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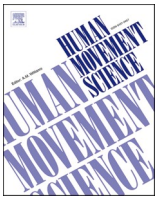

# Contributing factors to postural stability in Prader-Willi syndrome

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ABSTRACT

*Background:* Prader-Willi Syndrome (PWS) is a rare neurodevelopmental disorder affecting multiple functional parameters. This study examined postural stability and associated gait and neuromuscular factors in young adults with PWS.
*Methods:* Participants included 10 adults with PWS [7 M/3F; Body Fat % 40.61 ± 7.79]; ten normal weight (NW) adults [7 M/3F; Body Fat % 23.42 ± 7.0]; ten obese (OB) adults [7 M/3F; Body Fat % 42.40 ± 5.62]. Participants completed the Sensory Organization Test (SOT)®. Condition (C) specific and a composite equilibrium score (CES) were calculated (maximum = 100). Quadriceps strength was assessed using an isokinetic dynamometer. Three-dimensional gait analyses were completed along a 10 m walkway using a motion capture system and two force plates. A gait stability ratio (GSR) was computed from gait speed and step length (steps/m).
*Results:* The PWS group had lower scores for C1, C3, C4 and CES compared to the NW ($p < .039$ for all) and lower scores for C4 and CES than the OB ($p < .019$ for both) groups, respectively. In C5 (eyes closed, sway-referenced support) and C6 (sway-referenced vision and support), 33.3% of participants with PWS fell during the first trial in both conditions ($X^2$ [2] 7.436, $p = .024$) and ($X^2$ [2] 7.436, $p = .024$) but no participant in the other groups fell. Those with PWS showed higher GSR than participants with NW ($p = .005$) and those with obesity ($p = .045$).
*Conclusion:* Individuals with PWS had more difficulty maintaining standing balance when relying on information from the somatosensory (C3), visual-vestibular (C4) and vestibular systems (C5, C6). A more stable walk was related to shorter steps, slower velocity and reduced peak quadriceps torque. Participation in multisensory activities that require appropriate prioritization of sensory system(s) input for controlling balance in altered sensory environments should be routinely included. In addition, exercises targeting muscular force and power should be included as part of exercise programming in PWS.

## 1. Introduction

Prader-Willi syndrome (PWS) is a rare neurodevelopmental disorder and is the best characterized form of genetic obesity (Cassidy, Schwartz, Miller, & Driscoll, 2012). PWS negatively impacts the endocrine, neuromuscular, and musculoskeletal systems (Cassidy

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et al., 2012; Reus et al., 2011). Adults with PWS commonly have growth hormone deficiency, poor lean mass, high fat mass, hypotonia, poor bone mineral density (Cassidy et al., 2012) and increased (by 30%) risk of fractures (Butler et al., 2002). Cerebellar dysfunction has also been recently demonstrated in adults with PWS (Blanco-Hinojo et al., 2021).

Postural stability is the act of achieving, maintaining or restoring a state of balance during any activity (Pollock, Durward, Rowe, & Paul, 2000). The visual, somatosensory, and vestibular systems provide critical information contributing to postural stability (Peterka & Loughlin, 2004). Adults with PWS showed poor postural stability during standing (eyes open) with greater anterior-posterior (A/P) and medio-lateral (M/L) displacement of the center of pressure (CoP) compared to adults with and without obesity (Capodaglio et al., 2011; Galli et al., 2011). Muscle weakness in the ankle (Capodaglio et al., 2009) and/or muscle hypotonia (Galli et al., 2011) were identified as contributing factors. The presence of obesity in PWS could account for more CoP displacement (Menegoni et al., 2011). However, poorer postural stability in PWS than in non-syndromic obesity (Capodaglio, Menegoni, et al., 2011; Galli et al., 2011) suggests additional impairment. One factor could be impaired reception and integration of sensory information. Children with PWS have greater postural instability in conditions requiring contribution of the vestibular system, which indicates impairment in sensory reception and integration (Rose, White, Blanchard, Wilson, & Rubin, 2014).

Balance and gait are integral components of mobility and they share integratory neural signals at the level of the brainstem (Drew, Prentice, & Schepens, 2004). Walking is a task that requires postural stability and integration of multiple sensory inputs (Drew et al., 2004; Osoba, Rao, Agrawal, & Lalwani, 2019). Adults with PWS walk at a slower self-selected speed compared to controls with and without obesity (Cimolin et al., 2011b; Pamukoff, Holmes, Shumski, Garcia, & Rubin, 2020). Specifically, those with PWS spend a greater proportion of the gait cycle in stance compared with swing, and have a lower anterior step length (~1/3 of the length) when compared to controls of normal weight (Cimolin et al., 2011b). Other characteristics include longer transition time from standing with double to single base of support and less CoP displacement (Cimolin et al., 2017). These characteristics suggest a cautious and hypokinetic gait (Osoba et al., 2019). Hence, postural instability may contribute to compensatory gait modifications in those with PWS with the aim of increasing gait stability (Cromwell & Newton, 2004).

To date, most literature has evaluated factors affecting physical function in PWS by evaluating balance (Capodaglio, Menegoni, et al., 2011), muscular strength (Capodaglio et al., 2009) or gait (Cimolin et al., 2011a; Cimolin et al., 2017) separately or by evaluating the contribution of some factors such as hypotonia (Galli et al., 2011) or vision (Cimolin et al., 2011b) to postural stability. Thus, this study comprehensively evaluated physical function in adults with PWS by determining the contribution of sensory information to postural stability; and compared postural stability, spatiotemporal gait parameters and muscle strength, between adults with PWS to controls with and without obesity. We hypothesized that compared with controls, adults with PWS would have impaired postural stability and altered sensory integration, lower muscle strength, and gait features indicative of reduced mobility. A secondary exploratory aim was to determine associations between postural stability and muscular strength and spatiotemporal gait parameters in PWS.

## 2. Methods

### 2.1. Participants

Participants included ten adults ages 18–40 with PWS, ten adults with obesity but without PWS (with a body mass index >30 kg/m$^2$) and ten adults without PWS and without obesity (with a body mass index <25 kg/m$^2$ and > 17.9 kg/m$^2$) matched by age (±2 years) and sex. A sample size of ten participants per group was estimated based on a priori calculations for a one-way MANOVA ($f^2 = 0.75$, number of groups = 3, response variables = 10, $\alpha = 0.05$). Documented diagnosis for those with PWS included uniparental disomy ($n = 3$) and paternal deletion ($n = 7$). Seven participants with PWS were in growth hormone replacement therapy at 0.4–3 mg/dl daily doses. Exclusion criteria included a history of lower extremity surgery or fracture, injury in the lower extremity in the preceding six months, or neurologic or cardiovascular conditions that affected their ability to exercise. Female participants with confirmed pregnancy were also excluded.

Adults with PWS were recruited through study advertisements by the Prader-Willi California Foundation. Adults without PWS were recruited at the California State University Fullerton campus through fliers and word of mouth. All study procedures were approved by the Institutional Review Board at California State University Fullerton. Participants without PWS provided written consent and participants with PWS provided written assent and consent from their parent or legal guardian.

### 2.2. Procedures

Participants completed measurements in the following order: physical characteristics, sensory reception and integration, muscular strength, gait pattern and body composition during one visit. Participants with PWS were scheduled during the morning to maximize their energy level (Butler, Theodoro, Bittel, & Donnelly, 2007).

### 2.3. Measurements

#### 2.3.1. Physical characteristics and body composition

Body mass was obtained to the nearest 0.1 kg without shoes or heavy clothing using an electronic scale (ES200L; Ohaus, Pinewood, NJ, USA). Stature was measured to the nearest 0.1 cm at the end of inhalation using a wall-mounted stadiometer (Seca, Ontario, CA, USA). Body mass index (BMI) was computed by dividing body mass (kg) by stature (m$^2$). Body fat and lean mass were measured using a

full body dual x-ray absorptiometry scan (Lunar Prodigy Advance Plus; GE Healthcare, Milwaukee, WI). Air displacement plethysmography (BOD POD GS; COSMED USA Inc., Concord, CA) was used in participants with PWS because they were unwilling to have radiation ($n = 1$) and had metal rods and screws in the spine (n = 1).

#### 2.3.2. Sensory reception and integration

Sensory reception and integration contributing to postural control was evaluated using the sensory organization test® (SOT; Nashner, 1982; Nashner, Black, & Wall III, 1982). Anterior-poster sway is recorded while participants stand on moveable dual-force plates within a moveable three-sided visual surround. All participants completed the SOT® protocol on the SMART Balance Master® (NeuroCom International, Clackamas, OR) as described in the test manual. The test is comprised of three 20-s trials in each of six test conditions (firm support surface with eyes open [C1], firm support surface with eyes closed [C2], firm support surface and sway-referenced visual surround [C3], sway-referenced support surface with eyes open [C4], sway-referenced support surface with eyes closed [C5], and eyes open on a sway-referenced support surface and visual surround [C6]) in which the participant stands on a force platform that measures postural sway. A computer-calculated equilibrium score (ES) was recorded for each trial unless a fall was detected (0−100). A mean condition-specific equilibrium score (C1-C6) was calculated by averaging the scores across all three trials (0–100). A score of "0′ was assigned to a trial marked as a fall (a stepping reaction, hands touching the surround, or in cases where the participant required manual assistance from the overhead harness and/or test administrator). A weighted mean Composite Equilibrium Score (CES) for the six test conditions (0–100) was also generated by the SMART Balance Master® (Balance Master Operator's manual 2001, NeuroCom International Inc., Clackamas, OR). A CES close to 100 is associated with good postural stability and minimal sway while a lower CES indicates higher levels of sway and poor stability. When one or more falls were detected in any sensory condition a condition-specific score was not calculated. Participants completed a familiarization trial (one trial per condition) before completing three 20-s trials per sensory condition. The SOT has demonstrated good test-retest reliability for the CES (ICC: 0.76; $CI_{95\%}$: 0.46–0.90) in youth with PWS (Rose et al., 2014).

#### 2.3.3. Gait assessment

Three-dimensional gait analyses were completed along a 10 m walkway using a 9-camera Qualisys motion capture system (Qualisys, Goteburg, Sweden) and 2 force plates (AMTI, Waterdown MA) recording at 240 Hz and 2400 Hz, respectively (Pamukoff et al., 2020). Participants used their own footwear during testing because individuals with PWS commonly use orthotic devices and the intent was to capture habitual gait. Retroreflective markers were placed bilaterally on the heel counter, medial and lateral malleoli, and the first and fifth metatarsals and were removed after a standing calibration trial. Participants completed 5 practice trials to obtain self-selected walking speed and ensure that they could strike consecutive force plates without altering their gait. Walking speed was monitored using two timing gates positioned 2 m apart around the force plates and verified via anterior-posterior velocity of the pelvis segment. Five trials for each limb were used for analysis and deemed acceptable if both feet made full contact with force plates and participants were within 5% of their average practice trial speed. Only steps obtained during contact with force plates were used for analysis.

#### 2.3.4. Quadriceps strength

Isometric quadriceps function was assessed using an isokinetic dynamometer collecting at 2000 Hz (HUMAC Norm, Stoughton MA) (Vakula et al., 2019). Participants' dominant limbs (preferred limb to kick a ball) were positioned in 60 degrees of knee flexion and the axis of rotation was aligned with the knee joint center. The shank, thigh and torso were stabilized with Velcro straps, and the arm was affixed 2 cm above the medial malleoli. Prior to maximal assessments, participants completed submaximal contractions at 25%, 50%, 75% and 100% of their perceived maximal effort to serve as a warmup and acclimatization. Three maximal trials were completed with 1 min of rest in between trials.

### 2.4. Data processing

Marker trajectories and force plate data were low-pass filtered at 5 Hz and processed using Visual 3D (C-Motion, Germantown MD). A virtual foot segment was used where calibration markers were projected to be parallel to the floor (Vakula, Garcia, Holmes, & Pamukoff, 2022). The vertical ground reaction force was used to determine heel contact (>20 N) and toe off (<20 N). Step length (m) and step width (m) were defined as the distance between the proximal end-point of the foot segments at heel contact along the anterior-posterior and medial-lateral axes, respectively, and were normalized to body height for analyses. Double-limb support time (seconds) was defined as the time between heel contact of the leading foot to toe-off of the trailing foot. Single-limb support time (seconds) was calculated as: single limb support time = total stance time – double limb support time. Cadence (steps per minute) was calculated as: cadence = gait speed (m/s) * 60 / step length (m).The gait stability ratio (GSR), an indicator of postural stability during walking, was computed as: GSR = cadence (steps/s) / speed (m/s) (Cromwell & Newton, 2004).

Dynamometry data were analyzed using a custom LabVIEW program (National Instruments, Austin TX)(Vakula et al., 2019). Torque data were low-pass filtered at 50 Hz and normalized to lean mass. Peak torque was defined as the maximum torque signal, and early and late rate of torque development were defined as the linear slope of the torque signal during the first 100 ms and 100-200 ms following contraction onset, respectively. Contraction onset was defined as when the torque signal exceeded 3 standard deviations of the resting value. The trial with the highest peak torque was used for all analyses.

### 2.5. Statistical analyses

Data were screened for outliers and normal distribution by computing a z-score for skewness and kurtosis and late absolute and normalized RTD were the only variables identified not following a normal distribution. Descriptive means were calculated for participants' characteristics, SOT scores for conditions 1–4 and CES, gait spatiotemporal parameters and muscular strength. No mean data were available for C5 and C6 in the group with PWS due to multiple falls. Percent of falls were compared across the groups using Chi-Square analyses. Three by four repeated measures ANOVAS evaluated differences across groups for C1-C4. A one-way ANOVA was done to compare the CES among groups. One-way MANOVAS evaluated differences in mean scores for muscular strength and gait spatiotemporal parameters across the groups. Post-hoc comparisons were done using Tukey HSD tests. Statistical significance was set at $\alpha < 0.050$.

In those with PWS, one-tail Pearson or Rho correlation coefficients were used to examine potential associations between: 1) postural stability (C1 of the SOT), gait and normalized muscular strength measures and 2) gait and muscular strength. We calculated the 95% confidence intervals for the coefficients and interpreted their magnitudes as moderate (0.5–0.7) or large (>0.7).

## 3. Results

### 3.1. Participant characteristics

Demographic information is provided in Table 1. Participants with PWS had comparable height to other groups. Participants with PWS had greater body mass than those with NW ($p = .082$) and lower body mass than those with obesity ($p = .002$). Similarly, those with PWS had greater BMI and body fat than those with NW ($p = .009$ and $p < .001$, respectively) and lower BMI than those with obesity ($p = .001$). Those with PWS had lower lean mass than those with obesity ($p = .015$).

### 3.2. Postural stability

One participant with PWS did not complete the SOT test due to fear. Because of an invalid trial in one condition, data for one male with NW was omitted for that condition. One participant with PWS fell on all trials in C5 and C6, a second participant with PWS fell on all trials in C5 but only the first trial in C6. A third participant with PWS only fell on the first trial in C5 while a fourth participant with PWS fell on all three trials in C6. Specifically, during the first trial in C5 a greater proportion of participants with PWS fell (33.3%) while no participant in the other groups fell $X^2$ (2) = 7.436, $p = .024$. In C6, 33.3% of participants with PWS also fell on the first trial but no participant in the other groups fell $X^2$ (2) = 7.436, $p = .024$.

A three by four repeated measures ANOVA indicated a significant group by condition interaction ($p = .003$). Follow up post-hoc tests using the Bonferroni correction factor demonstrated that the group with PWS had lower C1, C3, C4 ES than the group with NW ($p < .039$ for all) and a lower C4 ES than the group with obesity ($p < .019$ for both), respectively. Moreover, there were no significant differences in C1-C4 between the group with NW and the group with obesity ($p > .327$ for all). A one-way ANOVA indicated significant differences among groups for CES ($p = .005$) and pairwise comparisons showed lower CES in the group with PWS compared to the group with NW and the group with obesity (Table 2).

### 3.3. Gait parameters

The one-way MANOVA comparing gait parameters was significant (Pillai's trace = 1.051, $F = 2.462$, $p = .009$, Table 3). Group effects were found for absolute and normalized step length, double-limb support time, gait speed and GSR ($p < .048$ for all). No group effects were found for absolute or normalized step width ($p = .141$ and $p = .261$, respectively), single-limb support time ($p = .257$) or cadence ($p = .081$). Post hoc comparisons indicated that those with PWS had smaller absolute and normalized step lengths than those with NW ($p = .003$ and $p < .001$, respectively) and smaller absolute step lengths than those with obesity ($p = .030$). Those with PWS had a longer double-limb support time and slower gait speed than those with NW ($p = .019$ and $p = .024$, respectively). Those with PWS showed higher GSR than participants with NW ($p = .005$) and those with obesity ($p = .045$). (See Table 4.)

**Table 1**
Participant characteristics for adults with Prader-Willi syndrome (PWS), normal weight (NW) and non-syndromic obesity, presented as mean ± SD.

| | Adults with PWS ($n = 10$) | Adults with NW (n = 10) | Adults with obesity (n = 10) | $p$-value |
|---|---|---|---|---|
| Sex (M/F) | 7/3 | 7/3 | 7/3 | n/a |
| Age (y) | 22.70 ± 5.21 | 23.01 ± 2.82 | 22.96 ± 2.39 | 0.980 |
| Height (cm) | 166.52 ± 14.56 | 166.68 ± 6.66 | 174.07 ± 8.99 | 0.210 |
| Body Mass (kg) | [a,b]79.09 ± 21.29 | 63.57 ± 5.03 | 105.45 ± 15.46 | <0.001 |
| BMI (kg/m$^2$) | [a,b]28.12 ± 5.43 | 22.86 ± 1.19 | 34.63 ± 3.01 | <0.001 |
| Body Fat (%) | [a]40.61 ± 7.78 | 23.42 ± 7.83 | 42.40 ± 5.62 | <0.001 |
| Lean Mass (kg) | [b]44.73 ± 11.01 | 46.74 ± 7.31 | 58.68 ± 12.18 | 0.012 |

[a] PWS different from NW ($p < .050$).
[b] PWS different from adults with obesity ($p < .050$).

**Table 2**
Group scores for the SOT conditions 1–4 and the composite equilibrium score (maximum score 100).

| | Adults with PWS | Adults with NW | Adults with obesity | *p*-value for PWS vs. NW | *p*-value for PWS vs. obesity |
|---|---|---|---|---|---|
| Condition 1 ($n = 9/10/10$) | [a]92.16 ± 2.60 | 95.06 ± 0.94 | 93.46 ± 2.55 | 0.021 | 0.603 |
| Condition 2 (n = 9/10/10) | 90.22 ± 3.93 | 92.63 ± 1.10 | 90.66 ± 2.83 | 0.224 | 1.000 |
| Condition 3 (n = 9/10/10) | [a]89.00 ± 4.76 | 92.70 ± 1.36 | 92.03 ± 2.00 | 0.038 | 0.111 |
| Condition 4 (n = 9/10/10) | [a,b]75.66 ± 12.21 | 89.90 ± 3.54 | 88.86 ± 4.48 | 0.001 | 0.002 |
| CES (n = 9/10/9) | [a,b]69.44 ± 13.99 | 83.88 ± 4.80 | 81.90 ± 6.29 | 0.005 | 0.020 |

Notes: PWS (Prader-Willi syndrome), NW (Normal Weight), CES (Composite Equilibrium Score); Means presented as means ± standard deviation.
[a] PWS different from NW ($p < .050$).
[b] PWS different from adults with obesity ($p < .050$).

**Table 3**
Muscular strength parameters in a group of adults with PWS, with obesity and with normal weight (NW), mean (SD).

| | Adults with PWS | | Adults with NW | | Adults with obesity | | Partial $\eta^2$ |
|---|---|---|---|---|---|---|---|
| Absolute peak torque (N*m) | [a,b]129.92 | (71.78) | 200.25 | (33.67) | 236.75 | (77.16) | 0.349 |
| Normalized peak torque ($N*m*kg^{-1}$) | [a,b]2.769 | (0.191) | 4.015 | (0.883) | 4.314 | (0.552) | 0.374 |
| Absolute early RTD ($N*m*s^{-1}$) | [a,b]453.892 | (459.525) | 1018.693 | (367.964) | 1118.605 | (470.072) | 0.335 |
| Normalized early RTD ($N*m*kg*s^{-1}$) | [a,b]9.327 | (8.401) | 22.423 | (9.077) | 18.668 | (5.395) | 0.357 |
| Absolute late RTD ($N*m*s^{-1}$) | [a,b]184.915 | (156.841) | 458.662 | (147.057) | 501.068 | (184.220) | 0.449 |
| Normalized late RTD ($N*m*kg*s^{-1}$) | [a,b]3.840 | (2.902) | 10.180 | (4.088) | 8.708 | (3.154) | 0.410 |

Notes: PWS (Prader-Willi syndrome), NW (Normal Weight).
[a] PWS different from adult with NW ($p < .050$).
[b] PWS different from adult with obesity ($p < .050$).

### *3.4. Quadriceps strength*

The one-way MANOVA comparing absolute and normalized quadriceps strength measures was significant (Pillai's trace = 0.850, F = 2.835, $p = .005$). Group effects were found for absolute and normalized peak torque, absolute and normalized early and late RTD ($p < .005$ for all). Those with PWS had lower absolute and normalized peak torque than those with NW or obesity ($p = .052$, $p = .002$ and $p = .002$, $p = .014$, respectively). Additionally, those with PWS had lower absolute and normalized early RTD compared to those with NW or obesity ($p = .019$, $p = .002$, and $p = .006$ and $p = .032$, respectively). Those with PWS had lower absolute and normalized late RTD when compared to those with NW or obesity ($p = .002$, $p < .001$and $p < .001$, $p = .010$, respectively).

### *3.5. Associations between measures of physical function in participants with PWS*

The C1 on the SOT was not significantly related to any gait or muscular strength parameters ($p > .065$ for all). Lower normalized step width ($r = -0.617$, $p = .029$, [−1.000, −0.098]) and greater gait speed ($r = 0.571$, $p = .042$, [0.027, 1.000]) were related to higher normalized peak torque. Higher gait speed was related to higher normalized late RTD (rho = 0.697, $p = .013$, [0.218, 1.000]). Higher GSR was related to shorter normalized step length ($r = -0.742$, $p = .007$ [−1.000, −0.322]), longer double-limb support time ($r = 0.632$, $p = .025$, C.I. 0.220, 1.000), slower gait speed ($r = -0.869$, $p < .001$, C.I. -1.000, −0.609), lower normalized peak torque ($r =$

**Table 4**
Gait parameters in a group of adults with PWS, with obesity and with normal weight (NW), mean (SD).

| | Adults with PWS | | Adults with NW | | Adults with obesity | | Partial $\eta^2$ |
|---|---|---|---|---|---|---|---|
| Step length (m) | [a,b].639 | (0.083) | 0.766 | (0.064) | 0.732 | (0.081) | 0.352 |
| Step width (m) | 0.112 | (0.054) | 0.087 | (0.042) | 0.126 | (0.0287) | 0.135 |
| Step length (% height) | [a].383 | (0.036) | 0.459 | (0.037) | 0.421 | (0.046) | 0.404 |
| Step width (% height) | 0.069 | (0.037) | 0.053 | (0.027) | 0.072 | (0.015) | 0.095 |
| Double-limb support time (s) | [a].169 | (0.033) | 0.128 | (0.016) | 0.172 | (0.034) | 0.350 |
| Single-limb support time (s) | 0.535 | (0.052) | 0.534 | (0.035) | 0.564 | (0.049) | 0.096 |
| Velocity (m/s) | [a]1.242 | (0.190) | 1.466 | (0.139) | 1.237 | (0.198) | 0.231 |
| Cadence (steps/min) | 116.53 | (8.51) | 114.87 | (5.96) | 108.52 | (8.15) | 0.170 |
| Gait Stability Ratio (steps/m) | [a,b]1.591 | (0.228) | 1.314 | (0.118) | 1.383 | (0.174) | 0.325 |

Notes: PWS (Prader-Willi syndrome), NW (Normal Weight).
[a] PWS different from adult with NW ($p < .050$).
[b] PWS different from adult with obesity ($p < .050$).

−0.760, $p = .005$, C.I. -1.000,-0.358), and lower normalized late RTD (rho = −0.709, $p = .011$, C.I. -1.000, −0.240). Scatterplots for these associations are presented in Figs. 1 and 2.

## 4. Discussion

This study supports previous findings that show poor postural stability in adults with PWS. We identified, impairments in the integration of visual, somatosensory and vestibular inputs for postural control in adults with PWS. Increased gait stability (i.e., a more cautious gait strategy) in those with PWS was associated with shorter step length, slower speed, less time in single limb support and lower force production.

While previous studies have shown postural instability in PWS (Capodaglio, Menegoni, et al., 2011; Cimolin et al., 2011b), the results of the SOT test provide new and rich information. In C3 of the test visual inputs are manipulated because the visual surround is sway-referenced. This condition requires the individual to rely more on somatosensory and vestibular inputs for maintaining upright balance. Cimolin and collaborators did not identify impairments in the contribution of visual input to postural stability using the Romberg ratio (Cimolin et al., 2011b) which is comparable to our results in conditions to C1 and C2 of the SOT. However, the present study suggests difficulties when non veridical visual information is presented. The higher postural sway in C3 in those with PWS compared with controls suggests an inability to increase the weighting of somatosensory and vestibular information to compensate for the inaccurate vision produced by sway-referencing the visual surround.

The high incidence of falls in the group with PWS in C5 and C6 also suggest a failure to rely on the vestibular system when both the visual and somatosensory inputs are manipulated (C5) or during conditions of sensory conflict in which the visual and somatosensory information is nonveridical (C6). Additionally, the higher level of postural sway in those with PWS compared to the controls in C4 indicate difficulties with appropriately weighting visual and vestibular inputs when somatosensory information is manipulated by sway-referencing the support surface. The results confirm impairments in the contribution of the vestibular system as shown previously in children with PWS (Rose et al., 2014), suggesting postural control does not improve with age and maturation of the vestibular system that is generally seen in people with neurotypical development (Hirabayashi & Iwasaki, 1995). Importantly, the repeated falls in some participants with PWS when exposed to the same sensory condition suggests an inability to adapt by appropriately prioritizing other sensory inputs to control balance. This places adults with PWS at a greater risk for falls in certain sensory environments. Further

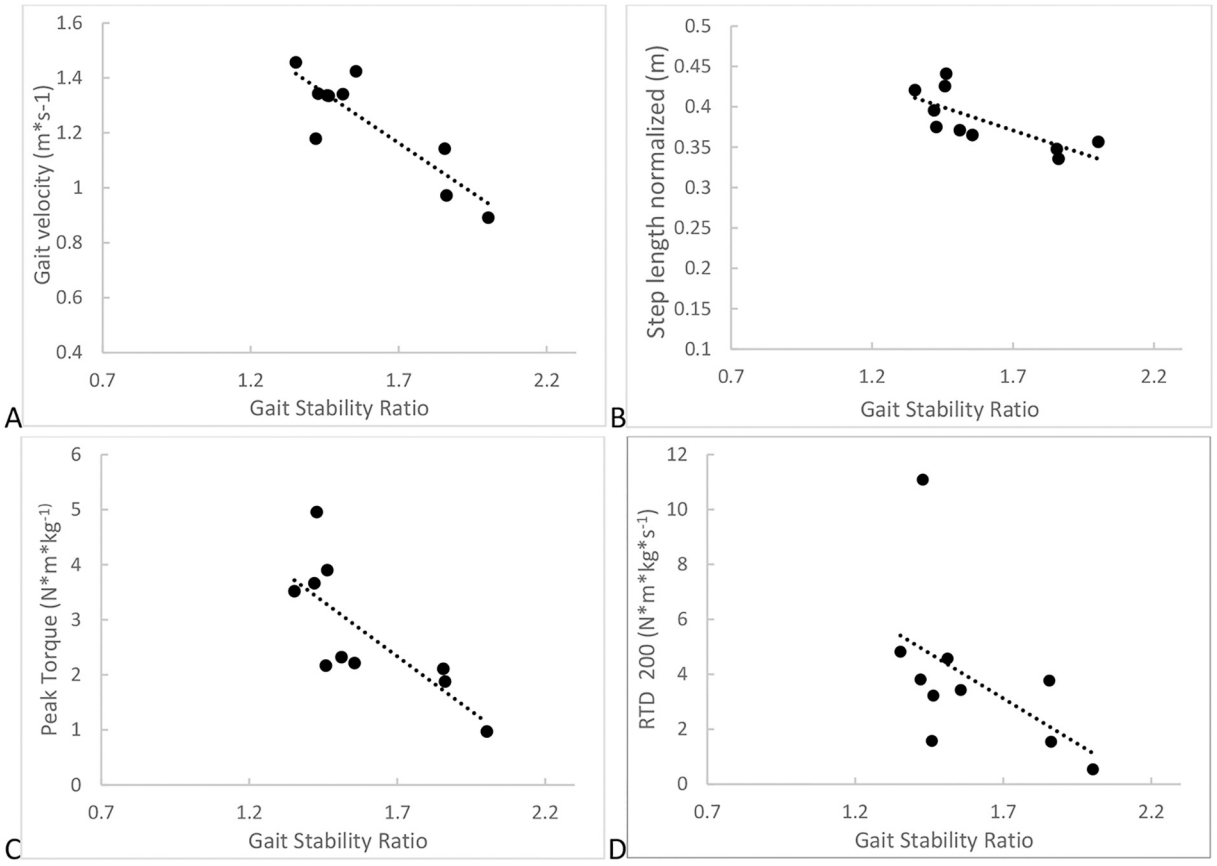


**Fig. 1.** Associations between the gait stability ratio, gait spatiotemporal parameters, and quadriceps strength parameters in participants with PWS (n = 10).

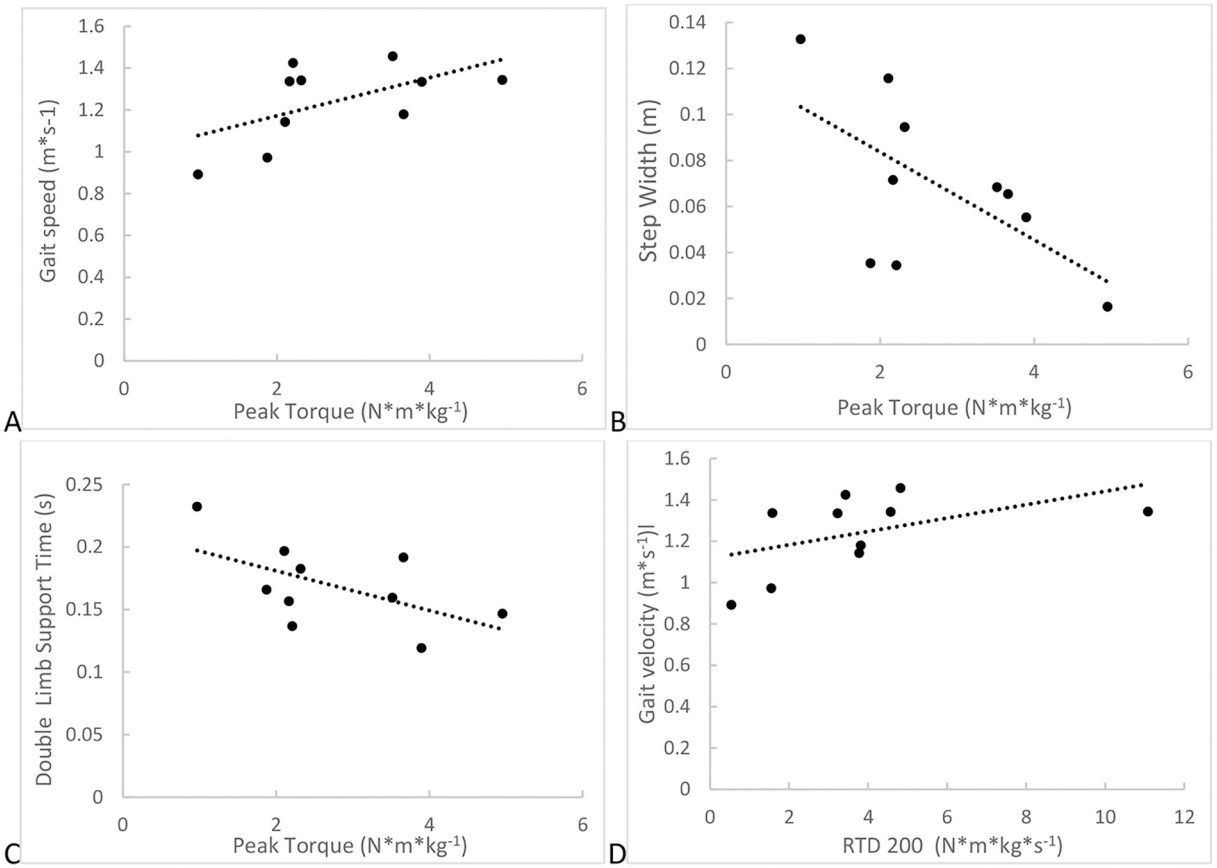


**Fig. 2.** Associations between quadriceps strength parameters and gait spatiotemporal parameters in participants with PWS ($n = 10$).

longitudinal studies should examine postural control throughout the lifespan in persons with PWS while also investigating whether exercise interventions that include a multisensory training component positively impact sensorimotor processes in person with PWS.

We confirmed similar findings as others for gait spatiotemporal parameters including a shorter normalized step length (Cimolin et al., 2021) and a slower self-selected speed (Cimolin et al., 2010) in PWS when compared to NW controls but no differences when compared to controls with obesity. This reduced normalized step length has been reported in adults with non-syndromal obesity (Lai, Leung, Li, & Zhang, 2008; Liu & Yang, 2017; Pataky, Armand, Muller-Pinget, Golay, & Allet, 2014). In older women with obesity, it was postulated that increased plantar pressure because of the excess mass might adversely affect mechanoreceptors resulting in reduced somatosensory feedback (Gonzalez, Gates, & Rosenblatt, 2020). This reduced somatosensory input may result in wider and shorter strides to maintain postural stability during gait. Increased step width typically reflects a strategy to increase frontal plane stability by widening the base of support (Vakula et al., 2022), but we did not observe differences between those with PWS and controls. Those with PWS may adopt slower speeds that contribute to reduced mobility without a commensurate gain in frontal plane stability from wider steps. The inability to modulate step width may contribute to lateral instability and laterally directed falls in those with PWS (Rogers & Mille, 2003). Future studies should evaluate how people with PWS modulate their gait in response to increased task demands such as increased gait speed, surface grade or clearing obstacles.

Participants with PWS spent a longer time in double support and took a greater number of steps per unit of distance, resulting in a higher GSR (Cromwell & Newton, 2004). Shortening step length without increasing cadence contributes to slower gait speed. Moreover, slower gait speed includes a longer period of double-limb support time, which may provide more stability (Lai et al., 2008; Liu & Yang, 2017). Longer time spent in double support has been shown in non-syndromic obesity (Vakula et al., 2022), and thus, may in part be due to excess adiposity in PWS. The increased time in double-limb support was related to higher GSR. Higher GSR is shown in older adults without PWS (Cromwell & Newton, 2004) and in young adults with obesity in comparison to controls with normal weight (Vakula et al., 2022). A higher GSR is indicative of a strategy to achieve greater stability during walking by minimizing the dynamic portions of the gait cycle. Unfortunately, while a higher GSR may reduce fall risk in the short-term, the slower gait speeds that result may be associated with increased fall risk in the long-term (Welmer, Rizzuto, Laukka, Johnell, & Fratiglioni, 2017). Therefore, strategies are needed in PWS to enhance gait speed to decrease morbidity.

Several studies have previously demonstrated poor muscular strength in adults (Pamukoff et al., 2020) and children with PWS (Lam et al., 2016). We also found lower quadriceps muscular strength and rate of torque development in those with PWS compared to controls (with obesity and with NW). These findings replicate previous findings in calf muscles of adults with PWS in which poor

muscular force development was related to diminished neural discharge rate and intrinsic capacity of their calf muscles to produce force (Pamukoff et al., 2020). Stimulation of the nervous system may improve generalized activation of the skeletal muscle and function in those with PWS when combined with physical training as shown in other conditions (Wang, Xiao, Yu, Zhou, & Fu, 2021). Increased muscle force and power to run, jump or exercise at moderate to high intensity, currently limited in persons with PWS (Rubin, Wilson, Dumont-Driscoll, & Rose, 2019), is important because it contributes to greater caloric expenditure (Butler et al., 2007) and can be improved with training (Rubin et al., 2019).

We found no association between upright postural stability (SOT C1 scores) and gait parameters or muscle force in the group with PWS. Cromwell and Newton (2004) also showed no correlations between balance and gait in older adults (Cromwell & Newton, 2004). Galli and colleagues suggested that postural instability in PWS and Elher-Danlos syndrome was related to muscular hypotonia and weakness, but did not measure muscular strength or investigate the associations (Galli et al., 2011). In individuals who suffered a stroke, muscle force was related to performance in C4, C5 and C6 of the SOT (Marigold, Eng, Tokuno, & Donnelly, 2004). Similarly, time to torque for knee flexors was only related to C5 and C6 of the SOT in children with developmental coordination disorder (Fong, Ng, & Yiu, 2013). Muscular strength correlated with postural sway in older adults when standing on compliant surfaces (Lord & Menz, 2000). Thus, studies showing associations between muscle function and balance showed results in conditions requiring vestibular input for maintaining postural stability. Because 33% of those with PWS fell in C5 and C6 we could not evaluate associations in these conditions. Nevertheless, the decreased force production and specifically lower RTD observed in those PWS is of concern as in healthy older adults lower knee extensors RTD was associated with multiple falls (Kamo et al., 2019). Future studies should ascertain the relative contributions of impaired muscle activation and sensorimotor processes to increased fall incidence in PWS populations (Butler et al., 2002).

Correlational analyses indicated that in the group with PWS, a more stable walk (indicated by greater GSR) was associated with shorter steps, slower velocity and lower peak torque. Additionally, greater peak torque was related to longer steps, increased velocity, and less time spent in double-limb support (correlation approached statistical significance with $r = -0.573$, $p = .083$). Likewise, greater late RTD, which depends on muscle mass (Cossich & Maffiuletti, 2020), was also associated with taking longer steps and increased velocity. In people without PWS muscular power is more strongly related than maximal strength to successful balance recovery (Han & Yang, 2015). Possibly in PWS, because of impairment in the activation of higher threshold motor neurons and larger muscle cells (Pamukoff et al., 2020), overall peak force was associated with gait parameters but early RTD was not. Additionally, as the gait speed was also low there is less power. Resistance training interventions aiming to increase muscle mass and power in those with PWS should be considered to potentially increase walking speed and balance recovery (Capodaglio et al., 2011; Mehta et al., 2012).

## 5. Study limitations and strengths

This study included a small number of participants. However, the rarity of PWS makes recruitment of large sample sizes difficult. Most of the participants with PWS were on GHRT (7/10), which positively influences muscle mass; however, comparisons based on GHRT were not possible. Regardless, the study had sufficient statistical power to detect major group differences. Additionally, the study design included two closely age and sex matched control groups with and without obesity which allowed us to investigate whether differences were solely related to excess adiposity or other neuromuscular characteristics of those with PWS. The study also included a comprehensive evaluation of physical function, including postural control, gait and muscle function. While we used a state-of-the-art test to identify impairments in sensorimotor processes contributing to upright balance, other factors likely contribute to recovery from a sudden loss of balance. The high incidence of falls in conditions 5 and 6 of the SOT in the PWS group limited group comparisons for those conditions. Additionally, we evaluated gait in a laboratory-based environment and force plate positioning may have constrained some aspects of spatiotemporal parameters (e.g., step length). Nonetheless, we still identified meaningful and expected differences between those with and without PWS, and values were similar to those previously reported (Vakula et al., 2022). Last, we explored potential associations between factors, but the cross-sectional design presents limitations related to causality and potential confounders.

## 6. Conclusion

We identified impairments in the contribution of visual, somatosensory and vestibular input to postural stability in adults with PWS. We also identified a more cautious and slower gait in those with PWS that was characterized by shorter steps and a longer time spent in double-limb support. We found that a more stable, yet slower gait in those with PWS was related to less quadriceps peak torque, and rate of torque development. Thus, we identified some aspects of physical function that could be targeted for intervention to improve balance as well as mobility in this population to reduce the risk of falls (Rose, 2010; Sherrington et al., 2020).

## CRediT authorship contribution statement

**Daniela A. Rubin:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Investigation, Supervision, Writing – original draft. **Debra J. Rose:** Methodology, Resources, Writing – review & editing. **Derrick L. Escano:** Investigation, Data curation, Writing – review & editing. **Skylar C. Holmes:** Investigation, Data curation, Writing – review & editing. **Steven A. Garcia:** Data curation, Writing – review & editing. **Derek N. Pamukoff:** Conceptualization, Funding acquisition, Methodology, Software, Investigation, Supervision, Writing – review & editing.

## Declaration of Competing Interest

The authors declare no conflict of interest with the information presented in this manuscript.

## Data availability

Data will be made available on request.

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