



Short communication

Limited correlations between clinician-based and patient-based measures of essential tremor severity



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ABSTRACT

Introduction: We investigated the relation between changes in clinician-based and patient-based measures of tremor severity, within the Fahn–Tolosa–Marin Tremor Rating Scale (TRS) and Visual Analogue Scale (VAS) in essential tremor patients.

Methods: Thirty-seven patients were assessed twice: on- and off-medication. Clinician-based, objective TRS assessments, consisting of part A (postures/movements) and part B (tremor-inducing tasks) were conducted by a blinded assessor using video-tapes. Patients completed TRS part C (limitations in activities of daily life) and indicated subjective tremor severity using VAS.

Results: Patients' total TRS and VAS scores improved on-medication (both $p < 0.001$). Mean improvement was 6.3 (sd 5.4) points on the total TRS and 2.3 (sd 2.3) points on the VAS score. Within the TRS, we found moderate correlations between changes in clinician-based TRS-B and patient-based TRS-C scores ($\rho = 0.387$, $p = 0.011$), but not between changes in clinician-based TRS-A and TRS-C scores ($\rho = 0.128$, $p = 0.232$). Moreover, changes in subjective VAS scores correlated with changes in total TRS ($\rho = 0.422$, $p = 0.007$), changes in TRS-C scores ($\rho = 0.367$, $p = 0.015$) and, more weakly, with changes in TRS-B scores ($\rho = 0.281$, $p = 0.049$), but again: not with changes in TRS-A scores ($\rho = -0.008$, $p = 0.482$).

Discussion: We found no correlation between changes in clinician-based TRS-A, and patient-based measures TRS-C or VAS scores, and a weak correlation between clinician-based TRS-B and VAS scores. The limited correlations between changes in clinician-based and patient-based measures of tremor severity suggest that the different scales measure different aspects of tremor severity and support the additional use of subjective patient-based assessments in clinical practice and clinical trials.

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1. Introduction

The Fahn–Tolosa–Marin Tremor Rating Scale (TRS) [1] is well known and widely used as a tool to assess tremor severity in clinical trials [2–4]. The TRS includes both clinician-based ratings in parts A and B, and patient-based ratings in part C (see Table 1). Part A comprises clinical assessment of tremor severity based on observation of tremor amplitude during rest, posture, movement and finger-to-nose maneuvers. Part B entails clinical assessment of severity during tremor-inducing task performance, including

writing, standardized Archimedes spirals, a line-drawing task and a water-pouring task. Together, parts A and B express tremor severity from a clinical point of view: an objective (impartial and unprejudiced) rating. Recently, a Movement Disorders Society task force recommended the use of the Fahn–Tolosa–Marin TRS, although it was expressed that parts A and B have been investigated more thoroughly, and that part C requires additional clinimetric study [5]. Part C is patient-based, and consists of a structured interview where patients rate the limitations they experience in daily life due to tremor. This interview is rather time consuming, and is not always used in clinical studies. Therefore, some clinical trials rely quite heavily on the clinician-based parts of the TRS.

Here, we investigate how well neurologist-based, objective assessments of changes in tremor severity (TRS-A and TRS-B) correlate with patient-based, subjective assessments of changes (TRS-C and VAS) upon taking medication. Intuitively, one would suspect

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Table 1
Different measures of tremor severity on/off medication: clinician-based and patient-based.

	TRS-A	TRS-B	TRS-C	VAS
Test details	Clinician-based assessment of standardized postures and movements	Clinician-based assessment of writing and task performance	Patient-based assessment of limitations in daily life	Patient-based assessment of tremor severity
Scoring range	0–24	0–32	0–32	0–10

TRS: tremor rating scale (Fahn–Tolosa–Marin), VAS: visual analogue scale.

these to correlate well; however, these intuitions have not been tested and may be deceiving. Correlations between some parts of the TRS and quality of life have been investigated before [6], but never direct correlations between changes in objectively and subjectively assessed tremor severity.

2. Methods

Thirty-seven essential tremor (ET) patients, who were participating in a neuroimaging study in the University Medical Center Groningen and the Academic Medical Center in Amsterdam, were assessed. The Medical Ethical Committees of both sites approved the study. Subjects participated after providing informed consent in accordance with the declaration of Helsinki. We included patients who had a definite diagnosis of ET according to the TRIG criteria [7]: all had bilateral upper limb action tremor in the absence of other neurological signs, and in addition disease duration had to be >5 years. Age at onset was <65 years, thereby excluding late-onset ET. The other supportive TRIG criteria, which are a positive family history and positive response to alcohol, were present in most patients but were not required for inclusion. Patients were all right-handed as assessed by the Annett Handedness scale. All subjects scored >25 on the Mini Mental State Examination ensuring proper understanding of tasks and questions. Exclusion criteria were neurological comorbidity, the use of medication affecting the central nervous system (other than tremor medication), and, because of the related imaging study, MR-related contra-indications.

Patients were assessed twice: on- and off-medication. On the day of on-medication testing, patients were instructed to take their medication at such a time prior to testing that it would be effective (adapted to medication type). On the day of off-medication testing, patients had quit their medication minimally three days before off-medication testing. TRS-A and -B were recorded on video, and supplemented with the drawings (two standardized Archimedes spirals, three straight lines, a written standard sentence, signature and date). An experienced movement disorders specialist (Dr. J.D. Speelman, AMC), who was blinded to medication status, determined TRS scores based on this material. AWGB scored TRS-C for all patients from Amsterdam, and AMMS for all patients from Groningen, while they were aware of medication status. Patients indicated VAS scores on each visit by marking a 10 cm line ranging from 'no tremor at all' (0) to 'worst tremor imaginable' (10).

First, differences in tremor severity measures on/off-medication were assessed using paired samples-t tests for normally distributed data, as tested using the Shapiro–Wilk test. Correlations between changes in tremor severity measures were assessed using Pearson's correlation coefficient (ρ). We used one-tailed testing because we hypothesized that larger changes in TRS scores would be related to larger changes in VAS scores. Note that a sample size of 37 patients has a power of 0.8045 to detect correlations of 0.4 for $\alpha = 0.05$ (one-tailed) [8].

3. Results

Thirty-seven ET patients participated in this study. Patients had a median age of 62 years (interquartile range 21, range 21–80) and a median age at onset of 22 years (interquartile range 34). The mean disease duration was 28 (sd 16) years. 92% of patients had a positive family history for tremor, whereas 43% reported a decrease of tremor upon alcohol-intake. Thirty-five patients were treated with propranolol, with a median dose of 80 mg daily (interquartile range 55), and two patients were treated with primidon. TRS scores varied, with a mean total TRS score of 25 (sd 9) off-medication, improving to a mean TRS score of 19 (sd 9) on-medication ($p < 0.001$). The mean change in TRS score was 6 (sd 5, range from –4 to 20). Patient-perceived tremor severity, as measured with VAS scores, also varied from mild to severe with a mean off-medication score of 6.2 (sd 2), ranging from 2.1 to 9.5 on a 10-

point scale. VAS scores improved on-medication to a mean score of 3.9 (sd 2.2, $p < 0.001$). The mean change in VAS score was 2.3 (sd 2.3, range from –2.0–7.5).

Correlations are depicted in Fig. 1. We found moderate correlations within the TRS between changes in clinician-based TRS-B and patient-based TRS-C scores, but not between changes in clinician-based TRS-A and TRS-C scores. Moreover, changes in subjective VAS scores correlated with changes in total TRS scores, changes in TRS-C and (weakly, <0.3) with changes in TRS-B scores, but again: not with changes in TRS-A scores.

4. Discussion

Overall, there is a moderate correlation between changes in tremor severity as rated in the combined three parts of the Fahn–Tolosa–Marin Tremor Rating Scale and subjectively experienced changes in tremor severity as expressed in VAS scoring.

However, when zooming in on our results, we find correlations between objective and subjective measures of improvement in tremor severity to be limited. When using the TRS and VAS as measures for changes on/off-medication, we found no correlation between changes in part A and C scores *within* the TRS, or between changes in TRS-A and VAS scores. This indicates that patients appraise medication-related changes in their tremor quite differently than clinicians when performing standard tests including posture and finger to nose maneuvers. This may be because TRS-A is known to be a crude measure that is insensitive to small changes in tremor amplitude [9], and because patients may base their impression of changes in tremor severity more heavily on abilities in daily life, rather than simply on tremor amplitude during standardized postures/movements. It is necessary to consider this result for clinical trials where tremor severity scores are used as outcome measures: our results show that a patient-based measure such as TRS-C or VAS adds important information on medication-related changes in tremor severity, in addition to clinician-based measures.

TRS-A and TRS-B include those tests that are typically done by most neurologists in the examination room to assess tremor. Our results suggest that although assessment of tremor during different postures/movements is key to tremor diagnosis, it is useful to recognize that changes in this assessment do not relate to patient-perceived improvement.

Regarding TRS-C, it is interesting to interpret our findings in relation to the scale that is recommended for quality-of-life assessment (QUEST) [5]. QUEST was made specifically for ET [10], and assesses slightly different aspects of tremor impact than TRS-C: quality of life versus limitations in activities of daily life. QUEST was found to correlate with TRS-A/B in single measurements [6,11], however, whether these correlations remain when assessing *changes in tremor severity* needs to be established. Some QUEST-subparts were also found to correlate with a subjective tremor severity measure that is comparable to VAS scoring [10,12], similar to the correlation we found between TRS-C and VAS. Whether QUEST and TRS-C correlate is also unknown: TRS-C was not

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