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ORIGINAL ARTICLE

Kinematics associated with treadmill walking in Rett syndrome

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ABSTRACT

Background and purpose: Individuals with Rett syndrome suffer from severely impaired cognitive and motor performance. Current movement-related therapeutic programs often include traditional physical therapy activities and assisted treadmill walking routines for those individuals who are ambulatory. However, there are no quantitative reports of kinematic gait parameters obtained during treadmill walking. The purpose of this research was to characterize the kinematic patterns of the lower limbs during treadmill walking as speed was slowly increased.

Methods: Seventeen independently ambulatory females diagnosed with a methyl-CpG-binding protein 2 gene mutation walked on a motorized treadmill while joint kinematics were obtained by a camera-based motion capture system and analysis software.

Results: Stride times progressively decreased as treadmill speeds increased. There were significant main effects of speed on sagittal knee and hip ranges of motion and hip velocity. There were large joint asymmetries and variance values relative to other ambulatory patient populations, although variance values decreased as walking speed increased.

Conclusions: The results indicate that individuals with Rett syndrome can adapt their kinematic gait patterns in response to increasing treadmill speed, but only within a narrow range of speeds. We suggest that treadmill training for ambulatory individuals with Rett syndrome may promote improved walking kinematics and possibly provide overall health benefits.

➤ IMPLICATIONS FOR REHABILITATION

- Walking is an activity that can counter the negative impacts of the sedentary lifestyle of many individuals with disabilities, including those individuals with Rett syndrome.
- Documentation of the lower limb kinematic patterns displayed during walking by ambulatory females with Rett syndrome can be used by clinicians to evaluate their patients' gait performance in response to therapeutic and pharmacological interventions designed to promote walking.
- The ability to adapt to increases in treadmill speed suggests that a training program of treadmill walking may be effective in promoting improved gait performance in individuals with Rett syndrome.

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Rett; walking; kinematics; training; physical activity

Introduction

Mutations in the gene coding for methyl-CpG-binding protein 2 (*MECP2*) result in the neurodevelopmental disorder Rett syndrome (RTT). Although a relatively rare condition, worldwide RTT affects approximately 1 in 10,000 live born females [1]. Those born with RTT appear to develop typically until 6–18 months of age, at which point they begin to experience losses in verbal and social interactivity, as well as regressions in both fine and gross motor skills. Stereotypical hand movements, breathing difficulties, apraxia, ataxia, muscle hypertonia, limb rigidity and bruxism are some of the disabling symptoms commonly observed. A period of stabilization ensues, but bipedal postural control and walking are severely compromised. Walking ability often continues to decline at later ages, such that ultimately less than half remain able to walk [2].

Loss of ambulatory skills results in a number of additional physical problems such as muscle atrophy, limb contractures, decreased cardio-respiratory fitness and low overall physical fitness. Suggested physical therapy for individuals with RTT has included physical exercise designed to increase physical fitness and to maintain walking ability. These therapies have ranged from traditional physical exercises and stretching [3], guided physical activities in a multi-sensory room [4], and hydrotherapy [5]. A recent report describes the effectiveness of providing an enriched sensori-motor environment during therapeutic sessions designed to promote the development of motor skills and physical endurance [6]. Many of the activities focused on walking and balance control with the results showing that the enriched environment led to improved outcomes beyond those observed when therapy occurred in more traditional therapeutic environments. Other authors have suggested that a program incorporating walking may have a range of benefits for individuals with RTT including improved physical fitness and positive influences on their quality of life and wellbeing [7].

There are several reports exploring the possibility of individuals with RTT incorporating treadmill walking into their therapeutic

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regimen. Lotan et al. [8], explored the use of a treadmill-walking program to promote both walking skills and physical fitness and reported high correlations between improved walking performance and physical fitness. While promising, this study was conducted with only four girls with RTT. Three girls with RTT served as participants for an exploratory investigation using robot-assisted walking [9]. Preliminary results indicated the girls tolerated the robotic system, suggesting that this might be a clinical tool that merits further investigation.

Gait training with motorized treadmills is standard practice with a variety of populations with gait disorders, including those with Parkinson's disease, cerebral palsy and stroke. The results of these studies indicate improvement in gait patterns after treadmill gait training. Multiple investigations have documented improvements in overground gait parameters in these populations with treadmill gait training [10–15]. Individuals with RTT have neurological issues that are generally different than those conditions listed above, however there is no *a priori* reason to suggest that treadmill training would not provide benefits to those with RTT. Currently, treadmill walking is often a component of therapy programs for those with RTT, however its efficacy is unknown.

Prior to exploring the efficacy of a treadmill-walking program for improving functional walking characteristics and possibly overall physical fitness, is important to identify some typical kinematic features associated with treadmill walking of individuals with RTT. Such information is necessary to evaluate any potential improvements stemming from a treadmill-walking program. Although Downs and her colleagues have completed extensive efforts to develop reliable and valid measures of RTT walking that can be used as clinical measures [16], currently there are no reports of lower limb quantitative kinematics obtained from individuals with RTT during treadmill walking.

An important characteristic of effective walking is the ability to adapt to different speeds. Therefore, we were interested in determining if RTT participants could modify their gait to keep pace with increases in treadmill speed. The basic, rhythmical, alternating-limb-pattern, driving locomotion has long been proposed to be the product of a network of spinal neurons that require the mediation of higher order structures for the complete expression of goal-directed walking. This network is commonly referred to as a central pattern generator i.e., CPG [17–19]. Tonic innervation of the spinal locomotion circuits is regulated by noradrenalin and serotonin neurons. Without this innervation, which [20] suggests is impaired in those with RTT due to hypofunctioning of aminergic neurons in the brainstem, proper functioning of the spinal circuit is impaired. However, input into the circuit from lower limb muscle spindles and foot contact information [21] can assist in activating the circuit and generating the basic locomotor pattern [22]. The well-documented toe walking exhibited by those with RTT is proposed to be an adapted behavior that generates increased spindle input to the spinal circuitry, thereby activating the circuit [20]. This suggests that the basic spinal locomotion circuity remains generally intact and can be activated with increased sensory input. Successful adaptation to increasing treadmill speed for those with RTT would also suggest that the neural mechanisms available to integrate peripheral sensory information remain intact.

Previous work by our group explored details of the temporal features of gait of individuals with RTT during both overground and treadmill walking [23]. It was reported there were increases in stance time, but decreases in swing and double support time, when comparing treadmill to overground gait. Additionally, treadmill walking resulted in decreased variance in the temporal gait parameters, indicating treadmill walking resulted in a more regularized gait.

The primary purpose of this investigation was to determine if individuals with RTT were able to adapt their lower limb kinematics and associated stride times as treadmill speed progressively increased. Secondary considerations included exploring the relationships between joint angles and joint velocities, the symmetry of the motion of the two legs, the variance associated with our measures and the possible prevalence of excessive knee joint motion in the horizontal plane and pelvis motion in the frontal plane.

Methods

Study participants

Seventeen females diagnosed with typical RTT based upon the Neul et al. [24] criteria and carrying pathogenic MCEP2 mutation served as participants in this study. They ranged in age from 4 to 20 with a mean age of 10.8, standard deviation ± 5.3 and were receiving treatment at the Blue Bird Circle Rett Center at Baylor College of Medicine in Houston, TX. All participants were able to independently walk without orthotics and none were taking medication that would be expected to impact their motor control function including benzodiazepines. All procedures were approved by the Institutional Review Boards of the Baylor College of Medicine (H-35835) and the University of Houston (00000855). Participants' parents provided written informed consent for their daughters.

Data collection

The task involved walking on a dual-belt motorized treadmill (Bertec®) with embedded force plates under each belt. Participants were secured in an overhead harness that eliminated the possibility of falls but did not provide postural support during walking. Walking was initiated at 0.1 m/s and was increased by 0.1 m/s every 20 s. This continued until either the parents indicated this was the maximum speed the participant could obtain, or the participant began to exhibit signs of discomfort such as vocalizations, hand or facial gestures. Depending upon the participant's gait pattern and treadmill speed, the 20 s of data collection resulted in 10–14 strides for each treadmill speed.

Kinematics are measures that describe the motion of the body or its segments without regard for the forces that cause the movement. Gait kinematics are often reported as joint angle measures and associated velocities. Kinematic data were collected at 100 Hz using a Vicon® 12-camera motion capture system in combination with the plug-in gait data processing software. Reflective markers were applied bilaterally on the heel, toe, ankle, knee, shank and hips prior to data collection. Ground reaction forces from the treadmill force plates were sampled at 1000 Hz and synchronized with the kinematic data. Kinematic and force data were used in combination to identify heel strike and toe off. Additional details regarding the data collection procedures can be obtained in Layne et al. [25].

Data processing and analysis

A preliminary assessment of the data revealed that all 17 participants were able to walk between the speeds of 0.2 and 0.5 m/s. Therefore, the decision to analyze the kinematics associated with the speeds of 0.2, 0.3, 0.4 and 0.5 m/s was made. A custom MATLAB (MathWorks®) script was used to filter the kinematic data with a Butterworth low-pass filter with a 6 Hz cutoff frequency. Bilateral heel strikes were detected and the data between consecutive ipsilateral heel strikes were saved as individual strides for both the right and left legs. Heel strikes were identified as the minimum position of the heel marker during each gait cycle. The toe marker minimum was used in the event that the participant was toe walking on particular strides. The kinematic data were then time normalized such that each stride was represented by 100 samples. The time normalized waveforms were then amplitude normalized such that the joint angle value at the instant of heel strike was zero degrees. For each normalized stride, sagittal plane knee and hip angles were obtained for each treadmill speed, for each participant. Maximum and minimum angular values were obtained and used to calculate the range of motion (ROM) for each stride. After the individual joint angles were obtained, the velocity curves for each angle were calculated. Peak angular velocity for each stride and each participant were also identified.

After the above processing was completed, the limb with the greater ROM, for each joint, was identified. The data were then organized by side (i.e., left or right), with strides of greater ROMs grouped together and strides with lesser ROMs grouped together. Symmetry indexes (SI) between greater and lesser joint angles were computed using the following formula [26]. A SI of 0 reflects perfect symmetry between the two limbs.

$$Symmetry\ Index = 1 - \frac{Lesser\ Angle}{Greater\ Angle}$$

After it was determined that there were no significant differences between the joint ROM and associated peak velocities, the data from the two limbs were collapsed for further processing and analysis. The data from each variable were then averaged for each participant at each gait speed, and group means were calculated. It was found that many of variables were not normally distributed based upon the results of the Shapiro-Wilk test of normality. Therefore, Friedman tests were used to determine if significant differences existed between the ROMs for each joint across the four treadmill speeds. Subsequently Wilcoxon tests were utilized, as appropriate, with an applied Bonferroni correction. An alpha level of $p < 0.05$ was adopted for significance. Pearson's correlation coefficients between a joint's ROM and its velocity, and between stride times, and ROMs were calculated. The above procedures were also applied to peak velocity values to determine if limb velocity changed in response to increasing treadmill speed. To assess if the variance of the dependent measures was influenced by treadmill speed, the F test for equality of variance was employed.

Occasionally our participants' feet would cross midline and land in front of their other foot. Therefore, we were interested in determining the degree of knee joint motion in the horizontal plane. We applied the same processing techniques for the knee motion in the horizontal plane as those used for sagittal joint angles. Additionally, Downs et al. [7] reported minimal vertical motion of the hip during overground walking in her participants with RTT, as assessed with the Actigraph GTX3 tri-axial accelerometer device. To determine if this reported lack of vertical hip motion is a common feature of RTT gait, we analyzed the motion of the pelvis in the coronal plane. Based on the literature, we identified the range (plus two standard deviations) of transverse knee motion for typical individuals and determined which of our participants exceeded that range. Similarly, we identified the range (minus two standard deviations) of the vertical motion of the hip and determined if any of our participants failed to reach the degree of motion demonstrated by typical walkers.

Table 1. Median stride times by speed and statistical comparisons.

Speed (m/s)	Median (s)	Comparison	Z value	p values
0.2	1.43			
0.3	1.27	0.2 vs 0.3	−4.525	0.000
0.4	1.21	0.3 vs 0.4	−4.505	0.000
0.5	1.17	0.4 vs 0.5	−4.368	0.000

Table 2. Correlations between stride times and kinematics.

Pearson correlation coefficients (R)	S Knee	S Hip
Joint ROM & Stride times	0.38*	0.59*
Joint angular velocities & Stride times	0.45*	0.60*

*Significant at $p < 0.01$.

Descriptive statistics of the number of participants who either exceeded the typical range of transverse knee motion or failed to display the typical amount hip vertical motion are reported.

Results

Table 1 displays that as treadmill speed increased from 0.2 to 0.5 m/s, our participants were able to decrease their stride times and continue walking. The Friedman test revealed a significant effect for speed ($\chi^2 = 86.698$, $p < 0.000$). However, only three of the 17 participants tested were able to continue walking up to the speed of 0.6 m/s. Thus, although our participants were able to adapt to the increasing treadmill speeds, that ability was limited to a narrow range of speeds.

Joint ROMs

The Friedman test revealed a significant main effect of speed on sagittal knee ROM ($\chi^2 = 11.047$, $p < 0.011$). Follow up Wilcoxon tests indicated that the ROM between the speeds of 0.2 and 0.3 m/s (0.2 median = 9.425, 0.3 median = 10.03, Z= −2.812, $p < 0.005$) and 0.2 and 0.4 m/s significantly differed (0.2 median = 9.425, 0.4 median = 9.99, Z= −2.445, $p < 0.014$). No other comparisons reached significance (Figure 1). Comparisons between sagittal hip ROM and treadmill speed revealed a significant main effect of speed (($\chi^2 = 14.012$, $p < 0.003$). Significant ROM differences existed between the ROM for speeds 0.2 and 0.3 m/s (0.2 median = 10.155, 0.3 median = 11.385, Z= −3108, $p < 0.003$). There were no other significant differences for hip ROM comparisons.

Joint peak velocities

For peak sagittal knee velocities (measured in degrees per second), the Friedman test approached significance ($\chi^2 = 7.238$, $p < 0.065$). The Friedman test for peak sagittal hip velocities revealed a significant main effect of treadmill speed ($\chi^2 = 14.633$, $p < 0.002$). There were significant increases between treadmill speeds of 0.2 and 0.3 m/s (0.2 median = 35.0, 0.3 median = 39.1, Z= −2.711, $p < 0.007$) and between the speeds 0.2 and 0.4 m/s (0.2 median = 35.0, 0.4 median = 45.3, Z= −2.711, $p < 0.007$). Interestingly, there was a significant decrease between the speeds 0.4 and 0.5 m/s (0.4 median = 45.0, 0.5 median = 39.5, Z= −2.744, $p < 0.006$). The Friedman test for the knee velocity in the horizontal plane revealed no significant differences across the four speeds ($\chi^2 = 4.575$, $p < 0.206$). Figure 2 displays the median angular velocities across the treadmill speeds and the associated R^2 values. Table 2 provides the correlation coefficients between the stride times and joint ROMs and angular velocities.

There were no significant changes in the SIs for the knee and hip in the sagittal plane. Figure 3 reflects that our participants'

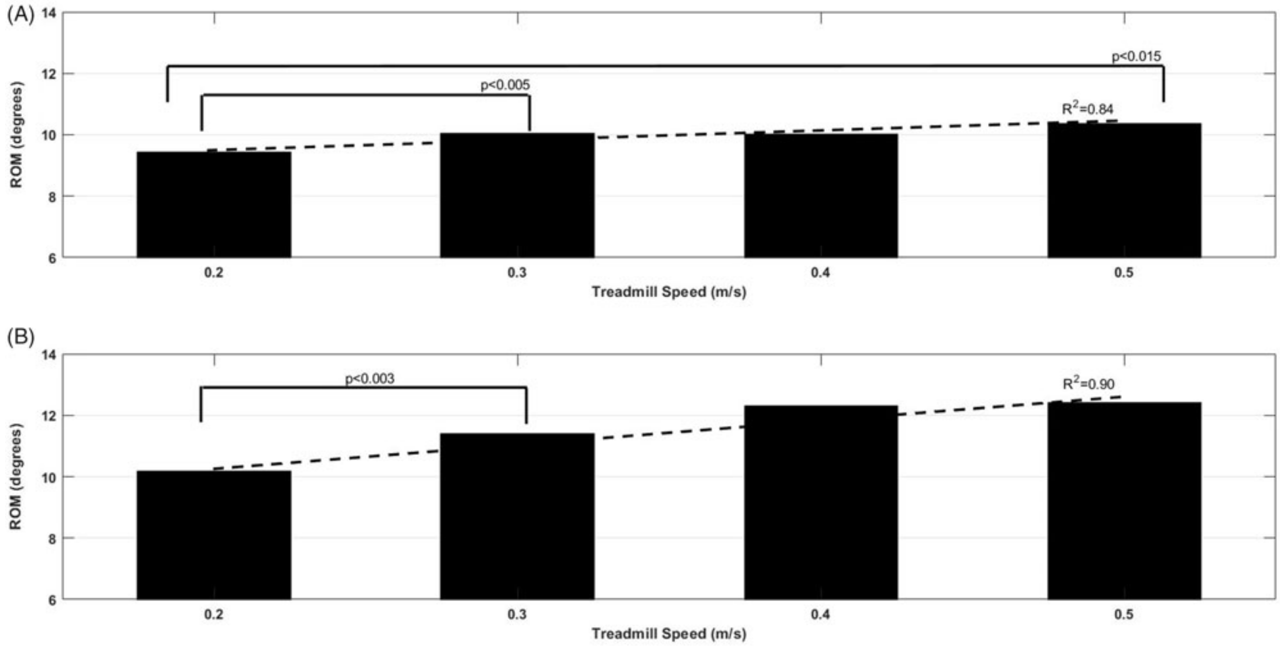

Figure 1. Median knee (A) and hip (B) ROM across treadmill speeds.

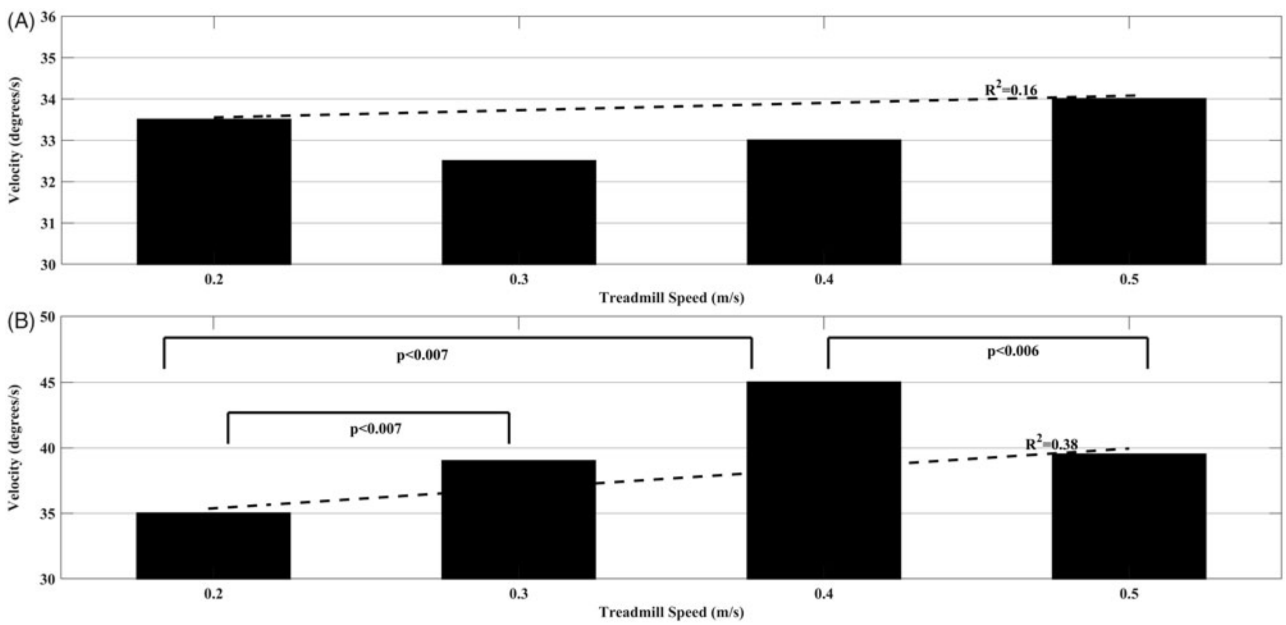

Figure 2. Median knee (A) and hip (B) joint angular velocity across speeds.

gait was asymmetrical, with all SI values being significantly greater than 0 (i.e., perfect symmetry).

Figure 4 illustrates the high correlations between the joints' ROM and their associated velocities as the treadmill speed increased.

The F tests assessing potential differences in the variance associated with joint ROM across speeds indicated that there were no differences resulting from changes in treadmill speed, although variance values were high. The same was true for the F tests comparing knee velocities across speeds. However, significant differences in variances were found for hip velocities between the speeds 0.2 vs 0.4 m/s (F = 2.444, $p < 0.006$), 0.2 vs 0.5 (F = 3.292, $p < 0.000$), and 0.3 vs 0.5 m/s (F = 2.169, $p < 0.015$). In all cases of significant F tests, the slower speed was always associated with the greater variances relative to the faster speed (Table 3).

Based on values obtained from typical individuals [27–29], a ROM of 10° was indicative of excessive motion in the transverse plane. There were only 13 instances, out of a possible 136, that exceeded this threshold across all speeds and both legs. There was no systematic effect of speed on knee transverse plane motion. To determine if our participants displayed typical pelvic motion in the coronal plane, we used a threshold of 0.7° as a minimum value. This value indicated if there was adequate peak motion in this plane [30,31]. Of the 136 measures, only six values

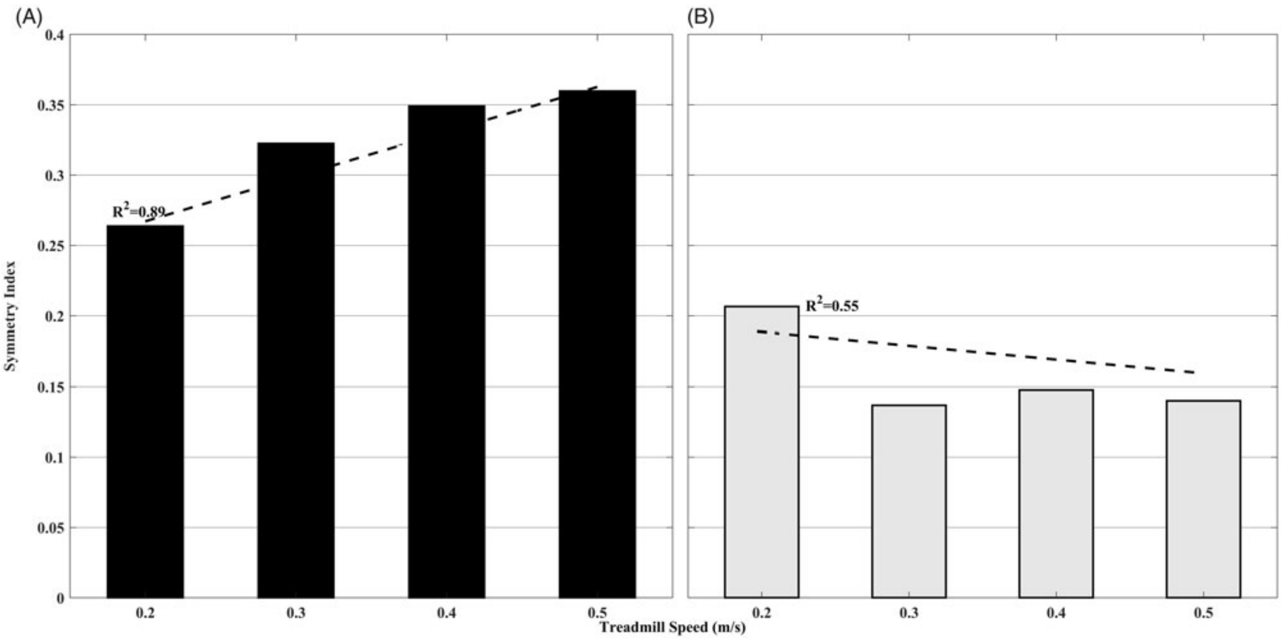

Figure 3. Symmetry index values for the sagittal plane motion knee (solid fill) and hip joints across treadmill speeds.

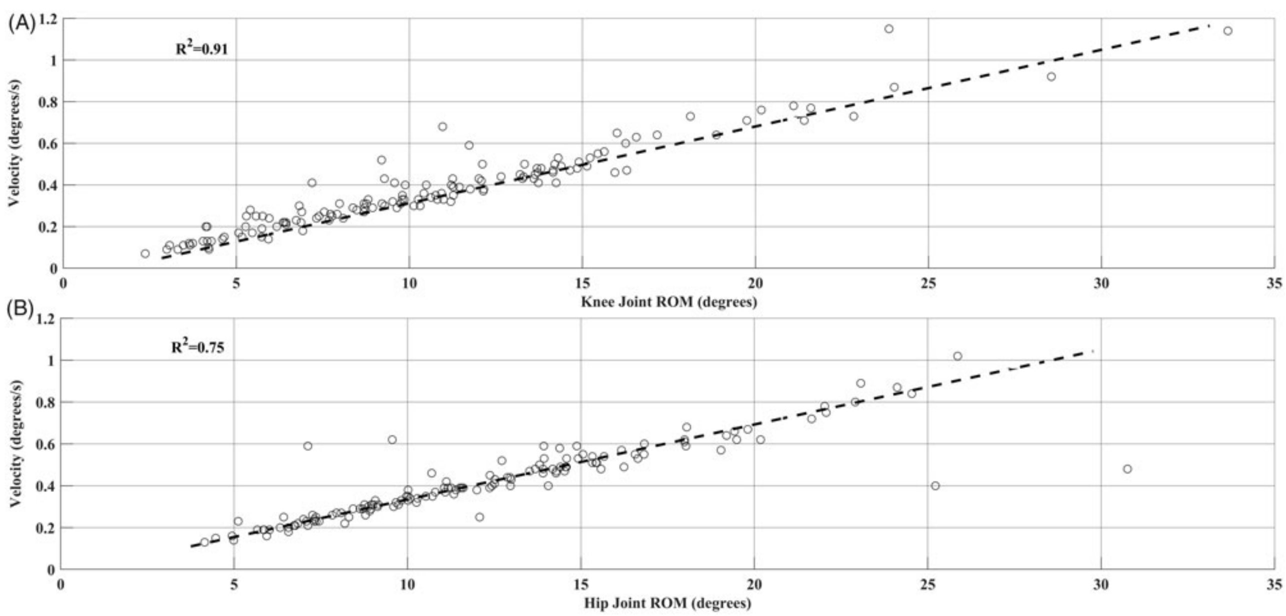

Figure 4. Relationships between ROM and associated angular velocities across treadmill speeds.

Table 3. Variance values for sagittal plane ROM, and joint velocities.

Speed (m/s)	Knee ROM (degrees)	Hip ROM (degrees)	Knee Velocity (m/s)	Hip Velocity (m/s)
0.2	25.9	32.0	0.048	0.071
0.3	35.8	30.3	0.046	0.047
0.4	34.8	23.1	0.043	0.029
0.5	21.7	19.9	0.027	0.022

fell below the minimum threshold value and these values were confined to just two participants. These data confirm that, with very few exceptions, our participants with RTT displayed a range of hip motion in the coronal plane associated with typical gait. The median transverse plane knee ROMs and median peak degrees of the hip in the coronal plane, across speeds, are displayed in Figure 5.

Discussion

In this report, we provide the first laboratory-based information regarding kinematic gait data collected from females with RTT. Characterizing the kinematic parameters associated with the walking of individuals with RTT is important to determine if pharmacological or therapeutic approaches are effective. We were interested in determining if individuals with RTT were able to successfully adapt their gait to increasing treadmill speeds. Successful adaptation would suggest that, despite abnormal kinematic parameters, the neurological mechanisms underlying sensory feedback responses associated with increased treadmill speed remain intact and participants can adapt their kinematic parameters accordingly.

As reported in Table 1, the participants were able to decrease their stride times as treadmill speed increased (just as has been

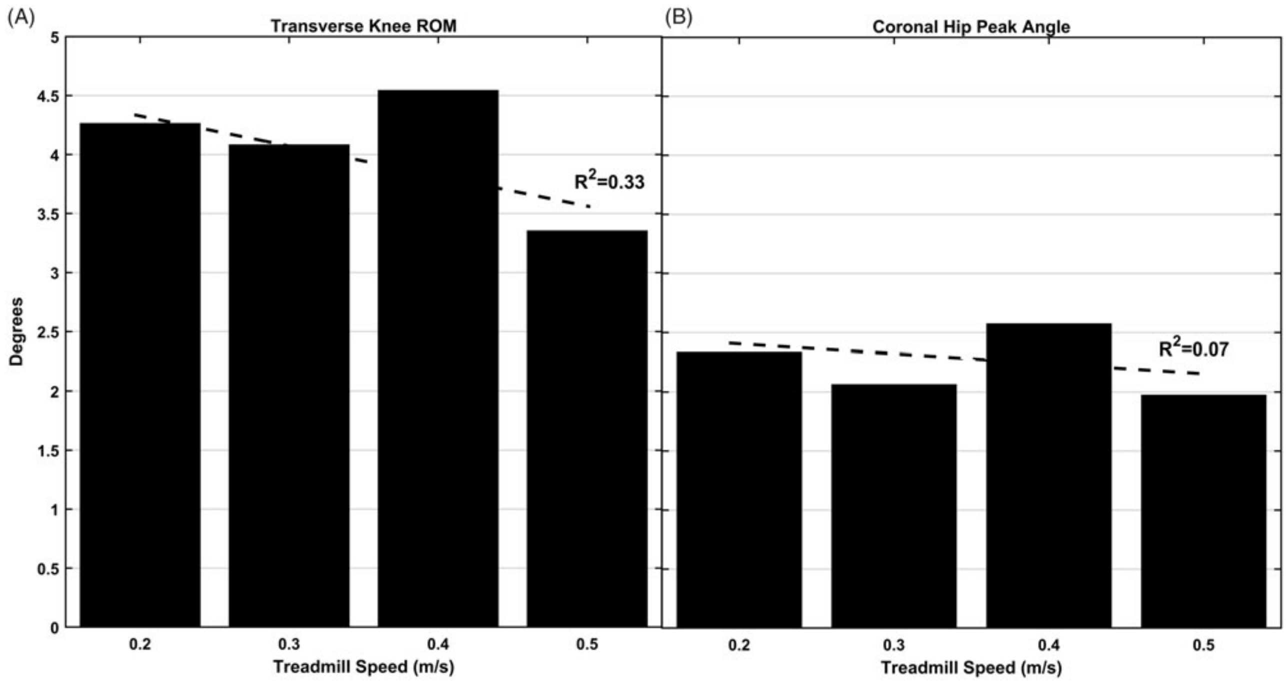

Figure 5. Median ROMs for knee transverse plane motion and median peak degrees for hip coronal plane motion across treadmill speeds.

demonstrated in a sample of typical participants [32]). However, these decreases occurred within a relatively narrow range of treadmill speeds (0.2–0.5 m/s). The average 10.5 year old in the Lythgo study, similar to the average age in this investigation, averaged 1.04 m/s with average stride times of 1.15 s when asked to adopt a slow gait [33]. To provide additional perspective, 9.5 year old children diagnosed with spastic diplegic cerebral palsy (CP) on average walked at a self-selected speed 0.86 m/s during overground walking [34]. This value is 72% greater than the maximum speed our participants walked on the treadmill. An additional study reported that 10 year old children with bilateral CP walked at 0.83 m/s on average, while those with unilateral CP walked on average at 1.01 m/s [35]. Although not necessarily surprising, these comparisons between children with CP and our similarly aged participants emphasize that girls with RTT walk significantly slower than those with CP.

Despite the minimal range of slow walking speeds, our participants did decrease their stride times such that they were able to maintain pace with the increasing treadmill speeds. This finding strongly suggests that our participants were able to both adequately detect sensory information indicating the treadmill speed was increasing as well as integrate that information and increase their lower limb velocities in response (thereby significantly decreasing stride times). This is consistent with Aoi et al.'s [21] assertion that foot contact information and muscle spindle input can activate the CPG and adjust the locomotor pattern to meet the lower limb movement demands associated with increasing treadmill speed. Consistent with the decrease in stride times, there are the significant increases in knee and hip ROMs and angular velocities associated with increases in treadmill speed. This has also been reported for a large range of typical individuals [36–38]. These significant main effects and the highly significant correlations between knee and hip ROMs and their associated angular velocities (see Figure 5) also reflect our participants' ability to modify their lower limb kinematic motion to adapt to increasing treadmill speed. Our data thereby suggest that participants have intact spinal locomotion circuity that can be regulated by sensory input and stimulated by walking within a narrow range of walking speeds. We speculate that our participants inability to increase their walking speed beyond 0.5 m/s may be primarily related to their failure to maintain attention on the walking task as well as their inability to preserve postural stability despite the safety that the harness provided. Although the spinal CPG may be able to produce the fundamental alternating lower limb motion necessary to walk, associated kinematics display a large amount of variance and the relationship between the two limbs is asymmetric. These features contribute to our participants' lack of postural stability, which prevents them from being able to further increase their walking speed.

Another notable feature of our participants' kinematics is the very small range of knee joint motion, despite some minimal but statistically significant speed-related increases. Consistent with our results, previous investigations have also reported minimal changes in knee motion associated with small increases in walking speed [39]. The median values ranged from 9.4 at 0.2 m/s to 10.3 at 0.5 m/s. This minimal knee ROM can be characterized as 'stiff-knee gait' (SKG) and contributes to the slow speeds at which our participants were able to walk. Typical individuals, when asked to walk at 0.3 m/s on a treadmill (the same speed that our participants walked at), had an average knee ROM of 46.1° and a hip ROM of 29.6° [39]. Carriero et al. [34] published data from a sample of children with spastic diplegia CP, aged 9.5 years. They reported a mean range of 41.3°, while an aged match sample of typically developing children displayed a ROM of 65.4°. Individuals post-stroke also exhibit significantly reduced knee ROM during gait [40,41]. For example, the post-stroke participants in Chen et al.'s [40] investigation displayed peak knee flexion of 37.8° with their paretic limb, while typical participants had average peak knee flexion values of 61.9°. Thus, even patient populations that have been characterized as displaying SKG had significantly greater knee motion than our participants. Concerning hip ROM in the sagittal plane, Carriero's et al. study [34] reported a range of 47.1° for children with CP and 49.9° for typically developing children. Again, these values are significantly greater than were observed in the current study.

Our sample of females with RTT have an extremely limited lower limb ROM as well as a limited range of walking speeds. Both post-stroke individuals and those with CP who exhibit stiff-knee gait also display compensatory kinematic strategies, primarily hip hiking and increased circumduction to ensure adequate toe clearing [40,42]. Interestingly, except in rare cases, our participants showed no tendency toward either of the traditional kinematic compensations associated with SKG. The treadmill speeds were such that, despite the limited of knee and hip ROMs, they were able to achieve enough toe clearance to maintain limb motion at the given speeds. This is consistent with a recent report that ambulatory females with RTT were able to walk on a treadmill [43]. However, this report did not indicate the speeds at which their participants walked, only that they walked for six minutes at their 'maximal' speed. As the treadmill speed exceeded 0.5 m/s, the vast majority of our participants exhibited signs of discomfort and treadmill speed was immediately decreased and testing discontinued. We hypothesize that, unlike those individuals with CP or post-stroke who walk faster than our participants and demonstrate compensatory kinematic strategies, our participants were unable to modify their gait with kinematic strategies that would enable them to walk at faster speeds. Possible factors that may contribute to our participants' slow gait speeds are discussed below.

There are several factors identified in the literature that are related to severely reduced lower limb ROMs, particularly that of the knee. Often, individuals with CP and post-stroke demonstrate SKG. This has been attributed to hyperactivity of the rectus femoris [40,44]. Another suggested cause of SKG is a lack of adequate push off at the ankle [45] leading to reduced knee velocity at toe off and reduced passive knee flexion [46,47]. Reduced hip joint velocity associated with weak hip flexors is also suggested to be a potential cause of SKG [48,49]. All of these muscle-related issues are likely factors in severely reduced lower limb ROMs and contributors to the slow walking speeds observed in the current study

Besides resulting in gait kinematics that significantly reduce the speed at which our participants could walk, these kinematic patterns are energy inefficient [40,50] with oxygen consumption and cost being elevated [51]. An investigation of 12 females with RTT walking for six minutes on a treadmill reported that energy production was low relative to typical individuals, resulting in fatigue within a few minutes of walking [43]. As observed in Figures 3 and 4, our participants had large symmetry indices and it is worth noting that there was a significant linear trend for knee flexion asymmetry to increase as treadmill speed increased (R^2=0.90). For comparative purposes, a gait study of individuals with peroneal nerve palsy displayed median knee joint angular asymmetry of 20% from perfect symmetry [52], while a group of typical individuals displayed a 3.7% deviation from perfect symmetry [53]. In contrast, our knee joint asymmetries ranged from 26% at 0.2 m/s to 36% at 0.5 m/s, reflecting a high degree of asymmetry. Significant kinematic asymmetries during gait are part of an overall pattern of lower limb motion that is energetically inefficient and will result in a rapid rate of fatigue development.

Although there was a high degree of knee motion asymmetry in the sagittal plane, this disordered motion pattern did not extend to motion in the transverse plane. Only 9.6% of the comparisons (13 of 136, see Results), displayed excessive motion in the transverse plane. This finding indicates that our participants' feet were rarely crossing over each other to the extent it would cause increased difficulty in walking. However, it is important to keep in mind that our findings were based on data obtained during treadmill walking. It is possible that, with the increased flexibility associated with overground walking, our participants would display a greater prevalence of crossing of their feet (i.e., greater lower body segment motion in the transverse plane). We suggest that the treadmill allows for less flexibility in the patterns of body segment motion relative to those during overground walking.

The findings indicate that our participants walked on the treadmill with vertical hip motion that fell within the range of typical walkers. Downs et al.'s [7] finding of minimal hip vertical motion may have been a function of the tri-axial accelerometers used in that investigation to record data during walking. Tri-axial accelerometer technologies are not generally used to obtain kinematic measures and require mathematical integration of the acceleration signal to ultimately obtain displacement data. Conversely, a camera-based motion analysis system, such as the one used in the current investigation, directly records the position of reflective makers and thereby increases the accuracy of the kinematic data, relative to accelerometer-based systems. Additionally, it is also plausible that the difference between our data and Downs et al.'s findings result from differences in lower limb segment motion associated with the treadmill versus overground walking mechanics. It is important to bear in mind that the reported findings were collected from individuals who could ambulate independently. Our findings of typical patterns of hip motion in the coronal plane further emphasizes that disordered patterns of lower limb motion are primarily limited to the sagittal plane in individuals with RTT.

The data from the current study provides evidence that a relatively large sample of ambulatory individuals with RTT are able to walk on the treadmill and modify their kinematic pattern such that they are able to increase their walking speed within a limited range. Despite kinematic patterns that lead to SKG, poor dynamic postural control and limited concentration on the walking task, we suggest that ambulatory RTT individuals may benefit from a physical activity program that includes regular bouts of treadmill walking [4–6,23,43]. Heart rate, cardiac vagal tone, mean arterial blood pressure, cardiac sensitivity to baroreflex, and transcutaneous partial pressures of oxygen sampled in females with RTT respond to treadmill walking in patterns that are similar to those of typical individuals [43].

Besides the possibility of improved physical fitness, a second potential benefit of a treadmill walking program would be improvements in gait kinematics and postural control dynamics, possibly resulting in increases in walking speed. Increases in walking speed have been reported to improve gait kinematics. For example, 20 post-stroke participants were exposed to a treadmill walking protocol that required them to walk as fast as possible. The results demonstrated that compared with their self-selected speed, walking as fast as possible improved the symmetry between their hemi-paretic and nonparetic limbs, as well as increases in knee and hip ROM [54]. Willerslev-Olsen, et al. [55] reported that the benefits of one month of daily treadmill training with 16 children with CP included significant increases in speed, improved dorsiflexion during the late portion of the swing phase and increase weight acceptance on the heel during early stance. The authors proposed that treadmill gait training may promote plasticity in the corticospinal tract driven by sensory input into the CPG, resulting in observed improvements in gait. Similar results following treadmill gait training were reported in individuals who had incomplete spinal cord injuries [56].

An important finding is that improvement in gait kinematics can be achieved by walking at less than an individual's maximal speed during treadmill training [54]. Although this study was completed with individuals with chronic stroke, it has direct relevance for those with RTT who often struggle to sustain their maximal achievable gait speed, even during treadmill walking. Given the above information, it is reasonable to hypothesize that ambulatory females with RTT will also benefit from a treadmill gait training protocol.

Although the number of participants in this investigation was substantial for the study methodology and the participant population, the absolute number was relatively limited. An additional limitation is the relatively large age range of our participants, thereby limiting our ability to make more definitive conclusions about gait parameters within a smaller participant age range. Future investigators may choose to restrict the age range of their participants, in addition to exploring the potential benefits of a treadmill-walking program.

In conclusion, our investigation has demonstrated that ambulatory females with RTT are able to adapt their stride times and lower limb kinematics in response to increases in treadmill belt speed, although within a limited range of gait speeds. Additionally, we have characterized several kinematic parameters associated with RTT, including very limited knee and hip ROM and significant asymmetrical motion. Our results suggest that treadmill gait training may be beneficial to individuals with RTT but that additional research is needed to explore this proposition.

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Disclosure statement

The authors report no declaration of interest.

Data deposition

The data supportive of this study can be found on Figshare at 10.6084/m9.figshare.7784789

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