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Essential Tremor Quantification During Activities of Daily Living

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Abstract

Background—Essential tremor (ET), characterized primarily by postural and kinetic tremor, is typically measured in the clinic with subjective tremor rating scales. These ratings are often used to adjust medications and assess efficacy in clinical trials. However, tremor ratings require the presence of a clinician and do not necessarily capture tremor fluctuations throughout the day during activities of daily living (ADL).

Objective—To evaluate the ability of motion sensors to discriminate tremor from voluntary posture and motion, classify tremor as postural or kinetic, and rate tremor severity during standardized tasks and non-standardized activities of daily living.

Methods—Ten subjects with ET wore motion sensors on the index finger and performed standardized motor tasks from the Washington Heights-Inwood Genetic Study of Essential Tremor (WHIGET) tremor rating scale (wTRS) and non-standardized ADL tasks. Four movement disorder specialists independently rated video segments of the standardized tasks but not the ADL tasks.

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Quantitative features were extracted from the motion sensors and used to develop mathematical models for predicting rating scores from kinematic data.

Results—The quantitative motion features were highly correlated with wTRS ratings for postural (r=0.90) and kinetic (r=0.80) tremors. Mathematical models produced tremor ratings that correlated strongly with clinician ratings of the wTRS tasks (mean r=0.80) and also produced ADL task ratings that correlated well with the most recent clinician wTRS ratings (mean r=0.72).

Conclusions—Recordings from motion sensors can be used to classify tremor as postural or kinetic and quantify tremor severity during both standardized and non-standardized activities.

Keywords

Essential tremor; tremor rating scale; Kinesia; gyroscopes; accelerometers

Introduction

Accurate quantification of tremor is critical in assessing response to essential tremor (ET) interventions. ET, characterized by postural and kinetic tremor, affects activities of daily living and may have a psychological impact, particularly when symptoms occur in public [1,2]. Activities most prominently affected are handwriting, eating, dressing and self-care. Postural and kinetic tremors typically occur in the forearms and hands, with a frequency range of 4–12 Hz that tends to decrease with age [3–5]. The relative contribution of postural and kinetic tremor in ET can vary, though recent data suggest that kinetic tremor is more severe than postural tremor in ET [6], and the neural mechanisms that cause the two types of tremor in ET remain largely unknown [3].

Currently, rating scales such as the Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) [7], Washington Heights-Inwood Genetic Study of Essential Tremor (WHIGET) tremor rating scale (wTRS) [8,9], and Fahn-Tolosa-Marin tremor rating scale [10] are used to evaluate ET during a clinical examination. Each tremor rating scale (TRS) rates tremor on a subjective, qualitative 0 – 4 scale, generally corresponding to (0) normal, (1) slightly abnormal, (2) mildly abnormal, (3) moderately abnormal, and (4) severely abnormal. While these rating scales have clinical utility, they require the presence of a clinician for scoring, are subject to clinical judgment and bias, and cannot be used for continuous monitoring of tremor fluctuation patterns throughout the day or in home environments. These limitations impede an objective, repeatable, and comprehensive evaluation of tremor severity.

Previously, accelerometers (actigraphy), gyroscopes, and electromyography (EMG) have been used extensively to obtain quantitative measurements of tremor in both Parkinson's disease (PD) and ET [7,11–14]. EMG activity correlates moderately with tremor scores [15,16], but accelerometers [17] and gyroscopes [18] provide stronger correlations. More recently, the built-in iPhone® accelerometer has been proposed as a quick and efficient means for clinicians to measure tremor frequency [19]. The motion sensing system used in the present study (Kinesia™, CleveMed) previously quantified tremor during standardized clinical exams of PD, with high correlations to the Unified Parkinson's Disease Rating Scale (UPDRS-III) [20], and ET, with high correlations to the TETRAS [7]. Home monitoring has typically been limited to actigraphs that only grossly detect when tremor occurs or quantify tremor severity at rest [17,18,21]. However, ET is most troublesome during voluntary movement or when holding posture against gravity. Therefore, the goal of this study was to demonstrate the feasibility of continuous home ET monitoring by determining if miniature motion sensors can 1) detect and classify tremor as postural or kinetic in spite of voluntary

motion artifact, 2) accurately rate tremor severity during standardized assessments and 3) accurately rate tremor severity during routine activities of daily living.

Patients and Methods

Subject Recruitment

Ten adults (7 male, 3 female; age, 56–83 years; disease duration, 10–40 years) with clinically diagnosed ET were recruited. Tremor ranged from 4.2 – 9.6 Hz with a mean of 6.1 Hz and a standard deviation of 0.9 Hz. Subject medication use was not altered as medication state (on/off) is not a factor in the clinical rating of tremor. All clinical testing was completed at CleveMed under the purview of the CleveMed Institutional Review Board (IRB), and all participants provided IRB approved informed consent.

Data Collection

Subjects wore a wireless motion sensor unit (Kinesia™, CleveMed; Supplementary Figure 1) on the index finger of the hand identified by the subject as being more affected by ET. When both hands were equally affected, the device was placed on the dominant hand. The light-weight (0.4 oz) sensor unit contained three orthogonal accelerometers for measuring linear acceleration and three orthogonal gyroscopes for measuring angular velocity. The sensor unit was placed on the dorsal side of the index finger between the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints. Motion data were sampled at 128 Hz and transmitted wirelessly to a PC for data storage.

During testing, each subject performed a sequence of eleven tasks including seven based on the wTRS [8,9] and four tasks that resembled more routine activities of daily living (ADLs) but were not part of any standardized rating scale. Before data collection, tasks were explained in detail to ensure each subject was familiar with them. Subjects performed each task for approximately fifteen seconds. The sequence of seven wTRS tasks included having the subjects place their hands in their laps (rest), hold their arms extended horizontally, repeatedly reach out and touch their noses, pour water between two cups, drink water from a cup, use a spoon to drink water, and draw a spiral. The sequence of four more general ADL tasks, not part of any standardized tremor evaluation, included typing on a computer keyboard, using a computer mouse to browse the internet, folding laundry, and using a TV remote control. These tasks were chosen to represent activities that might interfere with tremor measurement in the home. For example, typing on a keyboard includes repetitive motions that may resemble tremor, and folding laundry requires large movements in multiple frequency bands. The sequence of eleven tasks was repeated six times by each subject with a 3–5 minute rest period between each block of eleven tasks. While the tasks were being performed, kinematic data from the sensor unit was transmitted wirelessly to a laptop PC, and the subject's upper extremity was videotaped for subsequent clinical scoring.

Videos of the ten subjects performing the seven wTRS tasks were randomized and placed onto a secure web-based server for scoring by four experienced movement disorder specialists (JJ, DV, JP, RE) who were blinded to subject identity. The raters entered a 0 – 4 score for each task [9]. Since each subject repeated the tasks six times, 420 videos were scored in total (7 tasks×6 blocks×10 subjects). Given that clinical scoring validity has been demonstrated for the wTRS tasks [9] but not the generalized ADL tasks specific to this study, only the wTRS tasks were scored. Scores were averaged across the four raters to minimize variability.

Tremor Detection Signal Processing

Motion due to tremor must be distinguished from voluntary motion in order to classify and quantify tremor severity. Therefore, kinematic data were band pass filtered from 0.1 – 3.0 Hz (voluntary band) and from 4 – 12 Hz (tremor band), based on the typical frequency ranges for voluntary and tremor motion, respectively. The magnitude of the logarithm of the peak power of the x, y and z angular velocity signals in the voluntary band, which will be referred to as the "voluntary movement index" or VMI, was used to classify whether the subject was voluntarily moving. The midpoint between the average VMI across all subjects for the two tasks that do not require voluntary movement (rest, arms outstretched) and the average VMI across all subjects for the five tasks that require voluntary movement (nose-touching, pouring, drinking, spooning, spiral drawing) was used as a threshold for classifying tremor as "postural" or "kinetic" so the appropriate tremor quantification algorithm (postural or kinetic) could later be applied. We did not attempt to differentiate rest from static postures against gravity since rest tremor is usually not part of ET and can be excluded from this study.

The logarithm of the peak in the power spectrum in the tremor frequency band for each sensor type (accelerometers and gyroscopes) has previously been shown to correlate well with clinician scores even when the peak is broad [7,20]; therefore, the same method was performed in this study. In order to account for slight variations in orientation of the sensor on the finger, the magnitudes (Euclidean norm) of the accelerometer and gyroscope (x, y, z) signals were used. Correlation coefficients comparing these quantitative features to the average clinician score were calculated for each sensor type.

Standardized Tremor Severity Model

Two separate multiple linear regression models were derived from the motion sensor data: one model for rating postural tremor and another for rating kinetic tremor. The data collected during the seven wTRS tasks were classified as postural or kinetic based on the VMI and then used for the appropriate model development. Both models had the following general structure:

$$R = b_0 + B_a \cdot P_a + B_g \cdot P_g \quad (1)$$

where R is the average clinician rating, P_a and P_g are the processed peak powers of the accelerometer and gyroscope recordings as described above, and B_a, B_g, and b_0 are the regression coefficients.

The two models were tested using a "one left out" technique [22]. This meant a single regression was computed using all but one data point. The resulting regression model and coefficients were then used to compute an output score for the data point that was left out. The analysis was repeated leaving each data point out once. The coefficient of determination (r^2) and root-mean-square (RMS) error between regression model outputs and average clinician scores were computed for all generalization data.

Generalization to Activities of Daily Living

The major goal of this study was to demonstrate the feasibility of using motion sensors to accurately rate tremor severity during routine or spontaneous activities of daily living. Therefore, the algorithms developed from the wTRS task data were used to classify the type of activity (postural or kinetic) and rate the severity of tremor during the four ADL tasks that were not used in model development. Since standardized scoring does not exist for these

ADL tasks, scores output by the algorithms were compared to the average of the clinician wTRS scores given in the same data collection block.

Results

Motion Discrimination

Motion due to tremor must be discriminated from voluntary motion before tremor quantification is possible. Figure 1 shows sample data recorded during the nose-touching and laundry-folding tasks. Voluntary motion occurred in the low frequencies (<3Hz), while tremor occurred at higher frequencies (>4Hz). Folding laundry is a freeform motion that does not follow a rhythmic pattern, but tremor can still be distinguished from voluntary motion due to the sharpness of the tremor spectral peak.

In addition to distinguishing tremor from voluntary motion artifact, the quantification algorithm must determine if the subject is moving voluntarily, so the appropriate tremor rating model (postural or kinetic) can be applied. The VMI (see Methods) was used to determine if the subject was voluntarily moving the limb (Supplementary Figure 2A). The threshold VMI was approximately two standard deviations from the mean of either the movement or non-movement VMIs and classified over 96% of the tasks into the expected category (Supplementary Figure 2B). A few instances (12 out of 180) of the nose-touching, spiral drawing, and computer mouse tasks were classified as “non-movement” when the subject was performing the tasks at an extremely slow speed. Moreover, for a small number of tasks (8 out of 120) when the subject was not supposed to be moving (rest, arms outstretched), review of the videos revealed that the subject did in fact move voluntarily, and those tasks were correctly classified as “movement.”

Standardized Tremor Rating Model

The logarithm of the tremor spectral peak for each sensor type (accelerometer and gyroscope) was correlated with the average clinician score for each task (Table 1). The accelerometers produced higher correlations for some tasks, while the gyroscopes produced higher correlations for other tasks. Therefore, both sensor types were used in the analysis. On average, the quantitative features extracted from the motion sensors were highly correlated with wTRS scores for postural tremor (r=0.90), measured by the “arms outstretched” task, and for kinetic tremor (r=0.80), measured by the five wTRS tasks that required the subjects to move voluntarily.

The models described by Equation 1 were applied separately for each wTRS task performance according to classification based on the VMI. In order to test how well the models generalized to new data, a “one-left-out” analysis was performed (see Methods). The analysis demonstrated good correlations and low errors between model outputs (ratings) and clinician scores for the wTRS tasks (Figure 2).

Generalization to Activities of Daily Living

The tremor scoring algorithms (Eq. 1) were applied to the four ADL tasks, which were not clinically scored. The VMI was first used to determine if significant voluntary motion was present when the subject was performing the task so that the appropriate tremor scoring algorithm (postural or kinetic) could be applied. Scores produced by the algorithms correlated well with the average of the wTRS scores given in the same task block (Figure 3).

Discussion

This study represents the first step toward a system that can accurately quantify tremor during activities of daily living in the home. Specifically, we have shown that tremor can be discriminated from voluntary motion, classified as postural or kinetic, and quantified during generalized tasks simulating activities that an ET patient might perform throughout the day. Detecting voluntary movement, even in the presence of tremor (Figure 1), allows the appropriate tremor quantification model (postural or kinetic) to be applied. The laundry folding task is a good example of an activity in which movements contain multiple frequency components and do not follow a set pattern, but tremor can still be discriminated from voluntary motion and accurately scored for severity. We did not attempt to distinguish rest from static postures against gravity because our patients did not exhibit rest tremor, which is usually the case in ET.

The high correlations between clinician scores and the quantitative variables (Table 1) as well as between the clinician scores and the model outputs (Figure 2) are similar to what have been achieved previously for both PD [20] and ET [7]. The relatively low correlation between kinematic features and clinician scores during the rest task was again due to the fact that rest tremor did not occur in our patients. We conclude that motion sensors provide a standardized, objective measure of tremor severity, without the concern of inter-rater reliability.

Due to previous difficulties in distinguishing voluntary motion from tremor, most attempts at continuous tremor recording have used motion sensors either to measure the duration of tremor occurrence or to quantify tremor amplitude in the absence of voluntary motion [17,18,21]. We have demonstrated the feasibility of accurately rating the severity of tremor during non-standardized ADLs using algorithms based on motion sensors (Figure 3). The models developed with standardized clinic assessment tasks can be extrapolated to the home monitoring environment where tasks are not constrained. The slight overestimation of tremor severity seen in the laundry folding tasks (Figure 3C), particularly for mild tremor, is probably due to spectral power from voluntary motion extending into the tremor frequency range. However, if the goal is to monitor tremor continuously throughout the day, a few data points indicating higher than expected tremor scores when fast voluntary motion is occurring could be effectively “washed out” by low-pass filtering the continuous tremor rating over the course of the day. Although the device used in this study was large enough that it could possibly interfere with certain daily activities, smaller, more ergonomic sensor units and the possibility of using fewer motion capture channels are currently under investigation. Additionally, the subjects who participated in this study had mild to moderate tremor, as subjects with severe tremor were difficult to recruit. Further studies are planned to validate the system in patients with a wider variety of tremor types and severities in the actual home environment with continuous monitoring during normal activities of daily living.

Continuous classification and rating throughout the day may aid clinicians and researchers in therapy development and symptom management optimization for patients with both ET and other movement disorders. For example, a patient may experience the most severe tremors only during a specific activity in the home that cannot be replicated in the clinic. Likewise, a particular deep brain stimulation (DBS) paradigm or combination of medications may help patients in a manner not apparent by clinical evaluation alone but only visible with continuous home monitoring. Capturing tremor during the activities that impact patient quality of life most may help clinicians to optimize therapy for each patient’s specific needs. Additionally, independent quantification of postural and kinetic tremors may help researchers learn more about the neural mechanisms that cause the two types of tremors

and speed the development of new therapies that may target a specific type of tremor. Our results suggest that tremor detection, discrimination, and quantification with motion sensors generalizes to unconstrained activities, and in turn may enable monitoring during a patient's daily activities, which would provide clinicians with a more sensitive, quantitative assessment in the context of daily life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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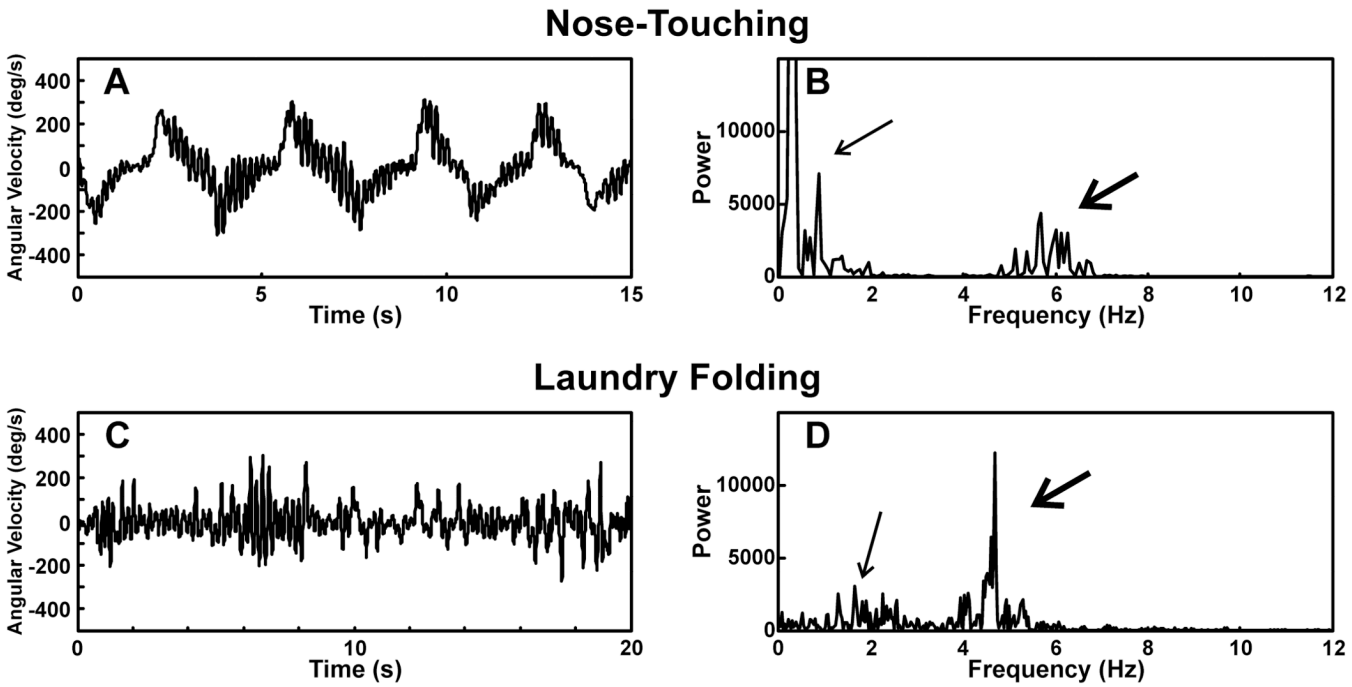

Figure 1.

A) Raw data recorded from the z-gyroscope during **nose-touching** task. The four slow waves are due to voluntary motion, while the fast oscillations are due to tremor. **B)** Power spectrum of the signal in **A.** The signal due to the voluntary motion is marked with a thin arrow, while tremor is marked with a thick arrow. **C)** Raw data recorded from the x-gyroscope during the **laundry folding** task. **D)** Power spectrum of the signal in **C**. The signal due to the voluntary motion is marked with a thin arrow, while tremor is marked with a thick arrow.

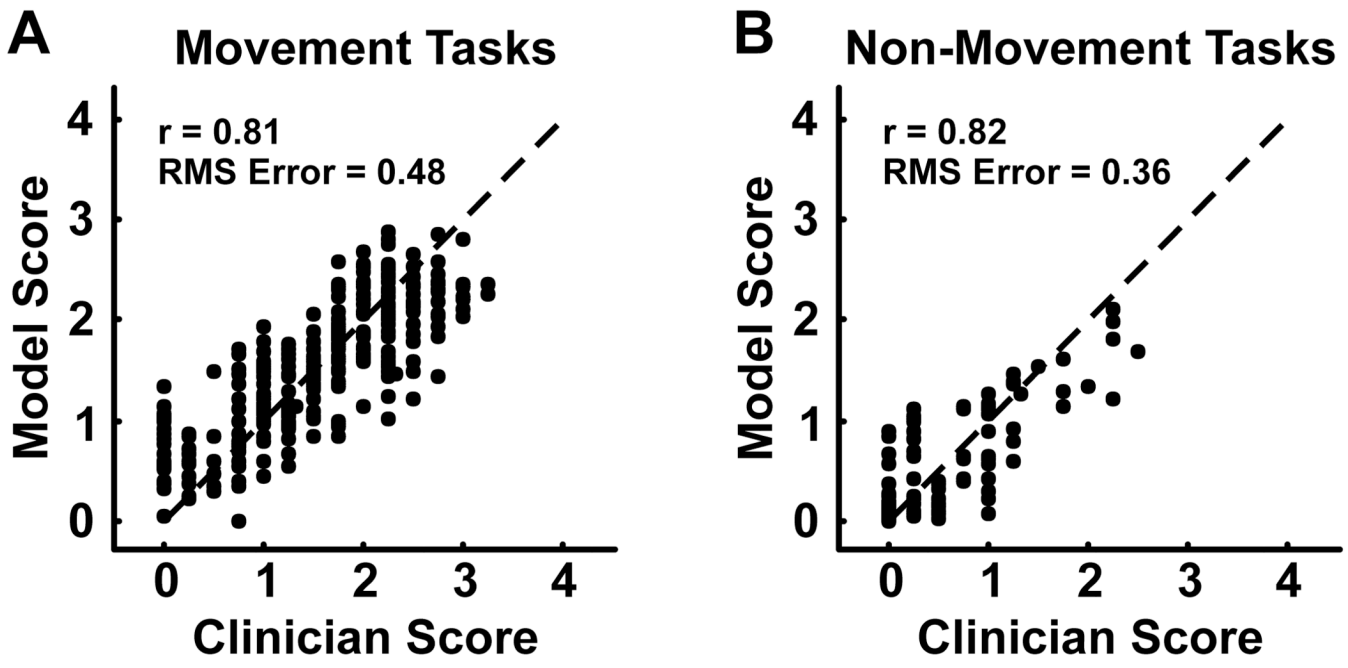

Figure 2.

The scores output by the "one left out" models are compared to the actual scores for tasks when voluntary movement was present (**A**) and tasks where there was no discernible voluntary movement (**B**). Each dot represents one of the 420 single wTRS task performances. Correlation coefficients and RMS errors are given for each tremor type. The dashed line corresponds to a perfect fit.

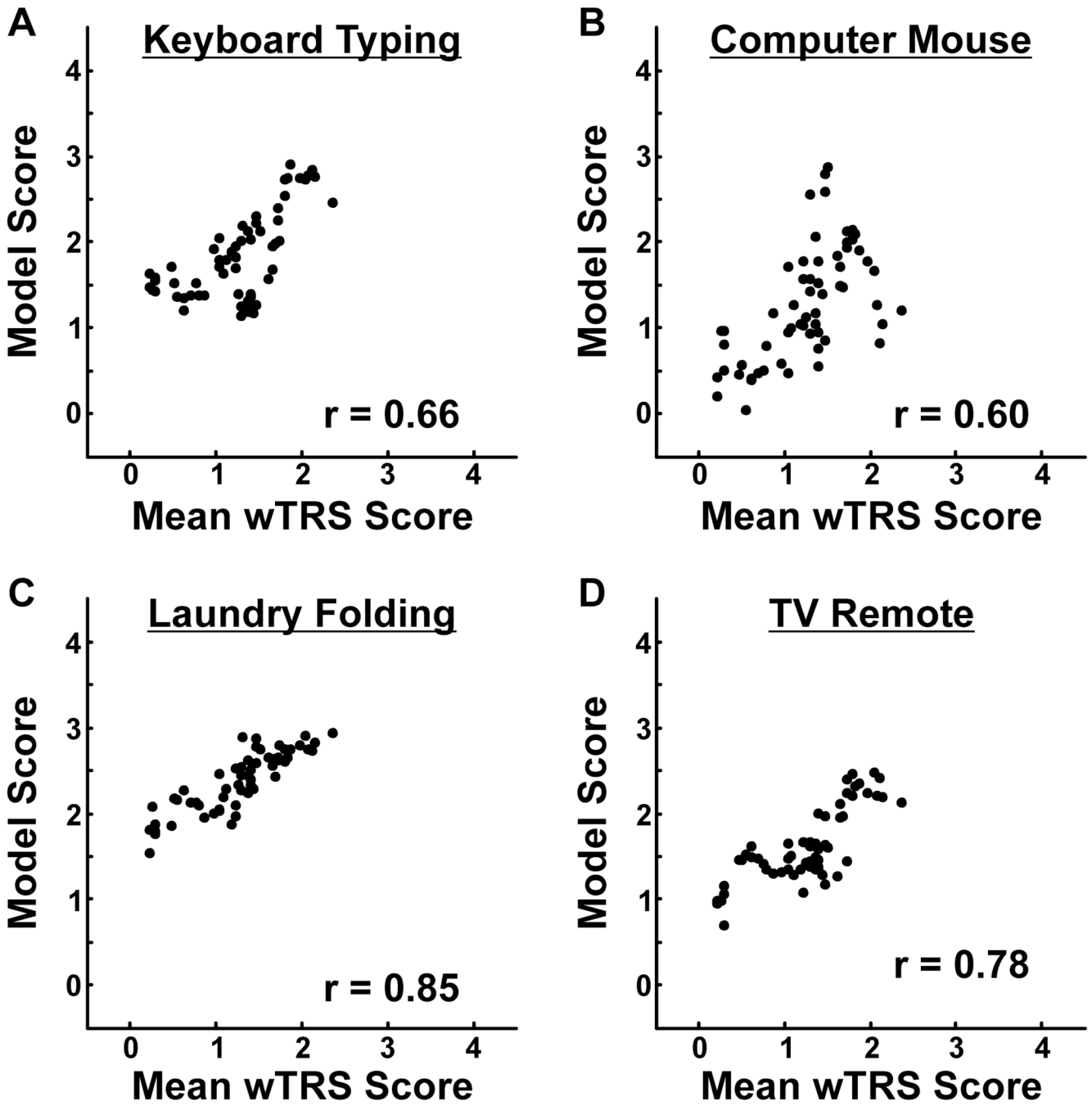

Figure 3.

The model output is compared to the mean of the clinician wTRS scores given by the clinicians in the same block for the (**A**) keyboard typing, (**B**) computer mouse, (**C**) laundry folding, and (**D**) TV remote tasks. Each dot represents one of the sixty task performances for each of the four ADL tasks. The correlation coefficient comparing the scores is shown for each task.

Table 1

Clinical Correlation.

Task	Acc.	Gyr.
Rest	0.57	0.60
Arms Outstretched	0.88	0.91
Nose-touching	0.78	0.69
Pouring	0.77	0.78
Drinking	0.87	0.90
Spoon	0.79	0.76
Spiral	0.83	0.87
Kinetic Mean	**0.81**	**0.80**

Correlations between clinician scores and kinematic data extracted from the accelerometers (Acc.) and gyroscopes (Gyr.) are shown for the wTRS tasks. The “Kinetic Mean” refers to the average correlation for the five tasks that require the subjects to move voluntarily.