Computerised analysis of writing and drawing by essential tremor phenotype

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ABSTRACT

We investigated whether computerised analysis of writing and drawing could discriminate essential tremor (ET) phenotypes according to the 2018 Consensus Statement on the Classification of Tremors. The Consensus scheme emphasises soft additional findings, mainly motor, that do not suffice to diagnose another tremor syndrome. Ten men and nine women were classified by blinded assessors according to Consensus Axis 1 definitions of ET and ET plus. Blinded scoring of tremor severity and alternating limb movement was also conducted. Twenty healthy participants acted as controls. Four writing and three drawing tasks were performed on a Wacom Intuos Pro Large digital tablet with a pressure-sensor mounted ink pen. Sixty-seven computerised measurements were obtained, comprising static (dimensional and temporal), kinematic and pen pressure features. The mean age of ET participants was 67.2±13.0 years and mean tremor duration was 21.7±19.0 years. Six were classified as ET, five had one plus feature and eight had two plus features. The computerised analysis could predict the presence and number of ET plus features. Measures of acceleration and variation of pen pressure performed strongly to separate ET phenotypes (p<0.05). Plus features were associated with higher scores on the Fahn-Tolosa-Marin Tremor Rating Scale (p=0.001) and it appeared that ET groups were mainly being separated according to severity of tremor and by compensatory manoeuvres used by participants with more severe tremor. There were, in addition, a small number of negative kinematic correlations suggesting some slowness with ET plus. Abnormal repetitive limb movement was also correlated with tremor severity (R=0.57) by clinical grading. Critics of the Consensus Statement have drawn attention to weaknesses of the ET plus concept in relation to duration and severity of ET. This classification of ET may be too biased towards tremor severity to assist in distinguishing underlying biological differences by clinical measurement.

INTRODUCTION

The concepts of syndrome and disease have long traditions as constructs of medical knowledge. Syndromes, delineated by phenomenology and pattern recognition, reflect the clinical features of a disorder. Disease entities are more likely to be informed by underlying aetiology or pathological mechanism. In the recent Consensus Statement on the Classification of Tremors, the Task Force on Tremor of the International Parkinson and Movement Disorder Society approached the problem of redefining essential tremor (ET) by separating syndromic (Axis 1) and disease (Axis 2) characters.[1] This recognises the possibility that a tremor syndrome such as ET has more than one aetiology and that a single aetiology produces several tremor syndromes. The scheme also attempts to address problems with previous classifications of ET.[2–4] Clinicians vary in their conception of ET, particularly as to what minor neurological abnormalities in addition to tremor are compatible with the diagnosis. The Consensus Statement should help to reduce grey areas with other disorders such as dystonic tremor[5] and tremor-dominant Parkinson's disease (PD).[6]

One important feature of the syndromic Axis 1 is the subclassification of the disorder into ET and ET plus. The additional plus criteria encompass patients who meet the basic ET definition but have, in addition, soft findings such as impaired tandem gait, questionable dystonic posturing, memory impairment or other mild neurological signs that do not suffice to diagnose another syndrome.[1] These distinctions may be relevant to impairments of motor control that seem to be present in some cases of ET. There is evidence for slowing of movement that, to a degree, resembles bradykinesia.[7–11] Some ET patients have signs of cerebellar dysfunction.[12] A challenge for the clinician is to discriminate soft additional motor findings on goal-directed or repetitive movement from the effects of the tremor itself.

The Consensus classification promotes more detailed phenotyping to try to unravel the aetiology of ET syndromes. Identifying ET plus features and understanding their significance to disease character is central to this aspiration of the Consensus scheme.

Writing and drawing are complex 'overlearned' activities that emphasise upper limb action tremor. In the clinic, pen and paper tests are useful in the diagnosis and monitoring of ET.[13] We will analyse a range of computerised measurements of writing and drawing tasks in ET. The aim is to look for correlations with the new Consensus Axis 1 classifications and with the minor motor accompaniments of ET syndromes.

METHODS

Ten men and nine women diagnosed with ET were recruited from the movement disorders service at Monash Health. Their mean age was 67.2±13.0 years and the mean duration of tremor symptoms was 21.7±19.0 years. All complied with the Axis 1 definition of ET in the 2018 Consensus Statement on the Classification of Tremors.[1] No subject met any of the Axis 1 exclusion criteria for ET and ET plus. Overall, 20 healthy participants (9 men and 11 women) acted as controls for the writing and drawing tasks. Their mean age was 64.3±12.0 years. A structured interview of ET subjects concentrated on clinical aspects of the tremor disorder. Scoring on the Fahn-Tolosa-Marin Tremor Rating Scale (FTM) was performed.[14] Patients were scored on items 3.4–3.8 of the Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS-III) to give a measure of impairment of limb repetitive movement.[15] A Montreal Cognitive Assessment (MoCA) was also conducted.[16]

Two movement disorders neurologists who were blinded to clinical information scored the FTM and MDS-UPDRS-III 3.4–3.8 from videotapes. Mean total scores were obtained for each subject. The blinded assessors were also provided with a summary of the structured clinical interview, the MoCA results and videotapes of goal-directed limb coordination and gait (normal and tandem). They then classified the ET disorder as defined in Axis 1 of the Consensus Statement. The Statement accepts that the identification of ET plus soft signs is subjective. Patients were classified as ET plus by the presence of any of the following features: impaired tandem gait, questionable dystonic posturing, memory impairment, mildly impaired goal-directed coordination of unknown significance, mildly impaired rapid alternating movement of unknown significance and tremor at rest. For each participant, a neurologist familiar with the case also phenotyped the tremor disorder from the videotape. A majority classification was then obtained on the presence or absence of plus features and on the number of plus features documented.

Patient and public involvement

Patients were first involved in this research when recruited though their treating neurologist and were not engaged in study development or design. Each participant assessed the burden of time and inconvenience associated with this research from material presented in the participant information and consent form. Participants will be informed of the outcome of the research, including scientific publications resulting from it, according to the terms of institutional research ethics committee approvals.

Digital tablet tasks

Participants were recorded while writing and drawing on a digital tablet (Wacom Intuos Pro Large, A3 sized) with a pressure-sensor mounted ink pen. The tablet was overlaid with a sheet of paper to normalise the experience as much as possible. The tablet was set on a standard height desk, positioned as was most comfortable to each participant. The following tasks were performed:
1. Writing the letter 'e' in series across a line.
2. Writing the letters 'bd' in series across a line.
3. Writing a standard sentence.
4. Usual written signature.
5. Drawing an Archimedes spiral
   a. In clockwise direction.
   b. In anti-clockwise direction.
6. Drawing two horizontal and two vertical lines.

When drawing, participants were asked to avoid touching the paper overlying the tablet surface with any part of their hand or arm. They were allowed to hold and use the ink pen in their customary manner for the writing tasks.

Data acquisition

Customised software was developed in c#, which was then integrated into the tablet to record the pen trajectories (x, y) and pen tip pressure on the tablet surface. The data were recorded at a sampling rate of 133 Hz, analysed in real-time using the customised software and stored as csv files.

Data preprocessing

The data were segmented using the pen tip pressure to separate movement on and above the tablet. Pen movements with pressure=0 were labelled as 'in-air' strokes; an 'on-tablet' stroke was any movement while pressure was >0. The data series for each task began at the start of the first on-tablet stroke and finished with the end of the final one. To remove the outlying data and noise caused by accidental touch of pen or hand on the tablet, two other preprocessing steps were conducted:

Step 1. The total length d of each segment was calculated as follows:

$$d = \sum_i^M \sqrt{(x_i - x_0)^2 + (y_i - y_0)^2}$$

where N is the total number of samples in a task; $i = 1$ for the starting segment; $i = N - 99$ for the ending segment and $M = i + 99$.

Segments of length $d < 2$ mm were considered as noise and discarded. This step was applied only to drawing tasks.

Step 2. To address accidental contact of the wrist or palm on the tablet, median filtering was applied. If the distance between two adjacent points was five times greater than the median value of the distances between

Table 1 Inventory of 67 computed features for writing and drawing

Feature type (units)	Feature abbreviation	Feature description	Feature dimension
Static features			
Dimensional (mm)	avgStrLenAir, medStrLenAir, maxStrLenAir, minStrLenAir, stdStrLenAir, iqrStrLenAir, avgStrLen, medStrLen, maxStrLen, minStrLen, stdStrLen, iqrStrLen	Average, median, maximum, minimum, SD and IQR of pen stroke length in air and on tablet surface.	$6 \times 2 = 12$
Temporal (s)	inAirT, onSurT, totalT, ratioAirtoSurT, satPreDur, noPause	Time in air; time on tablet surface; total time; ratio of air-to-surface time; duration with saturated pressure; number of pauses.	6
Kinematic features			
Velocity (mm·s^{-1})	avgVx, medVx, maxVx, stdVx, avgVy, medVy, maxVy, stdVy, ratioVxVy	Average, median, maximum and SD of pen tip velocity in x and y directions; ratio of pen tip median velocity in x and y.	$4 \times 2 + 1 = 9$
Acceleration (mm·s^{-2})	avgAx, medAx, maxAx, stdAx, avgAy, medAy, maxAy, stdAy, ratioAxAy	Average, median, maximum and SD of pen tip acceleration in x and y directions; ratio of median acceleration in x and y.	$4 \times 2 + 1 = 9$
Jerkiness (mm·s^{-3})	avgJx, medJx, maxJx, stdJx, avgJy, medJy, maxJy, stdJy, ratioJxJy	Average, median, maximum and SD of pen tip jerk in x and y directions; ratio of median jerk in x and y.	$4 \times 2 + 1 = 9$
Linear speed (mm·s^{-1})	avgS, medS, maxS, stdS	Average, median, maximum and SD of pen tip speed.	4
Angular speed (rad·s^{-1})	avgAngS, medAngS, maxAngS, stdAngS	Average, median, maximum and SD of pen tip angular speed.	4
Direction changes	Dx, Dy, Dxy, diffDxy	Total number of direction changes in x direction, y direction and both x and y directions; absolute differences in direction changes in either x or y.	4
Pen pressure features			
Pressure	avgP, medP, stdP, skewP, kurtP	Average, median and SD of pen tip pressure applied on the tablet surface; skewness and kurtosis of pressure.	5
Pressure differences	avgDiffP, medDiffP, stdDiffP, skewDiffP, kurtDiffP	Average, median and SD of pen tip pressure difference applied on the tablet surface; skewness and kurtosis of pressure difference.	5

the previous five adjacent points, this was considered an accidental touch and removed from the time series.

Feature extraction from writing and drawing tasks

Sixty-seven features were computed from the handwriting and drawing tasks. They are shown in table 1, divided into three sets: 18 static features (linear and time measures of strokes on and above the tablet surface); 39 kinematic features and 10 pen pressure features.

Statistical methods

The Shapiro-Wilk test for normal distribution of data was applied. The parametric one-way analysis of variance or non-parametric Kruskal-Wallis method was employed, as appropriate, to identify statistical significance. All p values were calculated using a multivariate model. The importance of computed features of writing and drawing was ranked based on Spearman correlation coefficient. A Pearson correlation coefficient was obtained for the two clinical motor rating scales. All computation, including statistical analysis, was performed using Matlab 2018b (MathWorks).

RESULTS

Thirteen subjects were classified as ET plus. Five had one plus feature (ET+1) and eight had two plus features (ET+2). Six subjects fulfilled the Consensus Axis 1 definition of ET, henceforth abbreviated as ET-0. These three groupings were used for the analysis of computerised features. The most common plus feature was rest tremor, in 10 subjects. Others were present as follows: minor motor signs (limb movement or gait), four; memory impairment, four and questionable dystonic posturing, three. All ET+2 subjects had rest tremor. Demographic and clinical details according to Axis 1 subtyping appear in table 2.

The ET plus groupings were, on average, 6 years older than ET-0. While this was not statistically significant, the ET+2 group had the highest mean age. Tremor duration showed no particular trend. The presence and number of ET plus features was associated with significantly higher FTM scores. MoCA scores showed similar distribution across the groups. Clinical scale results by ET phenotype are shown in figure 1.

Table 2 Demographic and clinical features according to Consensus Axis 1 definitions

	Control	ET-0	ET+1	ET+2	P value
Number	20	6	5	8	–
M:F	9:11	3:3	1:4	6:2	–
Age	64.3±12.0	62.8±16.5	61.4±11.6	74.0±8.5	0.191*
Age at tremor onset	–	37.7±18.5	51.2±13.1	46.3±22.4	0.505*
Tremor duration	–	25.2±23.2	10.2±5.8	26.4±19.7	0.300*
FTM score	–	16.0±9.2	20.4±3.8	39.8±13.1	**0.001***
MDS-UPDRS-III 3.4–3.8	–	1.0±1.6	2.5±4.8	4.4±4.0	0.063†
MoCA	–	25.8±4.2	25.2±3.3	24.5±3.6	0.80*

Values shown as mean±SD.
*By one-way analysis of variance.
†By Kruskal-Wallis.
FTM, Fahn-Tolosa-Marin Tremor Rating Scale; MDS-UPDRS-III, Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part III; MoCA, Montreal Cognitive Assessment.

Discriminating features for ET phenotype

This analysis is shown in table 3. Data from the 67 computerised measurements were not normally distributed and p values were derived by Kruskal-Wallis test. Drawing tasks were more effective in discriminating ET subgroups than writing. Drawing vertical and horizontal lines (Task 6) provided the strongest set of features to differentiate ET phenotype, followed by clockwise spiral drawing (Task 5a).

The analysis for drawing highlighted features related to acceleration and, especially with clockwise spirals, to variation of pen pressure (avgDiffP). For line drawing (Task 6), maximum angular speed and maximum jerk are only capable of differentiating ET+2 from the other ET groups, but not ET-0 from ET+1. Maximum angular speed and

maximum jerk were the only kinematic features that were negatively correlated with the presence of plus features.

In general, p values were less significant for the writing tasks. Most features for writing listed in table 3 fell into either static or acceleration-related kinematic categories.

ET versus controls

The features that best discriminated controls from the ET group as a whole concerned direction change and acceleration (table 4). Directional change measures ranked highest for each of the drawing tasks. Writing Task 3 showed one kinematic feature—median angular speed— that was negatively correlated with having ET.

Effect of tremor severity

Analysed by FTM tremor severity without regard to ET phenotype, the following patterns were seen (table 5). Drawing tasks had stronger correlations than writing tasks. Acceleration and direction change measures made up the majority of the highly correlated drawing parameters. Median acceleration performed best for each drawing task. For the writing tasks, static and pressure measurements had greater representation.

Effect of impaired repetitive movement

The aggregate MDS-UPDRS-III repetitive limb movement subscores 3.4–3.8 addressed perceived slowness of movement in ET. Overall, these motor disability scores were modest. A trend towards higher score in ET+2 was present (table 2).

Again, drawing had stronger correlation coefficients than writing (see table 6). Acceleration and direction change measures gave strong positive correlations with the MDS-UPDRS-III subscores, particularly for drawing. Static and pressure-related measures were well represented in writing, but with generally weaker correlations. Only when writing a standard sentence (Task 3) did MDS-UPDRS-III subscores correlate negatively with kinematic parameters for *y* direction and angular movement.
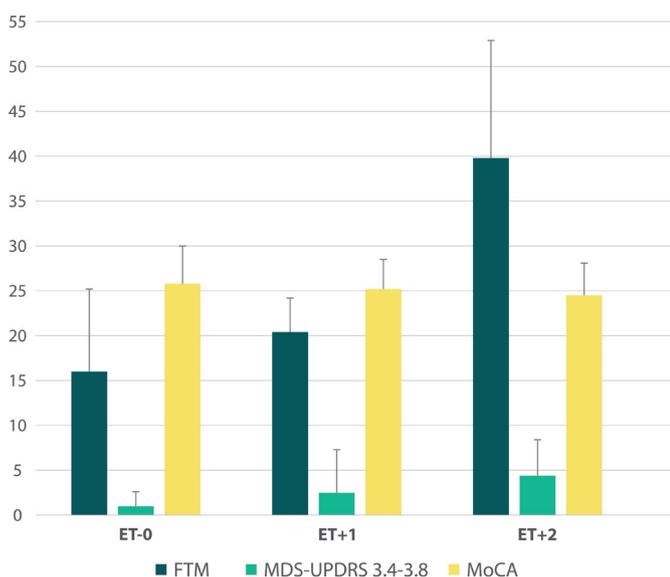

Figure 1 Clinical scale results by ET phenotype. Mean and SD shown by column height and error bars. ET, essential tremor; FTM, Fahn-Tolosa-Marin; MDS-UPDRS-III, Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part III, MoCA, Montreal Cognitive Assessment.

Table 3 Discriminative features for each task by ET phenotype

Task	Feature	Control (median±SD)	ET-0 (median±SD)	ET+1 (median±SD)	ET+2 (median±SD)	P value	Spearman correlation coefficient
Writing tasks							
1	stdStrLen	13.35±26.3	21.01±120	41.15±29.15	70.62±57.71	0.078*	0.51
	avgStrLenAir	83.77±35.47	99.18±63.96	76.75±18.41	128.08±37.9	0.077*	0.35
2	totalT	6.2±0.42	6.33±0.24	6.14±0.19	6.58±0.21	**0.01***	0.39
	ratioAxAy	1±0.21	0.90±0.14	0.66±0.25	1.41±0.62	**0.03***	0.46
3	avgDiffP	620.3±274.71	639.4±275.25	686±190.2	440±135.17	0.06*	−0.34
	ratioAirSurT	0.67±0.37	0.58±0.38	0.78±0.25	0.51±0.17	0.07*	−0.25
4	medAx	1±0.62	0.5±0.18	0.5±0.22	1±0.92	**0.03***	0.59
	avgAx	2.5±4.3	1.39±0.6	1.23±3.7	2.87±7.44	0.053*	0.55
Drawing tasks							
5a	avgDiffP	93.92±40.71	88.22±35.65	159.32±25.56	171.05±155.51	**0.018***	0.60
	skewDiffP	18.86±7.23	17.80±4.37	10.35±6.12	8.72±6.57	**0.030***	−0.56
5b	medAx	0.25±0.07	0.25±0.20	0.50±0.11	0.875±1.92	**0.042***	0.58
	Dxy	33.5±16.49	39±104.11	120±55.41	176.50±206.5	0.068*	0.54
6	medVx	4.75±1.24	3.25±3.80	6±4.07	16.25±15.31	**0.013***	0.66
	maxAngS	21.17±28.0	21.15±9.44	22.01±8.73	16.76±59.76	**0.016***	−0.54
	minStrLenAir	82.50±41.65	103.50±54.12	9±48.59	7.50±30.45	**0.017***	−0.65
	maxJx	50.08±86.2	50.26±22.0	50.19±19.9	39.29±170.2	**0.018***	−0.56

All features with p<0.05 are shown, otherwise the two features with lowest p values for each task. The p values and Spearman correlation coefficients were calculated for ET-0, ET+1 and ET+2.
*By Kruskal-Wallis.
ET, essential tremor.

There was a correlation (R=0.57) between the MDS-UPDRS-III subscores and FTM tremor severity (figure 2).

DISCUSSION

Our computerised analysis of standard writing and drawing activities was able to predict the presence and number of ET plus features. The statistical differences varied across study tasks. According to both p values and Spearman correlation, drawing—both of Archimedes spirals and of straight lines—proved more discriminative than writing. Kinematic measures reflecting acceleration and velocity were increased in the presence of ET plus features, while pen pressure was more variable. Compared with drawing, the writing tasks emphasised static measures. Most features listed in table 3 showed positive correlation with ET plus classifications, but two negative kinematic correlations—maximum angular speed and maximum jerk (the rate of acceleration change with respect to time)—provide some evidence of 'slowness' in ET+2.

The 67 features obtained from the computerised writing tablet record dimensional, kinematic and pressure measurements in relation to the pen tip. Virtually all facets of this skilled motor activity are captured by the technology. The challenge then is to interpret significant changes in individual features and in combinations of features, to understand how the clinical state of ET

Table 4 Most discriminative features by Spearman rank order correlation coefficient (in brackets) to differentiate ET from age-matched controls

Rank of features	Task 1	Task 2	Task 3	Task 4	Task 5a	Task 5b	Task 6
1	stdStrLen (0.48)	Dx (0.38)	kurtP (0.47)	maxStrLenAir (0.48)	Dxy (0.60)	Dx (0.63)	Dxy (0.64)
2	iqrStrLen (0.47)	maxStrLen (0.37)	skewP (−0.42)	Dxy (0.45)	Dx (0.60)	medAx (0.61)	medAx (0.63)
3	Dxy (0.39)	minStrLen (0.37)	medAngS (−0.37)	Dx (0.44)	medAx (0.58)	Dxy (0.60)	Dy (0.62)

Table 5 Spearman correlation analysis of raw FTM tremor score: top five computerised features for each task

Writing tasks							
Features Task 1	Spearman correlation coefficient	Features Task 2	Spearman correlation coefficient	Features Task 3	Spearman correlation coefficient	Features Task 4	Spearman correlation coefficient
stdStrLen	0.58	satPreDur	0.50	kurtP	0.46	Dxy	0.55
iqrStrLen	0.56	maxStrLen	0.49	ratioAxAy	0.45	Dx	0.53
maxStrLen	0.52	minStrLen	0.49	medStrLen	0.45	Dy	0.51
minStrLen	0.52	Dx	0.49	skewP	−0.44	maxStrLenAir	0.50
medStrLen	0.49	ratioJxJy	0.49	Dx	0.43	inAirTime	0.49

Drawing tasks					
Features Task 5a	Spearman correlation coefficient	Features Task 5b	Spearman correlation coefficient	Features Task 6	Spearman correlation coefficient
medAx	0.75	medAx	0.75	medAx	0.82
Dxy	0.73	Dxy	0.73	medAy	0.77
Dx	0.72	Dy	0.72	Dxy	0.70
Dy	0.71	Dx	0.71	Dy	0.68
medAy	0.68	medAy	0.65	medJy	0.64

disturbs the fine motor control involved in writing and drawing. Three different effects could be in play. First, the kinematic measurements record oscillations during pen strokes that correspond to the tremor itself. Second, individuals with ET adopt compensatory strategies to minimise loss of accuracy and legibility. Third, motor deficits that are independent of tremor could impair pen control. This includes minor degrees of dystonia, though questionable dystonic posturing was identified in only three subjects. By considering the features that separate ET from control pencraft and that correlate with FTM tremor severity, some conclusions about the influence of ET can be made.

Tremor oscillations consist of cycles of acceleration and deceleration with periodic changes in direction. A clear-cut finding is the number of positively correlated directional change and acceleration features. These were prominent in line and spiral drawing, both to

Table 6 Spearman correlation analysis of MDS-UPDRS-III limb bradykinesia score: top five computerised features for each task

Writing tasks							
Features Task 1	Spearman correlation coefficient	Features Task 2	Spearman correlation coefficient	Features Task 3	Spearman correlation coefficient	Features Task 4	Spearman correlation coefficient
iqrStrLen	0.58	satPreDur	0.64	ratioAxAy	0.50	Dxy	0.56
stdStrLen	0.54	ratioJxJy	0.55	Dx	0.44	Dx	0.53
Dxy	0.49	Dx	0.49	medAy	−0.40	Dy	0.52
Dy	0.47	maxStrLen	0.48	medAngS	−0.40	maxStrLenAir	0.51
Dx	0.45	minStrLen	0.48	Dxy	0.39	totalT	0.49

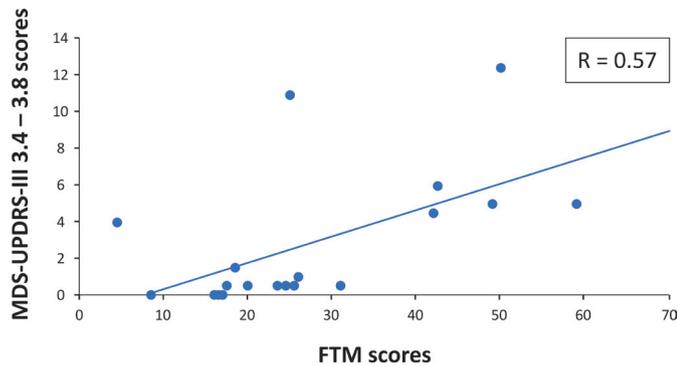|					
Drawing tasks					
Features Task 5a	Spearman correlation coefficient	Features Task 5b	Spearman correlation coefficient	Features Task 6	Spearman correlation coefficient
medAx	0.79	medAx	0.80	medAx	0.80
avgAx	0.66	Dx	0.68	medAy	0.71
medAy	0.64	medAy	0.67	medVx	0.65
Dx	0.63	Dxy	0.65	medVy	0.60
avgJy	0.63	Dy	0.62	Dxy	0.58

Figure 2 Tremor severity (FTM score) versus repetitive limb movement (MDS-UPDRS-III 3.4–3.8 score). FTM, Fahn-Tolosa-Marin Tremor Rating Scale; MDS-UPDRS-III, Movement Disorder Society-Unified Parkinson's Disease Rating Scale Part III.

separate ET from control data and as markers of ET severity. While the drawing tasks have long, continuous pen strokes, static features give more information about the up-and-down pen activity of writing. In ET, stroke length on the tablet when writing is somewhat higher (maxStrLen, minStrLen) and also more variable (stdStrLen, iqrStrLen). The same measurements show correlation with FTM score. It is not clear whether this represents an intrinsic change in motor control or is compensatory. Increased and more variable stroke length in the air and time in the air were significant findings in the signature Task 4, which is, for most people, their most overlearned writing action. ET patients, when they sign their name, spend more time hovering above the tablet. Finally, ET participants tended to use abnormal pen pressures. This was more apparent with writing than drawing tasks and was emphasised by the analysis for tremor severity. For Task 2, which required repetitive writing of 'bd', ET patients with greater FTM scores have constant high pressure (satPreDur), while findings in other writing tasks suggest that pressure may also be more variable. It seems likely that both the hovering behaviour with signature and the application pen pressures represent compensatory strategies to improve the accuracy of penmanship.

It is important to consider clinical differences between ET-0 and ET plus participants when interpreting these results. Those classified as ET plus were a little older than the ET-0 group, though mean tremor duration was actually greater for those without plus features. The difference in tremor severity between ET-0 and ET+1 was small, but ET+2 patients had FTM scores almost twice as great as either of the other subgroupings. While all ET+2 patients had rest tremor as a plus feature, additional scoring for the rest tremor amounted to less than 10% of their total FTM score; most of the difference was in other aspects of the scale, reflecting severity and distribution of non-resting tremor, and tremor-related disability. In previous research, the presence of rest tremor in ET has been correlated with duration and

severity of tremor.[17] The range of discriminative features for ET subtype showed some differences as well as similarities with those that separated ET from controls and which correlated with raw tremor severity. Pressure-related features became more sensitive to subtype in drawing. Static features were prominent with writing, with a suggestion of 'hovering' (more pen in-air time) in other writing tasks. The discriminative powers of direction change and acceleration measures, as discussed above, are probably linked to degree of tremor. It appeared that ET-0, ET+1 and ET+2 were mainly being separated according to the severity of tremor and by compensatory manoeuvres used by participants with more severe tremor. The question of slowness in ET plus, suggested by a small number of negative kinematic correlations, needs further examination.

An implication of the Axis 1 Consensus classification of ET is that 'minor motor' findings, which compose most of the list of plus features, may be relevant to aetiology and pathophysiology. A kinematic study of ballistic movement showed both slowness and overshoot in ET.[12] The abnormalities were greater in the presence of intention tremor, defined as tremor which increases towards the goal of an action. These findings were interpreted as indicating cerebellar dysfunction in ET. A number of studies have found that rapid alternating movements are performed abnormally slowly in ET.[8–10] In addition, the rhythmicity of repetitive hand movements is impaired.[11] While ET lacks a consistent pathological lesion, there are possible clinicopathological correlations of these motor deficits. The more common finding is a 'cerebellar ET' pattern—alterations in Purkinje cell axons and dendrites, including torpedo inclusions in proximal axons.[18] Loss of Purkinje cells, suggested by some[18 19] but not other studies,[20] is more contentious. Then there are a minority of ET brains in which brainstem Lewy bodies are present.[19 21] The neuropathology of ET is consistent with the heterogeneity of the ET syndrome and could explain impaired motor control.

There is, however, uncertainty about whether impairment of movement is truly independent of tremulous oscillations. That ET affects the fluency and rhythm of voluntary actions can easily enough be observed in the clinic. Slowness of movement in ET has, in some studies, been comparable in degree to the bradykinesia of early PD,[7 9] but there are important differences. Patients with ET generate normal movement amplitudes, without the pervasive underscaling of motor commands that occurs in PD.[8] Furthermore, a sequence effect—repetitive movements becoming smaller or slower—is not present in ET.[10] Some researchers have found slowness and irregularity of repetitive action in ET that is not fully accounted for by tremor.[10 11] Others, though, argue that slowness results from tremor, with signal-to-noise interference with movement above a certain threshold of tremor severity.[8] We tried to explore the relationship of slowness to ET phenotype by using the repetitive

limb movement subscores of the MDS-UPDRS-III as an independent yardstick. Although designed to measure parkinsonian bradykinesia, these scales evaluate speed, rhythm, amplitude and decrement together and do not insist on the strict Queen Square Brain Bank definition of bradykinesia (progressive reduction in speed and amplitude of repetitive actions).[22 23] Our impression was that the MDS-UPDRS subscores were mainly accrued from hesitations and loss of rhythm. Taking them as a representation of the disturbance of alternating movement that attends ET, we found limited evidence of 'slowness'. The writing of a full sentence (Task 5) showed negative correlations between MDS-UPDRS-III subscores and kinematic parameters for y direction and angular movement. Otherwise, kinematic parameters for acceleration, velocity and direction change mostly correlated positively with the MDS-UPDRS-III subscores, consistent with tremor effects. It is possible that measures of jerkiness (for instance, increased average pen tip jerk in the y direction for clockwise spirals) capture hesitancy and dysrhythmia in repetitive movement. A nexus between clinical measures of impaired repetitive movement and tremor severity was present. The positive correlation between MDS-UPDRS-III and FTM scores is illustrated by figure 2. As can be seen in figure 1, scores on both clinical scales increase in the presence of ET plus features.

We found significant differences between Axis 1 categories of ET as set out in the recent Consensus Statement on the Classification of Tremor. Many of the changes in writing and drawing relate to the severity of the tremor itself and to strategies employed to ameliorate its effects. The point should be made that these findings all relate to complex writing and drawing tasks and are not necessarily generalisable to other upper limb movement. While the Consensus definition of plus features emphasises soft motor signs, it also encompasses non-motor findings such as memory impairment, which may have created some heterogeneity in the motor performance of our ET plus groups.

The Consensus scheme seeks to facilitate the identification of biomarkers by deeper phenotyping of ET, enabling the discovery of specific etiologies. We found that this objective may be impeded by associations with tremor severity—for ET plus and for impaired repetitive movement in ET. Based on blinded classification, we found that ET plus subjects had higher FTM scores, particularly if two plus features were present. The MDS-UPDRS-III subscores, which attempt to quantify 'mild neurological signs' associated with ET plus, also correlated with tremor severity. Critics of the Consensus Statement have drawn attention to inherent problems with the ET plus concept in relation to duration and severity of ET.[24] Kinetic tremor worsens with the passage of time[25 26] and patients accumulate additional clinical features.[27 28] These include tremor at rest[17 29] or with intention[27] and gait and balance difficulty.[27 29–31] A syndromic subdivision of ET according to the Consensus Statement may be too biased towards tremor severity to assist in distinguishing underlying biological differences by clinical measurement.

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