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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 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 were 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.

1. Introduction

Essential tremor (ET) is a common movement disorder presenting with both motor and non-motor 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

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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.

2. Methods

2.1. 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.

2.2. 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.

2.3. 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].

2.4. 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 m from the beginning of the mat and stopped 3 m 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 [20,21]). 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.

2.5. 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 $\geq$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's *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.

3. Results

3.1. 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).

3.2. 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 × condition interaction was not seen, indicating that