



Reduced joint motion supersedes asymmetry in explaining increased metabolic demand during walking with mechanical restriction

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ABSTRACT

Recent research has highlighted the complex interactions among chronic injury- or disease-induced joint limitations, walking asymmetry, and increased metabolic cost. Determining the specific metabolic impacts of asymmetry or joint impairment in clinical populations is difficult because of concurrent neurological and physiological changes. This work investigates the metabolic impact of gait asymmetry and joint restriction by unilaterally (asymmetric) and bilaterally (symmetric) restricting ankle, knee, and combined ankle and knee ranges of motion in unimpaired individuals. We calculated propulsive asymmetry, temporal asymmetry, and step-length asymmetry for an average gait cycle; metabolic rate; average positive center of mass power using the individual limbs method; and muscle effort using lower limb electromyography measurements weighted by corresponding physiological cross-sectional areas. Unilateral restriction caused propulsive and temporal asymmetry but less metabolically expensive gait than bilateral restriction. Changes in asymmetry did not correlate with changes in metabolic cost. Interestingly, bilateral restriction increased average positive center of mass power compared to unilateral restriction. Further, increased average positive center of mass power correlated with increased energy costs, suggesting asymmetric step-to-step transitions did not drive metabolic changes. The number of restricted joints reduces available degrees of freedom and may have a larger metabolic impact than gait asymmetry, as this correlated significantly with increases in metabolic rate for 7/9 participants. These results emphasize symmetry is not by definition metabolically optimal, indicate that the mechanics underlying symmetry are meaningful, and suggest that available degrees of freedom should be considered in designing future interventions.

1. Introduction

Asymmetric walking is common after acute or chronic injuries or diseases, including amputations (Adamczyk and Kuo, 2015; Houdijk et al., 2009), knee or hip osteoarthritis (Mills et al., 2013), hip arthroplasty (Lugade et al., 2010), and stroke (Chen et al., 2005; Patterson et al., 2010; Wonsetler and Bowden, 2017). Gait asymmetry is quantified by spatiotemporal (Isakov et al., 1997; Nolan et al., 2003) and propulsive (Lewek and Sawicki, 2019) characteristics and is often accompanied by increased energetic requirements (Detrembleur et al., 2003; Mattes et al., 2000; Stoquart et al., 2012) thought to result from metabolically expensive step-to-step transitions (Houdijk et al., 2009;

Mahon et al., 2015). Specifically, reduced impaired limb propulsion leading to reduced peak instantaneous center of mass (COM) power (Farris et al., 2015; Mahon et al., 2015) may require increased collision work during double support or increased contralateral work in unimpaired single support (Donelan et al., 2002). Therefore, researchers have proposed that restoring walking symmetry may reduce energetic requirements (Finley and Bastian, 2017; Mahon et al., 2019).

However, the interaction between walking asymmetry and metabolic cost is inconsistently characterized in the literature. This relationship is further obscured by the numerous methods for quantifying asymmetry (propulsive, spatial, temporal) and by the diversity of interventions that target symmetry. Ankle-based exoskeletons (Awad et al., 2017) and

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prosthetic emulators (Quesada et al., 2016) can improve impaired limb propulsion but do not consistently reduce metabolic cost. Using feedback to guide unimpaired participants, researchers have induced step-length asymmetry (Nguyen et al., 2020) or step-time asymmetry (Ellis et al., 2013) and observed metabolic increases relative to participants' unaltered gait. However, others demonstrated step-time (Stenum and Choi, 2020) and step-length asymmetry (Sánchez et al., 2020) can be energetically optimal when unimpaired participants walk on a split-belt treadmill at different belt velocities. Repeated sessions of training on a split-belt treadmill (Reisman et al., 2013b) or walking with functional electrical stimulation (Awad et al., 2015) improved step-length asymmetry in clinical populations, and improved asymmetry correlated with reduced metabolic cost (Awad et al., 2015). However, in longitudinal studies, metabolic improvements could result from other benefits that accompany gait training including increased preferred walking speed (Reisman et al., 2013a; Tyrell et al., 2011) and muscle strength (Bohannon, 2007). Further, while some found a significant correlation between improved step-length (Awad et al., 2015) or foot placement (Finley and Bastian, 2017) symmetry and reduced metabolic cost, others observed that improved stance *time* asymmetry was moderately correlated with metabolic cost in persons post-stroke (Ryan et al., 2020). Additional research found no metabolic benefit to single-session reductions in step-length asymmetry in clinical populations (Nguyen et al., 2020; Padmanabhan et al., 2020; Sánchez and Finley, 2018). Characterizing the relationship between improved gait asymmetry and metabolic reductions requires further investigation.

Injury or disease-induced anatomical (Quesada et al., 2016) or physiological (Attias et al., 2016; Ong et al., 2019) changes that can unilaterally constrain joint and limb function make investigating the interactions among altered joint function, walking asymmetry, and metabolic cost especially challenging. Therefore, ankle (Huang et al., 2015; Wutzke et al., 2012) and knee (Lewek et al., 2012) bracing were previously used to limit joint range of motion (ROM) and induce gait asymmetry in unimpaired participants. This approach allowed investigators to isolate the biomechanical and energetic impacts of reduced joint ROM and walking asymmetry from the impacts of concurrent anatomical or physiological changes in clinical populations. However, asymmetry accompanied by joint restriction still makes it difficult to identify whether outcomes are a result of the asymmetry per se or a consequence of joint restriction. To isolate the metabolic impact of reduced joint ROM and induced asymmetry, we used knee braces and custom 3D-printed ankle stays to restrict ankle ROM, knee ROM, and ankle + knee ROM unilaterally and bilaterally. We hypothesize (h1a) that induced asymmetry will be more metabolically expensive than induced symmetry (bilaterally restricted joints) (h1b) due to energetically expensive step-to-step transitions. If increased metabolic cost in asymmetric gait indeed results from badly coordinated step-to-step transitions, then restoring symmetry with bilateral bracing should also eliminate expensive transitions. However, researchers have reported that simultaneous ankle and knee restriction is more metabolically expensive than ankle restriction (McCain et al., 2021), possibly because restricting additional joints or degrees of freedom (DOFs) lessens redundancy and restricts compensation. Thus, we hypothesized (h2) that as a proxy for available DOFs, the number of joints restricted will correlate with a metabolic increase in asymmetric and symmetric conditions.

2. Methods

Data Collection: UNC-Chapel Hill institutional review board approved procedures and consent forms signed prior to data collection by nine healthy adult participants (5 M/4F, 25.22 ± 0.30 years, 1.77 ± 0.13 m, 78.34 ± 15.9 kg). We recruited healthy adults without a history of surgery for lower extremity musculoskeletal injury or a lower extremity musculoskeletal injury in the past two years. Participants walked on an instrumented split-belt treadmill (Bertec, Columbus, OH,

USA) for eight conditions, each lasting 7 min, including: (1) *control*: no braces worn, (2) *braced*: knee braces worn unrestricted bilaterally; unilaterally restricted conditions: (3) *uni-ank*: unilaterally restricted ankle, (4) *uni-knee*: unilaterally restricted knee, and (5) *uni-a + k*: unilaterally restricted ankle + knee; and bilaterally restricted conditions: (6) *bi-ank*: bilaterally restricted ankles, (7) *bi-knee*: bilaterally restricted knees, and (8) *bi-a + k*: bilaterally restricted ankles + knees simultaneously. Our approach allowed reduction of available DOFs both symmetrically (0: *control*, *braced*; 2: *bi-ank*, *bi-knee* 4: *bi-a + k*) and asymmetrically (1: *uni-ank*, *uni-knee*; 2: *uni-a + k*). Walking speed (0.8 m/s) was chosen to accommodate the increased challenge associated with the *bi-a + k* condition. 3D-printed ankle stays secured to the foot/ankle dorsum restricted ankle ROM, and lockable donJoy T-ROM knee braces (DJO Global, Inc, Vista, CA, USA) restricted knee ROM. We only applied ankle stays unilaterally for *uni-ank* and *uni-a + k* conditions, and bilaterally for *bi-ank* and *bi-a + k* conditions. Knee braces were worn bilaterally for all conditions except the *control* condition. The *control* condition was performed last to eliminate additional static captures, and other conditions were performed in a random order. In *braced*, *uni-ank*, and *bi-ank* conditions knee ROM was unrestricted, in *uni-ank* and *uni-a + k* conditions knee ROM was unilaterally restricted, and in *bi-knee* and *bi-a + k* conditions knee ROM was bilaterally restricted.

We recorded rates of oxygen consumption and carbon dioxide production with a portable metabolic system (K5, Cosmed, Chicago, IL) for five minutes of quiet standing before walking and during walking conditions. The positions of 42 reflective markers attached to the pelvis and lower limb (McCain et al., 2019) were recorded using an eight-camera motion capture system (Vicon, Oxford, UK) sampling at 120 Hz; marker positions were filtered within OpenSim software (Delp et al., 2007) using a 6 Hz Butterworth filter. Ground reaction forces (GRFs) were recorded at 1200 Hz, then filtered with second-order low-pass Butterworth filter (cutoff frequency: 25 Hz). We collected surface electromyography (EMG) (Trigno, Delsys) at or above 1200 Hz bilaterally for tibialis anterior, soleus, lateral gastrocnemius, medial gastrocnemius, vastus lateralis, and biceps femoris. We filtered EMG with a 4th order bandpass filter (30 Hz/450 Hz), found the rolling root mean square (50 ms), smoothed data with a moving average (50 ms), and normalized EMG by representative EMG peaks.

Data Processing: We used an OpenSim full-body model (Rajagopal et al., 2016) altered to represent the lower limb and scaled according to participant anthropometry. Filtered marker data and personalized models were input into an inverse kinematic algorithm (Thelen and Anderson, 2006) to determine joint angular velocities and moments. We determined heel strike and toe-off timing with a custom MATLAB script using GRF data. Propulsive asymmetry (PA), temporal asymmetry (TA), step-length asymmetry (SLA), average positive COM power and weighted muscle effort were calculated as described below over 10 gait cycles for each limb and averaged across gait cycles for each subject and condition. We removed gait cycles bordering crossover steps and selected ten consecutive gait cycles nearest the end of the last two minutes of data collection to ensure metabolic steady state. To isolate the impact of joint ROM restriction from that of bracing mass, we calculated Δ metabolic cost, Δ PA, Δ TA, Δ average positive COM power, and Δ weighted muscle effort for restricted (*uni* & *bi*) conditions relative to the *braced* condition.

Measures of Asymmetry: We calculated asymmetry measures as the ratio of maximum contribution (between legs) to summed contribution (both legs) such that 0.5 indicates symmetry and larger values indicate increased asymmetry (Lewek et al., 2018). This ratio was calculated from integrated anteriorly directed GRFs for PA, from the percent gait cycle spent in single limb support for TA, and from average step-lengths for SLA. Step-lengths were determined from the sagittal distance in calcaneus marker locations at heel strikes.

Metabolic Rate: We calculated metabolic power from rates of oxygen consumption and carbon dioxide production measured during five minutes of quiet standing before the first condition and during the last

two minutes of each condition (Brockway, 1987). The net metabolic rate was determined as the difference in metabolic power for each walking condition and metabolic power of quiet standing, normalized by participant mass.

Average Positive COM Power: We calculated instantaneous external mechanical limb powers using individual limbs method (Donelan et al., 2002) in a custom MATLAB script. We calculated COM velocity for each gait cycle by integrating COM acceleration, determined from external forces and body mass, with integration constants determined such that sagittal velocity equaled treadmill speed and average vertical and medial COM velocities were zero. The dot product of COM velocity and each limb's mass normalized GRF gave instantaneous limb power. To obtain average positive COM power for a gait cycle we summed average positive limb power for each limb, where average positive limb powers for each limb and gait cycle were determined by integrating periods of positive instantaneous power and dividing by average corresponding gait cycle duration.

Weighted muscle effort: We determined average integrated muscle activity (a_m^{int}) by integrating normalized muscle activities and dividing by the number of gait cycles. Weighted muscle activity was found with the equation $\sum_{m=1}^{N_{muscles}} ((a_m^{int} * PCSA_m) / a_m^{MAX}) * 100$ where $PCSA_m$ is muscle physiological cross-sectional area (Rajagopal et al., 2016), a_m^{MAX} is the subjects max average integrated muscle activity for all conditions, and $N_{muscles}$ is the total number of muscles included bilaterally.

Statistical Analyses: We performed a one-way (factor levels: braced, bi-ank, bi-knee, bi-a + k) repeated measures reduced maximum likelihood (REML) analysis in SAS Statistical Software (SAS Institute, Cary, NC, USA) on asymmetry measures to ensure there was no significant differences in asymmetry among the braced, bi-ank, bi-knee, and bi-a + k conditions. Then we performed two-way repeated measures REML analysis in SAS to determine whether restriction symmetry (factor 1 levels: unilateral/bilateral) or restriction joint (factor 2 levels: ankle, knee, ankle + knee) were significant ($p_{REML} < 0.05$) factors outcome measures (PA, TA, SLA, average positive COM power, metabolic rate, weighted muscle effort, Δ metabolic rate, Δ average positive COM power, Δ weighted muscle effort). We visually inspected residuals in Q-Q plots for normality, and Grubb's test was used to determine and remove one outlier value in the metabolic data (participant P9, condition: bi-knee). Post-hoc analyses to determine significance between factor levels ($p_{ph} < 0.05$) included t-tests with Bonferroni corrections for multiple comparisons (uni-ank vs bi-ank, uni-knee vs bi-knee, uni-a + k vs bi-a + k) We used a custom MATLAB script to determine the Pearson correlation

coefficient (r) and significance ($p_{p} < 0.05$), calculate the coefficient of determination (R^2), and perform a simple linear regression analysis.

3. Results

Measures of Symmetry: Joint restrictions induced propulsive (Fig. 1A, $p_{REML} = 0.02$) and temporal (Fig. 1B, $p_{REML} < 0.01$) asymmetry in unilaterally compared to bilaterally restricted conditions. Furthermore, TA increased in uni-knee ($TA = 0.53 \pm 0.01$) and uni-a + k ($TA = 0.53 \pm 0.01$) conditions when compared to bi-knee ($TA = 0.51 \pm 0.01$, $p_{ph} < 0.01$) and bi-a + k ($TA = 0.51 \pm 2e^{-3}$, $p_{ph} < 0.01$) conditions, respectively. Restriction location significantly affected TA ($p_{REML} < 0.01$), and we found increased TA with knee ($p_{ph} = 0.02$) or ankle + knee ($p_{ph} < 0.01$) restrictions compared to ankle restriction. Post-hoc analysis did not find statistically significant differences between factor levels for propulsive asymmetry. Step-length asymmetry was not significantly affected by either factor (Fig. 1C). We analyzed the braced and bilaterally restricted conditions and found no significant change in asymmetry measures.

Metabolic Rate: Δ Metabolic rate (Fig. 2B) was also significantly affected by restriction symmetry ($p_{REML} < 0.01$) and by joints restricted ($p_{REML} < 0.01$), and there was a significant interaction between these factors ($p_{REML} < 0.01$). Symmetric knee restriction in bi-knee (0.71 ± 0.38 W/kg) and bi-a + k (1.21 ± 0.48 W/kg) conditions was more metabolically expensive than asymmetric knee restriction in uni-knee (0.13 ± 0.20 W/kg; $p_{ph} < 0.01$) and bi-a + k (0.40 ± 0.33 W/kg; $p_{ph} < 0.01$) conditions, respectively. Δ Metabolic rate did not significantly correlate with Δ propulsive asymmetry (Fig. 2C, $p_p = 0.89$) or Δ temporal asymmetry (Fig. 2D, $p_p = 0.92$).

Average Positive COM Power: Restriction symmetry had a significant effect on Δ average positive COM power (Fig. 3B, $p_{REML} = 0.03$) as bilaterally restricted conditions had increased Δ average positive COM power compared to unilaterally restricted conditions. Further, bi-a + k Δ average positive COM power (0.04 ± 0.06 W/kg) was significantly increased compared to uni-a + k Δ average positive COM power (-0.02 ± 0.05 W/kg, $p_{ph} = 0.03$). We found a significant ($p_p < 0.01$, $R^2 = 0.12$) positive correlation between Δ average positive COM power and Δ metabolic cost (Fig. 3C). Average positive and negative limb power during both double support periods and average instantaneous mechanical power of each limb normalized for a gait cycle were calculated and included for additional context (Supplemental Fig. 1).

Weighted Muscle Effort: Δ Weighted muscle effort (Fig. 4B, p_{REML}

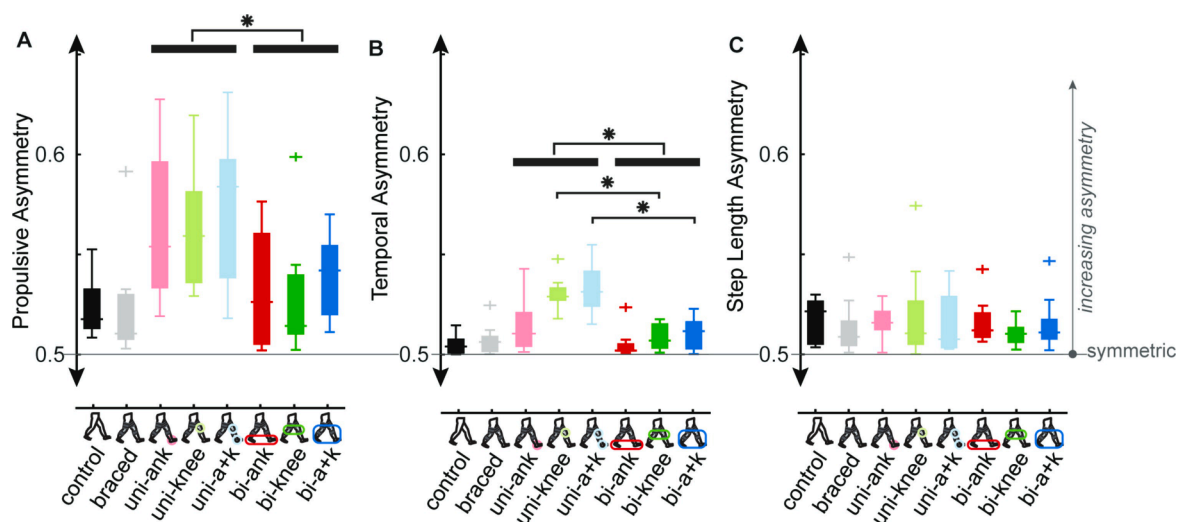


Fig. 1. Group (A) propulsive asymmetry, (B) temporal asymmetry, and (C) step-length asymmetry across conditions. Single asterisks (*) above horizontal bars indicate that the symmetry (unilateral/bilateral) nature of restriction had as significant effect on corresponding asymmetry values. Single asterisks above brackets indicate significant differences between specific conditions.

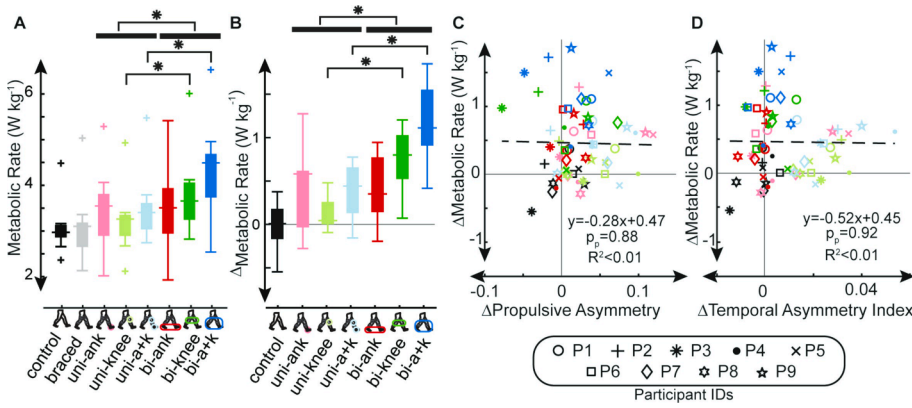


Fig. 2. Group (A) metabolic rate and (B) Δ metabolic rate for all conditions. Single asterisks (*) above horizontal bars indicate that the symmetry (unilateral/bilateral) nature of restriction had as significant effect on corresponding asymmetry values. Single asterisks above brackets indicate significant differences between specific conditions. Subject specific Δ metabolic rates plotted with (C) Δ propulsive asymmetry and (D) Δ temporal asymmetry showing resulting linear correlations with Pearson coefficient p-values.

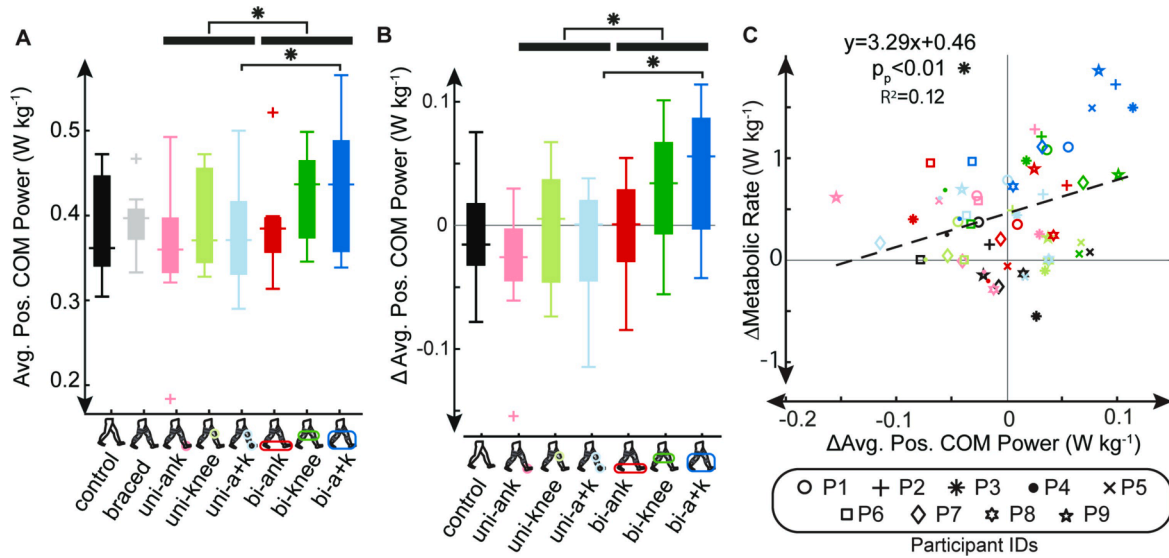


Fig. 3. Group (A) average positive COM power and (B) Δ average positive COM power for all conditions. Single asterisks (*) above horizontal bars indicate that the symmetry (unilateral/bilateral) nature of restriction had as significant effect on corresponding asymmetry values. Single asterisks above brackets indicate significant differences between specific conditions. Subject specific Δ metabolic rates plotted with (C) Δ average positive COM work and single asterisk (*) indicates significant correlation.

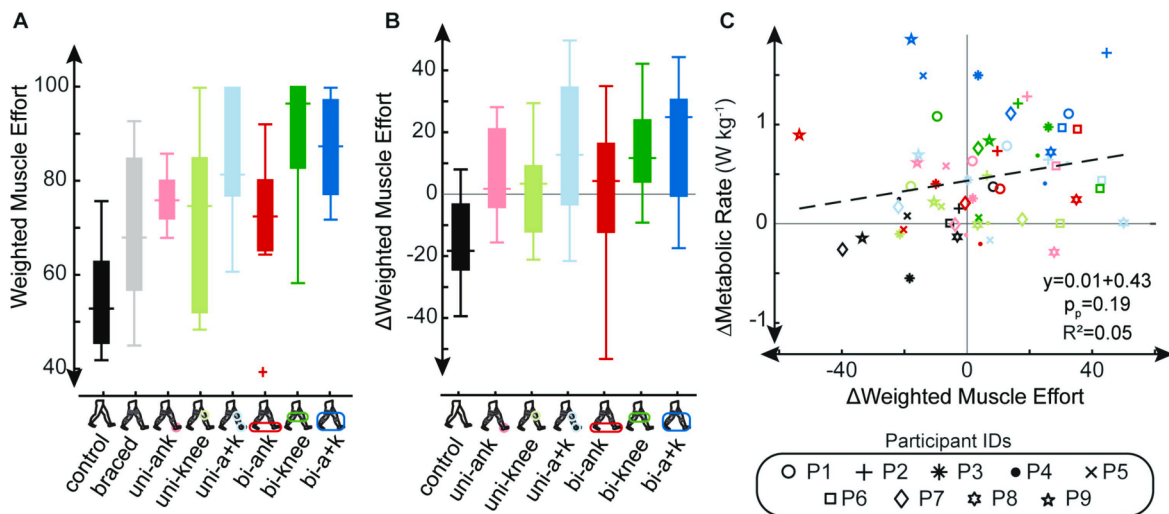


Fig. 4. Group (A) weighted muscle effort and (B) Δ weighted muscle effort for all conditions. Single asterisks (*) above solid bars indicate that the symmetry of restriction had as significant effect on corresponding asymmetry values. Single asterisks above brackets indicate significant differences between specific conditions. Subject specific Δ metabolic rates plotted with (C) Δ weighted muscle effort.

= 0.048) was significantly affected by the joint restricted, but not affected by restriction symmetry. Further, when the ankle and knee were restricted simultaneously, we found a significant increase in Δ weighted muscle effort ($p_{ph} = 0.04$) compared to ankle restriction alone. Δ Weighted muscle effort was not significantly correlated with Δ metabolic cost (Fig. 4C).

Correlation Between Δ Metabolic Cost and Restricted Degrees of Freedom: The number of constrained DOFs was significantly correlated with the Δ metabolic cost for seven participants (Fig. 5, P1, P2, P3, P6, P7, P8, P9; $p_p < 0.02$). The R^2 values for these seven participants were $0.63 < R^2 < 0.96$.

4. Discussion

We investigated the metabolic consequences of gait asymmetry and reduced DOFs using joint-specific restrictions with unimpaired participants. This builds upon previous work (Lewek et al., 2012; McCain et al., 2021; Wutzke et al., 2012) by applying multiple joint restrictions unilaterally and bilaterally to explore the metabolic impacts of asymmetry and joint restriction. Our approach elicited asymmetric and symmetric gait and demonstrated that asymmetry in and of itself does

not drive increased energy requirements. Instead, we found the number of restricted DOFs had the strongest correlation with metabolic rate. Our results suggest that rather than targeting walking symmetry, assistive technology or rehabilitative strategies that mitigate limb or joint impairments - thereby increasing functional DOFs - may have greater potential to reduce metabolic requirements.

Our approach successfully induced temporal and propulsive walking asymmetry, but induced asymmetry did not result in metabolic increases as hypothesized. Specifically, we found asymmetrically restricted conditions were less metabolically costly than symmetrically restricted conditions, and no significant correlation existed between Δ metabolic cost and asymmetry measures (Δ PA, Δ TA). These results reinforce that symmetry is not always metabolically optimal in unimpaired (Sánchez et al., 2019) or clinical (Roemmich et al., 2019; Sánchez and Finley, 2018) populations and suggest that walking asymmetrically with imposed restriction to one limb is more economical than walking symmetrically with bilaterally imposed restriction (Browne et al., 2021). Interestingly, any knee restriction had a larger impact on TA than did ankle restriction, indicating knee restriction may promote increased TA (Fig. 1B). It is possible that a knee restriction makes foot clearance a priority, with the resulting compensations, such as foot circumduction

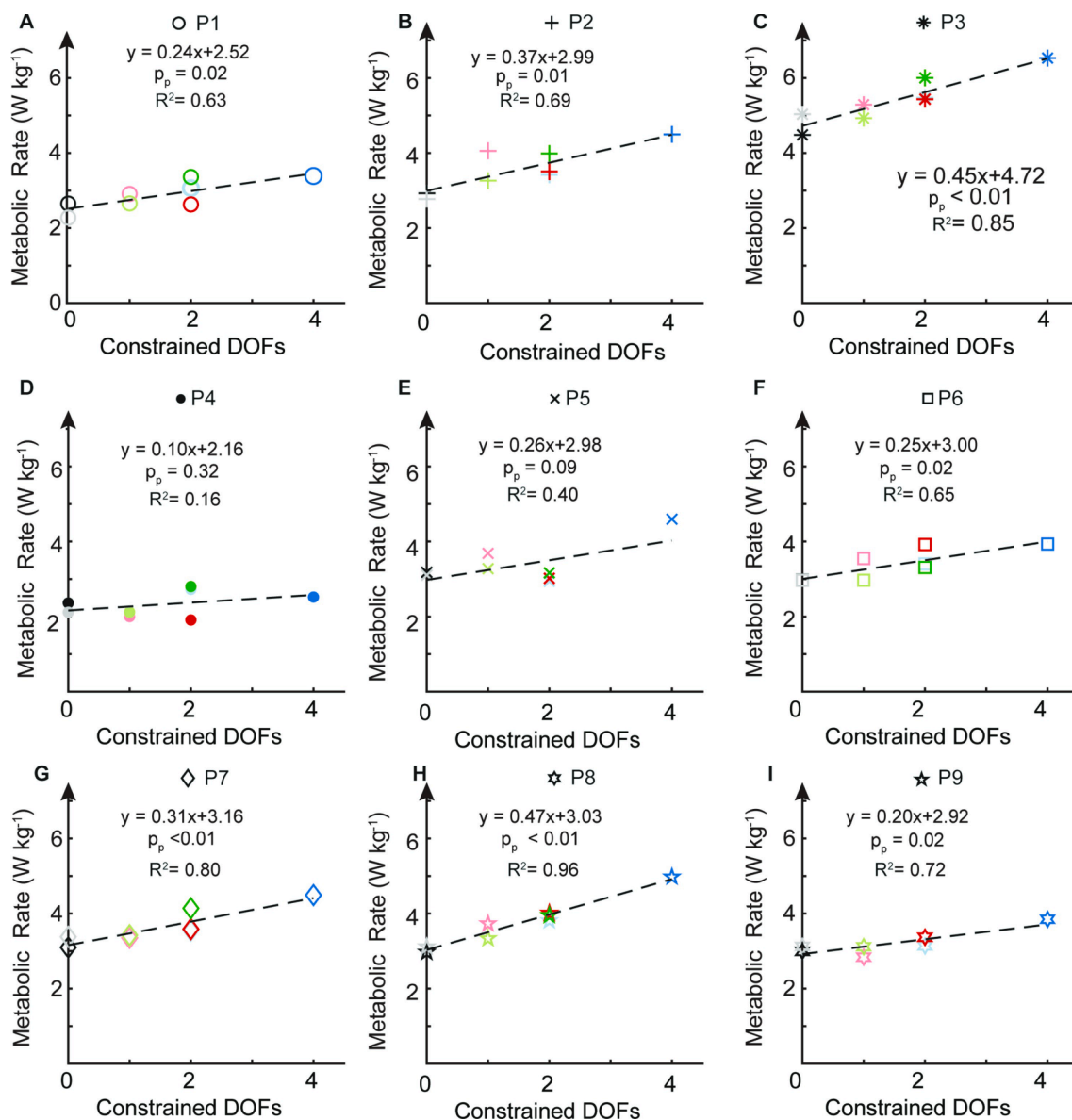


Fig. 5. The number of constrained DOFs is plotted with metabolic rate for all participants (A:I). A single asterisk indicates a significant Pearson correlation.

(McCain et al., 2021), impacting the duration of single limb support. Despite changes in TA and PA, we did not see any significant change in SLA. Unimpaired controls may compensate for restriction with temporal gait adaptations alone, whereas clinical populations may have less capacity to manipulate underlying gait parameters (Hak et al., 2013).

Despite our success in creating propulsive asymmetries, energetically expensive asymmetric step-to-step transitions were not at the root of metabolic increases as we hypothesized. Instead, we found symmetric conditions had larger total average positive COM power and correspondingly higher metabolic rates. It is possible that a decrease in gait cycle duration in the symmetrically restricted conditions could account for the larger average positive COM power. Likewise, we did not measure arm movement, which is known to increase with greater bilateral propulsion needs (Lewek et al., 2010), and has the potential to impact the COM work rate (Collins et al., 2009). However, we note the correlation observed between Δ metabolic cost and Δ average positive COM power (Fig. 3C) had a small R-squared value, and thus explains little variability in the metabolic data.

Additional muscle-level metabolic impacts could explain why Δ average positive COM power does not account for variability of this dataset, as muscle contractions not resulting in motion are not accounted for by COM power. Qualitatively, correlation between Δ weighted muscle effort and Δ metabolic cost (Fig. 4C) is similar to the correlation between Δ average positive COM power and Δ metabolic cost and is a better predictor of Δ metabolic cost than Δ PA or Δ TA. It is possible that inclusion of upper limb EMG measurements to account for arm movement needed to conserve angular momentum or back muscles used for trunk stability would improve this correlation; alternatively, muscles surrounding the hip may have been crucial to understand kinematic compensations and could strengthen the predictive quality of this relationship (Stenum and Choi, 2016). Future research could employ musculoskeletal simulation to investigate contributions of muscles difficult to measure experimentally.

Our results suggest metabolic increases may be driven by the number of restricted DOFs. We found that for seven of nine participants, metabolic rate and restricted DOFs were significantly correlated, and the number of restricted DOFs accounted for between 63% and 96% of the metabolic variability. These results echo previous research suggesting that reducing available DOFs limits compensatory strategies (Clark et al., 2010) the resulting gait may require increased metabolic cost (Mahon et al., 2015). This may explain inconsistencies in previous literature examining relationships between gait asymmetry and metabolic consequences. Specifically, improvement in paretic ankle DOF performance resulting from increased muscle strength may drive decreased energy requirements observed with repeated gait training (Awad et al., 2015); this would explain why the same benefits do not accompany single-session gait training that addresses symmetry but does not increase available DOFs (Sánchez and Finley, 2018).

Our results echo that asymmetry can be less metabolically expensive than symmetry (Browne et al., 2021; Sánchez et al., 2020), and suggest rehabilitative interventions targeting specific improvement in affected limb DOFs function rather than improvement in specific symmetry metrics may have more potential to reduce energy requirements. In this work, bilaterally restricted DOFs resulted in symmetric and energetically expensive gait; similarly, when instructed to improve symmetry, clinical populations may reduce the unaffected limb's performance, limiting available DOFs, and creating symmetric and metabolically detrimental gait. While counterintuitive, this may be the only achievable manner for individuals with large intralimb functional discrepancies to walk symmetrically. While the intention of targeting symmetry in patient populations is to improve impaired limb function to match unimpaired limb function, the method for restoring symmetry is not ensured. For example, limb symmetry is frequently used for return-to-play decisions following anterior cruciate ligament injury (Wellsandt et al., 2017). This metric can overestimate knee function (Wellsandt et al., 2017), possibly because athletes opt to reduce unimpaired limb function

to expedite their return-to-play, again creating symmetric, but undesirable, performance. In addition, recent work suggests transfemoral amputees have individualized, metabolically-optimal, levels of walking asymmetry such that any deviation is metabolically detrimental (Mahon et al., 2019). We suggest energetically optimal asymmetry may maximize impaired limb function such that increasing symmetry would require restricting the unimpaired limb, thereby reducing available DOFs.

There are several limitations to this work. On average, study participants were significantly younger than many patient populations which may impact generalization of these results. However, we note that our asymmetry measures were similar to reports for clinical populations in the literature (Allen et al., 2014; Awad et al., 2017; Little et al., 2020). Reported values for average positive COM power are slightly larger than values reported in previous ILM analysis for persons post-stroke and unimpaired participants (Farris et al., 2015). The asymmetry ratios we present do not indicate which limb contributes to asymmetry in unilateral conditions. However, we note that they allow us to calculate the magnitude of asymmetry consistently across unilaterally and bilaterally restricted conditions. Restricting ankle motion was accomplished using a 3D-printed polylactic acid ankle stay for ankle restricted conditions and otherwise removed; while results could be affected by added mass, the ankle stays weighed < 3 oz. Our participants wore knee braces bilaterally for all restricted conditions so the added mass of knee bracing was consistent across conditions and thus should not impact outcomes. Walking asymmetry and restricted DOFs are related in this work and their metabolic impact cannot be completely decoupled. However, our approach allowed for both symmetric and asymmetric DOFs reduction and therefore can provide insight into the relative metabolic impact of asymmetry and DOFs. In addition, we acknowledge that the chosen gait speed is slower than our participants typically walk; however, this speed was selected to ensure that participants would be challenged enough to elicit a metabolic impact while allowing participants to complete all braced conditions. The predictive power of weighted muscle effort and Δ weighted muscle effort metrics would likely be improved by a more extensive set of EMG measurements. We identified the metabolic data for one participant and trial as an outlier (P9, *bi-knee*); because much of our analyses related metabolic data to other outcomes, we removed that one data point (P9, *bi-knee*) from all analyses. Our correlation analysis did not account for participants as a random variable, and it is possible that if we had, the predictive power of the analyses could have increased. Further, a larger sample size may have allowed us to detect additional relationships.

In summary, we investigated the metabolic impacts of asymmetry and available DOFs using joint restriction unilaterally and bilaterally in unimpaired controls. We elicited increased asymmetry with unilateral compared to bilateral restrictions. Interestingly, symmetric restriction was more mechanically and metabolically expensive than asymmetric restriction, and changes in symmetry did not correlate with changes in metabolic cost. Further, we found the average positive COM power to be larger in the energetically expensive, symmetrically restricted conditions than in conditions with unilateral restrictions, suggesting asymmetric step-to-step transitions do not drive metabolic outcomes. Increased energetic requirements correlated significantly with changes in Δ average positive COM power and tended to correlate, although insignificantly, with weighted Δ EMG effort. Interestingly, we found a significant correlation between metabolic rate and the number of DOFs restricted for most participants, suggesting reducing available DOFs has a larger metabolic impact than asymmetry. These findings are not intended to discourage restoration of walking symmetry, but instead should emphasize importance of how symmetry is restored and suggest the inclusion of DOFs availability as a metric guiding future interventions.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jbiomech.2021.110621>.

References

- Adamczyk, P.G., Kuo, A.D., 2015. Mechanisms of Gait Asymmetry Due to Push-Off Deficiency in Unilateral Amputees. *IEEE Trans Neural Syst Rehabil Eng* 23, 776–785.
- Allen, J.L., Kautz, S.A., Neptune, R.R., 2014. Forward propulsion asymmetry is indicative of changes in plantarflexor coordination during walking in individuals with post-stroke hemiparesis. *Clin Biomech (Bristol, Avon)* 29, 780–786.
- Attias, M., Bonnefoy-Mazure, A., De Coulon, G., Cheze, L., Armand, S., 2016. Feasibility and reliability of using an exoskeleton to emulate muscle contractures during walking. *Gait Posture* 50, 239–245.
- Awad, L.N., Bae, J., O'Donnell, K., De Rossi, S.M.M., Hendron, K., Slood, L.H., Kudzia, P., Allen, S., Holt, K.G., Ellis, T.D., Walsh, C.J., 2017. A soft robotic exosuit improves walking in patients after stroke. *Sci. Transl. Med.* 9.
- Awad, L.N., Palmer, J.A., Pohl, R.T., Binder-Macleod, S.A., Reisman, D.S., 2015. Walking speed and step length asymmetry modify the energy cost of walking after stroke. *Neurorehabil Neural Repair* 29, 416–423.
- Bohannon, R.W., 2007. Muscle strength and muscle training after stroke. *J Rehabil Med* 39, 14–20.
- Brockway, J.M., 1987. Derivation of formulae used to calculate energy expenditure in man. *Hum Nutr Clin Nutr* 41, 463–471.
- Browne, M.G., Smock, C.S., Roemmich, R.T., 2021. The human preference for symmetric walking often disappears when one leg is constrained. *J Physiol* 599, 1243–1260.
- Chen, G., Patten, C., Kothari, D.H., Zajac, F.E., 2005. Gait differences between individuals with post-stroke hemiparesis and non-disabled controls at matched speeds. *Gait & Posture* 22, 51–56.
- Clark, D.J., Ting, L.H., Zajac, F.E., Neptune, R.R., Kautz, S.A., 2010. Merging of healthy motor modules predicts reduced locomotor performance and muscle coordination complexity post-stroke. *J. Neurophysiol.* 103, 844–857.
- Collins, S.H., Adamczyk, P.G., Kuo, A.D., 2009. Dynamic arm swinging in human walking. *Proceedings. Biological sciences* 276, 3679–3688.
- Delp, S.L., Anderson, F.C., Arnold, A.S., Loan, P., Habib, A., John, C.T., Guendelman, E., Thelen, D.G., 2007. OpenSim: open-source software to create and analyze dynamic simulations of movement. *IEEE transactions on bio-medical engineering* 54, 1940–1950.
- Detrembleur, C., Dierick, F., Stoquart, G., Chantraine, F., Lejeune, T., 2003. Energy cost, mechanical work, and efficiency of hemiparetic walking. *Gait Posture* 18, 47–55.
- Donelan, J.M., Kram, R., Kuo, A.D., 2002. Simultaneous positive and negative external mechanical work in human walking. *J. Biomech.* 35, 117–124.
- Ellis, R.G., Howard, K.C., Kram, R., 2013. The metabolic and mechanical costs of step time asymmetry in walking. *Proceedings. Biological sciences / The Royal Society* 280, 20122784.
- Farris, D.J., Hampton, A., Lewek, M.D., Sawicki, G.S., 2015. Revisiting the mechanics and energetics of walking in individuals with chronic hemiparesis following stroke: from individual limbs to lower limb joints. *J. NeuroEng. Rehabil.* 12, 24.
- Finley, J.M., Bastian, A.J., 2017. Associations Between Foot Placement Asymmetries and Metabolic Cost of Transport in Hemiparetic Gait. *Neurorehabilitation and Neural Repair* 31, 168–177.
- Hak, L., Houdijk, H., van der Wurff, P., Prins, M.R., Mert, A., Beek, P.J., van Dieën, J.H., 2013. Stepping strategies used by post-stroke individuals to maintain margins of stability during walking. *Clin Biomech (Bristol, Avon)* 28, 1041–1048.
- Houdijk, H., Pollmann, E., Groenewold, M., Wiggerts, H., Polomski, W., 2009. The energy cost for the step-to-step transition in amputee walking. *Gait Posture* 30, 35–40.
- Huang, T.P., Shorter, K.A., Adamczyk, P.G., Kuo, A.D., 2015. Mechanical and energetic consequences of reduced ankle plantarflexion in human walking. *The Journal of experimental biology.*
- Isakov, E., Burger, H., Krajnik, J., Gregoric, M., Marincek, C., 1997. Double-limb support and step-length asymmetry in below-knee amputees. *Scand. J. Rehabil. Med.* 29, 75–79.
- Lewek, M.D., Braun, C.H., Wutzke, C., Giuliani, C., 2018. The role of movement errors in modifying spatiotemporal gait asymmetry post stroke: a randomized controlled trial. *Clin Rehabil* 32, 161–172.
- Lewek, M.D., Osborn, A.J., Wutzke, C.J., 2012. The Influence of Mechanically and Physiologically Imposed Stiff-Knee Gait Patterns on the Energy Cost of Walking. *Arch. Phys. Med. Rehabil.* 93, 123–128.
- Lewek, M.D., Poole, R., Johnson, J., Halawa, O., Huang, X., 2010. Arm swing magnitude and asymmetry during gait in the early stages of Parkinson's disease. *Gait & posture* 31, 256–260.
- Lewek, M.D., Sawicki, G.S., 2019. Trailing limb angle is a surrogate for propulsive limb forces during walking post-stroke. *Clin Biomech (Bristol, Avon)* 67, 115–118.
- Little, V.L., Perry, L.A., Mercado, M.W.V., Kautz, S.A., Patten, C., 2020. Gait asymmetry pattern following stroke determines acute response to locomotor task. *Gait & Posture* 77, 300–307.
- Lugade, V., Wu, A., Jewett, B., Collis, D., Chou, L.-S., 2010. Gait asymmetry following an anterior and anterolateral approach to total hip arthroplasty. *Clin. Biomech.* 25, 675–680.
- Mahon, C.E., Darter, B.J., Dearth, C.L., Hendershot, B.D., 2019. The Relationship Between Gait Symmetry and Metabolic Demand in Individuals With Unilateral Transfemoral Amputation: A Preliminary Study. *Mil Med* 184, e281–e287.
- Mahon, C.E., Farris, D.J., Sawicki, G.S., Lewek, M.D., 2015. Individual limb mechanical analysis of gait following stroke. *J. Biomech.* 48, 984–989.
- Mattes, S.J., Martin, P.E., Royer, T.D., 2000. Walking symmetry and energy cost in persons with unilateral transtibial amputations: matching prosthetic and intact limb inertial properties. *Arch. Phys. Med. Rehabil.* 81, 561–568.
- McCain, E.M., Dick, T.J.M., Giest, T.N., Nuckols, R.W., Lewek, M.D., Saul, K.R., Sawicki, G.S., 2019. Mechanics and energetics of post-stroke walking aided by a powered ankle exoskeleton with speed-adaptive myoelectric control. *J. NeuroEng. Rehabil.* 16, 57.
- McCain, E.M., Libera, T.L., Berno, M.E., Sawicki, G.S., Saul, K.R., Lewek, M.D., 2021. Isolating the energetic and mechanical consequences of imposed reductions in ankle and knee flexion during gait. *J. NeuroEng. Rehabil.* 18, 1–13.
- Mills, K., Hettinga, B.A., Pohl, M.B., Ferber, R., 2013. Between-Limb Kinematic Asymmetry During Gait in Unilateral and Bilateral Mild to Moderate Knee Osteoarthritis. *Arch. Phys. Med. Rehabil.* 94, 2241–2247.
- Nguyen, T.M., Jackson, R.W., Aucie, Y., de Kam, D., Collins, S.H., Torres-Oviedo, G., 2020. Self-selected step length asymmetry is not explained by energy cost minimization in individuals with chronic stroke. *J. NeuroEng. Rehabil.* 17, 119.
- Nolan, L., Wit, A., Dudzinski, K., Lees, A., Lake, M., Wychowski, M., 2003. Adjustments in gait symmetry with walking speed in trans-femoral and trans-tibial amputees. *Gait Posture* 17, 142–151.
- Ong, C.F., Geijtenbeek, T., Hicks, J.L., Delp, S.L., 2019. Predicting gait adaptations due to ankle plantarflexor muscle weakness and contracture using physics-based musculoskeletal simulations. *PLoS Comput Biol* 15, e1006993.
- Padmanabhan, P., Rao, K.S., Gulhar, S., Cherry-Allen, K.M., Leech, K.A., Roemmich, R.T., 2020. Persons post-stroke improve step length symmetry by walking asymmetrically. *J Neuroeng Rehabil* 17, 105.
- Patterson, K.K., Gage, W.H., Brooks, D., Black, S.E., McLroy, W.E., 2010. Changes in Gait Symmetry and Velocity After Stroke: A Cross-Sectional Study From Weeks to Years After Stroke. *Neurorehabilitation and Neural Repair* 24, 783–790.
- Quesada, R.E., Caputo, J.M., Collins, S.H., 2016. Increasing ankle push-off work with a powered prosthesis does not necessarily reduce metabolic rate for transtibial amputees. *J. Biomech.* 49, 3452–3459.
- Rajagopal, A., Dembia, C.L., DeMers, M.S., Delp, D.D., Hicks, J.L., Delp, S.L., 2016. Full-Body Musculoskeletal Model for Muscle-Driven Simulation of Human Gait. *IEEE trans. bio-med. Eng.* 63, 2068–2079.
- Reisman, D.S., Kesar, T.M., Perumal, R., Roos, M.A., Rudolph, K.S., Higginson, J., Helm, E., Binder-Macleod, S., 2013a. Time course of functional and biomechanical improvements during a gait training intervention in persons with chronic stroke. *J. neurologic phys. Ther. JNPT* 37, 159–165.
- Reisman, D.S., McLean, H., Keller, J., Danks, K.A., Bastian, A.J., 2013b. Repeated Split-Belt Treadmill Training Improves Poststroke Step Length Asymmetry. *Neurorehabil Neural Repair*.
- Roemmich, R.T., Leech, K.A., Gonzalez, A.J., Bastian, A.J., 2019. Trading Symmetry for Energy Cost During Walking in Healthy Adults and Persons Poststroke. *Neurorehabil Neural Repair* 33, 602–613.
- Ryan, H.P., Husted, C., Lewek, M.D., 2020. Improving Spatiotemporal Gait Asymmetry Has Limited Functional Benefit for Individuals Poststroke. *J Neurol Phys Ther* 44, 197–204.
- Sánchez, N., Finley, J.M., 2018. Individual Differences in Locomotor Function Predict the Capacity to Reduce Asymmetry and Modify the Energetic Cost of Walking Poststroke. *Neurorehabil Neural Repair* 32, 701–713.
- Sánchez, N., Simha, S.N., Donelan, J.M., Finley, J.M., 2019. Taking advantage of external mechanical work to reduce metabolic cost: the mechanics and energetics of split-belt treadmill walking. *J Physiol* 597, 4053–4068.
- Sánchez, N., Simha, S.N., Donelan, J.M., Finley, J.M., 2020. Using asymmetry to your advantage: learning to acquire and accept external assistance during prolonged split-belt walking. *bioRxiv*, 2020.2004.2004.025619.
- Stenum, J., Choi, J.T., 2016. Neuromuscular effort predicts walk-run transition speed in normal and adapted human gaits. *J. experimental biology* 219, 2809–2813.
- Stenum, J., Choi, J.T., 2020. Step time asymmetry but not step length asymmetry is adapted to optimize energy cost of split-belt treadmill walking. *J Physiol* 598, 4063–4078.
- Stoquart, G., Detrembleur, C., Lejeune, T.M., 2012. The reasons why stroke patients expend so much energy to walk slowly. *Gait & Posture* 36, 409–413.

- Thelen, D.G., Anderson, F.C., 2006. Using computed muscle control to generate forward dynamic simulations of human walking from experimental data. *J. Biomech.* 39, 1107–1115.
- Tyrell, C.M., Roos, M.A., Rudolph, K.S., Reisman, D.S., 2011. Influence of Systematic Increases in Treadmill Walking Speed on Gait Kinematics After Stroke. *Phys. Ther.* 91, 392–403.
- Wellsandt, E., Failla, M.J., Snyder-Mackler, L., 2017. Limb symmetry indexes can overestimate knee function after anterior cruciate ligament injury. *J. orthopaedic & sports phys. therapy* 47, 334–338.
- Wonsetler, E.C., Bowden, M.G., 2017. A systematic review of mechanisms of gait speed change post-stroke. Part 1: spatiotemporal parameters and asymmetry ratios. *Top Stroke Rehabil* 24, 435–446.
- Wutzke, C.J., Sawicki, G.S., Lewek, M.D., 2012. The influence of a unilateral fixed ankle on metabolic and mechanical demands during walking in unimpaired young adults. *J. Biomech.* 45, 2405–2410.