Myoclonus

U.S. DEPARTMENT OF HEALTH
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National Institutes of Health

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What is myoclonus?

Myoclonus refers to sudden, brief involuntary twitching or jerking of a muscle or group of muscles. It describes a clinical sign and is not itself a disease. The twitching cannot be stopped or controlled by the person experiencing it. Myoclonus can begin in childhood or adulthood, with symptoms ranging from mild to severe.

Myoclonic twitches or jerks are caused by:

- sudden muscle contractions (tightening), called **positive myoclonus**, or
- muscle relaxation, called **negative myoclonus**.

Myoclonic jerks may occur:

- either alone or in sequence, in a pattern of movement or without pattern
- infrequently or many times per minute
- sometimes in response to an external event or when a person attempts to make a movement.

Myoclonus can be broadly categorized into:

- **Physiologic myoclonus** consists of a quick muscle twitch followed by relaxation. Examples are hiccups and the jerks or "sleep starts" that some people experience while drifting off to sleep. This form occurs in healthy people, causes no difficulties, and does not require medical treatment.
- **Pathologic myoclonus** may involve persistent, shock-like contractions in a group of muscles and is more widespread. They begin in one region of the body and spread to muscles in other areas. More severe cases can affect movement and severely limit a person's ability to eat, talk, or walk. This can be one of many signs indicating a wide variety of underlying disorders in the brain or nerves, secondary to certain medical conditions, or can be a reaction to certain types of medication.

What causes myoclonus?

Myoclonus may be caused:

- most commonly by a disturbance of the brain or spinal cord (the central nervous system, or CNS), or
- more rarely by an injury to the peripheral nerves (the nerves outside the CNS that connect to sensory organs and muscles, and relay information from/to the CNS).

Myoclonus can occur by itself or as one of several symptoms associated with a wide variety of nervous system disorders. For example, myoclonic jerks may develop in individuals with multiple sclerosis or epilepsy, and with neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, or Creutzfeldt-Jakob disease.

Myoclonus may also be seen in conjunction with infection, head or spinal cord injury, stroke, brain tumor, kidney or liver failure, chemical or drug intoxication, or metabolic disorders. Prolonged oxygen deprivation to the brain, called hypoxia, may lead to post-hypoxic myoclonus.

What are the types of myoclonus?

Classifying myoclonus is difficult because the causes and responses to therapy vary widely. Some of the commonly described types are:

- **Stimulus-sensitive myoclonus** is triggered by various external events, including noise, movement, and light. Being surprised may increase the sensitivity of the individual.
- **Sleep myoclonus** (or hypnic myoclonus) occurs during sleep and sleep transitions, often as one is dropping off to sleep. Some forms appear to be stimulus sensitive. While some people may not be troubled by, or need treatment, others may require treatment where myoclonus may be a symptom in more complex and disturbing sleep disorders.

- **Essential myoclonus** occurs on its own and is not influenced by abnormalities in the brain or nerves. Involuntary twitches or spasms can occur in people with no family history of the condition, and the cause may be unexplained (idiopathic). However, it also can appear among members of the same family—indicating that it may be an inherited disorder. It tends to be stable without increasing in severity over time. In some families there is an association of essential myoclonus with essential tremor or a form of dystonia (myoclonus-dystonia). Dystonia is a movement disorder in which sustained muscle contractions cause twisting and repetitive movements or abnormal postures.
- **Action myoclonus** is triggered by voluntary movement or even the intention to move. It may become worse during attempts at precise, coordinated movements. It can be the most disabling form of myoclonus affecting the arms, legs, and face. One of the causes may be brain damage that results from a lack of oxygen and blood flow to the brain, or it can be secondary to other medical or neurological conditions.
- **Cortical reflex myoclonus** originates in the cerebral cortex—the outer layer of the brain that is largely responsible for information processing. In this type, jerks usually involve only a few muscles in one part of the body, but jerks involving many muscles also may occur. It becomes more intense when a person attempts to move in a certain way (action myoclonus) or perceives a particular sensation.

- **Epileptic myoclonus** is the presence of myoclonus in people living with epilepsy. Myoclonus can occur as the only seizure manifestation, as one component of a seizure, or one of multiple types of seizures within an epilepsy syndrome. Some examples of syndromes with myoclonic seizures include:
  - **Juvenile myoclonic epilepsy** (JME) starts around puberty and involves myoclonic seizures usually of the neck, shoulders, or upper arms, as well as generalized tonic-clonic seizures (affecting the whole body).
  - **Myoclonic-astatic epilepsy** has generalized myoclonic jerks or seizures followed by a loss of muscle tone.
  - **Lennox-Gastaut Syndrome** occurs in childhood and involves multiple seizure types which are usually difficult to control, as well as intellectual disability.
  - **Progressive myoclonus epilepsy (PME)** is a group of disorders characterized by myoclonic seizures and other neurologic symptoms such as trouble walking or speaking. These rare disorders often get worse over time and sometimes are fatal. One of its many forms is **Lafora body disease** (or Lafora progressive myoclonus epilepsy), which is characterized by myoclonic seizures, progressive loss of memory, and impaired intellectual functions.

- **Reticular reflex myoclonus** originates in the brain stem, the part of the brain that connects to the spinal cord and controls vital functions such as breathing and heartbeat. Myoclonic jerks usually affect the whole body, with muscles on both sides of the body affected simultaneously. In some people, myoclonic jerks occur in only a part of the body, such as the legs, with all the muscles in that part being involved in each jerk. It can be triggered by either a voluntary movement or an external stimulus.
- **Palatal myoclonus** (or palatal tremor) is a regular, rhythmic contraction of one or both sides of the rear of the roof of the mouth, called the soft palate. The contractions are very rapid and may continue during sleep. The condition usually appears in adults and can last indefinitely. People with palatal myoclonus may note a "clicking" sound in the ear when the muscles in the soft palate contract. This can be idiopathic or secondary to injury in the brain stem or adjacent cerebellum.
- **Spinal myoclonus** originates in the spinal cord. In some instances, the myoclonic jerk involves the whole trunk, beginning in the thoracic (middle) spinal segments and spreading up and down, a phenomenon known as **propriospinal myoclonus**.
- **Peripheral myoclonus** refers to myoclonic jerks that originate from a peripheral nerve (outside of the brain and spinal cord) such as in hemifacial spasm (frequent spasms of the muscles on one side of the face).

What do scientists know about myoclonus?

Studies suggest that the following locations in the brain are involved in myoclonus:

- **Cerebral cortex**, which is the most common origin for myoclonus.
- **Brain stem**, which is close to structures that are responsible for the startle response—an automatic reaction to an unexpected stimulus involving rapid muscle contraction.

However, the specific mechanisms underlying myoclonus are not yet fully understood:

- Scientists believe that some types of stimulus-sensitive myoclonus may involve overexcitability of the parts of the brain that control movement.
- Laboratory studies suggest that an imbalance between chemicals called neurotransmitters may bring about myoclonus, with the end result being a lack of inhibition at some level (inhibition is a decrease in the rate of a chemical reaction, or its prevention).

Neurotransmitters carry messages between nerve cells. They are released by one nerve cell and attach to a protein called a receptor on neighboring (receiving) cells. Abnormalities or deficiencies in receptors for certain neurotransmitters may contribute to some forms of myoclonus, including receptors for:

- **Serotonin**, involved in modulating mood, cognition, reward, learning, memory, physiological processes, and more
- **Gamma-aminobutyric acid (GABA)**, which is involved in motor control

- **Glycine**, important for the control of motor and sensory functions in the spinal cord
- **Opioids**, involved in different functions related to analgesia, pain, and depression.

More research is needed to determine how these receptor abnormalities cause or contribute to myoclonus.

How is myoclonus diagnosed?

Following a review of the person's medical history and physical exam, a physician may order additional tests to confirm the diagnosis of myoclonus:

- **Electromyography (EMG)**, which measures electrical activity of muscle, is the commonly used method to diagnose myoclonus as well as nerve and muscle dysfunction
- **Electroencephalography (EEG)** uses electrodes attached to the scalp to record the electrical activity of the brain that may trigger the myoclonic jerk
- **Evoked potential studies** capture the electrical activity in the brain, brain stem, and spinal cord evoked by specific stimuli (i.e., tactile, auditory, visual stimulation)
- **Laboratory urine or blood tests** for possible causes and to rule out other conditions that may cause symptoms similar to myoclonus
- **Magnetic resonance imaging (MRI),** using computer-generated radio waves and a magnetic field, to produce three-dimensional images of the brain, spinal cord, nerve, and other tissue (including muscles).

How is myoclonus treated?

The first consideration is reversing or treating any underlying cause or origin of the myoclonus. However, many cases require symptomatic treatment if the myoclonus is disabling.

Several options are available to help treat myoclonus:

- **Clonazepam** is a medication that is commonly used to treat some forms of myoclonus. Dosages are increased gradually until the individual improves or side effects (such as drowsiness and loss of coordination) become bothersome. The beneficial effects of clonazepam may diminish over time if the individual develops a tolerance for the drug.
- Other drugs such as certain **barbiturates**, **phenytoin**, **levetiracetam**, **valproate**, and **primidone** are used to treat epilepsy in addition to myoclonus.
- **Multiple medications** may be required by some individuals for effective treatment. Although some medications have a limited effect when used individually, they may have a greater effect when combined with others that act on different pathways or mechanisms in the brain.
- **Hormonal therapy** (the use of hormones in medical treatment) may improve responses to antimyoclonic drugs in some people.

- **5-hydroxytryptophan (5-HTP)**, a building block of serotonin (a chemical made in the body that transmits nerve impulses), leads to improvement in individuals with some types of action myoclonus and progressive myoclonus epilepsy. However, the effectiveness of 5-HTP therapy varies between individuals, and sometimes this may even worsen the condition in some individuals. These differences in the effect of 5-HTP on people with myoclonus have not yet been explained.
- **Botulinum toxin injections** can reduce excess muscle activity by blocking the activity of a chemical that makes muscles contract at the cellular level. It is the first-line therapy for hemifacial spasm (frequent spasms of the muscles on one side of the face) and has been effective in treating some individuals with palatal myoclonus.

What research is being done?

The mission of the National Institute of Neurological Disorders and Stroke (NINDS) is to seek fundamental knowledge about the brain and nervous system and to use that knowledge to reduce the burden of neurological disease. NINDS is a component of the National Institutes of Health, the leading federal supporter of biomedical research in the world. As part of its mission, the NINDS supports research on myoclonus at its laboratories in Bethesda, Maryland and through grants to major research institutions across the country.

- Biomarkers are measurable indicators of some biological state or condition and are often necessary for predicting the nature and severity of a disease. A recent NINDS-funded study known as **Juvenile Myoclonic Epilepsy Connectome Project (JMECP)** aims to define biomarkers of JME. Using state-of-the-art imaging methods, researchers will measure altered structural and functional connections between brain regions in children and adolescents between 12 to 20 years of age with JME. Results may lead to novel clinical tools for diagnosis and personalized management for individuals with JME.
- Glycogen is a form of sugar that is used as an energy reserve in many cells. Lafora bodies (LBs) are unusual, glycogen-like inclusions found in cells of all tissues in individuals suffering from Lafora body disease (or Lafora progressive myoclonus epilepsy). NINDS-funded scientists hope to understand what goes wrong with glycogen storage in Lafora body disease, which could help provide clues to new treatments. In another study, NINDS-funded researchers will generate proteins that will help to degrade or break down LBs, which could lead to a novel therapeutic strategy to treat Lafora body disease.

- Researchers of the **Lafora Epilepsy Cure Initiative** determined the satisfactory performance of therapeutic agents against Lafora body disease and myoclonus epilepsy in pre-clinical trials with mice. A current NINDS-funded study will develop an **Early Diagnosis Campaign** to prepare a clinical trial ready group of people with early-stage and moderately advanced Lafora body disease and to identify clinical biomarkers of disease progression before advancing from mice therapeutics to human clinical trials.
- Botulinum toxin is a treatment for a variety of movement disorders. A NINDS study compared the use of ultrasound (using sound waves) and electrophysiologic guidance (using electrical stimulation and a needle) to precisely target muscles for **botulinum toxin injection to treat upper limb spasticity and focal hand dystonia**. Results may lead to improved treatment for movement disorders such as myoclonus.
- Animal models are being used to study the mechanisms involving myoclonus. For example, NINDS-funded scientists have developed **a mouse model of myoclonus-dystonia** (an inherited movement disorder characterized predominantly by myoclonus of the upper body and dystonia). A striking characteristic of this disorder is that motor symptoms improve with alcohol

consumption. Researchers tested the hypothesis that abnormal activity of the cerebellum (the part of the brain responsible for coordination and regulation of voluntary movement) causes myoclonus and dystonia in myoclonus-dystonia, and that by acting on targets in the cerebellum, alcohol injections normalize cerebellar activity to relieve motor symptoms. Results may provide a better understanding of the underlying neurological cause of myoclonus and dystonia in myoclonus-dystonia and provide targets for treatment options.

- Complex movement disorders (CMDs), defined as disorders in which individuals are affected by more than one movement disorder (such as parkinsonism and dystonia, or myoclonus and tremor), are a continuing challenge for diagnosis and treatment. NINDS-funded researchers are **recruiting individuals with familial and sporadic CMDs to identify genetic mutations that may cause these disorders**. Findings may lead to improvements in disease diagnosis and treatment.

In addition to NINDS, other NIH institutes and centers support research on movement disorders that include myoclonus. More information is available through the NIH RePORTER (https://projectreporter.nih.gov), a searchable database of current and previously funded research, as well as research results and publications.

Many neurological disorders do not have effective treatment options. Clinical studies offer hope for many people and an opportunity to help researchers find better ways to safely detect, treat, or prevent disease. For more information about finding and participating in a clinical study, visit Clinicaltrials.gov at https://clinicaltrials.gov. Use the search term "myoclonus" to find trials on this disorder.

Where can I get more information?

The National Institute of Neurological Disorders and Stroke conducts and supports a wide range of research on neurological disorders, including myoclonus. For information on other neurological disorders or research programs funded by the NINDS, contact in the Institute's Brain Resources and Information Network (BRAIN) at:

BRAIN
P.O. Box 5801
Bethesda, MD 20824
301-496-5751
800-352-9424
www.ninds.nih.gov

Interested individuals may wish to contact the following organizations for additional information on myoclonus:

National Organization for Rare Disorders (NORD)
55 Kenosia Avenue
Danbury, CT 06813-1968
203-744-0100
800-999-6673
https://www.rarediseases.org

MedlinePlus
U.S. National Library of Medicine, NIH
https://medlineplus.gov

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