Clinical neurophysiology for tremor

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Review article

Clinical neurophysiology for tremor: Common questions in clinical practice

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ABSTRACT

Background: A thorough history and physical examination may be insufficient for comprehensively studying patients with tremor. In such instances, neurophysiology serves as an adjunct to the physical examination.
Objectives: Our aim is to present compelling evidence supporting the utilization of neurophysiological studies in various tremor conditions.
Methods: A panel of global experts, convened by the Study Group on Clinical Neurophysiology for Movement Disorders, examined the application and utility of neurophysiology across diverse movement disorders.
Results: This manuscript provides a detailed methodology for electrophysiological studies in tremors helping to differentiate them from myoclonus, comparing tremor in parkinson vs atypical parkinsonisms, describing dystonic tremor, describing the differences between Parkinson and essential tremor and the characteristics of functional tremor.
Conclusions: Neurophysiological studies play a crucial role in characterizing tremor syndromes and aiding in their differentiation from other hyperkinetic movement disorders.

1. Introduction

When studying a patient with tremor, careful history and physical examination are crucial, but are sometimes not enough to provide a confident diagnosis. Clinical definitions and diagnostic criteria of tremor syndromes are not optimal and lack objectivity. For example, with regard to Essential tremor (ET), the correct diagnosis at the time of referral to a tertiary Movement disorder center was 50 % and 63 % in two independent cohorts [1,2]. For dystonic tremors it sometimes takes close to 10 years to reach the diagnosis [3,4].

Thus, measuring the movement with electrophysiological techniques can be a helpful extension of the physical examination. Although Clinical Neurophysiology (CNP) is perceived to be a useful diagnostic tool in tremor assessment, it is still not widely available. One of the reasons is lack of training, another reason might be the lack of consensus guidelines on how to perform and interpret tremor studies. This was confirmed in a recent survey performed by MDS Task Force on CNP [5]. We found that electrophysiological testing is heterogenious between different labs in tasks performed and equipment used.

In this article we discuss some major challenges for clinical diagnosis

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of tremor disorders and discuss the utlility of supplementing the clinical approach with objective clinical neurophysiological assessment to help improve the diagnosis of tremor disorders.

2. Methods

A group of experts with global representation was assembled by the Study Group on CNP for Movement Disorders. The result of a literature review and expert opinion were taken into account to provide suggestions on the following topics.

- How to use CNP to differentiate tremor from myoclonus
- How to use CNP to differentiate tremor in Parkinson's disease from tremor in atypical Parkinsonian syndromes
- How to use CNP to differentiate dystonic tremor from Essential tremor
- How to use CNP to differentiate essential tremor from Parkinson tremor
- How to use CNP to identify patients with (comorbid) functional tremor

3. Results

3.1. How to use CNP to differentiate tremor from myoclonus

3.1.1. Background

Tremor and myoclonus are both hyperkinetic movement disorders that typically affect the limbs. In most cases, symptoms worsen with action, which means patients can experience similar difficulties when performing simple activities of daily life, such as handling cutlery, writing or using their phone. Despite these similarities, distinguishing between tremor and myoclonus matters because the diagnostic work-up and treatment is different, both regarding medications and targets for deep brain stimulation in advanced disease. In fact, establishing the movement disorder phenotype is recommended as the first step of the diagnostic approach [6],and the question of whether the phenotype is really tremor or rather myoclonus, the most important tremor mimic, is on top. Clinical distinction between tremor and myoclonus can be reasonably straightforward, but is difficult in specific cases (Fig. 1). On the one hand of the clinical spectrum, a tremor is defined as an oscillating, rhythmic (i.e., regular) movement around a joint [7]. On the other hand, myoclonus is characterized by brief, shock-like jerks that appear irregularly [8].When the presentation adheres strongly to these descriptions, the phenotypes are relatively easy to recognise for experienced clinicians. However, in between is where the difficulties lie: when a tremor is irregular, it can look like a myoclonus, and when a myoclonus has a high frequency, it can resemble a tremor. In clinical practice, changes in diagnosis between cortical myoclonus, enhanced physiological tremor and functional tremor were found to occur most frequently on review of the diagnostic process in 773 patients [9].These are the categories of patients that are challenging to classify based on clinical assessment alone, and in these cases, clinical neurophysiology is most helpful.

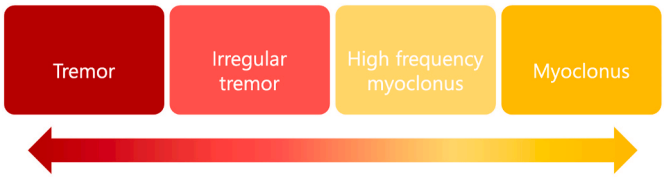

Fig. 1. Clinical spectrum ranging from tremor, to irregular tremor, to high frequency myoclonus, to myoclonus. Distinction on clinical grounds is most difficult in the middle two categories.

3.1.2. Neurophysiological approach

The two key clinical neurophysiological characteristics to distinguish between tremor and myoclonus are agonist-antagonist contraction pattern and rhythm regularity [9].Both can be assessed with surface EMG combined with accelerometry and do not necessarily require advanced analyses (Table 1).

First, the assessment of the agonist-antagonist contraction pattern is informative. Consistently synchronous discharges indicate myoclonus, whereas a predominantly alternating burst pattern is consistent with tremor. The occurrence of a synchronous agonist-antagonist contraction pattern at some point during the registration does not rule out tremor. For instance, rest tremor in essential tremor (ET) is reported to have a synchronous contraction pattern and this characteristic is used in some clinics to differentiate it from rest tremor in Parkinson's disease (PD) [10].Moreover, co-contraction can be a feature of dystonia, in which case it consists of phasic, synchronous bursts of activity of variable duration (>250 ms) instead of the short bursts seen in myoclonus [11]. Note that while the high diagnostic value of an alternating pattern in tremor versus a synchronous pattern in myoclonus is described in expert opinion reviews and is used in clinical practice, diagnostic test accuracy studies encompassing both tremor and myoclonus patients are lacking [9,11].

Secondly, the regularity with which the movements are repeated is equally important. An irregular pattern without a clear peak in the frequency spectrum and with a high frequency variability both within and between different postures and tasks fits with myoclonus; while a regular rhythm, a clear peak in the frequency spectrum and relatively low frequency variability throughout the registration are characteristics of tremor. Note that a high tremor frequency variability can be found in enhanced physiological tremor, dystonic tremor and functional tremor (FT), and has diagnostic value in distinguishing these from other tremor syndromes [12–14].

Combining the assessment of agonist-antagonist contraction pattern and the rhythm regularity allows to distinguish between a tremor and a myoclonus syndrome. After that first important distinction, the clinical neurophysiological work-up of myoclonus patients will focus on determining the anatomical substrate. This will include an assessment of EMG burst duration, and in some cases EEG-EMG co-registration to investigate a cortical origin by means of analyses such as jerk-locked back-averaging or EMG-EEG coherence, as discussed elsewhere [9,15,16].The clinical neurophysiological work-up of tremor patients on the other hand will focus on determining the type of tremor, for which several diagnostic tools with useful clinical neurophysiological criteria exist [12,17–19].

3.2. How to use CNP to differentiate tremor in Parkinson's disease from tremor in atypical parkinsonian syndromes

3.2.1. Background

3.2.1.1. Tremor in Parkinson's disease. Tremor is a core component of PD, present in more than 80 % of patients [20]. The typical 4–7 Hz

Table 1
Key clinical neurophysiological characteristics to differentiate tremor from myoclonus.

	Myoclonus	Tremor
Agonist-antagonist contraction pattern	Synchronous bursts, never alternating	Predominantly alternating bursts, can be temporarily synchronous
Rhythm regularity	Irregular No clear peak in the frequency spectrum High frequency variability within and between postures and tasks	Regular The narrow peak in the frequency spectrum Low frequency variability within and between postures and tasks*

'pill-rolling' type of rest tremor is distinctive for PD compared to the atypical parkinsonian syndromes such as progressive supranuclear palsy (PSP), multiple system atrophy (MSA) or corticobasal syndrome (CBS). The rest tremor is most commonly present in the distal upper limbs, and may also manifest in the lower limbs, tongue, or jaw [21]. It increases during cognitive tasks (counting backward, serial subtraction) or activity by the contralateral hand (tapping). The tremor is suppressed on voluntary activation of the limb, and may reappear on maintaining a stable posture after a pause of few seconds to a minute (re-emergent tremor). The frequency of rest tremor and postural tremor are considered similar when their difference does not exceed 1.5 Hz, with the re-emergent tremor having a slightly higher frequency (+0.4 Hz) than the rest tremor [22,23]. A pure postural tremor (about 8 Hz) may also be seen in PD, with a frequency difference of 3.5 Hz from rest tremor [22]. Additionally, a mild form of kinetic tremor exists in PD, with a higher frequency (+1 Hz) compared to rest tremor [21,23]. Orthostatic tremor may be present in PD (fast 13–18 Hz, intermediate 8–9 Hz, or slow 4–6 Hz) [24].

3.2.1.2. Tremor in atypical parkinsonian syndromes. Tremor is reported in about 42 % of PSP patients, and it is predominantly postural/action (20 %) than at rest (11 %) [25]. Tremor is predominantly present in the upper limbs (94 %), and is asymmetric in nearly half of the patients [25]. The typical tremor in MSA is a jerky, irregular postural tremor. The presence of fine myoclonic jerks (minipolymyoclonus) is thought to contribute to this movement [26]. While rest tremor is also seen in MSA, a typical pill-rolling tremor is rare (3.8 %) [27]. The cerebellar subtype of MSA (MSA-C) is associated with intention tremor [28].Tremor is present in almost half (55 %) of the patients of CBS, albeit not as the predominant feature [29].It is usually postural, and more irregular and faster (6–8 Hz) than PD tremor [30].There is often a combination of rest and postural/action tremors [30].Myoclonus is commonly present in CBS, and myoclonic jerks may be misinterpreted as tremor. In dementia with Lewy bodies (DLB), tremor manifests in about 45 %, and usually consists of rest, postural, and action components [31].The limb tremor in DLB is more commonly bilateral than PD, although, a pill-rolling rest tremor may be seen in DLB.

3.2.2. Neurophysiological approach

In routine clinical practice, the electrophysiological evaluation of parkinsonian tremor is performed using multichannel surface electromyography and at least a monoaxial accelerometer. The tremor is recorded at rest, on maintaining posture, and during kinetic activation [32].(22)It should be recorded continuously from resting position to the assumption of posture [32].(22)Tremor in PD consists of alternating EMG bursts in agonist/antagonist muscles, and when the hand is extended into posture, a suppression of the rest tremor typically occurs [32,33].Compared to a re-emergent tremor of PD, a pure postural tremor does not show this suppression, and it starts immediately on the assumption of posture, with a lower amplitude and larger frequency difference from the rest tremor [22].This can be demonstrated in the power spectrum or time-frequency representations (TFR) [34].Additionally, in the power spectrum, the pure postural tremor shows a wider peak than rest tremor in PD [21].A predominant postural tremor (non-re-emergent) indicates an atypical parkinsonian syndrome, especially when it is irregular, faster, and unaccompanied by a typical rest tremor. The tremor dominant frequency is higher in MSA than PD in both resting (5.50 v/s 4.76 Hz) and postural (7.27 v/s 5.6 Hz) conditions [35]. An additional clue supporting an atypical parkinsonian disorder is the jerky, irregular nature of the postural tremor. Electrophysiologically, these manifest as irregular, short duration (<50 ms), synchronous bursts akin to myoclonus rather than tremor [35].These are associated with cerebral potentials on EEG-EMG polygraphy with jerk-locked back averaging, reminiscent of cortical myoclonus [35].Recently, the presence of harmonics (integral multiples of the tremor dominant frequency) has been shown to be sensitive for discriminating PD (75 %) from MSA (4.5 %) [35]. Interestingly, in DLB, an overflow phenomenon has been described in the standing posture with outstretched arms, whereby, the tremor starts in the hands with a latency of 3–15 s followed by an overflow to the lower limbs in 5–30 s [31].

Thus, CNP is useful to document and classify tremors in parkinsonian disorders (Table 2). Several parameters should be noted, frequency (rest, posture, kinetic) with power spectrum and TFR analysis, presence of harmonics, burst duration, burst pattern (regular v/s irregular, alternating v/s synchronous), tremor amplitude, suppression of rest tremor on voluntary movement, re-emergent v/s pure postural tremor, and lower limb tremor (in selected cases). These features, taken together, yield valuable information, which can be helpful in distinguishing PD from the atypical parkinsonian syndromes, particularly in patients with overlapping clinical features in the early stages of the disease.

3.3. How to use CNP to differentiate dystonic tremor from essential tremor

3.3.1. Background

In 1984 Fahn defined dystonic tremor as repetitive movements displaying a coarse, irregular, jerky appearance without the necessity of overt dystonia [36]. In the dystonia 2013 consensus, dystonic tremor was considered to be a movement manifestation of dystonias [37] whereas in the 2018 tremor consensus, it was considered to be the result of the co-ocurrence of tremor and dystonia [7,38], However, the definition of dystonic tremor continues to be a matter of debate and recently the MDS Dystonia Study Group and Tremor Study Group suggested the term *tremor* to be reserved for movements exhibiting rhythmicity, *jerky dystonia* for rapid, repetitive dystonic movements resembling tremor and *dystonia-tremor syndrome* for coexisting movements [39].

However, for the pourpose of this review we will use the MDS 2018 tremor consensus definition, where Dystonic tremor is defined as a combined tremor syndrome in which dystonia and tremor are the main neurological signs [7]. The overall prevalence of clinical apparent tremor in dystonia is 53 % while dystonia can occur in patients with essential tremor up to 21 % [40]. Two subtypes of tremor in dystonia are distinguished; dystonic tremor (DT) where tremor appears in the dystonic part and tremor associated with dystonia (TAWD) where tremor presents in the non-dystonic area [7,23]. Head tremor is the most affected region for DT while head and arm tremor are commonly described in TAWD(40).

Clinically, tremor in dystonia could be irregular and jerky as well as regular and sinusoidal [36,41]. Patients with DT mostly present with irregular and jerky tremors whereas patients with TAWD often have regular and sinusoidal components. However, mixed tremor types have been documented in both DT and TAWD([36,40–42]). Irregular and jerky characteristics of DT are sometimes difficult to assess during clinical examination and have to be distinguished from myoclonus and functional tremor (FT) where the movements are mostly irregular [43–45]. Differentiation between DT/TAWD and ET and especially ET plus, which is characterized by additional signs of uncertain significance

Table 2
Characteristics of tremor in Parkinson' disease and atypical Parkinsonian syndromes.

Parkinson's Disease	Atypical Parkinsonism
- 4–7 Hz rest tremor (pill-rolling) - Suppression of rest tremor on voluntary movement - Re-emergent tremor (rarely, pure postural tremor) - Presence of harmonics	- Predominantly postural/action tremor (rest tremor, if present, rarely pill-rolling) - Faster tremor (rest and postural) - Jerky, irregular tremor (myoclonus) - Overflow phenomenon (DLB)

ET; essential tremor, DT; dystonic tremor, TAWD; tremor associated with dystonia; *Lower than DT, but higher than PD.

such as questionable dystonic posturing [7], is even more challenging in patients with regular and sinusoidal tremor particularly when dystonia is subtle since there is no definition of subtle or uncertain significant dystonia [21,46,47]. In addition, the interrater agreement on diagnosis among these types of tremor syndromes is poor [48]. Tremors in dystonia commonly occur during action or are task-specific, but can be presented at rest without being task specific at the unilateral upper limb mimicking Parkinson's disease tremor and ET plus [47,49–51]. Thus, clinical assessment alone might not be sufficient to diagnose and discriminate DT from other mimic tremor syndromes.

3.3.2. Neurophysiological approach

The basic neurophysiological features include peak frequency, frequency variability, EMG burst duration, synchronicity of bursts and amplitude [11]. A baseline co-contraction of EMG of the agonist and antagonist pairs as a feature of dystonia, defined as phasic, synchronous bursts of activities of variable duration (>250 ms) can be found [9,11,12]. This should be discriminated from short synchronous bursts with a duration <100 ms as seen in myoclonus. Tremor in dystonia can be visualized as rhythmic bursts with duration of 50–300 ms [11]. On inspection of EMG of the agonist-antagonist pairs, tremor in dystonia (both DT and TAWD) seems to have no consistent pattern with either synchronous or alternating contractions [14].

The peak frequency of DT and TAWD varies from 3 to 7 Hz and overlaps with ET, ET plus, PD and FT([52]). However, the frequency variability is higher in DT compared to ET, suggestive of tremor irregularity. This can be demonstrated with a higher frequency spread [41]of ≥1.75 Hz throughout the registration [12], larger half-power bandwidth of peak spectral analysis as well as greater tremor stability index [53] in DT compared to ET(14). Nevertheless, the use of high variability of tremor frequency cannot be applied in the differentiation of ET/ET plus from TAWD where tremor is more regular [14].

Rest tremor in dystonia should be distinguished from ET plus with rest tremor and PD. Again, the frequency can be overlapping at 5–7 Hz [54]. Synchronous EMG patterns at rest with increased amplitude during action compared to resting position are found in both DT and ET plus, making it indistinguishable between these 2 syndromes with basic neurophysiological features [47]. However, alternating EMG patterns and decrease amplitude with action with re-emerging tremor are the characteristic of PD tremor that are different from rest tremor in dystonia and ET(10).

Other neurophysiological characteristics of tremor in dystonia are based on the phenotypes of dystonia including overflow, mirror movement, the effect of sensory trick and reduction of tremor with null point.

Currently, there are no standard neurophysiological criteria for diagnosis of DT and TAWD with good sensitivity and specificity [21]. However, using a combination of basic features comprising of baseline co-contraction of EMG, irregular rhythmic EMG bursts with high frequency variability might suggest DT rather than ET(21). TAWD might need additional neurophysiological tests that underpin the physiology of dystonia to assist the differential diagnosis from ET. This includes the temporal discrimination threshold (TDT) and blink reflex recovery curve for tremors involving craniocervial muscles. The TDT is measured as the shortest interval to discriminate two tactile stimuli. Increased TDT and loss of the blink reflex recovery curve have been found in TAWD, contrary to ET([55,56]). An exception to this is the cases of musician dystonia in which TDT is not different from healthy musicians or healthy controls [57].

In conclusion, neurophysiological tests using polymyography and additional tests underlying the physiology of dystonia can be an important tools to assist the diagnosis of DT (Table 3). Considering significiant limitations of the clinical approach for the diagnosis of dystonia overall and dystonic tremors, these additional neurophysiolgical characteristics can serve as additional supportive criteria for diagnosis. It could potentially help address the major limitation of the current clinical diagnositic approach for dystonia based solely on clinical crtieria to a more objective, pragmatic pathophysiology based classfication which has prognostic and potential translational therapeutic implications.

Table 3
Different neurophysiological characteristics among ET, DT and TAWD.

Characteristics	ET	DT	TAWD
Baseline EMG	Silent EMG at rest	Phasic, synchronous bursts of activity of variable duration (>250 ms)	? (No dystonia at the tremor part)
Appearance of tremor	Postural Kinetic (Intentional)	Rest Postural, kinetic	Postural, kinetic
Pattern of EMG activities	Synchronous or alternating	Synchronous or alternating	Synchronous or alternating
Specific EMG activities	–	Overflow/mirror to the nearby/ contralateral muscles Effect of sensory trick Null point	–
Peak frequency (Hz)	5–12	3–7	5–7
Frequency variability			
- Frequency spread	Low	High	Low
- Half-band width	Low	High	Low
- Tremor stability index (TSI)	Low*	High	Low
Physiology of dystonia			
- Temporal discrimination threshold (TDT)	Normal TDT	High TDT (compared to ET)	High TDT (compared to ET)
- Blink reflex recovery curve (BRRC)	Normal BRRC	Loss BRRC	Loss BRRC

3.4. How to use CNP to differentiate ET from PD

3.4.1. Background

ET and PD characteristics were previously described in this article. Although usually easy to distinguish there are cases in which ET and PD can look similar, when there is ET with rest tremor for instance, or PD with pure postural tremor. The acceptance of the so-called soft signs such as bradykinesia in ET further complicates the differentiation [58].

3.4.2. Neurophysiological approach

Although the there is an overlap of PD and ET tremor frequencies, there are other characteristics that may help in differentiating both conditions [58]. As previously discussed, the so-called re-emergent tremor is a characteristic of PD tremor that can be measured on both accelerometers and EMG [21]. PD tremor also has a higer frequency tolerance, defined as the range of frequencies over which the tremor is stable, this can be calculated with the tremor stability index (TSI) on accelerometer data [53]. Another difference is given by the common presence of harmonic distortion in PD compared to ET([59]) but this may be just a correlate of higher tremor amplitud in PD (as harmonic distortion increases with amplitud) [21]. There is also a difference in muscle contraction pattern between antagonist muscles that is usually alternating in PD and synchronum in ET.

There are several groups tring to apply machine lerning strategics to differentiate both conditions, but arger datasets and independent cohorts analysis are nedded to further validate those techniques [58].

3.5. How to use CNP to identify patients with (comorbid) functional tremor

3.5.1. Background

3.5.1.1. Functional tremor. Functional neurological disorders (FND) are a common occurrence in general neurological clinics (15–30 %) [60,61] with FT being the most frequent one (50 %) [62] followed by functional dystonia, myoclonus and gait disorders. Certain signs taken from history or clinical examination aid an early and confident diagnosis, such as an acute, unusual onset, changing clinical presentations with fluctuations and remissions, distractibility, entrainment or tremor variability, as well as the co-activation sign. While a history of trauma or other psychological stressors might support a diagnosis of functional tremor, it is not required for the diagnosis. Taking a careful history as well as conducting a thorough clinical assessment leads to a diagnosis in most patients.

3.5.1.2. Comorbid functional tremor. FND may also occur in patients, who have been diagnosed with another neurologic tremor condition, such as essential tremor or Parkinson's disease. Out of 410 consecutive patients with functional motor disorders, 17.1 % had other comorbid neurological conditions, such as migraine and parkinsonism. This indicates that functional motor disorders often occur over the course of other neurological diseases. FT and functional weakness represented the most common phenotypes in this cohort [63].

In the literature, this is described as "functional overlay"([64]) and has more recently been coined FND comorbidity [65]. In clinical practice, the same neurophysiological tools are usually used to identify functional tremor and comorbid functional tremor [21].Neurophysiology has recently been shown to be helpful in identifying an underlying organic tremor that was masked by a functional tremor [66].However, to date there are no validated tools for identifying functional overlay in other tremor syndromes, which is an important knowledge gap.

3.5.2. Neurophysiological approach

A recent systematic review summarised the currently available evidence for the interpretation of neurophysiological investigations used to complement clinical assessment in these cases [11]. Surface EMG and accelerometery are useful tools to help identify variable muscle recruitment, variable burst duration, frequency variability, distractibility and entrainment, which are suggestive of FT. This can in turn help to distinguish between functional tremor and other neurologic tremor disorders [21].

More advanced analyses include the standard coherence analysis, which refers to a mathematical analysis looking at frequency correlation between tremor signals from bilateral muscle pairs. It shows higher coherence in bilateral muscle pairs in FT when compared to organic tremors (56 % vs. 4 %) [67]. The wavelet coherence analysis, looking at the variation of coherence over time, achieves even higher accuracy than standard coherence analysis alone [19]. Essential tremor might also be distinguished from FT by means of cumulant density, assessing the opposite of coherence [12].

To further strengthen the sensitivity and specificity of these techniques, different combinations of tests have been suggested as diagnostic tools to distinguish functional from organic tremor [11].

Tool I**:** Schwingenschuh et al. suggested and validated a test battery using surface EMG and accelerometery, which is highly sensitive (89.5 %) and specific (95.9 %) [67,68]. The suggested battery includes the following: Loading test, response to ballistic movement, coherence Test, tonic co-activation, tapping performance and tapping response. This set was based on previous findings suggesting a tonic discharge of antagonist muscles about 300 ms before tremor onset [23], increased tremor amplitudes in the loading test (response to weighting a limb), entrainment, change of tremor frequency or higher variability when tapping with the contralateral hand, less accurate tapping performance at requested frequencies, significant interlimb coherence in bilateral tremors [69], and transient arrest of tremor during ballistic movements of the other hand.

Tool II**:** A paper from Stouwe et al. also suggested a combination of high frequency variability throughout the entire tremor registration or provoked through distraction or entrainment as a sensitive (100 %) and specific (93 %) tool to distinguish FT versus organic tremor [12].

Tool III**:** A study showed that intralimb wavelet coherence analysis in addition to polymyography may also be a useful tool to distinguish organic from functional tremor as the number of periods without significant coherence was higher in functional tremor than in organic" tremor (PT, ET, EPT) [19]. For further details see Table 4.

In summary, clinical neurophysiology is not only a well-established tool to distinguish different types of organic tremors [70], but may also assist in distinguishing organic from functional tremor syndromes. The use of surface EMG and accelerometery is, to date, the most commonly used neurophysiological tool to do so and when a certain battery of tests is performed, shows high sensitivity and specificity.

3.5.3. Use of CNP to screen for functional tremor prior to invasive or lesional surgical treatment options

Whereas the majority of patients with tremor syndromes are managed pharmacologically, some therapy refractory cases may be referred for surgical treatment such as Deep brain stimulation (DBS) or MR-guided focused ultrasound (MRgFUS). DBS has successfully been used in these cases for several decades.

FND comorbidity in patients with other tremor diagnoses is often underdiagnosed and may indeed apply to up to 34 % of patients diagnosed with e.g., PD, of which approximately 40 % experience FT([71]). Due to surgical risks, potential complications and sub-optimal outcomes, careful screening for functional tremor and/or functional overlay is of utmost importance before surgical intervention is planned to avoid unnecessary and potentially harmful procedures or simply a lack of treatment effect [72].

To date, neurophysiological screening for functional tremors is not routinely done pre-operatively, and none of the mentioned testing tools are validated for distinction of patients with organic tremor syndromes and functional tremor overlay.

In a recent study, pre-operative screening of a cohort of tremor patients showed that the most commonly observed feature of functional tremor in surface EMG was distractibility as well as variability in appearance or frequency, while entrainment was relatively uncommon in this cohort [73]. 14 % of their patients were eventually diagnosed with a functional tremor disorder or an overlay of this matter [73] and surgery was therefore not performed.

The lack of data on FND comorbidity in tremor patients undergoing DBS surgery underpins the unmet need for further research in this field. A combination of clinical examination by a movement disorder specialist and a multidisciplinary team approach are mandatory to allows for an accurate diagnosis and should be performed before surgical interventions are planned. We recommend to add validated clinical neurophysiology in the routine work-up of these patients in order to avoid unnecessary surgical procedures, leading to improved patient outcomes, cost-effectiveness, and patient satisfaction.

4. Conclusion

Clinical neurophysiology is helpful in many situations to distinguish tremor from other hyperkinetic movement disorders. Examples of the tremor studies on different conditions can be found as a supplementary material.

The irregular frequency and the simultaneous contraction of agonist and antagonist muscles should make the clinician suspect of myoclonus, the burst duration and the correlation analysis of EEG and EMG signal con help to support the diagnosis when there is a cortical origin.

In the setting of parkinsonism syndromes, the lack of re-emergent

Table 4
Recommended tools to distinguish organic tremor from FT (adapted from Ref. [10]).

Suggested tool I ([63]) ([13])
- Incorrect tapping performance at 1, 3, and 5 Hz (max. 3 points)
- Entrainment, suppression, or pathological frequency shift at 1, 3, and 5 Hz (max. 3 points)
- Pause or 50 % reduction in amplitude or tremor with ballistic movements (1 point)
- Tonic co-activation before tremor onset (1 point)
- Coherence of bilateral tremors (1 point)
- Increase of peak tremor frequency with loading (1 point)
Cut-off score for a diagnosis of laboratory supported FT with 3 of 10 points.
Sensitivity of 89.5 % and specificity of 95.9 %
Suggested tool II ([12])
- Frequency change during entrainment
- Frequency change during distractibility
- Frequency variability >1.75 Hz
A score of ≥2 out of 3 positive tests suggests FT. Sensitivity of 100 % and specificity of 93 %
Suggested tool III - Wavelet coherence analysis ([18])
- Mean numbers of valleys >3.3; defined as the total number of upward crossing through the line of significant coherence AND
- The percentage of time that significant coherence existed <97 %
Both calculated for the time that tremor activity was present in both EMG signals of the muscle pair. Correctly classifies 83.7 % of all cases of organic and functional tremor

postural tremor, the jerkiness of the tremor, and the lack of harmonics point to an atypical parkinsonism.

Although there are not standard neurophysiological criteria for diagnosis of DT and TAWD, an irregular, long burst duration tremor with synchronis agonist-antagonist co-contraction plus the change in amplitude associated with specifical postures, point to those diagnosis.

ET can be differentiated from PD temor by looking at the presence of re-emergen tremor, the antagonist burst patter and the TSI.

Finally, probably the most useful application of electrophysiology in tremor is for functional cases in which the internal inconsistency can be proved during entrainment, ballistic movements and with loading tasks all this combined with coherence analysis which will give high sensitivity and specificity to the diagnosis.

CRediT authorship contribution statement

Petra Schwingenschuh: Writing – review & editing, Writing – original draft, Conceptualization. **Madelein Van der Stouwe:** Writing – review & editing, Writing – original draft, Conceptualization. **Sanjay Pandey:** Writing – review & editing, Writing – original draft, Conceptualization. **Stephanie Hirschbichler:** Writing – review & editing, Writing – original draft, Conceptualization. **Pattamon Panyakaew:** Writing – review & editing, Writing – original draft, Conceptualization. **Maja Kojovic:** Writing – review & editing, Writing – original draft, Conceptualization. **Adreesh Mukherjee:** Writing – review & editing, Writing – original draft, Conceptualization. **Marina AJ. Tijssen:** Writing – review & editing, Writing – original draft, Conceptualization. **Shabbir Hussain I. Merchant:** Writing – review & editing, Writing – original draft, Conceptualization. **Felipe Vial:** Writing – review & editing, Writing – original draft, Conceptualization.

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Ethical compliance statement

The authors confirm that the approval of an institutional review board and patient consent was not required for this work.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2024.107196.

References

[1] A. Schrag, A. Münchau, K.P. Bhatia, N.P. Quinn, C.D. Marsden, Essential tremor: an overdiagnosed condition? J. Neurol. 247 (12) (2000).
[2] S. Jain, S.E. Lo, E.D. Louis, Common misdiagnosis of a common neurological disorder, Arch. Neurol. 63 (8) (2006 Aug 1) 1100 [Internet][cited 2019 Feb 25] Available from: http://archneur.jamanetwork.com/article.aspx?doi=10.1001/archneur.63.8.1100.
[3] A.T. Powell, J.W. Bidewell, A.C. Walker, Diagnosing idiopathic dystonia: must it take so long? Aust. Health Rev. 18 (3) (1995).
[4] A. Macerollo, M. Superbo, A.F. Gigante, P. Livrea, G. Defazio, Diagnostic delay in adult-onset dystonia: data from an Italian movement disorder center, J. Clin. Neurosci. 22 (3) (2015).
[5] P. Kassavetis, R. Chen, C. Ganos, M. Hallett, M. Hamada, A. Latorre, et al., Global perceptions and utilization of clinical neurophysiology in movement disorders, Mov Disord Clin Pract 11 (4) (2024) 346–351.
[6] J Van De Wardt, A.M.M. Van Der Stouwe, M. Dirkx, J.W.J. Elting, B. Post, M.A. J. Tijssen, et al., Review: systematic clinical approach for diagnosing upper limb tremor, J. Neurol. Neurosurg. Psychiatry 91 (8) (2020 Aug 1) 822 [Internet][cited 2024 Oct 8]Available from:/pmc/articles/PMC7402459/.
[7] K.P. Bhatia, P. Bain, N. Bajaj, R.J. Elble, M. Hallett, E.D. Louis, 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. 33 (1) (2018) 75–87.
[8] R. Zutt, M.E. van Egmond, J.W. Elting, P.J. van Laar, O.F. Brouwer, D.A. Sival, et al., A novel diagnostic approach to patients with myoclonus, Nat Rev Neurol [Internet] 11 (12) (2015 Dec 10) 687–697 [cited 2018 Aug 22]Available from: http://www.nature.com/articles/nrneurol.2015.198.

[9] C.S.J. Everlo, J.W.J. Elting, M.A.J. Tijssen, A.M. Madelein van der Stouwe, Electrophysiological testing aids the diagnosis of tremor and myoclonus in clinically challenging patients, Clin Neurophysiol Pract [Internet] 7 (2022 Jan 1) 51–58 [cited 2024 Oct 8]Available from: https://pubmed.ncbi.nlm.nih.gov/35243186/.

[10] R. Nisticò, D. Pirritano, M. Salsone, F. Novellino, F. Del Giudice, M. Morelli, et al., Synchronous pattern distinguishes resting tremor associated with essential tremor from rest tremor of Parkinson's disease, Parkinsonism Relat. Disorders 17 (1) (2011 Jan) 30–33.

[11] S. van der Veen, M.R. Klamer, J.W.J. Elting, J.H.T.M. Koelman, A.M.M. van der Stouwe, M.A.J. Tijssen, The diagnostic value of clinical neurophysiology in hyperkinetic movement disorders: a systematic review, Parkinsonism Relat Disord [Internet] 89 (2021 Aug 1) 176–185 [cited 2024 May 1]Available from: https://pubmed.ncbi.nlm.nih.gov/34362669/.

[12] A.M.M. van der Stouwe, J.W. Elting, J.H. van der Hoeven, T. van Laar, K. L. Leenders, N.M. Maurits, et al., How typical are 'typical' tremor characteristics? Sensitivity and specificity of five tremor phenomena, Parkinsonism Relat. Disorders 30 (2016 Sep 1) 23–28.

[13] P. Schwingenschuh, T.A. Saifee, P. Katschnig-Winter, A. Macerollo, M. Koegl-Wallner, V. Culea, et al., Validation of "laboratory-supported" criteria for functional (psychogenic) tremor, Mov. Disord. 31 (4) (2016 Apr) 555–562 [Internet][cited 2018 Nov 23]Available from:.

[14] P. Panyakaew, H.J. Cho, S.W. Lee, T. Wu, M. Hallett, The pathophysiology of dystonic tremors and comparison with essential tremor, J. Neurosci. 40 (48) (2020 Nov 25) 9317–9326.

[15] S.H.I. Merchant, F. Vial-Undurraga, G. Leodori, J.A. van Gerpen, M. Hallett, Myoclonus: an electrophysiological diagnosis, Movement Disorders Clinical Practice. Wiley-Blackwell 7 (2020) 489–499 [Internet][cited 2020 Nov 8]Available from: https://pubmed.ncbi.nlm.nih.gov/32626792/.

[16] S. van der Veen, J.N. Caviness, Y.E.M. Dreissen, C. Ganos, A. Ibrahim, J.H.T. M. Koelman, et al., Myoclonus and other jerky movement disorders, Clin Neurophysiol Pract 7 (2022 Jan 1) 285–316 [Internet][cited 2024 Oct 8]Available from: https://pubmed.ncbi.nlm.nih.gov/36324989/.

[17] P. Schwingenschuh, P. Katschnig, S. Seiler, T.A. Saifee, M. Aguirregomozcorta, C. Cordivari, et al., Moving toward "' laboratory-supported "', Criteria for Psychogenic Tremor 26 (14) (2011) 2509–2515.

[18] A. Gironell, J. Kulisevsky, B. Pascual-Sedano, M. Barbanoj, Routine neurophysiologic tremor analysis as a diagnostic tool for essential tremor: a prospective study, J. Clin. Neurophysiol. 21 (2004).

[19] G. Kramer, A.M.M. Van der Stouwe, N.M. Maurits, M.A.J. Tijssen, J.W.J. Elting, Wavelet coherence analysis: a new approach to distinguish organic and functional tremor types, Clin. Neurophysiol. 129 (1) (2018 Jan) 13–20 [Internet][cited 2018 Nov 14]Available from: http://www.ncbi.nlm.nih.gov/pubmed/29136548.

[20] J.L. Sánchez, O. Buriticá, D. Pineda, C.S. Uribe, L.G. Palacio, Prevalence of Parkinson's disease and Parkinsonism in a Colombian population using the capture-recapture method, Int. J. Neurosci. 114 (2) (2004 Feb) 175–182 [Internet] [cited 2020 Dec 8]Available from: https://pubmed.ncbi.nlm.nih.gov/14702206/.

[21] G. Deuschl, J.S. Becktepe, M. Dirkx, D. Haubenberger, A. Hassan, R.C. Helmich, et al., The clinical and electrophysiological investigation of tremor, Clin. Neurophysiol. 136 (2022 Apr 1) 93–129.

[22] M.F. Dirkx, H. Zach, B.R. Bloem, M. Hallett, R.C. Helmich, The nature of postural tremor in Parkinson disease, Neurology 90 (13) (2018) e1095–e1102.

[23] G. Deuschl, P. Bain, M. Brin, Consensus statement of the movement disorder society on tremor, Mov. Disord. 13 (S3) (2008 Oct 20) 2–23 [Internet][cited 2020 Apr 6]Available from:.

[24] S. Leu-Semenescu, E. Roze, M. Vidailhet, A.P. Legrand, J.M. Trocello, V. Cochen, et al., Myoclonus or tremor in orthostatism: an under-recognized cause of unsteadiness in Parkinson's disease, Mov. Disord. 22 (14) (2007 Oct 31) 2063, 9. [Internet][cited 2024 Oct 9] Available from: https://pubmed.ncbi.nlm.nih.gov/17674413/.

[25] S. Fujioka, A.A. Algom, M.E. Murray, M.Y. Sanchez-Contreras, P. Tacik, Y. Tsuboi, et al., Tremor in progressive supranuclear palsy, Parkinsonism Relat. Disorders 27 (2016) 93 [Internet][cited 2024 Oct 9]Available from:/pmc/articles/PMC4887294/.

[26] G. Salazar, J. Valls-Solé, M.J. Martí, H. Chang, E.S. Tolosa, Postural and action myoclonus in patients with parkinsonian type multiple system atrophy [cited 2024 Oct 9]; Available from: https://onlinelibrary.wiley.com/terms-and-conditions, 2000.

[27] Y. Miki, S.C. Foti, Y.T. Asi, E. Tsushima, N. Quinn, H. Ling, et al., Improving diagnostic accuracy of multiple system atrophy: a clinicopathological study, Brain [Internet] 142 (9) (2019 Sep 1) 2813, 27. [cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/31289815/.

[28] P. Mailankody, M. Netravathi, P.K. Pal, Review of tremor in Parkinson's disease and atypical parkinsonian disorders, Neurol. India 65 (5) (2017 Sep 1) 1083–1090 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/28879902/.

[29] K. Kompoliti, C.G. Goetz, B.F. Boeve, D.M. Maraganore, J.E. Ahlskog, C. D. Marsden, et al., Clinical presentation and pharmacological therapy in corticobasal degeneration, Arch. Neurol. 55 (7) (1998 Jul) 957–961 [Internet] [cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/9678313/.

[30] G.M. Saranza, J.L. Whitwell, G.G. Kovacs, A.E. Lang, Corticobasal degeneration, Int Rev Neurobiol [Internet] 149 (2019 Jan 1) 87–136 [cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/31779825/.

[31] M. Onofrj, S. Varanese, L. Bonanni, J.P. Taylor, A. Antonini, E.M. Valente, et al., Cohort study of prevalence and phenomenology of tremor in dementia with Lewy bodies, J Neurol [Internet] 260 (7) (2013 Jul) 1731 [cited 2024 Oct 9]Available from:/pmc/articles/PMC3705145/.

[32] F. Vial, S.H.I. Merchant, P. McGurrin, M. Hallett, How to do an electrophysiological study of myoclonus, J. Clin. Neurophysiol. 40 (2) (2023) 93–99.

[33] F. Papengut, J. Raethjen, A. Binder, G. Deuschl, Rest tremor suppression may separate essential from parkinsonian rest tremor, Parkinsonism Relat. Disorders 19 (7) (2013 Jul) 693–697 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/23623196/.

[34] S. Alshimemeri, D. Vargas-Méndez, R. Chen, N. Lipsman, M.L. Schwartz, A. M. Lozano, et al., Functional tremor developing after successful MRI-guided focused ultrasound thalamotomy for essential tremor, J. Neurol. Neurosurg. Psychiatry 93 (6) (2022 Jun 1) 625–627 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/35473713/.

[35] Y. Okuma, K. Fujishima, H. Miwa, H. Mori, Y. Mizuno, Myoclonic tremulous movements in multiple system atrophy are a form of cortical myoclonus [cited 2024 Oct 9]; Available from: https://movementdisorders.onlinelibrary.wiley.com/doi/10.1002/mds.20346, 2004.

[36] S. Fahn, The varied clinical expressions of dystonia, Neurol Clin [Internet] 2 (3) (1984 Aug 1) 541–554 [cited 2024 Oct 3]Available from: https://europepmc.org/article/MED/6398404.

[37] A. Albanese, K. Bhatia, S.B. Bressman, M.R. Delong, S. Fahn, V.S.C. Fung, et al., Phenomenology and classification of dystonia: a consensus update, Mov. Disord. 28 (7) (2013 Jun 15) 863–873 [Internet][cited 2024 Sep 6]Available from: https://pubmed.ncbi.nlm.nih.gov/23649720/.

[38] S. Lalli, A. Albanese, Dystonic tremor: time to change, Mov Disord Clin Pract 11 (6) (2024 Jun 1) 605–612 [Internet][cited 2024 Sep 5]Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/mdc3.14010.

[39] S. Lalli, A. Albanese, Dystonic tremor: a tribute to stanley Fahn, Mov Disord Clin Pract [Internet] 11 (9) (2024 Sep 1) 1173–1174 [cited 2024 Oct 10]Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/mdc3.14171.

[40] A.G. Shaikh, S.B. Beylergil, L. Scorr, G. Kilic-Berkmen, A. Freeman, C. Klein, et al., Dystonia and tremor: a cross-sectional study of the dystonia coalition cohort, Neurology 96 (4) (2021 Jan 26) E563–E574 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/33046615/.

[41] A.G. Shaikh, H.A. Jinnah, R.M. Tripp, L.M. Optican, S. Ramat, F.A. Lenz, et al., Irregularity distinguishes limb tremor in cervical dystonia from essential tremor, J. Neurol. Neurosurg. Psychiatry 79 (2) (2008 Feb) 187 [Internet][cited 2024 Oct 9]Available from:/pmc/articles/PMC2737356/.

[42] M. Rudzińska, M. Krawczyk, M. Wójcik-Pedziwiatr, A. Szczudlik, A. Wasielewska, Tremor associated with focal and segmental dystonia, Neurol. Neurochir. Pol. 47 (3) (2013 Jan 1) 223–231.

[43] E. Apartis, L. Vercueil, To jerk or not to jerk: a clinical pathophysiology of myoclonus, Rev. Neurol. (Paris) 172 (8–9) (2016 Aug 1) 465–476 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/27568397/.

[44] H. Shibasaki, M. Hallett, What is the Bereitschaftspotential? Clinical Neurophysiology 117 (11) (2006 Nov) [Internet][cited 2019 Aug 4] 2341–56. Available from: https://linkinghub.elsevier.com/retrieve/pii/S138824570600229X.

[45] M. Hallett, Functional (psychogenic) movement disorders - clinical presentations, Parkinsonism Relat Disord [Internet] 22 (0 1) (2016 Jan 1) S149–S152 [cited 2020 Aug 18]Available from:/pmc/articles/PMC4662613/?report=abstract.

[46] E.D. Louis, M. Bares, J. Benito-Leon, S. Fahn, S.J. Frucht, J. Jankovic, et al., Essential tremor-plus: a controversial new concept, Lancet Neurol [Internet] 19 (3) (2020 Mar 1) 266–270 [cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/31767343/.

[47] N. Gupta, S. Pandey, Rest tremor in dystonia: epidemiology, differential diagnosis, and pathophysiology, Neurol Sci [Internet] 41 (9) (2020 Sep 1) 2377–2388 [cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/32328831/.

[48] J. Becktepe, F. Gövert, B. Balint, C. Schlenstedt, K. Bhatia, R. Elble, et al., Exploring interrater disagreement on essential tremor using a standardized tremor elements assessment, Mov Disord Clin Pract 8 (3) (2021 Apr 1) 371–376.

[49] A. Batla, R. Erro, M. Stamelou, S.A. Schneider, P. Schwingenschuh, C. Ganos, et al., Patients with scans without evidence of dopaminergic deficit: a long-term follow-up study, Mov Disord [Internet] 29 (14) (2014 Dec 1) 1820–1825 [cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/25350529/.

[50] A.F. Gigante, A. Berardelli, G. Defazio, Rest tremor in idiopathic adult-onset dystonia, Eur. J. Neurol. 23 (5) (2016 May 1) 935–939 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/26916971/.

[51] R. Erro, C. Sorrentino, M. Russo, P. Barone, Essential tremor plus rest tremor: current concepts and controversies, J Neural Transm [Internet] 129 (7) (2022 Jul 1) 835 [cited 2024 Oct 9]Available from:/pmc/articles/PMC9217824/.

[52] F. Bove, G Di Lazzaro, D. Mulas, F. Cocciolillo, D Di Giuda, A.R. Bentivoglio, A role for accelerometry in the differential diagnosis of tremor syndromes, Funct Neurol [Internet] 33 (1) (2018 Jan 1) 45–49 [cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/29633696/.

[53] Di Biase L, Brittain JS, Syed Ã, Shah A, Pedrosa DJ, Cagnan H, et al. Tremor Stability Index: a New Tool for Differential Diagnosis in Tremor Syndromes.

[54] S. Pandey, N. Sarma, Tremor in dystonia: a cross-sectional study from India, Mov Disord Clin Pract 4 (6) (2017 Nov 1) 858–863 [Internet][cited 2024 Oct 9] Available from: https://pubmed.ncbi.nlm.nih.gov/30868097/.

[55] G. Defazio, A.F. Gigante, G. Abbruzzese, A.R. Bentivoglio, C. Colosimo, M. Esposito, et al., Tremor in primary adult-onset dystonia: prevalence and associated clinical features, J. Neurol. Neurosurg. Psychiatry 84 (4) (2016 Apr 13) 404–408 [Internet][cited 2024 Oct 9]Available from: https://jnnp.bmj.com/content/early/2012/11/09/jnnp-2012-303782.

[56] R. Nisticò, D. Pirritano, M. Salsone, P. Valentino, F. Novellino, F. Condino, et al., Blink reflex recovery cycle in patients with dystonic tremor: a cross-sectional study, Neurology 78 (17) (2012 Apr 24) [Internet][cited 2024 Oct 9]1363–5. Available from: https://pubmed.ncbi.nlm.nih.gov/22496196/.
[57] F. Borngräber, M. Hoffmann, T. Paulus, J. Junker, T. Bäumer, E. Altenmüller, et al., Characterizing the temporal discrimination threshold in musician's dystonia, Sci. Rep. 12 (1) (2022 Dec 1).
[58] L. Angelini, G. Paparella, M. Bologna, Distinguishing essential tremor from Parkinson's disease: clinical and experimental tools, Expert Rev Neurother [Internet] (2024 Aug 2) [cited 2024 Sep 10]; Available from: https://www.tandfonline.com/doi/abs/10.1080/14737175.2024.2372339.
[59] A. Hossen, M. Muthuraman, Z. Al-Hakim, J. Raethjen, G. Deuschl, U. Heute, Discrimination of Parkinsonian tremor from essential tremor using statistical signal characterization of the spectrum of accelerometer signal, Bio Med. Mater. Eng. 23 (6) (2013) 513–531.
[60] A.J. Carson, B. Ringbauer, J. Stone, L. McKenzie, C. Warlow, M. Sharpe, Do medically unexplained symptoms matter? A prospective cohort study of 300 new referrals to neurology outpatient clinics, J. Neurol. Neurosurg. Psychiatry 68 (2) (2000 Feb) 207–210 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/10644789/.
[61] O. Ahmad, K.E. Ahmad, Functional neurological disorders in outpatient practice: an Australian cohort, J. Clin. Neurosci. 28 (2016 Jun 1) 93–96 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/26754851/.
[62] K.E. Anderson, A.L. Gruber-Baldini, C.G. Vaughan, S.G. Reich, P.S. Fishman, W. J. Weiner, et al., Impact of psychogenic movement disorders versus Parkinson's on disability, quality of life, and psychopathology, Mov. Disord. 22 (15) (2007 Nov 15) 2204, 9[Internet][cited 2024 Oct 9]. Available from: https://pubmed.ncbi.nlm.nih.gov/17876850/.
[63] M. Tinazzi, F. Morgante, E. Marcuzzo, R. Erro, P. Barone, R. Ceravolo, et al., Clinical correlates of functional motor disorders: an Italian multicenter study, Mov Disord Clin Pract [Internet] 7 (8) (2020 Nov 1) 920–929 [cited 2024 Oct 9] Available from: https://pubmed.ncbi.nlm.nih.gov/33163563/.
[64] A.B. Carter, The functional overlay, Lancet 2 (7527) (1967) 1196–1200 [Internet] [cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/4168390/.
[65] M.M. Kurtis, I. Pareés, Functional movement disorder comorbidity in Parkinson's disease: unraveling the web, Parkinsonism Relat. Disorders 82 (2021 Jan 1) 138–145 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/33092981/.
[66] S.H. Merchant, D. Haubenberger, M. Hallett, Mirror movements or functional tremor masking organic tremor, Clin Neurophysiol Pract [Internet] 3 (2018) 107–113 [cited 2018 Nov 23]Available from: http://www.ncbi.nlm.nih.gov/pubmed/30215019.
[67] P. Schwingenschuh, P. Katschnig, S. Seiler, T.A. Saifee, M. Aguirregomozcorta, C. Cordivari, et al., Moving toward "laboratory-supported" criteria for psychogenic tremor, Mov. Disord. 26 (14) (2011 Dec) 2509–2515.
[68] P. Schwingenschuh, T.A. Saifee, P. Katschnig-Winter, A. Macerollo, M. Koegl-Wallner, V. Culea, et al., Validation of "laboratory-supported" criteria for functional (psychogenic) tremor, Mov. Disord. 31 (4) (2016 Apr 1) 555–562 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/26879346/.
[69] M.J. Edwards, K.P. Bhatia, Functional (psychogenic) movement disorders: merging mind and brain, Lancet Neurol [Internet] 11 (3) (2012) 250–260, https://doi.org/10.1016/S1474-4422(11)70310-6.
[70] G. Deuschl, P. Krack, M. Lauk, J. Timmer, Clinical neurophysiology of tremor, Journal of Clinical Neurophysiology [Internet] 13 (2) (1996 Mar 1) 110–121 [cited 2018 Feb 18]Available from: https://insights.ovid.com/pubmed?pmid=8849966.
[71] B.D. Wissel, A.K. Dwivedi, A. Merola, D. Chin, C. Jacob, A.P. Duker, et al., Functional neurological disorders in Parkinson disease, J. Neurol. Neurosurg. Psychiatry 89 (6) (2018 Jun 1) 566–571 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/29549192/.
[72] K.A.M. Pauls, J.K. Krauss, C.E. Kämpfer, A.A. Kühn, C. Schrader, M. Südmeyer, et al., Causes of failure of pallidal deep brain stimulation in cases with pre-operative diagnosis of isolated dystonia, Parkinsonism Relat. Disorders 43 (2017 Oct 1) 38–48 [Internet][cited 2024 Oct 9]Available from: https://pubmed.ncbi.nlm.nih.gov/28690015/.
[73] C.Z. Chou, J.E. Ahlskog, B.T. Klassen, E.A. Coon, F. Ali, J.H. Bower, et al., Utility of routine surface electrophysiology to screen for functional tremor prior to surgical treatment of essential tremor, Clin Park Relat Disord (2022 Jan 1) [Internet][cited 2024 Oct 9];7. Available from: https://pubmed.ncbi.nlm.nih.gov/35928768/.