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Tremor and Other Hyperkinetic Movements

Brief Reports

Severity Stages in Essential Tremor: A Long-Term Retrospective Study Using the Glass Scale

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Abstract

Background: Few prospective studies have attempted to estimate the rate of decline of essential tremor (ET) and these were over a relatively short time period (less than 10 years). We performed a long-term study of severity stages in ET using the Glass Scale scoring system.

Methods: Fifty consecutive patients with severe ET were included. We retrospectively obtained Glass Scale scores throughout the patient's life. Common milestone events were used to help recall changes in tremor severity.

Results: According to the Glass Scale, the age distributions were as follows: score I, 40±17 years, score II, 55±12 years, score III, 64±9 years, and score IV, 69±7 years. A significant negative correlation between age at first symptom and rate of progression was found ($r=-0.669$, $p<0.001$). The rate of progression was significantly different ($p<0.001$) when the first symptom appeared at a younger age (under 40 years of age) compared with older age (40 years or older).

Discussion: Our results support the progressive nature of ET. Age at onset was a prognostic factor. The Glass Scale may be a useful tool to determine severity stages during the course of ET in a manner similar to the Hoehn and Yahr Scale for Parkinson's disease.

Keywords: Essential tremor, Glass Scale, essential tremor progression

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Introduction

Essential tremor (ET) is generally considered to be a neurodegenerative disease.[1,2] Prospective and longitudinal data have shown a progressive worsening in tremor scores over time. The average annual increase in tremor severity from baseline has been estimated to be between 3.1% and 5.3%. Nevertheless, to our knowledge, only four studies have attempted to estimate the rate of decline over time and they have all been performed over a relatively short period (less than 10 years).[3–6]

The Glass Scale was developed as a simple tool to measure the severity of ET in everyday clinical practice.[7] It is simple to use and quick to administer to ET patients with upper limb involvement (95% of patients). This scale has only four scores and its characteristics are similar to those of the Hoehn and Yahr Scale, the classical stage marker of Parkinson's disease.[8]

In this article, we used the Glass Scale to assess severity staging of ET using a retrospective method, which permitted a long-term evaluation. We hypothesized that the study could help to confirm the progressive nature of the disorder and to determine prognostic factors. It could also elucidate the usefulness of the Glass Scale as a marker of ET stage.

Methods

Fifty consecutive patients with severe ET (Glass Scale score III or higher) attending the Movement Disorders Unit at Sant Pau Neurology Department from January 2012 to September 2014 were included in the study (27 males, 23 females; mean age 72.5 years, range 60–79 years).

Diagnosis of ET was established using the consensus criteria established by the Movement Disorders Society.[9] All the patients

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Table 1. Demographic and Clinical Characteristic of Essential Tremor Patients.

Characteristics	Data
Age (years)	72.5 ± 12.4
Female gender	23 (46)
Education (years)	15.2 ± 2.0
Age at first symptom	40.1 ± 17.1
Tremor duration (years)	27.1 ± 7.7
Baseline asymmetry	1 (2)
Baseline head tremor	26 (52)
Baseline voice tremor	11 (22)
Family history of ET	44 (88)
Takes daily caffeine	5 (10)
Takes daily tremoric drugs	7 (14)
Takes daily antitremoric drugs	50 (100)

Abbreviation: ET, Essential Tremor.
Values represent mean ± SD or number (percentage).

fulfilled neurophysiological criteria for ET.[10] The study protocol was approved by the Hospital Ethics Committee and was performed in accordance with international ethical regulations. All subjects received and signed informed consent to participate.

The Glass Scale score is obtained by asking the patient a single question: "When you are seated at the table, how do you drink water from a glass with your dominant hand?"[7] By means of extensive interviews with the patients and their relatives, we retrospectively obtained Glass Scale scores throughout the patient's life. We asked when they first noted tremor in their arms (Glass Scale I), when tremor increased, making it difficult to drink from a glass using one hand (Glass Scale II), when tremor provoked the need to use both hands to drink (Glass Scale III), and when patients needed a straw to drink (Glass Scale IV). We used common milestone events to help to remember tremor severity changes, such as school leaving age, age of military service in the case of men, marriage, birth, or wedding of a child, and retirement. To simplify data collection, we did not include the second part (A and B) of the scale.

The two most reliable scores were I (symptoms first noticed) and III (when both hands were first needed to drink from a glass). Scores II and IV are more difficult to obtain precisely. For this reason, we used the time lapse between scores I and III to correlate disease progression rate and clinical predictors.

We assessed several clinical factors, on the basis of a chart review and on the patient's report, to correlate with ET worsening over time that could predict the rate of change: age at first symptom, gender, years of education, baseline head tremor, baseline voice tremor, family history of ET, baseline asymmetrical tremor, usual caffeine intake, tremoric drugs, and ET medications.

Statistical analysis

We initially performed a descriptive analysis. Categorical variables were reported as percentage and number of cases. Quantitative variables were presented as the mean ± standard deviation. We studied the possible relationship between quantitative variables and the time lapse between Glass Scale scores I and III using Pearson's correlation coefficient. When of interest, we added a scatterplot for easier understanding, and we used a box-plot for some variables. The Student *t*-test was used to compare quantitative variables in the two groups.

In all analysis, the statistical level of significance was established at 5% (alpha=0.05, two-sided). The statistical package used was IBM-SPSS (V 22.0).

Results

Fourteen patients were classified as Glass Scale score IV, and 36 as score III. Table 1 shows the demographic and clinical characteristics of the patients in our series. We found the following age distribution according to the Glass Scale scores: score I 40 ± 17 years, score II 55 ± 12 years, score III 64 ± 9 years, and score IV 69 ± 7 years (Figure 1). The mean time in years to reach each score was: score II 17 ± 10, score III 25 ± 13, and score IV 36 ± 15 years (Figure 1).

We found a significant negative correlation between age at first symptom of ET (Glass Scale score I) and time between scores I and III ($r=-0.669$, $p<0.0001$) (Figure 2).

No significant correlation was found between the other clinical variables studied and time between scores I and III: gender ($p=0.092$), years of education ($p=0.990$), baseline head tremor ($p=0.238$), baseline voice tremor ($p=0.358$), family history of ET ($p=0.097$), baseline asymmetrical tremor ($p=0.809$), usual caffeine intake ($p=0.888$), tremoric drugs ($p=0.768$), and ET medications ($p=0.766$).

We repeated the statistical analysis using two group of patients: patients in whom symptoms of ET first appeared before 40 years of age (n=19; 9 females; mean age of onset=20 ± 7 years), and patients in whom they appear at 40 years or older (n=31; 14 females; mean age of onset 52 ± 7 years). We found that patients who presented tremor at a younger age took 37 ± 10 years to reach stage III, while patients with debut at an older age took 17 ± 8 years. This difference was statistically significant ($p<0.0001$) (Figure 3).

Discussion

In this retrospective study covering a wide time span, we found that ET was a slow, progressive disorder, and that the rate of progression depended on the age of disease onset. The progressive course of the disease is in concordance with the four previous prospective studies. Elble[3] followed 44 ET patients over 4 years using accelerometry and found a 7.4% yearly worsening after baseline. Putzke et al.[4] prospectively analyzed 45 patients with a mean follow-up of 3.6 years.

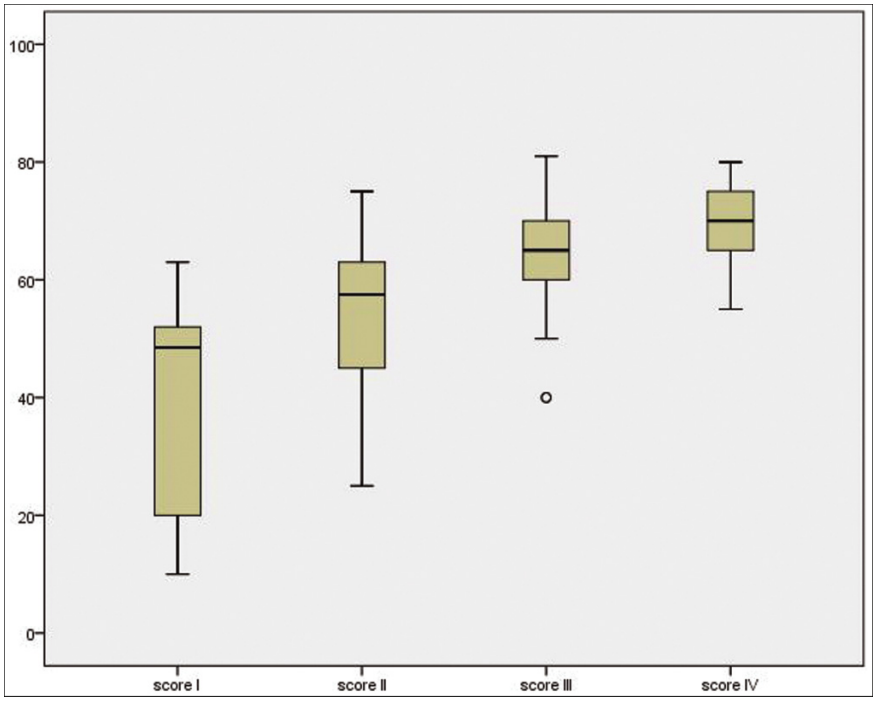

Figure 1. Glass Scale Scores and Age (years) of Patients in the Present Series. X axis: The Glass Scale; Y axis: Age (years).

They estimated a 12% annual worsening in clinical tremor ratings after baseline. In another study, Louis et al.[5] followed 83 patients for a mean of 5 years and found an average annual increase in tremor severity from baseline between 3.1% and 5.3%. The most recent longitudinal study, by Louis et al.,[6] had a mean follow-up of 5.8 years and was performed in 116 patients. The authors used the spirography test to quantify tremor and found worsening of spiral score at an average rate of 0.12 points per year.

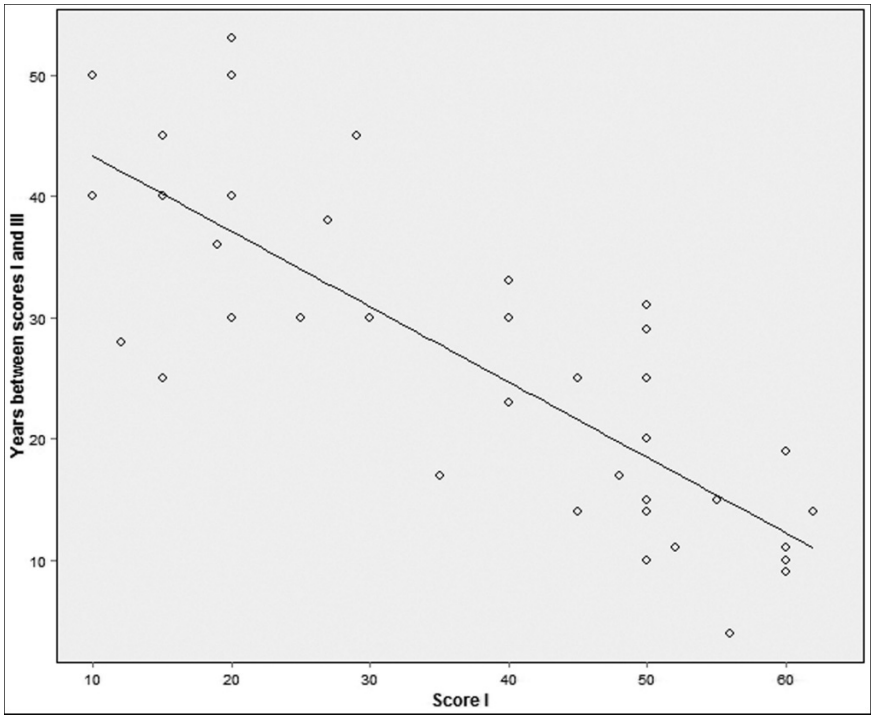

Figure 2. Correlation between Glass Scale Score I (age at first symptom) and Time Between Scores I and III ($r=-0.669$, $p<0.0001$). X axis: The Glass Scale; Y axis: Age (years).

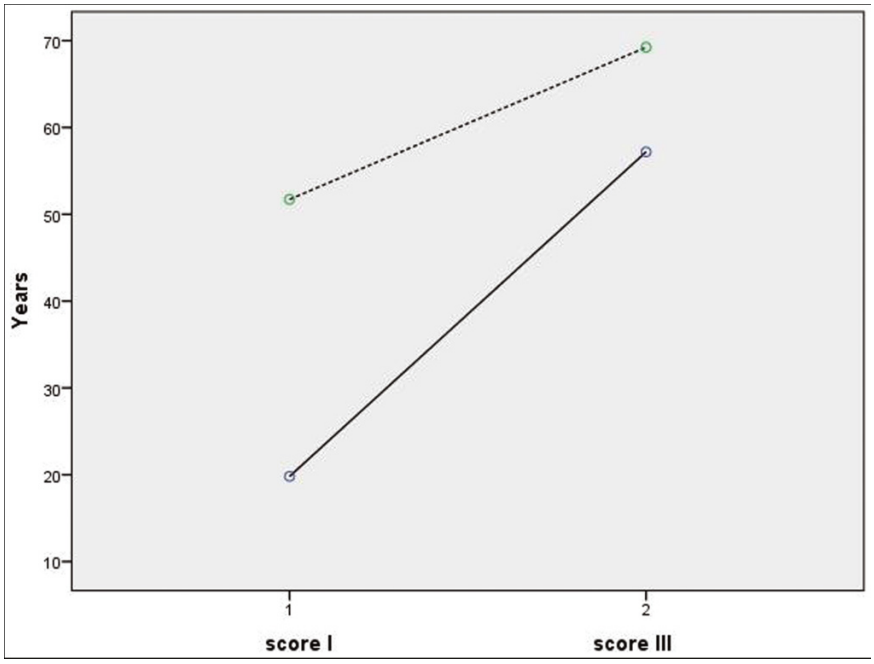

Figure 3. Rate of Progression to Reach Glass Scale Score III ($p<0.0001$) when Disease Begins Before 40 Years of Age (continuous line) and at 40 Years or Older (discontinuous line). X axis: The Glass Scale; Y axis: Age (years).

Studies on ET progression are difficult because they require a very long follow-up. Prospective studies reported to date had a relatively short follow-up, of 3–6 years. The Glass Scale assessment, however, does not imply the need for a clinical evaluation in person and is based solely on anamnesis of the patient and/or relatives. This point, together with the scale's simplicity, makes it suitable for retrospective studies. Another strength of the Glass Scale is that it is not susceptible to intra-subject variability as it collects data referring to a period of time rather than to a single assessment as when using presential clinical rating scales or accelerometry.

We consider ET to be a progressive disorder with several stages of severity. The Glass Scale may be useful in determining these levels. The Glass Scale score I corresponds to a mild severity stage when the patient may need occasional medication. Score II corresponds to a moderate severity stage, during which patients commonly need continuous drug therapy. Scores III and IV correspond to high severity stages when the patient often needs polytherapy and surgery. However, ET has a great clinical heterogeneity. Interestingly, in about 20–30% of patients, tremor did not worsen in longitudinal studies, although the follow-up periods were short. Louis et al. performed an interesting cross-sectional study of ET in 335 patients to determine the clinical situation of the disease at each 10-year milestone.[11] Each patient underwent a single evaluation of tremor severity. They found that after more than 40 years of ET duration, 20–60% of patients had a high tremor amplitude. Less than 10% of patients were incapacitated. The authors concluded that there is a progressive decade-by-decade decline in ET. However, patients with long disease duration did not converge at the same end-stage of severe functionally incapacitating tremor.

Clinical baseline predictors of worsening in ET have been analyzed in some previous prospective studies. Putzke et al.[4] found the asymmetrical self-reported tremor onset and asymmetrical tremor ratings at the first clinic visit to be significant predictive factors. In our study, only one of the patients recounted an asymmetrical onset. Louis et al. found no baseline factors that predicted annual change in ET.[5] In their second study, they found statistically significant differences in the rate of progression between familial and non-familial ET. The rate of change was higher in ET patients with a family history.[6] In our study, we did not find a significant correlation with this variable, although the series was biased as most ET patients in our series had a family history.

Interestingly, in our study we found a clear relationship between age at onset of the disease and rate of progression. We agree with the results of a previous retrospective study by Louis et al.[12] In that study, the rate of progression was estimated based on the tremor severity and reported disease duration at the time of evaluation. They found that patients with age of onset after 60 years progressed more rapidly. Furthermore, this finding is similar to other neurodegenerative disorders such as Parkinson's disease.[13] In fact, older age at onset is a poor prognosis marker and has a major progression rate.

The study has several limitations that make our estimates more conservative. The main limitation of our study is that it is retrospective and is subject to recall bias and low precision of data: the patient can remember approximate but not exact dates at which the severity of tremor changes. Another limitation is that although the Glass Scale has displayed a strong construct validity compared with the Tremor Clinical Rating Scale (weighted kappa=0.907) and high inter-rater validity (weighted kappa=0.937), several psychometric properties, such as floor and ceiling effects, are not known.[7] Moreover, it is only a

four-point scale, and, thus, lacks precision for a more fine-grained analysis of rate of progression. Another limitation is that the patients were enrolled in a clinic-based study. It has been described that there is a substantial difference between clinic and community ET cases in terms of the information they provide regarding their family history, thus affecting their estimate of rate of progression.[14] Finally, our sample of ET patients is biased for several clinical variables, thus limiting predictive analysis.

In conclusion, our study supports the progressive nature of ET. Age at onset of symptoms is a prognostic factor. If tremor begins before 40 years of age, the rate of progression is low. Finally, the Glass Scale may be a useful tool to determine severity stages during the course of ET, in a similar way to the Hoehn and Yahr Scale for Parkinson's disease.

References

1. Louis ED. Essential tremor. *Lancet Neurol* 2005;4:100–110, doi: http://dx.doi.org/10.1016/S1474-4422(05)00991-9.

2. Deuschl G, Elble R. Essential tremor: neurodegenerative or nondegenerative disease towards a working definition of ET. *Mov Disord* 2009;14:2033–2041, doi: http://dx.doi.org/10.1002/mds.22755.

3. Elble RJ. Essential tremor frequency decreases with time. *Neurology* 2000; 55:1547–1551, doi: http://dx.doi.org/10.1212/WNL.55.10.1547.

4. Putzke JD, Whaley NR, Baba Y, Wszolek ZK, Uitti RJ. Essential tremor: predictors of disease progression in a clinical cohort. *J Neurol Neurosurg Psyquiatry* 2006;77:1236–1237.

5. Louis ED, Agnew A, Gillman A, Gerbin M, Viner AS. Estimating annual rate of decline: prospective, longitudinal data on arm tremor severity in two groups of essential tremor cases. *J Neurol Neurosurg Psychiatry* 2011;82:761–765, doi: http://dx.doi.org/10.1136/jnnp.2010.229740.

6. Louis ED, Michalec M, Gillman A. Shaky drawing: what is the rate of decline during prospective follow-up of essential tremor? *BMJ open* 2014;4: e004626, doi: http://dx.doi.org/10.1136/bmjopen-2013-004626.

7. Gironell A, Martínez-Corral M, Pagonabarraga J, Kulisevky J. The Glass Scale: a simple tool to determine severity in essential tremor. *Parkinsonism Rel Disord* 2010;16:412–414, doi: http://dx.doi.org/10.1016/j.parkreldis.2010.04.001.

8. Hoehn M, Yahr M. Parkinsonism: onset, progression and mortality. *Neurology* 1967;17:427–442, doi: http://dx.doi.org/10.1212/WNL.17.5.427.

9. Deuschl G, Bain P, Brin M, et al. Consensus statement of the Movement Disorder Society on tremor. *Mov Disord* 1998;13(suppl 3):2–23, doi: http://dx.doi.org/10.1002/mds.870131303.

10. Gironell A, Kulisevsky J, Pascual-Sedano B, Barbanoj M. Routine neurophysiological tremor analysis as a diagnostic tool for essential tremor: a prospective study. *J Clin Neurophysiol* 2004;21:446–450, doi: http://dx.doi.org/10.1097/00004691-200411000-00009.

11. Louis ED, Gerbin M, Galecki M. Essential tremor 10,20,30,40: clinical snapshots of the disease by decade of duration. *Eur J Neurol* 2013;20:949–954, doi: http://dx.doi.org/10.1111/ene.12123.

12. Louis ED, Ford B, Barnes LF. Clinical subtypes of essential tremor. *Arch Neurol* 2000;57:1194–1198, doi: http://dx.doi.org/10.1001/archneur.57.8.1194.

13. Reinoso G, Allen JC Jr, Au WL, Seah SH, Tay KY, Tan LC. Clinical evolution of Parkinson's disease and prognostic factors affecting motor progression: 9-year follow-up study. *Eur J Neurol* 2015;22:457–63, doi:10.1111/ene.12476.

14. Louis ED, Barnes LF, Ford B, Ottman R. Family history information on essential tremor: potential biases related to the source of the cases. *Mov Disord* 2001;16:320–324, doi: http://dx.doi.org/10.1002/mds.1040.