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Functional Correlates of Gait and Balance Difficulty in Essential Tremor: Balance Confidence, Near Misses and Falls

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Abstract

Background—Although a mild objective abnormality of gait and balance has been observed in essential tremor (ET) cases in research settings, the clinical significance of this finding for patients is far from clear. In this study, we assessed whether ET patients subjectively experience more gait difficulty, more falls or near misses than controls.

Methods—Activities-specific Balance Confidence (ABC) scores were obtained in 59 ET cases (15 with head tremor and 44 without head tremor) and 82 controls enrolled in a clinical-epidemiological study.

Results—ABC scores were lower in ET cases than controls (61.8 ± 27.7 vs. 70.3 ± 28.1 , $p = 0.035$) of similar age (71.2 ± 14.6 vs. 71.6 ± 0.8 years), indicating significantly lower balance confidence in cases. The lowest scores (51.4 ± 26.9) were observed in cases with head tremor ($p = 0.02$). Near misses in the past year were the highest in cases with head tremor (67.3 ± 112.1) and lowest in controls (6.1 ± 33.3 , $p = 0.008$). The proportion who had had 5 near misses or falls in the past year was 11 (13.4%) for controls, 8 (18.2%) for cases without head tremor and 6 (40.0%) for cases with head tremor ($p = 0.048$). For the ABC score, we created a receiver operating curve (ROC) curve and optimal cut-off score to differentiate between our two most different groups, namely, ET with head tremor and controls. Using this cut-off (< 67), sensitivity and specificity were moderate.

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Conclusions—ET patients experience a loss of confidence in balance. The subgroup of patients with head tremor experienced the most gait and balance difficulty, with nearly one-in-two having had multiple near misses or falls during the previous year.

Keywords

essential tremor; balance; gait; falls; confidence

Introduction

Essential tremor (ET) is among the most highly prevalent neurological diseases.^{1–3} Interestingly, a mild abnormality of gait and balance has been observed in patients with ET.^{4–11} Besides revealing that the motor features of ET are not restricted to tremor,^{11, 12} the observation provides important physiological support for the view of ET as a disease of cerebellar system dysfunction.^{5, 8, 9, 11}

In existing studies, investigators used either simple bedside tests (tandem gait)^{5, 8, 10} or detailed laboratory-based quantitative approaches^{4, 6, 7, 9, 11} to document subtle, objective, case-control differences. Yet the clinical significance of these findings for the patients themselves is far from clear. Are abnormalities of gait and balance evident only during objective testing conditions or do patients themselves feel some subjective difficulty? Only two studies (combined n = 43 cases) attempted to assess if the patients thought their balance and walking were impaired in any way.^{6, 7} While one study ascertained relatively mild cases through the community,⁷ the other assessed severe cases who had already undergone deep brain stimulation surgery.⁶ Hence, a non-surgical, clinical sample has not been evaluated.

A clinical issue of prognostic significance is whether abnormalities of gait and balance in ET are translated into an increased risk for falls or near misses. Falls may cause physical injuries (fractures, head injuries) and are associated with increased risk of nursing home admission and higher mortality rates.¹³ Only one study examined this issue; with 30 ET cases and 28 controls, small differences were not significant.⁷ The same study⁷ reported that ET cases with head tremor experienced the most subjective gait and balance difficulty. Yet, as noted by the authors, theirs were *post hoc* analyses⁷ and no further work of this type has been reported. If substantiated, the importance of this finding is that it takes the first steps in identifying a subgroup of ET patients who are prone to greater gait difficulty and possible falls.⁷

This study had three aims: (1) to compare subjective functional measures of gait and balance in ET cases and controls. We used a clinical rather than a surgical or community-based sample of ET cases. (2) to assess whether cases are more prone to near falls or falls. (3) to evaluate in an *a priori* manner whether the subgroup of ET patients with head tremor is the most functionally impaired.

Methods

Participants

ET cases were enrolled in an ongoing (2000 – 2010) clinical-epidemiological study in New York.¹⁴ ET patients, age 18 years, came from two primary sources. First were patients whose neurologist was on staff at our center. These were selected using a random digit table from a computerized billing list. Second were patients who were cared for by their local doctor in the tri-state region (New York, New Jersey, Connecticut). Patients in the second group were members of the International Essential Tremor Foundation who had volunteered after having read advertisements for the study. During recruitment, participants from both

sources were invited to participate in this clinical-epidemiological study, whose broadly-stated goal was to elucidate the role of environmental toxins in tremor (i.e., it was not specifically advertised as a study of gait per se or gait-related disability). Prior to enrollment, all participants signed informed written consent approved by our University Institutional Review Board. ET cases qualified for enrollment if they had a diagnosis of ET using published diagnostic criteria (kinetic arm tremor rated ≥ 2 during at least 3 tests or head tremor).¹⁴ None had Parkinson's disease (PD) or dystonia. Normal controls were selected from the same set of zip codes within the New York metropolitan area as cases, and were recruited using random-digit telephone dialing. For statistical efficiency, controls were frequency-matched to ET cases by age, sex and race.¹⁵

Evaluation

Participants were evaluated in person by a trained tester who administered structured demographic and medical questionnaires and a Folstein Mini Mental Status Test (range = 0 – 30).¹⁶ The Cumulative Illness Rating Scale was a measure of medical comorbidity, assessing illnesses in 14 bodily systems (range = 0 – 42 [high co-morbidity]).¹⁷ Depressive symptoms were assessed with a ten-item version of the Center for Epidemiologic Study Depression (CESD) scale (0 – 10 [maximal depressive symptoms]).¹⁸ A videotaped neurological examination was performed, which included one test for postural tremor and five for kinetic tremor performed with each arm (12 tests total). A neurologist specializing in movement disorders used a reliable¹⁹ and validated²⁰ clinical rating scale to rate postural and kinetic tremor during each test: 0 (none), 1 (mild), 2 (moderate), 3 (severe), resulting in a total tremor score (range = 0 – 36).¹⁴ In addition, the motor portion of the Unified Parkinson's Disease Rating Scale (UPDRS)²¹ was videotaped. Head (i.e., neck) tremor in ET was coded as present or absent and was distinguished from dystonic tremor.⁸

In 2009, we added two self-reported measures of gait and balance difficulty. First, using the shortened 6-item version of the Activities-specific Balance Confidence (ABC-6) scale;^{22, 23} participants are asked to rate their level of confidence in performing 6 activities without losing their balance or becoming unsteady (0 [not at all confident] to 100 [completely confident]). The final score (range = 0 – 100) was the mean of the six 0 – 100 ratings. Second, as in other studies,⁷ we asked participants to indicate how many falls and how many near misses (i.e., when they felt they were going to fall but did not actually fall) they had had in the past year, and whether during that period they used a walking aid regularly in the house or when outside of the house.

We also added an objective measure of gait and balance. The Berg Balance Scale (BBS) is a 14-item test during which participants are rated on their ability to maintain balance while performing tasks such as retrieving an object from the floor and standing on one foot.²⁴ Each item is scored from 0 – 4 (total score = 0 – 56 [optimal balance]).

The current analyses were limited to participants enrolled as of 2009, which was the date when we added the two self-reported measures of gait and balance difficulty to the study assessment. Thus, data were available on 59 ET cases (71.2 $\pm$ 14.6 years of age; 34 [57.6%] female, and 57 [96.6%] white race) and 82 controls (71.6 $\pm$ 10.8 years of age; 49 [59.8%] female, and 75 [91.5%] white race).

Statistical Analyses

Analyses were carried out using SPSS (version 18.0.2; Chicago, Illinois). Demographic and clinical variables were compared using chi-square and Student's t-tests, when normally distributed. For continuous measures that were non-normal (e.g., ABC-6 scores, BBS scores), non-parametric approaches were used (e.g., Mann-Whitney test, Kruskal-Wallis

test, Spearman's r). For some analyses, we initially compared ET cases and controls using a Mann-Whitney test. Subsequent analyses then compared ET + H cases to controls and ET – H cases to controls; for these subsequent analyses, which involved two comparisons, a Bonferroni correction was applied, and the resultant level of statistical significance was adjusted from <0.05 to <0.025). We also created a receiver operating curve (ROC) for the ABC-6 score, BBS score and the number of near misses in order to examine the diagnostic performance of these three items when comparing our two most different groups, namely, ET+H and controls. Area under the curve (AUC) along with 95% confidence intervals (CIs) were calculated, and optimal cut-off scores were determined by choosing the value that produced the highest likelihood of a positive prediction of instability on these items. Sensitivity and specificity were calculated based on these cut-offs. We also considered the effects of several possible confounders. As our outcome variables were not normally distributed, even after log-transformation, it was not possible to adjust for confounders in linear regression models. Therefore, in logistic regression models, we divided the outcome variables (e.g., ABC-6 score, BBS scores) into low vs. high values, and then considered the independent association between diagnosis (ET+H vs. controls) and the outcome variable, while adjusting for the possible confounders. These analyses generated odds ratios (ORs) with 95% CIs. We compared the ORs in the unadjusted vs. adjusted models.

Results

Cases and controls were similar in terms of demographics and medical co-morbidities that could influence effective gait and balance (all $p > 0.05$, Table 1). Fifteen (25.4%) cases had head tremor.

Many gait and balance measures covaried with age: older age was associated with lower ABC-6 scores (Spearman's $r = -0.35$, $p < 0.001$), marginally more near misses in the past year (Spearman's $r = 0.16$, $p = 0.07$), and lower BBS scores (Spearman's $r = -0.56$, $p < 0.001$). Participants who used a walking aid in the house were older than those who did not (78.9 ± 17.4 [median 88.5] vs. 71.1 ± 12.1 [median 71.0] years, Mann-Whitney $z = 2.12$, $p = 0.03$).

ABC-6 scores were lower in ET cases than controls ($p = 0.035$), indicating significantly lower balance confidence in ET cases (Table 2). ABC-6 scores decreased as one progressed from controls to ET cases without head tremor (ET–H) to ET with head tremor (ET+H) (Kruskal-Wallis = 7.79, $p = 0.02$); indeed the highest ABC-6 scores were in controls and the lowest were in ET+H, Mann Whitney $z = 2.62$, $p = 0.009$). The number of near misses increased from controls to ET–H to ET+H (Kruskal-Wallis = 7.76, $p = 0.02$) such that near misses in the past year were the lowest in controls and highest in ET+H (Mann Whitney $z = 2.67$, $p = 0.008$). The proportion of participants who had ≥ 5 near misses or falls was 11 (13.4%) for controls, 8 (18.2%) for ET–H and 6 (40.0%) for ET+H (Spearman's $r = 0.17$, $p = 0.048$), indicating that nearly one-in-five ET–H cases and nearly one-in-two ET +H cases had had multiple near misses or falls in the previous year.

For each of the six items in the ABC-6, the participants who had a score ≤ 50 were designated as having low confidence with that task. For each task, low confidence occurred in approximately twice as many ET+H cases than controls (Table 3). The ABC-6 score was strongly inversely correlated with number of falls (Spearman's $r = -0.24$, $p = 0.005$) and number of near misses (Spearman's $r = -0.48$, $p < 0.001$) (i.e., lower balance confidence was a marker of more near misses and falls).

The BBS scores were lower in ET+H than controls (Table 2, Mann Whitney = 2.29, $p = 0.02$), indicating more difficulty performing balance tasks. There was a marginally

significant inter-group difference such that the lowest BBS scores were in ET+H, intermediate scores were in ET-H, and the highest scores were in controls (Kruskal-Wallis = 5.15, $p = 0.076$). A higher proportion of ET+H reported the need to use a walking aid in their house than did controls (20.0% vs. 3.8%, Fisher's Exact test $p = 0.048$, Table 2).

We also created ROC curves for the ABC-6 score, BBS score and the number of near misses in order to examine the diagnostic performance of these three items when comparing our two most different groups, namely, ET+H and controls. AUC and optimal cut-off scores were determined as were the sensitivity and specificity based on these cut-offs (Table 4). Values for sensitivity and specificity were moderate.

We considered age as a potential confounder. We also considered medication effects as many ET medications are anticonvulsants (phenobarbital, clonazepam, diazepam, gabapentin, primidone, topiramate, zonisamide) with the potential to affect gait and balance. We do not think depression was a confounder: CESD scores did not differ across the three groups (6.1 ± 4.7 [controls], 8.1 ± 6.3 [ET-H], 7.4 ± 6.8 [ET+H], Kruskal-Wallis = 2.86, $p = 0.24$). To assess confounding we first divided the ABC-6 into low vs. high values, with low values being those that were below the median of 76.7. In an initial unadjusted logistic regression model, ET+H (independent variable) was associated with an increased odds of having a lower ABC-6 score (OR = 5.10, 95% CI = 1.33 – 20.0, $p = 0.017$). In a logistic regression model that adjusted for age in years and the medications listed above (use vs. nonuse of one or more), ET+H was still independently associated with a lower ABC-6 score (OR = 4.26, 95% CI = 1.04 – 17.54, $p = 0.04$). We also divided the number of near misses into low vs. high values, with low values being those that were at the median of 0. In an initial unadjusted logistic regression model, ET+H (independent variable) was associated with an increased odds of having a high near miss value (OR = 3.71, 95% CI = 1.16 – 11.94, $p = 0.028$). In a logistic regression model that adjusted for age in years and medications, the magnitude of the OR was similar: OR = 3.35, 95% CI = 1.02 – 10.97, $p = 0.046$. Finally, we also divided the BBS scores into low vs. high values, with low values being those that were below the median of 54. In an initial unadjusted logistic regression model, ET+H (independent variable) was marginally associated with an increased odds of having a lower BBS score (OR = 3.36, 95% CI = 0.84 – 13.51, $p = 0.087$). In a logistic regression model that adjusted for age in years and medications, the magnitude of the OR did not change: OR = 3.57, 95% CI = 0.61 – 20.83, $p = 0.157$.

There was no correlation between the ABC-6 score and age of tremor onset (Spearman's $r = -0.14$, $p = 0.31$) or duration of ET (Spearman's $r = -0.07$, $p = 0.64$).

Discussion

ET cases reported greater subjective functional gait and balance impairment than controls, indicating that gait and balance problems in ET are not merely a subclinical phenomenon observed in the laboratory; patients themselves experience difficulty. We also noted that the subgroup of ET patients with head tremor was the most functionally impaired. Nearly one-in-five ET-H cases and nearly one-in-two ET+H cases had had multiple near misses or falls in the previous year. ET+H cases also functioned more poorly on a performance-based measure of balance that included common everyday activities (e.g., sitting to standing, retrieving an object from floor).

These findings have a number of potential clinical implications. First, we should consider whether a clinical assessment of balance should become part of routine clinical practice with ET patients rather than remaining restricted to research laboratory settings. Second, formal interventional trials (i.e., rehabilitation therapy) need to be undertaken to determine whether

balance, balance confidence, and functional mobility can be improved in ET. We are unaware of any such studies. Third, clinical trials of new ET medications, many of which are anticonvulsants, should formally assess whether the gait worsens with these medications; this is not currently assessed. Finally, a goal of medication development can be the improvement in gait. Such trials are currently underway for other forms of ataxia^{25, 26} but not for ET.

The earlier finding⁷ that ET cases with head tremor experience the most subjective gait and balance difficulty has been substantiated by the present study. We also reported in a previous study that ET cases with head tremor performed most poorly on tandem gait,⁸ suggesting that a disturbance of balance and head tremor may both be symptomatic of the same underlying pathophysiology, a disturbance of cerebellar regulation of the midline, which is distinct from its regulation of the limbs.

Our results may be compared with those from several previous studies. Our ET cases had a mean ABC-6 score of 61.8. The two other studies^{6, 7} that examined balance confidence in ET used the ABC-16, although the ABC-6 and ABC-16 correlate very highly²³ and are graded on the same scale. Parisi et al⁷ reported higher balance confidence scores in ET (mean ABC score approximately 90), although their cases were largely community-based and were on average approximately 13 years younger than ours (i.e., approximately 58 years vs. 71.2 years), contributing to their higher scores. Parisi et al⁷ also did not find differences in the BBS score or in the number of near falls, as we did; again, this could reflect the relatively mild ET in their sample. Earhart et al's⁶ ET cases were also nearly ten years younger than ours, but their ABC-16 scores were similar (66.0), perhaps a function of the severity of their cases (i.e., post-surgical cases).

Near misses were more frequently reported than were actual falls, which is not surprising and is not a finding unique to this study.⁷ Indeed, near misses may be a better measure of postural instability and loss of confidence than falls themselves. Previous studies have shown that near misses are a sensitive predictor of future falls²⁷ and, in some instances, are a better marker of instability than are falls themselves.²⁷

This study had limitations. We assessed medications that were most likely to be associated with ET and imbalance (i.e., anticonvulsant medications used in the treatment of ET) but recognize that other medications could also have played a lesser role. This study had strengths. We used a combination of widely-used and reliable scales to assess both self-reported measures of gait and balance and performance-based measures to obtain a broad, functionally-relevant view of gait and balance in ET.^{22, 24} Second, we extended our analyses to examine the issue of near falls and actual falls, a clinical issue with wider-reaching health consequences. Finally, we used a clinically-derived sample of cases to bring balance to the prior studies that have focused on the two extremes of ET cases (surgical or community-based samples of cases).

In summary, ET cases in general reported greater subjective functional gait and balance impairment than their counterparts without ET, indicating that the abnormalities of gait and balance in ET are not merely curiosities only evident during objective testing conditions but that patients themselves may experience subjective difficulty. The subgroup of ET patients with head tremor experienced the most difficulty; nearly one-in-two having had multiple near misses or falls during the previous year. Clinicians should consider incorporating an assessment of balance into their routine clinical evaluation of ET patients.

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Table 1

Demographic and clinical characteristics of ET cases and controls

	Controls (N = 82)	ET Cases (N = 59)
Age in years	71.6 ± 10.8	71.2 ± 14.6
Female sex	49 (59.8)	34 (57.6)
Education in years	16.2 ± 2.5	16.1 ± 2.3
White race	75 (91.5)	57 (96.6)
Mini Mental Status Test score	28.8 ± 1.6	28.7 ± 1.6
Cumulative Illness Rating Scale score	6.7 ± 3.3	6.5 ± 3.3
Total tremor score	20.7 ± 5.0	Not applicable
Age of tremor onset (years)	38.1 ± 20.6 ¹	Not applicable
Tremor duration (years)	33.2 ± 18.0 ²	Not applicable
Takes daily medication for tremor	30 (50.8)	Not applicable
Family history of ET or tremor	37 (62.7)	Not applicable
Wears corrective lenses ^a	75 (92.6)	51 (87.9)
Glaucoma ^a	10 (12.5)	5 (8.6)
Macular degeneration ^a	5 (6.3)	0 (0.0)
Cataracts ^a	16 (20.3)	6 (10.3)
Diabetes mellitus ^a	10 (12.3)	4 (7.0)
Numbness in feet ^a	18 (22.2)	12 (20.7)
Diagnosis of neuropathy ^a	9 (11.1)	5 (8.8)
Hip replacement ^a	2 (4.3)	0 (0.0)

Values are either mean ± standard deviation or number (percentage).

For some cells, n < 82 for controls and n < 59 for cases.

^aby self report on the medical questionnaire.

¹median = 40, range = 1 – 80, interquartile range = 35.

²median = 30, range = 5 – 76, and interquartile range = 27.

Table 2

Gait and balance in ET cases and controls

	Controls (N = 82)	ET Cases without Head Tremor (N = 44)	ET Cases with Head Tremor (N = 15)	All ET Cases (N = 59)
Age in Years	71.6 ± 10.8 (72.0)	67.1 ± 14.9 (71.0)	74.6 ± 15.6 (78.0) *	71.2 ± 14.6 (75.0)
Female sex	49 (59.8)	22 (50.0)	12 (80.0)	34 (57.6)
ABC-6 score	70.3 ± 28.1 (79.2)	68.2 ± 22.7 (74.6)	51.4 ± 26.9 (54.2) **	61.8 ± 27.7 (66.7) *
Near misses in the past year	6.1 ± 33.3 (0)	19.6 ± 67.6 (0)	67.3 ± 112.1 (2.5) **	26.3 ± 75.0 (0)
0	54 (65.9)	31 (70.5)	5 (33.3)	36 (61.0)
1 – 5	19 (23.2)	7 (15.9)	4 (26.7)	11 (18.6)
6 – 10	4 (4.9)	1 (2.3)	0 (0.0)	1 (1.7)
11 – 20	2 (2.4)	1 (2.3)	0 (0.0)	1 (1.7)
21 – 99	2 (2.4)	1 (2.3)	2 (13.3)	3 (5.1)
100 – 364	1 (1.2)	2 (4.5)	3 (20.0)	5 (8.5)
365 or more	0 (0.0)	1 (2.3)	1 (6.7)	2 (3.4)
Falls in the past year	0.6 ± 1.0 (0)	0.6 ± 1.2 (0)	0.6 ± 0.9 (0)	0.6 ± 1.0 (0)
0	54 (65.9)	32 (72.7)	10 (66.7)	42 (71.2)
1	16 (19.5)	8 (18.2)	2 (13.3)	10 (16.9)
2	8 (9.8)	2 (4.5)	3 (20.0)	5 (8.5)
3	1 (1.2)	1 (2.3)	0 (0.0)	1 (1.7)
4	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
5	1 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
>5	1 (1.2)	1 (2.3)	0 (0.0)	1 (0.0)
BBS score	52.4 ± 6.7 (55.0)	51.4 ± 9.7 (55.0)	47.3 ± 11.6 (51.0) *	50.4 ± 10.2 (54.0)
Uses a walking aid regularly in the house	3 (3.8)	1 (2.3)	3 (20.0) *	4 (6.9)
Uses a walking aid regularly when outside of the house	13 (16.7)	2 (4.9)	5 (35.7)	7 (12.7)

Values are mean ± standard deviation (median) or numbers (percentages) unless otherwise indicated.

For some cells, n < 82 for controls and n < 59 for cases.

ABC-6 = Activities-specific Balance Confidence-6 scale.

BBS = Berg Balance Scale score

* p < 0.05 compared with controls.

** p < 0.01 compared with controls.

Table 3

Proportion of participants with low balance confidence during different tasks on ABC-6

	Controls (N = 82)	ET Cases with Head Tremor (N = 15)
ABC 1 (stand on your tiptoes and reach for something)	10 (12.2%)	3 (20.0%)
ABC 2 (stand on chair and reach for something)	19 (23.2%)	8 (53.3%) [*]
ABC 3 (bumping into people on a crowded sidewalk)	8 (9.8%)	3 (20.0%)
ABC 4 (stepping on or off an escalator while holding the railing)	6 (7.3%)	3 (20.0%)
ABC 5 (stepping on or off an escalator while not holding the railing)	20 (24.4%)	7 (46.7%)
ABC 6 (walking on icy sidewalks)	27 (32.9%)	10 (66.7%) [*]

Low confidence was defined as a score < 50%.

^{*} p < 0.05 when compared with controls.

ABC-6 = Activities-specific Balance Confidence scale.

Table 4

Diagnostic performance of ABC-6 score, BBS score and reported falls when comparing ET+H and controls

	AUC (95% CI), p value	Best cut off point	Sensitivity	Specificity
ABC-6 score	0.71 (0.58 – 0.85), p = 0.009	67	0.73	0.65
Near misses in the past year	0.69 (0.53 – 0.85), p = 0.018	1	0.67	0.65
BBS score	0.70 (0.54 – 0.87), p = 0.025	51	0.67	0.79

ABC-6 = Activities-specific Balance Confidence-6 scale.

BBS = Berg Balance Scale score

AUC = area under the curve.