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The gait disorder of advanced essential tremor

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Summary

Gait disturbances of patients with essential tremor (ET) have been described anecdotally, but have never been investigated quantitatively. Recent studies provided evidence for a cerebellar-like hand tremor in some patients with ET. Therefore, we designed a study to assess cerebellar-like abnormalities of leg function. Twenty-five patients with ET, eight patients with cerebellar diseases (CD) and 21 age-matched healthy subjects were studied for their normal and tandem gait using a three-dimensional gait analysis system. During normal walking, CD and ET patients showed only slight abnormalities. However, ET patients exhibited abnormalities in tandem gait with an increased number of mis-steps and a broad-based, ataxic and dysmetric gait which was indistinguishable from the findings in CD. When ET patients were separated into groups of those with or without intention tremor of the hands, the gait disorder was found to be much more pronounced in the intention tremor group. Patients with this gait disorder were more severely disturbed in their activities of daily living, and suffer from an advanced stage of ET. The present results quantitatively describe a gait disturbance in advanced ET which affects tandem gait, but leaves normal gait almost unaffected. This is strong evidence for a cerebellar-like disturbance in ET.

Keywords: essential tremor; intention tremor; gait ataxia; cerebellar gait

Abbreviations: ADL = activities of daily living; CD = cerebellar disease; CV = coefficient of variation; ET = essential tremor; ET_{IT} = essential tremor with intention tremor; ET_{PT} = essential tremor with predominant postural tremor; HC = healthy control

Introduction

Essential tremor (ET) is a mostly autosomal dominant, monosymptomatic disease with predominant postural tremor of the hands or head, but voice, leg and trunk tremor are uncommon (Deuschl *et al*., 1998). Converging evidence from animal studies with the harmalin model of tremor (Elble, 1998; Wilms *et al*., 1999), PET studies (Hallett and Dubinsky, 1993; Wills *et al*., 1994; Boecker *et al*., 1996) and observations in patients with brain lesions (Dupuis *et al*., 1989; Kim and Lee, 1994; Qureshi *et al*., 1996; Nagaratnam and Kalasabail, 1997) has led to the hypothesis that ET comes from oscillatory activity within the Guillain–Mollaret triangle consisting of the olivo-cerebello-(rubral) pathways (Elble, 1998). Despite progress, we are far from clearly understanding the precise mechanisms of this oscillatory activity, but if these cerebellar circuits are abnormally activated in ET, it seems plausible to assume other cerebellar motor functions could be disturbed.

To test this hypothesis, we have analysed movements in a reach-to-grasp paradigm in patients with ET (Deuschl *et al*., 2000). We found that a subgroup of patients with ET had intention tremor indistinguishable from cerebellar tremor, an overshoot of voluntary hand movements and a slowing of movement. These are all features compatible with a cerebellar malfunction. Following this line of reasoning, the next step is to assess the lower extremity for possible abnormalities. Clinical experience suggests that the gait of patients with ET is normal, but quantitative analysis has never been performed. In a cerebellar gait disturbance, we expect a broad-based unstable and lurching gait pattern which has been assessed in some rare quantitative studies on cerebellar patients (Victor *et al*., 1959; Hallett *et al*., 1991).

The present study was designed to uncover possible abnormalities of gait in patients with ET. We investigated normal walking and tandem gait using a three-dimensional opto-electronic movement analysis system and compared patients with ET or cerebellar disease with age-matched healthy controls (HCs). We will demonstrate that patients with ET have an abnormal tandem gait, and this feature is found in those patients who also have clinical features of hand tremor, reminiscent of cerebellar abnormalities. Together with the new finding of a gait disorder in ET, this is further evidence for a cerebellar-like abnormality in ET.

Material and methods

Tremor rating scale

Tremor rating was performed for each side of the upper and lower limb and head tremor by trained neurologists on a five-point scale (0–4), according to a modified clinical tremor rating scale by Fahn and co-workers (Fahn *et al*., 1988). Intention tremor of the hands was considered to be present when the amplitude increased during visually guided movements towards a target during the terminal phase of the movement and if a position-specific tremor or a postural tremor emerging at the end of the movement was excluded (Deuschl *et al*., 1998). Intention tremor of the hands was rated in the terminal period of the finger–nose test. Intention tremor of the leg was measured when the patient made pointing movements with the leg (sitting position) attempting to touch the finger of the examiner with the big toe.

Handwriting, drawings and water pouring were also all rated according to the scale (Fahn *et al*., 1988). The maximum score was 88 points.

Disability in activities of daily living (ADL) and social handicap were rated according to a modified five-point (0–4) scale proposed by Bain and co-workers (Bain *et al*., 1993): 0 = able to do the activity without difficulty; 1 = able to do the activity with a little effort; 2 = able to do the activity with a lot of effort; 3 = nearly unable to do the activity by oneself; 4 = totally unable to do the activity by oneself. Maximum score was 88 points. Handicap was assessed with a questionnaire given to the subjects, asking if the tremor had stopped them carrying out different professional and private activities: 0 = no, 1 = yes, because the person is embarrassed by the tremor; 2 = yes, because of the physical difficulties produced by the tremor; and 3 = yes, because of both the physical difficulties and the embarrassment which were produced by the tremor. Maximum score was 27 points. Tremor rating was performed in both patient groups, those with ET and those with cerebellar disease (CD).

Gait analysis

Before gait analysis on a treadmill, the natural walking speed of each subject was measured during overground locomotion. The subjects were instructed to walk a distance of 13 m at their own selected comfortable speed on a walkway. In the central part of the 13 m, two infrared light barriers were installed 5 m apart. The gait velocity was calculated by measuring the time each subject needed to cover the 5-m distance (mean of four runs). For the measurement of the walking speed during tandem gait (mean of four runs), a red tape of 1.5 cm width was fixed on the walkway and the subjects were trained to walk the distance by placing one foot exactly in front of the other on the red line.

Subsequently, a complete gait analysis was carried out on a motor-driven treadmill (Woodway®), with a length of 2.2 m and a width of 0.7 m. As in the gait velocity measurements, the subjects walked barefoot during treadmill locomotion. The treadmill speed was adjusted exactly to the subject's individual gait velocity measured during normal and tandem gait. During normal locomotion on the treadmill, the subjects were instructed to let their arms swing freely. If necessary, the patients additionally were secured with a safety belt suspended from the ceiling of the laboratory (without weight support). During tandem gait, both on the walkway and on the treadmill, the subjects were trained to walk with their hands folded over their necks (if possible) to avoid different strategies of balance control, e.g. such as walking with horizontally outstretched arms. Just as on the walkway, the subjects were instructed to place one foot in front of the other on a line of red tape (1.5 cm width) that was fixed onto the middle of the lamella layers of the treadmill. Before recording, the subjects were given 5 min to familiarize themselves with treadmill locomotion and again 2 min before the recordings of tandem gait. Normal walking was assessed first. In addition to the movement analysis during tandem gait, mis-steps, defined as those steps taken with the whole foot outside the bounds of the red tape, were counted over 60 s.

For quantitative off-line analysis, the gait was recorded with an infrared movement analysis system (Qualisys, Sandvälen, Sweden), consisting of four infrared cameras and video processors (50 Hz sampling rate) connected to a Macintosh computer. Seven infrared light-reflective spherical markers (1.8 cm diameter) were attached to each leg (above the anterior superior iliac spine, the major trochanter, the lateral thigh, the knee joint, lateral malleolus, calcaneus and to the lateral forefoot above the head of the fifth metatarsal bone). Three trials of 20 s duration were recorded at identical treadmill speed for each condition. From these trials, 15–20 consecutive walking cycles were averaged for off-line analysis and calculation of the different spatio-temporal gait measurements with self-developed software, which has been described elsewhere (Stolze *et al*., 1997). The following gait variables were calculated: gait velocity, stride length, cadence, step width (which was corrected for the individual distance between medial and lateral malleolus corresponding to the marker on the lateral malleolus), foot angle (outward rotation denoted as positive), step height, gait cycle time, stance, swing and double limb support phase duration. The step width can have negative values if one foot crosses the other, especially during tandem gait. Additionally, an ataxia ratio measuring the regularity of the strides was calculated as a ratio of the standard deviation (SD) of foot placement in all three room directions [(SD of step length + SD of step width + SD of step height)/3]. For the kinematics of gait, the hip joint angle was measured between the markers fixed over the anterior superior iliac spine, the trochanter and the thigh. The knee joint angle was determined between the markers attached to the thigh, the knee and the lateral malleolus. The ankle joint angle was defined as the angle between the knee, lateral malleolus and forefoot markers.

Subjects

Twenty-five out-patients with ET were studied (for demographic data, see Table 1). All patients fulfilled the

Table 1 *Anthropometric data of patients with ET and intention tremor (ET_{IT}), ET with postural tremor (ET_{PT}), cerebellar disease (CD) and healthy controls (HC)*

	HC	ET	ET_{PT}	ET_{IT}	CD
No. and sex	21 (10 F, 11 M)	25 (12 F, 13 M)	10 (4 F, 6 M)	15 (8 F, 7 M)	8 (1 F, 7 M)
Age (years)	52.7 ± 15.2	50.3 ± 21.1	43.4 ± 19.5	55.3 ± 21.4	52.5 ± 17.3
Body size (m)	168.5 ± 27.5	172.6 ± 7.4	174.0 ± 8.9	171.5 ± 6.2	171.6 ± 6.1
Body weight (kg)	79.9 ± 23.7	74.6 ± 15.5	75.7 ± 20.5	73.7 ± 11.2	73.6 ± 6.5
Leg length (cm)	94.0 ± 5.3	93.4 ± 4.7	95.1 ± 5.6	92.2 ± 3.7	92.5 ± 4.3
Medication	None	Primidone (4) Propanolol (3)	Primidone (1) Propanolol (1)	Primidone (3) Propanolol (2)	Oxitriptane (1)
Family history		13 patients	7 patients	6 patients	
Age of onset of tremor (years)	34 ± 22	34 ± 23	35 ± 20		
Duration of tremor (years)	16 ± 15	21 ± 17	10 ± 6		

F = female; M = male.

diagnostic criteria of classical ET according to the consensus statement of the Movement Disorders Society (Deuschl *et al*., 1998). Medication for the treatment of ET (propanolol and primidone) was allowed (see Table 1). Besides a full neurological examination, the patients were assessed for the clinical features of ET by a standardized tremor rating scale (see above).

For some of the statistical analyses, the ET group was divided according to the presence of intention tremor of the hands into those patients with predominant postural tremor (ET_{PT}; 10 patients: four women, six men; mean age 43.4 years) and those with definite intention tremor (ET_{IT}; 15 patients: eight women, seven men; mean age 55.3 years). The demographic data of the patients and controls are shown in Table 1. The age, body size, weight and length were not significantly different. Patients and healthy subjects were excluded if either the history or the examination showed a hindrance or disease which interfered with an unrestrained gait, other than ET or CD (for the patient groups). All patients were physically active and completely independent. A normal or abnormal tandem gait performance was not an inclusion criterion for patients and subjects. Clinical examination of the patients with ET showed postural tremor in 92% and definite intention tremor in 60% of the patients. ET_{IT} patients were ~10 years older than the group of ET_{PT}, but the difference did not reach significance. The tremor score on the tremor rating scale was highest for the patients with ET_{IT} followed by CD, and it was significantly different between ET_{IT} and ET_{PT} (Table 2). Postural tremor of the arms was more severe in ET_{IT}. Voice tremor and head tremor were distributed equally between both ET groups. ADL and the handicap score were mostly altered in CD, followed by ET_{IT} and ET_{PT}.

Eight patients with CD (Table 1) of heterogeneous aetiology were compiled for a control group (one woman, seven men; mean age 52.5 years). Demographic and disease-related data of CD patients are shown in Table 3. All patients had a gait disturbance of variable extent, limb ataxia and intention tremor on neurological exam.

Twenty-one healthy subjects (10 women, 11 men; mean age 52.7 years) served as normal HCs for the data of the gait analysis. The subjects underwent a full neurological examination. The subjects were age matched (see Table 1) to the patients with ET and CD.

All patients and HCs gave their informed consent to participate in the study, which was approved by the ethical committee of The Christian-Albrechts-Universität zu Kiel.

Statistical analysis

For statistical analysis, means and SDs were calculated for the gait measurements derived from 15–20 gait cycles in each subject. Additionally, the coefficients of variation (CV) were calculated for stride length, step width, step height and foot angle to quantify the intra-individual variability. Groups were compared with the Kruskal–Wallis one-way analysis of variance. In the case of a significant influence of the group factor on the dependent variables, *post hoc* comparisons were calculated using the Mann–Whitney *U* test. The results were corrected for the influence of multiple comparisons according to Bonferroni. Correlation between the clinical tremor score, the ADL and the different gait measurements during normal walking and tandem gait were computed by use of Spearman's rho for ET, CD and the two subgroups ET_{PT} and ET_{IT}. The level of significance was set at $P < 0.05$.

Results

Gait analysis

The results of the gait analysis during normal free speed locomotion are shown in Fig. 1. Balance-related parameters are typically abnormal in CD and partially abnormal in ET, which is expressed in an enlarged step width (CD, 154 mm; ET, 149 mm; HC, 118 mm) and significantly outward-rotated foot angle in CD (19°) but normal in ET (14°) comparable with HC (14°). A more detailed analysis separating ET patients into those with (ET_{PT}) and without intention tremor (ET_{IT}) did not reveal further significant differences. The double limb support duration, which is the phase of the

Table 2 *Data of the tremor rating in ET with intention tremor (ET_{IT}), ET with postural tremor (ET_{PT}) and cerebellar disease (CD)*

	ET	ET_{PT}	ET_{IT}	CD
Tremor total score (max 88 pts)	16.9 ± 7.8	12.6 ± 4.1*	20.0 ± 8.4	16.0 ± 7.2
Postural tremor upper extremity (max 8 pts)	2.2 ± 1.3	1.7 ± 1.1	2.6 ± 1.3	
Postural tremor lower extremity (max 8 pts)	1.3 ± 1.5	1.7 ± 1.5	1.1 ± 1.4	
Intention tremor upper extremity (max 8 pts)	1.7 ± 1.8		2.9 ± 1.4	1.6 ± 1.7
Patients with intention tremor upper extr. (*n*)	15		15	8
Intention tremor lower extremity	0.6 ± 0.9		0.9 ± 1.0	2.8 ± 3.0
Patients with intention tremor lower extr. (*n*)	6		6	4
Voice tremor (max 4 pts)	0.5 ± 0.9	0.4 ± 1.0	0.5 ± 0.9	
Head tremor (max 4 pts)	0.6 ± 1.0	0.7 ± 1.1	0.6 ± 0.9	
Patients with voice tremor (*n*)	7	2	5	
Patients with head tremor (*n*)	8	3	5	
Activities of daily living score (max 88 pts)	17.3 ± 17.1	7.6 ± 4.5*,**	24.1 ± 19.5	33.6 ± 26.7
Handicap score (max 27 pts)	3.1 ± 4.7	1.6 ± 3.1***	4.1 ± 5.4	6.4 ± 6.4

Significant differences ($\alpha < 0.05$) are indicated: *$P < 0.05$ between ET_{IT} and ET_{PT}; **$P < 0.05$ between ET_{PT} and CD; ***$P < 0.01$. ET_{IT} = ET with intention tremor; ET_{PT} = ET with postural tremor; CD = cerebellar disease.

Table 3 *Disease-related data of the patients with cerebellar disease*

Patient no.	Age (years)	Sex	Disease duration (years)	Aetiology
1	69	M	1	OPCA*
2	84	F	2	Lindau tumour in the posterior fossa with cerebellar bleeding
3	46	M	1	Alcohol toxic
4	37	M	1	OPCA*
5	49	M	6	SCA 2†
6	39	M	14	SCA 3‡
7	36	M	13	Early-onset cerebellar ataxia
8	59	M	–	Cerebellar metastasis

*OPCA = multiple system atrophy of olivopontocerebellar type; †SCA 2 = spino-cerebellar ataxia type 2; ‡SCA 3 = spinocerebellar ataxia type 3 (Machado–Josephs disease).

walking cycle in which the feet are in contact with the ground, was significantly longer in CD, which can be interpreted as an increased need for stability during locomotion. Furthermore, some meaningful trends can be derived from these data. The speed of locomotion was reduced in CD (0.9 m/s) and in ET (1.0 m/s) as a well-known sign of the cerebellar gait disturbance compared with the HC (1.2 m/s). This reduction in walking speed was due mainly to a reduced and somewhat more variable stride length, while the cadence was relatively preserved.

Regarding the kinematics of gait, a significant difference in the so-called yield (or E1-extension phase) was detected. The yield describes the short flexing movement of the knee after the heel strikes the ground and body weight is loaded on the leg. This value was reduced in CD (4°) compared with HC (11°) and ET (10°), which means that the leg was held stiffly during heel strike. No further significant differences of the joint angles were found.

The major abnormalities were found for the balance-related parameters of tandem gait. In the group of ET patients, we were not able to find an influence of the medication (primidone or propanolol) on the performance of tandem gait. The basic finding is shown in Fig. 2 which shows the paths of the markers at the lateral malleolus during tandem gait. The normal gait shows a regular pattern of a half circle for each foot, with the straight line indicating the foot transport on the treadmill and the half-circle the active step around the contralateral foot. For the patients, this pattern is mildly (ET_{PT}) or grossly distorted (ET_{IT} and CD). Quantitative measurements are shown in Fig. 3. The step width, expressing the distance between both feet during the double limb support phase, should be around zero if one foot is placed directly in front of the other, such as when walking on a line. This holds true for HC where the mean width was 2 mm (range −35–37 mm) but not for CD (34 mm, range –17–83 mm) and ET (19 mm, range −24–97 mm) (Fig. 3B). Significantly, more mis-steps were counted over 60 s in CD (mean 9.1 ± 13, range 1–39) and ET (3.7 ± 7, range 0–25). The ataxia ratio was highest in CD (45.9 ± 18.4, range: 18.1–72.6) and also increased in ET (mean 30.5 ± 25.2, range 14.6–96.0) compared with HC (mean 22.1 ± 9.7, range 11.5–50.7). No differences were found for the phases of the walking cycle

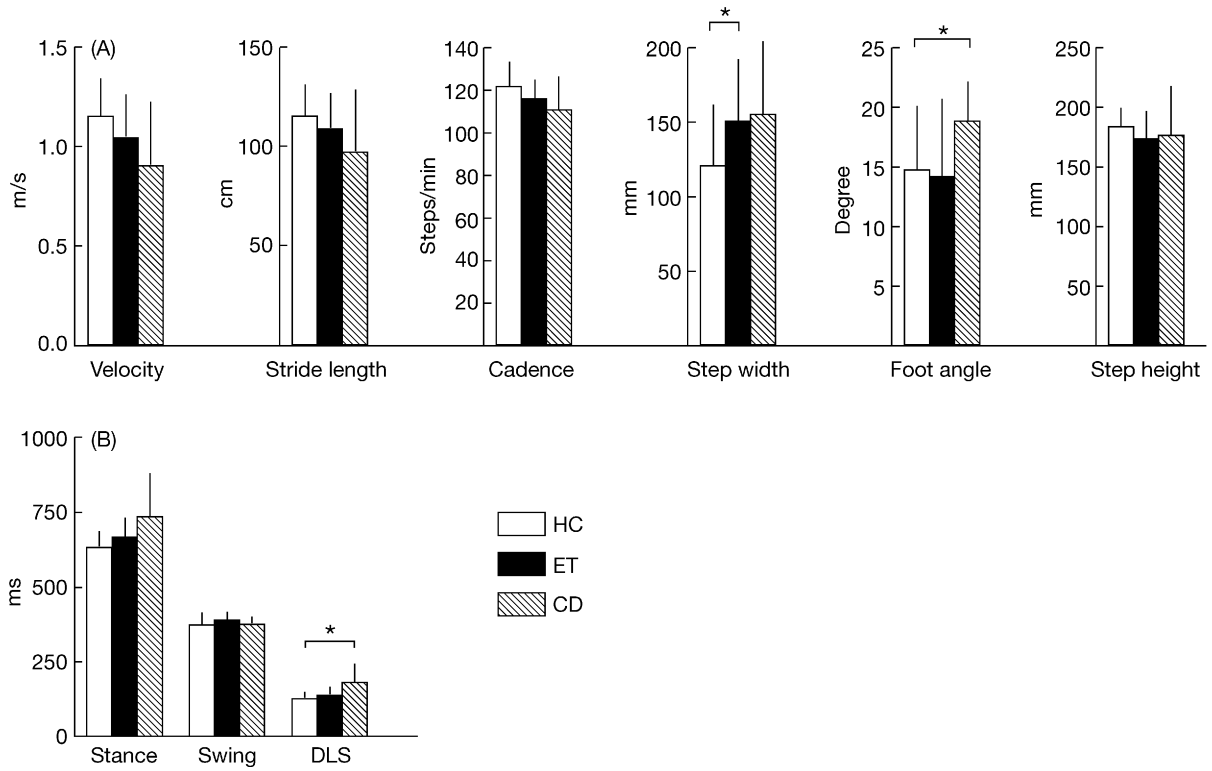

Fig. 1 Differences in gait parameters during normal locomotion between patients with essential tremor (ET), cerebellar disease (CD) and healthy controls (HC). (**A**) Spatial gait measurements. (**B**) Temporal gait values. Stance = stance phase duration; Swing = swing phase duration; DLS = duration of the double limb support phase. Significant differences ($\alpha < 0.05$) are indicated. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

(Fig. 3C). A more detailed analysis of the balance-related parameters splitting up the ET group into patients with and without intention tremor (ET_{IT} and ET_{PT}; Fig. 3D) showed that the abnormality of balance-related parameters was pronounced in the ET group with intention tremor of the hands. The step width was 6 mm for ET_{PT} (range −24–31) and 29 mm for ET_{IT} (range −8–97). The number of mis-steps was almost identical for ET_{PT} (0.5 ± 0.5, range 0–1) and HC (0.6 ± 1.3, range 0–5) but significantly enhanced for ET_{IT} (5.9 ± 8.1, range 0–25) and CD (9.1 ± 13, range 1–39). Similar differences were found for the ataxia ratio.

No significant differences between the groups were found for the velocity of tandem gait, the length of the steps or the cadence (Fig. 3A), but the intra-individual CV of the step length was significantly higher in CD (25%) and ET_{IT} (36%), compared with HC (10%) and ET_{PT} (9%), which means that the strides could not be placed correctly in front of each other. The same abnormality is found for the intra-individual CV of the step height for CD (40%) compared with ET_{IT} (24%), ET_{PT} (21%) and HC (21%), which is another expression of the increased variability of the stepping movement in the vertical direction for CD.

For the kinematics of tandem gait, a difference was found for the minimum hip angle, which was significantly decreased in CD (72°) compared with HC (119°). This indicates a more flexed hip in cerebellar patients, possibly indicating the protective gait in these patients.

The relationship of tremor characteristics and gait abnormalities

The next question is whether the gait abnormalities that have been demonstrated here are related to any specific clinical features of ET. For this reason, we have performed correlation analysis including the major clinical features of ET and the major gait abnormalities. We found that intention tremor of the hands was significantly correlated with the number of mis-steps ($r = 0.55$, $P < 0.005$) and the step width ($r = 0.46$, $P < 0.02$) of tandem gait. The same was found for the reduction of the ADL and step width ($r = 0.63$, $P < 0.001$) or mis-steps ($r = 0.52$, $P = 0.009$). Intention tremor and the reduction of ADL are also highly correlated, confirming the clinical experience that the patients with ET are most handicapped by their intention tremor. Interestingly, the balance-related gait parameters were not correlated with the severity of the intention tremor of the legs. Similar correlations were found for the patients with CD. The tremor is more severe and patients with ET_{IT} have a more serious disability, but these features are correlated neither with age nor duration of the disease.

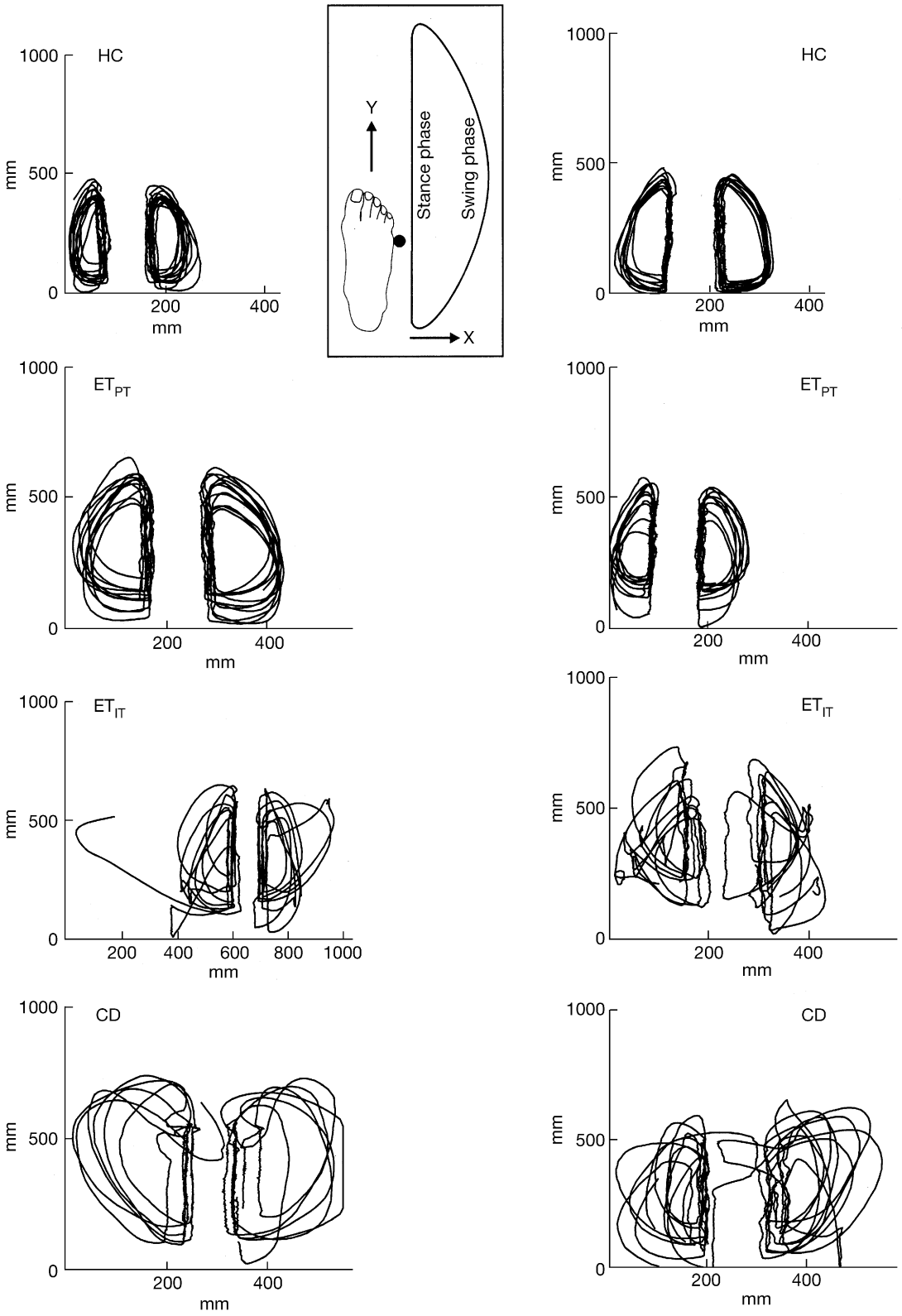

Fig. 2 Direct tracings of markers attached in projection on the fifth metatarsal bone of both feet in a view from above (see schematic drawing at the top) for healthy controls (HC), patients with ET and predominantly postural tremor (ET_{PT}), ET with intention tremor (ET_{IT}) and cerebellar disease (CD). Recordings were made during tandem walking on the treadmill over 20 s of continuous measurement. Note the dysmetric and even ataxic leg movements in ET_{IT} and CD.

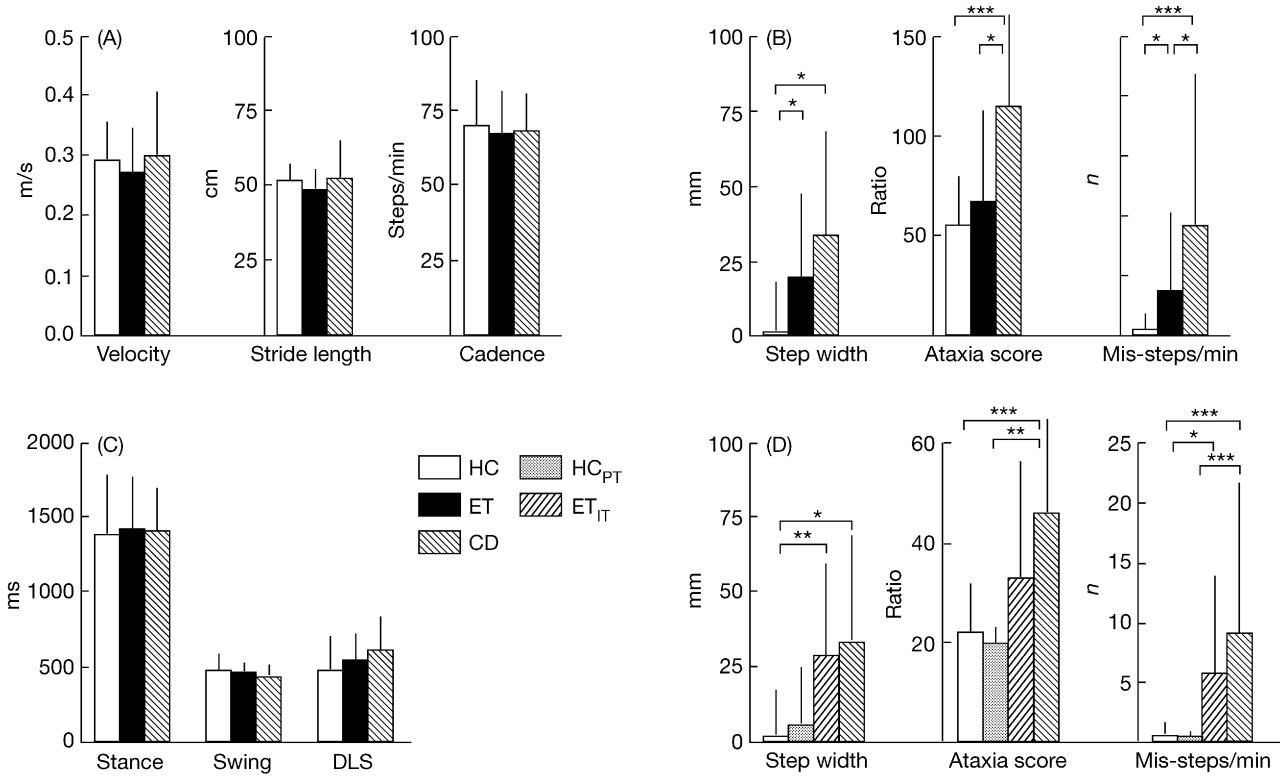

Fig. 3 Differences in gait parameters during tandem gait between patients with ET, cerebellar disease (CD) and healthy controls (HC). (**A**) Spatial gait measurements; (**B**) ataxia-related gait values; (**C**) temporal gait parameters. In **D**, ataxia-related gait parameters in ET are displayed separately for ET with intention tremor (ET_{IT}) and predominantly postural tremor (ET_{PT}). Stance = stance phase duration; Swing = swing phase duration; DLS = duration of the double limb support phase. Significant differences ($\alpha < 0.05$) are indicated. $^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

Discussion

The present quantitative study has demonstrated a gait disorder of patients with ET. This abnormality is very distinct, as the tandem gait is affected, but normal locomotion shows only subtle alterations. This gait disorder was most pronounced in the group of patients which exhibited intention tremor of the hands, which is a hallmark of an advanced disease stage. Ataxic tandem gait was indistinguishable from the gait disorder of CD, and thus the present data are further evidence for a dysfunction of the cerebellum or cerebellar outflow tracts in ET.

The gait disorder of ET

Anecdotal reports have already pointed out a small number of patients with ET exhibiting a gait disorder. This gait disorder has been described as bizarre and grotesque (Hornabrook and Nagurney, 1976) or ataxic (Critchley, 1972). Some of these early descriptions may be due to extreme manifestations of the gait disorder that we have shown here. Critchley (Critchley, 1949) has speculated that these cases may be due to a 'forme fruste' of an 'olivopontocerebellar atrophy' or a 'different kind of disease' (Critchley, 1972). Further evidence that the tandem gait of patients with ET is abnormal was provided by two clinical studies demonstrating abnormal tandem gait (Singer *et al*., 1994; Hubble *et al*., 1997) in almost 50% of the patients with ET.

Our study demonstrates that this gait disorder is more than an incidental finding and affects patients who suffer from an extreme variant of a subclinically frequent symptom of advanced ET. The following clinical clues help to identify these patients during tandem gait: (i) they have more than three mis-steps per minute, (ii) an enlarged step width and (iii) often show ataxic deviations of the feet during tandem gait; moreover, (iv) clinical analysis of their hand tremor often demonstrates intention tremor and the tremor-related disability of these patients is often severe. These observations may be of special interest for everyday clinical practice because whenever patients present with a more severe intention tremor or gait abnormalities, the diagnosis of ET is questioned and, in addition, further neurological tests are often undertaken unnecessarily. We propose including these features as part of the syndrome of more advanced ET.

Pathophysiological implications

These observations have some interesting pathophysiological implications. Our findings demonstrate that the gait disorder

of ET is indistinguishable from that of mild CD or lesions in the cerebellar outflow tracts (Victor *et al*., 1959; Hallett *et al*., 1991; Bastian and Thach, 1995; Diener and Nutt, 1997) because our control group of patients with CD showed the same type of abnormalities. Three abnormal features are considered to be typical for cerebellar gait. The first is a broad-based gait (Gilman, 1997). Although this could not be shown during normal walking in a recent study (Palliyath *et al*., 1998), we have shown this feature both for the patients with CD and for patients with ET during normal locomotion and tandem gait. Secondly, ataxic gait is defined as a disturbance of constant force and velocity execution resulting in a decomposition of movement (Nutt *et al*., 1993; Bastian and Thach 1995; Gilman, 1997; Rand *et al*., 1998). Such decomposed movements can be observed well in the original footpaths during the gait cycle in both CD and ET of our study during tandem gait (Fig. 2) and are underlined by the quantitative measurements of balance-related gait parameters (Fig. 3). Thirdly, dysmetria is considered a typical feature of cerebellar movement disorders both in experimental animal models following cooling of the paravermal zone (Udo *et al*., 1976) and in patients (Hallett *et al*., 1991; Diener and Nutt, 1997; Gilman, 1997). Overshooting leg movements are shown in the original traces of our gait study and have been identified by the ataxia ratio in the *x*, *y* and *z* direction for both CD and ET. The number of mis-steps may clinically reflect dysmetria, although poor balance leads to the same phenomenon.

For patients with ET, the question may arise as to whether inaccuracy of stepping is due simply to an intention tremor of the legs during stepping. Several observations dispute this hypothesis. First, the original traces show dysmetric movements with overshooting paths rather than a rhythmic tremor. Secondly, even patients without intention tremor of the legs exhibited decomposed ataxic leg movements. The most important argument against a simple effect of leg intention tremor is the lack of correlation between any of the critical gait parameters for the cerebellar gait disorder and the presence and severity of intention (or postural) tremor of the legs. In contrast, close correlations were found for the intention tremor of the arms and both step width and mis-steps. We interpret this finding to be a reflection of the severity of the disease.

These observations are in line with earlier studies from our group demonstrating cerebellar abnormalities in the upper extremity in ET (Bastian and Thach, 1995; Deuschl *et al*., 2000). We showed that almost half of the patients with ET have intention tremor as a classical sign of cerebellar tremor, overshoot of voluntary movements and slowness of movements. All these features are seen classically in CD. (Hallett and Dubinsky, 1993; Wills *et al*., 1994; Boecker and Brooks, 1998). Another observation relevant for the present question was the finding of a cerebellar-like abnormality of ballistic movements in ET (Britton *et al*., 1994), demonstrating a delay of the second agonist in the triphasic muscle activation underlying such fast goal-directed movements. The present results therefore uncover similar abnormalities in an extremity that is usually not involved in tremor of ET and further underline the independence of the tremor-dependent movement disorder and a further cerebellar dysfunction in ET. Although, it has also been demonstrated that lesions in the ventrolateral thalamus, a region which is a strong projection of the cerebellar outflow tracts, lead to uncoordinated movements of the hand (Bastian and Thach, 1995), in the same paper, overshooting and dysmetric movements have been demonstrated only in patients with a lesion in the lateral cerebellum (including the dentate nucleus). However, we cannot exclude that a functional disturbance not only within the cerebellum, but also of its target region may cause the condition of a disturbed tandem gait.

How can such an obvious cerebellar-like disorder in patients with ET be interpreted? Converging evidence favours the idea that ET originates within the olivo-cerebellar circuit. For the harmaline model of ET, animal studies have shown the inferior olive to be the source of oscillating activity that subsequently is distributed through the cerebellum via brainstem nuclei to the spinal cord (Elble, 1998; Wilms *et al*., 1999). Clinical studies have demonstrated a disappearance of ET following localized lesions of the cerebellum and pontine nuclei (Nagaratnam and Kalasabail, 1997), and PET studies have demonstrated the cerebellum to be hyperactive in ET. A plausible explanation for our findings is that such rhythmic activity of the cerebellum affects the normal function of cerebellar feed-forward functions that are necessary to execute a smooth and regular movement. Although these studies have now established a cerebellar-like deficit in ET, they open up some new questions. We do not know whether these abnormalities are present only as long as the tremor persists or whether they are permanent. Studies before and after medical or surgical treatment may answer this question. It is also unknown whether such cerebellar-like abnormalities also extend into the vestibulo-cerebellar system. In our clinical experience, the absence of oculomotor disturbances is an indicator that distinguishes the cerebellar disorder of ET from primary CD. However, this does not exclude the possibility that systematic oculomotor studies may uncover subtle disturbances in these patients.

In conclusion, we have demonstrated a typical gait disturbance of ET that can be demonstrated clinically during normal neurological exam. More than three mis-steps per minute is abnormal. Thus, tandem gait is the relevant clinical test to uncover this disturbance. As the abnormality must be related to cerebellar function including the cerebellar outflow pathways, this is further evidence that the cerebellum and/or pathways and structures which are connected with the cerebellum are critically involved in the generation of ET. This approach opens a new line of integrative studies in patients with ET, hopefully leading to a better understanding of this mysterious movement disorder.

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