

Brainstem Reticular Myoclonus

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Clinical Syndromes and Definitions

Myoclonus is defined as ‘quick movement of muscle.’ The resulting brief jerks are shock-like involuntary movements due to either a muscle contraction (positive myoclonus) or a brief interruption of contraction of active muscles (negative myoclonus). The term myoclonus initially included a variety of involuntary movements including tics. In 1903, Lundborg proposed the first classification to help specify this entity. Today, myoclonus can be classified based on clinical features, pathophysiology, or cause. On the basis of the clinical characteristics and electrodiagnostic studies, a relatively accurate site of origin in the nervous system can be predicted. Myoclonus can arise from the cortex, brainstem, spinal cord, and rarely from peripheral nerves. Those arising from the brainstem include exaggerated startle, reticular reflex myoclonus, and palatal myoclonus/tremor.

Exaggerated startle diseases or hyperekplexias (Greek for ‘to startle excessively’) refer to the brief, explosive, and overblown response to unexpected, mainly auditory stimuli but less frequently to visual or somesthetic stimuli. They were first described in 1958 by Kirstein and Silfverskiold; the definitive description in a large Dutch family occurred in 1966. Clinically, the hyperekplexias are characterized by three major features. A generalized stiffness in response to handling occurs after birth and disappears by 1 year of age. With time, an exaggerated response to sound stimulation becomes evident especially when the patient is anxious, tired, or frightened. An inconsistent generalized stiffness lasting a few seconds follows the startle and frequently leads to falls and injury. Periodic limb movements during sleep, hypnagogic myoclonus, hernias (umbilical, inguinal, and epigastric), epilepsy, swallowing, and respiratory problems in children, and sudden infant death syndrome may also be concomitantly present. Intelligence is usually normal, but mild mental retardation may be observed. On examination, affected infants may exhibit head retraction reflex, increased muscle tone, and hypokinesia. Adults have wide-based gait without ataxia with an exaggerated head retraction reflex.

The hyperekplexias are largely thought to be familial, but sporadic forms are known to occur. The major autosomal dominant forms are mapped to chromosome 5q33–35; a variety of missense mutations have also been

identified in the glycine receptor (GLRA1) gene. Glycine is the most common inhibitory neurotransmitter in the nervous system and its receptor consists of five subunits (3α and 2β); mutations located on the $\alpha 1$ subunit are associated with these diseases. Normally glycine receptors are linked to chloride channels and oppose depolarization. Abnormalities in the receptor lead to decreased inhibition of neuronal activity. Genetic associations are not known to occur with sporadic hyperekplexias, which can result from brainstem infarct, hemorrhage, and encephalitis. Although clonazepam is considered the drug of choice, other benzodiazepines, phenobarbital, vigabatrin, phenytoin, carbamazepine, chlorodiazepoxide, propofol, fluoxetine, 5-hydroxytryptophan, and piracetam can be tried.

Reticular reflex myoclonus was first described in 1977 by Hallet et al. and is thought by some to be a fragment of a generalized form of epilepsy originating in the brainstem. Rat models with urea-induced myoclonus have been well studied, and extensive electrodiagnostic studies including intracellular recordings implicate the nucleus reticularis gigantocellularis of the brainstem. Paroxysmal depolarization shifts (PDS), the most elemental component of a seizure discharge, are found in these regions. Reticular reflex myoclonus appears to be the human version of the brainstem myoclonus in rats. Some experts assert that seizures are a cortical phenomenon, and reticular reflex myoclonus should be considered nonepileptic.

Clinically, these patients have generalized jerks affecting mainly the proximal and flexor regions but are found all over the body. They can be elicited by voluntary movements or by sensory stimulation. Reticular reflex myoclonus was initially described in a patient with post-hypoxic myoclonus (Lance–Adams syndrome) and has been described with renal insufficiency. Single cases were reported in a patient with parkinsonism plus myoclonus, Lyme disease, procarbazine therapy, and neck trauma.

Diagnosis

Reticular reflex myoclonus can be differentiated from the hyperekplexias by several features. Although both appear to need a sensory stimulus to evoke the myoclonus, auditory stimulation is paramount in the startle syndromes. Hyperekplexia patients have the greatest sensitivity to

taps in the mantle regions (head, upper chest, and back), while the reticular reflex myoclonus patients greatest sensitivity to taps is in the distal limbs. Presence of spontaneous and action-induced jerks characterize the reticular reflex myoclonus, which have an electromyographic (EMG) burst duration of 10–30 ms. EMG burst duration of more than 75 ms is characteristic of the startle syndromes. When cranial nerves are involved in the reticular reflex myoclonus, the sternocleidomastoid muscle is activated first. Thyrotropin-releasing hormone is thought to have stimulatory effect on the reticular neurons in the medulla and may exaggerate this type of myoclonus. This may be helpful diagnostically in patients with reticular reflex myoclonus. Like exaggerated startle, reticular reflex myoclonus is usually treated with clonazepam. 5-Hydroxytryptophan can be beneficial in patients with reticular reflex myoclonus as well.

p0035 Other forms of startle syndromes have been described worldwide for more than 100 years. The startle syndromes, including reticular reflex myoclonus, share a characteristic rostrocaudal progression of muscle contraction and lack of habituation. These syndromes exhibit some variability in excessive startle. The jumping Frenchmen of Maine was first described in the family of French–Canadian lumberjacks in Moosehead, Maine in 1878. In Indonesia and Yemen, the afflicted are referred to as ‘latah’ and are usually women. In Siberia, these individuals are referred to as Myriachit and in Louisiana, as ‘ragin Cajun.’ There is some debate that these disorders may be psychogenic or functional in nature but should be distinguished from startle epilepsy.

p0040 Palatal tremor is the currently accepted term for what used to be called palatal myoclonus. In the past, this condition was referred to as rhythmic palatal myoclonus, oculopalatal myoclonus, palatal nystagmus, brainstem myorhythmia, and palatal myorhythmia. It is a rhythmic involuntary tremor of the soft palate and can be unilateral or bilateral. It is classified into symptomatic or essential palatal tremor (SPT or EPT, respectively). SPT results from the rhythmic contraction of the levator veli palatini muscle and EPT from tensor veli palatini. Nucleus ambiguus may be the site of origin for SPT and the trigeminal nucleus for EPT. While other brainstem findings may be

evident in patients with SPT, EPT patients have rhythmic clicking in the ear with no other brainstem findings. Pathologic evaluation consistently reveals contralateral hypertrophic degeneration of the inferior olive in SPT patients but not in EPT patients. Magnetic resonance imaging reveals a similar enlargement of the inferior olive and a T2 hyperintensity in the same region. The initial assumption that the lesion had to be within the triangle of Guillain–Mollaret is no longer considered to be completely accurate. Disruptions in other connections may lead to this type of clinical phenomenon also.

Treatment

Surgical and medical treatments for palatal tremor are frustrating. Antiepileptics and sedatives like benzodiazepines can provide some benefit. Botulinum toxin injections can be tried, but administration is difficult and the results are not reliable. Frequent injections are needed with unpredictable results.

Further Reading

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Relevant Websites

www.movementdisorders.org – Movement Disorder Society
www.myoclonus.com

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Non-Print Items

Abstract:

Brainstem reticular myoclonus is a form of myoclonus that includes exaggerated startle, reticular reflex myoclonus, and palatal myoclonus/tremor. Clinical history/examination and electrophysiological tools are fundamental to accurate recognition and diagnosis. Treatment is available for some forms of brainstem reticular myoclonus.

Keywords: Brainstem reticular myoclonus; Exaggerated startle; Hyperekplexias; Myoclonus; Palatal myoclonus/tremor; Reticular myoclonus; Reticular reflex myoclonus

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