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Feasibility of wearable technology for 'real-world' gait analysis in children with Prader-Willi and Angelman syndromes

Running head: Feasibility of wearable technology

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Data availability statement

Data available on request from the authors.

ABSTRACT

Background: Prader-Willi syndrome (PWS) and Angelman syndrome (AS) are neurodevelopmental disorders in need of innovative 'real-world' outcome measures to evaluate treatment effects. Instrumented gait analysis (IGA) using wearable technology offers a potentially feasible solution to measure ''real-world' neurological and motor dysfunction in these groups. **Methods:** Children (50% female; 6-16 years) diagnosed with PWS (n=9) and AS (n=5) completed 'real-world' IGA assessments using the Physilog®5 wearable. PWS participants completed a laboratory assessment and a 'real-world' long walk. The AS group completed 'real-world' caregiver-assisted assessments. Mean and variability results for stride time, cadence, stance percentage (%) and stride length were extracted and compared across three different data reduction protocols. **Results:** The wearables approach was found to be feasible, with all participants able to complete at least one assessment. This study also demonstrated significant agreement, using Lin's concordance correlation coefficient (CCC), between laboratory and 'real-world' assessments in the PWS group for mean stride length, mean stance % and stance % CV (n=7, CCC: 0.782 – 0.847, p = 0.011 – 0.009). **Conclusion:** 'Real-world' gait analysis using the Physilog®5 wearable was feasible to efficiently assess neurological and motor dysfunction in children affected with PWS and AS.

Keywords: inertial sensors, gait analysis; Angelman syndrome; Prader-Willi syndrome, wearable technology, children, neurological dysfunction, motor dysfunction.

INTRODUCTION

Prader-Willi syndrome (PWS) and Angelman syndrome (AS) are neurodevelopmental disorders caused by genetic or epigenetic changes at the 15q11.2-q13 imprinted region (Kalsner and Chamberlain, 2015). Children with PWS typically have mild intellectual disability (ID), hyperphagia, and challenging behaviours (Cassidy et al., 2012). The AS phenotype is characterised by severe ID, minimal or absent speech, movement or balance disorder, and behavioural uniqueness (Bird, 2014).

Infants with PWS typically walk at 24 months (Cassidy et al., 2012), then face ongoing difficulties with gait initiation and termination (Cimolin et al., 2017), reduced stride length and cadence (Vismara et al., 2007), and lack of gait symmetry (Cimolin et al., 2020). In children with AS, walking is typically delayed until three or five years (Bindels-de Heus et al., 2020), followed by ataxic and irregular gait (Williams et al., 2006). Other AS gait characteristics include crouch gait (Bindels-de Heus et al., 2020), spastic diplegia (Dan et al., 2001) and dystonia (Ferlazzo et al., 2021).

Formal assessment of gait may have clinical benefits in both PWS and AS. In PWS, assessments could guide personalised physiotherapy programs (Cimolin et al., 2011, Cimolin et al., 2019). These are important for PWS given known links between physical activity and bone strength, muscle mass, and weight maintenance (Rubin et al., 2013). In children with AS, monitoring of gait dysfunction from a young age would improve understanding of the mechanisms that might be targeted to avoid severe gait outcomes (i.e., wheelchair use) (Clayton-Smith and Laan, 2003). Gait assessments could also be used as an outcome measure in clinical trials (Grieco et al., 2018).

Instrumented gait analysis (IGA) is a sensitive and objective tool for the measurement of spatiotemporal aspects of gait and three-dimensional (3D) gait analysis. Traditionally spatiotemporal aspects of gait have been examined using electronic walkways or optoelectronic systems, both within laboratory settings (Toro et al., 2003). More recently, spatiotemporal IGA techniques in 'real-world' non-laboratory settings have been explored with both paediatric and adult clinical groups, using wearable devices (Ilg et al., 2019, Carcreff et al., 2020). Such 'real-world' measures have potential advantages for children with disability, who may have difficulty accessing gait laboratories, and who may not be comfortable being assessed in the laboratory setting.

The aim of this study was to test the feasibility of 'real-world' IGA using the Physilog®5 wearable in children with PWS and AS. We hypothesised that assessments would be feasible, and that 'real-world' data would be in agreement with laboratory data.

METHODS

Participants.

Fourteen children (PWS: n=9; AS: n=5; 6-16 years old) were recruited from a previous cohort (Baker et al., 2020) via an addendum to the FREE FX study (Table 1). Most participants were engaged in regular physical activity (Supplementary Table S1). Exclusion criteria were: (i) significant non-PWS/AS medical or neurological condition/s (i.e., stroke, malignancies, severe head trauma, congenital heart disease, liver or renal failure, inadequate control of seizures); and (ii) recent injuries/pain that could affect gait. This study was approved by the Royal

Children's Hospital Human Research Ethics Committee (HREC 33066 and HREC 34227). All participants had a legally acceptable representative provide consent.

Gait assessment protocols.

Participants wore lace-up runners or skate/leisure shoes with Gait Up Physilog®5 inertial sensors (Gait Up; Lausanne, Switzerland) secured below the lateral malleolus or centrally below laces or Velcro in line with the inferior lateral malleolus. The Physilog®5 has high levels of agreement with typical clinical gait analysis set-ups (Carcreff et al., 2018, Bourgeois et al., 2014, Carroll et al., 2021). Sensors were turned on remotely and left to continuously record across each assessment.

The PWS group completed two indoor gait assessments: (i) laboratory assessment within a research centre (15 metre track; 3-4 laps with turns around a pole; (ii) 'real-world' long walk assessment of two minutes in a quiet public hospital corridor with one turn. The AS group was asked to complete one 'real-world' assessment: either (i) assisted short walks at home/research centre (i.e., assessor to caregiver or with caregiver up and back); or (ii) assisted long walk within the hospital. In 'real-world' assessments conversations were permitted to help the child feel comfortable. Encouragement was allowed in all assessments. Height (cm) and weight (kg) were measured on day of testing whilst barefoot (stadiometer). Leg length was measured in a supine position (McRae, 2006).

Data reduction protocols.

Three data reduction protocols were explored: (i) Turns; (ii) Turns+; (iii) walking episode segmentation. The Turns protocol is based on excision of the first and last two cycles and all cycles with a turning angle (TA) >20 degrees (one or both legs). The Turns+ protocol repeats Turns but with additional excision of one full cycle before and after each turn (using TA>20 degrees). Cycles with missing data on a primary spatiotemporal parameter (one or both legs) were removed in both Turn and Turn+ protocols.

The segmentation protocol classifies walking segments of 4+ sequential cycles (i.e., ~8+ steps) without extreme results for turning angle (indicating a turn or distraction) deemed at >25 degrees (selected to accommodate AS out-toeing), stance percentage (%) (indicating a pause) and peak angle velocity (indicating loss of steady-state gait). (Supplementary note S2 and Supplementary Figure S1).

For each assessment, the total cycles remaining after the data reduction protocol were analysed for mean and coefficient of variation (CV) of stride time, cadence, stance % and stride length. Gait parameters were calculated across all step data (left and right combined). Assessments with <8 cycles after data reduction were considered void.

Statistical analyses.

In the PWS group with repeat assessments, the level of agreement between laboratory and 'real-world' assessments for each data reduction protocol was analysed using paired t-tests and Lin's concordance correlation coefficient (CCC) (Lin, 1989), with the paired t-test used to detect systematic bias. Both Estimation plots and Bland-Altman plots showing the bias and upper and lower 95% Limits of Agreement (LoA) were analysed. Using repeated measures

one-way ANOVA we tested for differences between the three data reduction protocols. This was performed independently in the data collected from the AS group, the laboratory PWS, and the 'real-world' PWS data. All analyses were conducted using software STATA (http://www.stata.come).

RESULTS

Feasibility

All participants completed at least one assessment (Figure 1). One PWS participant was unable to complete the 'real-world' long walk due to inappropriate footwear on the day (laboratory assessment performed barefoot). One PWS participant was re-entered into the caregiver assessment due to behavior on the day (results in Supplementary Table S2). All remaining PWS participants (n=7) completed two assessments. The assessments completed by AS participants included: laps at the research centre (n=1); laps at home: (n=2); long walk at hospital (n=2). For one AS participant and one PWS participant, there were <8 cycles remaining after segmentation. Here, a modification that replaced the requirement for 4+ consecutive cycles to 3+ cycles was used to maintain the data. The same data collected from the AS home assessment was voided for the Turns+ protocol and could not be retrieved. All other assessments were compatible with Turn, Turns+ and segmentation data reduction protocols.

Agreement between laboratory and 'real-world' assessments

Agreement was tested in the PWS participants with repeat data (n=7; see Supplementary Table S3 for gait cycle and segmentation data). The results analysed using the segmentation protocol

had a high level of agreement between laboratory and 'real-world' settings for three parameters (Table 2, Supplementary Tables S4-5, Supplementary Figures S2-3). These were mean stance % (CCC: 0.782, p = 0.009), mean stride length (CCC: 0.847, p = 0.004) and stance % CV (CCC: 0.798, p = 0.011) (Table 2). High agreement was also observed for the Turns protocol (mean stance %: CCC: 0.710, p = 0.029: mean stride length: CCC: 0.805, p = 0.007) (Supplementary Table S4). Using Turns+, only mean stride length was significant (CCC: 0.783, p = 0.010) (Supplementary Table S5). Stride time and cadence parameters (mean and CV) were not in agreement using any data reduction protocol explored in this study. Based on the paired t-test, there were no significant differences between laboratory and 'real-world' results. This indicates lack of systematic bias for all parameters evaluated in this study (Table 2, Supplementary Tables S4-5, Figure 2, Supplementary Figures S4-5).

Comparison of data reduction protocols

Repeated measures one way ANOVA was used to compare data reduction protocols in AS and PWS groups. Parameters significantly different between data reduction protocol in the AS group included stride time (Turns+ < Turns, p = 0.049), stride length (Turns < Turns+, p = 0.014); stride length CV (segmented < Turns, p = 0.027) (Figure 3A-B, Supplementary Figure S6). Parameters different in PWS 'real-world' data included: cadence CV (segmented < Turns, p = 0.002) and stance % CV (segmented < Turns, p = 0.044). Differences between Turns and Turns+ for mean parameters were also observed (p = 0.037 to 0.050) (Figure 3C, Supplementary Figure S5). In the PWS laboratory data stride length (segmented < Turns+; p =

0.040) and stance % CV (segmented < Turns+; p = 0.013) were different across protocols (Figure 3D, Supplementary Figure S8).

DISCUSSION

This study has demonstrated feasibility of 'real-world' gait analysis with children who have PWS and AS, using the Physilog® wearable. Mean stance %, mean stride length and stance % CV from 'real-world' assessments showed a high level of agreement with the laboratory results (segmentation > Turns > Turns+). These findings warrant further research into wearable technologies applied in more typical 'real-world' settings. If found to be similar to the data gathered in a laboratory context, this could free-up assessment of gait by minimising the need for a formal laboratory assessment.

This study also shows that the data reduction protocol can impact results in 'real-world' assessments. For example, in the AS data, while no outliers were observed using the segmentation protocol, some participants' Turns/Turns+ results were too high to be considered a good measurement of motor functioning (e.g., stride time CV: Turns = 72.98; Turns+ = 59.93) (Figure 3A).

Other reduction protocols are being developed to segment wearables data (summarised in Supplementary Table S6). These include targeting segments based on the number of successive strides (often at least three) and stride time/velocity, discrete wavelet decomposition with decision tree algorithms, normalised autocorrelation-based analysis, application of selective thresholds, and machine learning (Carcreff et al., 2020, Del Din et al., 2016, Tamburini et al., 2018). The segmentation protocol in this study differs from those described

in previous literature due to: (i) targeting steady-state gait rather than episodes of walking *per se* (i.e., only well-regulated walking episodes); and (ii) no requirement for setting of baseline thresholds in a laboratory assessment. It was also developed for children with PWS and AS, thus has features not explored in other models including a wider angle for classifying turns that was used to capture out-toeing by children who have AS.

A strength of this study is that it accommodated for differences in ability to cooperate and follow assessment instructions. This approach is important for research of children with ID, where motor and cognitive difficulties often co-occur and where there is growing acceptance in the gait field that different approaches are needed for clinical monitoring (Hallemans et al., 2019).

A limitation of this study is the small sample size of the groups. Furthermore, due to absence of a control group, it is not clear if the lack of agreement observed for stride time and cadence data (mean and CV), is a PWS-specific finding, or a more general phenomenon related to the different assessment demands. Similarly, we do not know if the high agreement observed for stance % and stride length for PWS will extend to other groups, including the AS group.

In conclusion, this study demonstrated that it is feasible to use Physilog® wearable to measure gait performance in children with PWS and AS in 'real-world' settings. For three parameters (mean stance %, mean stride length, stance % CV) agreement with laboratory data was high, indicating that these are likely the most stable gait parameters explored in this study. These findings support further research into gait assessment outside the laboratory environment.

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Conflicts of Interest: The authors declare no conflict of interest.

REFERENCES

Baker, E. K., Butler, M. G., Hartin, S. N., Ling, L., Bui, M., Francis, D., Rogers, C., Field, M. J., Slee, J., Gamage, D., Amor, D. J. & Godler, D. E. 2020. Relationships between UBE3A and SNORD116 expression and features of autism in chromosome 15 imprinting disorders. *Transl Psychiatry,* 10**,** 362.

Bindels-De Heus, K., Mous, S. E., Ten Hooven-Radstaake, M., Van Iperen-Kolk, B. M., Navis, C., Rietman, A. B., Ten Hoopen, L. W., Brooks, A. S., Elgersma, Y., Moll, H.

A. & De Wit, M. Y. 2020. An overview of health issues and development in a large clinical cohort of children with Angelman syndrome. *Am J Med Genet A,* 182**,** 53-63.

Bird, L. M. 2014. Angelman syndrome: review of clinical and molecular aspects. *Appl Clin Genet,* 7**,** 93-104.

Bourgeois, A., Mariani, B., Aminian, K., Zambelli, P. Y. & Newman, C. J. 2014. Spatio-temporal gait analysis in children with cerebral palsy using, foot-worn inertial sensors. *Gait Posture,* 39**,** 436-42.

Carcreff, L., Gerber, C. N., Paraschiv-Ionescu, A., De Coulon, G., Newman, C. J., Aminian, K. & Armand, S. 2020. Comparison of gait characteristics between clinical and daily life settings in children with cerebral palsy. *Sci Rep,* 10**,** 2091.

Carcreff, L., Gerber, C. N., Paraschiv-Ionescu, A., De Coulon, G., Newman, C. J., Armand, S. & Aminian, K. 2018. What is the Best Configuration of Wearable Sensors to Measure Spatiotemporal Gait Parameters in Children with Cerebral Palsy? *Sensors (Basel),* 18.

Carroll, K., Kennedy, R. A., Koutoulas, V., Bui, M. & Kraan, C. M. 2021. Validation of shoe-worn Gait Up Physilog®5 wearable inertial sensors in adolescents. *Gait Posture,* 91**,** 19-25.

Cassidy, S. B., Schwartz, S., Miller, J. L. & Driscoll, D. J. 2012. Prader-Willi syndrome. *Genet Med,* 14**,** 10-26.

Cimolin, V., Cau, N., Galli, M., Pau, M., Parisio, C., Saezza, A., Grugni, G. & Capodaglio, P. 2019. Gait strategy and body composition in patients with Prader-Willi syndrome. *Eat Weight Disord*.

Cimolin, V., Cau, N., Galli, M., Santovito, C., Grugni, G. & Capodaglio, P. 2017. Gait initiation and termination strategies in patients with Prader-Willi syndrome. *J Neuroeng Rehabil,* 14**,** 44.

Cimolin, V., Galli, M., Grugni, G., Vismara, L., Precilios, H., Albertini, G., Rigoldi, C. & Capodaglio, P. 2011. Postural strategies in Prader-Willi and Down syndrome patients. *Res Dev Disabil,* 32**,** 669-73.

Cimolin, V., Pau, M., Cau, N., Leban, B., Porta, M., Capodaglio, P., Sartorio, A., Grugni, G. & Galli, M. 2020. Changes in symmetry during gait in adults with Prader-Willi syndrome. *Comput Methods Biomech Biomed Engin***,** 1-8.

Clayton-Smith, J. & Laan, L. 2003. Angelman syndrome: a review of the clinical and genetic aspects. *J Med Genet,* 40**,** 87-95.

Dan, B., Bouillot, E., Bengoetxea, A., Boyd, S. G. & Cheron, G. 2001. Distinct multi-joint control strategies in spastic diplegia associated with prematurity or Angelman syndrome. *Clin Neurophysiol,* 112**,** 1618-25.

Del Din, S., Godfrey, A., Galna, B., Lord, S. & Rochester, L. 2016. Free-living gait characteristics in ageing and Parkinson's disease: impact of environment and ambulatory bout length. *Journal of neuroengineering and rehabilitation,* 13**,** 46-46.

Ferlazzo, E., Ascoli, M., Abate, F., Gasparini, S., Mastroianni, G., Cianci, V., Ferrigno, G., Sueri, C., D'agostino, T. & Aguglia, U. 2021. Dystonia in Angelman syndrome: a common, unrecognized clinical finding. *J Neurol*.

Grieco, J. C., Romero, B., Flood, E., Cabo, R. & Visootsak, J. 2018. A Conceptual Model of Angelman Syndrome and Review of Relevant Clinical Outcomes Assessments (COAs). *Patient*.

Hallemans, A., Van De Walle, P., Wyers, L., Verheyen, K., Schoonjans, A. S., Desloovere, K. & Ceulemans, B. 2019. Clinical usefulness and challenges of instrumented motion analysis in patients with intellectual disabilities. *Gait Posture,* 71**,** 105-115.

Ilg, W., Seemann, J., Giese, M., Traschütz, A., Schöls, L., Timmann, D. & Synofzik, M. 2019. Towards ecologically valid biomarkers: real-life gait assessment in cerebellar ataxia. *bioRxiv***,** 802918.

Kalsner, L. & Chamberlain, S. J. 2015. Prader-Willi, Angelman, and 15q11-q13 Duplication Syndromes. *Pediatr Clin North Am,* 62**,** 587-606.

Lin, L. I. 1989. A concordance correlation coefficient to evaluate reproducibility. *Biometrics,* 45**,** 255-68.

Mcrae, R. 2006. *Pocket book of Orthopaedics and fractures*, Churchill Livingstone.

Rubin, D. A., Cano-Sokoloff, N., Castner, D. L., Judelson, D. A., Wright, P., Duran, A. & Haqq, A. M. 2013. Update on body composition and bone density in children with Prader-Willi syndrome. *Horm Res Paediatr,* 79**,** 271-6.

Tamburini, P., Storm, F., Buckley, C., Bisi, M. C., Stagni, R. & Mazzà, C. 2018. Moving from laboratory to real life conditions: Influence on the assessment of variability and stability of gait. *Gait Posture,* 59**,** 248-252.

Toro, B., Nester, C. & Farren, P. 2003. A review of observational gait assessment in clinical practice. *Physiotherapy Theory and Practice,* 19**,** 137-149.

Vismara, L., Romei, M., Galli, M., Montesano, A., Baccalaro, G., Crivellini, M. & Grugni, G. 2007. Clinical implications of gait analysis in the rehabilitation of adult patients with "Prader-Willi" Syndrome: a cross-sectional comparative study ("Prader-Willi" Syndrome vs matched obese patients and healthy subjects). *J Neuroeng Rehabil,* 4**,** 14.

Williams, C. A., Beaudet, A. L., Clayton-Smith, J., Knoll, J. H., Kyllerman, M., Laan, L. A., Magenis, R. E., Moncla, A., Schinzel, A. A., Summers, J. A. & Wagstaff, J. 2006. Angelman syndrome 2005: updated consensus for diagnostic criteria. *Am J Med Genet A,* 140**,** 413-8.

Figure 1. Study workflow. Summary of recruitment and assessment outcomes for 14 children recruited into the study. AS = Angelman syndrome; PWS = Prader-Willi syndrome.

Figure 2. Estimation plots for CV data from paired t-test using segmentation protocol. (A). Mean stance %; **(B)** stance percentage (%) CV; **(C)** mean stride length; **(D)** stride length CV. Analysis included all PWS participants that successfully completed both laboratory and 'real-world' (RW) assessments (n=7). Lab = Laboratory assessment. RW = 'real-world' assessment. CV = coefficient of variation. As per difference estimates in Table 2 and Supplementary Tables S4-5, no difference estimate was significant using paired t-test ($p<0.05$).

Figure 3. Comparison of results across data reduction protocol (Turns / Turns+ / segmentation). (A) Angelman syndrome (AS) stride time CV. **(B)** AS stride length CV **(C)** Prader-Willi syndrome (PWS) 'real-world' cadence CV; **(D)** PWS laboratory stance percentage (%) CV. P-value significant if <0.05 using repeated measures ANOVA.

Table 1. Medical data for PWS and AS participants

ID	Age	Sex	Diagnosis	Autism features (SCQ)	Full scale IQ	Low muscle tone	Flat feet	Orthotics	Scoliosis	Falls (last 12 months)
PWS1	6.51	M	Deletion	10	89	Yes	No	NR	No	innumerable
PWS2	11.99	M	UPD	20	66	No	No	Yes	Yes	0
PWS3	8.18	F	UPD	21	50	Yes*	No	NR	No	Yes – many
PWS4	10.89	M	Deletion	14	47	Yes	Yes	NR	Yes	0
PWS5	14.32	F	UPD	17	60	Yes	No	NR	Yes	Yes+
PWS6	9.59	F	UPD	17	70	Yes	No	NR	Yes	3 to 4
PWS7#	8.31	M	UPD	18	49	Yes	No	NR	No	4 to 6
PWS8[A]	16.08	F	UPD	15	45	Yes	Yes	Yes	No	Yes+
PWS9[A]	7.01	F	UPD	25	40[B]	Yes	Yes	Yes	No	5 to 6
AS1	7.24	M	Deletion	14	23	Yes*	Yes	AFO	No	1
AS2^	10.24	F	UBE3A mutation	11	28	Yes	No	AFO	No	several
AS3^	7.43	M	UBE3A mutation	17	33	Yes	No	AFO	No	several
AS4	6.70	F	Paternal UPD	14	30	No	No	NR	No	~12 – 20

AS5	6.93	M	UBE3A mutation	11	27	Yes	Yes	Insoles	No	2

Note: Genotype was classified using original diagnostic reports. Full scale IQ scores for AS participants are ratio IQ scores derived from the Mullen Scales of Early Learning. #PWS participant providing raw data in Supplementary Figure S1. [A]Not included in agreement analysis due only one of two assessments completed (refer to Figure 1). [B]Full scale IQ was at floor level (i.e., 40 on Wechsler scales); ^sibling dyad. *also reported hyper extensible joints. +amount of falls unspecified. AFO = ankle foot orthosis; AS: Angelman syndrome; IQ: intelligence quotient; NR: Not reported; PWS: Prader-Willi syndrome; SCQ: Social Communication Questionnaire; UBE3A = ubiquitin-protein ligase E3A; UPD = uniparental disomy.

Table 2: Level of agreement between laboratory and real-world assessments in children who have Prader-Willi Syndrome (PWS) using the segmentation protocol (N = 7).

	Concordance correlation coefficient (CCC)				Difference				
	Est	SE	p	95% CI	Est	SE	p	95% CI	95% LOA
Mean data									
Stride time (seconds)	0.258	0.391	0.529	(-0.51, 0.80)	0.029	0.041	0.510	(-0.07, 0.13)	(-0.19, 0.24)
Cadence (steps/minute)	0.243	0.395	0.555	(-0.52, 0.79)	-3.272	4.676	0.510	(-14.7, 8.17)	(-27.5, 21.0)
Stance percentage (% cycle)	0.782	0.155	**0.009**	(0.26, 0.95)	0.473	0.448	0.333	(-0.62, 1.57)	(-1.85, 2.80)
Stride length (metres)	0.847	0.124	**0.004**	(0.37, 0.97)	-0.027	0.027	0.349	(-0.09, 0.04)	(-0.17, 0.11)
Variability data									
Stride time (CV)	-0.062	0.299	0.837	(-0.57, 0.48)	-1.657	1.014	0.153	(-4.14, 0.82)	(-6.91, 3.60)
Cadence (CV)	0.007	0.318	0.983	(-0.55, 0.56)	-1.379	0.880	0.168	(-3.53, 0.77)	(-5.94, 3.18)
Stance percentage (CV)	0.798	0.156	**0.011**	(0.25, 0.96)	0.189	0.255	0.487	(-0.44, 0.81)	(-1.14, 1.51)
Stride length (CV)	0.480	0.332	0.226	(-0.31, 0.88)	0.018	1.253	0.989	(-3.05, 3.08)	(-6.48, 6.52)

Note: Difference = real-world - laboratory. CCC = Lin's concordance correlation coefficient; CI = confidence interval; Est = estimate; LOA = limits of agreement (Bland and Altman); SE = standard error; p = p-value.