EMG signal was recorded with a 16-bit analogue-to-digital converter (PCI-DAS6402/16, Measurement computing corporation, Massachusetts, USA), at a sampling rate of 2400Hz. All EMG and force data were collected in Qualysis Track Manager (version 2.7-2.9, Qualysis Motion Capture Systems, Sweden) and processed in Spike2 (version 2.7.10, Cambridge Electronic Design Ltd, Cambridge, UK).

Measures of activities of daily living

Participants performed a series of ADL tasks in the following order; stair ascent and stair descent, walking, and sit-to-walk transitions, during a single visit to the human performance laboratory at Glasgow Caledonian University. The number of trials performed for each activity as stated in the protocol was a pragmatic decision to enable high-quality data to be collected while safeguarding patients against high levels of fatigue.

Participants performed three stair ascent and descent trials using a four-step instrumented staircase with a force plate (Kistler, 9286BA, Switzerland) embedded in the second step, aligned with a second Kistler force plate in the walkway. Participants ascended the stairs, turned and descended, ensuring the test leg landed on both force plates (walkway and second step). A successful trial was defined as the entire foot landing within the boundaries

of the force plate with no obvious signs of targeting the plate. The use of handrails was permitted if required, step-over-step (alternate leg on each step) was preferred; however, when this was not possible step-by-step (both legs on the same step with test leg as lead leg) was permitted.

Participants performed seven successful walking trials at a self-selected walking speed. A successful trial was defined as above and within ±10% of movement time (Brower timing system, Draper, Utah, USA).

A standard armchair (height 48cm) was placed on the walkway next to the force plate. Participants sat with their back against the chair and test leg on the force plate, they were instructed to stand up, walk 3.6m before turning and returning to a seated position. The use of the chair arms was permitted if required. For the purpose of this analysis, the stance phase (onset of force to toe-off), from three sit-to-walk trials was used.

For all activities, the stance phase was analysed, defined as initial contact (ground reaction force exceeded 20N) to toe-off (ground reaction force fell below 20N). During walking the stance phase was also split into four sub-phases; loading (0-14.9% of stance), early-stance (15-39.9%), mid-stance (40-59.9%) and late-stance (60-100%) with an additional pre-stance phase (-150ms to initial contact) (17). Stair ascent and descent were each split into two sub-phases; walk-to-stair transition (stance on the floor force plate) and continuous (stance on the force plate embedded in the stairs).

Participants performed a series of maximal voluntary isometric contractions (MVIC), using an isometric dynamometer (Biodex 4 Pro, Biodex Medical Systems Inc, New York, USA). Participants were seated with their knee and hip flexed at 50deg and 90deg respectively. Following a series of warm-up contractions, participants performed 3 flexion/extension MVIC's lasting 3s with 30s rest for the hamstrings and quadriceps respectively. For the gastrocnemius participants were seated with their knee at full extension and foot in anatomically neutral. Following a series of warm-up contractions, participants performed a series of 3 plantarflexion MVIC's lasting 3s with 30s rest. Data was analysed over a 500ms window: 250ms either side of peak force for hamstrings and quadriceps and 250ms either side of peak EMG amplitude for gastrocnemius.

Symptom severity

Participants completed the knee injury and osteoarthritis survey (KOOS) (32) and self-reported the duration of their symptoms.

Data Management

EMG data was Butterworth 4th order zero-lag bandpass filtered at 20-450Hz. The average root mean squared amplitude (RMS_{amp}) was calculated for the stance phase, subsequent sub-phases defined above and normalised to MVIC RMS_{amp} (33–35). RMS_{amp} was chosen as it is suggested to be more robust and directly linked to electrical power, having more physiological significance over linear envelope (33,36). MVIC's were used for normalisation over peak dynamic amplitude because it is believed that MVIC's provide an estimate of neuromuscular control and information about muscle activation enabling individual

variation which precludes direct comparison to be taken into account (33,34,36). In individuals with KOA normalisation to MVIC has been used to understand neuromuscular control alterations (3,35,37–39) and serves to provide a physiological reference (40).

Muscle co-activation was calculated using RMS_{amp} normalised to MVIC, normalised RMS_{amp} data was used to calculate muscle co-activation using equation (1), where $lowerEMG_i$ and $higherEMG_i$ are respectively the lowest and highest RMS_{amp} at sample i, division by 100 takes the average across the normalised interval (41). Muscle co-activation strategies were explored using the following muscle groups: quadriceps ([Q] VL; RF; VM):gastrocnemius ([G] MG; LG); gastrocnemius(G):hamstrings ([H] ST; BF) hamstrings(H):quadriceps(Q); and medial ([M] VM; ST; MG):lateral ([L] VL; BF; LG) and muscle pairs: VL:VM; ST:BF; MG:LG. Muscle groups involving multiple muscles, the mean RMS for the muscles involved was used. To explore agonist:antagonist versus medial:lateral muscle co-activation the following muscle combinations where used: H:Q and VL:VM.

$$\text{Co-activation Index} = \frac{\sum_{i=1}^{100} \frac{\text{lowerEMG}_i}{\text{higherEMG}_i}\left(\text{lowerEMG}_i + \text{higherEMG}_i\right)}{100} \quad (1)$$

Statistical Analysis

Descriptive statistics including means, standard deviations, and frequencies of the demographics were determined. Skewness, kurtosis, and boxplots were obtained to examine the distribution and identify outliers for all variables. Hierarchical sensitivity analysis was performed with 1) all data; 2) extreme outliers (>3* interquartile range (IQR))

removed; 3) all outliers (>1.5*IQR) removed; 4) all outliers and device users removed ('valid data'); 5) valid data with 1.5*IQR outliers associated with low MVIC or pain during MVIC included. Device users were defined as individuals who used the stairs handrails and/or a walking-aid whilst performing the ADL tasks. Once extreme outliers were removed some variables remain insignificant whilst others became significantly different between individuals with KOA and controls (data not presented), this did not change when further outliers were removed (42). The main analysis was run with only extreme (3*IQR) outliers removed. Sensitivity analysis was performed with and without device users; there was no difference between device users and non-device users.

Repeated measures ANOVA followed up with Bonferroni *post hoc* test was performed to compare muscle co-activity within each activity. Pearson's correlations between muscle co-activation combinations within the same activity, and partial correlations controlling for muscle strength and age assessed hypothesis 1 (muscle co-activation would be high across all muscle combinations within a given activity). Correlation strength was defined as r<0.1 no association; r=0.1-0.29 weak; r=0.3-0.49 moderate; r>0.49 strong association (43). Hypothesis 2 (muscle co-activation will be higher in the medial:lateral than agonist:antagonist pairs) was assessed with paired sample T-Tests using VL:VM and H:Q combinations. The VL:VM co-activation provides a clear metric for medial:lateral co-activation to provide neuromuscular control of the knee joint, as the vastii muscles were general joint stabilisers (26). Repeated measures ANOVA (muscle co-activation-by-activity) followed up with Bonferroni *Post hoc* test addressed hypothesis 3 (muscle co-activation will be higher during more challenging activities). All statistical analysis was conducted using SPSS (version 22.0 Chicago, USA) with alpha set at 0.05.

Results

A total of 77 individuals with KOA were recruited from Rheumatology Clinics (N=15), general practitioner practices (n=4) and a local newspaper advert (N=58) (Table 1), 13 (17%) people had missing data for the stairs.

Gait

During gait, VL:VM demonstrated higher muscle co-activation than ST:BF during pre-stance, loading, early-stance, and MG:LG during loading. During mid-stance, late-stance and overall-stance MG:LG was higher than ST:BF and VL:VM. Medial:lateral co-activation was higher than Q:G, G:H during pre-stance and loading; H:Q, G:H during early-stance, mid-stance, and overall-stance; H:Q, Q:G, G:H during late-stance (waveform data in supplement A).

Within the same phase of walking, correlations between muscle co-activation combinations ranged from no-association to strong positive associations (Figure 1; Supplement B). Pre-stance ranged from r=0.264 (P=0.025, ST:BF-VL:VM) to r=0.897 (P<0.001, H:G-Q:G), loading range from r=0.070 (P=0.557, H:G-VL:VM) to r=0.682 (P<0.001, H:Q-ST:BF) of which 87% of combinations were significant, for early-stance r=0.296 (P=0.011, H:Q-MG:LG) to r=0.739 (P<0.001, H:G-H:Q), mid-stance ranged r=0.105 (P=0.374, MG:LG-VL:VM) to r=0.759 (P<0.001, Q:G-VL:VM) of which 73% of combinations were significant, late-stance ranged from r=0.073 (P=0.547, H:Q-MG:LG) to r=0.708 (P<0.001, Q:G-VL:VM) of which 87% of combinations were significant, and overall-stance ranged from r=0.159 (P=0.191, H:Q-MG:LG) to r=0.721 (P<0.001, H:Q-H:G and H:Q-ST:BF) of which 93% of combinations were

significant. The strength of the associations decreased when controlling for age and muscle strength.

Muscle co-activation was significantly higher for VL:VM than H:Q for loading (P=0.008), early-stance (P<0.001), mid-stance (P<0.001), late-stance (P<0.001) overall-stance (P<0.001), there was no difference for pre-stance (P=0.319, Figure 2).

Stair negotiation

Medial:lateral gastrocnemius co-activation was higher than VL:VM during stair ascent transition (SUT), and continuous stair descent (SDC), while MG:LG and VL:VM were similar and higher than ST:BF during continuous stair ascent (SUC) and descent transition (SDT). Medial-lateral co-activation was higher than H:Q, H:G during SUT, SUC, and SDC; Q:G during SUT and SDT. During SDC Q:G was similar to H:G; M:L, and higher than H:Q.

Within the same phase of stair negotiation, correlations across muscle co-activation ranged from no association to strong positive associations (Figure 1, supplement B). Stair ascent transition ranged from r=-0.004 (P=0.976, MG:LG-VL:VM) to r=0.850 (P<0.001, H:G-ST:BF) of which 60% of combinations were significant, SUC ranged from r=0.079 (P=0.548, Q:G-MG:LG) to r=0.784 (P<0.001, H:G-H:Q) of which 60% of combinations were significant. During SDC correlations ranged from r=-0.006 (P=0.984, H:Q-MG:LG) to r=0.816 (P<0.001 H:Q-ST:BF) with 60% of combinations significant, whilst SDT ranged from r=0.003 (P=0.984, ST;BF-MG:LG) to r=0.722 (P<0.001, H:Q-ST:BF) of which 60% of combinations were significant. The strength of the associations decreased when controlling for age and muscle strength.

Muscle co-activation was significantly higher for VL:VM than H;Q across all phases of stair negotiation (P<0.001; Figure 2).

Sit-to-walk

During sit-to-walk VL:VM demonstrated higher muscle co-activation than ST:BF and MG:LG, whilst M:L was higher than H:Q, Q:G and H:G. Sit-to-walk demonstrated a weak (r=0.251, P=0.032, H:Q-MG:LG) to strong associations (r=0.727, P<0.001, H:Q-H:G; Figure 1; Supplement B). Muscle co-activation was higher in VL:VM than H:Q (P<0.001) during sit-to-walk (Figure 2).

Muscle co-activation across activities

Muscle co-activation was significantly different within the same muscle co-activation combination across activities and phases (P<0.001) for all muscle co-activation combinations (Figure 3). Muscle co-activation was significantly (P<0.05) different across 65.5% (H:Q); 61.8% (H:G); 63.6% (Q:G); 70.9% (M:L); 74.5% (VL:VM); 47.2% (ST:BF); 72.7% (MG:LG) of activity combinations. Pre-stance was significantly different to loading; early-stance; overall-stance; sit-to-walk and stair negotiation across all muscle combinations except ST:BF. Pre-stance was significantly different to loading; mid-stance and late-stance for ST:BF. Mid-stance and late-stance were different to loading; overall-stance; sit-to-walk for all muscle combinations. Overall-stance was different to sit-to-walk (H:G) and SUC (all combinations except H:G; ST:BF); sit-to-walk was different to SUC (all combinations except ST:BF) and stair ascent and descent phases were also different to each other for all combinations except ST:BF.

Discussion

The results indicate that muscle co-activation was positively correlated across different muscle combinations within the same activity. Medio-lateral co-activation within the quadriceps was higher than anterior-posterior co-activation across all activities in KOA. Muscle co-activation was higher during more challenging activities (stair negotiation) than less challenging activities (gait).

Investigations into muscle co-activation in KOA typically focus on walking. This study aimed to explore muscle co-activation across different ADL, during which different muscle co-activation strategies were observed. Overall muscle co-activation was deployed when the limb is preparing to, and accepts weight and starts to transition towards single limb support. It appears that overall muscle co-activation is a strategy adopted when the limb is least stable, in more vulnerable positions requiring all muscles to activate simultaneously to stabilise the joint. During transitions from single-to-double limb support and when increased muscle force is required to propel the body from a flexed position into extension (mid-stance and late-stance; sit-to-walk; stair ascent) selective muscle co-activation was utilised. Specifically high muscle co-activation in MG:LG and VL:VM which are thought to act as joint stabilisers, contribute towards rotational moments or increase compressive loads to facilitate moment generation needed to direct ground reaction forces, and potentially increase medial joint stability (11,26,27,44,45). Our results demonstrated neither overall nor selective muscle co-activation was prominent, with a combination of both strategies utilised. Mills et al. (11) a systematic review of 14 papers, highlighted that during walking

specific muscle co-activation is believed to play a role in distributing loads, whilst Lloyd and Buchanan (18) found in their modelling study that specific muscle co-activation (H:Q) contributed to muscular support in response to static valgus-varus loads. These results suggest that both muscle co-activation strategies are modulated throughout different phases of walking or other activities to increase joint stability; distribute joint loads and support joint moments at the potential cost of increased compressive loads.

Within the same activity, the same patients demonstrated high or low muscle co-activity across all muscle combinations. With increasing age and the addition of joint space narrowing associated with KOA, the passive restraints (e.g. ligaments) become increasingly lax (39,44). To prevent lateral joint opening and the transfer of load medially higher antagonist muscle force is required (46). Higher antagonist muscle activation is thought to increase joint stiffness (46), however, the ability to adopt movement strategies which remain normal is lost with muscle weakness (39). Alterations in muscle co-activation strategies may therefore, try and accommodate this lack of joint stability. Individuals with selective high muscle co-activation may be at an increased risk of disease progression as a result of high joint loads combined with high joint pressures associated with high muscle co-activation.

VL:VM co-activation was higher than H:Q in individuals with KOA across all activities except pre-stance. H:Q co-activation increases joint stiffness to counteract joint instability (2). Hamstrings activation is thought to increase joint stiffness and reduce loads on the anterior cruciate ligament by reversing the shear force on the tibia counterbalancing the main knee flexion moment, at the expense of increased patellofemoral and tibiofemoral load (28).

VL:VM co-activation has been suggested to be a response to joint space narrowing, increased joint stiffness and joint surface loading (2,3,19,37,47). Flaxman et al., also identified the vastii muscles as general joint stabilisers bracing the knee (26,27). When combined with increased joint contact pressures associated with high muscle co-activation, this may increase the risk for cartilage degeneration (1–3,6,12–14,18,19,21). Hodges et al. (48) found that increased duration of medial (vastus medalis:semimembranosus) co-activation was associated with medial cartilage loss in medial KOA, whilst Zeni et al (12) found high medial co-activation controlled medial laxity and instability in medial KOA. Lateral (vastus lateralis:biceps femoris) co-activation was inversely related with medial cartilage loss in KOA (48), and is thought to unload the medial compartment (3,6,15,17). According to findings from Bae et al (49), tibiofemoral OA is either confined to the medial compartment or generalized over the medial and lateral compartments. Several studies in medial and generalised KOA are in support of selective lateral activation (3,6,15,17), however, others do not (1,44,45). These results appear to be consistent with medial and generalised KOA across the literature. Three studies investigated muscle co-activation and included medial KOA patients only, with mixed results. Rudolph et al (39) and Lewek et al (45) found higher medial activation whilst Lewek et al (37) demonstrated high lateral muscle co-activation. Including both medial and generalised KOA in this study may dilute any compartmental differences if they exist however further research is required to understand muscle co-activation differences between medial tibiofemoral and generalised disease.

Muscle co-activation across activities was significantly different. It was hypothesised that muscle co-activation would be higher during more challenging activities such as stair negotiation compared to less challenging activities such as gait. Muscle co-activation was

higher during stair negotiation than overall-stance and sit-to-walk, where overall-stance was higher than sit-to-walk. This is potentially due to a combination of greater joint instability and muscle force required to perform more challenging activities, whereby knee joint stability is required to propel the body up each step or control the lowering of the body down each step. During pre-stance the results demonstrated higher Q:G, and similar Q:H activity to Schmitt and Rudolph (1), where Q:G, G:H, and MG:LG are low whilst Q:G, M:L, VL:VM, ST:BF appear to be increasing in preparation to accept load (1,3) and slow the acceleration of the joint. During loading our results were higher compared to the literature, and higher than pre-stance except for MG:LG which is in keeping with the literature showing a peak in quadriceps activity (3,6). Additionally, high medial:lateral co-activation during loading was found which is similar to Heiden et al (17). During early-stance all combinations were lower than loading in line with Schmitt and Rudolph (1), whilst M:L remained higher than other combinations (17). During Mid- and late-stance no studies using the same equation MG:LG which increased, peaking during late-stance. Muscle co-activation was higher during sit-to-walk across all combinations compared to gait except for loading and overall-stance, stair ascent was higher than sit-to-walk and gait except for loading and overall stance. During continuous stair ascent muscle co-activation was higher than ascent transition for ST:BF and MG:LG. Muscle co-activation during stair descent was generally higher than gait and lower than continuous ascent and ascent. During more biomechanically challenging activities requiring greater muscle activation elevated co-activation is expected. This was shown in KOA patients in this study.

This study has a number of strengths and limitations. Firstly it is a relatively large convenience sample (N=77) with substantial sensitivity analysis performed prior to and

during the statistical analysis. We did not screen or grade participants for radiographic disease severity making comparisons with previous literature difficult. MVIC's were performed for the hamstrings and quadriceps however reference contractions were performed for the gastrocnemius to prevent discomfort to the patient. During stair negotiation and sit-to-walk transition participants were permitted to use the handrails, step-by-step stair negotiation style, and chair arm. Whilst this showed muscle co-activation during normal daily living, this meant movement was not standardised across the entire sample. Sensitivity analysis indicated that this did not affect the results presented here. Other studies which looked at muscle co-activation during stair negotiation did not allow the use of handrails. Muscle co-activation was higher in the study participants compared to the values reported for individuals with KOA in the literature (2,15,37,38). It is unclear why muscle co-activation values where so high compared to the literature possible explanations include: varying disease severity, participant demographics. Differences in signal processing as the studies which used the same equation and normalisation methods used linear envelope to process their data rather than RMS, whilst others used difference co-activation equations, normalisation methods, different time epochs over which the data was analysed. Alternatively, low muscle activation during MVIC as a result of not fully activating the musculature or really low muscle activation may elevate the normalised EMG.

To conclude, muscle co-activation patterns appear to be high across all muscle combinations within the same activity. Higher muscle co-activation was observed during more challenging activities which require greater stability. Whilst neither overall nor selective muscle co-activation was prominent it appears they modulate in unison to maintain joint stability and respond to the demands upon the joint. Whilst high muscle co-activation appears to be a

mechanism to maintain joint stability it may also increase the susceptibility of cartilage damage and risk of incidence and progression of KOA.

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Author contributions

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Figure legends

Figure 1 Correlations of muscle co-activation for individuals with KOA within the same activity for A) Sit-to-walk VL:VM and H:Q (r^2 =0.716**), B) Early-stance MG:LG and H:Q (r^2=0.408**), C) Loading H:Q and VL:VM (r^2=0.299*), D) Stairs continuous ascent MG:LG and HQ (r^2=-0.094) *P<0.05 ** P<0.01.

Figure 2 Muscle co-activation for vastus lateralis:medalis (Black) and hamstrings:quadriceps (Spotted) across different activities for individuals with KOA. Significant differences between medial:lateral and hamstrings:quadriceps *P<0.05; **P<0.01; †P<0.001.

Figure 3 Muscle co-activation combinations during A) phases of walking B) activities of daily living for individuals with KOA

Figure 1

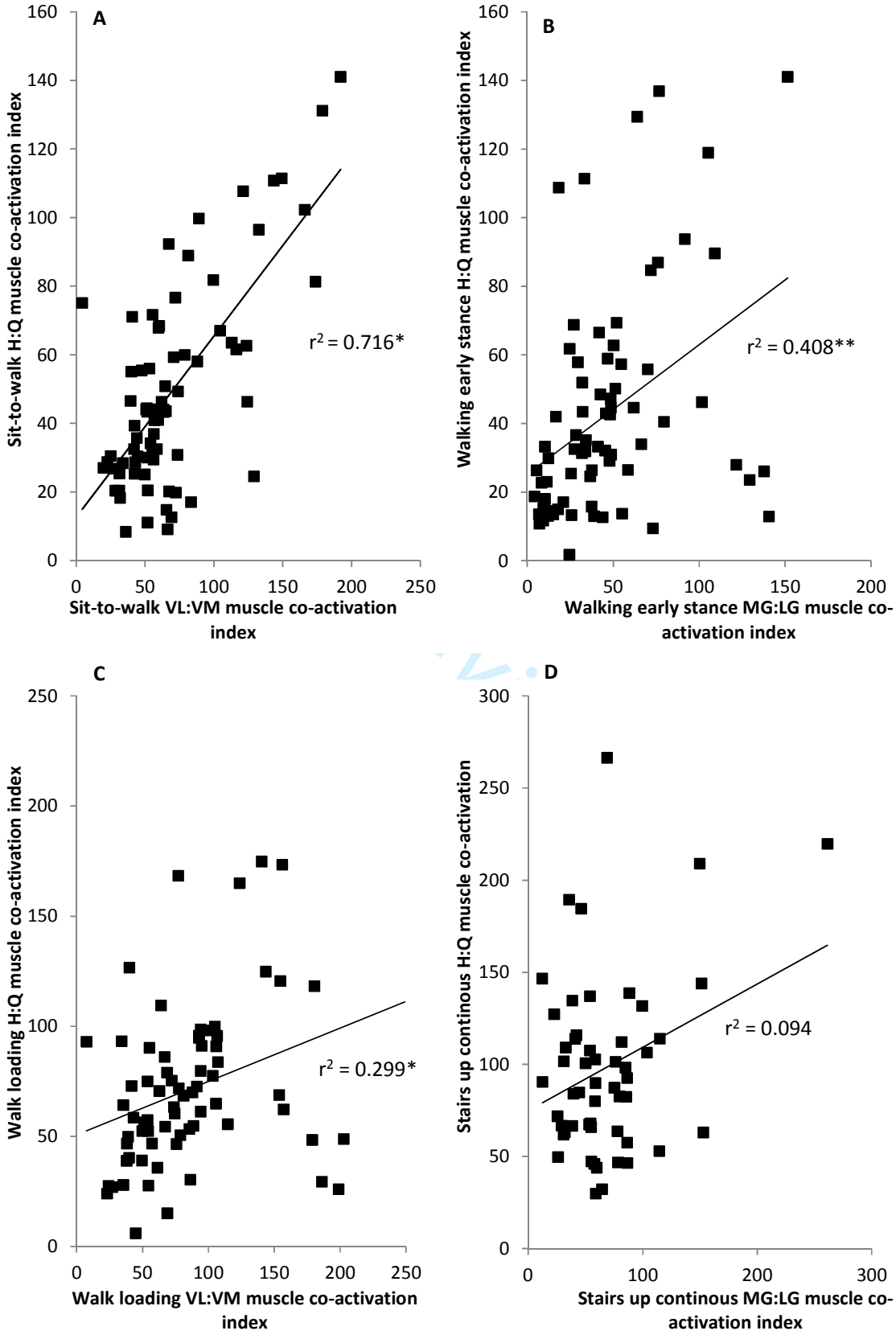

A
Sit-to-walk H:Q muscle co-activation index
Sit-to-walk VL:VM muscle co-activation index
r² = 0.716*
B
Walking early stance H:Q muscle co-activation index
Walking early stance MG:LG muscle co-activation index
r² = 0.408**
C
Walk loading H:Q muscle co-activation index
Walk loading VL:VM muscle co-activation index
r² = 0.299*
D
Stairs up continous H:Q muscle co-activation
Stairs up continous MG:LG muscle co-activation index
r² = 0.094

Figure 2

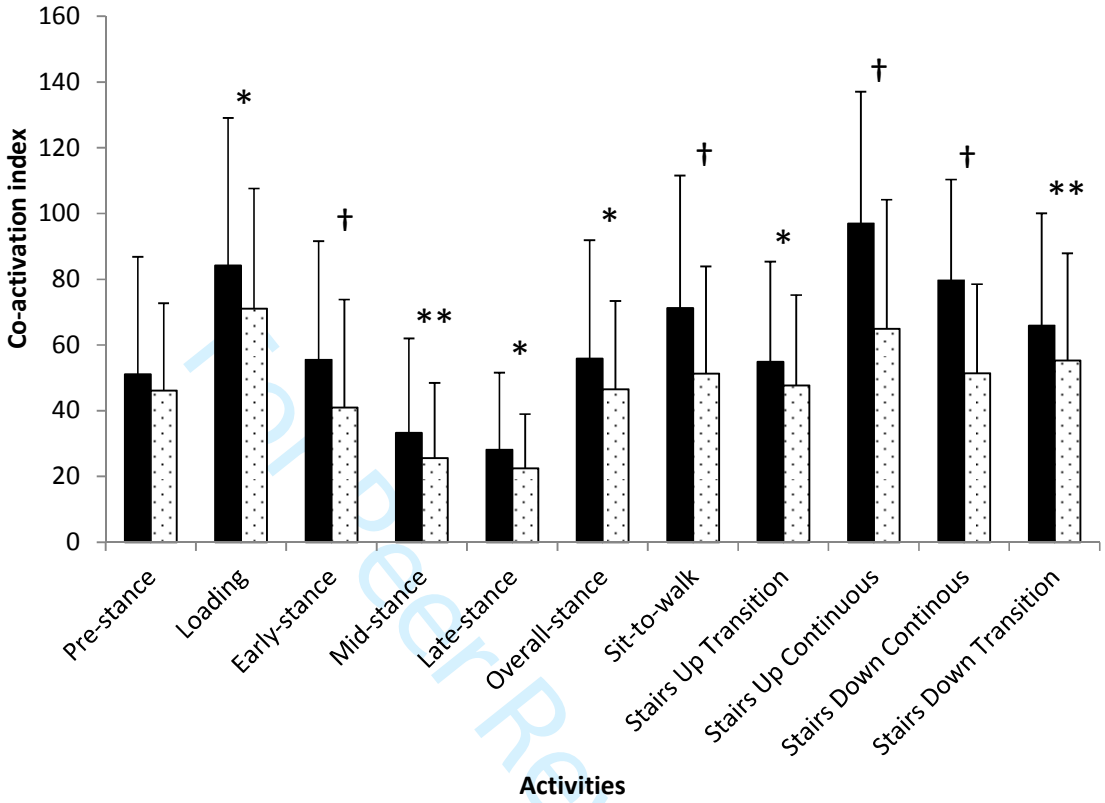
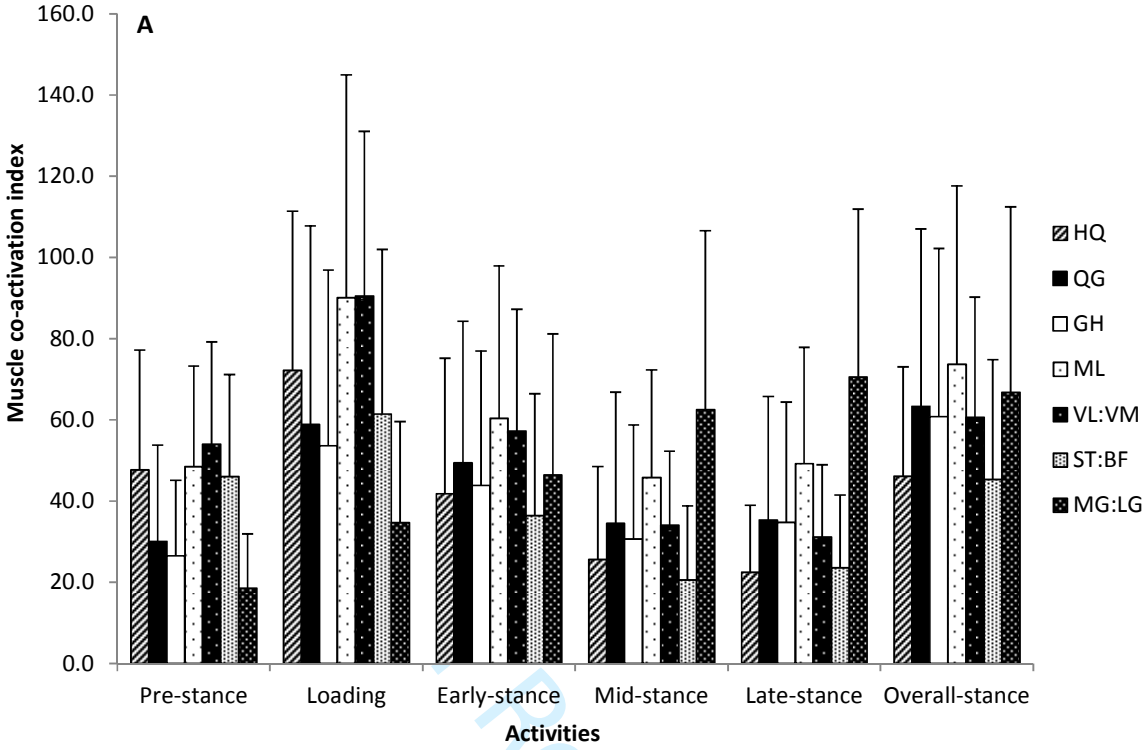
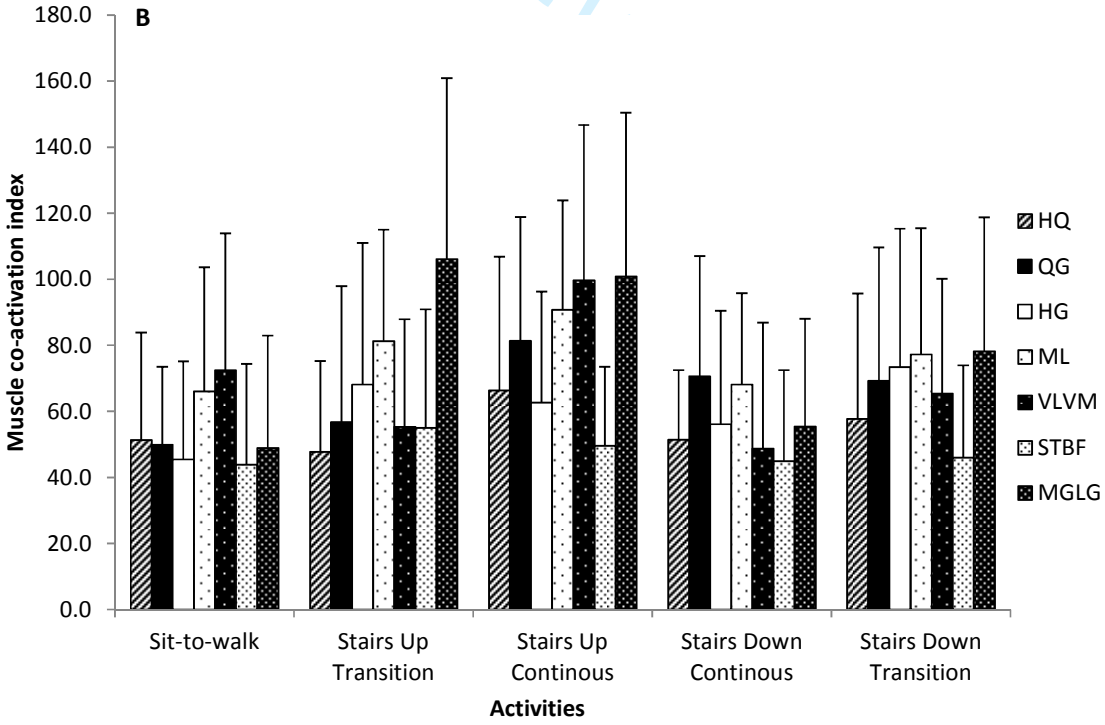


Figure 3


A
Muscle co-activation index
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
Pre-stance
Loading
Early-stance
Mid-stance
Late-stance
Overall-stance
Activities
HQ
QG
GH
ML
VL:VM
ST:BF
MG:LG


B
Muscle co-activation index
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
Sit-to-walk
Stairs Up Transition
Stairs Up Continous
Stairs Down Continous
Stairs Down Transition
Activities
HQ
QG
HG
ML
VLVM
STBF
MGLG

1 **Tables**

Table 1: Patient demographics and activities of daily living data presented as means (SD)

Characteristic	**KOA (n = 77)**
Age, years	62.5 (8.1)
Females, %	48 (62%)
Height, m	1.66 (0.11)
Body mass, kg	81.5 (19.4)
BMI, kg/m^2	29.4 (6.0)
Duration of symptoms, yrs	9.3 (9.2)
KOOS pain	56.8 (17.6)
KOOS symptoms	54.7 (19.4)
KOOS activities of daily living	65.2 (20.1)
KOOS sports and recreation	33.8 (24.9)
KOOS quality of life	39.1 (21.3)
Activities of daily living	
Walking Speed, m/s	1.05 (0.15)
Walking stick used, Yes (%)	2 (3%)
Chair arm used, Yes (%)	53 (69%)
Stairs walking styles (KOA=64 C=16)	
Ascent, SOS (%)	60 (94%)
SBS (%)	4 (6%)

Descent, SOS (%)	56 (88%)
SBS (%)	8 (12%)
Handrail used, Yes (%)	26 (41%)

KOA = knee osteoarthritis; BMI = bodymass index; SOS = step-over-step; SBS = step-by-step; KOOS = knee injury and osteoarthritis outcome survey

SUPPLEMENTARY MATERIAL

Supplement A. Waveform data for individual muscles, muscle groups, and muscle co-activation during gait

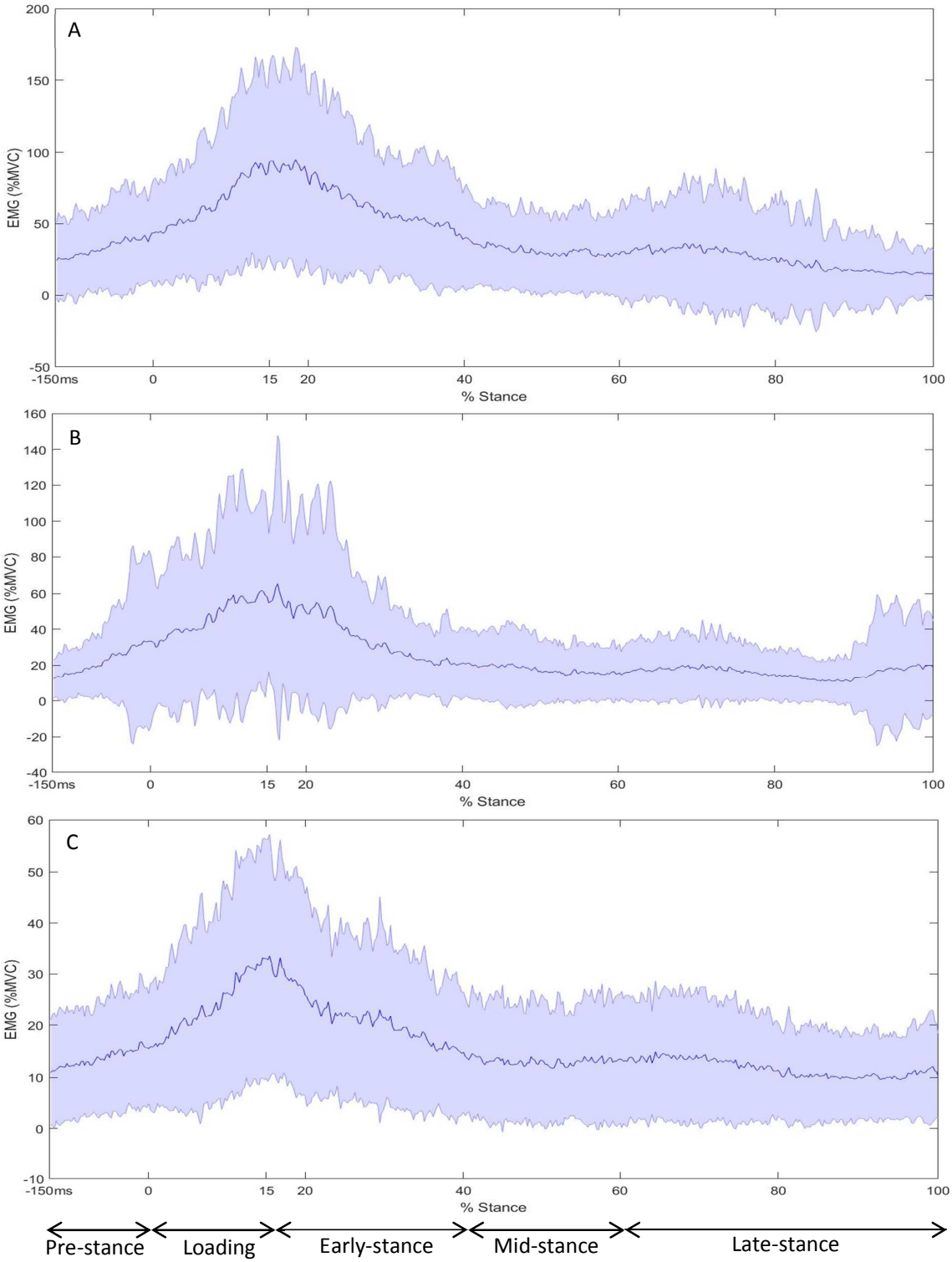


Figure S1. Mean (solid line) and standard deviation (shaded cloud) for individual quadriceps muscles A) vastus lateralis B) vastus medalis C) rectus femoris during gait

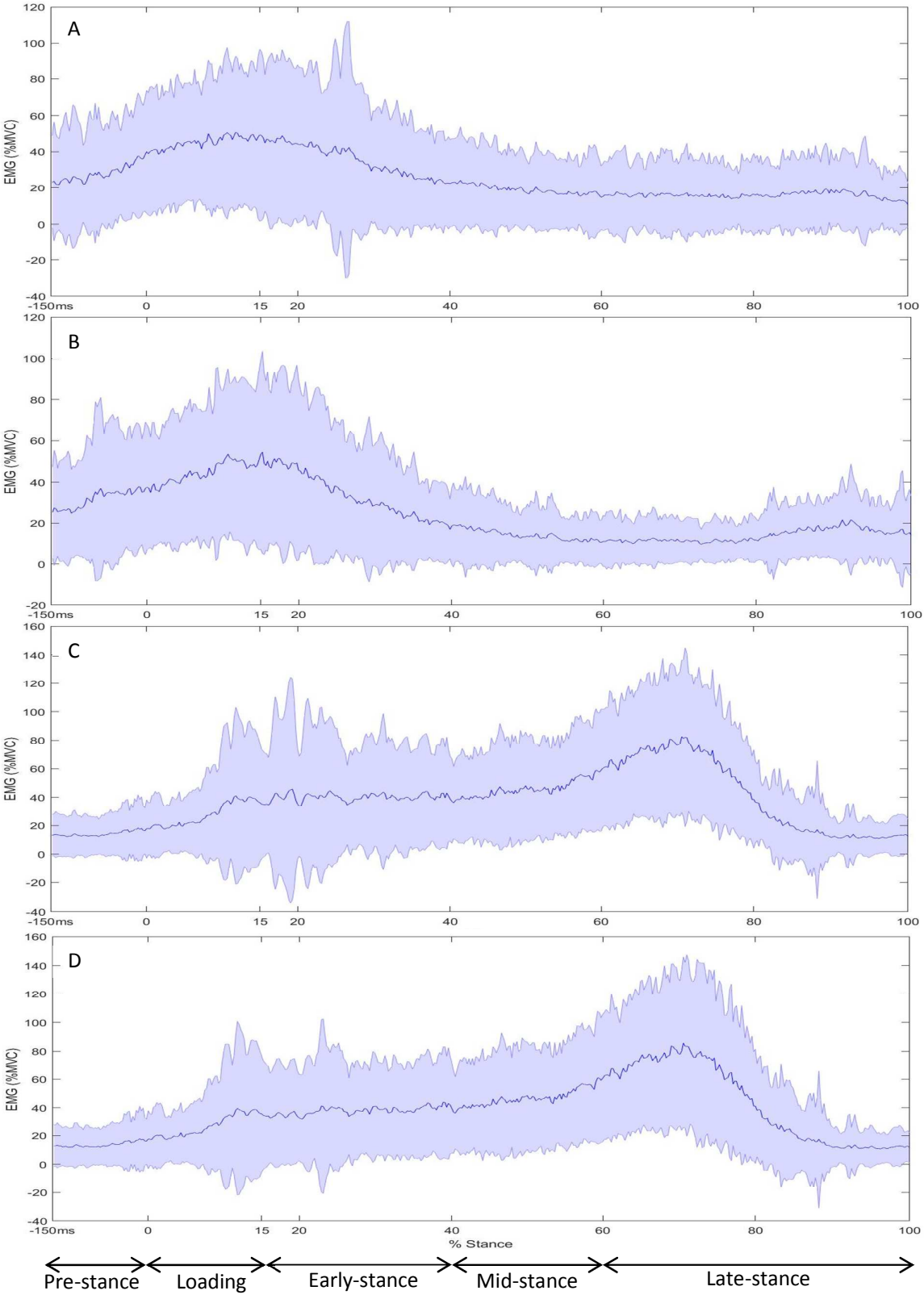


Figure S2. Mean (solid line) and standard deviation (shaded cloud) for individual hamstrings and gastrocnemius muscles A) biceps femors B) semitendinosus C) lateral gastrocnemius D) medial gastrocnemius during gait

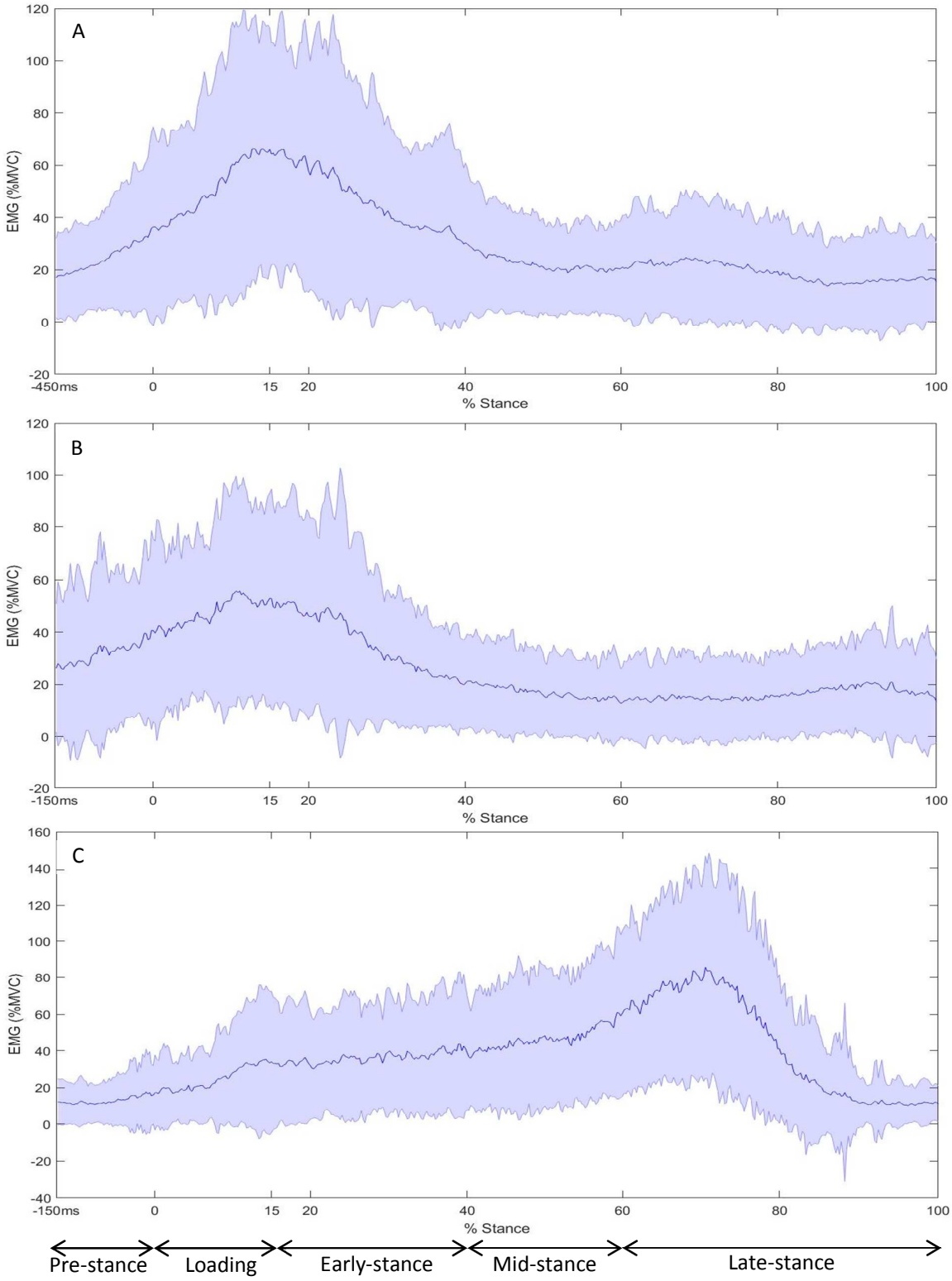


Figure S3. Mean (solid line) and standard deviation (shaded cloud) for A) quadriceps B) hamstrings C) gastrocnemius muscle groups during gait.

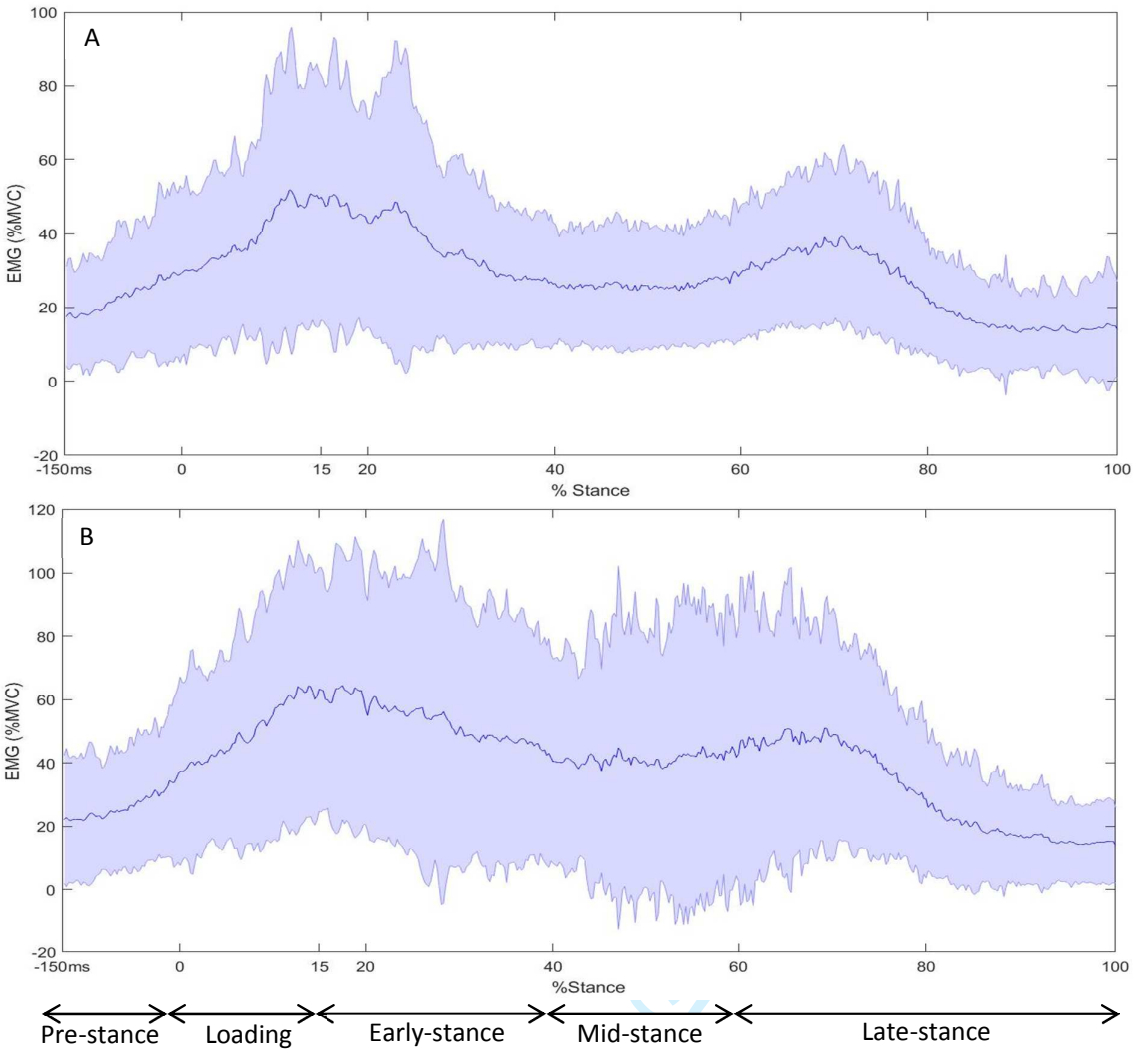


Figure S4. Mean (solid line) and standard deviation (shaded cloud) for A) medial B) lateral muscle groups during gait.

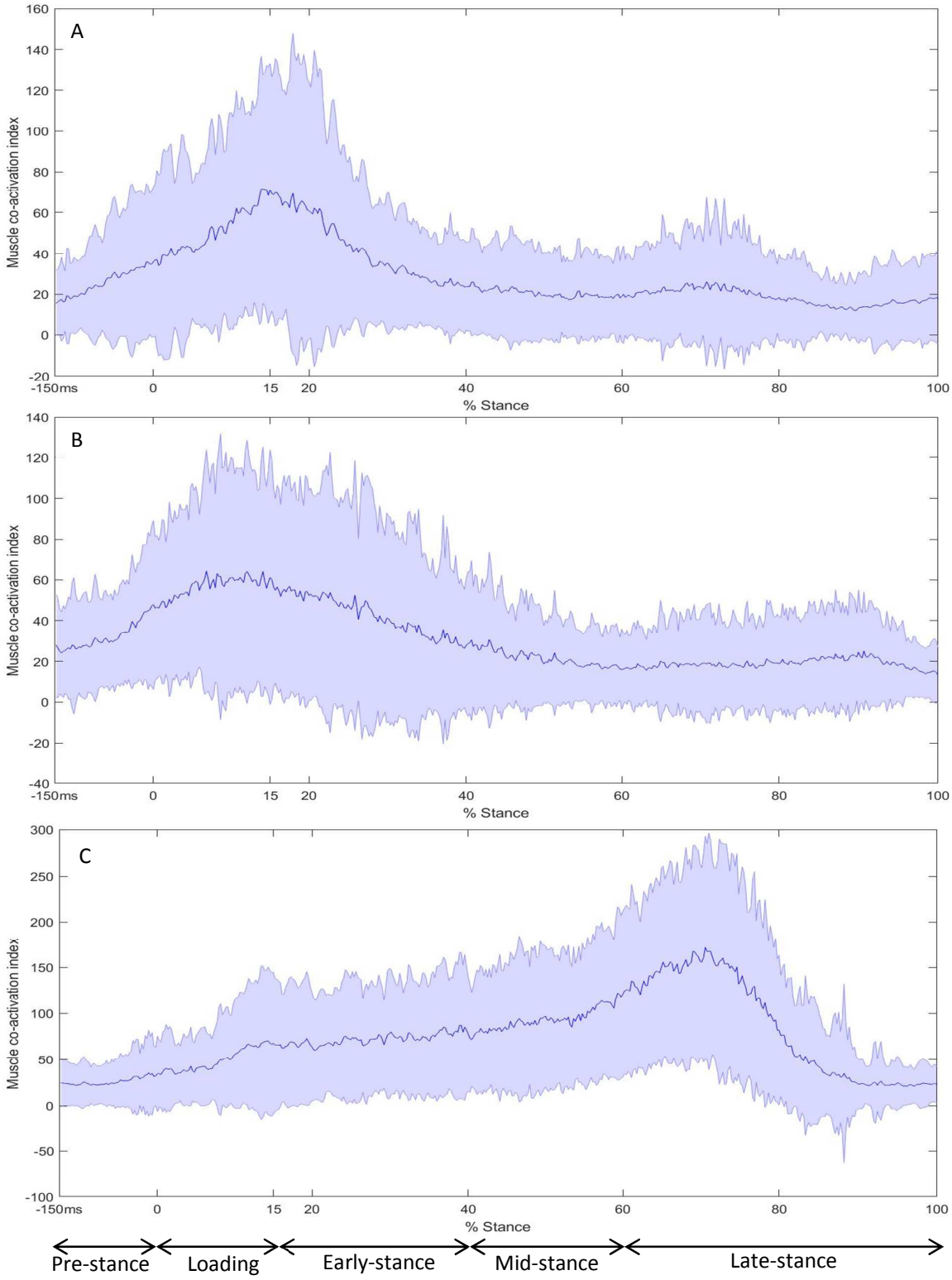


Figure S5. Mean (solid line) and standard deviation (shaded cloud) for individual muscle co-activation index combinations A) vastus lateralis:medalis B) semitendinosus:biceps femors C) medial:lateral gastrocnemius during gait.

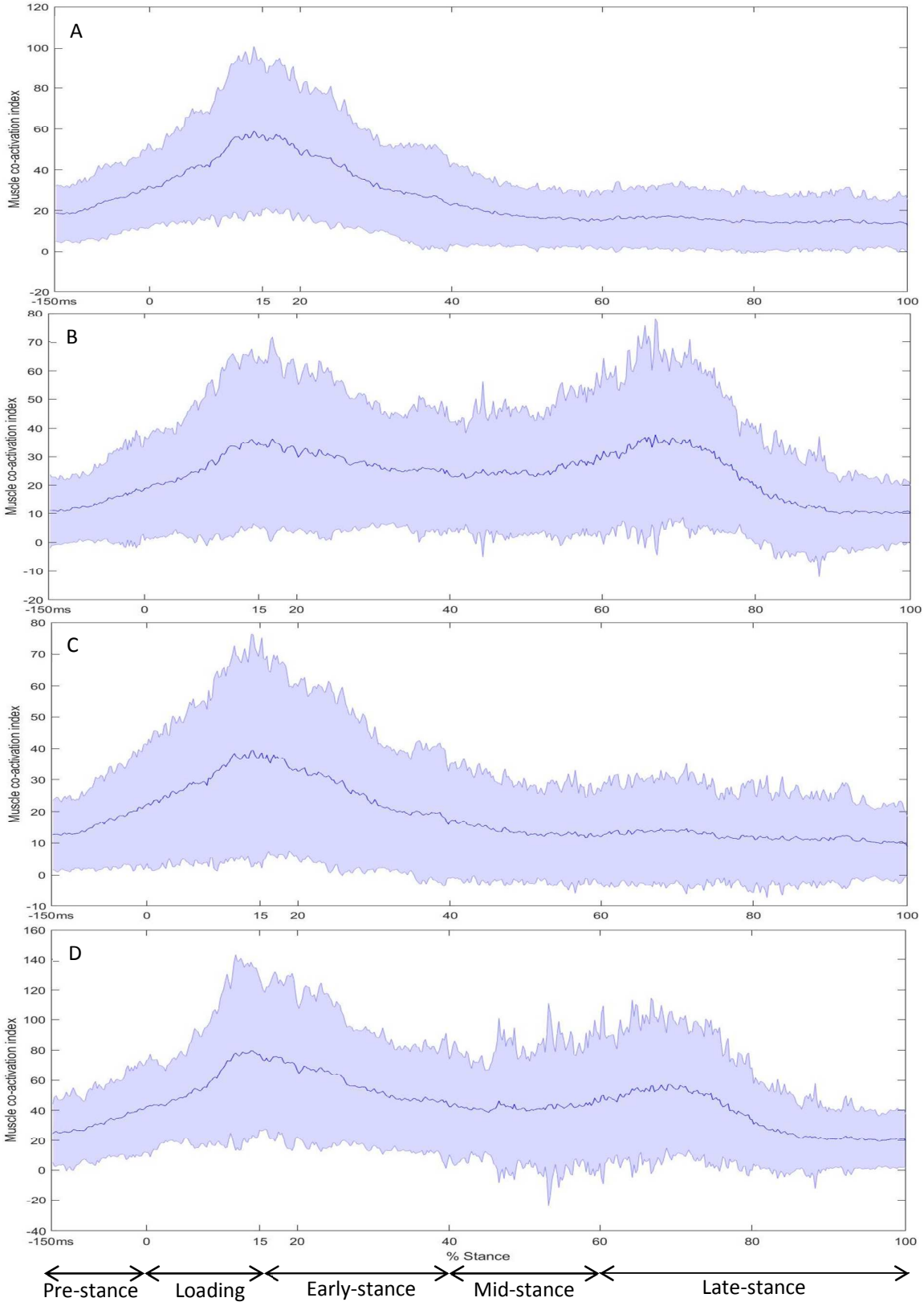


Figure S5. Mean (solid line) and standard deviation (shaded cloud) for A) hamstrings:quadriceps B) quadriceps:gastrocnemius C) gastrocnemius:hamstrings D) medial:lateral muscle group co-activation combinations during gait.

Supplement B Pearson's correlation coefficients for comparison of muscle co-activation across muscle combinations within the same activity or phase for individuals with KOA.

Table 1. Pearson's correlation coefficients for Walk Pre-stance *P<0.05; **P<0.01

	Q:G	H:G	VL:VM	ST:BF	MG:LG
H:Q	0.549**	0.555**	0.544**	0.464**	0.477**
Q:G		0.897**	0.472**	0.483**	0.635**
H:G			0.474**	0.459**	0.640**
VL:VM				0.264*	0.509**
ST:BF					0.364**

Table 2. Pearson's correlation coefficients for Walk Loading *P<0.05; **P<0.01

	Q:G	H:G	VL:VM	ST:BF	MG:LG
H:Q	0.441**	0.564**	0.299*	0.682**	0.303*
Q:G		0.750**	0.518**	0.307**	0.560**
H:G			0.070	0.415**	0.563**
VL:VM				0.226	0.335**
ST:BF					0.294*

Table 3. Pearson's correlation coefficients for Walk Early-stance *P<0.05; **P<0.01

	Q:G	H:G	VL:VM	ST:BF	MG:LG
H:Q	0.642**	0.739**	0.408**	0.550**	0.296*
Q:G		0.557**	0.594**	0.305**	0.358**
H:G			0.373**	0.651**	0.408**
VL:VM				0.423**	0.295*
ST:BF					0.364*

Table 4. Pearson's correlation coefficients for Walk Mid-stance *P<0.05; **P<0.01

	Q:G	H:G	VL:VM	ST:BF	MG:LG
H:Q	0.624**	0.740**	0.534**	0.671**	0.185
Q:G		0.456**	0.759**	0.428**	0.228
H:G			0.397**	0.743**	0.169
VL:VM				0.465**	0.105
ST:BF					0.231*

Table 5. Pearson's correlation coefficients for Walk Late-stance *P<0.05; **P<0.01

	Q:G	H:G	VL:VM	ST:BF	MG:LG
H:Q	0.552**	0.682**	0.533**	0.582**	0.073
Q:G		0.364**	0.708**	0.302**	0.378**
H:G			0.406**	0.616**	0.243*
VL:VM				0.447**	0.265*
ST:BF					0.079

Table 6. Pearson's correlation coefficients for Walk Overall-stance *P<0.05; **P<0.01

	Q:G	H:G	VL:VM	ST:BF	MG:LG
H:Q	0.676**	0.721**	0.364**	0.721**	0.159
Q:G		0.599**	0.646**	0.466**	0.369**
H:G			0.279*	0.706**	0.297*
VL:VM				0.335**	0.371**
ST:BF					0.276*

Table 7. Pearson's correlation coefficients for Sit-to-Walk *P<0.05; **P<0.01

	H:G	Q:G	VL:VM	ST:BF	MG:LG
H:Q	0.727**	0.661**	0.716**	0.649**	0.251*
H:G		0.704**	0.414**	0.721**	0.342**
Q:G			0.533**	0.607**	0.364**
VL:VM				0.435**	0.270*
ST:BF					0.355**

Table 8. Pearson's correlation coefficients for stair negotiation. UT- ascent transition; UC- ascent continuous; DC – descent continuous; DT – descent transition; *P<0.05; **P<0.01

	H:Q UC	H:Q DC	H:Q DT	H:G UT	H:G UC	H:G DC	H:G DT	Q:G UT	Q:G UC	Q:G DC	Q:G DT	VL:VM UT	VL:VM UC	VL:VM DC	VL:VM DT	ST:BF UT	ST:BF UC	ST:BF DC	ST:BF DT	MG:LG UT	MG:LG UC	MG:LG DC	MG:LG DT
H:Q UT	0.671**	0.722**	0.795**	0.615**	0.621**	0.487**	0.411**	0.708**	0.654**	0.490**	0.621**	0.564**	0.453**	0.460**	0.513**	0.581**	0.450**	0.612**	0.537**	0.031	0.084	0.115	0.087
H:Q UC		0.692**	0.788**	0.819**	0.784**	0.532**	0.550**	0.440**	0.540**	0.462**	0.411**	0.403**	0.359**	0.502**	0.308*	0.664**	0.686**	0.598**	0.564**	-0.050	-0.094	0.016	-0.021
H:Q DC			0.842**	0.721**	0.712**	0.698**	0.590**	0.496**	0.543**	0.418**	0.492**	0.427**	0.407**	0.434**	0.510**	0.547**	0.476**	0.816**	0.653**	-0.097	-0.114	-0.006	0.001
H:Q DT				0.790**	0.659**	0.613**	0.637**	0.621**	0.582**	0.609**	0.691**	0.585**	0.545**	0.574**	0.583**	0.568**	0.473**	0.732**	0.722**	-0.068	-0.103	0.008	0.019
H:G UT					0.846**	0.797**	0.807**	0.519**	0.557**	0.540**	0.496**	0.391**	0.346**	0.459**	0.376**	0.850**	0.668**	0.744**	0.722**	0.017	-0.138	0.049	0.103
H:G UC						0.692**	0.647**	0.418**	0.532**	0.365**	0.375**	0.326**	0.252*	0.351**	0.330**	0.713**	0.639**	0.709**	0.603**	-0.034	-0.116	0.015	0.042
H:G DC							0.780**	0.416**	0.547**	0.483**	0.447**	0.171	0.215	0.196	0.224	0.677**	0.549**	0.690**	0.693**	0.064	0.011	0.098	0.161
H:G DT								0.300*	0.386**	0.384**	0.414**	0.178	0.167	0.195	0.222	0.732**	0.563**	0.620**	0.710**	0.041	-0.079	0.163	0.190
Q:G UT									0.597**	0.667**	0.794**	0.719**	0.622**	0.516**	0.628**	0.341**	0.214	0.477**	0.289*	0.058	-0.034	0.115	0.140
Q:G UC										0.660*	0.594**	0.700**	0.711**	0.689**	0.610**	0.498**	0.344**	0.438**	0.495**	-0.022	0.079	0.076	0.082
Q:G DC											0.712**	0.593**	0.658**	0.640**	0.560**	0.488**	0.439**	0.500**	0.474**	0.323*	0.285*	0.234	0.333*
Q:G DT												0.573**	0.534**	0.401**	0.557**	0.415**	0.286*	0.445**	0.443**	0.115	0.061	0.044	0.085
VL:VM UT													0.795**	0.753**	0.868**	0.232	0.114	0.303*	0.326*	-0.004	0.073	0.095	0.006
VL:VM UC														0.888**	0.873**	0.053	-0.082	0.296*	0.179	0.149	0.154	0.165	0.176
VL:VM DC															0.784**	0.237	0.183	0.318*	0.200	0.157	0.193	0.190	0.191
VL:VM DT																0.234	0.105	0.394**	0.303*	0.098	0.099	0.125	0.159
ST:BF UT																	0.823**	0.733**	0.813**	0.078	0.090	0.129	0.206
ST:BF UC																		0.723**	0.723**	0.202	0.200	0.175	0.243
ST:BF DC																			0.802**	0.026	-0.041	0.067	0.125
ST:BF DT																				-0.076	0.012	-0.008	0.003
MG:LG UT																					0.864**	0.736**	0.775**
MG:LG UC																						0.705**	0.733**
MG:LG DC																							0.754**

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