

Marshall University

Marshall Digital Scholar

Physical Therapy Faculty Research

Physical Therapy

1-2020

Improvement in overground walking after treadmill-based gait training in a child with agenesis of the corpus callosum

Gena Henderson

Matthew Beerse

Huaqing Liang

Diego Ferreira

Jianhua Wu

Follow this and additional works at: https://mds.marshall.edu/physical_therapy_faculty



Part of the [Physical Therapy Commons](#)

1
2
3 1 **Improvement in overground walking of a child with agenesis of the corpus callosum after**
4
5 2
6 **treadmill-based gait training**
7
8 3
9

10 4 **Abstract**

11
12 5 **Background and Purpose:** Agenesis of the corpus callosum (ACC) is a rare congenital brain
13
14 6 defect that produces a wide variety of cognitive and motor impairments. Literature is scarce
15
16 7 regarding this population's response to physical rehabilitation. Treadmill-based gait training
17
18 8 (TT) has been shown to improve walking ability in some pediatric populations, but has not been
19
20 9 investigated in children with ACC.
21
22

23
24 10 **Case Description:** Our subject was a 13-year-old female with ACC and cortical visual
25
26 11 **impairment who ambulated independently using a reverse walker for household and short**
27
28 12 **community distances.** We implemented a **home-based TT intervention** (two phases of 3-
29
30 13 month training over six months) and **conducted a lab-based gait analysis** at four time points:
31
32 14 baseline, after each of two training phases, and 3 months after cessation of training. The
33
34 15 intervention consisted of weekly bouts of TT. Phase 1 incorporated 15-minute forward,
35
36 16 backward, and incline walking; Phase 2 continued this protocol and added another 10-minute
37
38 17 short-burst interval training. Data collected at each lab visit included spatiotemporal parameters
39
40 18 and kinematics (joint angles) during overground and treadmill walking.
41
42

43
44 19 **Outcomes:** After both phases of training, our subject increased step length, decreased step width
45
46 20 and foot progression angle, **and decreased variability of most spatiotemporal parameters.**
47
48 21 Further, after Phase 2 our subject increased peak extension at the hip, knee and ankle, **decreased**
49
50 22 **crouch gait, and improved minimum foot clearance during overground walking. Most gait**
51
52 23 **improvements were retained for three months after cessation of the intervention.**
53
54
55
56
57
58
59
60

1
2
3 24 **Discussion:** This report demonstrates that TT may be a safe and effective treatment
4
5 25 **paradigm for children with ACC. Future research should investigate the effect of**
6
7 26 **intervention dosage on gait improvements and generalization in individuals with ACC.**
8
9
10 27
11
12 28
13
14 29
15
16 30
17
18 31
19
20 32
21
22 33
23
24 34
25
26 35
27
28 36
29
30 37
31
32 38
33
34 39
35
36 40
37
38 41
39
40 42
41
42 43
43
44 44
45
46 45
47
48 46
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review Only

47 Introduction

48 Agenesis of the corpus callosum (ACC) is a congenital brain defect; its exact incidence is
49 not well documented, but the highest estimates place it as occurring in seven of every 1000
50 births.¹ A wide variety of presentations, ranging from normal IQ and motor function to
51 significant cognitive and motor impairments can be seen in ACC.²⁻⁴ The incidence of specific
52 presentations is unclear in the literature. A survey by Moes, Schilmoeller & Schilmoeller⁵
53 reported that developmental delay was present in 66-79% of children with ACC and noted
54 significantly delayed attainment of most gross motor milestones when compared to a typically
55 developing sibling group. In contrast, a meta-analysis by D'Antonio, et al.² reported gross motor
56 delays in just 4.4% of children with isolated complete ACC and cognitive delays in 15.2% and
57 17.3% of children with isolated partial and complete ACC, respectively.

58 Although the presentation of ACC varies significantly, it has been reported to affect
59 individuals at all levels of the International Classification of Functioning, Disability and Health
60 framework⁶, including Body Structures and Functions, Activities, and Participation. Some of the
61 most common sensorimotor impairments reported in individuals with ACC include low muscle
62 tone, decreased cognitive function, difficulties in learning, and poor sensory processing, balance
63 and bilateral coordination.^{2,4,5,7-9} Delayed gross motor skills have been reported in children with
64 low muscle tone¹⁰ **and in children with** decreased cognition¹¹, suggesting that children with
65 ACC who demonstrate hypotonia or cognitive delays may also be at risk for motor delays.
66 Interestingly, Meyer, Roricht & Niehaus³ reported on six individuals who were incidentally
67 discovered to have callosal agenesis without any symptoms other than an inconsistent difficulty
68 with achieving heel-toe gait. This suggests that abnormalities in gait may be present in otherwise

1
2
3 69 unaffected individuals with ACC. However, the specific characteristics of gait in children with
4
5 70 ACC have not been examined in the literature.
6

7
8 71 Additionally, despite evidence of the potential for motor delays in children with ACC^{2,5,9},
9
10 72 there is a lack of literature describing this population's response to rehabilitation. Chiappedi &
11
12 73 Bejor¹ recommend that rehabilitation, including physical therapy (PT), begin early in children
13
14 74 with ACC to minimize secondary complications and take advantage of the plasticity of the young
15
16 75 child's nervous system. Akbal¹² described a case in which a 2-year-old child with ACC
17
18 76 responded well to conventional PT intervention, gaining the ability to sit, stand, and walk with an
19
20 77 assistive device over the course of five years of treatment. Pacheco, Queiroz, Niza, da Costa &
21
22 78 Ries¹³ also reported improved postural control and transfers in a 2-year-old child with ACC
23
24 79 following PT intervention that focused on functional training. Examination of the efficacy of
25
26 80 specific training protocols, as well as the response of older children to therapy, is lacking.
27
28
29

30
31 81 Treadmill training (TT) has **shown** its efficacy in accelerating the onset of walking and
32
33 82 improving the quality of gait pattern in infants with Down Syndrome¹⁴⁻¹⁷ although the literature
34
35 83 supporting its efficacy in other populations is inconclusive.^{15,18} However, improved walking
36
37 84 speed following some TT protocols has been observed in children with cerebral palsy (CP)¹⁹⁻²¹
38
39 85 and in ambulatory young children with developmental delay¹⁸. In their systematic review,
40
41 86 Dewar, Love & Johnston²⁰ noted that ambulatory children with CP who participated in TT that
42
43 87 progressively increased belt speed demonstrated the **greatest increase** in walking speed.
44
45 88 Backward walking on a treadmill has also been reported to improve postural control²², step
46
47 89 length, walking speed, and postural symmetry²³ in children with hemiplegic CP. Incline walking
48
49 90 on a treadmill has been found to increase the activity of the hip, knee, and ankle extensors in
50
51 91 healthy young adults.²⁴ Further, Bjornson, Moreau & Bodkin²⁵ found that a TT protocol
52
53
54
55
56
57
58
59
60

1
2
3 92 utilizing short-burst interval training (SBIT) globally improved walking performance in children
4
5 93 with CP, increasing overground walking speed, Timed Up-and-Go performance, and amount of
6
7
8 94 time spent engaging in moderate-to-high intensity walking during the day. As reduced capacity
9
10 95 for rapid force generation is strongly correlated with decreased functional walking ability²⁶ and
11
12 96 slower walking velocities²⁷ in individuals with CP, SBIT may potentially present an effective
13
14
15 97 approach to augmenting training effects in other populations. However, to our knowledge, a TT
16
17 98 paradigm including these components has not been investigated in children with ACC.

19 99 The purpose of this study, therefore, is to investigate the effect of a novel treadmill
20
21 100 intervention paradigm on the gait parameters of a child with ACC. This intervention was
22
23
24 101 designed with two phases, the first of which incorporated **15 minutes of** forward, backward, and
25
26 102 incline walking (Phase 1), and the second of which maintained the protocol of Phase 1 and added
27
28 103 **another 10 minutes of** SBIT (Phase 2). We hypothesized that our subject would improve (a)
29
30 104 spatiotemporal gait parameters, such as increasing walking speed and step length, and (b) joint
31
32 105 kinematics, such as increasing peak joint extension angles, following Phase 1 of TT, that our
33
34 106 subject would demonstrate greater improvements in these same parameters following Phase 2,
35
36 107 and that the improvements would persist three months following cessation of the TT protocol.
37
38
39

40 108

42 109 **Patient Information**

44 110 Our subject was a 13-year-old female with ACC and cortical visual impairment **that**
45
46 111 **limited her vision both at a distance and in her lower visual field.** This study was approved
47
48 112 by the institutional review board at the hosting university. A **parent consent** form was signed by
49
50 113 the parent and assent was obtained from the subject.
51
52

53
54 114

115 **Clinical Findings**

116 **At baseline, our subject demonstrated hypotonia throughout her trunk and**
117 **extremities. She also demonstrated weakness about her trunk and lower extremities, most**
118 **notably her abdominals, hip extensors, and ankle plantarflexors, as evidenced by a**
119 **crouched stance and excessive anterior pelvic tilt during both standing and walking. She**
120 **ambulated with modified independence using a reverse walker for household and short**
121 **community distances and was able to transition independently in and out of her walker**
122 **from both short-sitting on a chair and sitting on the floor. Her height and body mass**
123 **increased** from 116.5 to 122cm and from 26.3 to 27.4 kg, respectively, between visit 1 (before
124 intervention) and visit 4 (three months after intervention).

126 **Therapeutic Intervention**

127 The subject received an intervention that consisted of once-weekly bouts of TT for two
128 phases of twelve weeks each. All TT sessions were conducted by the same licensed physical
129 therapist in the subject's home on a Life Fitness T3i home fitness treadmill (Rosemont, IL) **with**
130 **a 137cm x 51cm belt.**

131 *Phase 1*

132 The protocol consisted of ten minutes forward incline walking followed by five minutes
133 backward walking (Table 1); no rest was provided between forward and backward walking. This
134 phase of the training protocol was designed to increase walking speed by combining progressive,
135 incremental increases in belt speed with incline and backward walking to increase demand on
136 hip, knee, and ankle extensors.^{24,28}

1
2
3 137 The subject wore shoes and bilateral supramalleolar orthoses during the training. During
4
5 138 forward walking, the subject held an anterior bar on the treadmill independently. During
6
7
8 139 backward walking, the subject was given bilateral hand-held assist by the therapist. For forward
9
10 140 walking, treadmill speed was initially set at 0.22 m/s, generally considered the minimum speed
11
12 141 for household ambulation.²⁹ Speed was increased as quickly as possible, so long as the subject
13
14 142 visually appeared to achieve near-full knee extension in terminal swing and maintain an upright
15
16 143 trunk for >75% of steps (Table 1). Speed was progressively increased up to 1.34 m/s, the typical
17
18 144 walking speed for community ambulators.²⁹ After a speed of 1.34 m/s was reached, the grade
19
20 145 was increased by the increment of 0.5% and the speed was lowered when necessary. For
21
22 146 backward walking a similar pattern was followed, although treadmill speed was only increased
23
24 147 up to 0.36 m/s due to the subject's difficulty coordinating backward stepping and intolerance to
25
26 148 higher speeds.

30 149 *Phase 2*

31
32
33 150 The protocol consisted of the protocol **at phase 1** immediately followed by ten minutes
34
35 151 of SBIT consisting of alternating bouts of 30-second slow walking and 30-second fast walking
36
37 152 (Table 1). This resulted in a total training time of 25 minutes for each session during Phase 2.
38
39 153 Treadmill speed was adjusted following the same guidelines set forth in Phase 1. For the SBIT,
40
41 154 the "slow" speed was set to 75% and the "fast" speed to 150% of the current forward walking
42
43 155 speed.

46 156

48 157 **Timeline of gait evaluation**

49
50 158 Gait data **were** collected in our lab at four time-points: before the intervention (visit 1),
51
52 159 within one week of completing Phase 1 (visit 2) and Phase 2 (visit 3) of the intervention, and
53
54 160 three months after cessation of the intervention (visit 4). Gait data were collected using an eight-

1
2
3 161 camera Vicon motion capture system (Vicon, Denver, CO) with a Plug-In Gait Lower Body
4
5 162 marker set and a sampling rate of 100 Hz. Reflective markers were placed bilaterally on the
6
7 163 **anterior superior iliac spine, posterior superior iliac spine**, lateral thigh, lateral knee, lateral
8
9 164 tibia, lateral ankle, heel, and toe. Anthropometric measures including height, weight, and leg
10
11 165 length were collected. The subject walked barefoot overground **at a self-selected speed** for five
12
13 166 good trials **in which the subject walked through the 10m camera field without stopping** with
14
15 167 a reverse walker, and on a treadmill **at various speeds while holding onto an anterior bar** for
16
17 168 two minutes. **Three treadmill speeds were used: her overground walking speed from the**
18
19 169 **first visit, twice that speed, and three times that speed (which was approximately the top**
20
21 170 **speed she achieved during TT); these speeds ranged from 0.4 to 1.2 m/s.**

22
23
24
25
26 171 Gait data were processed using Vicon Nexus 2.3 (Vicon, Denver, CO). Gait events (heel-
27
28 172 strike and toe-off) were manually labeled for overground trials and were **identified** using an
29
30 173 **anterior/posterior (AP) velocity** change of each heel marker for treadmill trials; a velocity
31
32 174 change from positive to negative indicated a heel-strike event and a change from negative to
33
34 175 positive indicated a toe-off event.^{30,31} Spatiotemporal parameters and joint kinematics were
35
36 176 calculated **for both overground and treadmill walking** using custom MATLAB (Mathworks,
37
38 177 Natick, MA) programs.

39
40
41
42 178 Step length was calculated as the AP difference between the ipsilateral and contralateral
43
44 179 heel markers at heel strike. Step width was calculated as the medial/lateral (ML) difference
45
46 180 between the heel markers at heel strike. Foot progression angle (FPA) was calculated as the
47
48 181 angle between the toe marker and the heel marker in reference to the line of forward progression.
49
50 182 Positive FPA values represent out-toeing, while negative FPA values represent in-toeing.
51
52
53 183 Temporal variables included cycle, stance, swing, and double support times of gait cycle. Cycle
54
55
56
57
58
59
60

1
2
3 184 time was defined as the elapsed time between two consecutive ipsilateral heel strikes. Stance
4
5 185 time was defined as the time between each ipsilateral heel strike and subsequent toe off, while
6
7
8 186 swing time was defined as the time between each ipsilateral toe off and subsequent heel strike.
9
10 187 Double support time was calculated for the first double support phase of each gait cycle.

11
12 188 We determined peak joint extension angles at the hip, knee, and ankle. Hip joint angles
13
14 189 were calculated as the angle between the vector formed by the knee and thigh markers and a line
15
16
17 190 perpendicular to the vector formed by the ipsilateral ASIS and PSIS, projected onto the sagittal
18
19 191 plane. A positive angle represents hip flexion and a negative angle represents hip extension.
20
21 192 Knee joint angles were calculated as the angle between the vector formed by the knee and thigh
22
23 193 markers and the vector formed by the knee and tibia markers; angles were subtracted from 180°
24
25
26 194 to give the anatomical angle. Ankle joint angles were calculated as the angle between the vector
27
28 195 formed by the knee and ankle markers and the vector formed by the heel and toe markers. Angles
29
30 196 were subtracted from 90°; positive values represented dorsiflexion and negative values
31
32
33 197 represented plantarflexion. Joint angles were time-normalized to 100% of a full gait cycle, and
34
35 198 peak joint extension angles were defined as the maximum angle at each joint for each gait cycle.
36
37 199 Normalized trials across each visit were then averaged together to produce mean angles for each
38
39 200 joint. **As kinematic patterns of treadmill walking at each visit were found to be similar,**
40
41
42 201 **regardless of speed, we collapsed the kinematic treadmill data across all speeds prior to**
43
44 202 **further analysis.** To investigate the variability of our variables, coefficient of variation (CV)
45
46 203 was calculated as the ratio of standard deviation to mean value for each variable. All trials within
47
48 204 each visit were combined when calculating the CV.

49 205 Additionally, our subject demonstrated a crouched gait pattern at baseline, an often-
50
51
52 206 progressive abnormality associated with increased knee flexion, decreased foot clearance in
53
54
55
56
57
58
59
60

1
2
3 207 swing phase³², and increased fatigue.³³ We therefore evaluated both progression of crouch,
4
5 208 defined as the amount of knee flexion at initial contact³⁴, as well as minimum foot clearance
6
7 209 (MFC). To calculate MFC, the trajectory of the toe marker during swing phase of each step was
8
9 210 plotted and visually identified as either a bimodal pattern with two peaks or a unimodal pattern
10
11 211 with only one peak (Fig. 1a-b).³⁵ The percentage of steps following a bimodal pattern was
12
13 212 calculated. MFC was calculated on all steps following a bimodal pattern and was defined as the
14
15 213 minimum vertical height **of the toe marker** between the two peaks of the toe marker during
16
17 214 swing phase³⁶.
18
19
20
21
22

215

216 **Outcomes**

217 *Treadmill intervention*

218 The subject completed 10/12 recommended training sessions over each phase of
219 intervention. Missed sessions were due to subject illness or travel. **The subject was able to**
220 **tolerate increases in treadmill parameters at most visits without report of adverse effects**
221 (Table 1).

222 *Overground spatiotemporal gait parameters and variability*

223 **The subject demonstrated improvements in some overground spatial gait**
224 **parameters over the course of study. Although her walking speed initially increased after**
225 **Phase 1, this increase was not maintained after Phase 2 and returned to baseline by visit 4**
226 **(Table 2); cadence followed a similar pattern (Fig 2a). Step length increased by 36.9% from**
227 **visit 1 to visit 4 (Fig 2c). Step width decreased at visits 2 and 3 and remained 48.3%**
228 **decreased from baseline at visit 4; it demonstrated substantially greater improvements**

1
2
3 229 following Phase 2 than following Phase 1 (Fig 2e). FPA decreased consistently across all
4
5 230 visits, demonstrating an 18.4% decrease from baseline at visit 4 (Fig 2g).
6

7
8 231 Several spatiotemporal parameters demonstrated decreased variability over the
9
10 232 course of the study. Variability of cadence (Fig 2b), step length (Fig 2d), FPA (Fig 2h), cycle
11
12 233 time, stance time, and swing time (Table 2) all decreased across the course of the study.
13
14 234 Step width variability was less consistent, increasing initially but returning to baseline by
15
16 235 visit 4 (Fig 2f).
17

18
19 236 *Overground peak joint extension angles*
20

21 237 All peak joint extension values were found when the joints were in flexed positions;
22
23 238 however, their values substantially decreased following Phase 2 of the intervention (Table
24
25 239 3). At visit 4, peak hip extension was 19.57° (21.6% increase from baseline), peak knee
26
27 240 extension was 23.93° (13.0% increase from baseline), and peak ankle plantarflexion was
28
29 241 2.49° (60.6% increase from baseline). The measured changes in our subject's joint angles
30
31 242 generally exceed the minimal detectable change for healthy adults³⁷, indicating that these
32
33 243 changes are outside the measurement error associated with motion capture.
34
35

36
37 244 *Overground crouch angle*
38

39
40 245 Crouch angle worsened between visits 1 and 2 but demonstrated a notable improvement
41
42 246 following Phase 2 (Table 3). Average crouch angle decreased to 23.97° at visit 3 and was
43
44 247 32.33° at visit 4, remaining 12.6% decreased from baseline.
45

46
47 248 *Overground minimum foot clearance*
48

49 249 The subject demonstrated improvements in MFC both during and after training. While
50
51 250 both bimodal (Fig 1c) and unimodal (Fig 1d) trajectories were seen at all visits, the
52
53 251 percentage of steps in which the toe marker followed a bimodal trajectory increased to
54
55
56
57
58
59
60

1
2
3 252 **34.9% by visit 4, a 29.3% increase from baseline (Fig. 1e). Typically developing children**
4
5 253 **demonstrate a MFC of approximately 2 cm³⁸; our subject's MFC during steps with a**
6
7 254 **bimodal trajectory increased to 1.46 cm by visit 4, a 33.9% increase from baseline (Fig 1f).**

255 *Treadmill peak joint extension angles and crouch angles*

12 256 Kinematic patterns were distinct between overground and treadmill walking at all visits,
13
14 257 with treadmill patterns more closely approximating typical movement (Fig. 3). **At visit 4, peak**
15
16 258 **hip extension was 16.67° (35.1% increase from baseline), peak knee extension was 20.13°**
17
18 259 **(29.7% increase from baseline), and peak ankle plantarflexion was -0.84° (112.2% increase**
19
20 260 **from baseline). Like overground walking, peak joint extension during treadmill walking**
21
22 261 **demonstrated greater improvements following Phase 2 than following Phase 1 and retained**
23
24 262 **for three months after cessation of the intervention. Crouch angles during treadmill**
25
26 263 **walking also demonstrated notable improvements; it decreased to 13.97° at visit 3 and was**
27
28 264 **21.25° at visit 4, remaining 30.0% decreased from baseline.**

266 **Discussion**

37 267 Overall, TT was found to be a **safe**, well-tolerated, and effective paradigm to improve the
38
39 268 walking ability of our subject with ACC. TT is regarded as an effective rehabilitation tool not
40
41 269 only because it allows for controlled, repetitive practice of stepping, but because its parameters
42
43 270 can be modulated to induce specific desired gait adaptations.¹⁵ For example, typically developing
44
45 271 children adapt to faster walking speeds by increasing step length and cadence.³⁹ Our subject with
46
47 272 ACC demonstrated similar adaptation by walking overground with increased step length **and**
48
49 273 **peak extension angle at the hip, knee, and ankle joints** following training. Additionally, the
50
51 274 width of the treadmill belt provides an environmental constraint to the medial-lateral base of

1
2
3 275 support during walking; this pattern also appeared to generalize to overground walking as our
4
5 276 subject decreased both her step width and FPA following training. **While some of our observed**
6
7 277 **changes in overground walking speed and cadence did exceed the reported minimally**
8
9 278 **clinically important differences (MCID) of children with cerebral palsy⁴⁰, they lacked**
10
11 279 **consistency. For this reason, we believe that the changes in these parameters represents**
12
13 280 **variability rather than clinically important differences; this also suggests that published**
14
15 281 **MCID values for other pediatric populations may not be valid for children with ACC.**
16
17

18
19 282 SBIT has been proposed as an effective way to increase muscle power and promote
20
21 283 higher stride rates during community walking in children with CP.²⁵ Our subject's primary gait
22
23 284 abnormalities at baseline were her decreased walking speed and crouched gait pattern. Weakness
24
25 285 of the plantarflexors is strongly associated with crouch gait.⁴¹ A SBIT protocol, therefore, could
26
27 286 address both impairments by increasing demand on the plantarflexors and facilitating increased
28
29 287 community walking speed. Our subject's **reduced** crouch following Phase 2 of our intervention
30
31 288 suggests that it may have been effective at improving strength in this muscle group. Both
32
33 289 backward and incline walking are known to **increase** the demand on hip and knee extensors and
34
35 290 ankle plantarflexors in healthy adults^{24,28}, however no improvements in crouch or peak joint
36
37 291 extension were noted during overground walking following Phase 1. Increases in walking speed
38
39 292 increase demand on the plantarflexors in typically developing children.³⁹ It may be that only the
40
41 293 SBIT component of Phase 2, which involved walking at the highest speeds, generated sufficient
42
43 294 challenge to our subject's plantarflexors to induce strength gain. Further, we saw improvements
44
45 295 in our subject's MFC following Phase 2 of training. At baseline she demonstrated low foot
46
47 296 clearance, placing her at risk for trip-related falls⁴²; she also demonstrated a high percentage of
48
49 297 steps with a unimodal toe trajectory, which has been proposed as a strategy to minimize falls in
50
51
52
53
54
55
56
57
58
59
60

1
2
3 298 other special populations.³⁵ In addition to demonstrating increased MFC over time, she also
4
5 299 demonstrated an increasing percentage of steps wherein her toe trajectory followed a bimodal
6
7 300 pattern. This suggests that her gait pattern improved to such a degree that she was not obligated
8
9 301 to use as many compensations to clear her foot during swing phase. Crouch gait frequently leads
10
11 302 to abnormal joint kinematics in the swing phase of gait³², so the improvements in crouch may
12
13 303 have enabled our subject to achieve more normalized foot clearance. Additionally, the changes in
14
15 304 variability of spatiotemporal parameters represent clinically meaningful improvements. Impaired
16
17 305 variability of movement can be seen in a variety of special populations and limit the efficiency of
18
19 306 performance.^{31,43,44} Given her excessive variability at baseline, our subject's ability to decrease
20
21 307 the variability of several spatiotemporal parameters may represent improved movement
22
23 308 consistency, rhythmic timing control, and postural stability during gait.
24
25
26
27

28 309 Our subject produced a significantly more typical gait pattern on the treadmill than she
29
30 310 did overground, suggesting that she can produce a much more normalized pattern than she
31
32 311 utilizes during daily walking activities. The moving belt of the treadmill is known to provide a
33
34 312 stimulus that encourages push-off and regular stepping.⁴⁵ A trend toward a more upright gait
35
36 313 pattern with increased hip and knee extension in stance was noted over time, as was increased
37
38 314 movement into plantarflexion near toe-off, suggesting an improved push-off. The improvements
39
40 315 seen during treadmill walking suggest that our training paradigm was effective at improving the
41
42 316 subject's ability to walk at faster speeds, with a more upright posture and a more normalized gait
43
44 317 pattern. Generalization of these improvements to overground walking was more limited; similar
45
46 318 changes were seen, but to a lesser degree than were exhibited during treadmill walking. It is
47
48 319 critical to note, however, that our subject has a cortical visual impairment that has the potential to
49
50 320 alter her overground gait pattern; **her lower field limitations, in particular, may predispose**
51
52
53
54
55
56
57
58
59
60

1
2
3 321 **her to choose strategies that allow her to respond easily to unexpected obstacles.** We
4
5 322 proposed that she was capable of producing such a normalized gait pattern on a treadmill **within**
6
7 323 **a relatively fixed environment**, but she chose a more cautious gait pattern during overground
8
9 324 walking **due to her limited visual ability to perceive the environment.** Alternatively, the
10
11 325 dosage of **our TT intervention** might be insufficient to allow for complete generalization **from**
12
13 326 **treadmill** to overground walking. Pilot work investigating the effects of SBIT on children with
14
15 327 CP found overground walking speed improved only in the group which trained at a high
16
17 328 frequency of 5 times per week.²⁵ However, many aspects of our subject's **spatiotemporal**
18
19 329 **parameters** improved from visit 1 to 4, which **supports, to a certain degree**, the dosage of our
20
21 330 training.

22
23
24
25
26 331 **Given a single subject in our study**, the generalizability of our findings **is limited to the**
27
28 332 **wide variety of presentations within individuals with ACC.** Another **limitation** was that our
29
30 333 subject walked overground at a higher speed at visit 2 than at other visits. While it is possible
31
32 334 that Phase 1 of our training protocol induced this, its lack of persistence with continued training
33
34 335 suggests that this instead represents natural variability in the subject's gait speed. Several gait
35
36 336 parameters demonstrated apparent declines from baseline at this visit; notably, crouch increased,
37
38 337 peak joint extension decreased, and MFC decreased with an increased percentage of atypical toe
39
40 338 trajectories in swing phase. Rather than representing adverse effects of our training protocol, we
41
42 339 believe that these are simply compensations observed during fast walking. This is also supported
43
44 340 by a lack of these compensations during treadmill walking at visit 2, when speed was controlled
45
46 341 and comparable to other visits. This alteration in preferred overground walking pace at visit 2
47
48 342 represents a confounding factor when comparing the relative effectiveness of the two phases of
49
50 343 our protocol. **Finally, the discrepancy in training time between the two phases also**
51
52
53
54
55
56
57
58
59
60

1
2
3 344 **represents a confounding factor when comparing their relative effectiveness. Although we**
4
5 345 **believe that the SBIT component of Phase 2 represents a novel task for our subject, we**
6
7 346 **cannot be certain that its inclusion did not simply increase the dosage of task-specific**
8
9 347 **walking practice on the treadmill from 15 to 25 minutes, and that it was the dosage**
10
11 348 **increase rather than the specifics of the SBIT that caused the increased improvements seen**
12
13 349 **following Phase 2.**
14

15
16
17 350 Overall, this study demonstrates that TT can be a safe and effective treatment paradigm
18
19 351 to use for improving the gait patterns of children with ACC. Future research is needed to
20
21 352 determine if these findings can be reproduced **and generalized** in other individuals with ACC,
22
23 353 specifically those of different ages and who present with different motor impairments.
24
25 354 Additionally, more TT protocols, particularly with different SBIT designs, should be investigated
26
27 355 in this population to determine if increased generalization to overground walking can be seen
28
29 356 with increased dosage **for individuals with ACC.**
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

357 **References**

- 358 1. Chiappedi M, Bejor M. Corpus callosum agenesis and rehabilitative treatment. *Ital J*
359 *Pediatr.* 2010;36:64.
- 360 2. D'Antonio F, Pagani G, Familiari A, et al. Outcomes Associated With Isolated Agenesis
361 of the Corpus Callosum: A Meta-analysis. *Pediatrics.* 2016;138(3).
- 362 3. Meyer BU, Roricht S, Niehaus L. Morphology of acallosal brains as assessed by MRI in
363 six patients leading a normal daily life. *J Neurol.* 1998;245(2):106-110.
- 364 4. Siffredi V, Anderson V, Leventer RJ, Spencer-Smith MM. Neuropsychological profile of
365 agenesis of the corpus callosum: a systematic review. *Dev Neuropsychol.* 2013;38(1):36-
366 57.
- 367 5. Moes P, Schilmoeller K, Schilmoeller G. Physical, motor, sensory and developmental
368 features associated with agenesis of the corpus callosum. *Child Care Health Dev.*
369 2009;35(5):656-672.
- 370 6. Kovac ML, Simeonsson RJ. Agenesis of the corpus callosum: classifying functional
371 manifestations with the ICF-CY. *Disabil Rehabil.* 2014;36(13):1120-1127.
- 372 7. Bigler ED, Rosenstein LD, Roman M, Nussbaum NL. The clinical significance of
373 congenital agenesis of the corpus callosum. *Arch Clin Neuropsychol.* 1988;3(2):189-200.
- 374 8. Mueller KL, Marion SD, Paul LK, Brown WS. Bimanual motor coordination in agenesis
375 of the corpus callosum. *Behav Neurosci.* 2009;123(5):1000-1011.
- 376 9. Sauerwein HC, Lasseonde M. Cognitive and sensori-motor functioning in the absence of
377 the corpus callosum: neuropsychological studies in callosal agenesis and callosotomized
378 patients. *Behav Brain Res.* 1994;64(1-2):229-240.

- 1
2
3 379 10. Strubhar AJ, Meranda K, Morgan A. Outcomes of infants with idiopathic hypotonia.
4
5 380 *Pediatr Phys Ther.* 2007;19(3):227-235.
6
7
8 381 11. Smits-Engelsman B, Hill EL. The relationship between motor coordination and
9
10 382 intelligence across the IQ range. *Pediatrics.* 2012;130(4):e950-956.
11
12 383 12. Akbal A. Long Term Outcomes of Physical Therapy A Patients With Agenesis of The
13
14 384 Corpus Callosum. *Ortadogu Medical Journal.* 2013;5(3):85-87.
15
16
17 385 13. Pacheco SC, Queiroz AP, Niza NT, da Costa LM, Ries LG. Pediatric neurofunctional
18
19 386 intervention in agenesis of the corpus callosum: a case report. *Rev Paul Pediatr.*
20
21 387 2014;32(3):252-256.
22
23
24 388 14. Angulo-Barroso RM, Wu J, Ulrich DA. Long-term effect of different treadmill
25
26 389 interventions on gait development in new walkers with Down syndrome. *Gait Posture.*
27
28 390 2008;27(2):231-238.
29
30
31 391 15. Damiano DL, DeJong SL. A systematic review of the effectiveness of treadmill training
32
33 392 and body weight support in pediatric rehabilitation. *Journal of neurologic physical*
34
35 393 *therapy : JNPT.* 2009;33(1):27-44.
36
37
38 394 16. Ulrich DA, Ulrich BD, Angulo-Kinzler RM, Yun J. Treadmill training of infants with
39
40 395 Down syndrome: evidence-based developmental outcomes. *Pediatrics.* 2001;108(5):E84-
41
42 396 E84.
43
44
45 397 17. Wu J, Looper J, Ulrich BD, Ulrich DA, Angulo-Barroso RM. Exploring effects of
46
47 398 different treadmill interventions on walking onset and gait patterns in infants with Down
48
49 399 syndrome. *Developmental Medicine & Child Neurology.* 2007;49(11):839-945.
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 400 18. Valentin-Gudiol M, Mattern-Baxter K, Girabent-Farres M, Bagur-Calafat C, Hadders-
4
5 401 Algra M, Angulo-Barroso RM. Treadmill interventions in children under six years of age
6
7 402 at risk of neuromotor delay. *Cochrane Database Syst Rev.* 2017;7:Cd009242.
8
9
10 403 19. Chrysagis N, Skordilis EK, Stavrou N, Grammatopoulou E, Koutsouki D. The effect of
11
12 404 treadmill training on gross motor function and walking speed in ambulatory adolescents
13
14 405 with cerebral palsy: a randomized controlled trial. *Am J Phys Med Rehabil.*
15
16 406 2012;91(9):747-760.
17
18
19 407 20. Dewar R, Love S, Johnston LM. Exercise interventions improve postural control in
20
21 408 children with cerebral palsy: a systematic review. *Dev Med Child Neurol.*
22
23 409 2015;57(6):504-520.
24
25
26 410 21. Moreau NG, Bodkin AW, Bjornson K, Hobbs A, Soileau M, Lahasky K. Effectiveness of
27
28 411 Rehabilitation Interventions to Improve Gait Speed in Children With Cerebral Palsy:
29
30 412 Systematic Review and Meta-analysis. *Physical therapy.* 2016;96(12):1938-1954.
31
32
33 413 22. El-Basatiny HM, Abdel-Aziem AA. Effect of backward walking training on postural
34
35 414 balance in children with hemiparetic cerebral palsy: a randomized controlled study. *Clin*
36
37 415 *Rehabil.* 2015;29(5):457-467.
38
39
40 416 23. Kim SG, Ryu YU, Je HD, Jeong JH, Kim HD. Backward walking treadmill therapy can
41
42 417 improve walking ability in children with spastic cerebral palsy: a pilot study. *Int J*
43
44 418 *Rehabil Res.* 2013;36(3):246-252.
45
46
47 419 24. Franz JR, Kram R. The effects of grade and speed on leg muscle activations during
48
49 420 walking. *Gait Posture.* 2012;35(1):143-147.
50
51
52 421 25. Bjornson KF, Moreau N, Bodkin AW. Short-burst interval treadmill training walking
53
54 422 capacity and performance in cerebral palsy: a pilot study. *Dev Neurorehabil.* 2018:1-8.
55
56
57
58
59
60

- 1
2
3 423 26. Moreau NG, Falvo MJ, Damiano DL. Rapid force generation is impaired in cerebral
4
5 424 palsy and is related to decreased muscle size and functional mobility. *Gait Posture*.
6
7 425 2012;35(1):154-158.
8
9
10 426 27. Geertsen SS, Kirk H, Lorentzen J, Jorsal M, Johansson CB, Nielsen JB. Impaired gait
11
12 427 function in adults with cerebral palsy is associated with reduced rapid force generation
13
14 428 and increased passive stiffness. *Clin Neurophysiol*. 2015;126(12):2320-2329.
15
16
17 429 28. Cipriani DJ, Armstrong CW, Gaul S. Backward walking at three levels of treadmill
18
19 430 inclination: an electromyographic and kinematic analysis. *The Journal of orthopaedic*
20
21 431 *and sports physical therapy*. 1995;22(3):95-102.
22
23
24 432 29. Middleton A, Fritz SL, Lusardi M. Walking speed: the functional vital sign. *Journal of*
25
26 433 *aging and physical activity*. 2015;23(2):314-322.
27
28
29 434 30. Zeni JA, Richards JG, Higginson JS. Two simple methods for determining gait events
30
31 435 during treadmill and overground walking using kinematic data. *Gait & posture*.
32
33 436 2008;27(4):710-714.
34
35
36 437 31. Beerse M, Henderson G, Liang H, Ajisafe T, Wu J. Variability of spatiotemporal gait
37
38 438 parameters in children with and without Down syndrome during treadmill walking. *Gait*
39
40 439 *& Posture*. 2019;68:207-212.
41
42
43 440 32. van der Krogt MM, Bregman DJ, Wisse M, Doorenbosch CA, Harlaar J, Collins SH.
44
45 441 How crouch gait can dynamically induce stiff-knee gait. *Ann Biomed Eng*.
46
47 442 2010;38(4):1593-1606.
48
49
50 443 33. Lundh S, Nasic S, Riad J. Fatigue, quality of life and walking ability in adults with
51
52 444 cerebral palsy. *Gait Posture*. 2018;61:1-6.
53
54
55
56
57
58
59
60

- 1
2
3 445 34. Rozumalski A, Schwartz MH. Crouch gait patterns defined using k-means cluster
4
5 446 analysis are related to underlying clinical pathology. *Gait Posture*. 2009;30(2):155-160.
6
7
8 447 35. Alcock L, Galna B, Lord S, Rochester L. Characterisation of foot clearance during gait in
9
10 448 people with early Parkinsons disease: Deficits associated with a dual task. *Journal of*
11
12 449 *biomechanics*. 2016;49(13):2763-2769.
13
14
15 450 36. Winter DA. Foot trajectory in human gait: a precise and multifactorial motor control task.
16
17 451 *Physical therapy*. 1992;72(1):45-53; discussion 54-46.
18
19 452 37. Wilken JM, Rodriguez KM, Brawner M, Darter BJ. Reliability and Minimal Detectible
20
21 453 Change values for gait kinematics and kinetics in healthy adults. *Gait Posture*.
22
23 454 2012;35(2):301-307.
24
25
26 455 38. Liang H, Ke X, Wu J. Transitioning from the level surface to stairs in children with and
27
28 456 without Down syndrome: Motor strategy and anticipatory locomotor adjustments. *Gait*
29
30 457 *Posture*. 2018;66:260-266.
31
32
33 458 39. Schwartz MH, Rozumalski A, Trost JP. The effect of walking speed on the gait of
34
35 459 typically developing children. *Journal of biomechanics*. 2008;41(8):1639-1650.
36
37
38 460 40. Oeffinger D, Bagley A, Rogers S, et al. Outcome tools used for ambulatory children with
39
40 461 cerebral palsy: responsiveness and minimum clinically important differences.
41
42 462 *Developmental medicine and child neurology*. 2008;50(12):918-925.
43
44
45 463 41. Steele KM, van der Krogt MM, Schwartz MH, Delp SL. How much muscle strength is
46
47 464 required to walk in a crouch gait? *Journal of biomechanics*. 2012;45(15):2564-2569.
48
49 465 42. Begg R, Best R, Dell'Oro L, Taylor S. Minimum foot clearance during walking:
50
51 466 strategies for the minimisation of trip-related falls. *Gait Posture*. 2007;25(2):191-198.
52
53
54
55
56
57
58
59
60

- 1
2
3 467 43. Fetters L. Perspective on Variability in the Development of Human Action. *Physical*
4
5 468 *Therapy*. 2010;90(12):1860-1867.
6
7
8 469 44. Smith BA, Stergiou N, Ulrich BD. Patterns of gait variability across the lifespan in
9
10 470 persons with and without down syndrome. *Journal of neurologic physical therapy :*
11
12 471 *JNPT*. 2011;35(4):170-177.
13
14
15 472 45. Thelen E. Treadmill-elicited stepping in seven-month-old infants. *Child development*.
16
17 473 1986;57(6):1498-1506.
18
19 474
20
21 475
22
23
24 476
25
26 477
27
28 478
29
30
31 479
32
33 480
34
35 481
36
37 482
38
39 483
40
41 484
42
43 485
44
45 486
46
47 487
48
49 488
50
51 489
52
53
54
55
56
57
58
59
60

490 Table 1: Details of the completed treadmill training protocol.

	Session	Forward speed (m/s)	Forward incline (% grade)	Backward speed (m/s)	Backward incline (% grade)	Interval training speed (slow/fast, in m/s)
Phase 1	1-3	1.03	3.0	0.27	0.5	n/a
	4-5	1.07	3.0	0.27	0.5	n/a
	6	1.07	3.0	0.31	0.5	n/a
	7	1.12	3.0	0.31	0.5	n/a
	8-9	0.94	3.5	0.31	0.5	n/a
	10	0.98	3.5	0.31	0.5	n/a
Phase 2	1	0.98	3.5	0.31	0.5	0.72/1.43
	2-3	1.03	3.5	0.31	0.5	0.72/1.43
	4	1.07	3.5	0.31	0.5	0.72/1.43
	5	1.07	3.5	0.36	0.5	0.76/1.52
	6	1.07	3.5	0.36	0.5	0.72/1.43
	7	1.07	3.5	0.36	0.5	0.76/1.52
	8	1.07	3.5	0.36	1.0	0.76/1.52
	9	1.12	3.5	0.36	1.0	0.76/1.52
	10	1.12	3.5	0.27	1.5	0.76/1.52

491
492 At Phase 2, the slow and fast interval training speeds were 75% and 150% of the forward walking speed, respectively. Total training
493 time for each session in Phase 1 was 15 minutes (10 minutes forward, and 5 minutes backward). Total training time for each session in
494 Phase 2 was 25 minutes (10 minutes forward, 5 minutes backward, and 10 minutes intervals). n/a: not applicable.
495

496 Table 2: Mean (SD) and coefficient of variation (CV) of temporal gait variables during overground walking

		Speed	Cycle time	Stance time	Swing time	Double support
		(m/s)	(sec)	(sec)	(sec)	time (sec)
Mean (SD)	Visit 1	0.30 (0.06)	1.17 (0.25)	0.82 (0.19)	0.36 (0.08)	0.23 (0.09)
	Visit 2	0.39 (0.17)	1.15 (0.12)	0.82 (0.10)	0.33 (0.07)	0.25 (0.07)
	Visit 3	0.23 (0.06)	1.47 (0.10)	1.00 (0.11)	0.46 (0.06)	0.27 (0.06)
	Visit 4	0.28 (0.13)	1.24 (0.07)	0.84 (0.08)	0.40 (0.04)	0.22 (0.07)
CV	Visit 1	20.0	21.0	23.5	23.5	36.6
	Visit 2	42.1	10.6	12.0	20.3	29.5
	Visit 3	23.7	6.9	10.5	13.1	22.7
	Visit 4	44.2	5.7	9.5	10.7	32.0

497
498 Note that for gait analysis, visit 1 was before the intervention, visit 2 was after phase 1 (three months) of the intervention, visit 3 was
499 after phase 2 (another three months) of the intervention, and visit 4 was the follow-up (three months after phase 2 of the intervention).
500 Variability is expressed as the coefficient of variation (CV).
501
502
503
504
505
506
507
508
509
510
511

512 Table 3: Mean (standard deviation) of peak extension angles at the hip, knee, and ankle and crouch angle during overground (OG) and
513 treadmill (TM) walking.
514

	Hip angle		Knee angle		Ankle angle		Crouch angle	
	(degrees)		(degrees)		(degrees)		(degrees)	
	OG	TM	OG	TM	OG	TM	OG	TM
Visit 1	24.97	25.69	27.51	28.62	6.33	7.38	36.98	30.35
	(12.10)	(5.25)	(12.77)	(6.90)	(12.62)	(3.45)	(4.90)	(7.30)
Visit 2	26.36	25.82	34.97	29.69	11.93	5.05	43.78	31.77
	(8.52)	(6.28)	(11.80)	(4.99)	(12.96)	(4.75)	(13.55)	(4.64)
Visit 3	18.58	16.64	17.94	12.91	6.69	1.66	23.97	13.97
	(10.08)	(7.72)	(6.73)	(4.61)	(3.83)	(3.42)	(6.14)	(5.03)
Visit 4	19.57	16.67	23.93	20.13	2.49	-0.84	32.33	21.25
	(15.84)	(8.61)	(8.65)	(4.14)	(12.78)	(2.60)	(4.69)	(3.90)

515
516 At the hip, negative values represent hip extension while positive values represent hip flexion. At the knee, negative values represent
517 knee hyperextension while positive values represent knee flexion. At the ankle, negative values represent plantarflexion while positive
518 values represent dorsiflexion. Crouch is defined as the amount of knee flexion present at initial contact. Note that for gait analysis,
519 visit 1 was before the intervention, visit 2 was after phase 1 (three months) of the intervention, visit 3 was after phase 2 (another three
520 months) of the intervention, and visit 4 was the follow-up (three months after phase 2 of the intervention).
521
522

523

524

1
2
3 525 **Figure captions**

4
5 526
6
7
8 527 Fig 1: Toe trajectories in swing phase and minimum foot clearance **during overground walking**
9
10 528 at visits 1-4. A representative (a) bimodal and (b) unimodal toe trajectories during swing phase,
11
12 529 averaged (c) bimodal and (d) unimodal trajectories at each visit, (e) percent of steps which
13
14 530 demonstrated bimodal trajectories at each visit, and (f) minimum foot clearance during bimodal
15
16 531 steps at each visit.
17
18

19 532
20
21 533 Fig 2: Mean (SD) and coefficient of variation (CV) of gait variables during overground walking
22
23 534 at visits 1-4. (a) Cadence mean, (b) cadence CV, (c) step length mean, (d) step length CV, (e)
24
25 535 **step width mean, (f) step width CV, (g) foot progression angle mean, and (h) foot progression**
26
27 536 angle CV. Note that visit 1 was before the intervention, visit 2 was after phase 1 (three months)
28
29 537 of the intervention, visit 3 was after phase 2 (another three months) of the intervention, and visit
30
31 538 4 was the follow-up (three months after phase 2 of the intervention).
32
33
34

35 539
36
37 540 Fig 3: Mean joint kinematics over a **time-normalized** gait cycle at visits 1-4 at the (a) hip, (b)
38
39 541 knee, and (c) ankle during both overground (OG) walking, represented by a dashed line, and
40
41 542 treadmill (TM) walking, represented by a solid line. Positive joint angles represent flexion and
42
43 543 negative joint angles represent extension. Toe-off during OG walking is represented by a vertical
44
45 544 grey line, and toe-off during treadmill walking is represented by a vertical black line. Note that
46
47 545 visit 1 was before the intervention, visit 2 was after phase 1 (three months) of the intervention,
48
49 546 visit 3 was after phase 2 (another three months) of the intervention, and visit 4 was the follow-up
50
51 547 (three months after phase 2 of the intervention).
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Fig 1:

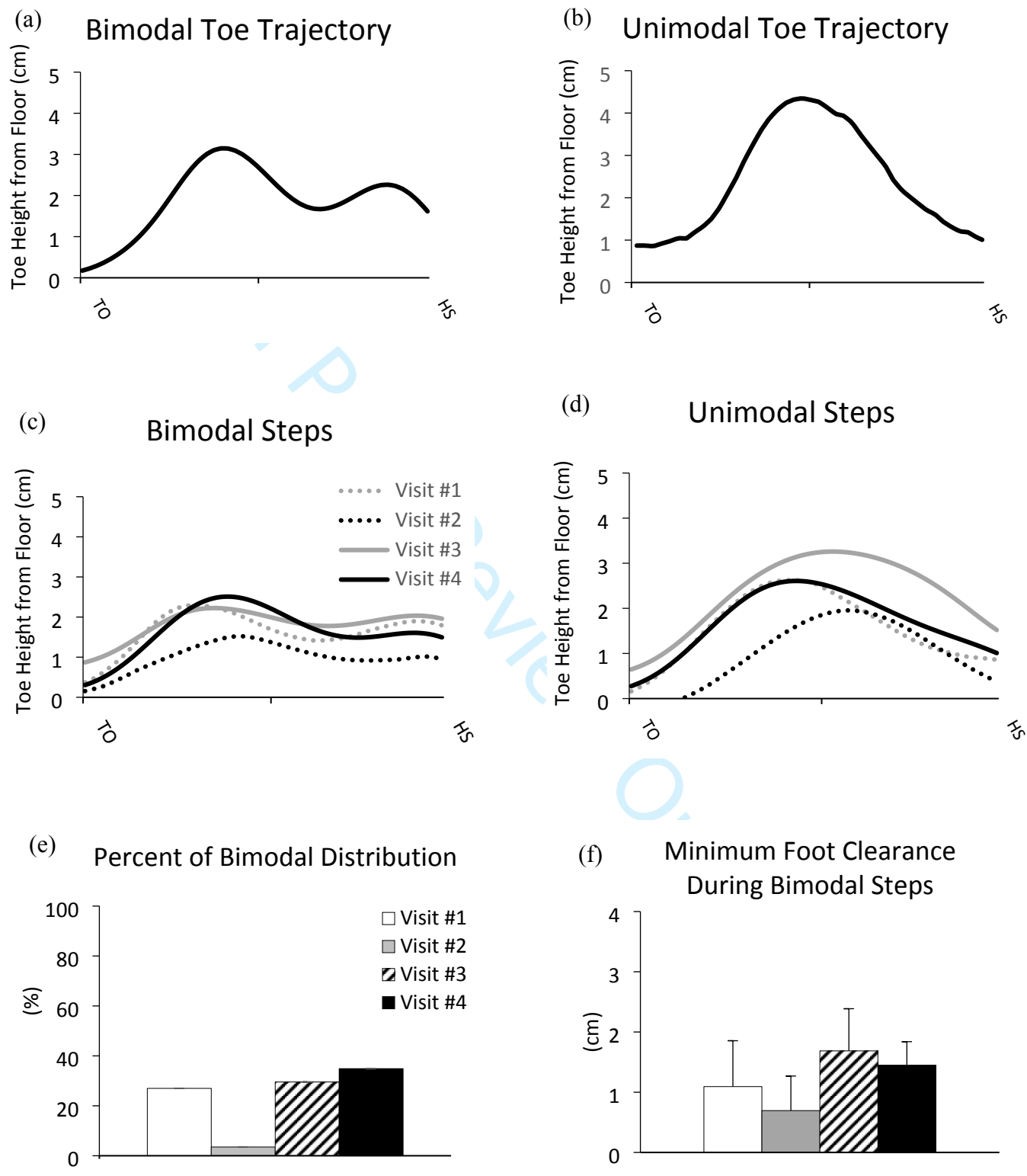


Fig 2:

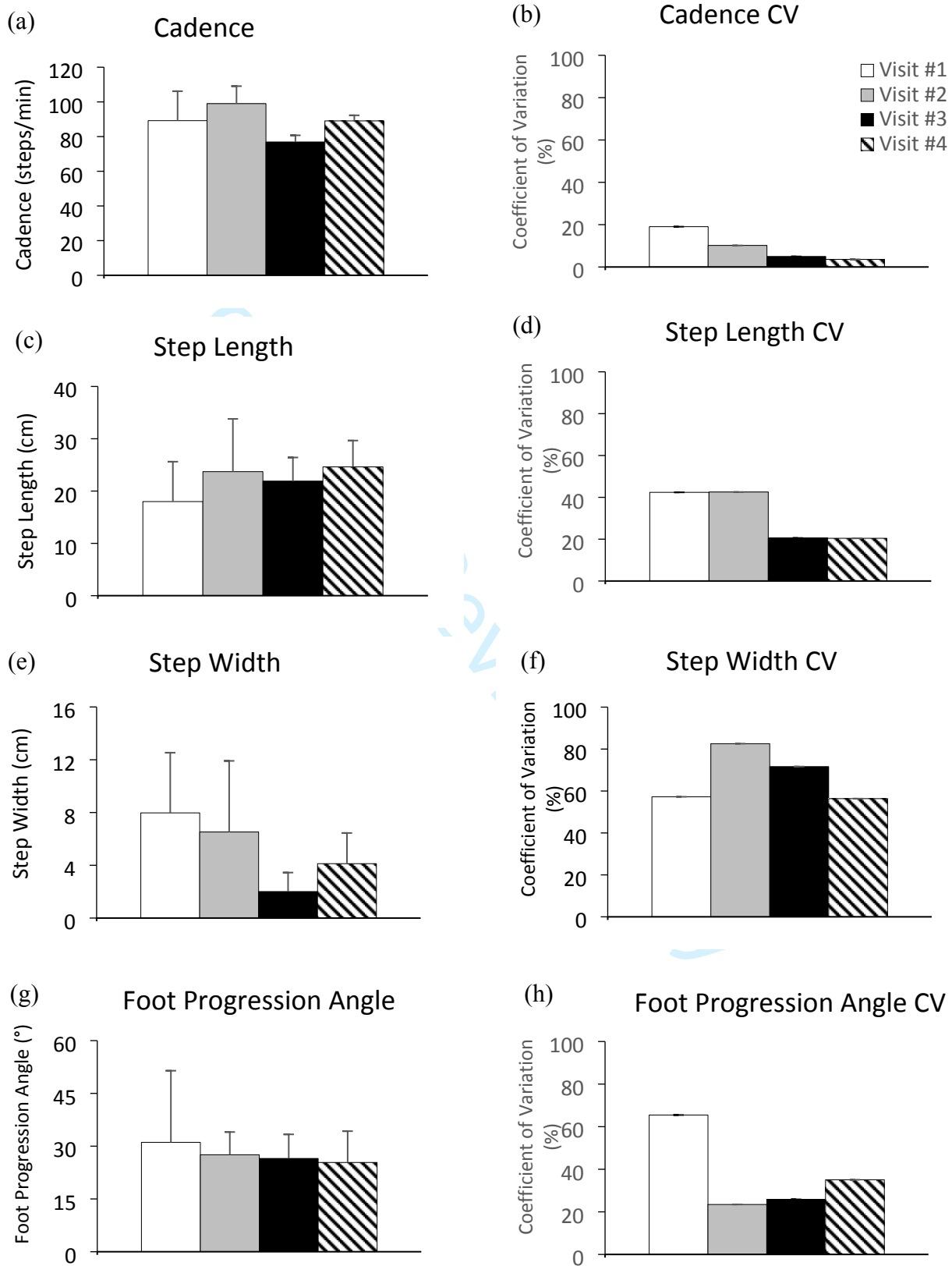


Fig 3:

