Movement Disorders
CLINICAL PRACTICE

RESEARCH ARTICLE

Physiology of Tremor Reduction by Putting the Hands Together in Essential Tremor

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ABSTRACT: Background: Essential tremor is a common movement disorder, characterized by 4–12 Hz tremor of the hands and arms that can affect many activities of daily living. It has been reported by patients that when performing tasks bimanually their tremor is reduced, but why this happens is unknown.
Objectives: We measured patients' tremors in different conditions when performed with 1 hand and 2 hands to observe if bimanual task performance changes the characteristics of the tremor.
Methods: A total of 10 patients with essential tremor participated in the study. Electromyographic electrodes were attached bilaterally to the wrist flexor and extensor muscles, and accelerometers were attached to the dorsum of the hands. For each condition, holding a cup, wingbeat, and extending both arms up, data were collected with a single hand and bimanually with the hands touching.
Results: When the hands were touching, there was a significant decrease in both accelerometric and electromyographic power at the tremor frequency. In addition, there was a decrease in coherence between accelerometer and electromyography on the same side. There was no change in the tremor frequency.
Conclusions: Tremor amplitude does decrease when the hands are together. Together, the characteristics underlying the decrease in tremor amplitude may indicate a decrease in power of the central oscillator driving the tremor, which we speculate is attributed to the differences in unimanual and bimanual motor control. However, given the small sample size, we note that future hypothesis-driven studies with an a priori power analysis will be required to further explore this phenomenon.

Essential tremor (ET) is a common movement disorder affecting the limbs during action, both posture and kinetic action.[1,2] The tremor associated with ET has a frequency in the range of 4 to 12 Hz and has been well characterized clinically and physiologically.[3] ET has central and peripheral components.[4] The central component arises from the firing of central oscillators and shows no change in the frequency with weight loading. This component has the greater power of the tremor. The peripheral component decreases in frequency with mass loading. It may be very small and/or entrained to the central component. The amplitude of ET has also been found to generally increase with age along with a decrease in tremor frequency.[5–7]

Tremor can impair the quality of life and limit the ability to perform daily activities. To restore function, multiple treatments for ET have been developed. Pharmacological options have been shown to decrease upper limb tremor amplitude by close to half,[8,9] but nearly half of patients eventually discontinue use of this option because of the lack of continued efficacy and/or adverse effects.[10] More invasive treatments, including deep brain stimulation and focused ultrasound, are often recommended to those who have exhausted pharmacological therapies. Peripheral nerve stimulators worn on the wrist aim to decrease tremor using a nonsurgical approach to decrease tremor and have shown improvements in tremor rating scale scores.[11] Modifying limb mechanics, such as weight loading of a tremulous limb,[12] orthotics to modify hand movements,[12] and modification of handheld devices by introducing a stabilizing counter movement,[13] have also been explored and show varying potential to decrease tremor.

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An interesting observation in patients with ET is that they naturally tend to put hands together to do different tasks, such as using a key, or holding a cup, because they find that this strategy reduces the tremor. This reduction could happen as a mechanical phenomenon secondary to left–right phase cancellation or there may also be a central phenomenon involving sensory integration. Whether there is an actual reduction of tremor amplitude and the mechanisms of that reduction have not been studied, and systematic exploration of this may provide further insight to the pathophysiology of ET and ultimately aid in the design of new therapies. Therefore, the objective of this study was to investigate the reduction in tremor amplitude produced by putting hands together in patients with ET and define whether the mechanism of this reduction is mechanically or centrally mediated.

Methods

A total of 10 patients with ET (6 women) gave their written informed consent, and the protocol was approved by the National Institutes of Health Institutional Review Board. The cohort had a mean age of 63 ± 16 years and an average disease duration of 39.8 ± 9.6 years. ET diagnosis was evaluated and confirmed by a movement disorder specialist according to the Movement Disorder Society new criteria.[1] Patients continued on their regular course of medications for the study, including tremor-reducing medications, and were restricted from consuming caffeine or alcohol 12 hours before the experimental session. Inclusion criteria included being diagnosed with ET, demonstrating a clear central tremor component during a tremor study performed by our group prior to this research study, being right-hand dominant per the Edinburgh Handedness Inventory, and having a clinician-rated score of at least 2 in 1 hand and 1.5 in the other hand during posture, wingbeat, or finger-to-nose testing as rated by The Essential Tremor Rating Assessment Scale (TETRAS).

Data were collected in 1 experimental session. Surface electromyography (EMG) was used to record from bilateral extensor carpi radialis (ECR) and flexor carpi radialis muscles, and triaxial accelerometers (ACCs) were attached to the back of each of the patient's hands. Recordings were performed during 4 different conditions. These included the patient holding a cup, wingbeat, and extending both arms up with hands in 2 different orientations, palm posture and forward posture (see Fig. 1). For each condition, data were collected while maintaining the condition's position with a single hand (left only, right only) and bimanually with the hands touching. For the wingbeat and cup hold conditions, the fingers were interlocked when touching. All recordings were for 60 seconds each and were completed with and without a 1-lb weight.

Both EMG and triaxial ACC data were collected using a Neuroscan Synamps 32-channel EEG system (Compumedics USA, Charlotte, NC) and analyzed offline using in-house Matlab scripts (version 2019a; Mathworks, Natick, MA). EMG and ACC data were bandpass filtered at 20 to 300 Hz and 2 to 20 Hz, respectively. ACC triaxial data were combined into a single axis by calculating the root sum square.[14,15] EMG data were rectified before further processing. Both EMG and ACC data were converted into the frequency domain using a Fast Fourier Transform to calculate the power in the tremor frequency for each patient. The maximum power in the tremor frequency range as well as the frequency value for that range were then recorded for each patient. Coherence of the left and right EMG, left and right ACC, and ipsilateral EMG-ACC for the left and right sides separately were also calculated using the Matlab neurospec 2.2 package. For statistical comparisons, the extensor muscles were used.

Statistical Analysis

A linear mixed model was performed separately using ACC power, EMG power, and ACC-EMG coherence (EMG-ACC left, EMG-ACC right) as outcome variables. For each model, we included condition (wingbeat, cup hold, arms extended), weight (no weight, with 1 lb), and touch (bimanual, unimanual) as fixed effects (independent variables). In addition, we included TETRAS score, handedness (right or left), and tremor dominance (ie, whether the tremor was larger in amplitude on the left or right side) as additional fixed effects. The model also included a random intercept for patient, which accounts for correlated observations within person.

A linear mixed model was also performed separately using ACC left/right coherence and EMG left/right coherence as outcome variables. For each model, we included condition, weight, and touch as fixed effects (independent variables). In addition, we included TETRAS score as an additional fixed effect. Patient identification was treated as a random effect. For all analyses, we assessed whether the results were robust to outliers. Criteria for outliers were observations that were greater than 3 standard deviations (SDs) higher than the mean ACC or EMG measurements. These outliers can be visualized when reviewing the raw data in the Supplementary Material.

Overall variable significance was shown using F statistics. Specific coefficient estimates were shown as well to determine the direction and magnitude of the effect. For individual within-condition comparisons, a Bonferroni correction was applied.

For plotting purposes, the ratio of the unimanual to bimanual data was taken for each condition (bimanual/unimanual). This improved the ability to visualize changes in the primary outcome measures. Specifically, any shift above or below 1 indicates an increase or decrease relative to the unimanual condition. Plots that show the raw power and coherence values can be found in the Supplementary Material.

Results

TETRAS Scores

Participants had an average TETRAS performance score of 29.25 (SD = 7.50) of a possible 72, with a higher score

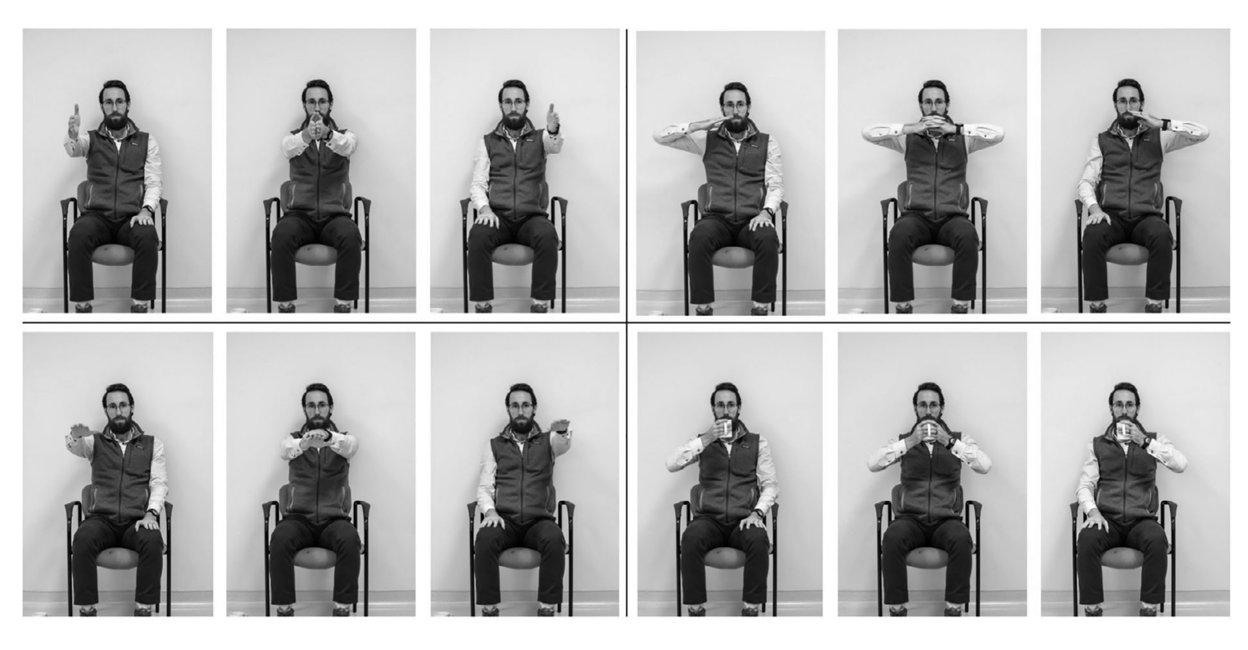

FIG 1. Images depicting each of the 4 conditions: palm posture (top left), forward posture (bottom left), wingbeat (top right), and cup hold (bottom right). For each condition, the middle left and right-most pictures depict the left-only and right-only unimanual tasks, respectively, and the middle image depicts the bimanual task.

indicating a larger tremor amplitude. When comparing the total scores for left and right sides, 8 of the10 patients were found to have larger amplitude tremor on the right side. See Table S1.

ACC Power

ACC power was significantly lower when the hands were touching relative to when they were not touching ($\beta = 82.654$; standard error [SE] $= 28.58$; $P = 0.004$). We also found a significant effect of TETRAS score, with increasing TETRAS score correlating with higher ACC power ($\beta = 78.826$; SE $= 10.59$; $P < 0.001$), but no effect of condition, weight, handedness, or tremor dominance. This analysis was robust to removing outliers in ACC power. See Figure 2 and refer to Figure S1 for raw values.

EMG Power

We found marginally lower EMG power, but not strictly significant at the 0.05 level, when the hands were touching relative to when they were not touching ($\beta = 0.159$; SE $= 0.084$; $P = 0.059$). Higher EMG power was related to the dominant hand ($\beta = -0.319$; SE $= 0.084$; $P < 0.001$), higher TETRAS score ($\beta = 0.158$; SE $= 0.058$; $P = 0.29$), and condition ($F = 7.217$; $P < 0.001$). For condition, subsequent statistical tests for condition revealed a significant difference in EMG power, with forward posture being significantly higher than bimanual cup hold ($\beta = 0.483$; SE $= 0.12$; $P < 0.001$) and wingbeat ($\beta = 0.453$; SE $= 0.12$; $P < 0.001$). We did not find a significant effect of tremor dominance or weight.

We found that with EMG power as the outcome variable, the statistical model was not robust to removing outliers of EMG power. With the removal of outliers, we found that EMG power was significantly lower when the hands were touching relative to when they were not touching ($\beta = 0.115$; SE $= 0.04$; $P = 0.001$). Similar to the analysis when not removing outliers, we did find significant effects of handedness ($\beta = -0.081$; $P = 0.021$), TETRAS score ($\beta = 0.069$; SE $= 0.03$; $P = 0.035$), and condition ($F = 11.541$; $P < 0.001$). For condition, subsequent statistical tests revealed significantly higher EMG power during cup hold compared with both the forward ($\beta = 0.249$; SE $= 0.05$; $P < 0.0001$) and palm ($\beta = 0.159$; SE $= 0.05$; $P = 0.006$) postures as well as higher power for the wingbeat condition relative to both the forward ($\beta = 0.227$; SE $= 0.05$; $P < 0.00001$) and palm ($\beta = 0.137$; SE $= 0.05$; $P = 0.031$) postures. In this analysis, we also found a significant positive correlation with weight ($\beta = 0.138$; SE $= 0.04$; $P < 0.001$), but no significant effect of tremor dominance. See Figure 2 and refer to Figure S1 for raw values.

ACC Frequency

To better understand the changes in the tremor amplitude, we also analyzed the frequency peak values for each patient to assess whether there was a shift in the frequency. ACC frequency was not significantly different when the hands were touching relative to when they were not touching. We did find that higher ACC

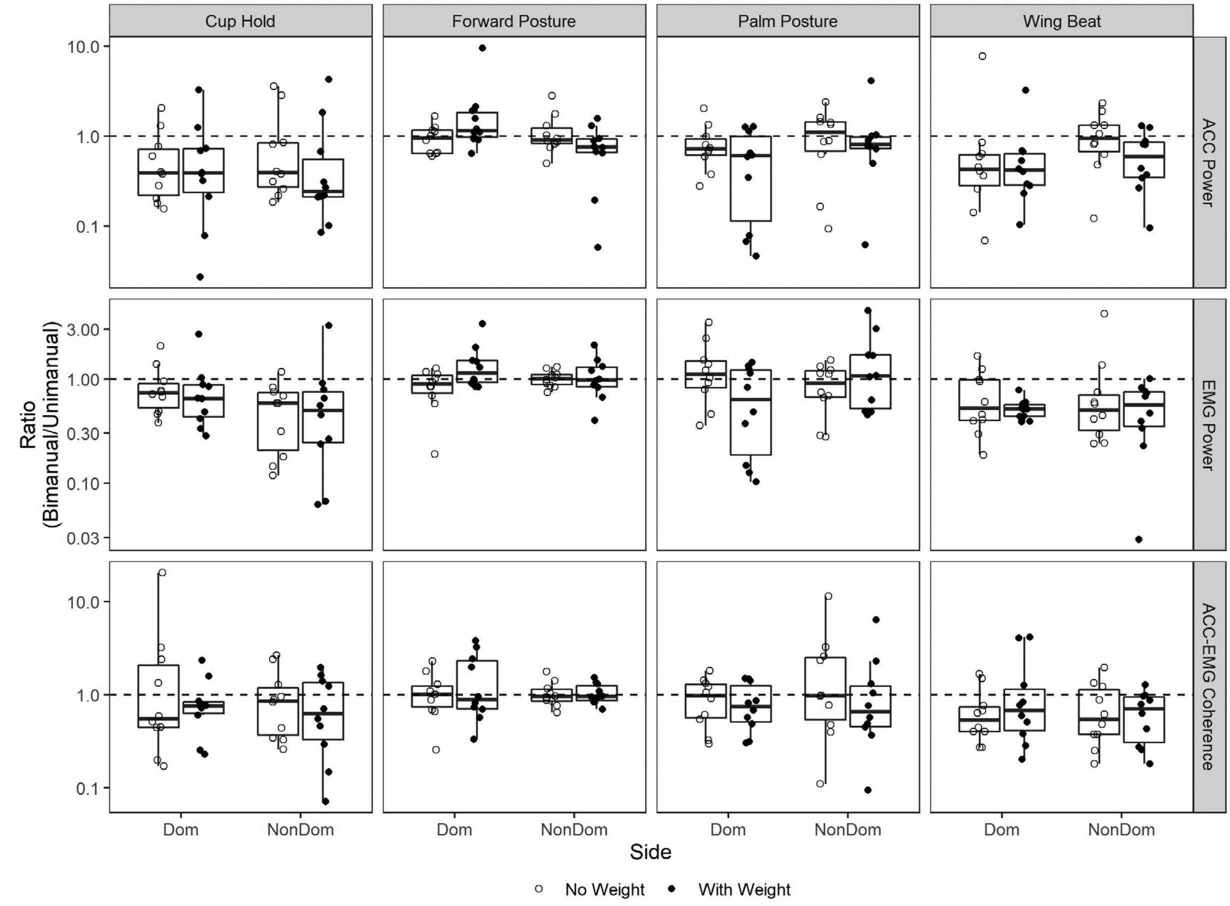

FIG 2. Accelerometer (ACC) power, electromyographic (EMG) power, and ipsilateral EMG-ACC coherence. For the ACC data, power of the root sum square of the 3 axes of the ACC in the tremor frequency were used for calculation. For the EMG data, power was calculated using the extensor muscle activity in the tremor frequency. For the EMG-ACC coherence analysis, values were calculated in the tremor frequency between the ipsilateral accelerometer signal and the extensor muscle signal. All calculations were performed for the 4 conditions, without weight, and with the addition of a 1 lb weight. For all plots, dominant (Dom) and nondominant (NonDom) sides are normalized (bimanual/unimanual), such that any shift above or below 1 indicates an increase or decrease in ACC power at the tremor frequency during the bimanual task relative to the unimanual task for each condition. The y axis is displayed in log format.

frequency was related to the nondominant hand ($\beta = 0.154$; SE $= 0.051$; $P = 0.003$) and condition ($F = 8.534$; $P = < 0.001$). Subsequent statistical tests for condition revealed significantly higher ACC frequency for palm posture compared with forward posture ($\beta = -0.235$; SE $= 0.073$; $P = 0.007$), cup hold ($\beta = 0.345$; SE $= 0.073$; $P < 0.001$), and wingbeat ($\beta = 0.275$; SE $= 0.073$; $P < 0.001$) conditions. We found no effect of tremor dominance, TETRAS score, or weight. This analysis was robust to removing outliers in ACC frequency. See Figure S2.

Coherence Between Ipsilateral EMG and ACC

Ipsilateral ACC-EMG (left ACC with left EMG; right ACC with right EMG) coherence was significantly lower when the hands were touching relative to when they were not touching ($\beta = 0.073$; SE $= 0.02$; $P = 0.001$). We also found a significant effect of condition ($F = 5.746$; $P = 0.001$). Subsequent statistical tests revealed significantly higher ipsilateral coherence in forward posture relative to wingbeat ($\beta = 0.121$; SE $= 0.03$; $P < 0.001$). We did not find a significant effect of handedness, tremor dominance, or weight. This analysis was robust to removing outliers in ACC-EMG coherence. See Figure 2 and refer to Figure S1 for raw values.

Coherence for Bilateral EMG and ACC

For both left/right ACC ($\beta = 0.354$; SE $= 0.03$; $P < 0.001$) and left/right EMG ($\beta = 0.068$; SE $= 0.02$; $P < 0.001$) coherence, we found that coherence is significantly higher when the hands are touching relative to when they are not touching. We also found a significant effect of condition (ACC: $F = 8.402$ [$P < 0.001$]; EMG: $F = 3.148$ [$P = 0.027$]). Refer to Figure S3.

For the ACC coherence analysis, subsequent comparisons revealed a significantly higher coherence in the cup hold ($\beta = -0.128$; SE $= 0.03$; $P = 0.003$), palm posture ($\beta = -0.141$; SE $= 0.03$; $P = 0.0008$), and wingbeat ($\beta = -0.173$; SE $= 0.03$; $P < 0.00001$) conditions relative to the forward posture condition. For the EMG coherence analysis, subsequent comparisons also revealed significantly higher coherence in palm posture versus forward posture conditions ($\beta = -0.067$; SE $= 0.02$; $P = 0.023$). We did not find a significant effect of weight or TETRAS score for either comparison. Both analyses were robust to removing outliers.

Discussion

Here we present data to quantify the clinical observation that bringing the hands together reduces tremor amplitude. We find that bimanual task performance does indeed reduce the tremor without a change in tremor frequency. Moreover, our data allow us to examine how the action of bringing the hands together acts to reduce tremor amplitude. We report that this action reduces both ACC power and EMG power. In addition, there is a decrease in the ipsilateral EMG-ACC coherence and an increase in the side-to-side ACC and EMG coherences. To our knowledge, this is the first study to describe how bimanual task performance decreases the amplitude of the tremor.

The Essential Tremor Rating Assessment Scale

The significance of TETRAS in the ACC and EMG analyses may be due to the fact that a higher tremor amplitude would likely be associated with an increased TETRAS score as well as higher power on both EMG and ACC signals. We believe that this is likely the case, which is also supported by the lack of significance of this variable in the coherence analyses. If TETRAS score had an influence on the change of tremor characteristics between the unimanual and bimanual conditions, we would have expected coherence to be sensitive to TETRAS score.

Handedness

The analysis of EMG power includes a significant effect of handedness, namely, that EMG power was higher for the dominant side relative to the nondominant side. We believe that this makes sense given that on average there was a higher TETRAS score on the right side relative to the left. The patients who participated were all right-handed, and thus their dominant hand had overall more tremor. Importantly, we did not find a significant effect of tremor dominance. We believe that this suggests that the underlying changes that relate to the decrease in tremor are not unique to the tremor dominant and nondominant sides. Thus, the change seems less likely to be driven by the amplitude of the tremor.

Weight

The analysis of EMG power shows—during the analysis without outliers—a significant effect of weight. We believe that this makes sense as this means that there was lower EMG power in the condition with the 1-lb weight. This suggests that at least some of the dampening of the tremor could be due to a change in the peripheral component. By changing the limb mechanics by touch, this component may show a decrease.[16] However, we also note that there is a nonsignificant effect of weight in any other outcome measure, and thus this effect may also be driven by the removal of outliers.

Condition Breakdown

The lack of significant effect of condition for the change in ACC power—and no significant change in tremor frequency—suggests that the central component is more sensitive to the effect of using 2 hands. The rationale here is that we see a decrease that is unchanged by the position of the upper limbs (ie, a change in condition). In contrast, the EMG power is sensitive to condition, which may suggest that either the position of the arms or the corresponding EMG activity required to hold the given position affects how much performing a task with 2 hands decreases the tremor amplitude. The specific condition comparisons reveal that EMG power is significantly larger for the forward and palm postures, which would support this.

Given that the majority of the differences in the conditions across the various comparisons were between forward/palm posture and cup hold/wingbeat conditions, we speculate that these differences manifest from the proximal versus distal nature of the tasks. Forward and palm posturing extend the arms, may require more muscle activation to maintain, and also may be contaminated by other movements. An alternate explanation is that with the cup hold and wingbeat conditions, the fingers were interlocked, making a stronger connection between the 2 sides. This does not explain the differences seen in the coherence data for palm posture versus forward posture, although this difference is only significant in 1 comparison. This may be attributed to the change in the angle of the shoulder joint or the muscle groups involved in maintaining the posture for each of the conditions.

Phase Considerations

There was a clear change in the limb mechanics going from the not-touching to touching conditions from what was 2 separate objects into what might be considered 1 larger tremulous object. The decrease in tremor amplitude is unlikely to have risen from a phase cancellation of the tremulous limbs touching. It is common for ET tremor frequency to be similar in both limbs outside of the early stages of the disease, but for a phase cancellation to happen, the frequencies would have to be nearly inverse.[17] Although the frequencies will be similar, the chances are low that they would be perfectly aligned to cancel each other out. If the frequencies were different and simply added, then there would be periodic low and high points (beats), and this was not present (see Fig. S4).

Perhaps the biggest argument against phase cancellation is that there were decreases in both EMG and ACC powers, which supports a change in the central oscillator. With a phase cancellation effect, one would expect to see only a decrease in ACC power.

Change in Central Oscillator

Likely the most important finding, and the most surprising, is that the power of the EMG decreased when the 2 hands were coupled. To date, the oscillators of the 2 upper limbs are thought to be independent and believed not to be significantly influenced by afferent input. However, the decrease in EMG power suggests that putting the hands together does have at least some influence on the oscillators and may in fact alter the motor command. This would indicate that although each hand is receiving most of the motor commands from the contralateral motor cortex, when both hands act together for a common goal there may be a place in the brain where the activity of both hands is also coordinated. There is some evidence that this is done by the dominant motor cortex, which shows less disinhibition than the nondominant side when the subject is involved in a bimanual common goal task. This is in contrast to a bimanual dual-goal task, in which case both sides show the same level of disinhibition.[18] This control is likely coordinated through interhemispheric interactions[19] as well as the ipsilateral uncrossed corticospinal pathway.[20]

Based on this previous work and our current findings, we hypothesize that the common goal dual-task control mechanism may play a role in dampening the tremor in ET when both hands engage in a common goal. In fact, in common goal tasks, there is a "give and take" interaction between both limbs, with the force of 1 arm increasing while the force of the other arm decreases to reach a goal.[18] Those commands may "overwrite" the tremor outputs, explaining the observed phenomenon.

Conclusions

We have shown that performing a bimanual task does change the physiological characteristics of the tremor and therefore is an effective way to reduce tremor amplitude in ET. This information gives us a better understanding of the physiopathology of ET and may provide guidance for the development of therapies for this syndrome. One limitation to our study is that we studied only static positions, which may not be as representative of more common tasks of daily living, such as drinking from a cup or using keys. Future work could investigate whether we see similar changes during action. A second limitation of our study is that we had a small sample size. We note that although this does not impact the novelty of our findings, we believe that future studies will be required to explore whether the change in physiological characteristics of tremor during bimanual tasks is truly linked to a change in the central oscillator.

Author Roles

1. Research Project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

P.M.: 1B, 1C, 2A, 2C, 3A, 3B
F.V.: 1B, 1C, 2A, 2C, 3A, 3B
T.O.: 1B, 1C, 3A
G.N.: 2A, 2B, 2C, 3B
I.K.: 1A, 1B, 1C, 3B
D.H.: 1A, 1B, 1C, 2A, 2C, 3B
D.E.: 1A, 1B, 1C, 2A, 2C, 3B
M.H.: 1A, 1B, 1C, 2A, 2C, 3B

Disclosures

Ethical Compliance Statement: Data acquisition were in accordance with our institutional ethics committee—the Combined Neurosciences National Institutes of Health Institutional Review Board—and were in line with the Declaration of Helsinki. The patients presented in this manuscript signed a written consent for the case, and all procedures were verbally described to the patient before signing. All authors have read and approved this manuscript. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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Supporting Information

Supporting information may be found in the online version of this article.

Figure S1 Raw accelerometer (ACC) power, electromyographic (EMG) power, and ipsilateral accelerometer–electromyography coherence values for unimanual and bimanual tasks. For the ACC data, power of the root sum square of the 3 axes of the ACC in the tremor frequency was used for calculation. For the EMG data, power was calculated using the extensor muscle activity in the tremor frequency. For the EMG-ACC coherence analysis, values were calculated in the tremor frequency between the ipsilateral accelerometer signal and the extensor muscle signal. All calculations were performed for the 4 conditions, without weight and with the addition of a 1 lb weight. For all plots, unshaded circles represent raw values that were greater than 3 standard deviations from the mean.

Figure S2 Tremor frequency values of individual subjects. Accelerometer data were converted into the frequency domain using a Fast Fourier Transform to calculate the power in the tremor frequency for each patient. The frequency value with the highest power was recorded for unimanual and bimanual tasks of each condition. This is shown for all conditions without (top row) and with (bottom row) the addition of a 1 lb weight.

Figure S3 Accelerometer and electromyographic coherence for unimanual and bimanual tasks. Coherence values in the tremor frequency were calculated between the left and right accelerometer signals and the left and right extensor muscles. These calculations were performed for all 4 conditions without weight and with the addition of a 1 lb weight.

Figure S4 Raw accelerometer traces showing an example of changes in the raw signal during unimanual and bimanual task performance during the cup hold condition.

Table S1 Summary of patient demographics and scores for The Essential Tremor Rating Scale (TETRAS).