RESEARCH ARTICLE

Defining the Rhythm: Developing a New Method to Describe Tremor and Myoclonus

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ABSTRACT: Background: The hallmark feature of tremor is rhythmicity, which can be quantified using power spectral density (PSD) analysis. However, tremor exhibits considerable variability, ranging from highly regular to more irregular patterns. Similarly, rhythmicity in myoclonus varies, but it typically manifests as arrhythmic jerks.
Objectives: To develop PSD-based measures of movement regularity for the classification of tremor and myoclonus.
Methods: Electromyography data from 153 patients were analyzed retrospectively, including orthostatic tremor (OT) (n = 36), essential tremor (ET) (n = 40), hand dystonic tremor (DT) (n = 42), and limb cortical myoclonus (n = 35). Five PSD analysis-derived variables were assessed: peak prominence, peak-to-broadband power ratio, peak frequency, peak width, and harmonics. Discriminant analysis evaluated classification accuracy across groups.
Results: Peak prominence was highest in OT and higher in ET than DT or myoclonus. Peak-to-broadband power ratio showed similar trends. Peak frequency differed across groups, with myoclonus highest and OT exceeding ET and DT. Peak width was larger in myoclonus and, to a less extent, in DT compared with ET. Harmonics were greater in OT and ET compared with DT and myoclonus. Discriminant analysis correctly classified 86.3% of cases, with overlap between ET and DT. Receiver operating characteristic (ROC) curve analysis for peak prominence and width demonstrated high classification accuracy between ET and DT.
Conclusions: Our findings represent a promising step toward establishing objective, PSD-based measures for the classification of tremor and myoclonus. These tools could enhance diagnostic accuracy and deepen insights into these disorders. © 2025 The Author(s). *Movement Disorders* published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society.

Key Words: essential tremor; orthostatic tremor; dystonic tremor; myoclonus; power spectral density analysis

Tremor is defined as an involuntary, rhythmic, oscillatory movement of a body part.[1] Its hallmark feature, rhythmicity, distinguishes it from other hyperkinetic movement disorders, providing a valuable diagnostic advantage. These regular muscle discharges can be readily identified using basic electrophysiological techniques such as surface electromyography (EMG). However, tremor rhythmicity may range from highly regular to somewhat irregular.[2-4] While regularity is a key feature of tremor, it can also be seen in myoclonus. Certain forms of cortical and high-frequency myoclonus may exhibit rhythmicity that visually resembles tremor, complicating the clinical distinction between the two conditions.[5] Aside from these exceptions, myoclonus is typically considered the opposite of tremor, as it is usually characterized by arrhythmic jerks.[5,6]

Despite advances in understanding tremor and myoclonus, the translation of neurophysiological concepts

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into clinical practice remains limited. A key challenge lies in identifying neurophysiological characteristics that accurately reflect observable rhythmicity. The absence of standardized, objective metrics has led to imprecise clinical terminology. For instance, terms such as "jerky" are often used to describe "irregular" tremor—a description that may appear contradictory. This term is frequently applied to dystonic tremor (DT), yet it introduces ambiguity, as "jerk" is synonymous with myoclonus. Describing tremor as "jerky" could imply the presence of brief, abrupt muscle contractions (ie, myoclonus) superimposed on the tremor, further complicating differentiation between these phenomena.

A well-established method for quantifying movement rhythmicity, as recorded via EMG or accelerometery, is the estimation of power spectral density (PSD) using the fast Fourier transform or related techniques. The presence of a peak in the PSD is often regarded as a reliable indicator of rhythmicity; however, no objective definition of a PSD peak currently exists.[4] When visually apparent, peak frequency can aid in diagnosing tremors with distinct frequencies, such as orthostatic tremor (OT) and essential tremor (ET).[1,7] Conversely, for DT or myoclonus, the presence of a PSD peak is less well-studied and may be ambiguous or absent.

Beyond identifying peaks, more sophisticated PSD-derived measures remain underexplored.[8,9] One such feature, peak width (also termed full width at half maximum—FWHM—and half-power bandwidth in previous literature[4,10]), reflects the range of frequencies contributing to the tremor signal and it has been proposed to distinguish ET from ET-plus and DT.[11,12] A broader peak width may correspond to greater irregularity observed during visual inspection, though this relationship has yet to be systematically investigated. Other potential PSD features, such as the prominence of peak activity relative to the underlying broadband PSD, could offer valuable insights. In theory, more regular movements would exhibit less contamination from non-rhythmic activity, resulting in a more prominent peak. Additionally, a regular movement pattern may be inferred from the presence of harmonics at integer multiples of the fundamental tremor frequency. Strong synchronization of motor unit spike trains would enhance tremor regularity, resulting in pronounced harmonics in both the neural drive and the EMG signal.[13]

To test these concepts and develop objective measures of movement regularity, we analyzed four distinct conditions: OT, characterized by extreme regularity and a clear PSD peak; myoclonus, typically irregular; ET, noted for its regularity; and DT, considered less regular than ET and often described as "jerky," though still classified as tremor. We extracted PSD-derived measures across these conditions and demonstrated that they form a spectrum of regularity. Furthermore, these measures, when combined, effectively differentiate between the conditions.

Methods

Patients

Data from 153 patients who underwent tremor or myoclonus EMG recording, at UCL Queen Square Institute of Neurology, London, UK, between 2019 and 2023 were retrospectively collected and analyzed. Medical records for all participants were systematically reviewed to confirm the final diagnosis (further details are provided in Data S1). The cohort comprised 36 patients with OT (28 female, mean age 65.4 ± 9.7 years, mean disease duration 6.8 ± 5.6 years), 40 with ET (22 female, mean age 64.6 ± 8.5 years, mean disease duration 9.5 ± 6.5 years), 42 with hand DT (25 female, mean age 58.7 ± 9.5 years, mean disease duration 8.2 ± 5.4 years), and 35 with upper limb cortical myoclonus (20 female, mean age 45.8 ± 18.5 years, mean disease duration 5.4 ± 4.2 years), diagnosed according to the current criteria.[1,14] The study protocol was approved by the local institutional review board and conducted in accordance with the Declaration of Helsinki.

EMG Recording and Analysis

EMG recording is detailed in Data S1. Examples of raw EMG traces are provided in Figure 1A.

Signal analysis was performed in MATLAB (Version 2020a, MathWorks Inc., Natick, MA, USA). For all EMG recordings, PSD was calculated using Welch's periodogram with a Hann window twice the length of the sampling rate and a frequency resolution of 0.1 Hz. From the PSD, a peak of activity was identified by selecting the maximum value within predefined frequency ranges for each condition: 1–20 Hz for OT, 1–12 Hz for ET and DT, and 1–48 Hz for myoclonus, excluding harmonics (see later). These ranges were chosen based on the expected peak frequencies for each group while avoiding high-amplitude, non-tremor-related EMG activity from being erroneously selected. The peak detection process used MATLAB's 'findpeaks' function and was visually confirmed.

Once a peak was identified, five key variables were extracted. The first variable was peak prominence, calculated as the ratio of peak power to the underlying EMG power at the same frequency. The underlying EMG power was estimated by interpolating the PSD after excluding the peak and surrounding values using a cubic function, then selecting the PSD value at the peak frequency from this interpolated spectrum. The second variable was the peak-to-broadband power ratio (PB ratio), where broadband power was defined as the average PSD between 1 and 48 Hz (excluding the peak and
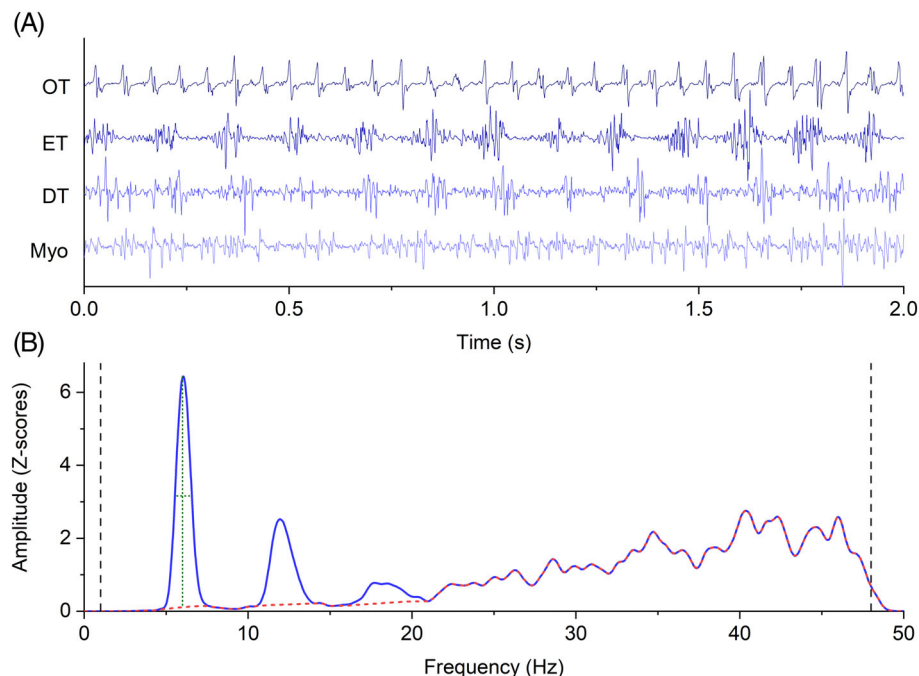
FIG. 1. (A) Electromyography (EMG) traces of the four conditions explored, showing maximum rhythmicity in orthostatic tremor (OT) (upper row), progressively decreasing in essential tremor (ET), dystonic tremor (DT), and myoclonus (Myo). (B) Example of power spectral densities (PSDs) from a patient with ET and graphical representation of features used to extract the main variables. Black vertical dashed lines represent the range (1–48 Hz) from which broadband EMG activity, used to calculate the PB ratio, was selected. The dashed red line indicates the PSD where activity from harmonics and peak frequency was interpolated to measure broadband activity and peak prominence (vertical dotted green line). The horizontal dotted green line represents peak width. See article text for further information. [Color figure can be viewed at wileyonlinelibrary.com]

harmonics) using the same interpolation approach. The third variable was the peak frequency itself, while the fourth was the peak width at half prominence.[11,12] Finally, the fifth variable was the number of harmonics, defined as regions of the PSD at frequencies that were integer multiples of the peak frequency, where power exceeded the underlying EMG power by at least three standard deviations, as determined using the interpolation method. A graphical explanation of these variables is provided in Figure 1B. To investigate the possible contribution of voluntary muscle activity associated with posture to the PSD observed in myoclonus, we compared these data to PSDs obtained from surface EMG in 72 healthy subjects, as detailed in Data S1.

Statistical Analysis

Statistical analyses were carried out with SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Equality of covariance matrices was tested by means of Box's test. A multivariate analysis of variance (MANOVA) was performed to investigate simultaneous differences across the four different patient groups (OT, ET, DT, myoclonus), which were included as a fixed factor. Dependent variables, each having four levels corresponding to the four patient groups, included peak prominence, PB ratio, peak frequency, peak width, and number of harmonics.

To investigate differences in individual variables between groups, the MANOVA was followed by five univariate between-group analyses of variance (ANOVAs). For variables showing statistically significant effects, Bonferroni-corrected post hoc comparisons were conducted to identify specific group differences. Post hoc tests included t-tests for peak prominence, PB ratio, peak frequency, and peak width, while the Mann–Whitney U test was applied for the number of harmonics.

Finally, a discriminant analysis was performed to assess whether a linear combination of the five outcome variables could effectively discriminate among the four patient groups. Prior probabilities for group classification were based on the observed group sizes.

Results

A graphical summary of the PSDs and their peak features is provided in Figure 2. Box's test for equality of covariance matrices was not significant ($P = 0.18$), and Levene's test for equality of error variances showed no significant results for any of the tested variables (all $P > 0.05$).

Using Pillai's trace, the MANOVA showed a significant effect of "group" ($F_{15,441} = 35.864$, $P < 0.001$). The one-way ANOVAs all showed significant main
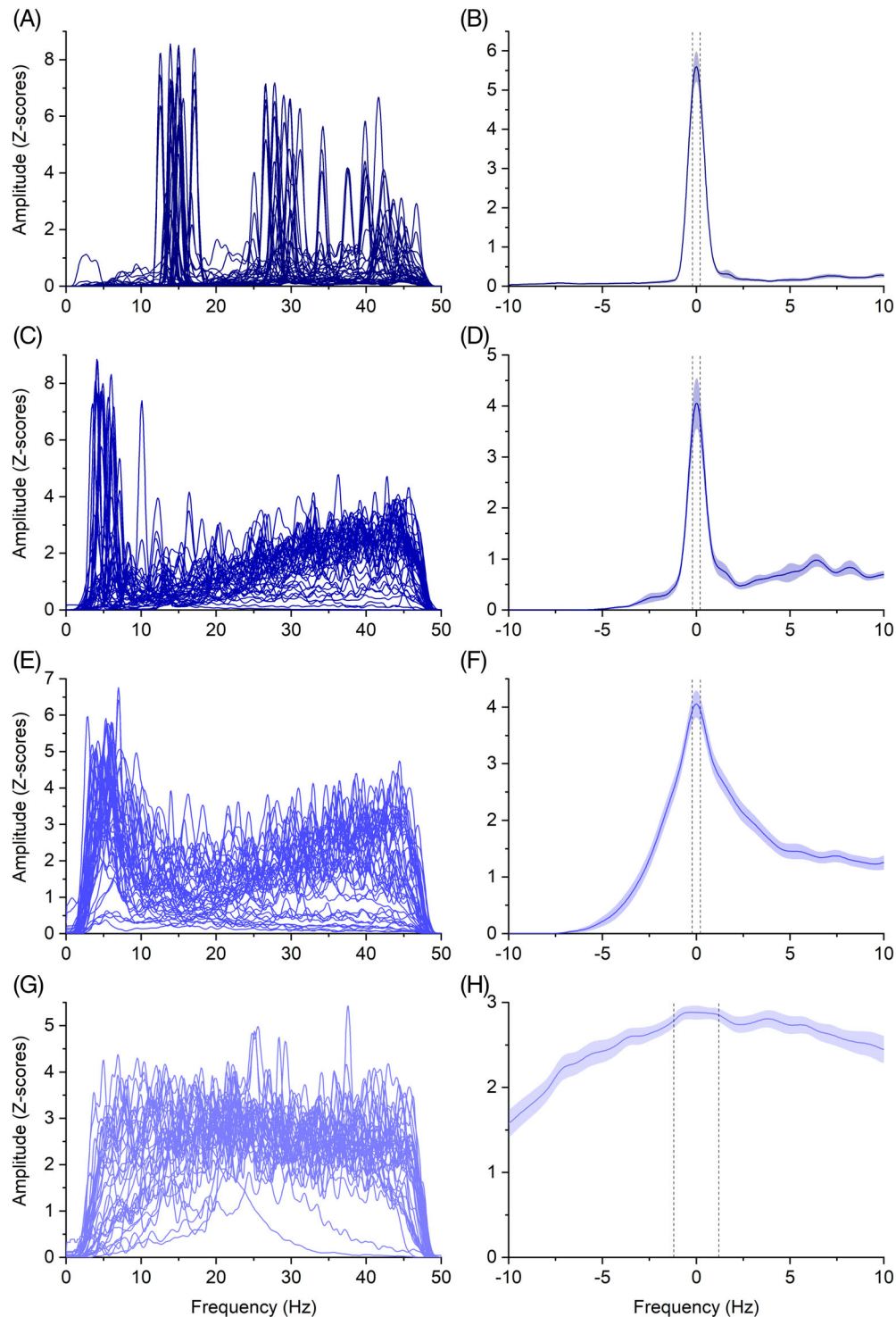
FIG. 2. In (A, C, E, G) power spectral densities (PSDs) from all subjects from orthostatic tremor (OT), essential tremor (ET), dystonic tremor (DT), and myoclonus patients are shown, respectively. To facilitate visual comparison, voltage values were converted into Z-scores and offsets were subtracted. (B, D, F, H) show frequency-centred peaks of activity for OT, ET, DT, and myoclonus, respectively. OT exhibited narrower and more pronounced peaks in the PSD compared with other conditions. In contrast, the PSD peaks for ET, DT, and myoclonus became progressively broader and less prominent relative to surrounding EMG activity. Black dashed lines represent the standard error of the mean for frequency and shaded areas represent the standard error of the mean for the signal. [Color figure can be viewed at wileyonlinelibrary.com]

effects of factor "group" (peak prominence: $F_{3,149} = 59.351$, $P < 0.001$; PB ratio: $F_{3,149} = 31.115$, $P < 0.001$; peak frequency: $F_{3,149} = 141.768$, $P < 0.001$; peak width:

$F_{3,149} = 52.556$, $P < 0.001$; harmonics: $F_{3,149} = 77.810$, $P < 0.001$). Post hoc comparisons on peak prominence showed significantly larger values in OT compared with

the other groups (all $P < 0.001$). This was also the case for ET compared with DT and myoclonus ($P = 0.001$ and $P < 0.001$), while the difference between DT and myoclonus was not significant ($P = 0.686$), albeit the first showed larger values (Fig. 3A). Post hoc tests on PB ratio showed similar but weaker results, with OT having significantly larger values than ET, DT, and myoclonus (all $P < 0.001$), while the same variable was not significantly different in the last three groups (Fig. 3B). The four groups showed marked differences in frequency of peak activity, with myoclonus being significantly larger than the other three (all $P < 0.001$) and OT showing larger values than ET and DT (both $P < 0.001$). Conversely, the same variable was not significantly different when comparing ET and DT ($P = 0.951$) (Fig. 3C). Peak width was significantly larger in myoclonus compared with OT, ET, and DT (all $P < 0.001$) and significantly larger, albeit to a less extent, in DT compared with ET ($P = 0.023$) and OT ($P = 0.019$). The same variable, however, did not yield statistically different values when comparing OT and ET ($P = 0.945$) (Fig. 3D). Post hoc comparisons on the number of harmonics showed a significantly larger value in OT, compared with the other three groups (all $P < 0.001$). The same was true when comparing ET with DT and myoclonus (both $P < 0.001$), while there was no significant difference between the last two groups (p > 0.05), as both groups showed no harmonics (Fig. 4).

Data S1 and Figure S1 present the PSDs of healthy subjects and patients with myoclonus, together with their statistical comparison. The finding confirms that the observed peaks in myoclonus PSDs below ~39 Hz are not solely due to postural activation.

Discriminant analysis revealed three discriminant functions (DFs), each significantly separating the four patient groups ($P < 0.001$, < 0.001, and 0.002, respectively). Variance explained and canonical R^2 were 63.3%/0.91, 35.3%/0.853, and 1.4%/0.306 for DF1, DF2, and DF3, respectively. In combination, these functions significantly differentiated the four groups ($A = 0.043$, $\chi^2(15) = 465.343$, $P < 0.001$). The correlations between outcomes and the DFs revealed that frequency and width significantly loaded on DF1 ($r = 0.719$ and 0.443, respectively). By contrast, peak prominence and harmonics loaded significantly on DF2 ($r = 0.645$ and $r = 0.702$, respectively), while PB ratio significantly loaded on DF3 ($r = -0.674$). Details about single-subject scores are depicted in Figure 5. When classified according to the DFs, 86.3% of original cases were correctly identified, specifically 97.2% of OTs (35/36, 1 identified as ET), 60% ETs (24/40, 16 identified as DTs), 100% of DTs and 97.1% myoclonus (34/35, 1 identified as DTs). The difficult discrimination between ET and DT might be due to some overlapping features, such as peak frequency and PB ratio, which
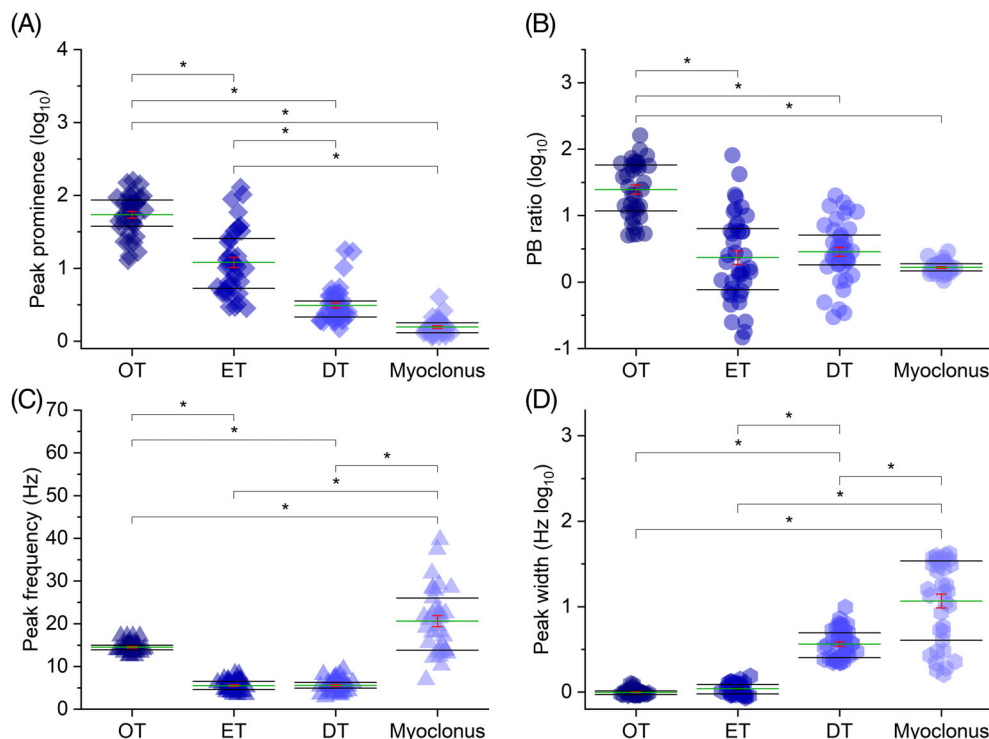

FIG. 3. (A–D) Post hoc comparisons for peak prominence, peak-to-broadband power ratio (PB ratio), peak frequency, and peak width, respectively, for the four patient groups investigated (orthostatic tremor [OT], essential tremor [ET], dystonic tremor [DT], and myoclonus). Brackets with asterisks indicate statistically significant comparisons. To facilitate visual comparison across the four groups, y-axis values have been converted into $\log_{10}$ values for peak prominence, PB ratio, and peak width. Raw values are summarized in Table S1. [Color figure can be viewed at wileyonlinelibrary.com]
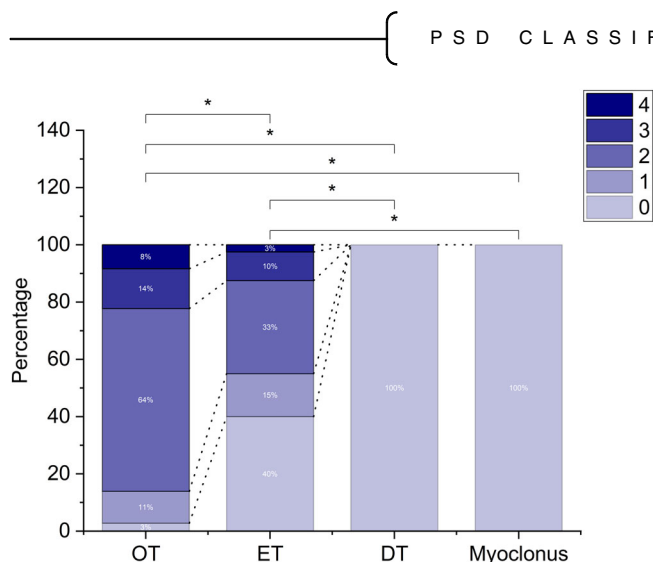
FIG. 4. Percentages of cases in each group (orthostatic tremor [OT], essential tremor [ET], dystonic tremor [DT], and myoclonus) where variable numbers of harmonics (ranging from 9 to 4) were present. Brackets with asterisks indicate statistically significant comparisons. Black dashed lines join areas in the stacked bars corresponding to the same number of harmonics. Overall, OT showed the largest number of harmonics, followed by ET. No harmonics were observed in the DT and myoclonus recordings. [Color figure can be viewed at wileyonlinelibrary.com]
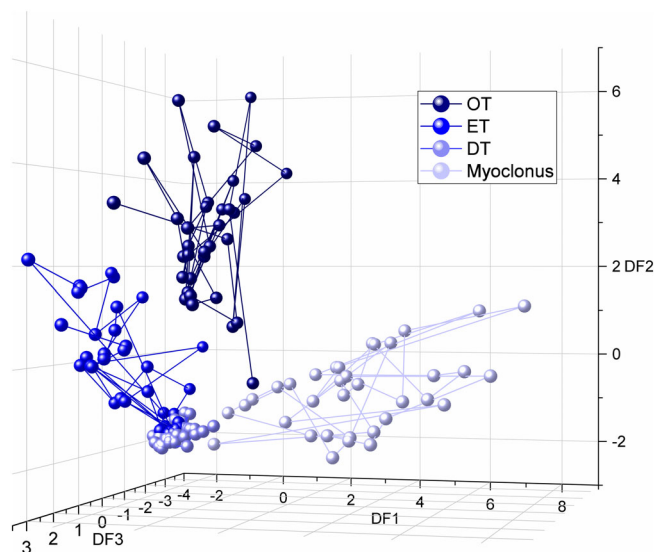

FIG. 5. Clustering of power spectral density (PSD) features obtained in orthostatic tremor (OT), essential tremor (ET), dystonic tremor (DT), and myoclonus according to the three discriminant functions (DF1, DF2, DF3), represented by three different axes. Overall, DF1 and DF2, which explained the largest variance, could easily discriminate OT and myoclonus from other groups, while ET and DT were the groups most difficult to separate. See article text for details. [Color figure can be viewed at wileyonlinelibrary.com]

did not show statistically significant differences (Fig. 3) and may have decreased the accuracy of the discriminant analysis. Therefore, we further explored the possibility of discriminating ET and DT by focusing on spectral features showing statistically significant differences between these two groups (peak prominence and

peak width). To this end, we calculated receiver operating characteristic (ROC) curves separately for both variables. This analysis, shown in Figure S2, yielded high classification accuracy for both variables (area under the curve [AUC] 0.905 for peak prominence and 0.963 for peak width). The optimal cut-offs were 6.53 for peak prominence (sensitivity 87.5%, specificity 83.3%) and 1.76 Hz for peak width (sensitivity 92.8%, specificity 92.5%). Moreover, to further explore the discriminative value of peak width between tremor and myoclonus, we performed a post hoc ROC analysis comparing DT and myoclonus (see Data S1), as these two groups showed the closest overlap in peak width distribution. The AUC was 0.78, indicating moderate/good discriminative ability (Fig. S3). The optimal cut-off value for peak width was 2.21 Hz. This threshold yielded a sensitivity of 100% and a specificity of 88.57%.

Discussion

In this study, we analyzed five measures extracted from the PSD: peak prominence, PB ratio, frequency of peak activity, peak width, and number of harmonics. While the individual measures demonstrated varying results, they collectively highlighted significant differences among the tremor subtypes (OT, ET, DT) and between these and cortical myoclonus, aligning with their distinct phenomenological characteristics. Furthermore, discriminant analysis combining all outcome measures successfully separated the four patient groups, with the exception of ET and DT. However, these two groups were more effectively distinguished using peak prominence and peak width, underscoring the utility of specific spectral features for finer diagnostic differentiation.

Peak Prominence and PB Ratio

The peak prominence of the PSD reflects how distinctly the most prominent signal (the peak) stands out from the background activity at a specific frequency. The PB ratio is a similar concept, but it compares the peak power to a broader measure of background activity, encompassing the average power across the entire frequency range considered (1–48 Hz). This allows the peak power to be assessed relative to the overall EMG activity, making it possible to distinguish tremor-related muscle activity (the peak) from background noise due to non-specific muscle activity. The group with the highest prominence was OT, which showed a statistically significant difference compared with the others. Conversely, the ET peak was significantly more prominent than both DT and myoclonus, while DT and myoclonus did not differ significantly, though DT displayed a larger value. The PB ratio demonstrated a similar pattern of results, albeit weaker, since only OT

showed statistically significant differences with the three other groups (Fig. 3A,B).

These measures are relatively new, as only a few studies have applied similar approaches in this context.[8] High synchronization among motor units at the tremor frequency has already been demonstrated in ET.[15] However, increased peak power is also observed in the "voluntary drive frequency band," attributed to voluntary contraction during posture holding. Additionally, peripheral feedback loops can influence motor unit discharge during tremor.[16] This indicates that background activity at frequencies matching or differing from the tremor frequency may be related to voluntary movements, afferent inputs, or other EMG activity unrelated to tremor.

Our findings suggest that tremor in ET and OT is driven by highly synchronized motor unit discharges, as previously indicated.[7,15,16] This synchronization results in a tremor-related peak in the PSD that is much larger than the EMG activity associated with posture. In contrast, in DT, dystonic activity, and lower tremor rhythmicity, likely reduces the gap between the peak and background noise. This suggests that only part of the dystonic activity follows a regular pattern contributing to tremor, while irregular and continuous dystonic activity persists in the background. Lastly, the findings in myoclonus align with expectations: a clear visible peak is absent, with irregular muscle discharges creating high noise levels and either a minimal or non-existent peak. Interestingly, DT and myoclonus did not differ in terms of peak prominence. This finding may reflect a shared feature: a modest contrast between peak frequency power and background EMG activity. In DT, this could arise from the overlap of tremulous and irregular dystonic bursts, along with voluntary postural activity (see Fig. S2). A similar background pattern may apply to myoclonus; however, in this case, low peak prominence may also reflect a flatter spectral profile (due to lower or absent rhythmicity), where the peak frequency is closely surrounded by nearby frequencies of similar power. This would also explain the broader peak width in this group.

Beyond the individual findings for each condition, we have demonstrated that these two measures—particularly peak prominence—can be used to reliably identify a PSD peak, as opposed to relying on visual inspection. Given that it answers the question "Is there a peak?", this measure could become a valuable tool for precisely defining a tremulous disorder as tremor.

Frequency of Peak Activity

This measure identifies the predominant frequency at which muscle discharges occur. As expected from previous studies,[1,11,12] there is no significant frequency difference between ET and DT, while OT shows a significantly higher frequency (Fig. 3C).[1] Interestingly, myoclonus results indicate not only a wide frequency range (8–40 Hz), but also the presence of very high frequencies. The most remarkable aspect is that these frequencies overlap with the beta frequency band, which is typically associated with high corticomuscular coherence observed in cortical myoclonus.[6,17,18]

Peak Width

The width of the peak activity defines the range of dominant frequencies. A wider peak width suggests that muscles fibers can synchronously discharge across multiple frequencies rather than a single one, resulting in a broader, "bell-shaped" peak in the PSD rather than a sharp peak. This measure reflects the range of frequencies that contribute, with varying power, to tremor or myoclonus, offering insight into whether the phenomenon is driven by a single or multiple oscillatory activities, or a single oscillator influenced by interfering noise that alters the tremor frequency.

Our results indicate that myoclonus exhibits a larger peak width, likely due to irregular, multifrequency muscle discharges typical of arrhythmic phenomena, where no single dominant frequency emerges (Fig. 3D). A similar, broad peak width with more distinct peak prominence has been observed in cortical tremor, a form of rhythmic cortical myoclonus resembling tremor but sharing the same pathophysiology as cortical myoclonus.[5,19]

DT also shows a broader peak width compared with ET and OT (Fig. 3D), suggesting higher frequency variability in DT. This characteristic has been proposed based on clinical observations of DT's jerkiness and has been previously assessed using other measures, such as cycle-to-cycle frequency variability in the time domain or the tremor stability index (TSI), which captures frequency variability by examining the interquartile range of instantaneous frequency changes.[12,20,21] Thus, the broader peak width observed in DT complements TSI results, indicating that both frequency-domain and time-domain measures consistently reveal increased variability in DT compared with other tremor types.

Comparable results to ours were achieved using similar measures of tremor power, namely half-width power (HWP) and FWHM.[11,12] The former quantifies tremor power by measuring the area under the curve between the rising and falling edges of the peak at half-peak power, while the latter provides a measure of frequency, specifically capturing the range of frequencies involved,[12] which corresponds to our peak width. Similar to our results, FWHM was significantly higher in DT compared with ET, while HWP was lower.[12] This finding suggests the presence of multiple oscillators with irregularities in both amplitude and frequency in DT or that superimposed dystonic contractions could disrupt the rhythmicity of the tremor.

In conclusion, the width of peak activity provides a measure of "regularity," answering the question: "Is this tremor or myoclonus more or less regular?". This measure could be particularly valuable, as studies suggest that more regular tremors may respond better to non-invasive central stimulation compared with irregular ones.[2,3,22]

Number of Harmonics

The presence of harmonics has been observed in the PSD of tremor signals, particularly in studies on tremor in PD.[23-25] The functional significance of these harmonics remains under debate. It is possible that they reflect true physiological phenomena, as previous studies have found significant corticomuscular and corticocortical coherence at double the tremor frequency in PD and voluntarily simulated tremor.[24,25] This interpretation is further supported by the observation of different scalp topography of corticomuscular coherence for the basic and first harmonic frequencies in PD tremor.[26] While not directly tested here, this would support the presence of different neural generators in OT and ET, which could help differentiate them from DT and myoclonus, similar to what was reported previously between ET and PD tremor.[27] Another possible explanation is that harmonics arise from sensory feedback from mechanoreceptors activated by muscle contractions associated with tremor.[24] According to this view, the clearer and more numerous harmonics found in OT and ET in the present study may be a result of stronger and more synchronous tremor discharges, as demonstrated by the larger peak prominence and narrower peak width found in these conditions, compared with DT and myoclonus.

The EMG signal itself may also contribute to harmonics in the PSD, potentially due to the nonlinearity of tremor waveforms.[23,24,28] It is important to note that the steepness of tremor discharges can have physiological meaning. The sum of individual motor unit action potentials correlates linearly with the neural drive to the muscle.[29] The higher the level of motor unit synchronization, the steeper the rise and fall of the EMG bursts related to tremor.[29-31] It has been suggested that the amplitude and number of harmonics in the EMG PSD depend on the steepness of the rising and falling edges in tremor discharges.[32] In this view, our findings suggest that EMG discharges in OT are driven by the activity of a highly synchronous neural generator, while the descending activity in ET, DT, and myoclonus is more temporally dispersed.

Conclusions

In this study, we demonstrated that our five outcome measures can objectively characterize tremulous involuntary movements, determining whether a movement qualifies as tremor, its regularity, and its predominant frequency or frequency range. Individual measures were able to differentiate OT, ET, DT, and myoclonus to different degrees. Combining all measures in a linear discriminant analysis allowed us to effectively separate these four movement disorders, providing significant segregation across them, with the exception of ET and DT (Fig. 5).

The inclusion of OT, ET, DT, and myoclonus was based on their distinct clinical features. We hypothesized that these disorders represent a spectrum, ranging from a highly regular, single-frequency-driven phenomenon (OT) to an irregular, multifrequency phenomenon (myoclonus). Our results support this hypothesis, positioning OT and myoclonus at opposite ends of the spectrum, with ET and DT lying in between. The partial overlap in certain features, such as peak frequency and PB ratio, which lacked significant differences, may explain the limited accuracy of the discriminant function in separating ET and DT. By focusing exclusively on spectral features that demonstrated statistically significant differences between the two groups—specifically, peak prominence and peak width—DT and ET could be classified with high accuracy. The area under the ROC curve values were 0.905 for peak prominence and 0.963 for peak width, highlighting their strong discriminative power.

The presence of some overlap between DT and ET is not surprising. This might be due to diagnostic challenges[33,34] or the broad inclusion of ET cases, including those classified as ET-plus and questionable dystonia that may have clustered with DT cases. Nevertheless, we believe that these findings overall point to a potential pathophysiological link between ET and DT. While peak frequency and PB ratio are similar between the two, ET exhibits higher peak prominence and narrower peak width compared with DT, suggesting that DT is characterized by greater background muscle activity and more variable frequencies, likely due to the influence of underlying dystonia. These differences may reflect different physiological mechanisms.[12,35-39]

Our findings should be interpreted with caution due to the retrospective design of the study and the lack of in-depth phenotyping, such as differentiation of ET-plus. Additionally, our analysis relied on diagnosis-specific frequency windows, which restricts the generalizability of the method for prospective diagnostic use. Although this approach was necessary to avoid misclassifying tremor-related activity amid nonspecific EMG signals, future studies should aim to develop classifiers based on unified frequency ranges without prior diagnostic assumptions and while also taking tremor severity into account. Furthermore, our study focused on group-level comparisons rather than establishing quantitative thresholds for clinically meaningful spectral peaks. While we identified systematic differences

across conditions, future research is needed to validate cut-offs that could support objective diagnostic criteria. Nonetheless, we believe our results provide valuable insights into tremor and cortical myoclonus characterization, particularly in differentiating ET from DT, thereby aiding clinical diagnosis and advancing understanding of the pathophysiology of these disorders. ●

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Bhatia KP, Bain P, Bajaj N, et al. Consensus statement on the classification of tremors. From the Task Force on Tremor of the International Parkinson and Movement Disorder Society. Mov Disord 2018;33(1):75–87.

2. Schreglmann SR, Wang D, Peach RL, et al. Non-invasive suppression of essential tremor via phase-locked disruption of its temporal coherence. Nat Commun 2021;12(1):363.

3. Nieuwhof F, Toni I, Buijink AWG, van Rootselaar AF, Warrenburg BPC, Helmich RC. Phase-locked transcranial electrical brain stimulation for tremor suppression in dystonic tremor syndromes. Clin Neurophysiol 2022;140:239–250.

4. Deuschl G, Becktepe JS, Dirkx M, et al. The clinical and electrophysiological investigation of tremor. Clin Neurophysiol 2022;136:93–129.

5. Latorre A, Rocchi L, Magrinelli F, et al. Unravelling the enigma of cortical tremor and other forms of cortical myoclonus. Brain 2020;143(9):2653–2663.

6. Latorre A, Belvisi D, Rothwell JC, Bhatia KP, Rocchi L. Rethinking the neurophysiological concept of cortical myoclonus. Clin Neurophysiol 2023;156:125–139.

7. Antelmi E, Rocchi L, Cocco A, et al. Cerebellar and brainstem functional abnormalities in patients with primary orthostatic tremor. Mov Disord 2018;33(6):1024–1025.

8. Heida T, Wentink EC, Marani E. Power spectral density analysis of physiological, rest and action tremor in Parkinson's disease patients treated with deep brain stimulation. J Neuroeng Rehabil 2013;10:70.

9. Luft F, Sharifi S, Mugge W, et al. A power spectral density-based method to detect tremor and tremor intermittency in movement disorders. Sensors (Basel) 2019;19(19):4301.

10. Elble RJ, McNames J. Using portable transducers to measure tremor severity. Tremor Other Hyperkinet Mov (N Y) 2016;6:375.

11. Rajan R, Anandapadmanabhan R, Vishnoi A, et al. Essential tremor and essential tremor plus are essentially similar electrophysiologically. Mov Disord Clin Pract 2024;11(2):136–142.

12. Panyakaew P, Cho HJ, Lee SW, Wu T, Hallett M. The pathophysiology of dystonic tremors and comparison with essential tremor. J Neurosci 2020;40(48):9317–9326.

13. Dideriksen JL, Gallego JA, Holobar A, Rocon E, Pons JL, Farina D. One central oscillatory drive is compatible with experimental motor unit behaviour in essential and parkinsonian tremor. J Neural Eng 2015;12(4):046019.

14. Latorre A, van der Veen S, Pena A, et al. IAPRD new consensus classification of myoclonus. Parkinsonism Relat Disord 2024;132:107216.

15. Gallego JA, Dideriksen JL, Holobar A, et al. The phase difference between neural drives to antagonist muscles in essential tremor is associated with the relative strength of supraspinal and afferent input. J Neurosci 2015;35(23):8925–8937.

16. Puttaraksa G, Muceli S, Gallego JA, et al. Voluntary and tremorogenic inputs to motor neuron pools of agonist/antagonist muscles in essential tremor patients. J Neurophysiol 2019;122(5):2043–2053.

17. Brown P, Farmer SF, Halliday DM, Marsden J, Rosenberg JR. Coherent cortical and muscle discharge in cortical myoclonus. Brain 1999;122(Pt 3):461–472.

18. Grosse P, Guerrini R, Parmeggiani L, Bonanni P, Pogosyan A, Brown P. Abnormal corticomuscular and intermuscular coupling in high-frequency rhythmic myoclonus. Brain 2003;126(Pt 2):326–342.

19. Latorre A, Rocchi L, Magrinelli F, et al. Reply: Pentameric repeat expansions: cortical myoclonus or cortical tremor? And cortical tremor: a tantalizing conundrum between cortex and cerebellum. Brain 2020;143(10):e88.

20. Shaikh AG, Jinnah HA, Tripp RM, et al. Irregularity distinguishes limb tremor in cervical dystonia from essential tremor. J Neurol Neurosurg Psychiatry 2008;79(2):187–189.

21. Bove F, Di Lazzaro G, Mulas D, Cocciolillo F, Di Giuda D, Bentivoglio AR. A role for accelerometry in the differential diagnosis of tremor syndromes. Funct Neurol 2018;33(1):45–49.

22. Pascual-Valdunciel A, Ibanez J, Rocchi L, et al. Frequency-selective suppression of essential tremor via transcutaneous spinal cord stimulation. Mov Disord 2024;39(10):1817–1828.

23. Sapir N, Karasik R, Havlin S, Simon E, Hausdorff JM. Detecting scaling in the period dynamics of multimodal signals: application to parkinsonian tremor. Phys Rev E Stat Nonlinear Soft Matter Phys 2003;67(3 Pt 1):031903.

24. Pollok B, Gross J, Dirks M, Timmermann L, Schnitzler A. The cerebral oscillatory network of voluntary tremor. J Physiol 2004;554(Pt 3):871–878.

25. Timmermann L, Gross J, Dirks M, Volkmann J, Freund HJ, Schnitzler A. The cerebral oscillatory network of parkinsonian resting tremor. Brain 2003;126(Pt 1):199–212.

26. Raethjen J, Govindan RB, Muthuraman M, Kopper F, Volkmann J, Deuschl G. Cortical correlates of the basic and first harmonic frequency of parkinsonian tremor. Clin Neurophysiol 2009;120(10):1866–1872.

27. Muthuraman M, Hossen A, Heute U, Deuschl G, Raethjen J. A new diagnostic test to distinguish tremulous Parkinson's disease from advanced essential tremor. Mov Disord 2011;26(8):1548–1552.

28. Deuschl G, Lauk M, Timmer J. Tremor classification and tremor time series analysis. Chaos 1995;5(1):48–51.

29. Negro F, Farina D. Linear transmission of cortical oscillations to the neural drive to muscles is mediated by common projections to populations of motoneurons in humans. J Physiol 2011;589(Pt 3):629–637.

30. Farina D, Negro F, Jiang N. Identification of common synaptic inputs to motor neurons from the rectified electromyogram. J Physiol 2013;591(10):2403–2418.

31. Farina D, Merletti R, Enoka RM. The extraction of neural strategies from the surface EMG: an update. J Appl Physiol (1985) 2014; 117(11):1215–1230.

32. Benito-León J, Serrano JI, Louis ED, et al. Essential tremor severity and anatomical changes in brain areas controlling movement sequencing. Ann Clin Transl Neurol 2019;6(1):83–97.

33. Becktepe J, Govert F, Balint B, et al. Exploring interrater disagreement on essential tremor using a standardized tremor elements assessment. Mov Disord Clin Pract 2021;8(3):371–376.

34. Rajan R, Pandey S, Anandapadmanabhan R, Srivastava AK. Interrater and intrarater agreement on the 2018 consensus statement on classification of tremors. Mov Disord 2018;33(12):1966–1967.

35. Erro R, Fasano A, Barone P, Bhatia KP. Milestones in tremor research: 10 years later. Mov Disord Clin Pract 2022;9(4):429–435.

36. DeSimone JC, Archer DB, Vaillancourt DE, Wagle Shukla A. Network-level connectivity is a critical feature distinguishing dystonic tremor and essential tremor. Brain 2019;142(6):1644–1659.

37. van den Berg KRE, Helmich RC. The role of the cerebellum in tremor-evidence from neuroimaging. Tremor Other Hyperkinet Mov (N Y) 2021;11:49.

38. Panyakaew P, Jinnah HA, Shaikh AG. Clinical features, pathophysiology, treatment, and controversies of tremor in dystonia. J Neurol Sci 2022;435:120199.

39. Nieuwhof F, Toni I, Dirkx MF, et al. Cerebello-thalamic activity drives an abnormal motor network into dystonic tremor. Neuroimage Clin 2022;33:102919.

Supporting Data

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