How Well Do Commonly Used Co-Contraction Indices Approximate Lower Limb Joint Stiffness Trends during Gait?

Geng Li¹, Mohammad S. Shourijeh¹, Di Ao¹, Carolyn Patten², Benjamin J. Fregly^{1*}

¹ Rice Computational Neuromechanics Laboratory, Department of Mechanical Engineering, Rice University, Houston, TX, United States

² Biomechanics, Rehabilitation, and Integrative Neuroscience Lab, Department of Physical Medicine & Rehabilitation, School of Medicine, University of California, Davis, Davis, CA, United States

* Correspondence:

Benjamin J. Fregly
fregly@rice.edu

Keywords: muscle co-contraction, co-contraction index, joint stiffness, electromyography (EMG), EMG-driven modeling.

Abstract

Muscle co-contraction generates joint stiffness to improve stability and accuracy during limb movement but at the expense of higher energetic cost. The quantification of joint stiffness generated from muscle co-contraction is difficult through both experimental and computational means for its benefit and cost to be assessed. Quantification of muscle co-contraction may offer an alternative path for estimating joint stiffness. By choosing the commonly used Co-Contraction Indices (CCIs) to represent muscle co-contraction, this study investigated the feasibility of using CCI to approximate lower limb joint stiffness trends during gait. A calibrated EMG-driven musculoskeletal model of a hemiparetic individual post-stroke from a previous study was used to generate the quantities required for CCI calculation and model-based estimation of joint stiffness. A total of 14 classes of CCIs for various combinations of antagonistic muscle pairs were calculated based on two common CCI formulations, each with 7 types of quantities that included variations of electromyography (EMG) signals and joint moments from the muscles. Correlations between CCIs and model-based estimates of sagittal plane stiffness of the lower extremity joints (hip, knee, ankle) were computed. Although moderate to strong correlation was observed between some CCI formulations and the corresponding joint stiffness, these associations were highly dependent on the methodological choices made for CCI computation. The overall findings of this study were the following: (1) the formulation proposed by Rudolph et al. (2000), CCI_I , was more correlated with joint stiffness than that of Falconer and Winter (1985); (2) Moment-based CCI_I from individual antagonistic muscle pairs was more correlated than EMG-based CCI_I ; (3) EMG signals with calibrated electromechanical delay and joint moment generated by individual muscle without normalization to a reference value were the most correlated for EMG-based CCI_I and moment-based CCI_I , respectively. The combination of antagonistic muscle pairs for most correlated within each CCI class was also identified. By using CCI to approximate joint stiffness trends, this study may open an alternative path to studying joint stiffness.

1 Introduction

Muscle co-contraction refers to the simultaneous activation of muscles on opposite sides of a joint and is arguably an important mechanism used by the nervous system to regulate joint stability (Hirokawa et al., 1991; McGill et al., 2003) and provide movement accuracy (Gribble et al., 2003; Missenard et al., 2008). It is further argued that individuals who have suffered orthopedic injuries or neuromuscular disorders use elevated levels of muscle co-contraction (Lamontagne et al., 2000; Rudolph et al., 2000; Higginson et al., 2006; McGinnis et al., 2013) to generate additional joint stiffness so as to compensate for the lack of joint stability (Gollhofer et al., 1984; Kuitunen et al., 2002; Mohr et al., 2018), although evidence in support of this premise is equivocal (Banks et al., 2017). While co-contraction increases joint stiffness that may improve stability (Latash and Huang, 2015) and accuracy (Wong et al., 2009) of limb movement, it does so at the expense of increased energetic cost (Moore et al., 2014). Quantification of joint stiffness is therefore critical to the understanding of how this quantity adds both benefit and cost to dynamic joint movements such as gait. However, joint stiffness is difficult to either measure experimentally (Pfeifer et al., 2012) or calculate computationally as its determination requires appropriate interpretation of muscle recruitment strategies and muscle-tendon modeling (Sartori et al., 2015).

Quantification of muscle co-contraction may offer an alternative for estimating joint stiffness. Although muscle co-contraction and joint stiffness have been found to be related in previous studies (Kuitunen et al., 2002; McGinnis et al., 2013; Collins et al., 2014), the relationship between these two quantities remains poorly understood, as initially noted by Hortobágyi and Devita (2000). One issue is that previous studies have quantified joint stiffness primarily in the form of quasi-stiffness. Joint quasi-stiffness is described as the gradient of the torque-angle curve rather than the true characterization of joint stiffness (Rouse et al., 2013). Since joint quasi-stiffness does not change for different levels of muscle co-contraction, it is not an accurate representation of joint stiffness generated by muscle co-contraction. From another perspective, quasi-stiffness represents response in joint moment due to changes in not only joint position but also muscle activation and joint velocity (Sartori et al., 2015). To address these concerns, joint stiffness is defined in the present study as the elastic response to only changes in joint position. This definition follows the recommendation of Latash and Zatsiorsky (1993) and provides a reasonable basis for the evaluation of the relationship between muscle co-contraction and joint stiffness.

The Co-Contraction Index (CCI) is a commonly used method for quantifying muscle co-contraction. Two common variants of CCI (Falconer and Winter, 1985; Rudolph et al., 2000) allow clinical researchers to make a fast and easy assessment of muscle co-contraction using surface electromyography (EMG) data. EMG-based CCIs have been used to quantify muscle co-contraction in a number of studies (Kellis, 1998; Di Nardo et al., 2015; Banks et al., 2017). However, the more representative method to quantify muscle co-contraction is through estimating individual muscle forces (Kellis et al., 2003), which may require advanced capabilities in neuromusculoskeletal modeling and simulation. Simulation-based studies can estimate muscle forces and compute CCI with either muscle forces (Trepczynski et al., 2018) or the joint moments generated by individual muscles (Souissi et al., 2018). Since CCI is commonly used by the clinical community, it can be used to investigate the relationship between muscle co-contraction and joint stiffness during gait.

Computation of CCI involves choosing from a wide selection of methods. Previous studies have examined how differences in method affect the results of CCI (Knarr et al., 2012; Banks et al., 2017; Souissi et al., 2017). Knarr et al. (2012) calculated CCI based on a formulation by Rudolph et al. (2000) using normalized joint moments from an antagonistic pair of muscles, while Souissi et al. (2017) calculated CCI based on a formulation by using the sum of antagonist moments around each joint. Not only would these choices result in varied CCI outcomes, but they also could affect how the

relationship between co-contraction and joint stiffness is interpreted. It would, therefore, be valuable to evaluate how different methodological choices for calculating a CCI affect the CCI's ability to approximate joint stiffness trends.

This study provides a quantitative evaluation of the relationship between lower extremity muscle co-contraction indices and corresponding joint stiffness during gait for an individual post-stroke. A total of 14 different classes of CCIs were investigated and their correlation with joint stiffness calculated by a personalized neuromusculoskeletal model was assessed. The 14 different classes of CCIs were calculated applying two commonly used formulations (Falconer and Winter, 1985; Rudolph et al., 2000), and each with 7 types of quantities used to represent muscle co-contraction: 4 variations of EMG signals; 2 types of joint moment generated by individual muscles, normalized or not; and the sum of joint moment generated by antagonistic muscles. For CCIs computed from individual pairs of antagonistic muscles, all possible combinations of eligible muscles were covered (12 for the hip joint, 16 for the knee joint, and 3 for the ankle joint). Based on the correlation observed between different CCI calculation methods and joint stiffness, we provide recommendations for the CCI calculation methods that best approximate joint stiffness trends. These recommendations are tailored to fit clinical practice and different levels of capability in neuromusculoskeletal modeling and simulation.

2 Methods

2.1 Experimental data

Ten cycles of previously published walking data collected from a hemiparetic male subject post-stroke (Meyer et al., 2017) were used for this study. The subject (height 1.70 m, mass 80.5 kg, age 79 years) walked on a split-belt instrumented treadmill (Bertec Corp., Columbus, OH) at a self-selected speed of 0.5 m/s for multiple gait cycles, while motion capture (Vicon Corp., Oxford, UK), ground reaction (Bertec Corp., Columbus, OH) and EMG data (Motion Lab Systems, Baton Rouge, LA) were collected. EMG signals were collected from 16 muscles in each leg (Table 1) using a combination of surface and indwelling electrodes at a frequency of 1000 Hz (Meyer et al., 2017). For more details about the data collection and the experimental protocol, see Meyer et al. (2017).

2.2 EMG data processing and EMG-driven model calibration

Collected EMG data were high-pass filtered at 40 Hz, demeaned, rectified, and low-pass filtered at a variable cutoff frequency of 3.5/period of the gait cycle being processed (Lloyd and Besier, 2003) while using a 4th order zero phase-lag Butterworth filter (Meyer et al., 2017). Filtered EMG data were subsequently normalized to the maximum value over all trials and resampled to 101 normalized time points for each gait cycle. Normalized EMG data for each gait cycle were offset by the minimum value so that the minimum EMG value for each gait cycle was zero. These processing procedures represent the basic approach for processing EMG adopted by other studies for the quantification of muscle co-contraction (Rosa et al., 2014). The EMG signals processed under the aforementioned procedures were defined as the basic EMG signals, *EMG_{basic}*.

An EMG-driven model was used to calibrate parameters of the model, including a few for conditioning basic EMG to muscle excitation along with those for musculotendon force functions, within an optimization process to match the joint moments produced by the muscles in the model with those calculated from inverse dynamics (Meyer et al., 2017). The conditioning of the EMG signals involved adding an electromechanical delay and applying a muscle-specific EMG scale factor to *EMG_{basic}*. The electromechanical delay is defined as the duration from the instant an electrical

signal is received to the instant a force response is generated by the muscle. The electromechanical delay was assumed to be fixed for all the muscles in each leg (Meyer et al., 2017), which was determined by the optimization to be 82 ms and 93 ms for the left and right side, respectively. The muscle-specific scale factor (Table 1) was used to account for the difference between the true maximum EMG value and maximum value over all experimental trials. The EMG signals resulted from calibration for both electromechanical delay and scaling were defined as fully calibrated EMG signals, $EMG_{calibrated}$.

To isolate the underlying effect of the two EMG parameters on quantification of co-contraction, we introduced two additional types of EMG signals: 1) scaled EMG signals EMG_{scaled} , which are EMG signals normalized to the optimized maximum EMG value but without electromechanical delay; 2) delayed EMG signals $EMG_{delayed}$, which are electromechanically delayed EMG signals but not normalized to the optimized maximum value. These signals were obtained by

$$EMG_{scaled} = EMG_{basic} \times \text{scale factor}$$

$$EMG_{delayed} = \frac{EMG_{basic}}{\text{scale factor}}$$

The EMG-driven model calibration process also provided estimates of force and joint moment(s) generated by each muscle during walking. The muscle force and joint moment were passed onto CCI computation and joint stiffness estimation.

2.3 CCI computation

CCI values were computed from the two commonly used formulations. CCI_1 was based on the study by Rudolph et al. (2000):

$$CCI_1(t) = \frac{Inpt_L(t)}{Inpt_H(t)} (Inpt_L(t) + Inpt_H(t))$$

CCI_2 was based on the work by Falconer and Winter (1985):

$$CCI_2(t) = \frac{2 \times Inpt_L(t)}{(Inpt_L(t) + Inpt_H(t))}$$

For both formulations, the lower input $Inpt_L$ represents input quantity with lower absolute magnitude, and higher input $Inpt_H$ represents input quantity with higher absolute magnitude sampled at time instant t , which is each of the 101 normalized time points (0 – 100% of gait cycle at 1% increment) of a gait cycle. For EMG-based CCI, the input quantities include the aforementioned four types of EMG signals (EMG_{basic} , EMG_{scaled} , $EMG_{delayed}$, and $EMG_{calibrated}$). For moment-based CCI, the input quantities include joint moment from an antagonistic pair of muscles, actual values (M_{mus}), or values normalized to maximum values over all selected trials ($M_{mus\ norm}$) and the sum of antagonist moment around the joints M_{sum} . This study uses a notation to specify the formulation and input quantities used to compute CCI, e.g., $EMG_{delayed}$ -based CCI_1 means the CCI values are calculated using delayed EMG signals based on Rudolph et al. (2000) formulation.

CCI_1 can also be seen as the product of two terms where one term represents the ratio between antagonist muscle activities while the other represents the sum of antagonist muscle activities:

$$CCI_1(t) = AR(t)SQ(t)$$

where antagonist ratio AR represents the ratio of the antagonist quantities used for CCI computation and sum of antagonist quantities for CCI calculation SQ represents the sum of the antagonist quantities:

$$AR(t) = \frac{Inpt_L(t)}{Inpt_H(t)}$$

$$SQ(t) = Inpt_L(t) + Inpt_H(t)$$

In addition to varying the types of quantities used to compute CCI, this study also investigated how the difference in constituent muscles for an antagonistic pair could affect the relationship between CCI and joint stiffness. CCI was computed for three lower limb degrees of freedom (DOFs) in the sagittal plane: hip, knee, and ankle flexion and extension for both non-paretic side and paretic side. Lower extremity muscles were classified by their functional roles during gait (Table 1), and one muscle was selected from each of the agonist group and the antagonist group to form various combinations of antagonistic pairs. Antagonistic muscle pairs consisting of small muscles that were not major contributors to overall joint stiffness (less than 2% on average) were not included for the subsequent analyses. The majority of the EMG-based CCI in previous studies was computed using EMG signals measured from surface muscles (Rosa et al., 2014) because the alternative indwelling EMG method is invasive and not universally available. Therefore, despite the availability of indwelling EMG data of deep muscles (iliacus, psoas, tibialis posterior, extensor, and flexor digitorum longus), the analyses in this study focused on CCI computed from surface EMG signals of muscles for the findings to be more applicable in clinical settings. Antagonistic muscle pairs consisting of the aforementioned deep muscles were not included for the subsequent analyses either. After removing antagonistic pairs consisted of small or deep muscles from consideration, CCI values from 12 antagonistic muscle pairs for hip joint, 16 for knee joint, and 3 for ankle joint were analyzed.

2.4 Estimation of joint stiffness

Sagittal plane stiffness of the lower extremity joints (hip, knee, and ankle) of the subject was estimated using a model-based formulation (Shourijeh and Fregly, 2020):

$$K_j = \sum_{i=1}^n K_{mus\ i} = - \sum_{i=1}^n \left(\frac{\partial r_{ij}}{\partial \theta_j} F_i^T - r_{ij}^2 \frac{\partial F_i^T}{\partial l_i^{MT}} \right)$$

where stiffness K_j of DOF j is equal to the sum of the individual muscle stiffnesses $K_{mus\ i}$. r_{ij} represents the moment arm of the i^{th} muscle about DOF j . θ_j is the joint angle about DOF j . F_i^T and l_i^{MT} represent the tendon force and muscle-tendon length of muscle i . The model-based stiffness formulation assumes a rigid-tendon muscle model. As moment arms and muscle-tendon lengths of the musculoskeletal model (Meyer et al., 2017) were represented by surrogate models in the form of polynomials of joint kinematics, muscle stiffness around a joint could be computed analytically. Joint stiffness was estimated at the same % points of gait at which CCI was evaluated.

2.5 Statistical Analyses

The strength of association between CCI (CCI_1 or CCI_2) and joint stiffness (K_{joint}) was determined by the Pearson correlation coefficients using the *corrcoef* function in MATLAB (MathWorks, Natick, USA) between the two time series for each of the 10 gait cycles analyzed.

$$r_{1j} = \text{corrcoef}(CCI_{1j}, K_j)$$

$$r_{2j} = \text{corrcoef}(CCI_{2j}, K_j)$$

Since AR and SQ were available, the correlation between these CCI_1 components and joint stiffness was also investigated to elucidate which component was the main driver for correlation r_1 .

The Wilcoxon rank sum test implemented in MATLAB as the *Ranksum* function was used to compare the mean correlation coefficient between the two classes of data (10 correlation coefficients per class for 10 gait cycles). The analysis tested the null hypothesis that the two classes of data came from samples with continuous distributions possessing equal medians.

3 Results

A consistency across trials was observed in the estimates of joint stiffness at all three joints (Figs. 1A and 1B, 1st row). For the hip joint on each side, joint stiffness continued to increase in the early in the stance phase (0 – 15% gait cycle), maintained at the level for the remainder of the stance phase (15% – 55% gait cycle) and continued to decrease during late stance and swing phases (55% – 100% gait cycle). For the knee joint on each side, joint stiffness continued to increase early in the stance phase (0 – 20% gait cycle) and began to gradually decrease from the peak value. For the ankle joint on the non-paretic side, joint stiffness continued to rise during the stance phase (0 – 60%) before descending and on the paretic side, joint stiffness continued to increase in the early in the stance phase (0 – 20% gait cycle), maintained at the level for the remainder of the stance phase (20% – 65% gait cycle) and continued to decrease during swing phases (65% – 100% gait cycle). Examples of CCI results were also plotted to visualize the correlation between joint stiffness and CCI (Figs. 1A and 1B, 2nd row: EMG-based CCI_1 , 3rd row: moment-based CCI_1 , 4th row: EMG-based CCI_2 and 5th row: moment-based CCI_2).

Correlation r_1 between the values of CCI_1 and joint stiffness were moderate ($0.5 < r_1 < 0.7$, Moore et al., 2015) for the hip joint, strong ($r_1 > 0.7$) for the knee joint and moderate ($0.5 < r_1 < 0.7$) for the ankle joint (Fig. 2). The highest mean values of r_1 for EMG-based and moment-based CCI_1 were 0.51 and 0.70, respectively at the hip joint on the non-paretic side; 0.59 and 0.66 at the hip joint on the paretic side; 0.81 and 0.85 at the knee joint on the non-paretic side; 0.91 and 0.91 at the knee joint on the paretic side; 0.57 and 0.38 at the ankle joint on the non-paretic side; 0.76 and 0.59 at the ankle joint on the paretic side.

Correlation r_2 between the values of CCI_2 and joint stiffness were moderate ($0.5 < r_2 < 0.7$) for the hip joint, moderate ($0.5 < r_2 < 0.7$) for the knee joint, weak ($0.3 < r_2 < 0.5$) for the ankle joint on the non-paretic side and moderate ($0.5 < r_2 < 0.7$) on the paretic side (Fig. 3). The highest mean value of r_2 for EMG-based and moment-based CCI_2 were 0.69 and 0.64 respectively at the hip joint on the non-paretic side; 0.54 and 0.38 at the hip joint on the paretic side; 0.64 and 0.79 at knee joint on the non-paretic side; 0.60 and 0.79 at the knee joint on the paretic side; 0.40 and 0.42 at the ankle joint on non-paretic side; 0.59 and 0.62 at the ankle joint on the paretic side.

Differences in the mean between best-in-class correlations indicated that r_1 was higher than r_2 in most cases (Table 2). For $EMG_{delayed}$ and $EMG_{calibrated}$ cases at the hip (non-paretic side) and M_{mus} class at the ankle (both sides), best-in-class mean values of r_2 were higher than those of r_1 .

Correlation between SQ and joint stiffness was generally stronger than that between AR and joint stiffness (Fig 4), suggesting the association between CCI_1 and joint stiffness is driven more by the SQ component. Correlation between AR and joint stiffness in some cases was in the range from negative to low positive, yet the correlation between CCI_1 and joint stiffness was at the moderate-to-strong level because of the high correlation between SQ and joint stiffness.

4 Discussion

This study evaluated how well different CCI formulations approximate lower extremity joint stiffness trends during gait. Although moderate to strong correlation was observed between some CCI formulations and corresponding joint stiffness, this correlation was highly dependent on the methodological choices made for CCI computation. The following observations summarize the conditions under which high CCI correlations with joint stiffness were obtained: (1) CCI_1 formulation (Rudolph et al., 2000) was more correlated than CCI_2 formulation (Falconer and Winter, 1985); (2) Moment-based CCI_1 from individual antagonistic muscle pairs was more correlated than EMG-based CCI_1 ; (3) M_{mus} and $EMG_{delayed}$ were the most correlated for moment-based CCI_1 and EMG-based CCI_1 , respectively. These findings could be used as preliminary foundation for predicting joint stiffness from EMG-based measurement of muscle co-contraction.

Correlation between CCI_1 and joint stiffness was higher than for CCI_2 for most cases (Table 2), whether CCI was EMG-based or moment-based. Joint stiffness K_{joint} is a sum of the stiffness generated by all the individual muscles K_{mus} . The SQ term in the CCI_1 formulation was more effective at characterizing this summation than any term in the CCI_2 formulation. This effectiveness became more pronounced when the quantities used for CCI computation from each muscle were accurate proxies for the corresponding K_{mus} . On the other hand, the CCI_2 formulation was more suitable for quantifying the ratio of quantities from two antagonist muscles. This observation is demonstrated by the high correlation between results from CCI_2 and those from the AR term in CCI_1 . Close examination also showed that CCI_2 values reached a peak in magnitude in the swing phase (~60 to 100% gait cycle) comparable to that during the stance phase (0% to ~60% gait cycle) at several joints (Fig. 1A and 1B). This phenomenon was deemed unlikely to be physiological. This exposes the limitation of the CCI_2 formulation that when the two quantities from antagonist muscles become close in magnitude, CCI_2 would report a high level of co-contraction regardless of how small both quantities might be, as CCI_2 focuses on quantifying the ratio between the two quantities. Since the CCI_1 formulation was a better choice than CCI_2 for approximating joint stiffness trends, the subsequent discussion will focus on the methodological choices involved in calculating CCI_1 .

For each joint, the best correlation between M_{mus} -based CCI_1 results and joint stiffness was generally higher than the best correlation between any EMG-based CCI_1 results and joint stiffness. The higher correlation between M_{mus} -based CCI_1 and joint stiffness was because the joint moments produced by individual muscles could serve as a more accurate proxy for K_{mus} than could EMG signals. Additional analyses revealed that $\frac{\partial F}{\partial l} r^2$ was the dominant term in K_{mus} (responsible for > 95% of K_{mus} magnitude) for the vast majority of the muscles included in the model. The $\frac{\partial F}{\partial l}$ term can be further expressed as the product of muscle force F_{mus} and a complex function consisting of geometric and dynamic muscle parameters. M_{mus} is the product of moment arm r and muscle force F_{mus} , both being present in the

283 $\frac{\partial F}{\partial l} r^2$ term. In contrast, EMG amplitude partially reflects F_{mus} . However, it is well known that the
 284 relationship between EMG amplitude and F_{mus} is not linear, especially when large force is generated
 285 (Buchanan et al., 2004). As a result, the joint moment generated by a muscle carries more
 286 information about joint stiffness generation than does the EMG signal of the muscle. Previous studies
 287 concluded that moment-based CCI offered a more complete description of muscle activity and joint
 288 loads than does EMG-based CCI (Knarr et al., 2012; Souissi et al., 2017). This study built upon this
 289 conclusion and found that moment-based CCI_I also provided better ability at approximating joint
 290 stiffness trends than the EMG-based CCI_I .

291 Among the moment-based CCI_I methods, the ones based on M_{mus} were most likely to achieve the
 292 highest correlation with joint stiffness as compared to the ones based on either M_{sum} or M_{mus_norm} . The
 293 majority of the muscles analyzed articulate more than one DOF. Some muscles articulate DOFs that
 294 were not analyzed in this study, e.g. hip adduction-abduction and ankle inversion-eversion. Some
 295 muscles even switch their roles during dynamic tasks. For instance, although psoas is primarily a hip
 296 flexor, it has a minor ab/adduction role in our musculoskeletal model and switches between being a
 297 hip adductor and a hip abductor during gait. By summing the moments, we could not separate the
 298 collective muscle activities and allocate the precise proportion of muscle activities of each joint to
 299 account for stiffness generation. Therefore, the M_{sum} -based CCI_I correlated poorly with joint stiffness
 300 for joints with multiple DOFs (i.e., the hip and ankle) but correlated well with joint stiffness for joints
 301 with only a single DOF (i.e., the knee joint). A previous comparison study by Knarr et al. (2012) on
 302 CCI methods used the M_{mus_norm} value to compute a CCI. In our study, for most antagonistic pairs
 303 analyzed, the M_{mus_norm} -based CCI_I had a lower correlation with joint stiffness than did the M_{mus} -
 304 based CCI_I because of a lower correlation between the SQ term and joint stiffness for M_{mus_norm} -based
 305 CCI_I than M_{mus} -based CCI_I . As Souissi et al. (2017) argued, the use of a normalized moment did not
 306 allow distinguishing between the force-producing capacity of the agonist and antagonist muscle.
 307 Therefore, the relative contribution of each quantity to the SQ term was distorted by the
 308 normalization. In contrast, computation of the M_{mus} -based CCI_I could potentially include two
 309 antagonistic muscles that the sum of the joint moment generated by these muscles would correlate
 310 well with joint stiffness. In other words, the SQ term in CCI_I , which is equal to the sum of the M_{mus}
 311 quantities, would help CCI_I to also correlate well with joint stiffness. However, to obtain reliable
 312 M_{mus} data, one must use a calibrated musculoskeletal model. Consequently, the moment-based CCI is
 313 less frequently adopted by the clinical community than the more accessible alternatives, e.g. the
 314 EMG-based CCI.

315 For a clinical setting, the simplest and easiest approach is to use a CCI that requires only EMG data.
 316 However, EMG processing methods affect the correlation between EMG-based CCIs and joint
 317 stiffness. From the EMG_{basic} signals, two modifications were applied to obtain the other types of
 318 processed EMG signals. One modification was adding electromechanical delay from EMG_{basic} to
 319 $EMG_{delayed}$. The delays were set to 82 and 93 ms for the non-paretic side and paretic side respectively,
 320 based on the optimal values found via the EMG-driven model. This modification increased the
 321 correlation between CCI_I and K_{joint} . As previously discussed, EMG signals are able to convey partial
 322 information about joint stiffness because of the relationship between EMG amplitude and F_{mus} .
 323 Introducing electro-mechanical delay improves the synchronization between an EMG signal the
 324 resulting muscle force. Consequently, the correlation between the EMG signal and K_{mus} increases,
 325 resulting in an increased correlation between the $EMG_{delayed}$ -based CCI_I and K_{joint} . The second
 326 modification was applying a muscle-specific scale factor (Table 2), i.e. from EMG_{basic} to EMG_{scaled}
 327 and from $EMG_{delayed}$ to $EMG_{calibrated}$. This modification did not produce a clear improvement in the
 328 correlation between resultant CCI_I and K_{joint} . Applying the scale factor did not change the ability of

the EMG signals to represent K_{mus} , and the correlation between scaled EMG signal and K_{mus} remained the same as before scaling. However, the muscle-specific scale factor did change the relative contribution of muscle EMG amplitudes to the SQ term in the CCI_1 formulation. In some cases, a change in SQ caused a decrease in the correlation between resultant CCI_1 and K_{joint} . Although applying muscle-specific scale factors changed muscle force estimates during the calibration of the EMG-driven musculoskeletal model, these scale factors did not consistently increase the correlation between CCI_1 and K_{joint} . Excluding the uncertain effect of scaling and including the improvement from adding electromechanical delay, $EMG_{delayed}$ -based CCI_1 appeared to be the most suitable choice for the purpose of approximating joint stiffness trends.

This study presented CCI data from muscles from which EMG data could be obtained by surface measurement. Although indwelling EMG data for some muscles were also collected from the subject studied, these muscles were excluded from the CCI analysis, since EMG data would not be available from them in a clinical setting. Contrary to the general trends noted above, some discrepancies existed: 1) at the hip, the correlation between CCI_2 and K_{joint} was better than that between CCI_1 and K_{joint} ; 2) at the ankle, the correlation between M_{mus} -based CCI_1 and K_{joint} was lower than between EMG-based CCI_1 and K_{joint} . However, when CCI was recalculated by including muscles with available indwelling EMG data, these discrepancies mostly disappeared. Among the muscles omitted were iliocacus and psoas, two primary hip flexors. If included on the non-paretic side, the iliocacus – bflh pair would become the new leader for correlation between CCI_1 and K_{joint} for the EMG_{basic} , EMG_{scaled} , and $EMG_{delayed}$ cases and the psoas – bflh pair for the $EMG_{calibrated}$ case. All held a higher correlation with K_{joint} than did their CCI_2 counterparts. Also among the omitted muscles were edl and tibpost, one primary dorsi-flexor, and one primary plantar-flexor muscle. The mean correlation between M_{mus} -based CCI_1 and K_{joint} for the edl – tibpost pair on the non-paretic side was found to be 0.89, higher than that between any EMG-based CCI_1 and K_{joint} (highest mean = 0.57). Even though indwelling EMG measurements are invasive, the measurement technique seems to provide valuable information on muscle co-contraction and joint stiffness.

One limitation of this study was that the joint stiffness used for comparison with different CCI methods was obtained from a neuromusculoskeletal model instead of experimentally usually a joint perturbation technique. A model-based approach was used since the perturbation approach is difficult to implement experimentally, especially for dynamic tasks such as gait (Pfeifer et al., 2012). The model-based approach has been reported to generate joint stiffness estimates that compare well with experimental joint stiffness measurements for isometric conditions (Pfeifer et al., 2012; Sartori et al., 2015). A published model for estimating joint stiffness (Shourijeh and Fregly, 2020) was used in the present study, and the model parameters were calibrated using a validated EMG-driven modeling process (Meyer et al., 2017). Thus, the model closely reproduced the subject's experimental joint moments when the subject's experimental EMG and kinematic data were used as input, suggested that the estimated muscle forces and thus joint stiffness values are likely to be at least reasonable.

Another limitation of this study was that it analyzed gait data collected from only a single hemiparetic subject. Although the collection of sixteen channels (including 6 indwelling) of EMG from each leg of the subject during walking was time-consuming and not a common practice, it facilitated the calibration of our musculoskeletal model. Despite analyzing one subject limits our ability to draw more general conclusions that could be applied to the stroke population, at the same time, this dataset provided a unique opportunity to build a musculoskeletal model of the subject and calibrate the model parameters using an EMG-driven framework that did not require prediction of any missing EMG signals (Sartori et al., 2014). Another benefit of the data set was that the

indwelling EMG data allowed us to demonstrate that the use of these data improved CCI correlation with joint stiffness at the hip and ankle.

In conclusion, this study demonstrated the feasibility of using various CCIs to approximate lower limb joint stiffness trends during gait. Numerous methodological choices for CCI computation were examined. Key methodological choices to achieve the highest possible correlation between CCI and joint stiffness should include the use of CCI_1 formulation and the use of M_{mus} or $EMG_{delayed}$ as the quantities for computing moment-based or EMG-based CCI_1 . Antagonistic muscle pairings that yielded the highest correlations between CCI and joint stiffness were also identified. These recommendations on the methodological choices were provided for researchers with different levels of neuromusculoskeletal modeling capability. By using CCI to approximate joint stiffness trends, this study may open an alternative approach to estimate joint stiffness, which is difficult to obtain through either computational modeling or experimental measurement.

5 Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

6 Author Contributions

Conceptualization: GL DA MSS BJF
Funding acquisition: BJF
Data collection: BJF CP
Investigation: GL DA MSS BJF
Methodology: GL DA MSS BJF
Formal analysis: GL DA MSS BJF
Supervision: MSS BJF
Drafting the Manuscript: GL MSS BJF
Revising the Manuscript: GL DA MSS CP BJF

7 Acknowledgments

This work was conducted with support from the Cancer Prevention and Research Institute of Texas (CPRIT) funding RR170026. The authors would like to thank Marleny Arones for her assistance with analyzing the data.

8 Reference

- Banks, C. L., Huang, H. J., Little, V. L., and Patten, C. (2017). Electromyography Exposes Heterogeneity in Muscle Co-Contraction following Stroke. *Front. Neurol.* 8, 699. doi:10.3389/fneur.2017.00699.
- Buchanan, T. S., Lloyd, D. G., Manal, K., and Besier, T. F. (2004). Neuromusculoskeletal modeling: estimation of muscle forces and joint moments and movements from measurements of neural command. *J. Appl. Biomech.* 20, 367–395. doi:10.1123/jab.20.4.367.
- Collins, A. T., Richardson, R. T., and Higginson, J. S. (2014). Interlimb symmetry of dynamic knee joint stiffness and co-contraction is maintained in early stage knee osteoarthritis. *J.*

- 413 *Electromyogr. Kinesiol.* doi:10.1016/j.jelekin.2014.03.010.
- 414 Di Nardo, F., Mengarelli, A., Maranesi, E., Burattini, L., and Fioretti, S. (2015). Assessment of the
415 ankle muscle co-contraction during normal gait: A surface electromyography study. *J.*
416 *Electromyogr. Kinesiol.* doi:10.1016/j.jelekin.2014.10.016.
- 417 Falconer, K., and Winter, D. A. (1985). Quantitative assessment of co-contraction at the ankle joint
418 in walking. *Electromyogr. Clin. Neurophysiol.* 25, 135–149.
- 419 Gollhofer, A., Schmidtbleicher, D., and Dietz, V. (1984). Regulation of muscle stiffness in human
420 locomotion. *Int. J. Sports Med.* 5, 19–22. doi:10.1055/s-2008-1025874.
- 421 Gribble, P. L., Mullin, L. I., Cothros, N., and Mattar, A. (2003). Role of Cocontraction in Arm
422 Movement Accuracy. *J. Neurophysiol.* 89, 2396–2405. doi:10.1152/jn.01020.2002.
- 423 Higginson, J. S., Zajac, F. E., Neptune, R. R., Kautz, S. A., and Delp, S. L. (2006). Muscle
424 contributions to support during gait in an individual with post-stroke hemiparesis. *J. Biomech.*
425 doi:10.1016/j.jbiomech.2005.05.032.
- 426 Hirokawa, S., Solomonow, M., Luo, Z., Lu, Y., and D'Ambrosia, R. (1991). Muscular co-contraction
427 and control of knee stability. *J. Electromyogr. Kinesiol.* doi:10.1016/1050-6411(91)90035-4.
- 428 Hortobágyi, T., and Devita, P. (2000). Muscle pre- and coactivity during downward stepping are
429 associated with leg stiffness in aging. *J. Electromyogr. Kinesiol.* doi:10.1016/S1050-
430 6411(99)00026-7.
- 431 Kellis, E. (1998). Quantification of Quadriceps and Hamstring Antagonist Activity. *Sport. Med.* 25,
432 37–62. doi:10.2165/00007256-199825010-00004.
- 433 Kellis, E., Arabatzi, F., and Papadopoulos, C. (2003). Muscle co-activation around the knee in drop
434 jumping using the co-contraction index. *J. Electromyogr. Kinesiol.* doi:10.1016/S1050-
435 6411(03)00020-8.
- 436 Knarr, B. A., Zeni, J. A., and Higginson, J. S. (2012). Comparison of electromyography and joint
437 moment as indicators of co-contraction. *J. Electromyogr. Kinesiol.*
438 doi:10.1016/j.jelekin.2012.02.001.
- 439 Kuitunen, S., Komi, P. V., Kyrolainen, H., and others (2002). Knee and ankle joint stiffness in sprint
440 running. *Med. Sci. Sports Exerc.* 34, 166–173.
- 441 Lamontagne, A., Richards, C. L., and Malouin, F. (2000). Coactivation during gait as an adaptive
442 behavior after stroke. in *Journal of Electromyography and Kinesiology* doi:10.1016/S1050-
443 6411(00)00028-6.
- 444 Latash, M. L., and Huang, X. (2015). Neural control of movement stability: Lessons from studies of
445 neurological patients. *Neuroscience* 301, 39–48. doi:10.1016/j.neuroscience.2015.05.075.
- 446 Latash, M. L., and Zatsiorsky, V. M. (1993). Joint stiffness: Myth or reality? *Hum. Mov. Sci.*
447 doi:10.1016/0167-9457(93)90010-M.
- 448 Lloyd, D. G., and Besier, T. F. (2003). An EMG-driven musculoskeletal model to estimate muscle
449 forces and knee joint moments in vivo. *J. Biomech.* doi:10.1016/S0021-9290(03)00010-1.

- 450 McGill, S. M., Grenier, S., Kavcic, N., and Cholewicki, J. (2003). Coordination of muscle activity to
451 assure stability of the lumbar spine. *J. Electromyogr. Kinesiol.* doi:10.1016/S1050-
452 6411(03)00043-9.
- 453 McGinnis, K., Snyder-Mackler, L., Flowers, P., and Zeni, J. (2013). Dynamic joint stiffness and co-
454 contraction in subjects after total knee arthroplasty. *Clin. Biomech.*
455 doi:10.1016/j.clinbiomech.2012.11.008.
- 456 Meyer, A. J., Patten, C., and Fregly, B. J. (2017). Lower extremity EMG-driven modeling of walking
457 with automated adjustment of musculoskeletal geometry. *PLoS One* 12, 1–24.
458 doi:10.1371/journal.pone.0179698.
- 459 Missenard, O., Mottet, D., and Perrey, S. (2008). The role of cocontraction in the impairment of
460 movement accuracy with fatigue. *Exp. brain Res.* 185, 151–156.
- 461 Mohr, M., Lorenzen, K., Palacios-Derflinger, L., Emery, C., and Nigg, B. M. (2018). Reliability of
462 the knee muscle co-contraction index during gait in young adults with and without knee injury
463 history. *J. Electromyogr. Kinesiol.* doi:10.1016/j.jelekin.2017.10.014.
- 464 Moore, D. S., Notz, W. I., and Fligner, M. A. (2015). *The basic practice of statistics*. Macmillan
465 Higher Education.
- 466 Moore, I. S., Jones, A. M., and Dixon, S. J. (2014). Relationship between metabolic cost and
467 muscular coactivation across running speeds. *J. Sci. Med. Sport* 17, 671–676.
468 doi:https://doi.org/10.1016/j.jsams.2013.09.014.
- 469 Pfeifer, S., Vallery, H., Hardegger, M., Riener, R., and Perreault, E. J. (2012). Model-Based
470 Estimation of Knee Stiffness. *IEEE Trans. Biomed. Eng.* 59, 2604–2612.
471 doi:10.1109/TBME.2012.2207895.
- 472 Rosa, M. C. N., Marques, A., Demain, S., Metcalf, C. D., and Rodrigues, J. (2014). Methodologies to
473 assess muscle co-contraction during gait in people with neurological impairment - A systematic
474 literature review. *J. Electromyogr. Kinesiol.* doi:10.1016/j.jelekin.2013.11.003.
- 475 Rouse, E. J., Gregg, R. D., Hargrove, L. J., and Sensinger, J. W. (2013). The difference between
476 stiffness and quasi-stiffness in the context of biomechanical modeling. *IEEE Trans. Biomed.*
477 *Eng.* 60, 562–568. doi:10.1109/TBME.2012.2230261.
- 478 Rudolph, K. S., Axe, M. J., and Snyder-Mackler, L. (2000). Dynamic stability after ACL injury: who
479 can hop? *Knee Surgery, Sport. Traumatol. Arthrosc.* 8, 262–269. doi:10.1007/s001670000130.
- 480 Sartori, M., Farina, D., and Lloyd, D. G. (2014). Hybrid neuromusculoskeletal modeling to best track
481 joint moments using a balance between muscle excitations derived from electromyograms and
482 optimization. *J. Biomech.* doi:10.1016/j.jbiomech.2014.10.009.
- 483 Sartori, M., Maculan, M., Pizzolato, C., Reggiani, M., and Farina, D. (2015). Modeling and
484 simulating the neuromuscular mechanisms regulating ankle and knee joint stiffness during
485 human locomotion. *J. Neurophysiol.* 114, 2509–2527. doi:10.1152/jn.00989.2014.
- 486 Shourijeh, M. S., and Fregly, B. J. (2020). Muscle Synergies Modify Optimization Estimates of Joint
487 Stiffness During Walking. *J. Biomech. Eng.* 142, 011011. doi:https://doi.org/10.1115/1.4044310.
- 488 Souissi, H., Zory, R., Bredin, J., and Gerus, P. (2017). Comparison of methodologies to assess

- 489 muscle co-contraction during gait. *J. Biomech.* doi:10.1016/j.jbiomech.2017.03.029.
- 490 Souissi, H., Zory, R., Bredin, J., Roche, N., and Gerus, P. (2018). Co-contraction around the knee
491 and the ankle joints during post-stroke gait. *Eur. J. Phys. Rehabil. Med.* 54, 380–387.
492 doi:10.23736/S1973-9087.17.04722-0.
- 493 Trepczynski, A., Kutzner, I., Schwachmeyer, V., Heller, M. O., Pfitzner, T., and Duda, G. N. (2018).
494 Impact of antagonistic muscle co-contraction on in vivo knee contact forces. *J. Neuroeng.*
495 *Rehabil.* 15, 101. doi:10.1186/s12984-018-0434-3.
- 496 Wong, J., Wilson, E. T., Malfait, N., and Gribble, P. L. (2009). Limb Stiffness Is Modulated With
497 Spatial Accuracy Requirements During Movement in the Absence of Destabilizing Forces. *J.*
498 *Neurophysiol.* 101, 1542–1549. doi:10.1152/jn.91188.2008.
- 499

Table 1: Muscles analyzed in this study. The functional role of each muscle is indicated as FLEX – flexor, EXT – extensor, DF – dorsi-flexor, PF – plantar-flexor. A shaded cell for functional role indicates muscle has switched role during gait. EMG scale factor is the scale factor applied to the basic EMG signal of a muscle to account for the difference between true maximum and maximum observed experimentally.

Muscle Name and Abbreviation	EMG Source	Functional Role			EMG Scale	
		Hip	Knee	Ankle	L	R
adductor brevis (addbrev)	adductor longus	FLEX			0.14	0.05
adductor longus (addlong)		FLEX			0.33	0.07
adductor magnus distal (addDist)		EXT			0.07	0.05
adductor magnus ischial (addmagIsch)		EXT			0.05	0.05
adductor magnus middle (addmagMid)					0.07	0.05
adductor magnus proximal (addmagProx)		FLEX			0.13	0.05
gluteus maximus superior (glmax1)	gluteus maximus	EXT			0.32	0.20
gluteus maximus middle (glmax2)		EXT			0.33	0.20
gluteus maximus inferior (glmax3)		EXT			0.32	0.20
gluteus medius anterior (glmed1)	gluteus medius	EXT			0.71	0.62
gluteus medius middle (glmed2)		EXT			0.69	0.63
gluteus medius posterior (glmed3)		EXT			0.69	0.62
gluteus minimus anterior (glmin1)					0.32	0.15
gluteus minimus middle (glmin2)					0.30	0.16
gluteus minimus posterior (glmin3)		EXT			0.30	0.15
iliacus (iliacus)	iliopsoas *	FLEX			0.05	0.05
psoas (psoas)		FLEX			0.99	0.82
semimembranosus (semimem)	semimem	EXT	FLEX		0.34	0.40
semitendinosus (semiten)		EXT	FLEX		0.30	0.40
biceps femoris long head (bflh)	bflh	EXT	FLEX		0.76	0.38
biceps femoris short head (bfsh)			FLEX		0.76	0.39
rectus femoris (recfem)	rectus femoris	FLEX	EXT		0.48	0.28
vastus medialis (vasmed)	vastus medialis		EXT		0.27	0.50
vastus intermedius (vasint)			EXT		0.31	0.44
vastus lateralis (vaslat)	vastus lateralis		EXT		0.32	0.11
lateral gastronemius (gaslat)	gasmed		FLEX	PF	0.05	0.12
medial gastronemius (gasmed)			FLEX	PF	0.14	0.14
tibialis anterior (tibant)	tibialis anterior			DF	0.61	1.00
tibialis posterior (tibpost)	tibialis posterior *			PF	0.05	0.05
peroneus brevis (perbrev)	peroneus longus			PF	0.05	0.98
peroneus longus (perlong)				PF	0.05	0.99
peroneus tertius (pertert)				DF	0.05	0.99
soleus (soleus)	soleus			PF	0.65	0.96
extensor digitorum longus (edl)	edl *			DF	1.00	0.26
flexor digitorum longus (fdl)	fdl *			PF	1.00	0.05

* measured using indwelling EMG

Table 2: Mean difference in the highest correlation for each case between both CCI methods. The method which produces a higher correlation with K_{joint} for each case is identified in the corresponding table cells. Blue shading indicates mean correlation r_1 is higher than r_2 , whereas red shade indicates the mean correlation r_2 is higher than r_1 . Each value in the Overall column is the mean of values from the corresponding Hip, Knee, and Ankle column.

	Non-paretic side				Paretic side			
	Hip	Knee	Ankle	Overall	Hip	Knee	Ankle	Overall
EMG basic	CCI_2 (0.38)*	CCI_1 (0.08)	CCI_1 (0.38)*	CCI_1 (0.03)	CCI_2 (0.02)	CCI_1 (0.26)*	CCI_1 (0.12)	CCI_1 (0.12)
EMG scaled	CCI_2 (0.22)*	CCI_2 (0.01)	CCI_1 (0.14)	CCI_2 (0.03)	CCI_2 (0.08)	CCI_1 (0.30)*	CCI_1 (0.16)	CCI_1 (0.13)
EMG delayed	CCI_2 (0.18)*	CCI_1 (0.17)*	CCI_1 (0.43)*	CCI_1 (0.14)	CCI_1 (0.05)	CCI_1 (0.38)*	CCI_1 (0.17)*	CCI_1 (0.20)
EMG calibrated	CCI_2 (0.05)	CCI_1 (0.17)*	CCI_1 (0.16)	CCI_1 (0.09)	CCI_1 (0.10)*	CCI_1 (0.32)*	CCI_1 (0.17)*	CCI_1 (0.20)
Moment muscle	CCI_1 (0.06)	CCI_1 (0.06)	CCI_2 (0.04)	CCI_1 (0.02)	CCI_1 (0.28)*	CCI_1 (0.12)*	CCI_2 (0.03)	CCI_1 (0.12)
Moment sum	CCI_1 (0.15)*	CCI_1 (0.44)*	CCI_1 (0.52)*	CCI_1 (0.37)	CCI_1 (0.30)*	CCI_1 (0.40)*	CCI_1 (0.28)*	CCI_1 (0.32)

* indicates statistically significant Wilcoxon rank sum test result ($p < 0.05$)

Common Co-Contraction Indices versus Joint Stiffness

Figure 1: Stiffness, sample CCI_1 and CCI_2 values (mean $\pm$ 1 standard deviation) around lower extremity joints of the subject during gait for (A) non-paretic side data in blue, and (B) paretic side data in red. The antagonistic pair of muscles selected for CCI computation are identified in the legend of the subplot. EMG-based CCI shown in the figure is computed using $EMG_{delayed}$ signals and moment-based CCI are computed using unnormalized joint moment and then normalized by the maximum value over all gait trials analyzed.

Figure 2: Correlation between CCI_1 and joint stiffness K_{joint} . Bars are at the mean value of the Pearson correlation coefficient, and error bars are at 1 standard deviation (+/- depending on the sign of mean value). Each muscle combination for antagonistic pairing displayed in the figure represents the best-in-class correlation between K_{joint} and CCI_1 computed using a specific type of quantity: (1) EMG_{basic} (in blue); (2) EMG_{scaled} (in red); (3) $EMG_{delayed}$ (in orange); (4) $EMG_{calibrated}$ (in purple); (5) M_{mus} (in green). Bar (6) represents the correlation between K_{joint} and CCI_1 computed using the sum of the antagonist moment around each joint, M_{sum} (in cyan).

Common Co-Contraction Indices versus Joint Stiffness

Figure 3: Correlation between CCI_2 and joint stiffness K_{joint} . Bars are at the mean value of the Pearson correlation coefficient and error bars are at 1 standard deviation (+/- depend on the sign of mean value). Each muscle combination for antagonistic pairing displayed in the figure represents the best-in-class correlation between K_{joint} and CCI_2 computed using a specific type of quantity: (1) EMG_{basic} (in blue); (2) EMG_{scaled} (in red); (3) $EMG_{delayed}$ (in orange); (4) $EMG_{calibrated}$ (in purple); (5) M_{mus} (in green). Bar (6) represents the correlation between K_{joint} and CCI_2 computed using the sum of the antagonist moment around each joint, M_{sum} (in cyan).

Figure 4: Correlation between CCI_1 terms (AR and SQ) and joint stiffness. Bars are at the mean value of the Pearson correlation coefficient, and error bars are at 1 standard deviation (+/- depending on the sign of mean value). Blue bars are for AR , and red bars are for SQ . Dark lines are at the mean value of the correlation coefficient between CCI_1 and joint stiffness.

545 **Data Availability Statement**

546 The datasets analyzed for this study are available on request from the corresponding author.