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Peer reviewed

## RESEARCH ARTICLE

# Feasibility of dual-task gait to estimate Alzheimer's related cognitive decline in Down syndrome

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## Abstract

**Introduction:** The striatum and frontal lobes have been shown to have early Alzheimer's disease (AD) neuropathology and are critical for motor and cognitive function. We hypothesized gait would be associated with early-stage dementia in Down syndrome (DS), a cohort at risk for AD.

**Methods:** Twenty-eight participants with DS were enrolled in the study. Participants walked at their self-selected pace and while completing a dual task (counting, obstacle, or counting+obstacle).

**Results:** All participants were able to complete the self-paced condition and 78.57–96.42% completed the dual-task conditions. There was a trend for greater dual-task effects on gait velocity based on dementia diagnosis. Gait velocity had stronger associations with clinical dementia assessments than age or diagnosis.

**Discussion:** A dual-task gait paradigm is feasible to conduct with adults with DS and is associated with age and cognitive impairment. Dual-task gait may serve as an indicator of early stage dementia in DS.

## KEYWORDS

aging, dementia, dual-task effect, gait speed, trisomy21

## 1 | INTRODUCTION

Down syndrome (DS) is the most common genetic cause of intellectual disability (ID) with 6000 individuals born in the United States each year.<sup>1</sup> DS is caused by full or partial triplication of chromosome 21.<sup>2</sup> The amyloid precursor protein (APP) is located on chromosome 21, and with triplication, there is a 50% overexpression of this protein. The overexpression of APP is thought to lead to the accumulation of amyloid beta (A $\beta$ ) in the brain.<sup>3</sup> Consequently, by age 40, virtually all individuals with DS have Alzheimer's disease (AD) characteristic brain neuropathology.<sup>4</sup> However, on average, clinical dementia is diagnosed at 55,<sup>5</sup> and prior research shows that not everyone with DS will display clinical dementia symptoms, despite significant neuropathology.<sup>6</sup>

Given the disconnect between pathology and dementia symptoms, there is a need for other clinical markers of disease progression. These markers could eventually be used to identify individuals most at risk for dementia and the time to clinical onset of disease.

While gait may seem automatic, it requires high-level cognitive functioning, including multi-faceted stimuli integration and processing, to be performed successfully.<sup>7</sup> Notably, frontal lobe areas including the dorsolateral pre-frontal cortex, anterior cingulate, orbitofrontal lobes, and supplementary motor area are required for planning and organizing movement while the basal ganglia coordinate and time movements.<sup>7</sup> The frontal lobes and basal ganglia are therefore critical for gait. The frontal lobes and striatum are also often the first brain regions to accumulate A $\beta$  observed in positron emission tomography

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(PET) studies in DS.<sup>8</sup> Thus, given the early-stage involvement of gait-related brain regions in AD progression, gait may be a promising marker of early-stage dementia, specifically mild cognitive impairment (MCI). In fact, studies investigating gait and dementia in non-DS populations show declines in gait before dementia symptoms emerge. In particular, slower gait velocity is associated with worse memory, executive function, and global cognition.<sup>9</sup> Moreover, slower baseline gait velocity is associated with greater declines over time suggesting that changes in gait may precede cognitive decline.<sup>9</sup> Other studies find that decreases in gait velocity occur 12 years before MCI.<sup>10</sup> Furthermore, those with impaired gait are more likely to develop AD relative to non-impaired peers.<sup>11</sup> Adding gait velocity to the predictive model of prodromal, early-stage dementia greatly improves diagnostic accuracy.<sup>12</sup>

To detect early stages of AD, dual tasks can be used to increase sensitivity to detect changes. Dual-task gait paradigms are used in the typically developing population to evaluate MCI<sup>13-17</sup> and AD.<sup>16,18</sup> Studies show a greater decrease in gait velocity under dual-task conditions among MCI compared to healthy controls,<sup>16</sup> and at times the only detectable gait difference between MCI and controls were under dual-task conditions.<sup>14</sup> However, few studies have examined dual-task gait in DS and have only examined a young population.<sup>19,20</sup> These few studies have found a greater dual-task effect among people with DS when completing a digit span task<sup>20</sup> and certain motor tasks (eg, buttoning shirt).<sup>19</sup> However, the relationship between dual-task gait and AD progression in DS has yet to be described. Furthermore, identifying possible covariates will also be critical for the design of any future studies of gait in an aging DS population. Sex has been shown to modify the relationship between age and gait in neurotypical individuals without DS.<sup>21</sup> Furthermore, in a study of aging in AD the association between amyloid measured via PET was associated with gait and cognition only in women.<sup>22</sup> Therefore, sex might be a significant covariate to account for. Moreover, because dual tasks are cognitively demanding it will be important to determine whether individuals with greater ID can complete the tasks and whether the level of ID is associated with gait performance.

The current study evaluates the feasibility of conducting a dual-task gait evaluation in older individuals with DS. Second, we sought to determine the role of ID and sex as possible covariates that may influence gait. We hypothesized that slower gait velocity, shorter step length, and wider base would be associated with greater ID, while sex would not be associated with gait measures. Finally, we evaluated the strength of the relationship between gait measures and age, dementia diagnosis, and cognitive measures. We hypothesized that gait measures would be more impaired and dual-task effects would be larger in older individuals, possible dementia, and worse cognitive performance.

## 2 | METHODS

### 2.1 | Participants

Research procedures were approved by the University of Kentucky Institutional Review Board. Participants completed approved

### RESEARCH IN CONTEXT

- 1. Systematic review:** The authors conducted a literature search via PubMed to review studies on gait, dementia, and Alzheimer's disease (AD). Dual-task gait speed has been shown to slow among typically developing individuals with mild cognitive impairment (MCI) or AD.
- 2. Interpretation:** Our findings demonstrate that a dual-task gait paradigm is feasible in the Down syndrome (DS) population and gait performance is associated with diagnosis and age.
- 3. Future directions:** The current study proposes that gait performance is a feasible and objective measure that is associated with dementia diagnosis and age in DS. However, future longitudinal studies are needed to further understand: (1) longitudinal change in gait, (2) the prognostic utility of gait performance, and (3) the association between gait performance and neuroimaging biomarkers (ie, white matter integrity, cerebral blood flow, amyloid load).

protocols for informed consent or assent with guardian approval. Participants were community residing men and women with DS recruited through local DS support groups and residential facilities in Kentucky, southern Indiana, and southern Ohio. To be considered eligible for the gait procedures participants must be currently enrolled in the parent RO1 study (R01-HD064993). Participants were eligible for the RO1 study if they (1) had a karyotype diagnosis of trisomy 21, (2) were at least 25 years old, (3) were in stable general medical condition and medications for at least 3 months prior to study, (4) were willing to participate in semi-annual visits including magnetic resonance imaging (MRI) scans, and (5) had English speaking skills (both participant and informant). The gait-specific inclusion criteria required the participant to be able to ambulate without an assistive device (ie, cane), and be capable of walking up and down stairs. If at any point during the testing session the participant was deemed to be at high fall risk, the testing session was terminated.

### 2.2 | Gait assessment

First, leg length was measured as the distance from the greater trochanter to the floor. Next, participants completed the gait assessment. Gait performance was measured using the GAITRite™ system (CIR Systems, Havertown, PA). The GAITRite™ is a 16-foot long portable walkway, made of foam carpet with sensors, that measures multiple temporal (eg, velocity) and spatial (eg, step length) gait characteristics. Velocity, step length, and base width were the primary variables of interest. Velocity and step length were normalized to the individual participant's average leg length.

**TABLE 1** Description of each condition

Condition	Single/Dual task	Description
Self-paced	Single	Walking at a self-selected pace
Obstacle	Single	Walking at a self-selected pace and stepping over an obstacle placed at 1.5 meter from the start of the GaitRite™ mat
Self-paced + counting	Dual	Walking at a self-selected pace while counting aloud
Obstacle + counting	Dual	Walking at a self-selected pace and stepping over an obstacle placed at 1.5 meter from the start of the GaitRite™ mat while counting aloud

Participants completed five trials in each of four conditions. Each trial was completed in the time required to traverse the 16-foot (4.88 meter) GAITRite™ mat. The four conditions included (1) single-task trials of self-paced walking, (2) obstacle walking, (3) dual-task conditions including counting while performing self-paced walking, and (4) counting while performing obstacle walking (Table 1). The obstacle was two small yoga blocks laid horizontally across the mat (Figure 1). The height of the obstacle was 4 inches, less than the average stair step. Counting was used as a dual cognitive task. Given possible issues with hearing and visual acuity in DS,<sup>23</sup> a verbal counting task was selected. For each trial, a random number between 1 and 10 was selected and the participant was asked to count up by one from the randomly selected number.

### 2.3 | Cognitive assessment, intellectual disability, and consensus diagnosis

Clinical assessments included the Brief Praxis Test (BPT), Severe Impairment Battery (SIB), and the Dementia Questionnaire for People with Intellectual Disabilities (DMR). The BPT consists of 20 items that directly measure dyspraxia, requiring minimal verbal demands and instead using simple behavioral output.<sup>24</sup> Low scores on the BPT indicate severe dyspraxia. The SIB<sup>25</sup> was developed to assess cognition in severely impaired individuals. Using one-step commands and gestural cues, the SIB allows for non-verbal responses and partially correct

responses to assess behavioral and cognitive symptoms in individuals with severe dementia. Lower SIB scores indicate more severe deficits. The DMR<sup>26</sup> is a diagnostic screening tool that measures behavioral and cognitive dysfunction as reported by caregivers or guardians. Higher scores on the DMR indicate more severe dysfunction. DMR raters for the current study were caregivers and/or legal guardians that were responsible for daily care of the participants either in the home or an assisted living facility. Because BPT, SIB, and DMR scores were skewed, the scores were transformed for analysis. Formulas for transformations are provided in Tables S1–S3 in supporting information. While analyses used the transformed values, plots are depicted in raw values to facilitate interpretation.

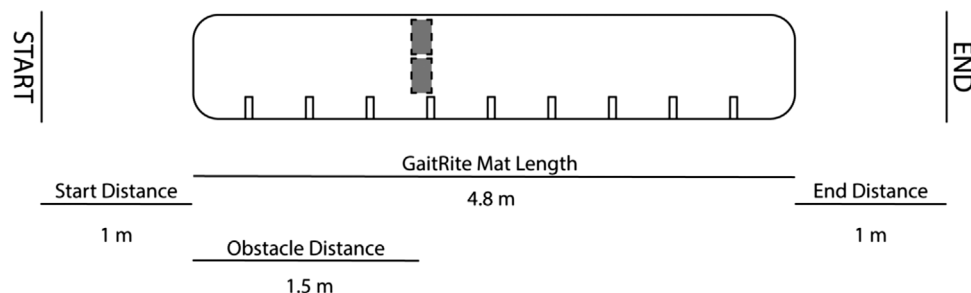
ID level was based on prior testing, which was abstracted from medical records when available. In addition, baseline scores we obtained as part of the parent R01. The tests used in medical records were usually Stanford Binet, Wechsler Intelligence Scale for Children. For the R01 we used the Kaufmann Brief Intelligence Test (KBIT) and the Peabody Picture Vocabulary Test (4th edition).

An expert panel of neurologists and neuropsychologists used NINCDS-ADRDA criteria to reach a consensus diagnosis. In the current cohort, participants were diagnosed with no dementia ( $n = 23$ ), likely impaired ( $n = 4$ ), or uncertain ( $n = 2$ ). The likely impaired cohort had some detectable cognitive decline, also considered MCI. The uncertain cohort met the criteria for dementia but had substantial medical conditions, sensory impairment, or other social factors (eg, change in home setting or guardian) that may have contributed to the clinical impression. For simplicity the likely impaired and uncertain groups were combined to create a possible dementia cohort ( $n = 6$ ).

### 2.4 | Statistical analysis

Gait parameters for each trial were extracted from the GaitRite™ software. Trials were excluded if the participant stopped walking while on the mat or did not follow directions. A minimum of three trials was required for the condition to be analyzed. The three to five trials were averaged to generate a single velocity, step length, and base width value for each condition.

First, we determined whether participants not completing a condition was primarily related to lack of time rather than any participant characteristic; for example, if a participant's study visit was running

**FIGURE 1** GaitRite™ set-up

behind schedule and we ran out of time to complete the entire gait protocol before they had to leave. To ensure there were no differences in completion rate based on key participant characteristics we compared age, ID, and consensus diagnosis across those who completed all conditions versus those who did not complete at least one condition. Age was determined to be non-normally distributed based on the Shapiro-Wilk test. The non-parametric version of the *t*-test, Mann-Whitney U, was used to compare age across condition completion groups. Chi-square tests with Fisher *P*-value correction compared ID and consensus diagnosis across condition completion groups.

To determine whether sex and ID were confounders for gait performance we used data from the self-condition only and modeled relationships using linear regression. Sex was associated with step length ( $P = .015$ ) and ID was significantly associated with base width ( $P = .046$ ). Thus, sex was included as a covariate in further models of step length and ID was included in future models of base width. We also evaluated sex and ID as possible confounders for dual-task effects. ID was significantly associated with the dual-task effect of self + counting versus self on velocity ( $P = .002$ ), step length ( $P = .001$ ), and base width ( $P = .015$ ). Thus, ID is included as a covariate when assessing associations among age, diagnosis, and dual-task effects.

Linear mixed models were used to measure the effect of condition, sex, ID level, and age on gait velocity, step length, and base width. Separate models were fit for velocity, step length, and base width. Participant as the random intercept was fit as the null model. Then main effects and interactions of the fixed effects (eg, age and disease diagnosis) were fitted using the maximum likelihood method. Post hoc comparisons used the false discovery rate correction. To reduce the number of comparisons and because the primary interest is dual-task effects, condition comparisons were limited to self versus self + counting, self + obstacle, and self + counting and obstacle conditions. Mixed model analyses were completed using the “lme4,” “lmerTest,” and “performance” packages in R.

Next, the associations between gait and cognitive measures were evaluated to determine how these associations compared to the relationships among age, diagnosis, and cognitive measures. Separate linear regressions for each gait outcome and cognitive measure were used to determine the relationships between gait and cognition. Only gait data from the self-paced condition was used to reduce the number of statistical comparisons. Additional separate models estimated the relationships between age and cognitive measure and diagnosis and cognitive measure. All models controlled for level of ID. Linear regression analyses used the “lm” package. All analyses were completed in R 3.6.1 and alpha of 0.05 was used.

### 3 | RESULTS

A total of 28 ( $n = 13$  female) participants completed the gait study. Participants ranged in age from 25 to 59, and on average were 36.61 (SD = 6.98) years old. The majority of participants had borderline/mild intellectual disability ( $n = 16$ ) and no dementia ( $n = 22$ ). Full participant characteristics are provided in Table 2.

**TABLE 2** Participant demographics

	No dementia ( $n = 22$ )	Other/possible ( $n = 6$ )	Overall ( $n = 28$ )
Sex			
Female	11 (50.0%)	2 (33.3%)	13 (46.4%)
Male	11 (50.0%)	4 (66.7%)	15 (53.6%)
Age			
Mean (SD)	35.6 (5.60)	40.2 (10.6)	36.6 (6.98)
Median [Q1, Q2]	35.5 [32.3, 35.5]	38.5 [32.0, 38.5]	35.5 [31.8, 35.5]
Intellectual disability			
Borderline/mild	13 (59.1%)	3 (50.0%)	16 (57.1%)
Moderate	9 (40.9%)	3 (50.0%)	12 (42.9%)
Missing any condition			
No	17 (77.3%)	4 (66.7%)	21 (75.0%)
Yes	5 (22.7%)	2 (33.3%)	7 (25.0%)

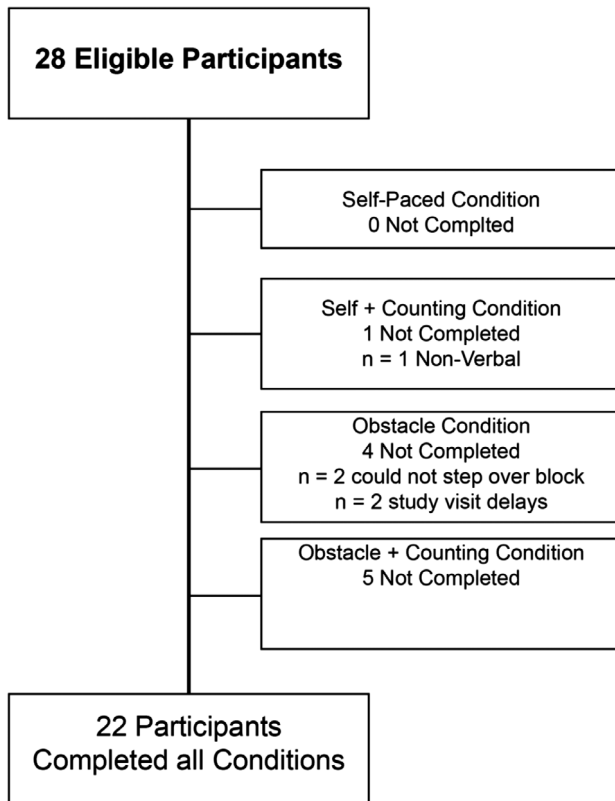
Abbreviation: SD, standard deviation.

#### 3.1 | Feasibility

On average it took 25 to 30 minutes to complete three practice trials and five test trials for each condition. All participants completed the self-selected pace condition. Twenty-seven (96.42%) participants completed the self + counting condition, 24 (85.71%) completed the obstacle condition, and 22 (78.57%) completed the obstacle + counting condition. One participant did not complete the self + counting and obstacle + counting because they were non-verbal. Two participants did not complete the obstacle or obstacle + counting conditions because they could not step over the block without touching it. Two participants did not complete the obstacle or obstacle + counting conditions because study visit delays reduced the time available to complete the full dual-task gait paradigm (Figure 2). Overall, 28 participants were included in the dataset; 28 had self, 27 had self + counting, 24 had obstacle, and 22 had obstacle + counting condition data. There were no significant differences between people with DS who completed the gait task versus those that did not in terms of age ( $P = .37$ ), ID ( $P = .99$ ), or consensus diagnosis ( $P = .62$ ).

#### 3.2 | Condition effect

There was a significant effect of condition on normalized gait velocity ( $F(3, 73.19) = 11.91, P < .001$ ). Significant differences are depicted in Figure 3A. Additionally, there was a significant effect of condition on normalized step length ( $F(3, 73.05) = 10.12, P < .001$ ), controlling for sex. Significant differences are depicted in Figure 3B. There was no effect of condition on normalized base width ( $F(3, 75.51) = 0.251, P = .860$ ), controlling for ID level. Because the greatest difference was between self and self + counting conditions for velocity, indicating a



**FIGURE 2** Participant flowchart

larger dual-task effect, the self versus self + counting dual-task effect on velocity was evaluated.

### 3.3 | Associations with clinically relevant outcomes

There was a trend for an interaction between age and condition in estimating normalized velocity ( $F(3, 73.38) = 2.18; P = .097$ ). Applying the false discovery rate correction, there was a trend for the age slope for the self + counting ( $P = .076$ ) and the obstacle and counting ( $P = .076$ ) conditions to be more negative than the self condition (Figure 4). Diagnosis was not significantly associated with normalized velocity when added to the model ( $P = .318$ ).

There was no significant relationship between age and step length or an interaction between age and condition (both  $P_s > .05$ ), controlling for sex. Similarly, there was no significant relationship between age and base width or an interaction between age and condition (both  $P_s > .05$ ), controlling for ID. Diagnosis was not significantly associated with step length or base width when added to the model (both  $P_s > .05$ ).

### 3.4 | Associations with dual-task effect

Controlling for ID, we evaluated the association of the velocity dual-task effect with age and diagnosis. Age was not associated with the velocity dual-task effect ( $P = .468$ ), and therefore was dropped from the model. There was a trend for diagnosis to be associated with the

velocity dual-task effect ( $P = .096$ ). Those with Uncertain/Possible dementia had a 13% greater dual-task effect than those with No Dementia (Figure 5A). ID was significantly associated with dual-task effect ( $P = .001$ ). Individuals with Borderline/Mild ID had a 22% greater dual-task effect than those with Moderate ID (Figure 5B).

Next, we tested the association between self and self + counting condition velocities and cognitive measures. Furthermore, we evaluated the strength of the gait and cognitive measure associations controlling for age, diagnosis, and cognitive measure associations. Detailed model results are provided in Tables S1–S3.

Normalized velocity during the self condition had a significant association with SIB ( $P = .003$ ; Figure 6A). As normalized velocity increased, SIB total score increased as well. Age ( $P = .718$ ) and ID ( $P = .338$ ) were not associated with SIB total score, but there was a trend for diagnosis to be associated with SIB total score ( $P = .075$ ). Those with Uncertain/Possible dementia had lower SIB scores than those with No Dementia.

Normalized velocity during the self + counting condition had a significant association with SIB ( $P = .004$ ; Figure 6B). As normalized velocity increased, SIB total score increased as well. Age ( $P = .501$ ) and diagnosis ( $P = .200$ ) were not associated with SIB total score, but there was a trend for ID to be associated with SIB total score ( $P = .076$ ). Those with Moderate ID tended to have lower SIB scores than those with Mild/Moderate ID.

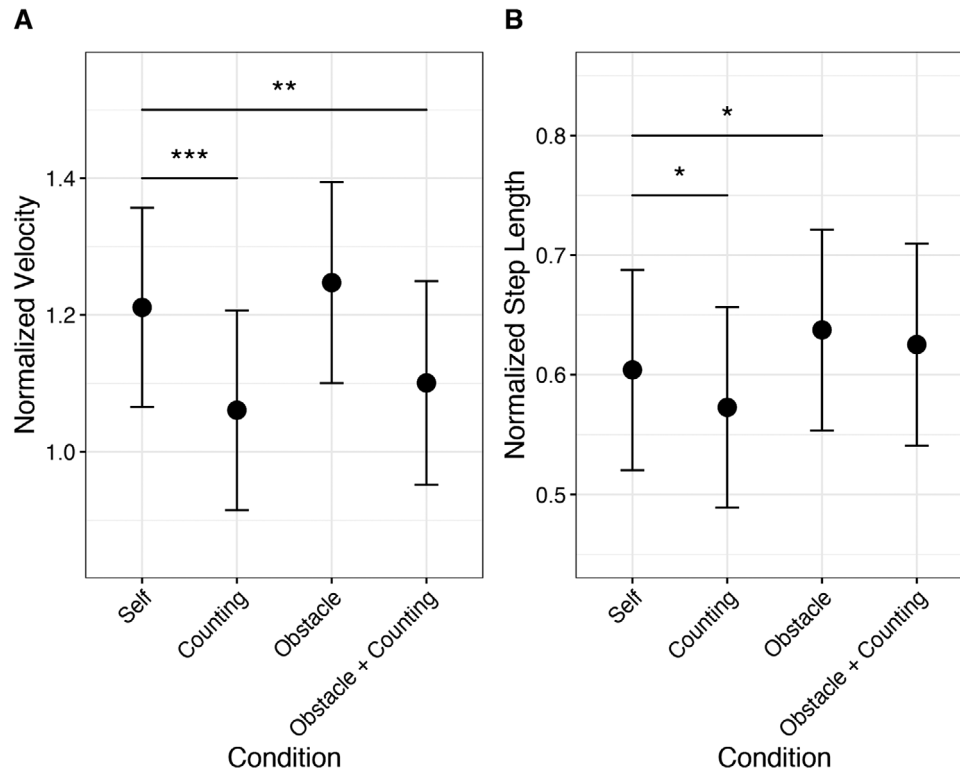
There was a trend for normalized velocity during the self + counting condition to associate with DMR ( $P = .065$ ; Figure 6C). As normalized velocity increased, DMR total score decreased. Age ( $P = .571$ ) and ID ( $P = .622$ ) were not associated with DMR total score, but there was a significant association with diagnosis ( $P = .002$ ). Those with Uncertain/Possible dementia had higher DMR scores than those with No Dementia.

There were no associations observed among normalized velocity, age, diagnosis, or ID. Also, there were no significant associations between dual-task effects and any cognitive measure (Tables S1–S3).

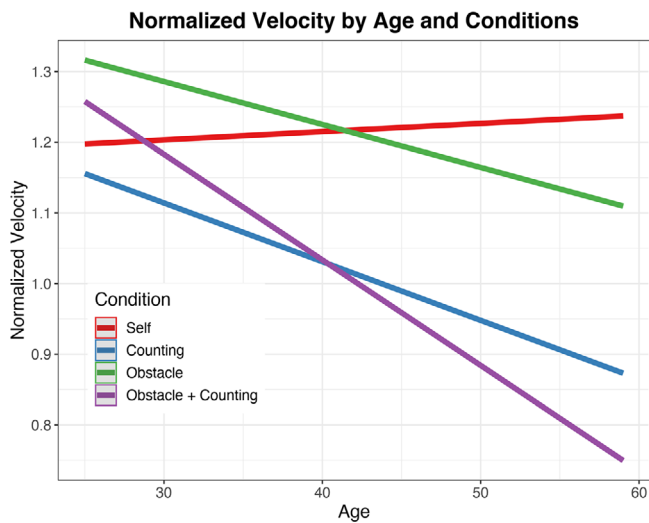
## 4 | DISCUSSION

The current study evaluated the feasibility of dual-task gait assessment in an aging DS population and whether gait performance had clinical relevance. The main findings from this study reveal dual-task gait can successfully be conducted in an aging DS population and that ID and sex were meaningful covariates. Our hypotheses were partially supported. While ID was significantly associated with wider base width and velocity dual-task effects we also found sex was associated with step length. Despite normalizing for leg length, the effect of sex is thought to be consistent with generally taller stature in males being associated with longer step length. Furthermore, gait speed and dual-task effects on gait speed were associated with age and cognitive measures, but we did not observe associations across all gait measures and all cognitive measures.

Dual-task gait paradigms have been evaluated in young to middle-aged adults with DS.<sup>19,20</sup> The ages in each of these studies range from



**FIGURE 3** Effect of condition on normalized velocity and step length. \*\*\* $P < .001$ ; \*\* $P < .01$ ; \* $P < .05$



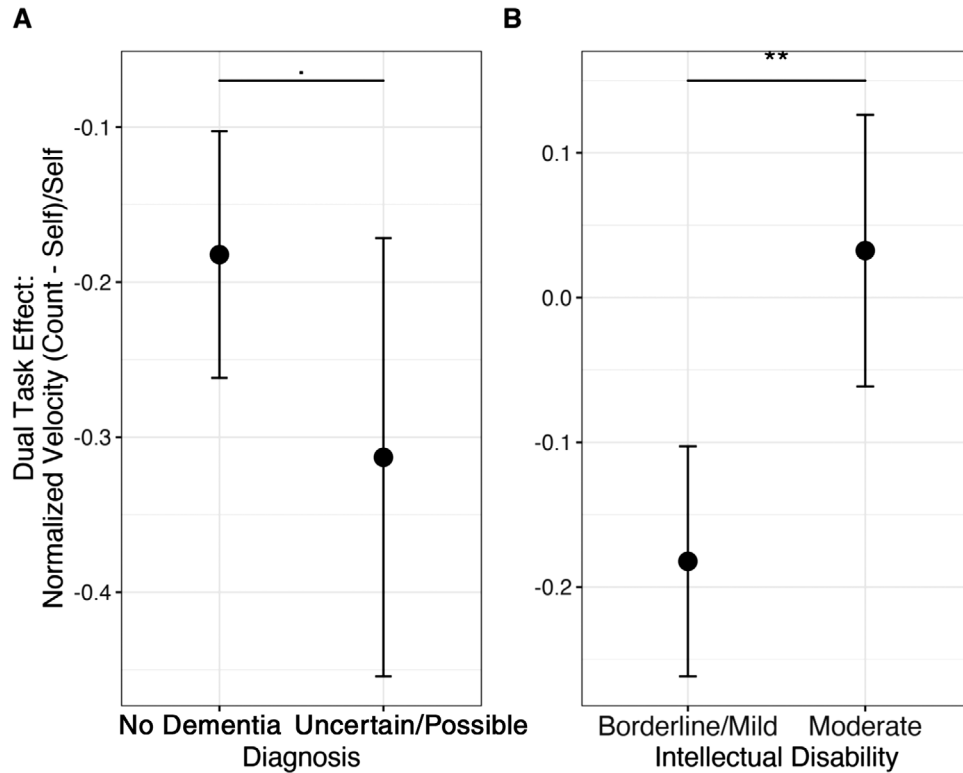
**FIGURE 4** Effect of age and condition on normalized velocity

16 to 39 with an average age of 23<sup>19</sup> and 25.<sup>20</sup> These prior studies evaluated whether there were greater dual-task effects among individuals with DS compared to those with other intellectual disabilities or typically developing individuals.<sup>19,20</sup> While greater dual-task effects were observed for DS participants compared to typically developing individuals, the impact of age or dementia were not evaluated. The current study addresses a novel question in the DS and dual-task literature by demonstrating aging individuals with DS can complete both a standard and added dual-task gait paradigm.

The current study found that the greatest dual-task effect was observed for velocity in the self + counting versus self-paced condition. In previous studies of dual-task gait in non-DS individuals with MCI the counting task also had the greatest impact on gait velocity.<sup>27</sup> Furthermore, similar to previous work evaluating different tasks for dual-gait paradigms,<sup>28</sup> the current study found limited effect of adding a physical obstacle to step over. Thus, the current results indicate that individuals with DS exhibit similar dual-task effects as non-DS peers, specifically demonstrating greater impairment due to cognitive interference than motor interference.

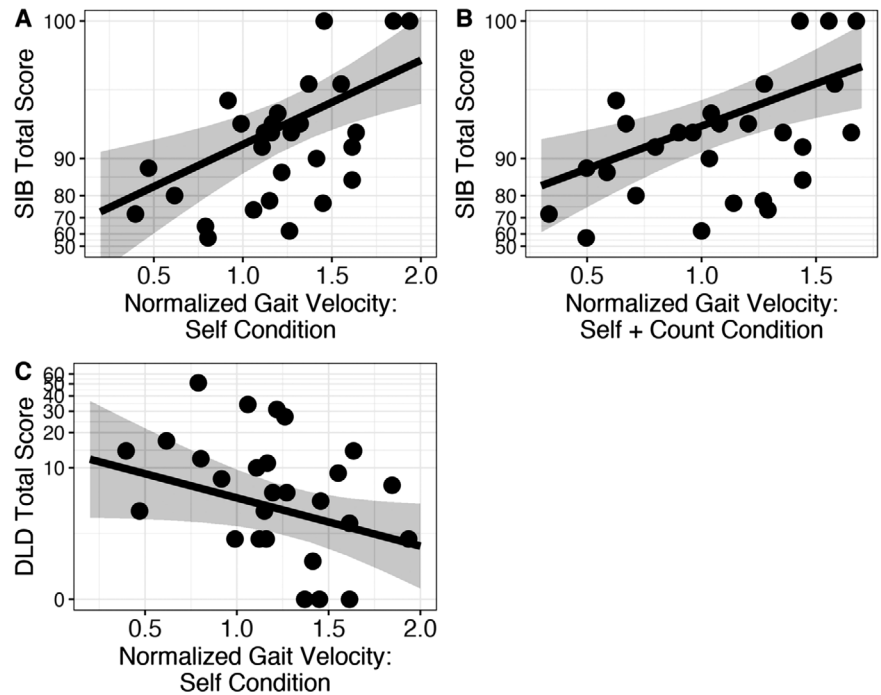
Furthermore, the current study adds critical information regarding the roles of ID and sex on gait performance. Studies of ID and gait have demonstrated worse gait performance and greater dual-task effects among young adults and children with ID.<sup>19,20,29</sup> The current study found the degree of ID in DS is associated with base width and influences whether dual-task effects are observed. Dual-task effects, namely differences in gait velocity during counting versus self-paced condition, were only observed in those with borderline/mild ID. The dual-task effect was reduced, or non-existent, within the moderate ID cohort. Most likely, the dual-task effect was not observed because gait velocity during the self-paced condition had already slowed enough that adding the counting task did not reduce gait velocity further for those with moderate ID.<sup>19,30-32</sup>

The second aim of the current study was to elucidate the relationship between gait performance and clinically relevant variables including age, diagnosis, and cognitive measures. We found that gait speed was tended to be slower in older individuals during dual-task



**FIGURE 5** Dual-task effects on normalized velocity by diagnosis and intellectual disability.  $P < .01$ ;  $***P < .001$ ;  $**P < .01$ ;  $*P < .05$ . A, There was a trend for diagnosis to be associated with the degree of dual-task effect observed. There was a trend for the uncertain/possible diagnosis group to experience a greater dual-task effect than those with no dementia. B, Individuals with moderate intellectual disability (ID) had significantly less of a dual-task effect than those with borderline/mild ID

**FIGURE 6** Association between clinical and gait assessments. Note: While values on Y-axis depict the raw scores of the Severe Impairment Battery (SIB) and the Dementia Questionnaire for People with Intellectual Disabilities (DMR), the Y-axis has been transformed to reflect the non-linear transformations used. A, There was a significant positive association between normalized velocity during the self condition and SIB total score. B, There was a significant positive association between normalized velocity during the self + counting condition and SIB total score. C, There was a significant negative association between normalized velocity during the self condition and DLD total score, whereby greater velocity was associated with less impairment





conditions, but remained relatively stable during the self-paced condition. In the typically developing population, decreases in gait velocity<sup>33–35</sup> occur in aging. For gait velocity, these changes are most evident after age 60,<sup>33</sup> with an exponential decline in gait speed after age 80.<sup>34</sup> Given the current cohort had a maximum age of 59 and average age of 37, it is promising that dual-task gait velocity tended to be slower as it may then indicate early effects of brain pathologies.

In addition to evaluating the effect of age on gait, we sought to determine whether those with possible dementia also have worse gait performance than those with no dementia. Dementia was not associated with velocity, step length, or base width. Prior studies investigating AD in the typically developing population have observed slower gait velocity and shorter step length in AD.<sup>36</sup> Moreover, gait performance<sup>39</sup> and particularly gait velocity under dual-task conditions<sup>40</sup> have differentiated between MCI and AD patients from cognitively normal individuals. Given the small sample size and only observing individuals with possible dementia in the current cohort, the current study may not have provided the power to detect differences based on early-stage diagnosis. However, there was a trend for possible dementia to be associated with greater dual-task effects. Individuals with uncertain/possible dementia showed greater dual-task effects than those without dementia. Because dual tasks can increase the sensitivity to detect changes, this could be why differences in dual-task effects were seen across diagnosis groups, but not differences in velocity, step length, or base width.<sup>19</sup>

Of note, analyses revealed that individuals with greater ID showed less of a dual-task effect. This indicates a possible floor effect, whereby those with greater ID have experienced enough gait impairment, as seen in the self-paced condition, such that their gait performance does not decline more during a dual-task. A floor effect hypothesis is supported by the typically developing literature, which has shown individuals with lower global intelligence have slower gait<sup>37</sup> and individuals with reduced cognitive functioning show steeper declines in gait speed.<sup>38</sup> However, in our follow-up analyses we found no significant difference between levels of ID and self-paced gait velocity. Rather, while individuals with borderline/mild ID had consistent decreases in velocity during the self + counting compared to self condition, the moderate ID group had a more variable response (Figure S1 in supporting information). This finding is important as it suggests that dual-task gait may impact those with greater ID differently. Future studies of gait in DS should account for the level of ID and also assess whether the effect of ID on dual-task effects is age dependent.

Because dual-task effects may be limited in individuals with greater ID we evaluated the relationship between gait velocity during self-paced or self + counting conditions and cognitive performance. Examining cognitive performance provides the opportunity to quantify more subtle differences that may be indicative of early-stage dementia. Prior studies have found significant relationships between speed and stride length with the MMSE in MCI patients<sup>16</sup> and executive function.<sup>41</sup> In support of these prior studies, the current study found a strong positive association between gait speed and SIB performance. Furthermore, gait speed outperformed age and diagnosis in estimating SIB performance. Thus, gait performance, particularly gait speed,

strongly estimates global cognitive performance supporting prior findings that gait impairment may precede objectively measured cognitive impairment.<sup>7,10</sup>

## 4.1 | Limitations

There are limitations to the current study. First, the data are cross-sectional and therefore it is not possible to determine how gait changes with age. While we observed age-related differences, without longitudinal data we cannot distinguish age-related change versus dementia status cohort effects. Furthermore, without longitudinal data we cannot predict future dementia conversion based on initial gait performance. Predicting conversion from gait performance is critical to determining whether changes in gait precede or result from AD-related changes in DS.

Gait performance in people with DS is more variable than in the typically developing population.<sup>42</sup> While successful condition manipulation was observed, suggesting a dual-task effect, this effect varied by ID and may also vary by age or diagnosis. However, given the small sample size and variability, we were likely unable to detect differences related to diagnosis above and beyond the effects of condition and ID. Future, larger scale studies with variable cognitive diagnoses will be needed to replicate and expand the findings of the current study.

Finally, because we emphasized completing the self and self + counting conditions we did not randomize the order of conditions. Thus, later conditions (obstacle or obstacle + counting) may be differentially impacted by fatigue. However, we believe the fatigue effect to be minimal as no participant discontinued their participation due to fatigue and dual-task effects were not more prominent during later conditions.

## 4.2 | Conclusion

Analysis of dual-task gait is feasible within the older DS population. ID and sex are important covariates and should be controlled for in gait testing. While controlling for ID and sex, gait performance and dual-task effects were associated with clinical measures of cognition. Future studies should track gait performance longitudinally and determine whether dual-task gait changes with AD progression and whether dual-task gait can predict clinical dementia onset in DS.

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## CONFLICTS OF INTEREST

The authors have no relevant conflicts of interest to disclose.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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