Effects of external and internal cues on gait function in Williams syndrome

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A B S T R A C T

Williams syndrome (WS), a rare genetically based neurodevelopmental disorder, is characterized by gait abnormalities that resemble basal ganglia-parkinsonian deficits in the internal regulation of stride length. In the current study, we explored whether visual or attentional cues would improve gait function in adults with WS, when compared to adults with Down syndrome (DS) and neurologically normal controls. The spatiotemporal characteristics of gait were measured using the GAITRite walkway while participants walked with visual cues set at 20% greater than preferred stride length (externally cued), or with an attentional strategy of maintaining the stride length without the assistance of visual cues (internally cued). Although the WS and DS groups were able to achieve the criterion and normalize stride length in both conditions, the WS group significantly reduced their gait speed and cadence in the externally cued condition when compared to controls. In the internally cued condition, the WS group also showed reduced speed and increased intra-individual variability in speed and stride time. These findings suggest that the primary deficit is not one of difficulty regulating stride length in WS, but rather indicates more widespread dysfunction within visuomotor regions.

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1. Introduction

Williams syndrome (WS) is a rare genetically based disorder, affecting 1 in 20,000 births, with more recent estimates of 1 in 7500 [1], caused by a microdeletion on a section of chromosome 7 including approximately 28 genes. The unique cognitive profile of WS has been well documented; this profile includes mild-to-moderate intellectual disability, with relative strengths in the verbal domain and face recognition, but with poor abilities in the visuospatial domain [2]. These characteristics are assumed to be related to specific dysfunction in the dorsal visual pathway in individuals with WS, an area which underpins the processing of spatial information associated with visually-guided movement; in contrast, ventral visual areas, which subserve perceptual processes such as object and face recognition, seem to be preserved [3]. Although several studies have shown visuomotor deficits within both upper limb and gait function in individuals with WS [4–7], the neural basis of the visuomotor abnormalities observed in WS are, as yet, unclear.

Anecdotal and clinical observations indicate that visuomotor deficits in WS are more pronounced during more complex motor tasks, such as descending stairs or walking across uneven surfaces [5,8]. The results of our previous research on the spatiotemporal gait patterns associated with WS indicate that, when compared to a neurologically intact control group, individuals with WS are characterised by slow, wide-based (broad distance between the feet) and variable gait; however, we concluded that the primary deficit appears to be difficulty in regulating stride length rather than cadence (stepping frequency) [7]. More specifically, the WS group showed a consistently reduced stride length at any given increase in speed, with a disproportionate increase in cadence as speed increased. Accordingly, the gait disturbances observed in WS resembled basal ganglia-parkinsonian deficits in the internal regulation of stride length [9,10].

Imaging studies have shown that, when compared with healthy controls and individuals with Down syndrome (DS), the volume of the caudate nuclei and basal ganglia is significantly reduced in individuals with WS [11–14]. In contrast, individuals with DS show relatively preserved volume of the basal ganglia and posterior (parietal and occipital) regions, whereas frontal, temporal and cerebellar regions are typically reduced in size [15,16]. Imaging studies, however, have shown either preserved or increased volume of the cerebellum in WS [11,13,14,17,18]. Nevertheless, biochemical differences (reduction of the neurotransmitter N-acetylaspartate) in the cerebellum have been observed during performance on visuospatial and visuomotor tasks in WS [19]. One of the most consistent findings to date, in the imaging studies in WS, is primary dysfunctions in the dorsal visual stream of the posterior parietal cortex [3,20,21]. However, it is not clear how these
abnormalities in visuomotor regions in WS are related to the control of gait function.

Some insights regarding the underlying mechanisms of abnormal gait in WS may be gained by employing similar paradigms to those used in patients with Parkinson’s disease (PD). Several studies have demonstrated that, when PD patients are provided with visual cues to guide their stride length, a normalization of speed and stride length can be achieved [10,22–25]. Azulay et al. [26] have suggested that the external visual cues may bypass the deficient basal ganglia-supplementary motor loop—a loop that fails to provide internal cues for the initiation of a motor sequence. However, these cues might influence the attention of individuals, which ultimately might affect their gait patterns; indeed, techniques that manipulate attention have been shown to be effective in normalizing the gait patterns in PD [27].

The underlying mechanisms for the normalization of gait in PD with the use of visual cues are still subject to debate. One possible explanation is that visual cues focus attention on the stride length, and thereby enable conscious compensatory mechanisms to circumvent the affected areas in the basal ganglia-supplementary motor loop, via the lateral premotor cortex [28]. An alternative explanation for facilitation of movement by visual cues in PD concerns the effects of optic flow—that is, the perceived motion of the stripes induced by the walking patient. As Azulay et al. [29] suggested, specific visuomotor (cerebello-cortical) pathways, particularly responsive to visual cues, may bypass the damaged basal ganglia in PD. However, the extent to which external or internal cues would be effective in improving the gait in individuals with WS, as has been demonstrated in PD, remains unclear.

The aim of the current study was to examine the effect of external and internal cueing on the spatiotemporal gait patterns in individuals with WS, when compared to both individuals of a similar chronological age and IQ with Down syndrome (DS) and a group of typically developing controls. Because most individuals with WS show mild-to-moderate intellectual disability, gait studies in this population are faced with particular challenges with respect to selecting an appropriate comparison group. For instance, differences between individuals with normal IQ and individuals with WS could be ascribed solely to intellectual disability. Thus, individuals with DS were used as a comparison group in the current study, because this population have been frequently compared to IQ-matched individuals with WS in the context of their unique neurological profiles. Individuals with DS show unique gait adaptation to maintain walking stability; that is, walking slower, with shorter, wider steps [30], although it is not yet clear how the differences in cortical and subcortical structures observed in these syndromes are related to gait function.

In the current study, we employed external visual cueing with the use of horizontal floor markers set at a criterion stride length. Performance in this condition was compared to the gait patterns with internal cueing—an attentional strategy of maintaining an image or representation of the stride length, without the assistance of visual cues. We hypothesized that, if the abnormal gait in WS resembles a parkinsonian-basal ganglia pattern, the effect of both visual cues and the attentional strategy should be effective in improving the spatiotemporal gait patterns. Alternatively, if the abnormal gait pattern in WS is more consistent with widespread abnormalities in visuomotor regions—specifically, the dorsal stream and cerebellum—we expected that neither visual cueing nor attentional strategies would be associated with any improvements in the spatiotemporal gait patterns.

2. Method

2.1. Participants

A total of 9 individuals with WS participated in the study and were recruited through the Williams Syndrome Family Support Group (Victoria) and Genetic Health Services Victoria. The participants with WS provided informed consent according to the declaration of Helsinki. In all cases, a diagnosis of WS was confirmed using fluorescent in situ hybridisation (FISH) testing for elastin, a gene found in the critical 7q11.23 deletion region, as well as confirmation either by a medical geneticist or family physician. Participants were excluded if they exhibited another neurometabolism disorder other than WS, severe joint contractures that impaired gait function, or visual deficits—such as strabismus, diminished visual acuity, amblyopia, or reduced stereopsis.

The participants with DS were recruited through the Down Syndrome Association of Victoria (DSAV) and through a longitudinal study of behavioural and emotional disturbance in people with intellectual disability [31], after informed consent was obtained. There were 9 participants with DS (Trisomy 21) who were matched to each WS individual on chronological age and IQ—as assessed on the Wechsler Adult Intelligence Scale—III (WAIS-III). The typically developing controls were recruited through social networks after informed consent and consisted of 9 participants matched as closely as possible to the other groups according to age and gender.

Table 1 shows the sample characteristics for the WS, DS, and control groups. One-way analysis of variance (ANOVA) revealed between group differences for height (F(2,24) = 14.424, p = 0.001), with both the clinical groups being shorter than controls (WS, p < 0.01; DS, p < 0.01). There were no differences in IQ scores between the WS and DS groups, and neither age nor weight differed across the WS, DS, and control groups.

2.2. Apparatus

The GAITRite walkway (CIR Systems Inc., Clifton, NJ, USA) was used to measure spatial and temporal gait parameters. The GAITRite is an 830 cm long × 89 cm wide walkway, with pressure sensors arranged in a horizontal grid. The sensors are arranged in a 48 × 48 grid pattern and each sensor is separated by 1.27 cm. The walkway is connected to a Windows based PC via an interface cable and the GAITRite application software. Although gait data were collected over 8.3 m only, a 14.3 m walkway was used to minimise effects associated with initial acceleration and final deceleration during each walk. After each trial, data were collected and analysed via the application software. All data were collected in the Clinical Research Centre for Movement Disorders and Gait at the Kingston Centre, Australia.

3. Procedure

Participants completed five walking trials in three different conditions in order. In the preferred walking condition, participants were instructed to walk at their preferred (normal) speed. In the externally cued condition, visual cues, consisting of horizontal laminated white strips, were placed along the 14.3 m walkway on the floor at intervals of 20% greater than their normal preferred stride length. Participants were instructed to walk while stepping on the white strips to the end of the walkway. Third, in the internally cued condition, participants were asked

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>WS (n = 9)</th>
<th>DS (n = 9)</th>
<th>Controls (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.1 (5.2)</td>
<td>28.8 (5.8)</td>
<td>24.3 (3.1)</td>
</tr>
<tr>
<td>Male/female</td>
<td>5/4</td>
<td>3/6</td>
<td>3/6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.6 (8.8)*</td>
<td>151.8 (9.2)*</td>
<td>172.2 (5.9)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>65.8 (18.2)</td>
<td>76.0 (15.0)</td>
<td>70.6 (12.7)</td>
</tr>
<tr>
<td>VlQ</td>
<td>63.2 (6.7)</td>
<td>56.7 (6.1)</td>
<td>-</td>
</tr>
<tr>
<td>VRQ</td>
<td>65.7 (6.6)</td>
<td>60.0 (8.0)</td>
<td>-</td>
</tr>
<tr>
<td>PIQ</td>
<td>65.3 (7.0)</td>
<td>60.7 (3.7)</td>
<td>-</td>
</tr>
</tbody>
</table>

*Significant p < 0.05, relative to controls.
to use an attentional strategy by walking at 20% greater than preferred stride length without the assistance of the visual markers. Participants were asked to walk with the same size steps as before (with the white strips) by keeping the step size in mind.

4. Data analysis

The GAITRite software produces both mean values for gait measures and step-to-step values, which were used to calculate variability—representing fluctuations in gait variables across the steps within a single walk. Gait variability was measured using coefficient of variation (CoV; SD/mean × 100), which is a common method to express variability in this domain [32]. The primary dependent measures that were analysed as were follows: speed (cm walked per second), cadence (steps per minute), stride length (combined length of left and right footfalls in full gait cycle), double support (percentage of time both feet are grounded in a complete gait cycle), and heel-to-heel base of support (perpendicular distance from the heel point of one footfall to the line of progression of the opposite foot). CoV values were also calculated for stride time (variability in time elapsed between the first contacts of two consecutive footfalls of the same foot).

To examine baseline differences in the average gait parameters and CoV values across the three groups—WS, DS and controls—we conducted one-way analyses of variance (ANOVAs), using height as a covariate. To explore differences between the three groups during the externally and internally cued conditions, we developed a gait ratio. That is, for each of the gait measures, we divided the value in the cued conditions by the value in the preferred or baseline condition. This ratio reflects a relative change from baseline to cued conditions where each participant acts as their own control. Given that the gait ratio controlled for group differences at baseline, we conducted one-way analyses of variance (ANOVAs) to compare mean gait ratios for each gait variable across the groups.

5. Results

5.1. Baseline preferred walking

Table 2 shows average values for the gait measures for the preferred (baseline) walking condition. ANCOVA was used to compare the three groups on the gait measures in this condition, with height as a covariate. Although cadence did not differ across the groups during preferred walking, speed \( F(2,23) = 5.872, p = 0.009 \), stride length \( F(2,23) = 11.659, p = 0.001 \) and base of support \( F(2,23) = 3.305, p = 0.05 \) did vary significantly across these groups. Additional ANCOVAs, exploring each pair of groups at a time, were conducted. As Table 2 shows, these analyses revealed that, although the DS group showed significantly reduced speed when compared to controls \( F(1,15) = 12.560, p = 0.003 \), both the intellectually disabled groups showed a significantly reduced stride length \( WS vs controls: F(1,15) = 10.201, p = 0.006; DS vs controls: F(1,15) = 30.232, p < 0.001 \). Both WS and DS groups also showed a significantly increased base of support relative to controls \( WS vs controls: F(1,15) = 16.272, p = 0.001; DS vs controls: F(1,15) = 7.243, p = 0.017 \).

5.2. Baseline intra-individual variability

Coefficient of variation (CoV) was used as a measure of intra-individual variability at baseline. Separate ANCOVAs, with height as a covariate, showed that intra-individual variability of speed \( F(2,23) = 4.925, p = 0.017 \), stride time \( F(2,23) = 5.829, p = 0.009 \) and stride length \( F(2,23) = 3.438, p = 0.045 \) varied across the groups (see Table 2). Further comparisons between groups revealed that both the intellectually disabled groups showed increased CoV values for speed when compared to controls \( WS vs controls: F(1,15) = 7.139, p = 0.017; DS vs controls: F(1,15) = 6.128, p = 0.027 \). However, the DS group showed more variability in stride time than controls \( F(1,15) = 7.503, p = 0.016 \), while the WS group showed increased variability of stride length relative to controls \( F(1,15) = 7.605, p = 0.015 \).

5.3. Effects of cues on gait function

Fig. 1 shows the distribution of the ratios of externally and internally cued to preferred values on the three key gait measures: speed, stride length and cadence. Values above or below one on each graph represents the magnitude and direction of change from baseline. Specifically, values that exceed one indicate that the gait parameter was higher in the cued condition relative to the baseline condition. A value of one indicates no effect of the cues on gait parameters.

When speed was subjected to a one-way ANOVA, both externally \( F(2,24) = 3.653, p = 0.042 \) and internally \( F(2,24) = 3.215, p = 0.04 \) cued conditions differed across groups. Additional ANOVAs, contrasting two groups at a time, were conducted. The WS group reduced their gait speed when compared to the controls in both the externally \( F(1,16) = 12.735, p = 0.003 \) and internally \( F(1,16) = 10.332, p = 0.005 \) cued conditions. There were no significant differences between the DS and control groups, nor between the WS and DS groups on gait speed in either of these cued conditions.

A similar pattern of results emerged for cadence, but significant differences between groups were revealed only during the externally cued condition \( F(2,24) = 3.681, p = 0.041 \). As further analyses revealed, only during the externally cued condition did the WS group show a greater reduction in cadence relative to the controls \( F(1,16) = 12.795, p = 0.003 \). No significant differences emerged between DS and controls, nor between WS and DS groups, in either of the cued conditions.

As Fig. 1 shows, for the ratio of stride length to preferred walking, neither the WS nor the DS groups differed in their mean ratios relative to controls in the externally or internally cued conditions. To determine whether participants were able to increase stride length to achieve the criterion, we conducted further analyses with one-way ANOVAs on mean values for stride length deviation (difference between criterion stride and actual stride length). These analyses showed that there were no significant differences across groups for both externally \( F(2,24) = 0.445, p = 0.646 \) and internally \( F(2,24) = 2.618, p = 0.094 \) cued conditions. All the groups were able to achieve the criterion stride with a reasonable degree of accuracy—mean stride length deviation ranged from 6 to 9 cm for all groups. Thus, all groups were able to increase their
stride length to achieve the criterion stride in both of the cued conditions.

Further analyses were conducted to ascertain whether or not the WS and DS groups could effectively use external and internal cues to increase stride length to values comparable to the control group in the preferred walking condition—and thus normalize their gait pattern. ANCOVA was used to compare gait characteristics in the WS and DS groups with the preferred gait parameters of controls at baseline, with height as a covariate.

Table 3 shows mean values for each of the gait parameters in preferred (baseline) walking in controls, as well as during internal and external cues in the WS and DS groups. Stride length did not significantly differ across the groups for either the externally cued ($F(2,23)=2.122$, $p=0.143$) or internally cued conditions ($F(2,23)=2.751$, $p=0.085$), suggestive of normalization of stride length in both the WS and DS groups. In contrast, both speed (external: $F(2,23)=3.502$, $p=0.047$; internal: $F(2,23)=4.263$, $p=0.027$) and cadence (external: $F(2,23)=8.010$, $p=0.002$; internal: $F(2,23)=10.652$, $p=0.001$) did vary across these groups. Additional comparisons between the groups using separate ANCOVAs, with height as a covariate, revealed that the WS group had more difficulty in adjusting to cues to walk at control parameters. As shown in Table 3, these analyses revealed that the WS group differed significantly from controls in both speed (external: $F(1,15)=9.661$, $p=0.007$; internal: $F(1,15)=6.469$, $p=0.022$) and cadence (external: $F(1,15)=63.238$, $p<0.001$; internal: $F(1,15)=51.551$, $p<0.001$) when using external or internal cues to increase their stride length. After adjusting for height, there were no significant differences between DS and controls, nor between WS and DS groups, in either of the cued conditions.

Table 1. Box-plots showing the distribution of ratio variables for speed, stride length and cadence in the externally and internally cued conditions. The value of one represents no change from baseline, whereas a value above (increase) or below (decrease) one corresponds to the magnitude and direction of change from baseline (preferred) walking.

*Significant $p<0.05$.

Table 3

<table>
<thead>
<tr>
<th>Gait variable</th>
<th>Controls</th>
<th>WS</th>
<th>DS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speed (cm/s)</td>
<td>Baseline</td>
<td>141.0 (7.0)</td>
<td>97.9 (21.2)**</td>
</tr>
<tr>
<td></td>
<td>External</td>
<td>96.8 (29.4)</td>
<td>99.4 (22.5)</td>
</tr>
<tr>
<td></td>
<td>Internal</td>
<td>100.4 (19.7)*</td>
<td>104.8 (26.4)</td>
</tr>
<tr>
<td>Cadence (steps/min)</td>
<td>Baseline</td>
<td>112.5 (3.8)</td>
<td>75.9 (8.6)**</td>
</tr>
<tr>
<td></td>
<td>External</td>
<td>84.2 (24.6)</td>
<td>87.0 (18.4)</td>
</tr>
<tr>
<td></td>
<td>Internal</td>
<td>84.2 (24.6)</td>
<td>87.0 (18.4)</td>
</tr>
<tr>
<td>Stride length (cm)</td>
<td>Baseline</td>
<td>155.0 (7.1)</td>
<td>155.2 (25.4)</td>
</tr>
<tr>
<td></td>
<td>External</td>
<td>139.3 (23.5)</td>
<td>139.3 (23.5)</td>
</tr>
<tr>
<td></td>
<td>Internal</td>
<td>139.3 (23.5)</td>
<td>139.3 (23.5)</td>
</tr>
</tbody>
</table>

*Significant $p<0.05$; **significant $p<0.01$, adjusted for height.
5.4. Effects of cues on intra-individual variability

Coefficient of variation (CoV) ratios were analysed using one-way ANOVA to examine group differences in intra-individual variability on the key gait measures. Mean CoV ratios differed significantly across groups when an attentional strategy was used in the internally cued condition for both speed ($F(1,24) = 5.183, p = 0.014$) and stride time ($F(1,24) = 8.844, p = 0.001$) (see Fig. 1). Further comparisons between the groups for the internally cued condition revealed that the WS group demonstrated a greater increase in variability of speed relative to the controls ($F(1,16) = 10.076, p = 0.006$). The WS group also showed a greater increase in stride time variability relative to the controls during the internally cued condition ($F(1,16) = 12.300, p = 0.003$). There were no other significant differences in adaptation of gait variability between DS and control groups or between WS and DS groups in both internally and externally cued conditions.

6. Discussion

In the current study, we compared the spatiotemporal gait patterns of individuals with WS, individuals with DS, and typically developing adult controls, when adjusting their gait to external or internal cues to increase stride length. The gait variables were interpreted in terms of a ratio of cued to preferred walking. This ratio provides a reference point that represents the magnitude and direction of change from baseline. In addition, the current study tested the degree to which individuals with WS and DS could achieve the criterion stride length in the presence of external and internal cues, and whether gait could be improved to approximate normal gait patterns. The results of the current study do not support the hypothesis that WS individuals would show improvement in gait that resembles patients with PD, when using cues to increase their stride length. Overall, the results indicate that the WS group were characterized by greater difficulty walking with cues relative to controls, with a greater reduction in both gait speed and cadence when adjusting to external cues, and reduced speed and increased gait variability when using internal cues. To utilize external and internal cues, and thus to achieve the criterion stride length similar to the DS group and controls, individuals with WS needed to adjust other gait variables such as speed and cadence. In addition, these specific gait measures were differentially affected by externally vs internally cued movements in WS.

In summary, neither external nor internal cues appeared to be effective in improving the overall spatiotemporal gait patterns in individuals with WS. In contrast, the DS group did not show any significant differences in the ratio of cued to baseline walking for both speed and cadence relative to controls, although there was a non-significant trend for greater difficulty in adjusting both speed and cadence during cued walking in the DS group. Thus it should be acknowledged that these findings may not necessarily reflect more preserved gait regulation in DS, but rather may indicate more profound deficits in both externally and internally guided movements in individuals with WS relative to controls. However, all groups were able to achieve the criterion stride length with reasonable accuracy and, at least for stride length, both external and internal cues were effective in normalizing gait. In our previous study we found that, during unobstructed walking at different speeds, the regulation of stride length seemed to be impaired in adults with WS, with increased cadence used as a compensatory strategy for reduced stride length [7]. However, the results of the current study indicate that individuals with WS are able to utilize external or internal cues to normalize their stride length; nevertheless, gait function was not normalized in the same way as has previously been observed in PD patients, with greater reduction in other gait parameters such as speed and cadence in the WS group. These results are therefore not consistent with a parkinsonian gait pattern, and suggest that deficits in more widespread visuomotor regions are likely to be responsible for the abnormalities of gait in affected individuals.

Another important finding in the current study was the reduced speed and increased intra-individual variability in speed and stride time in individuals with WS, at least during internally cued movements, when compared to controls. Increased variability in stride time has been reported previously in PD patients [33] and cerebellar ataxia [34]. However, temporal variability in gait has been shown to be a more defining characteristic of cerebellar dysfunction [35]. The finding of increased CoV of speed in individuals with WS may also be considered an indicator of neurobiological dysfunction [36], as intra-individual variability is a measure of the ability to produce consistent performance across steps within the same task. However, an alternative explanation for the slowing in gait speed and increased gait variability in WS during internally guided movement may be that such individuals exhibit deficits in executive function and attention [37,38]. Arguably, internally generated movements are more complex, requiring increased allocation of attention and executive control that would be required to update the motor plan continuously. In agreement with this hypothesis, increased activation of the dorsolateral prefrontal cortex and anterior cingulate cortex has been demonstrated during internally vs externally generated movements [39]. In functional terms, the current findings are consistent with more recent evidence of increased variability in stride time, observed in patients with dementia of the Alzheimer’s type, with gait variability showing an association with the degree of impairment in executive function in these patients [40]. Thus, in our WS group, the increased cognitive processing associated with internally generated movements may compete for attentional allocation with the automatic motor task of walking, thereby exceeding limited attentional resources.

Movements generated by externally guided stimuli involve different pathways from movements involved in internally guided actions [41,42]. The role that the dorsal visual stream plays in mediating sensory-motor transformations for externally guided movements has been well documented [43]. Dorsal stream deficits may represent the neural basis for the greater deterioration in gait function when movements are externally generated in individuals with WS. Indeed, both behavioural [4,37,44,45] and neuroimaging studies [3,20,21] have provided evidence for specific dysfunction in the dorsal visual stream in WS.

In contrast, internally generated movements are associated with greater activation in regions typically associated with cognitive operations when compared to movements in response to external feedback [39,41,42]. Behavioural evidence in children with WS indicates specific weaknesses in the executive control of behaviour within the visuospatial domain [37]; reduced activation has been found in regions subserving such cognitive operations in WS including the dorsolateral prefrontal and anterior cingulate cortex [46]. This evidence implies that the neural basis for the deficits in the internal regulation of movement, involving greater utilisation of attention and executive control, is likely to be associated with specific impairments within the fronto-parietal circuits in individuals with WS [37].

A possible explanation for the greater difficulty in adjusting to visual cues during walking in the WS group relative to controls may relate to the distinct neurological profile of individuals with WS. On neurological testing, Trauner et al. [47] found greater impairment in both gross and fine motor coordination and cerebellar functions in children with WS when compared to age and IQ-matched children with DS. However, in imaging studies cerebellar volume has been shown to be relatively preserved in WS [13]; in contrast, in individuals with DS, cerebellar size has been found to be reduced, whereas the volume of the basal ganglia is preserved [15,16]. It is not entirely clear from these findings what contribution the cerebellum might make to the additional deficits in adapting gait to external cues in WS.

There are several limitations to this study. Firstly, the sample size was small in the current study; however, this study has demonstrated
the distinct advantages of instrumented gait analysis in detecting subtle changes in gait function in rare genetic disorders. Nevertheless, future research should overcome the inherent constraints on sample size in gait studies in WS by conducting larger-scale studies in both children and adults with WS. Secondly, the low tone and ligamentous laxity, common in individuals with DS, might have affected the adaptive gait parameters in this group [30]. These biomechanical limitations may have contributed to unique gait adaptation to maintain stability—specifically reduced gait speed across all conditions. Indeed, individuals with WS show their own unique musculoskeletal limitations including hypotonia and joint limitation, which may affect gait function; although, in the current study, WS participants with severe joint contractures were excluded. Finally, a direct comparison of auditory and visual cues would have been helpful in determining whether individuals with WS show specific deficits in externally vs internally guided movement. Future studies could employ rhythmic auditory cueing techniques, such as the use of a metronome, to determine whether the abnormal alterations in gait speed and variability could be improved in individuals with WS.

The empirical findings from this study support the clinical observation that individuals with WS show abnormalities in adaptive gait patterns, such as when descending stairs or walking across uneven surfaces [5,8]. The current study found that, for individuals with WS, the external visual cues were not effective in improving gait when compared to typically developing adult controls. Furthermore, internally generated movement was associated with reduced speed and increased gait variability, suggestive of impairment in fronto-parietal circuits in WS. These findings imply that the viability of alternative processing pathways for externally and internally guided movement is substantially reduced in individuals with WS, and this difficulty may involve deficits within fronto-parietal regions that underpin the unique gait patterns in WS.

Acknowledgements

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References


