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Editorial

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Tremor is a highly prevalent neurological disorder and the most common movement disorder. The most frequent tremor, essential tremor (ET), affects up to 5.6% of world's population. Parkinson's disease (PD), affecting about 10 million people worldwide, is also commonly present with tremor. The third most common movement disorder, dystonia, affecting 3 million people globally, has associated tremor in 50% of instances. Tremor is often easy to diagnose as a symptom, but further granularity for its phenomenological and etiological classification has produced controversies. Many studies have attempted to find the mechanistic underpinning of ET or tremor in dystonia, but discrepancies in opinions still exist. This special volume in the *Journal of Neurological Sciences* is dedicated to "tremors". The volume comprises the most up-to-date reviews covering various aspects of common and uncommon tremor syndromes. The content covers clinical neurology, classification scheme, and mechanistic theories for tremor genesis.

The new Consensus Statement on the Classification of Tremors defines tremors as an involuntary, rhythmic, and oscillatory movement which may involve one or several body parts. The proposed classification scheme uses two axes: history and phenomenology of tremor comprise axis 1, while etiology comprises axis 2 [1]. In this issue, Latorre and colleagues further discuss such an approach to classifying tremor according to the axes [2]. The typical ET phenotype features bilateral hand action tremor with or without head, voice, and lower limb tremor. ET is often familial, but isolated tremor without a family history is not uncommon. ET often presents with subtle neurological signs of uncertain signficance including impaired tandem gait, dystonia, memory impairment, rest tremor, or other focal neurological deficits; such combinations are termed ET plus. The term ET plus is also controversial as outlined by Louis and Bain in this issue [3].

ET pathogenesis is often localized to the cerebellum; however, other theories also exist. For example, environmental exposures to β-carboline alkaloids and the consequent olivocerebellar hyperexcitation, cerebellar GABA deficiency, climbing fiber synaptic pathology with related cerebellar oscillatory activity, and extracerebellar oscillatory activity are thought to be possible in ET [4]. On the contrary, the Parkinson's tremors may be the result of altered oscillations and synchronization in two partially overlapping central motor circuitries, i.e., the cerebello-thalamo-cortical and the basal ganglia-cortical loops [5,6]. Panyakaew and colleagues suggest a shared biological mechanism explaining the co-occurrence of dystonia and tremors. Panyakaew and colleagues also discuss the limitations and corresponding controversy of different definitions of dystonic tremors [6].

The differential diagnosis of essential tremor also includes functional tremor, drug induced tremor, and uncommon tremor [7,8,9]. The most common drugs associated with tremor include amiodarone, selective serotonin (and norepinephrine) reuptake inhibitors (SSRIs/SNRIs), amitriptyline, lithium, valproate, β-adrenoceptor agonists, dopamine receptor antagonists, VMAT2 inhibitors, and drugs of abuse such as ethanol and cocaine [8]. Drug induced tremor usually resembles essential or parkinsonian tremor, but phenomenology is determined by the offending pharmacological compound. Dystonic or functional tremors may show unilateral, task-specific, position-dependent tremor or sudden onset, distractibility, entrainment and arrest with contralateral movements [7,8].

Tremors may also occur in many other rare neurological disorders. They can be debilitating and sometimes treatable and hence should not be missed. The tremors in rare diseases include orthostatic tremor,

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Holmes tremor, palatal and oculopalatal tremor, cortical tremor, some genetic forms of tremor including fragile X-associated tremor/ataxia syndrome as well as tremor associated with neuromuscular disorders, multiple sclerosis, and Wilson's disease [9].

Clinical tremor rating scales are advantageous as they assess the tremor severity (amplitude), anatomical distribution, triggers, and impact on activities of daily living, as well as the quality of life. Motion transducers and surface electromyography can be of help in discerning properties of tremor, determination of tremor frequency, and its changes in amplitude and frequency over time [10]. Although motion transducers exceed all clinical rating scales in precision and accuracy, they are limited by the within-subject random variability in tremor amplitude. It is proposed that instrumented measures and scales should be viewed as complementary techniques to quantifying tremor amplitude. Telemedicine provides a set of challenges but opens opportunities to assess patients' tremor. Modern sensors may improve the limitations of visual observations. Wearable technology opens avenues for clinicians and patients to assess tremor during daily life situations [11,12].

The treatment of tremors consists of discontinuation of the offending drugs in case of drug induced tremors. Pharmacotherapies for ET include propranolol, primidone, topiramate, zonizamide, and botulinum toxin [13,14]. When conventional therapy fails, deep brain stimulation and MRI guided focused ultrasound may be considered [13,15,16]. Different lesion sites are discussed for different tremor indications [15]. Pascual-Valdunciel and colleagues review the peripheral electrical stimulation (PES) literature, summarizing its effectiveness, safety, and clinical translatability [17]. The review further proposes guidelines for assessing tremor in the context of evaluating new therapies that combine the strengths of clinician assessments, patient evaluations, and novel motion sensing technology [17].

There is no drug that consistently alleviates the resting tremor in PD. Dopaminergic drugs can reduce the tremor but there is a significant fraction of PD patients whose tremor does not respond. This has led to a novel classification of two subtypes: dopamine-responsive and dopamine-resistant tremors, with the dopamine-responsive tremor subtype having greater disease severity and increased prevalence of dyskinesia [5,13]. Benztropine, levodopa, dopamine agonists, clozapine, mirtazapine, and zonizamide reduce tremor in PD [13].

The field of tremor is very active, with improvements in classification, understanding of pathophysiology, and treatments. We are pleased to have obtained contributions from world experts on these topics. We are grateful to all of them, and you will be too after reading this outstanding collection of articles.

Declaration of Competing Interest

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A.G.S has nothing to declare.

M.H. is an inventor of patents held by NIH for an immunotoxin for the treatment of focal movement disorders and the H-coil for magnetic stimulation; in relation to the latter, he has received license fee payments from the NIH (from Brainsway). He is on the Medical Advisory Boards of CALA Health and Brainsway (both unpaid positions). He is on the Editorial Board of approximately 15 journals and receives royalties and/or honoraria from publishing from Cambridge University Press, Oxford University Press, Springer, Wiley, Wolters Kluwer, and Elsevier. He has research grants from Medtronic, Inc. for a study of DBS for dystonia and CALA Health for studies of a device to suppress tremor.

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