

## Brief Reports

## Do Bradykinesia and Tremor Interfere in Voluntary Movement of Essential Tremor Patients? Preliminary Findings

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### Abstract

**Background:** The aim of this study was to determine whether tremor and bradykinesia impacted a dexterous activity performed by patients with essential tremor (ET).

**Methods:** Core bradykinesia was assessed in 27 controls and 15 patients with ET using a rapid alternating movement (RAM) task. Then, participants performed a “counting money” counting tasks while equipped with inertial measurement units to detect and quantify tremor during movement. The time required to perform subsections of the tasks and the rate of failure (errors) were compared between groups using Mann–Whitney U tests and a chi-square test, respectively.

**Results:** Patients with ET presented with significant bradykinesia during the RAM task and had more tremor during the counting money task. However, the time required to perform the task and rate of failure were similar between groups.

**Discussion:** Results show that even though bradykinesia was detected during fast movements, and that tremor was present during a task requiring dexterity, both symptoms did not interfere with the performance of patients with ET. This pilot study suggests that there may be a threshold at which tremor will become problematic. Determining this threshold for a wide range of daily activities may help determine when it is appropriate to initiate treatment for patients with ET.

**Keywords:** Activities of daily living, accelerometer, essential tremor, core bradykinesia

**Citation:** Goubault E, Nguyen HP, Ayachi FS, Bogard S, Duval C. Do bradykinesia and tremor interfere in voluntary movement of essential tremor patients? Preliminary findings. *Tremor Other Hyperkinet Mov.* 2017; 7. doi: 10.7916/D822319X

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**Editor:** Elan D. Louis, Yale University, USA

**Received:** March 1, 2017 **Accepted:** May 23, 2017 **Published:** June 22, 2017

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**Funding:** None.

**Financial Disclosures:** None.

**Conflicts of Interest:** The authors report no conflict of interest.

**Ethics Statement:** This study was performed in accordance with the ethical standards detailed in the Declaration of Helsinki. The authors' institutional ethics committee has approved this study and all patients have provided written informed consent.

### Introduction

Essential tremor (ET) is a movement disorder characterized by postural and kinetic tremor,<sup>1,2</sup> typically in the forearms and hands, with a frequency range of 4–12 Hz that tends to decrease with age.<sup>3–5</sup> Kinetic tremor is more severe than postural tremor in ET, and is present at a significantly higher rate.<sup>6</sup> Kinetic tremor has the potential to interfere with activities of daily living,<sup>1,2</sup> especially if that activity requires fine dexterous movements. However, little is known about the relationship between tremor amplitude and its influence on the performance of activities of daily living. There are also suggestions that core bradykinesia is a clinical feature of ET,<sup>7–9</sup> although this remains controversial.<sup>5,7</sup> Bradykinesia, typically the slowness of movements observed in some disorders like Parkinson's disease or advanced ET,

can be influenced by external factors like tremors, muscle weakness, rigidity and bradyphrenia.<sup>10</sup> Also, slowness of movement can be caused by a “voluntary” reorganization of movement speed to deal with the involuntary movement because of kinetic tremor. Core bradykinesia refers to slowness of movement that is independent of the need for accuracy, or slowness of movement that is not influenced by the fact that the amplitude of involuntary movement is close or superior to that on the intended voluntary movement. Here, core bradykinesia was defined as the slowness of movement detected during fast repetitive movements that is not caused by the need for accuracy, nor by the fact that the amplitude of the intended movement is close or inferior to that of the intended movement, i.e., a low signal-to-noise ratio.

The aim of this study was to determine if tremor or core bradykinesia had a deleterious influence on an activity of daily living requiring dexterity performed by patients with mild-to-moderate ET. To do so, core bradykinesia was first assessed using a standard rapid alternating movement (RAM) task. Then, tremor was quantified using inertial measurement units (IMUs) positioned strategically over limbs of interests while participants performed a “counting money” task.

## Methods

### Participants

Twenty-seven healthy control participants (14 females, 13 males;  $62.9 \pm 7.7$  years old; height =  $1.68 \pm 0.08$  m; weight =  $68.12 \pm 12.7$  kg; Mini Mental State Examination (MMSE) score =  $29.2 \pm 1$ ) and 15 age-matched participants diagnosed with ET (10 females, 5 males;  $62.4 \pm 8.3$  years old; height =  $1.67 \pm 0.09$  m; weight =  $72.11 \pm 14.3$  kg; MMSE score =  $29 \pm 1$ ; TETRAS upper limb score =  $0.53 \pm 0.71$ ) were recruited for the study. Patients were either treated ( $N=5$ ; topiramate ( $N=2$ ), propranolol ( $N=2$ ), clonazepam ( $N=1$ )) or not ( $N=10$ ) and had kinetic tremor ranging from no visible tremor to moderate tremor in either the dominant hand or in both hands (clinical score from 0 to 3 of the Essential Tremor Rating Assessment Scale assessed by two trained evaluators using video recordings). Healthy control participants were recruited through the Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal, while participants with ET were recruited through the Centre Hospitalier de l'Université de Montréal with the help of clinicians specializing in movement disorders. To be included, participants with ET must have a clinical diagnosis of ET according to the ET criteria.<sup>11</sup> We excluded participants who required assistance to walk, who had any orthopedic conditions that may have prevented them from performing the required tasks, who used any medication that could cause hyperkinetic disorders, or who had an MMSE score below 25/30 at the time of the experiment. None of the recruited participants reached the exclusion criteria and none of the participants exhibited any physical limitations or pain that could affect their ability to perform the tasks. The institutional research ethics review board approved this research and each participant read and signed an informed consent form.

### Experimental protocol

Participants performed three trials of RAM task, with a minute rest between trials.<sup>7,12-14</sup> The aim of the task is to assess core bradykinesia in participants with ET. During the RAM task, participants were sitting on a chair, arms extended in front of them, and were asked to rotate a ball with their dominant hand as fast (speed) and as much amplitude (angle) as possible for 10 seconds, while maintaining their non-dominant hand stable. Participants were asked to wait for a visual stimulus (light) before starting the task. The rotational speed and angle were measured using rotational sensors as attached to the ball by a 1.2 meters long wooden dowel (Figure 1D). These sensors have an accuracy of 0.3 degrees. Raw data from rotation sensors were acquired at 100 Hz using DasyLab11.0 (Data Acquisition System Laboratory, DasyTec, Amherst, NH, USA).

Participants also performed two trials of a daily living task consisting of counting money with a minute rest between trials. For this task,

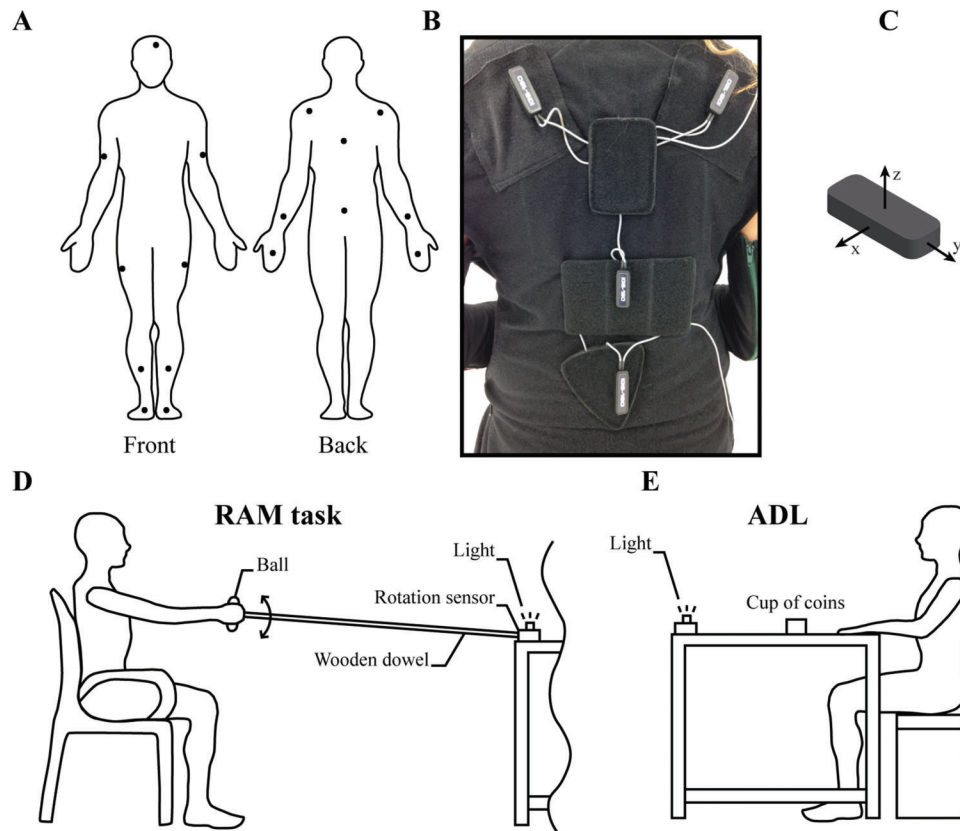
participants were sitting with both hands positioned on the table. They were asked to wait for a visual stimulus (light) to initiate the task (Figure 1E). When cued, they were required to reach for a cup containing an unknown amount of coins, empty the content in one hand, count the amount of money, put back the coins in the cup, and reposition each hand on the table at their initial position. Participants were instructed to keep coins in their hands while counting. To assess the impact of tremor and core bradykinesia in real-life conditions, participants were instructed to do the “counting money” task at their preference pace as they would do in their daily life. The amounts of money (\$4.60 and \$3.35) were different for the two trials to avoid a memory effect that could affect the results, and the order of presentation was randomized. The number and type of coins used for each amount were similar for all participants (\$4.60: one two-dollar, one one-dollar, five quarters, three dimes, one nickel. \$3.35: one two-dollar, four quarters, three dimes, one nickel). Participants performed this task while wearing the Animazoo IGS-180 motion capture suit (Synertial UK Ltd, Lewes, UK). The IGS-180 (Figure 1A–C) is equipped with 17 IMUs (OS3D, Inertial Lab, VA, USA) positioned on each limb to capture full-body three-dimensional movements. Each IMU comprises an accelerometer (three-axis linear acceleration), a gyroscope (three-axis angular velocity) and a magnetometer (magnetic north heading). Raw data from each IMU were acquired at 60 Hz. At the time of the experiment, participants with ET experienced visible tremor exclusively in the hands. For this reason, only the IMUs positioned on the hands were used for the analysis.

### RAM performance analysis

RAM data were band-passed filtered between 0.1 and 10 Hz<sup>7</sup> using a third-order Butterworth filter. The 10 Hz cut-off frequency was chosen because it allows for inclusion of all frequency components related to the RAM task.<sup>7,15-17</sup> The first cycle of the pronation–supination task was removed to ensure that the initiation component was not a part of RAM performance analysis. The last two seconds of the recording were also removed as fatigue may confound results.<sup>7,13,15</sup> Peaks of RAM signal were identified for analysis. The RAM task was analyzed using previously studied parameters.<sup>7,13,15</sup> These are 1) mean duration of each pronation–supination cycle in seconds, representing the time taken to perform a complete pronation–supination cycle averaged over one trial; 2) mean angular velocity of a full cycle of pronation–supination in degrees per second over one trial; 3) maximal angular velocity of a full cycle representing the highest mean velocity of a full cycle of pronation–supination in degrees per second over one trial; 4) maximal instantaneous angular velocity over one trial; 5) mean angular displacement over a full cycle of pronation–supination in degrees. For each participant, the average of the three trials was calculated for all the RAM characteristics. The five RAM characteristics were compared between groups using Mann–Whitney U tests with  $\alpha=0.05$ .

### Daily living task performance analysis

**Pre-processing.** Studies have shown that tremor is more pronounced in distal joints.<sup>3-5</sup> The counting money task was done with the hands,



**Figure 1. Sensor placement and experimental setup.** (A) Diagram of the 17 sensors and their location on the suit. (B) A close-up view of the sensors on the shoulders, trunk and hip. (C) The orientation of the axes on the sensor. Using the right-hand Cartesian coordinate system, the y-axis line is aligned along the length of the inertial sensor while the x-axis is aligned along the width of the sensor. (D) Spatial schematic of the RAM task. (E) Spatial schematic of the “counting money” task.

so we concentrated our efforts on IMUs positioned on the hands. Earth gravity detected by accelerometers positioned on the hands was removed using quaternions, which represent the fusion of accelerometer, gyroscope and magnetometer data to obtain sensor orientation. This process allowed us to isolate the time series associated with the movement.<sup>18</sup> Then, the signals in x, y, and z were decomposed using empirical mode decomposition into five intrinsic mode functions (IMFs), which can be used to identify distinct frequency bands associated with physical or physical pattern associated with ET.<sup>19,20</sup> Visual inspections of the spectra revealed that only the first two IMFs contained frequencies between 3 and 12 Hz, which is the frequency band where tremor is normally present.<sup>21–23</sup> Therefore, the sum of the time series associated with the first two IMFs was calculated to detect and quantify tremor during the “counting money” task. The obtained signal was then divided into 1-second windows to detect and quantify tremors in the x, y, and z direction.

**Detection and quantification of tremor during movement.** The power spectral density was computed for each 1-second window in each direction (x, y, z). The peak power, defined in this study as the power estimation around the dominant frequency with  $\pm 0.5$  Hz band width, was calculated only if the dominant frequency was between 3 and 12 Hz.

If the peak power of the 1-second window was out of the usual tremor frequency band, the tremor amplitude was considered irrelevant (i.e., within the physiological range), and set to zero for that particular 1-second window. When detectable, tremor amplitude was measured by summing peak power in x, y, and z direction. The amount of tremor for each participant was then calculated as the mean of tremor in the left and right hands. We also assessed the power distribution, representing the relative power percentage within the 3.5–7.5 Hz over the total amount of power. This was used in the past to assess the relative importance of tremor oscillations during voluntary movement.<sup>24,25</sup>

#### Segmentation of the dexterous task for performance assessment.

The “counting money” task was visually divided into five segments using video recordings: Segment 1, from initial position to when the participants reach for the cup containing coins; Segment 2, from having the cup in hand to when participants put back the cup on the table after they emptied the content of the cup onto one hand; Segment 3, from putting back the cup on the table to when participants finished counting the amount of money in their hands; Segment 4, from having counted the amount of money to when participants put back the coins into the cup; Segment 5, from putting back the coins into the cup, to when participants put back their hands on the table at their initial position.

The time required to perform each segment was then calculated for the two trials. The corresponding segments were summed over the two trials before comparing groups using a Mann–Whitney U test. Moreover, we set success criteria based on the errors (result of money count and drop coins during counting) reported during the testing. If participants made an error during counting (wrong amount, dropping money or cup), they failed the task. The rate of failure between groups was compared using chi-square tests. All the analysis was done in R (R Core Team (2016), R Foundation for Statistical Computing, Vienna, Austria).  $p < 0.05$  was used as the test threshold for statistical significance.

## Results

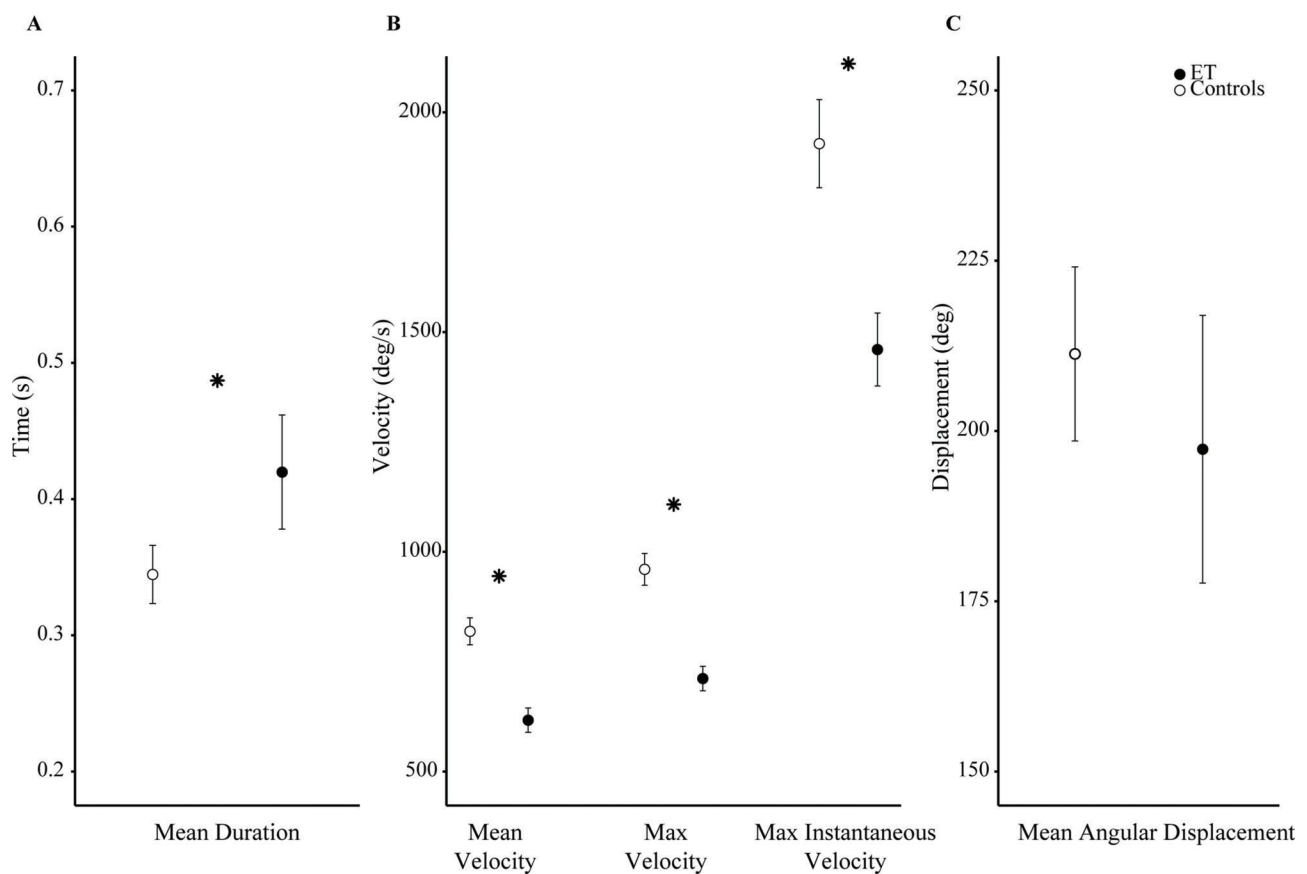
### RAM performance

Mann–Whitney U tests revealed that mean duration of pronation–supination cycle (Figure 2A) was significantly longer for participants with ET ( $W=136$ ,  $p=0.042$ ; with  $W$  representing the sum of ranks of the smallest group) than control participants, indicative of core bradykinesia. This finding was supported by significant reduction of mean

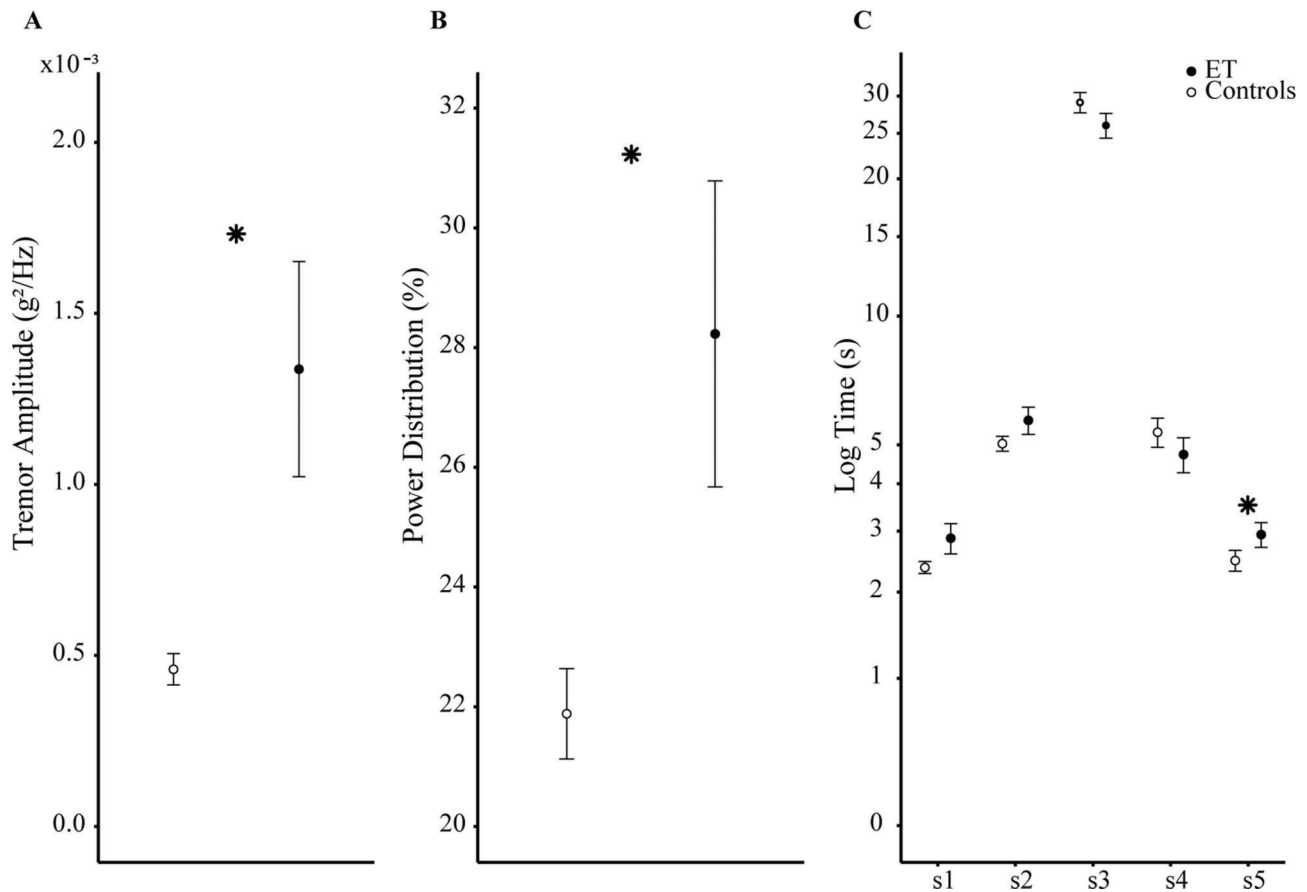
angular velocity ( $W=345$ ,  $p < 0.001$ ), maximal angular velocity ( $W=357$ ,  $p < 0.001$ ), and maximal instantaneous angular velocity ( $W=319$ ,  $p < 0.001$ ) (Figure 2B). Slowness of movement was not accompanied by reduced amplitude of movement since angular displacement over a full cycle of pronation–supination was statistically similar between groups (Figure 2C) ( $W=224$ ,  $p=0.293$ ).

### Tremor

The amplitude of tremor during the dexterous tasks was significantly higher for participants with ET ( $W=73$ ,  $p=0.0002$ ) (Figure 3A). Power percentage within the 3.5–7.5 Hz band was significantly higher for participants with ET, indicate the presence of abnormal oscillations during the tasks ( $W=101$ ,  $p=0.0051$ ) (Figure 3B). We found, however, no significant difference between groups in the time required to the first four segments of the “counting money” tasks (Segment 1,  $W=158$ ,  $p=0.093$ ; Segment 2,  $W=157.5$ ,  $p=0.114$ ; Segment 3,  $W=237$ ,  $p=0.821$ ; Segment 4,  $W=230$ ,  $p=0.773$ ). Segment 5 was the exception where controls were significantly faster to get back in the initial position ( $W=139.5$ ,  $p=0.0313$ ) (Figure 3C). Chi-square tests



**Figure 2. RAM performance comparison between controls and ET.** (A) Mean duration of pronation–supination cycles  $\pm$  SE. (B) Mean angular velocity of pronation–supination cycles  $\pm$  SE (left); maximal angular velocity of pronation–supination cycles  $\pm$  SE (center); maximal instantaneous angular velocity over the pronation–supination task  $\pm$  SE (right). (C) Mean angular displacement of pronation–supination cycles  $\pm$  SE for control participants (white) and participants with ET (black). The stars indicate a significant difference.



**Figure 3. Tremor and performance comparison between controls and ET during the counting money task.** (A) Tremor amplitude averaged over the two “counting money” tasks  $\pm$  SE. (B) Power distribution averaged over the two “counting money” tasks  $\pm$  SE. (C) Time required to do each segment of the dexterous task  $\pm$  SE for control participants (white) and participants with ET (black). The stars indicate a significant difference. s1, Reach cup; s2, Reach money; s3, Count money; s4, Put back money into the cup; s5, Put the hands on the table.

revealed no significant difference between the two groups in failure proportion ( $\chi^2(1)=0.259$ ,  $p=0.611$  for “counting money 1”;  $\chi^2(1)=0.221$ ,  $p=0.638$  for “counting money 2”).

### Discussion

This experiment revealed that patients with ET presented with core bradykinesia when their ability to perform RAMs was compared with a group comprising of healthy participants. Patients with ET presented a significantly higher tremor amplitude during the dexterity task, but the time required to perform the task and rate of failure were, in a great proportion, similar between groups.

Results presented here support the notion that core bradykinesia can be detected in patients with ET when they perform fast repetitive movements.<sup>7</sup> The lack of difference between groups in the angular displacement indicates that while patients were slower in performing RAM, they retained the ability to generate as large a movement amplitude as healthy controls. In some patients with Parkinson’s disease, we have shown that both core bradykinesia and hypokinesia are present when performing RAM.<sup>15</sup> More importantly, the fact that

the amplitude of movement was similar for each group eliminates the possibility that differences in movement time seen between groups were due to a difference in strategy; i.e., smaller rotations resulting in reduced time between rotational peaks.

Results from the dexterous task performance demonstrate that patients having mild to moderate treated or untreated tremor could perform an activity requiring dexterity as well as their counterpart in the control group. Indeed, the rate of failure was similar between groups, despite having detectable tremor during movement. Furthermore, the core bradykinesia observed during the RAM task had no influence on the time required to perform the dexterous task. These results may explain why bradykinesia is not considered a clinical feature of ET. It is reasonable to believe that more severe tremor amplitudes would increase the time required to perform an activity of daily living by forcing the individual to reduce movement speed in an attempt to improve accuracy. The amplitude threshold at which this occurs could be explained by a signal-to-noise ratio approach, where the signal is the voluntary movement and the noise the involuntary movement.<sup>26</sup> Past a certain signal-to-noise ratio, the rate of failure as

well as the time required to perform a specific task would increase dramatically. Finding this signal-to-noise ratio threshold would greatly help to determine when it is time to treat ET. It would then be possible to assess the efficiency of current treatments in increasing this signal-to-noise ratio. Here, there was an increase of power percentage within the frequency band associated with tremor, but it was not high enough to play a detrimental role during voluntary movement.

One obvious limit of this study is the low sample size. To build a more comprehensive model of interaction between tremor and activities of daily living (signal-to-noise ratio model), the present results must be confirmed in a larger group of patients, with more variability of tremor amplitude between them. Furthermore, building such a model would require testing different activities of daily living having different amplitudes of displacement and velocity between them. Only then would it be possible to determine the deleterious signal-to-noise ratio for the motor repertoire that represents daily activities. This would allow us to predict the breadth of the motor repertoire available to a patient for a specific tremor score assessed clinically, allowing treating physicians to make informed decisions on the timing and efficacy of their treatments.

The results show that even though core bradykinesia could be detected during fast movements and tremor during slow movements, neither symptom affected the performance of an activity of daily living that required dexterity in patients with mild to moderate ET. These results highlight the need to better understand the motor repertoire available to patients according to their tremor severity before determining the best treatment options.

### Acknowledgments

We would like to thank the volunteers from the Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal for their participation in the study and the medical doctor Sylvain Chouinard for his help with recruitment. We would also like to extend our acknowledgments to Elisabeth Mai Le and Noushin Roofigari for their help in data collection.

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