Assessing tremor severity

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Abstract

A clinical rating scale which measured the severity of tremor in 20 patients (12 with essential tremor and 8 with "dystonic" tremor) was assessed at specific anatomical sites for both inter and intra-rater reliability using four raters. The scores obtained with the scale were compared with the results of upper limb accelerometry, an activity of daily living self-questionnaire and estimates of the tremor induced impairment in writing and drawing specimens. The results show that, for the purposes of routine assessment and therapeutic trials, a clinical rating scale can produce reliable results which are a more valid index of tremor induced disability than standard postural accelerometry.

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During the last two decades there have been an increasing number of clinical trials evaluating the effect of drugs on tremor severity. In practice these trials have relied heavily on accelerometry as the objective method of measurement, and clinical rating systems and patient self-assessments as the subjective methods. The purpose of this study was to determine whether or not a clinical rating scale could be used reliably to evaluate the severity of tremor in patients with essential tremor and postural limb tremor associated with dystonia. Furthermore, the scores obtained by using the scale were compared with the results of upper limb accelerometry, two assessments of dominant hand function (handwriting and drawing a spiral) and a patient activity of daily living self-questionnaire.

The rating scale used is illustrated in Appendix 1 and was chosen after experimenting with various alternatives which established that clinicians found the combination of a "discrete step" verbal scale and a numerical (0–10) analogue scale helpful for scoring. It is slightly unusual in having more steps than most tremor rating scales,[1-8] but this tends to increase its precision and reliability.[9] As the number of scale steps increases, so does the difficulty of consistent judgement. However, by also decreasing the significance of a "unit" error, true score variance is altered advantageously for reliability.[10]

The scale relies on the examiners having some experience of movement disorders and

utilises a cognitive process whereby an observer ascribes a number to a phenomenon to indicate its degree of membership to a set. The technical term for this process is "fuzzy logic".[11] The scale differed from previous tremor rating scales not only in providing a broader gradation system,[1-8] but also by relating tremor magnitudes to different body parts,[1 4] including the head,[2 5] and in addition we avoided inclusion of measurements of disability and handicap within the scale.[1 4 5] To our knowledge the inter and intra-rater reliability of previous tremor rating scales and their validity as a measure of tremor induced disability have never been assessed formally. Similarly, the validity of standard accelerometry as a measure of tremor induced disability has not been documented.

The rating scale which we developed (Appendix 1) was subjected to validation against a disability self-questionnaire, accelerometry and scores for the degree of impairment seen in spirography and handwriting specimens, techniques commonly employed in clinical trials. The inter and intra-rater reliability of the rating scale and of the spirography and handwriting scores were then measured.

Patients

Twenty patients with postural tremor of their upper limbs were recruited from the clinic of the National Hospital for Neurology and Neurosurgery, Queen Square. Twelve patients were diagnosed as having pure essential tremor and eight had postural limb tremor in association with torticollis (dystonia). Ten of the patients had tremor of the lower limbs, 10 had head tremor (of whom 8 had torticollis) and in 6 a vocal tremor was detected. Ten were male and 10 female. Their average age was 64·5 years (range 26–82 years) and their mean duration of tremor 14·2 years (range 2–49 years). Nineteen were right handed and one, who wrote with the right hand, was ambidexterous. None of the patients had other significant illnesses and all the assessments were carried out without interrupting their medication. The patients were not aware of their scores.

Definitions

The various components of tremor were defined by an Ad Hoc committee of the Tremor Research Group [TRIG] in the following way.[12]

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1) Rest Tremor: tremor occurring when the muscles are not voluntarily activated and the relevant body part is completely supported against gravity.

2) Postural Tremor: tremor present while voluntarily maintaining a position against gravity.

3) Kinetic Tremor: tremor during any form of movement.

4) Intention Tremor: the pronounced exacerbation of kinetic tremor towards the end of a goal directed movement.

These definitions were familiar to the raters and were used in this study.

Methods

A) Validation of the Scale

Each patient was sent an "activities of daily living" (ADL) self-questionnaire to document the extent of their tremor induced disability. The questionnaire consisted of an inventory of 25 different activities of daily living and is based on that used in previous studies (Appendix 2).[13][14] Each patient was asked to circle the number (next to each item) which described most accurately how easy or difficult it was for them to perform the relevant activity. The sum of the scores for each item were then converted into percentages, with zero implying no disability and the higher the percentage the more disabled the patient.

Two weeks later the patients attended a grading clinic during which their tremors were independently rated by four doctors using our clinical rating scale. The severity of each patient's head, vocal, right upper limb, left upper limb, right lower limb and left lower limb tremors were scored separately (from 0–10) by each rater. For each anatomical site the components of tremor (rest, postural, kinetic and intention) were scored individually (see Appendix 1). During the grading clinic the patients had their tremors videotaped and their upper limb postural tremors measured by accelerometry. They were also asked to draw a spiral and give a specimen of their handwriting to one of the raters. To reduce any systematic bias the order of all these assessments was randomised. The spirals were drawn and handwriting done with the pen held normally and the wrist resting on the table and the patient seated.

Accelerometry

Accelerometry was performed on the pronated outstretched upper limbs, whilst the patients were sitting. Miniature piezo-resistive linear accelerometers (with vertical as the dimension of recording) were attached to the dorsal aspect of each hand in the second interspace, 1 cm proximal to the metacarpophalangeal joints. The devices weighed 6 g and had flat frequency responses from steady state acceleration to 300 Hz with a sensitivity of 50 m V/g (g = 9·81 m/s²). The postural tremor in each hand was then recorded for one minute. The accelerometer signals were amplified and analysed on-line, using a Hewlett Packard 5420 A signal analyser,[15] to produce an average of ten overlapping spectra which displayed the root mean square (rms) magnitude of the frequency components as a function of frequency. Measurements were taken for each hand of the frequency (Hz) of the dominant peak and of its magnitude scaled in rms acceleration, units of g (which were converted to m/s²).

Clinical Grading

The clinical grading of the various components of tremor was performed in the following way: the rest component of head tremor was assessed with the patients lying flat on a couch, with the head supported by pillows, and the postural component whilst the patients were sitting without head support looking straight ahead. The postural component of leg tremor was scored whilst each patient was sitting with the relevant leg extended and the rest component when the foot was placed on the floor. The upper limbs were, once again, assessed with the patients sitting. The rest component of tremor was scored whilst the arms were relaxed and totally supported in the patient's lap and the postural component whilst they were outstretched, with the hands pronated and fingers spread (as for accelerometry). The kinetic component was measured during the transit phase of the finger-nose test and the intention component as the subject's index finger approached a target (the tip of a patella hammer) placed at the limit of reach. Vocal tremor was scored by asking each patient to say their own name, address and birthday and to hold a note by singing "aah".

B) The Reliability of the Scale

The inter and intra-rater reliability of the scale was assessed using videotape of the patients seen in the assessment clinic and the same raters. Two video assessment sessions were carried out; the first (A) one month and the second (B) two months after the initial assessment in clinic. Once again the specific tremors were scored according to site and were subdivided into rest, postural, kinetic and intention components. However, during the video assessments the postural component of upper limb tremor was rated whilst the hands were held pronated in front of the patient's nose (but not quite touching) with the shoulders abducted to the horizontal.

No comparisons have been made between the clinic and video assessments because several difficulties have become apparent in estimating tremor severity from videotapes. Notably, most standard VHS video-recorders present the viewer with complete images at a rate of 25 Hz (alternate lines are changed at 50 Hz). Consequently, for a tremor with a frequency of 5 Hz, there are 5 picture frames per tremor cycle; whereas only 2·5 frames per tremor cycle occur if the frequency is 10 Hz. This produces a differential effect whereby more information is lost the faster the tremor frequency and thus there is a greater reduction in the apparent amplitudes of high

compared with low frequency tremors. The apparent amplitude of a tremor seen on a videoscreen also depends on the distance of the observers from the screen and the size of the images; which is influenced by the amount of zoom used by the cameraman.

Immediately after each video session the spirography specimens were ascribed scores independently by each rater. The spirals had been photocopied to provide four anonymous sets of twenty and within each set the order of the spirals had been randomised. Each rater ranked the twenty spirals from best (normal) to worst (most tremulous) and then ascribed each spiral a score from 0 (normal) to a possible maximum of 10 (extremely tremulous); although in practice 0–8 was the range of scores given. An identical procedure was used for rating the handwriting specimens which were again scored after each video session (A and B). The order in which the spirals and handwriting were assessed by each rater was also randomised.

The inter and intra-rater reliabilities of the assessments of each tremor component (rest, postural, kinetic and intention) at each anatomical site and the scores for spirography and handwriting were calculated using Cohen's Kappa coefficient.[16–18] This provides a measure of the degree of inter-observer agreement for pairs of observers assigning individual observations subjectively to one of a range of categories. Similarly, the intra-observer reliability (comparison of observations made by a single observer at two different times) can be measured. Kappa scores are conventionally interpreted as follows[17]:

Kappa Coefficient	Strength of Agreement
< 0	Poor
0–0·20	Slight
0·21–0·40	Fair
0·41–0·60	Moderate
0·61–0·80	Substantial
0·81–1·00	Almost perfect

The validity of the scale was assessed by measuring the correlation between the mean scores for the postural components of head (pHT), right upper limb (pRUL), left upper limb (pLUL), right lower limb (pRLL) and left lower limb (pLLL) tremors of the patients and their activity of daily living (ADL) scores, spirography and handwriting impairments and upper limb acceleration and

frequency. In our correlation (regression) analysis we used the mean of the raters' scores as recorded in the clinic and the mean of their first assessments of each patients spirography and handwriting impairments.

Results
Reliability
The inter and intra-rater reliabilities for the postural component of head and limb tremor, expressed as Cohen's Kappa coefficients, are illustrated in table 1. The rating scale proved to have good inter and intra-rater test-retest reliability for assessing the postural components of head and upper limb tremor, which are the principal sites affected by essential and "dystonic" tremor, and fair-moderate for lower limb postural tremor. However, the Kappa coefficients for the inter-rater reliability of vocal tremor assessments were poor-fair (Kappa values of −0·008–0·32). This was because of disagreement between the raters as to which of the patients had vocal tremor.

The inter-rater reliability of the assessments of spirography and handwriting impairment were 0·56–0·90 (moderate–almost perfect) and 0·31–0·83 (fair–almost perfect) respectively and the intra-rater reliability was 0·58–0·91 (moderate–almost perfect) for handwriting and 0·36–0·88 (fair–almost perfect) for spirography. The raters had great difficulty in applying the terms kinetic and intention tremor to real life observations, in spite of having previously agreed on these definitions. For instance the Kappa values for the inter-rater reliability of right upper limb kinetic and intention tremor components were 0·02–0·65 (slight – substantial) and −0·03–0·54 (poor-moderate) respectively. This reflects the practical difficulty of defining the boundaries of an intention tremor when kinetic and postural components are also present. Consequently, during the second video assessment "intention" tremor was not scored and, by confining attention to recording the severity of the kinetic tremor seen midway through a movement, greater inter-rater agreement was obtained; for example 0·44–0·66 (moderate–substantial) for the right upper limb.

Kappa analysis was not performed on the rest components of tremor as these were observed too infrequently to produce meaningful results. Furthermore, it is the action

Table 1 Reliability of the rating scale for assessing postural tremor

A Inter-rater reliability

Site of Tremor	Kappa Value	Strength of Agreement
Right upper limb	0·60–0·81	moderate–almost perfect
Left upper limb	0·55–0·77	moderate–substantial
Right lower limb	0·28–0·49	fair–moderate
Left lower limb	0·39–0·59	fair–moderate
Head	0·58–0·84	moderate–almost perfect
	(P of Kappa less than 0·01)	

B Intra-rater reliability

Site of Tremor	Kappa Value	Strength of Agreement
Right upper limb	0·72–0·85	substantial-almost perfect
Left upper limb	0·62–0·76	substantial
Right lower limb	0·40–0·54	fair–moderate
Left lower limb	0·23–0·56	fair—moderate
Head	0·71–0·78	substantial
	(P of Kappa less than 0·01)	

Table 2 Correlation coefficients (r-values) for the relationships between spirography and handwriting impairment, right upper limb acceleration and frequency, the mean of the raters' scores for the postural component of head tremor (pHT), and right upper (pRUL) and lower (pRLL) limb tremor and the disability self-questionnaire (ADL). (* implies significance at the 1% level.)

	ADL	Spirography impairment	Writing impairment	pRUL score
Spirography impairment	0·659*			
Writing impairment	0·686*	0·917*		
pRUL score	0·628*	0·804*	0·762*	
pRUL acceleration	0·039	0·406	0·343	0·655*
pRUL frequency	0·248	0·196	0·159	0·206
pHT score	0·398			0·039
pRLL score	0·055			

rather than the rest component of tremor which would be expected to contribute to the difficulties experienced by patients in their daily living activities.

Validity

Correlation coefficients (r-values) for some of the relationships between spirography and handwriting impairment, right upper limb accelerometry, the raters' scores for the postural component of head and right upper and lower limb tremor and the disability self-questionnaire are shown in table 2. The raters' scores for the right upper limb postural tremor component in each patient correlated well with the results obtained from the disability self-questionnaire and acceleration in the same arm, as well as handwriting and spirography. In contrast the frequency and acceleration values from right upper limb accelerometry were poorly correlated with disability, spirography and handwriting (table 2).

The correlation coefficients (r-values) for the relationships between the frequencies, acceleration and raters' scores for the postural component of tremor in the right compared with the left upper limbs were 0·22, 0·51* and 0·72* respectively (*significant at 1% level); indicating significant symmetries in the clinical severities and RMS acceleration of the tremors in the upper limbs, but asymmetry of the peak frequencies. Similarly, the severity of postural tremor in the patients' left lower limbs was highly correlated with that in the right (0·976*), again suggesting a high degree of symmetry as judged by the raters.

The grand averages of the patients' scores

Table 3 The grand averages of the patients' scores. The values shown are the averages of all those obtained from the patients during the grading clinic, from the first spirography/handwriting assessment and from the self questionnaire (ADL%).

	Mean	Range
ADL%	17	0–49
Writing impairment (0–10)	3·0	0–8
Spiral impairment (0–10)	3·6	0–8
pRUL acceleration (m/s²)	0·537	0·04–2·04
pLUL acceleration (m/s²)	0·385	0·03–1·35
pRUL frequency (Hz)	5·45	2·4–8·8
pLUL frequency (Hz)	5·12	2·4–6·8
pRUL (0–10)	2·8	0–8
pLUL (0–10)	2·4	0–7
pRLL (0–10)	0·4	0–2
pLLL (0–10)	0·4	0–2
pHT (0–10)	1·1	0–5

are shown in table 3, which gives an impression of the "state" of our "average" patient and of the range of scores observed.

The percentage of patients reporting difficulty with each item in the activities of daily living self questionnaire are shown in appendix 2.

Discussion

A quick, reliable and valid method of assessing postural tremor is necessary if changes in tremor behaviour are to be documented routinely and the results of clinical trials appraised. A clinical rating scale has advantages over accelerometry because no apparatus is required, it is cheaper, and more practical and the results are more comprehensible and meaningful to most physicians (and patients). Furthermore, accelerometry is not widely available in clinical practice.

The design of this study was deliberately meant to mimic a "typical" multicentre crossover therapeutic trial, as this was one of the intended uses of the scale. The four raters were therefore specifically chosen because of their varied countries of training and practice (UK, USA, France and India). Furthermore, the timings of the initial assessment clinic and the two video sessions (A and B) were arranged to simulate the schedule of a crossover trial (in which twenty patients were assessed (grading clinic) and then entered into a trial, reassessed after one month (video session A), crossed over and rerated one month later (video session B)). None of the raters had been given any previous experience of the rating scale before the assessment clinic; apart from a short briefing on how to use it.

A sample size of twenty patients and four raters were used, because these were considered to be the largest numbers manageable in a single clinic.

The results show that a clinical grading scale can provide a reliable method of assessing postural tremor severity, particularly of the upper limbs and head; which are the principle sites affected by essential tremor and the
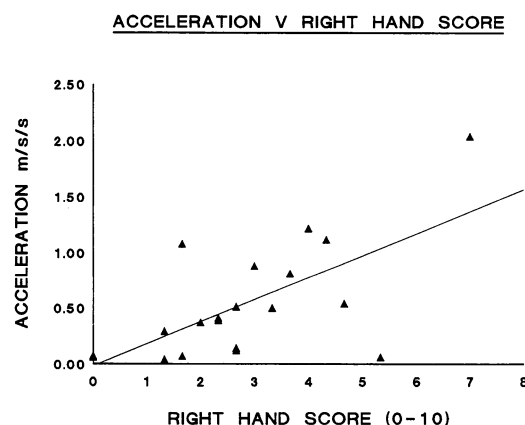
ACCELERATION V RIGHT HAND SCORE

Figure The graph shows the relationship between acceleration (m/s²) and tremor score (0–10) of the postural component of right upper limb tremor. (Correlation coefficient, 0·655*). (* significant at p < 0·01).

tremor associated with dystonia. These results correlated well with the patients own disability ratings (table 2). In contrast accelerometry, which has become a standard technique for assessing tremor in clinical trials and provides a quantitative measurement of upper limb tremor (fig), is not a valid method of assessing the functional significance of postural tremor upon patients (table 2). It does, however, provide an accurate way of measuring two tremor indices; the frequency of the principal peak in a spectrum and the magnitude (root mean square acceleration) of that peak.

There are several specific reasons why the raters produced better correlations than accelerometry with the patients' self-reported disability:

Firstly, the accelerometers used could only record postural upper limb tremor in one spatial dimension (vertical). This deficiency could have been avoided by using triaxial accelerometry, albeit at greatly increased cost and complexity. Second, the raters were able to appreciate the behaviour of the whole limb whereas the accelerometer can only reflect activity at one site. Third, and perhaps most significantly, the raters were all greatly impressed by what looked like intermittent "jumps" of the patients' hands. These infrequent, "aperiodic" but sudden increases in tremor amplitude would be the events most likely to cause a patient to spill a cup of coffee or ruin a piece of writing. However, these low frequency, high displacement components, characteristic of essential tremor as well as dystonia,[19] produced little effect on the dominant peak of the averaged spectra obtained by accelerometry.

Assessments of spirography and handwriting impairment were highly correlated with one another and with disability as well as with right upper limb postural tremor grades (table 2). Furthermore, the inter and intra-rater reliabilities for these two tasks varied from fair to almost perfect. In each case one rater performed well below the level of the other three; had this not been the case both inter and intra-rater agreements would have been almost perfect. In spite of this, assessment of either spirography or handwriting provides a valid and convenient measure of the disability caused by postural tremor. Spirography could be developed to provide a quick and practical way of reassessing patients by postal survey, providing the way in which a spiral is drawn has been standardised beforehand. The use of spirography in this way has the advantages of convenience and cost. It is more likely to reflect the day to day state of a patient's tremor because it avoids the anxiety that accompanies hospital attendance. The potential for a systematic bias caused by a training effect is also minimised because most patients will have learnt to write and draw in childhood and have practiced subsequently. It is thus unlikely that their performances will improve during the course of a clinical trial merely because of a training effect. In contrast, hospital based accelerometric assessments have been shown to produce a significant trend towards lower tremor amplitudes at successive evaluations in untreated patients with essential tremor.[20] Consequently, accelerometry will overestimate the beneficial effect of both drugs involved in a comparison study (for example, propranol versus primidone) and also the effects of treatment and placebo in a double blind placebo-controlled cross over study.

A feature of this clinical rating scale is the way in which tremor magnitude is related to specific anatomical sites. We suggest that when using it the individual scores for tremor severity at different sites are not amalgamated or averaged. Retention of the separate identities of the scale's components prevents unnecessary loss of useful information about the differential responses or natural histories of these site specific tremor components. For instance we found that in those patients with head tremor, eight of whom had torticollis, the severity of head tremor correlated poorly with that of postural tremor in the right upper limb (correlation coefficient: 0·227); suggesting that they are produced by two separate but associated mechanisms.

As tremors all vary continuously with time and with the position and state of activity of the patient's limbs, it is perhaps not surprising that neurologists appear to be better than accelerometry at evaluating such complex four dimensional behaviour in terms of its effect on people's lives. We conclude that, for the purposes of therapeutic trials, a clinical rating scale can produce reliable results, which are a more valid index of tremor induced disability than standard postural accelerometry. Consequently, emphasis on accelerometry should be avoided. The validity of accelerometry could possibly be improved upon by recording during specific tasks, such as spirography or a tracking task (rather than a standard posture), but this remains to be established. Grading spirography and handwriting would appear to be useful because the impairment seen in these tasks correlated well with disability. Standardising the way in which a spiral is drawn and improving analytical methods could lead to a way of carrying out postal assessments.

In this study we have demonstrated that a clinical rating scale can be analysed by a statistical method to provide a measure of the inter and intra-rater reliability of the specific raters involved. This information could be critical to the design of a therapeutic trial; as it allows the trial organisers to drop specific raters and/or switch to a different (more reliable) method of assessment. It also provides some indication of the number of patients required to show a specific magnitude of therapeutic effect. Without this information the results of any trial depending upon a clinical rating scale could be questioned.

No other tremor rating scale has been evaluated for inter and intra-rater reliability or been shown to be valid as an index of disability.

Appendix 1

The rating scale: An example is shown of a patient with grade 5 postural tremor (P) and grade 1 rest tremor (R) of the right upper limb. An identical system was used for grading tremor of the other limbs, voice and head.

Right upper limb
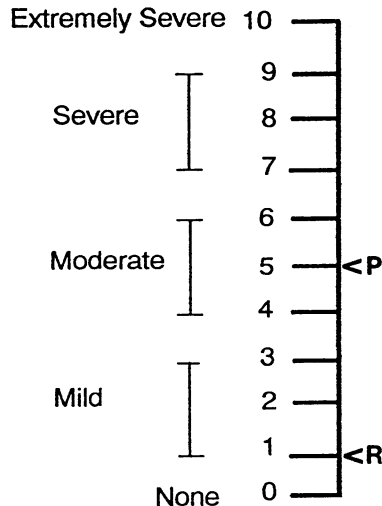
Appendix 2

Illustrates the activities of daily living self-questionnaire. The right hand column shows the percentages of patients reporting difficulties with each item.

Activities of daily living:

For each item circle the number which describes how easy or difficult it is for you to perform the activity.

						Percentage of patients reporting difficulty with each item %
1	Cut food with a knife and fork.	1	2	3	4	50
2	Use a spoon to drink soup.	1	2	3	4	65
3	Hold a cup of tea.	1	2	3	4	80
4	Pour milk from a bottle or carton.	1	2	3	4	45
5	Wash and dry dishes.	1	2	3	4	20
6	Brush your teeth.	1	2	3	4	20
7	Use a handkerchief to blow your nose.	1	2	3	4	0
8	Use a bath.	1	2	3	4	40
9	Use the lavatory.	1	2	3	4	10
10	Wash your face and hands.	1	2	3	4	10
11	Tie up your shoelaces.	1	2	3	4	15
12	Do up buttons.	1	2	3	4	35
13	Do up a zip.	1	2	3	4	20
14	Write a letter.	1	2	3	4	70
15	Put a letter in an envelope.	1	2	3	4	45
16	Hold and read a newspaper.	1	2	3	4	60
17	Dial a telephone.	1	2	3	4	40
18	Make yourself understood on the telephone.	1	2	3	4	5
19	Watch television.	1	2	3	4	5
20	Pick up your change in a shop.	1	2	3	4	40
21	Insert an electric plug into a socket.	1	2	3	4	15
22	Unlock your front door with the key.	1	2	3	4	30
23	Walk up and down stairs.	1	2	3	4	40
24	Get up out of an armchair.	1	2	3	4	35
25	Carry a full shopping bag.	1	2	3	4	45

KEY: 1 Able to do the activity without difficulty.
2 Able to do the activity with a little effort.
3 Able to do the activity with a lot of effort.
4 Cannot do the activity by yourself.

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