

Dystonia

Making a Difference Today

Dystonia is a chronic neurological movement disorder that causes muscles to contract involuntarily, forcing certain parts of the body into abnormal and sometimes painful movements or postures. Any part of the body can be affected, including the legs, arms, neck, face, eyes, and vocal cords. Symptoms can often emerge during childhood. Some forms of dystonia, termed primary, are inherited. Other secondary forms of dystonia result from a physical trauma, stroke, tumor, or exposure to certain drugs or toxins. Most cases, however, have no known cause.

Dystonia affects at least 300,000 people in North America, making it the third most common movement disorder after Parkinson's disease and tremors. Yet dystonia is not very well known and is often misdiagnosed, sometimes as a psychological illness. Early symptoms—such as deteriorating handwriting, foot cramps, a voice tremor, or rapid blinking—can be very mild, but over time these symptoms can worsen and, in children and young adults, spread to other areas of the body. In such cases, the disorder eventually may cause severe disabilities, interfering with nearly all aspects of everyday living, including walking, sitting, sleeping, eating, and talking.

The emotional and financial impact on individuals and their families is enormous. The average dystonia patient spends \$12,000 a year for basic medical management, and the annual cost to the U.S. economy is at least \$13.5 billion.

Research Brings Greater Understanding

Although there is, as yet, no cure for dystonia, past funding from the National Institutes of Health (NIH) has helped scientists make giant strides forward in understanding the disorder and, thus, in diagnosing and treating it. Researchers have linked dystonia to an abnormality in the basal ganglia, structures deep within the brain that help initiate and control body movements. Exactly what goes wrong in the basal ganglia is still unclear, but evidence points to an imbalance of dopamine and other neurotransmitters that help cells in the brain communicate with each other.

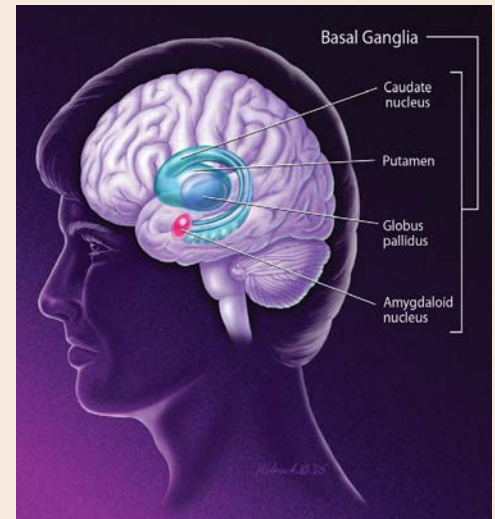
In 1997, scientists announced that they had identified and cloned the gene responsible for early-onset generalized dystonia, a particularly disabling form of the disorder that begins in childhood. This gene, called DYT1, produces an abnormal version of a previously unknown protein, now called torsinA. Scientists are now attempting to determine exactly what role torsinA plays in the development of dystonia. Since the identification of DYT1, researchers have identified three more of the dozen or so genes linked to inheritable forms of dystonia.

Treatment Advances

Medications that help correct neurotransmitter imbalances have been the mainstay of treatment for dystonia, but these drugs are not always effective and often produce severe side effects. One of the first big treatment breakthroughs came in the late 1980s with the discovery that botulinum toxin, when injected directly into the affected muscle, blocks the neurotransmitter acetylcholine, thus reducing the involuntary muscle contractions characteristic of dystonia. The Food and Drug Administration has now approved two botulinum toxins for the treatment of certain types of dystonia. More are under investigation.

Although past treatment advances have significantly improved the lives of people with dystonia, they are not a cure. Backed by NIH grants, researchers are actively searching for new treatments that will slow, prevent, or reverse this disabling disorder, rather than just lessen its symptoms.

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Dystonia has been linked to abnormalities in the basal ganglia, structures deep within the brain that help control movement. What goes wrong in the basal ganglia is still unknown, although some types of dystonia appear to involve an imbalance of dopamine and other neurotransmitters.

Continued funding for research could lead to:

- The development of new drugs that cause fewer side effects and work for longer periods of time than current ones.
- More effective surgical treatments.
- Greater understanding of the genetic and environmental factors that play a role in the development of dystonia.
- The discovery of a biomarker—a biochemical abnormality that all patients with dystonia might share—that could be detected by a simple chemical test or other screening technique before symptoms develop.



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Dystonia

Making a Difference Tomorrow

Dystonia is a disabling and often progressive brain disease. Did you know that:

- An estimated 300,000 people in North America are living with dystonia, making it the third most common movement disorder after Parkinson's disease and tremors.
- Dystonia affects more people than better known disorders, such as muscular dystrophy, Huntington's disease, and Lou Gehrig's disease.
- Symptoms of dystonia can strike at any age, even in children as young as 5 years old. Dystonia during childhood is often the most disabling.

Research Offers Hope for the Future

Federally funded basic research has helped scientists come closer to understanding the neurological causes of dystonia. With continued funding, researchers will be able to build on this knowledge to develop better diagnostic procedures, treatments, and preventive interventions.

Research is proceeding on several fronts. Using the latest brain imaging and mapping techniques, scientists are trying to better understand what precisely goes awry in the brain to cause dystonic symptoms. They are investigating, for example, the physiology of dystonic movements—how the electrical signals that control movements flow to and from the brain. They are also trying to decipher why the symptoms of some forms of dystonia can be temporarily controlled by “sensory tricks,” such as touching an affected body part.

On the genetics front, scientists are actively searching for additional genes with defects linked to dystonia. Such research is important because it helps unravel the complex neurochemical pathways involved in the disorder and, thus, promises to lead to new and more targeted treatments. Recent scientific advances have made it possible to create animal models that carry the mutated form of the human DYT1 gene. These models will greatly speed up our knowledge of how the DYT1 gene causes dystonia. And they will be useful in testing new therapies. Researchers are also trying to understand why only 30 percent to 40 percent of people with the abnormal DYT1 gene develop symptoms of dystonia—and how to identify those individuals before the symptoms appear.

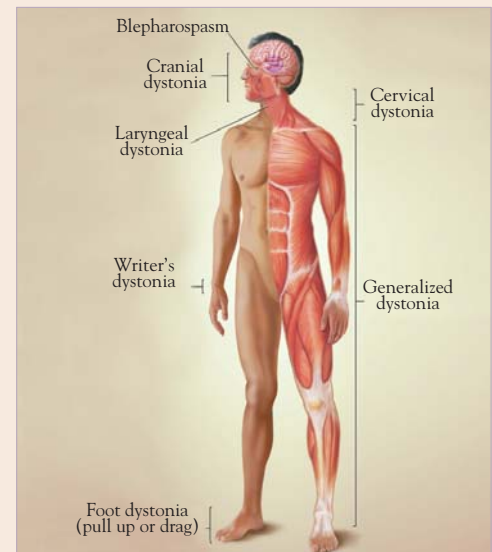
One of the most promising areas of dystonia research involves the study of torsinA, the protein linked to generalized dystonia, a particularly debilitating inherited form of the disorder. This protein was unknown just a few years ago. Scientists are now trying to determine how both normal and mutant torsinA affect cellular processes within the brain. Studies have shown that it's possible to selectively repress expression of mutant torsinA using an RNA inhibitor (RNAi)—a finding that may lead to new treatment possibilities.

Other researchers are studying the effectiveness of deep brain stimulation—a reversible surgical procedure that implants electrodes into specific areas within the basal ganglia—for treating patients who have dystonia. With the aid of a small implanted generator, the electrodes are “turned on” to an individually determined frequency to help correct abnormal brain circuits and, thus, relieve the abnormal movements and postures associated with dystonia. In 2003, the Food and Drug Administration approved deep brain stimulation for the treatment of dystonia in people whose symptoms fail to respond to medication. As of yet, scientists cannot predict which people with dystonia will respond to this therapy.

Hope for Other Disorders

Because dystonia is closely related to other movement disorders, including Parkinson's disease, essential tremor, and Huntington's disease, findings from dystonia research have wide ramifications. The discovery of the protein torsinA, for example, has opened a fascinating new avenue of research for scientists studying a number of neurological disorders, including the recent finding that torsinA appears to protect against the toxic accumulations of proteins that underlie Parkinson's disease. Only with continued funding, however, will scientists be able to make the new medical breakthroughs needed to help the millions of Americans whose lives have been devastated by dystonia and other movement disorders.

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Dystonia can affect any area of the body, including the vocal cords (laryngeal dystonia), face (cranial dystonia), hand (writer's dystonia), eyelids (blepharospasm), and neck and shoulder (cervical dystonia). It can also affect many parts of the body simultaneously (generalized dystonia).

Already research has led to:

- The identification and mapping of several genes directly linked to dystonia, including the DYT1 gene, which is responsible for a particularly disabling form of the disorder.
- The discovery of the protein torsinA, which appears to play a critical role in the major form of generalized dystonia in children and young adults.
- Botulinum toxin treatments, which can relieve dystonia symptoms in some people.
- Improvements in surgical treatments for dystonia, including deep brain stimulation.



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