Amplitude Fluctuations in Essential Tremor. A Prospective Study

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Background

Essential tremor (ET) may be classified as a pathological tremor in the physiological tremor frequency range (McAuley and Marsden, 2000). Because of such characteristics, spectral analysis of ET signal often reveals multiple frequency components of significant amplitude which may be due to the amplitude and frequency modulation of tremor signal (Gresty and Buckwell, 1990). Such variations may lead difficult to quantify tremor severity in ET subjects using quantitative motor assessment system (QMAS), biasing outcomes of any clinical trial for ET.

In order to assess temporal amplitude variability in patients with ET using a standardized approach, we prospectively evaluated postural and kinetic arms tremor of patients with ET in a clinical setting every 2 hours for 6 hours from 8:00AM (T0) using the Kinesia™ system (Great Lakes NeuroTech Inc.) as QMAS (see fig. 1) and The Essential Tremor Rating Assessment Scale (TETRAS), developed by The Tremor Research Investigation Group (TRIG) (Elble et al., 2008).

The Kinesia system assessments showed to correlate significantly with TETRAS scores in patients with ET (Giuffrida et al., 2009; Mostile et al., 2010).

Methods

Study Population

Patients diagnosed at the Parkinson's Disease Center and Movement Disorders Clinic (PDCMDC), Baylor College of Medicine who satisfied the TRIG diagnostic criteria for definitive or probable ET (Findley and Koller, 1995) were detected and enrolled in the study. All enrolled patients gave a written informed consent to participate in the research protocol which was approved by the Institutional Review Board for Human Research at Baylor College of Medicine. The study included subjects aged between 18 and 75 inclusive which were complied with the test requirements.

Experimental setting and procedure

All the enrolled ET patients attended for a single scheduled day the PDCMDC. Patients were requested not to take any pharmacological medication for tremor the day of the test and to abstain from caffeinated beverages, alcohol and tobacco for at least 12 hours prior to assessment.

On the day of the assessment, before the QMAS recording, each enrolled patient was first rated using TETRAS by a first rater (RF). Then, postural (arms outstretched) and kinetic (finger-to-nose) arms tremor was measured using QMAS every 2 hours intervals for 6 hours from 8:00AM [8:00 (T0), 10:00 (T2), 12:00 (T4), 14:00 (T6)].

Subjects were videotaped performing the tasks. Single subjects consecutively performed each assessment twice during every time-interval. At the end of the study, videos were randomized and blindly rated by an independent rater (TY) using the TETRAS items for upper limbs tremor.

Results

Twelve ET subjects were enrolled (age: 50.25 ± 20.58 years; age at onset: 32 ± 21.66 years). TETRAS scores for upper limbs postural (arms outstretched) and kinetic tremor were respectively 1.71 ± 0.45 and 1.79 ± 0.5. For each time-interval of assessment, QMAS and video scores were directly correlated and they showed good intra-rater reliability (see tab. 1 and tab. 2).

Fig.1. Kinesia™ wireless system (QMAS) and video-guided tasks:

Tab.1. Correlation between QMAS and video average scores[a] for time-intervals

N = 12	Postural task	Kinetic task
T0 * ** *** †		
Right Hand	0.708 (0.01)	0.775 (0.003)
Left Hand	0.776 (0.003)	0.734 (0.007)
T2 *		
Right Hand	0.665 (0.018)	0.906 (< 0.001)
Left Hand	0.776 (0.003)	0.724 (0.008)
T4 **		
Right Hand	0.74 (0.006)	0.849 (< 0.001)
Left Hand	0.717 (0.009)	0.796 (0.002)
T6 ***		
Right Hand	0.898 (< 0.001)	0.781 (0.003)
Left Hand	0.86 (< 0.001)	0.734 (0.007)

Tab.2. QMAS and Video scores intra-rater reliability[b]

| N = 12		QMAS score		Video Scores	
		Postural task	Kinetic task	Postural task	Kinetic task
T0	Right Hand	0.869 (< 0.001)	0.938 (< 0.001)	0.767 (0.004)	0.927 (< 0.001)
	Left Hand	0.897 (< 0.001)	0.836 (0.001)	0.736 (0.006)	0.886 (< 0.001)
T2	Right Hand	0.781 (0.003)	0.872 (< 0.001)	0.59 (0.044)	0.816 (< 0.001)
	Left Hand	0.788 (0.002)	0.957 (< 0.001)	0.747 (0.005)	0.939 (< 0.001)
T4	Right Hand	0.638 (0.026)	0.91 (< 0.001)	0.545 (0.067)	0.81 (0.001)
	Left Hand	0.774 (0.003)	0.932 (< 0.001)	0.755 (0.005)	0.845 (0.001)
T6	Right Hand	0.849 (< 0.001)	0.977 (< 0.001)	0.535 (0.073)	0.749 (0.005)
	Left Hand	0.811 (0.001)	0.976 (< 0.001)	0.826 (0.001)	0.977 (< 0.001)

Notes:
(a) Between first and second evaluation. Data are: Pearson r (p). * ** *** Sig. correlation for both hands and tasks. † Sig. correlation with in-person rated TETRAS items for both hands and tasks.
(b) Correlations between first and second evaluations for each time-interval. Data are: Pearson r (p).

Results

QMAS scores at T0 significantly correlated with in-person rated TETRAS scores as well as with subsequent time-intervals instrumental scores. No significant differences were detected among time-intervals QMAS average measurements using ANOVA. There was a maximal percent variation from T0 in tremor amplitude as determined by the QMAS estimates of 23% for postural task-right hand, 18% for postural task-left hand and 9% for kinetic task-both hands. Test for equality of variance showed high measurements variability for high QMAS scores at T0. Such difference in variability remained generally stable through the 6 hours of assessment (see fig. 2).

Fig.2. QMAS scores variability among time-intervals (T0 score cut-offs are median values)
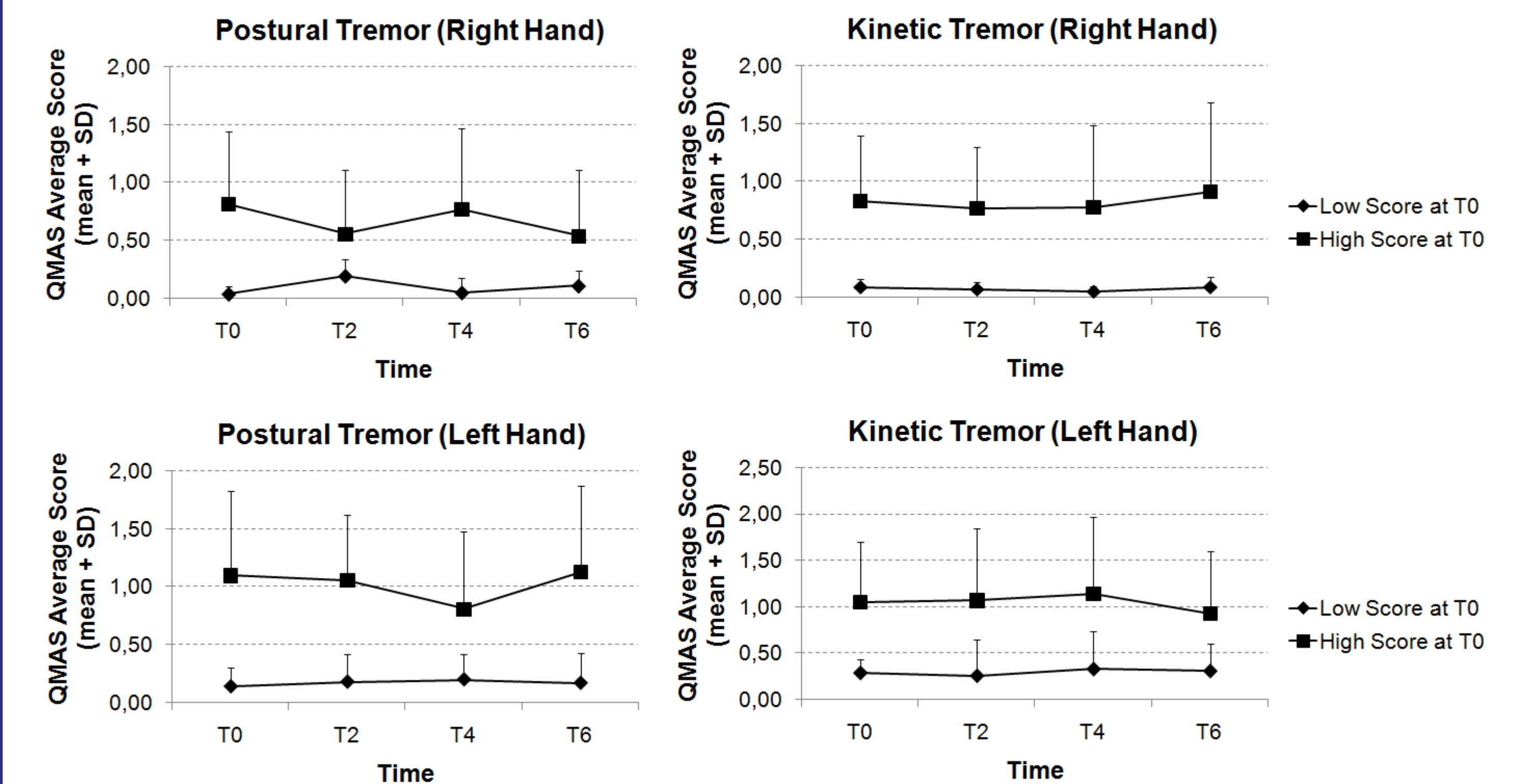
Conclusions

Morning instrumental measures of amplitude may predict subsequent hourly assessments. High amplitude tremor may be associated with high intra-assessment variability.

References:
- Giuffrida JP, Riley DE, Maddux BN, Heldman DA. Clinically deployable Kinesia technology for automated tremor assessment. Mov Disord. 2009;24:723-30.
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