

NIH Public Access

Author Manuscript

Gait Posture. Author manuscript; available in PMC 2014 July 01.

Published in final edited form as:

Gait Posture. 2013 July ; 38(3): 403-409. doi:10.1016/j.gaitpost.2013.01.006.

Cognitive Motor Interference During Dual-Task Gait in Essential Tremor

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Abstract

Background—Functional ambulation requires concurrent performance of motor and cognitive tasks, which may create interference (degraded performance) in either or both tasks. People with essential tremor (ET) demonstrate impairments in gait and cognitive function. In this study we examined the extent of interference between gait and cognition in people with ET and controls during dual-task gait.

Methods—We tested 62 controls and 151 ET participants (age range: 72–102). ET participants were divided into two groups based on median score on the modified Mini Mental State Examination. Participants walked at their preferred speed, and performed a verbal fluency task

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Conflict of interest disclosure:

None of the authors report a conflict of interest with respect to financial or personal relationships with organizations that may have an influence on the work.

Author Roles

Ashwini K. Rao: Research project: conception, organization and execution; Statistical Analysis: Design, execution, review and critique; Manuscript preparation: writing the first draft, review and critique

Jasim Uddin: Research project: organization, execution; Statistical Analysis: execution and review and critique; Manuscript Preparation: Review and critique

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while walking. We analyzed gait velocity, cadence, stride length, double support time, stride time, step width, step time difference, coefficient of variation (CV) of stride time and stride length.

Results—Verbal fluency performance during gait was similar across groups (p=0.68). Velocity, cadence and stride length was lowest whereas step time difference (p=0.003), double support time (p=0.009), stride time (p=0.002) and stride time CV (p=0.007) were highest for ET participants with lower cognitive scores (ETp-LCS), compared with ET participants with higher cognitive scores (ETp-HCS) and controls. ETp-LCS demonstrated greatest interference for double support time (p=0.005), step time difference (p=0.013) and stride time coefficient of variation (p=0.03).

Conclusions—ETp-LCS demonstrated high levels of cognitive motor interference. Gait impairments during complex tasks may increase risk for falls for this subgroup and underscore the importance of clinical assessment of gait under simple and dual-task conditions.

Keywords

Essential tremor; gait; dual-task; cognitive-motor interference

Introduction

Essential tremor (ET) is a common movement disorder presenting with both motor and nonmotor impairments [1]. Gait and balance impairments have been observed, both on tandem walk [2] and on standardized clinical assessments of balance [3]. Gait impairments include decreased velocity and cadence, increased time in double support, and step time asymmetry [3, 4]. Gait and balance impairments are functionally significant because they may predispose people with ET to fear of falls, near falls or falls [5].

ET participants also present with cognitive deficits, including memory, executive function and visual attention, above and beyond what is seen in age-matched controls [6, 7]. Cognitive deficits are clinically relevant because they are associated with poor performance in activities of daily living [8]. While pathological changes underlying cognitive deficits in ET are unclear, factor analysis of motor and non-motor signs show that cognitive changes do not fall in the same domain as motor changes, suggesting that cognitive and motor signs may arise from independent pathological processes [9]. Population-based studies report that ET is associated with increased risk for dementia, suggesting cognitive changes in ET may be related to Alzheimer's disease [10, 11]. However, the similarity of cognitive deficits in ET to those seen after cerebellar dysfunction indicate that cognitive deficits could arise from cerebellar-thalamo-cortical pathway dysfunction [12].

Functional ambulation in the community requires coordinated motor and cognitive skills. Cognitive demands of gait are typically evaluated with dual-task methodology, in which subjects perform a cognitive task concurrently with gait [13]. Changes in gait during performance of a concurrent cognitive task are indicative of cognitive-motor interference. Increased interference during dual-task conditions was reported in elderly participants [14] and stroke patients [15] and was associated with increased fall risk, highlighting the importance of studying dual-task gait.

While there is independent evidence of gait and cognitive impairments in ET, there are no studies of cognitive motor interference. In this study we examined if performance of a cognitive task during walking produced gait impairments in ET participants and controls. We used verbal fluency as the cognitive task because of its effectiveness in producing interference during gait [13]. Our aim was to examine if a sub-group of ET participants had greater cognitive-motor interference. We hypothesized that ET participants with lower cognitive scores would demonstrate greater cognitive-motor interference compared with ET

participants with higher cognitive scores and controls. Therefore, we divided ET participants into two groups based on scores on the modified Mini Mental State Examination (mMMSE). Given the strong association of age with cognitive deficits [9], a second aim of the study was to examine the influence of age on cognitive-motor interference. We hypothesized that ET participants with low cognitive scores (ETp-LCS) would demonstrate cognitive-motor interference in excess of that seen in participants with higher cognitive scores and controls, even into advanced age.

Methods

Subjects

Participants were enrolled as future brain donors to the Essential Tremor Centralized Brain Repository (ETCBR) at Columbia University, a national repository for collection of ET brains. Recruitment was done through (1) advertisements in the International Essential Tremor Foundation website and newsletters, (2) advertisements on the Tremor Action Network website, and (3) an ETCBR study website (www.essentialtremor.us). The target population included people with ET and spousal controls living broadly across the United States (including 34 States). The diagnosis of ET was re-confirmed in each ET participant using published diagnostic criteria (moderate or greater amplitude kinetic tremor during three or more activities, or a head tremor, in the absence of Parkinson's disease (PD)). Spousal controls were recruited if they did not have a diagnosis of ET. We excluded participants with dementia (mMMSE score < 40), other neurological disorders (such as stroke, PD or dystonia), orthopedic impairments that impair walking, or depression. We excluded participants with dementia because 1) they would have had difficulty completing the task, and 2) we wanted to maintain within-group homogeneity in ETp-LCS All participants signed a written informed consent form, approved by the institutional ethics committee.

Testing

Participants were tested at home on a single day by a trained tester, which allowed us to 1) examine performance in a familiar environment, and 2) recruit a large sample of subjects who would not have been able to travel the long distance to our hospital. In order to minimize differences in testing conditions across subjects, prior to testing, we ensured that subjects had access to a well-lit hallway long enough to accommodate the GAITRite[®] mat. Most participants had a hallway with wood flooring while few had pile carpeting. We placed corkboard under the GAITRite mat in order to make the support surface consistent (we established the reliability of measuring gait parameters with the cork board under the Gaitrite mat). Testing consisted of two parts, a clinical assessment and quantitative gait assessment. Participants were provided with rest, as needed, during testing.

Clinical assessment

All ET participants and controls underwent a clinical assessment that included collection of demographic and clinical data, which included age, gender, highest educational degree, and age at tremor onset. ET participants also underwent a standardized videotaped neurological examination [16] and a modified Mini Mental State Examination (mMMSE, range = 0-57, higher scores indicating better function) [17].

Quantitative gait assessment

The GAITRite, a 4.6 m long computerized mat (CIR Systems, Havertown, PA), was placed in the middle of a quiet hallway in the subjects' home to collect gait data. The mat registers the location and timing of each footfall. Subjects began walking 3 meters from the beginning

of the mat and stopped 3 meters beyond the end of the mat to record steady-state gait on the mat without the influence of gait initiation and termination. ET participants and controls performed three trials for each of two conditions: (a) standard walk, in which participants were asked to walk at their preferred speed; and (b) dual-task walk, during which participants performed verbal (category) fluency while walking. On each dual-task trial subjects were given a letter of the alphabet ("B") and were requested to name aloud as many animals as they could that began with that letter (e.g., "Bear", "Bat"), while walking at their preferred speed. The order of testing conditions was randomized. Participants were not given instructions regarding task priority and were requested not to use assistive devices during data collection.

Data were analyzed by AKR and JU, who were blinded to clinical diagnosis and age. We analyzed the following gait measures by computing the average of three trials per condition: velocity, stride length, cadence, stride time, double support time, step time difference, step length difference, step width, and coefficient of variation (CV) in stride time and stride length. On average, participants walked 10 steps per trial, enabling us to use 30 steps for computing variability. While some authors suggest that 30 steps may be adequate for computing variability [18], others recommend using hundreds of steps [19]. We used our data to provide an estimate of variability for comparison across groups, as seen in the literature (see [20] and [21]). Verbal fluency was only tested under dual-task conditions- we recorded the number of animals that each participant was able to name correctly across the three trials. Repetitions and incorrect responses were excluded.

Statistical Analysis

In order to examine if a sub-group of ET participants were at a greater risk of functional gait difficulty, we divided ET participants into two groups based on scores on the mMMSE (median value= 50). ET participants with scores 50 were classified as having higher cognitive test scores (ETp-HCS) and cases with scores <50 were classified as having lower cognitive test scores (ETp-LCS). Published data indicate that mMMSE scores <50 are associated with mild functional deficits [8].

Statistical analyses were performed in SPSS (version 18.0) by AKR. Clinical characteristics of ET participants and controls were compared with one-way analysis of variance (ANOVA) or Student t-test for continuous variables and χ^2 tests for categorical variables. For gait measures, we conducted analysis of covariance (ANCOVA), with group (ETp-LCS, ETp-HCS, control) and condition (standard walk, dual-task walk) as factors. We used ANCOVA in order to correct for baseline differences between groups. Since age was different across groups, this was entered as a covariate. Gait measures that demonstrated a significant main effect of group and age, and significant group × condition interaction effect were subsequently entered into a linear regression analysis to examine the independent effects of age and condition on gait. We used age and group as independent predictors of gait in separate models (model 1: predictor= group; model 2: predictors= group, age). Outliers (n=2) were excluded from the analysis if they were > 2 standard deviations from the mean.

Results

Demographic and Clinical Characteristics

Sample size was estimated based on our previous study on tandem gait impairments [2]. We recruited 162 ET participants and 63 controls (Total= 225). One ET participant and one control were excluded because they could not perform the task without assistive devices. Ten ET participants were excluded prior to analysis because their score on the mMMSE was

below 40/57. The final sample of 213 subjects included 61 ETp-LCS, 90 ETp-HCS and 62 controls.

Clinical characteristics of our sample are presented (Table 1). Both groups of ET participants (ETp-LCS and ETp-HCS) were of similar age but were older than controls (ETp-LCS, p = 0.0001 and ETp-HCS, p = 0.007). No differences were seen across groups in gender, highest educational degree or age at which tremor began (Table 1).

Quantitative Gait Analysis

Mean, standard deviation and significance values are presented in Table 2. Gait velocity, stride length and cadence demonstrated a main effect of group. Post-hoc analysis indicated that ETp-LCS had significantly lower velocity, stride length and cadence compared with ETp-HCS and controls. No difference was seen between ETp-HCS and controls. Under dual task walk, velocity, stride length and cadence decreased for all groups (main effect of condition). Group \times condition interaction was not seen, indicating that performance under dual task walk worsened similarly for all groups. Finally, velocity, stride length and cadence decreased with increasing age for all groups (main effect of age).

Stride time and double support time also demonstrated a main effect of group. Post hoc analysis demonstrated that ETp-LCS had the highest stride time and double support time compared with ETp-HCS and controls. No difference was seen between ETp-HCS and controls. Both variables demonstrated a significant group × condition interaction, as seen in Figure 1. While all three groups worsened under dual task walk, the increase in stride time (Fig.1A) and double support time (Fig. 1B) was highest for ETp-LCS. Step width was higher in ETp-LCS compared with ETp-HCS and controls, as seen on post-hoc analysis, and increased with age for all groups, as seen by a main effect of age.

Step time difference (Fig. 1C) and stride time CV (Fig. 1D) were higher (i.e. more impaired) for ETp-LCS compared with ETp-HCS and with controls, as seen by a main effect of group and post-hoc comparisons. During dual-task walk, step time difference and stride time CV were higher for all groups (main effect of condition) though the increase in variability was highest for ETp-LCS group (group × condition interaction). With increasing age, all groups demonstrate higher step time difference and stride time CV. In contrast, stride length CV was not different across groups, or conditions, though there was an effect of age (p=0.0001).

In summary, dual-task walk impaired gait for all three groups. However, for some variables (stride time, double support time, step time difference and stride time CV) the influence of the dual-task walk was most pronounced for ETp-LCS.

Effect of Age on Cognitive-Motor Interference

Gait variables that demonstrated significant group and condition main effects, and group \times condition interaction effect were further analyzed to examine the interaction of age on cognitive-motor interference (Table 3). In the simple model, diagnostic group was a significant predictor of stride time, double support time, step time difference and stride time CV under both standard walk and dual-task walk conditions. In the complex model, group and age were significant predictors of double support time, step time difference and stride time CV under dual-task conditions. Figure 2 shows results for double support time (2A), step time difference (2B) and stride time CV (2C) under dual-task conditions. The slope of the linear regression fit is clearly different for ETp-LCS, indicating that performance of these participants worsened under dual task gait with increasing age. These results indicate that under dual-task conditions, group was an independent predictor of gait impairments above and beyond the effect of age.

Cognitive Function

The mMMSE was administered only to ET participants. Item analysis of the mMMSE indicated that ETp-LCS performed worse on two items, orientation to place (p=0.04) and calculation (p=0.01) compared with ETp-HCS. As seen in Table 1, all groups performed comparably on verbal fluency during dual task walk. Thus, our results indicate that verbal fluency during dual-task performance was not impaired in ET participants. However, control of gait under dual-task performance was impaired, particularly for ETp-LCS.

Discussion

Gait and balance impairments are commonly seen in ET participants. These problems are not merely a subclinical phenomenon observed in the laboratory; emerging data indicate that people with ET experience more fear of falls, near falls and associated morbidities [22]. Some subgroups of ET patients could be at increased risk of these difficulties, and it would be important for clinicians to be aware of this.

In this study, ET participants with lower scores on the mMMSE (ETp-LCS) had more gait impairments during dual-task walk as compared with ET participants with higher cognitive test scores (ETp-HCS) and controls. In contrast, all three groups (ETp-LCS, ETp-HCS and controls) performed comparably on the cognitive task (verbal fluency). While all groups demonstrated some worsening of gait under dual-task walk, ETp-LCS demonstrated the greatest cognitive motor interference. This was particularly true for stride time, double support time, step time difference and stride time CV.

Functional ambulation often requires concurrent performance of walking and cognitive tasks (such as remembering items on shopping lists). Increased cognitive motor interference during complex dual-task conditions may be associated with increased risk for falls and decreased quality of life. Our study is the first to demonstrate cognitive motor interference in a particular subgroup of ET participants (i.e., those with lower cognitive scores), who could be at a greater risk for functional gait difficulty.

Increase in stride time and stride time CV under dual-task conditions has previously been reported in elderly people with mild cognitive dysfunction and dementia [23], and people with PD [24]. For elderly people with cognitive or neurological dysfunction, increase in stride time and stride time variability under dual-task conditions is associated with increased risk for falls [24, 25]. In contrast, a recent study reported that dual task walk was not predictive of falls in people with PD [26]. However, the subjects in that study were younger than participants in our study, as well as elderly people with mild cognitive dysfunction [23] and elderly people with dementia. It is possible that the predictive value of dual task walk for falls increases with age, though this remains to be tested.

The relationship of cognitive motor interference and fall risk has not been studied in ET. Our results indicate that ETp-LCS have greater impairments in gait. Whether greater gait impairments result in increased fall risk needs to be tested. Assessment of cognitive-motor interference is not currently part of routine clinical examination of ET participants [7]. Our results support inclusion of dual-task gait to identify ET participants who may be at a greater risk for functional gait difficulty [5].

While ETp-LCS had lower gait velocity, stride length and cadence compared with ETp-HCS and controls, all groups worsened similarly under dual-task conditions. Slowing of gait speed with increasing task complexity in elderly subjects is well-documented [13], and may be associated with structural changes in the pre-frontal cortex, suggested to be involved with performance of both cognitive tasks and control of gait speed [27].

ET participants and controls performed similarly on verbal fluency during gait despite differences in cognitive ability (scores on mMMSE). The phenomenon of worsening gait control while maintaining performance of a cognitive dual-task has been demonstrated previously in PD [28]. In these studies, healthy young subjects prioritized gait control at the cost of performance on the cognitive task [28]. PD participants, on the other hand, prioritized performance of the cognitive task at the cost of postural stability during gait [28]. Similar results have been reported in elderly subjects. The prioritization of the cognitive task has the effect of worsening gait impairments and increasing the risk for falls. Our cohort of ETp-LCS did not prioritize gait control, which may place them at a higher risk for falls. It remains to be tested whether ET participants can prioritize their gait performance on explicit instructions, as has been demonstrated in the elderly [29] and in PD [30].

Our study has some limitations. Since we did not administer the mMMSE to control subjects, it is unclear whether they had a similar range of scores compared with ET participants. However, even if some of the controls had had lower scores on the mMMSE, this would have biased our results towards the null hypothesis. Second, we did not collect data on falls, which would allow us to examine the relationship between gait impairments under dual-task conditions and falls. Third, we did not test verbal fluency as a single task. However, since we were primarily interested in the influence of a cognitive dual task on gait, any differences in verbal fluency performance as a single task would not influence our conclusions.

To summarize, our results show that ET participants demonstrate gait impairments above and beyond those seen in the healthy elderly. These gait impairments worsen during the performance of a concurrent cognitive task during gait, particularly in ET participants with lower scores on a cognitive test. The results underscore the importance of clinical assessment of gait under simple and dual-task conditions in ET [5].

Acknowledgments

We thank all ET subjects, their families and control subjects for participating in the study. We did not receive any writing assistance for preparing this manuscript.

Sources of Funding:

This work was supported by the National Institutes of Health (Bethesda, MD) under grant number 5R01NS042859. The funding source did not have a role in the design and implementation of the project, or in the writing of the manuscript. Ashwini K Rao conducted the statistical analyses.

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Research Highligts

- We examined if performance of a cognitive task (verbal fluency) during walking produced gait impairments (i.e. cognitive-motor interference) in ET participants and controls
- No differences were seen in the performance of the cognitive task
- ET participants with low scores on a cognitive test demonstrated the highest interference, particularly for double support time, step time difference and stride time variability
- Clinical assessment of gait in ET participants should include testing under simple and dual-task conditions.

Rao et al.

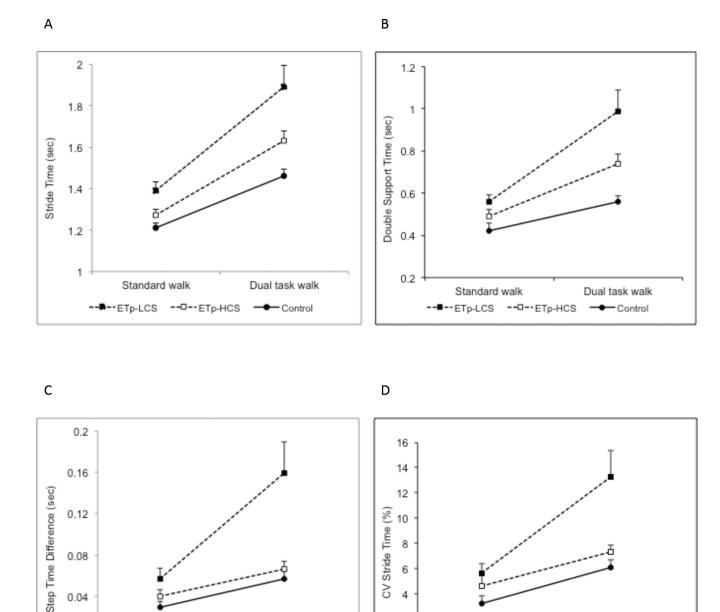


Figure 1.

Standard walk

---ETp-LCS --O--ETp-HCS

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Mean \pm standard error for stride time (A), double support time (B), step time difference (C) and stride time CV (D) for standard walk and dual-task walk for ETp-LCS (filled square), ETp-HCS (empty square) and controls (filled circle).

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Standard walk

--ETp-LCS --O--ETp-HCS

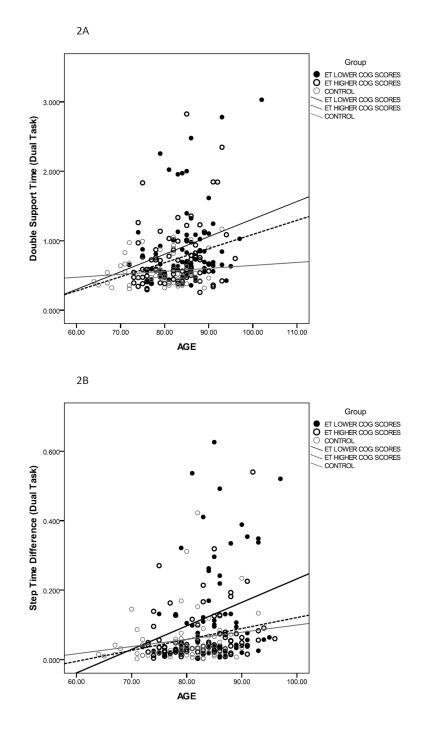
Dual task walk

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Dual task walk

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Rao et al.



Rao et al.

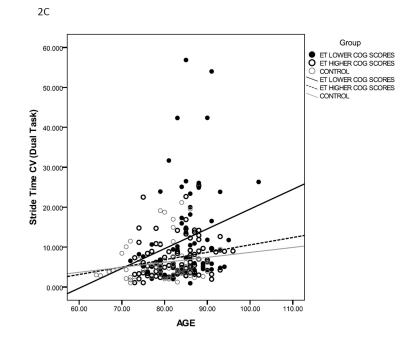


Figure 2.

Relationship between age and double support time (A) step time difference (B) and Stride time CV (C) for ETp-LCS (filled black circles), ETp-HCS (empty black circles) and controls (empty grey circles) under dual-task conditions. Linear regression fit is shown for all three groups (ETp-LCS: thick black line; ETp-HCS: black dashed line; Controls: grey line).

Table 1

Clinical Characteristics of Participants

	ET participants with Lower Cognitive Scores	ET participants with Higher Cognitive Scores	Controls	p Value
Number of subjects	61	06	62	•
Mean Modified	44.7 (2.29)	53.3 (1.90)	NT	0.0001 ^a
MMSE score (SD)	40-49	50–57		
Range				
Mean Age, years (SD)	84.4 (5.9)	82.6 (5.6)	79.6 (6.6) *	0.0001 ^a
Range	72–102	72–97	68–94	
Female Gender (percent)	42 (68%)	55 (61%)	40 (65%)	0.79 <i>b</i>
Highest Education category (SD)				
1=No degree	Э	2	NT	0.19b
2= High-school diploma	23	29		
3= Associates degree	5	6		
4= Bachelor degree	13	25		
5=Masters degree	11	17		
6= Doctorate or equivalent	9	8		
7= Trade school	0	0		
Age of Tremor Onset, Years (SD)	43.3 (23.42)	40.1 (21.84)	N/A	0.43 <i>a</i>
Dual-task Verbal fluency score	1.85 (1.00)	1.85 (0.93)	1.61 (0.77)	0.68c

Gait Posture. Author manuscript; available in PMC 2014 July 01.

 a^{a} = Student's t-test;

b =Chi square test;

 $c_{= One-way ANOVA;}$

NT = not tested; N/A = Not applicable;

 $\frac{*}{2}$ Tukey Post-hoc analysis revealed that controls were younger than ET participants with lower cognitive scores (p=0.0001) and ET participants with higher cognitive scores (p=0.007). There was no age difference between the two ET groups (p=0.173); Statistically significant values in bold

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Group × Condition		0.81	0.2	0.26	0.03	0.005	0.4	0.22	0.013	0.44	0.03
Age		0.0001	0.005	0.0001	900.0	0.0001	0.002	0.23	0.0001	0.0001	0.0001
Condition		0.003	0.021	0.035	0.465	0.46	0.21	0.11	0.02	0.34	0.33
sis	ETp- HCS vs C	0.11	0.06	0.57	0.18	0.29	0.71	0.7	0.8	0.54	0.76
hoc analy	ETp- LCS vs C	0.0001	0.0001	0.003	0.001	0.003	0.03	0.07	0.01	0.06	0.006
Group post-hoc analysis	ETp-LCS Vs ETp- HCS	0.001	0.003	0.004	0.01	0.029	0.04	0.1	100.0	0.14	0.005
Group		0.0001	0.0001	0.004	0.002	0.009	0.05	0.15	0.003	0.15	0.007
rols	DTW	0.71 (0.24)	0.93 (0.20)	86.01 15.46)	0.56 (0.21)	1.46 (0.32)	0.11 (0.46)	0.05 (0.07)	0.03 (0.03)	6.12 (4.76)	5.34 (2.94)
Controls	SW	0.99 (0.33)	1.08 (0.21)	101.55 (11.98)	0.42 (0.29)	$ \begin{array}{c} 1.21 \\ (0.21) \end{array} $	$\begin{array}{c} 0.01 \\ (0.41) \end{array}$	0.03 (0.05)	0.03 (0.05)	3.24 (4.8)	4 (4.54)
HCS	DTW	0.61 (0.26)	0.85 (0.24)	78.27 (17.78)	0.74 (0.43)	$ \begin{array}{c} 1.63 \\ (0.48) \end{array} $	0.12 (0.04)	0.06 (0.07)	0.04 (0.08)	7.33 (4.84)	6.91 (4.93)
ETp-HCS	SW	$\begin{array}{c} 0.89 \\ (0.31) \end{array}$	1.03 (0.23)	97.04 (14.46)	0.49 (0.32)	$ \begin{array}{c} 1.27 \\ (0.28) \end{array} $	0.11 (0.03)	0.04 (0.06)	0.03 (0.02)	4.59 (8.40)	4.59 (4.83)
LCS	DTW	0.46 (0.21)	0.73 (0.21)	70.30 (20.07)	0.99 (0.77)	1.89 (0.83)	0.14 (0.05)	0.16 (0.24)	0.04 (0.08)	13.28 (16.17)	8.55 (8.68)
ETp-LCS	SW	0.72 (0.24)	0.91 (0.23)	89.11 (15.31)	0.56 (0.26)	1.39 (0.32)	0.12 (0.04)	0.06 (0.08)	$\begin{array}{c} 0.11 \\ (0.58) \end{array}$	5.66 (5.77)	5.85 (4.93)
		Velocity, m/sec (SD)	Stride length, m (SD)	Cadence, steps/min (SD)	Stride time, sec (SD)	Double support time, sec (SD)	Step width, m (SD)	Step length difference, m (SD)	Step time Difference, sec (SD)	CV stride length, % (SD)	CV Stride time, % (SD)

Gait Posture. Author manuscript; available in PMC 2014 July 01.

ETp-LCS = ET participants with lower cognitive test scores; ETp-HCS = ET participants with higher cognitive test scores; C= control; SW= Standard walk; DTW= Dual-task walk; SD= Standard deviation; CV= Coefficient of variation; Statistically significant values in bold

Rao et al.

Table 3

Regression Model and Coefficients for Select	Gait Measures
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	Regression Model: Group	odel: Group	Regression Model: Group and Age	Iodel: Grou	ıp and Age	
	Coefficient	P Value	Coefficient Group	P Value	Coefficient Age	P Value
Stride Time Standard walk	-0.214	0.002	-0.14	0.03	0.243	0.0001
Stride Time Dual-task walk	-0.27	0.0001	-0.24	0.001	0.102	0.13
Double Support Time Standard walk	-0.146	0.03	-0.069	0.32	0.26	0.0001
Double Support Time Dual-task walk	-0.31	0.0001	-0.24	0.0001	0.222	0.001
Step Time difference Standard walk	-0.14	0.03	-0.068	0.33	0.257	0.0001
Step Time difference Dual-task walk	-0.25	0.0001	-0.19	0.005	0.21	0.003
Stride Time CV % Standard walk	-0.114	60.0	-0.048	0.49	0.222	0.002
Stride Time CV % Dual-task walk	-0.28	0.0001	-0.22	0.001	0.19	0.005

CV= Coefficient of variation; Statistically significant values in bold