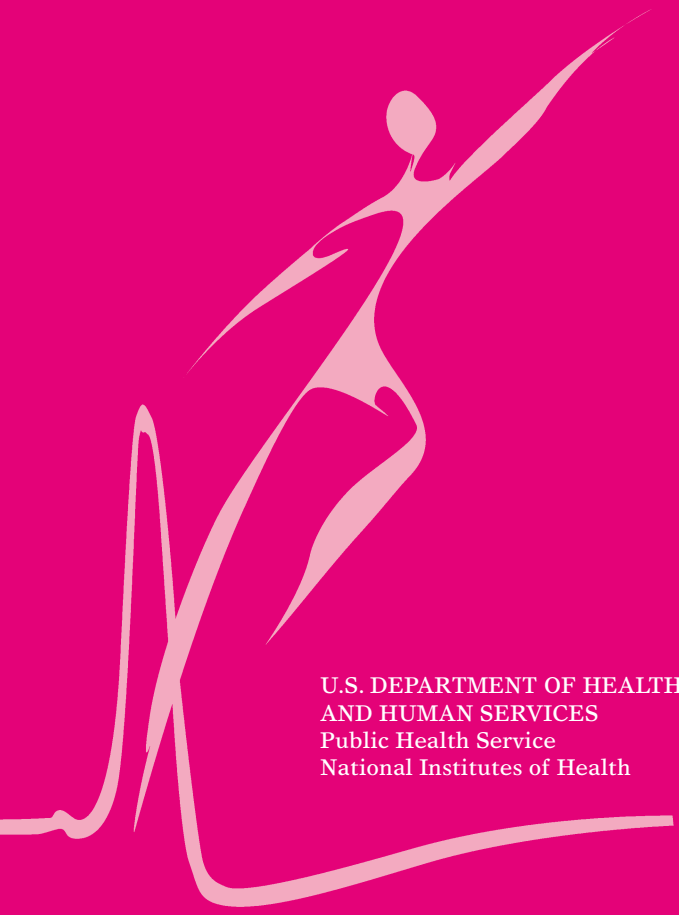
Myoclonus



U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES
Public Health Service
National Institutes of Health

Myoclonus

What is myoclonus?

Myoclonus describes a clinical sign and is not itself a disease. It refers to sudden, involuntary twitching or jerking of a muscle or group of muscles. Myoclonic twitches or jerks usually are caused by sudden muscle contractions, called positive myoclonus, or by muscle relaxation, called negative myoclonus. Myoclonic jerks may occur alone or in sequence, in a pattern or without pattern. They may occur infrequently or many times each minute. Myoclonus sometimes occurs in response to an external event or when a person attempts to make a movement. The twitching cannot be controlled by the person experiencing it.

In its simplest form, myoclonus consists of a muscle twitch followed by relaxation. A hiccup is an example of this type of myoclonus. Other familiar examples of myoclonus are the jerks or "sleep starts" that some people experience while drifting off to sleep. These simple forms of myoclonus occur in healthy people and cause no difficulties.

When it is more widespread, myoclonus may involve persistent, shock-like contractions in a group of muscles. In some cases, myoclonus begins in one region of the body and spreads to muscles in other areas. More severe cases of myoclonus can affect movement and severely limit a person's ability to eat, talk, or

walk. These types of myoclonus may indicate an underlying disorder in the brain or nerves.

What are the causes of myoclonus?

There are several different causes of myoclonus. For example, myoclonus may be seen in conjunction with infection, head or spinal cord injury, stroke, brain tumors, kidney or liver failure, lipid storage disease, chemical or drug intoxication, or other disorders. Prolonged oxygen deprivation to the brain, called hypoxia, may result in posthypoxic myoclonus. 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 and neurodegenerative diseases such as Parkinson's disease, Alzheimer's disease, or Creutzfeldt-Jakob disease. Myoclonic jerks also may occur in persons with epilepsy.

What are the types of myoclonus?

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

- **Action myoclonus** is triggered or intensified by voluntary movement or even the intention to move. It may be made worse by attempts at precise, coordinated movements. Action myoclonus can be the most disabling form of myoclonus and can affect the arms, legs, and face. This type of myoclonus may be caused by brain damage that results from a lack of oxygen and blood flow to the brain.

- **Cortical reflex myoclonus** originates in the cerebral cortex—the outer layer of the brain that is responsible for much of the information processing that takes place in the brain. In this type of myoclonus, jerks usually involve only a few muscles in one part of the body, but jerks involving many muscles also may occur. Cortical reflex myoclonus can be intensified when a person attempts to move in a certain way (action myoclonus) or perceive a particular sensation.
- **Essential myoclonus** occurs in the absence of apparent abnormalities in the brain or nerves. Its involuntary twitches or spasms can occur in people with no family history, but it also can appear among members of the same family—indicating that it sometimes may be an inherited disorder. Essential myoclonus 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.
- **Palatal myoclonus**, also called 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 persist 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.
- **Progressive myoclonus epilepsy (PME)** is a group of disorders characterized by myoclonus, seizures, and other neurologic symptoms

such as trouble walking or speaking. These rare disorders often get worse over time and sometimes are fatal. Studies have identified many forms of PME. One example is **Lafora body disease**, which occurs only when a child inherits two copies of a defective gene, one from each parent. Lafora body disease is characterized by myoclonus, seizures, and dementia (progressive loss of memory and other 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. Reticular reflex myoclonus can be triggered by either a voluntary movement or an external stimulus.
- **Stimulus-sensitive myoclonus** is triggered by a variety of external events, including noise, movement, and light. Surprise may increase the sensitivity of the individual.
- **Sleep myoclonus** occurs during sleep and sleep transitions, often as one is dropping off to sleep. Some forms appear to be stimulus-sensitive. Some persons with sleep myoclonus are rarely troubled by, or need treatment for, the condition. However, myoclonus may be a symptom in more complex and disturbing sleep disorders, and may require treatment by a doctor.

What do scientists know about myoclonus?

Most myoclonus is caused by a disturbance of the brain and spinal cord (the central nervous system); although rare cases of myoclonus are caused by an injury to the peripheral nerves (the nerves outside the central nervous system that connect to sensory and other organs, muscles, and blood vessels and relay information from/to the CNS). Studies suggest that several locations in the brain are involved in myoclonus. One such location, for example, is in the brain stem close to structures that are responsible for the startle response, an automatic reaction to an unexpected stimulus involving rapid muscle contraction.

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 underlie myoclonus. 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. This attachment signals the receiving cell to act in a certain way.

There is some evidence that abnormalities or deficiencies in the receptors for certain neurotransmitters may contribute to some forms of myoclonus. Receptors that appear to be related to myoclonus include those for two important inhibitory neurotransmitters: serotonin and gamma-aminobutyric acid (GABA). Other receptors with links to myoclonus include those for opiates and glycine, the latter an inhibitory neurotransmitter important for the

control of motor and sensory functions in the spinal cord. More research is needed to determine how these receptor abnormalities cause or contribute to myoclonus.

How is myoclonus treated?

Treatment of myoclonus focuses on medications that may help reduce symptoms. Clonazepam is commonly used to treat myoclonus. Dosages of clonazepam usually are increased gradually until the individual improves or side effects become bothersome. Drowsiness and loss of coordination are common side effects. The beneficial effects of clonazepam may diminish over time if the individual develops a tolerance for the drug.

Many of the other drugs used for myoclonus, such as barbiturates, phenytoin, levetiracetam, valproate, and primidone, also are used to treat epilepsy. Each has side effects that may impact which medication a doctor selects for an individual patient.

Some studies have shown that doses of 5-hydroxytryptophan (5-HTP), a building block of serotonin, leads to improvement in individuals with some types of action myoclonus and PME. However, other studies indicate that 5-HTP therapy is not effective in all people with myoclonus, and, in fact, may worsen the condition in some individuals. These differences in the effect of 5-HTP on people with myoclonus have not yet been explained, but they may offer important clues to underlying abnormalities in serotonin receptors.

The complex origins of myoclonus may require the use of multiple medications for effective treatment. Although some medications have

a limited effect when used individually, they may have a greater effect when used with others that act on different pathways or mechanisms in the brain. By combining several drugs, physicians can often achieve greater control of myoclonic symptoms. Hormonal therapy also may improve responses to anti-myoclonic drugs in some people.

What research is being done?

Within the Federal government, the National Institute of Neurological Disorders and Stroke (NINDS), a component of the National Institutes of Health, has primary responsibility for sponsoring research on neurological disorders. 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.

Scientists are seeking to understand the underlying biochemical basis of involuntary movements and to find the most effective treatment for myoclonus and other movement disorders.

NINDS investigators are evaluating the role of neurotransmitters and receptors in myoclonus. If abnormalities in neurotransmitters or receptors are found to play a role in causing myoclonus, future research can focus on determining the extent to which genetic alterations are involved and on identifying the nature of those alterations. Scientists also may be able to develop drug treatments that target specific changes in the receptors to reverse abnormalities, such as the loss of inhibition, and to enhance mechanisms that compensate for these abnormalities. Identifying receptor abnormalities also may

help researchers develop diagnostic tests for myoclonus. NINDS-supported scientists are studying various aspects of PME, including the basic mechanisms and genes involved in this group of diseases.

Where can I get more information?

The National Institute of Neurological Disorders and Stroke conducts and support 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:

Opsoclonus Myoclonus Support Network, Inc.
2116 Casa Linda Drive
West Covina, CA 91791
626-315-8125
sangreenca@yahoo.com

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

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