

Electrophysiologic Assessments of Involuntary Movements: Tremor and Myoclonus

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Tremor is defined as a rhythmical, involuntary oscillatory movement of a body part. Although neurological examination reveals information regarding its frequency, regularity, amplitude, and activation conditions, the electrophysiological investigations help in confirming the tremor, in differentiating it from other hyperkinetic disorders like myoclonus, and may provide etiological clues. Accelerometer with surface electromyogram (EMG) can be used to document the dominant frequency of a tremor, which may be useful as certain frequencies are more characteristic of specific etiologies than others hyperkinetic disorders. It may show rhythmic bursts, duration and activation pattern (alternating or synchronous). Myoclonus is a quick, involuntary movement. Electrophysiological studies may helpful in the evaluation of myoclonus, not only for confirming the clinical diagnosis but also for understanding the underlying physiological mechanisms. Electroencephalogram (EEG)-EMG correlates can give us important information about myoclonus. Jerk-locked back-averaging and evoked potentials with recording of the long-latency, long-loop reflexes are currently available to study the pathophysiology of myoclonus.

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Although the diagnosis of tremor is usually based on the patient's history and neurological examinations but, in some cases, investigation by electrophysiological studies such as electromyogram (EMG) examination is needed for correct diagnosis. Fourier analysis is useful to quantify amplitude and frequency of tremors. Myoclonus may originate from the cerebral cortex, subcortical structures, brainstem, spinal cord or peripheral nerve. The more specific localization of the focus requires the various electrophysiologic studies, including EMG correlates, electroencephalogram (EEG)-EMG polygraph, jerk-locked back averaging of EEG, cortico-muscular coherence, evoked potentials, long loop reflex, and transcranial magnetic stimulation. Deciding whether myoclonus is cortical, subcortical, brainstem, spinal or peripheral in origin is important for the therapeutic strategy of myoclonus.

Tremor

In order to describe a particular tremor, the following aspects are included: 1) the affected area (head, chin, jaw, vocal cords, upper or lower extremity, body), 2) the activation condition (rest, posture, non-goal directed movements, eventually specific tasks), 3) the frequency of tremor (low, less than 4 Hz; medium, 4-7 Hz; high, above 7 Hz). The general neurologic examination is important for the differential diagnosis of tremor. We should find any akinesia, rigidity, Froment's sign for upper and lower extremity and coactivation sign of psychogenic tremor, postural abnormalities, dystonia, spasticity, ataxia, and signs of neuropathy in patients with tremor. Specific data from the medical history should be described. Attention is needed regarding information about the onset of tremor, family history, alcohol sensitivity, associated diseases, medication, and drug abuser.

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Electrophysiologic Investigations for the Diagnosis of Tremor

Electromyogram

EMG studies can be helpful in the diagnosis of tremor. In order to support the diagnosis of tremor, surface EMG is sufficient, and needle recordings are rarely necessary. It is the best method to identify the involved muscles and limb segment.¹ Inspection of the EMG signal of a tremor reveals whether the tremor is regular or irregular. In some instances, there are some discrepancies between clinical analysis of tremor and EMG analysis of tremor. Therefore EMG studies are needed for proper diagnosis of tremor. In a tremor, asynchronous signal would be described as alternating. In essential tremor, the frequency varies from 4 to 11 Hz with synchronous activity in antagonist muscles. Accelerometer with weights on the hands can show a shift in peak frequency with exaggerated physiologic tremor and a constant frequency with essential tremor.

EMG is another reliable method of assessing primary orthostatic tremor² and of confirming or excluding asterixis³ in case of high-frequency irregular tremors. In rubral tremor or Holmes' tremor, its frequency ranges from 2.5 to 4 Hz, affects proximal muscles more than distal muscles and it has a tendency to increase in amplitude with prolonged postures. EMG reveals bursts of activity lasting 125 to 250 msec and alternating activity in antagonist muscle. It can be helpful for the diagnosis of dystonic tremor. In dystonic tremor, it has a frequency of 4 to 7 Hz and with irregular amplitude that occurs in an affected body part. The value of EMG is limited for the differential diagnosis of essential and parkinsonian tremor.⁴

However, it is often necessary for targeting botulinum injection treatment.

Fourier analysis

The uses of time series analysis for tremor are well established.¹ The mathematical and technical requirement are not trivial, and they bear some pitfall. Fourier analysis is useful to quantify amplitude and frequency of tremors. For some tremors, like Holmes' tremor and primary orthostatic tremor, the frequency is a most valuable diagnostic tool.³

Graphic tablet analysis

Graphic tablets have been introduced for the analysis of writing tremor and to measure the extent of action and intention tremor.⁵ It can be used for diagnostic purposes and especially for treatment monitoring.

Long term recording

Long term recording of tremor EMG usually for one or several days is used for the study of drug effects.⁶

Median nerve somatosensory evoked potentials and jerk-locked averaging and EEGs

The differential diagnosis of myoclonus and tremor may be impossible by only clinical investigation. For this reason, these classic electrophysiologic techniques may be necessary.

Myoclonus

Myoclonus is sudden, brief, jerky, shock-like, involuntary movements arising from the central nervous system and involving extremities, face, and trunk.⁷ Myoclonus can be described as action myoclonus (activated by voluntary movement), reflex myoclonus (activated by sensory stimulation). Some involuntary movements are abolished during sleep. However, rhythmic segmental myoclonus and brainstem (palatal) myoclonus persisted during sleep. Myoclonic jerks usually represent brief muscle contractions (positive myoclonus) but may also be produced by equally brief lapses of muscle contraction (negative myoclonus or asterixis), and both types may be observed in the same patient such as in posthypoxic action myoclonus.

In other words, positive myoclonus jerks originate from rapid, active contractions of a muscle or group of muscles. Less common, a brief loss of muscle tone in agonist muscles followed by a compensatory jerk of antagonistic muscle groups produces negative myoclonus. Asterixis, as seen in hepatic encephalopathy and the postural lapses of posthypoxic myoclonus are examples of negative myoclonus. It is essential to distinguish myoclonus from other hyperkinetic movement disorders.

Myoclonus is distinguished from tics because the latter can be controlled by an effort of will, at least temporarily, whereas myoclonus cannot. Tics are usually complex, stereotyped movements accompanied by an urge to move, with relief of this inner tension after the tic has occurred. The ability to suppress a tic and their waxing and waning character usually helps differentiate tics from myoclonus. Rhythmic myoclonus may be confused with tremor. Its frequency is often slower than the commonly observed tremors, it is present at rest, is not modified significantly by voluntary movements and often persists during sleep. Its square-wave character, with an interval between each brief burst, differs from the mores sinusoidal character of tremor, seen in essential tremor.

Myoclonus may also be confused with chorea, especially if multifocal and asynchronous, but in chorea the movements continue in a constant flow, randomly distributed over the body and randomly distributed in time. Many patients with dystonia have brief muscle jerks repetitively (myoclonic dystonia). However, dystonia is easily distinguished from myoclonus by the more sustained, twisting character of the distinctive dystonic postures.

Electrophysiologic Investigations for the Diagnosis of Myoclonus

Myoclonus can be classified in various ways, depending on which aspect is focused on but it is usually classified with the underlying physiologic mechanism or the causation. According to the pathophysiologic mechanisms, myoclonus is classified into three main categories; cortical, subcortical, and spinal. Among these three categories, cortical myoclonus is most commonly encountered. Electrophysiological studies can show an anatomical localization for myoclonus. The anatomical origin of the myoclonus sometimes provides good hints as to the treatment.

Cortical myoclonus

Cortical myoclonus is the most common form of myoclonus observed clinically. Cortical myoclonus is more often disabling to the patient and sometimes intractable to various treatments. It usually arises from a hyperexcitable focus within the sensory-motor cortex. In general, cortical myoclonus typically involves an arm, leg of the face and is triggered by action of intention. The physiologic characteristics of cortical myoclonus are 1) an associated EMG discharge of very short duration (usually less than 50 ms) 2) synchronous antagonists activity 3) EEG correlate 4) an EEG spike preceding the myoclonus by a short interval (20 ms in case of hand myoclonus) and localized the area of the contralateral central region corresponding to the involved muscle (around C3 and C4 in case of hand myoclonus) detected by back averaging technique, and 5) pathologic enlargement of early component of somatosensory evoked potentials (SEP), often accompanied by enhanced long-latency, long loop EMG discharge (C-reflex).¹⁰ Cortical myoclonus is often stimulus sensitive, with muscle stretch often being the critical stimulus.¹¹ This stimulus-sensitivity can be more easily explained if the sensory rather than the motor cortex is hyperexcitable. Most patients with cortical reflex myoclonus show enlarged SEP following electrical stimulation of median nerve stimulation, the P25-N33 component is enlarged, whereas the first major cortical negative peak N20 reflecting arrival of the sensory volley in the cortex is usually normal size. Since the giant SEP is not seen in other types of myoclonus, its demonstration is diagnostically significant in cortical myoclonus. In many patients, the cortical reflex or action myoclonus may be focal, involving the stimulated or active limb, suggesting an exaggeration of cortical long loop reflexes and intracortical processing of motor activity. In some, however more extensive myoclonic jerks suggest additional disinhibition, with intrahemispheric and interhemispheric spread of excitation via cortico-cortical and transcallosal pathways.¹² This extensive spread of excitation must be relevant to the generalization of seizures seen in these patients. With this regards, cortical myoclonus can be

considered as a fragment of focal epilepsy.¹³ However, cortical myoclonus is not disease-specific. It is most commonly seen in a group of diseases such as progressive myoclonic epilepsy (PME), and also seen in other diseases, including juvenile myoclonic epilepsy, postanoxic myoclonus,¹¹ corticobasal degeneration,¹⁴ Alzheimer's disease,¹⁵ olivopontocerebellar atrophy, advanced Creutzfeldt-Jakob disease, metabolic encephalopathy, Rett syndrome,¹⁶ and celiac disease. PME is a heterogeneous group of inherited disorders,¹⁷ including Unverricht-Lundborg disease, Lafora disease neuronal ceroid lipofuscinosis, mitochondrial disease, sialidosis, dentatorubral-pallidolusian atrophy, benign adult familial myoclonic epilepsy,¹⁸ and Angelman syndrome.¹⁹

Subcortical-reticular myoclonus

Reticular myoclonus may occur spontaneously, in response to various peripheral stimuli of during voluntary action. The myoclonic jerks are brief, lasting between 10-30 ms. Its distinctive features are as follows; 1) the myoclonic jerks tend to be generalized. Axial and proximal muscles are mainly involved, causing neck flexion, shoulder elevation with trunk and knee extension 2) the cortical EEG correlates, if present, is not time-locked to the EMG event, and the SEP is not enlarged 3) the sequence of activation of muscles is different (up the brainstem and down the spinal cord). The trapezius is activated first, suggesting an origin at the level of medulla.²⁰ Reticular myoclonus, both spontaneous and reflex, may be seen in metabolic encephalopathies, postanoxic myoclonus and in PME.²¹ Both cortical and reticular myoclonus may be present in the same patient, reflecting hyperexcitability at multiple levels of the central nervous system. The exaggerated startle response is also considered as a form of brainstem reticular myoclonus. Unlike reticular myoclonus, spontaneous myoclonic jerks are uncommon, and are mostly evoked by sudden noise or light, instead of muscle stretch or intention.

Negative myoclonus

Negative or asterixis occurs when a muscle contraction is suddenly interrupted. It can be seen in either cortical or subcortical lesions. It is often associated with metabolic or toxic encephalopathy,²² but unilateral asterixis is reported in patients with ischemic or hemorrhagic disorders, especially those involving the thalamus.²³ Epileptic negative myoclonus was also reported.²⁴ One negative peak at the contralateral central region and the following negative peak at the contralateral frontal region was demonstrated by back averaging technique in this patient.

Segmental and spinal myoclonus

Segmental myoclonus is usually indicative of a focal structural lesion and its clinical features are rather distinctive. The myoclonic jerks are usually rhythmic; tend to persist during

sleep and usually not stimulus-sensitive. There is no EEG correlates and the SEPs are not enlarged. The characteristics of segmental myoclonus are as follows; 1) may be uni or bilateral 2) may be associated with contraction of external ocular muscles, those of larynx, neck, diaphragm, trunk and limb, 4) has a rhythm of 2 Hz (range 80-180/min) and is most often due to brainstem stroke, although it has been reported with multiple sclerosis, brain tumors, syringobulbia, obstructive hydrocephalus and encephalitis.²⁵

Segmental myoclonus of spinal origin involves muscles controlled by one or a few contiguous segments of the spinal cord. Propriospinal myoclonus is a less common distinctive form of myoclonus, involving activity over extensive lengths of the spinal cord rather than a segmental distribution.²⁶ The myoclonic jerk tend to be repetitive and cause symmetrical often violent, axial flexion. The neck, trunk, hip and knees may be involved. It occurs spontaneously, often occurs during sleep, and may be elicited by taps to the trunk and limbs. EMG polygraph suggested that the myoclonic discharges spread up and down from a spinal generator. The involvement of propriospinal pathway is suggested by the pattern of muscles recruitment (trunk and proximal limbs bilaterally) and the relatively slow conduction velocity, with latencies between stimuli and reflex response in the order of 100 ms.²⁷

The electrophysiologic assessment of involuntary movements is not as widely used as traditional EMG tests. However, it can give some contributions to clinician to make a proper diagnosis and optimal management of involuntary movements.

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