

# Headache



National Institute of Neurological Disorders  
and Stroke  
National Institutes of Health

Hope Through Research

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# Introduction

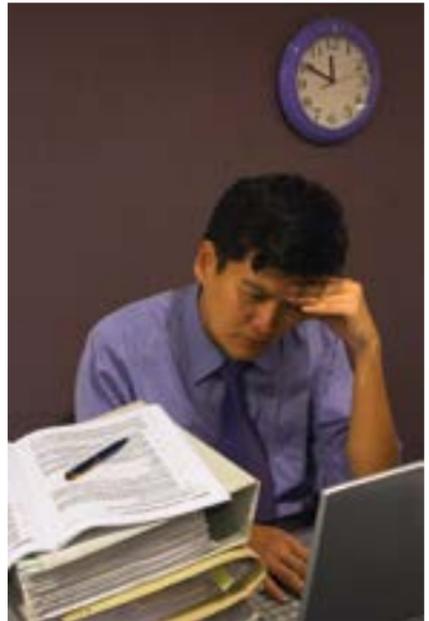
You're sitting at your desk, working on a difficult task, when it suddenly feels as if a belt or vice is being tightened around the top of your head. Or you have periodic headaches that occur with nausea and increased sensitivity to light or sound. Maybe you are involved in a routine, non-stressful task when you're struck by head or neck pain. Perhaps you have daily head pain that just won't go away.

Sound familiar? If so, you've suffered one of the many symptoms of headache that can occur on their own or as part of another disease or health condition.

Anyone can experience a headache. Nearly 2 out of 3 children will have a headache by age 15. More than 9 in 10 adults will experience a headache sometime in their life. Headaches are the most frequent neurological condition and our most common form of pain, yet relatively little is known about what causes them.

Certain types of headache run in families. Episodes of headache may ease or even disappear for a time and recur later in life. It's even possible to have more than one type of headache at the same time.

Headaches can range in frequency and severity of pain. Some individuals may experience headaches once or twice a year, while others may experience headaches more than 15 days a month.



Headaches are the most common form of pain and range in frequency and severity. Without proper treatment headaches can interfere with daily activities.

Headaches are called chronic in nature when they occur more than 14 days a month. Some headaches may last for weeks at a time. Pain can range from mild to disabling and may be accompanied by symptoms such as nausea or increased sensitivity to noise or light, depending on the type of headache.

Headache is a major reason cited for days missed at work or school as well as visits to the doctor. Headaches cost the U.S. billions of dollars a year in direct costs and lost productivity. Indirect costs are difficult to determine, such as the potential impact of severe chronic headaches in children and how they might restrict academic progress or social engagement.

Without proper treatment, headaches can be severe and restrict daily activities.

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## Why Headaches Hurt

Information about touch, pain, temperature, and vibration in the head and neck is sent to the brain by the trigeminal nerve, one of the 12 cranial nerves that start at the base of the brain.

The nerve has three branches that relay sensations from the scalp, the blood vessels inside and outside of the skull, the lining around the brain (the meninges), and the face, mouth, neck, ears, eyes, and throat.

Brain tissue itself lacks pain-sensitive nerves and does not feel pain. Headaches occur when pain-sensitive nerve endings called *nociceptors*<sup>1</sup> are activated in response to things that may bring on a headache (such as stress, certain foods or odors, or use of medicines).

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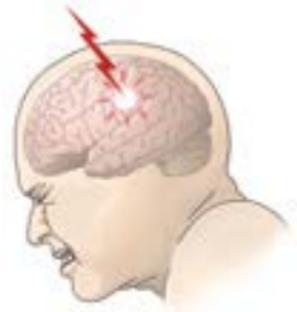
<sup>1</sup> Terms in italics appear in the Glossary found at the end of this document.

The nociceptors send messages through the trigeminal nerve to the brain stem and then to the thalamus, the brain’s “relay station” for pain sensation from all over the body, and then onto the parts of the cortex (the brain’s outer layer) involved in sensory and emotional processing. Other parts of the brain may also be part of the process, causing nausea, vomiting, diarrhea, trouble concentrating, and other neurological symptoms.

## When to See a Doctor

Not all headaches require a physician’s attention. People who experience uncontrolled recurring headaches, however, should be seen by a doctor. This is even more important in children. Most headaches are benign, but headaches can signal a more serious disorder that requires prompt medical care. Immediately call or see a physician if you or someone you’re with experience any of these symptoms:

- Very sudden, severe headache that may be accompanied by a stiff neck.
- Severe headache accompanied by fever, nausea, or vomiting that is not related to another illness.
- Sudden “worst” headache, often accompanied by confusion, weakness, double vision, or loss of consciousness (called a “thunderclap” headache because it occurs suddenly and severely).
- Headache that worsens over days or weeks or has changed in pattern or behavior.



A very sudden, severe headache accompanied by a stiff neck, or by fever, nausea, or vomiting requires prompt medical care.

- Headache following a head injury.
- Headache occurring with a loss of sensation or weakness in any part of the body, which could be a sign of a stroke.
- Headache associated with convulsions.
- Headache associated with shortness of breath.
- New onset of two or more headaches a week.
- Persistent headache in someone who has been previously headache-free, particularly someone over age 50.
- New headaches in someone with a history of cancer immune suppression or HIV/AIDS.
- Headache that occurs with upright position and goes away when lying flat.

## Diagnosing Your Headache

The circumstances under which you experience a headache can be key to diagnosing its cause. Keeping a headache journal can help a physician better diagnose your type of headache and determine the best treatment. After each headache, note the time of day when it occurred; its intensity and duration; any increased sensitivity to light, sound, or odors; nausea or vomiting; activity immediately prior to the headache; use of prescription and nonprescription over-the-counter medicines; amount of sleep the previous night; any stressful or emotional conditions; any influence from weather or daily activity; foods and fluids consumed in the past 24 hours; and any known health conditions at that time. Women should record the days of their menstrual cycles. Include notes about other family members who have a history of headache or other

disorder. A pattern may emerge that can be helpful to reducing or preventing headaches.

Once the doctor has reviewed your medical and headache history and conducted a physical and neurological exam, lab screening and diagnostic tests can help rule out or identify conditions that might be the cause of the headaches. Blood tests and urinalysis can diagnose brain or spinal cord infections, blood vessel damage, and toxins that affect the nervous system. Testing a sample of the fluid that surrounds the brain and spinal cord (obtained through a procedure called a lumbar puncture) can detect infections, bleeding in the brain (called a brain hemorrhage), and measure any buildup of pressure within the skull. Diagnostic imaging, such as with computed tomography (CT) and magnetic resonance imaging (MRI), can detect irregularities in blood vessels and bones, certain brain tumors and cysts, brain damage from head injury, brain hemorrhage, inflammation, infection, and other disorders. Neuroimaging also gives research doctors a way to see what's happening in the brain during headache attacks. An electroencephalogram (EEG) measures brain wave activity and can help diagnose brain tumors, seizures, head injury, and inflammation that may lead to headaches.

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## Headache Types and Their Treatment

*The International Classification of Headache Disorders* ([www.ihc-classification.org/en/](http://www.ihc-classification.org/en/)), published by the International Headache Society, is used to classify more than 150 types of primary and secondary headache disorders. The major types are discussed below.

## Primary Headache Disorders, including Migraine

*Primary headaches* occur independently and are not caused by another medical condition. It's uncertain what sets the process of a primary headache in motion. A cascade of events that affect blood vessels and nerves inside and outside the head sends pain signals to the brain. Brain chemicals and inflammatory molecules are involved in creating head pain, as are changes in nerve cell activity (called *cortical spreading depression* in the case of migraine headaches).

Primary headache disorders are divided into four main groups: migraine, tension-type headache, cluster headache and trigeminal autonomic cephalgias (a group of short-lasting but severe headaches), and a miscellaneous group.

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## Migraine

If you suffer from migraine headaches, you're not alone. About 12 percent of the U.S. population experience migraines, one form of *vascular* headaches. Migraine headaches are characterized by a buildup of throbbing and pulsating pain caused by the activation of nerve fibers within the wall of brain blood vessels of the meninges. Migraine headaches are recurrent attacks of moderate to severe pain that is throbbing or pulsing and often strikes one side of the head. Untreated attacks last from 4 to 72 hours. Other common symptoms are increased sensitivity to light, noise, and odor, as well as nausea and vomiting. Routine physical activity, movement, or even coughing or sneezing can worsen migraine pain.

Migraines occur most frequently in the morning, especially upon waking. Some people have migraines at predictable times, such as before menstruation or on weekends following a stressful week of work. Many people feel exhausted or weak following a migraine but are usually symptom-free between attacks.



Caffeine (or caffeine withdrawal) is one of many triggers for migraine headaches.

A number of factors can increase the risk of having a migraine and trigger the headache process. Although migraine triggers vary from person to person, they include sudden changes in weather or environment, too much or not enough sleep, strong odors or fumes, emotion, stress, overexertion, loud or sudden noises, motion sickness, low blood sugar, skipped meals, tobacco, depression, anxiety, head trauma, hangover, some medications, hormonal changes, and bright or flashing lights. Overusing analgesic medication or missing doses of preventive medications may also cause headaches. In some 50 percent of migraine sufferers, foods or ingredients can induce headaches. These include aspartame, caffeine (or caffeine withdrawal), wine and other types of alcohol, chocolate, aged cheeses, monosodium glutamate, some fruits and nuts, fermented or pickled goods, yeast, and cured or processed meats. Keeping a diet journal can help identify food triggers.

**Who Gets Migraines?** Migraines occur in both children and adults, but affect adult women three times more often than men (perhaps due to hormonal triggers). There is evidence that migraines are genetic,

with most migraine sufferers having a family history of the disorder. They also frequently occur in people who have other medical conditions. Depression, anxiety, bipolar disorder, sleep disorders, and epilepsy are more common in individuals with migraine than in the general population. Migraine sufferers—in particular those individuals who have pre-migraine symptoms referred to as *aura*—have a slightly increased risk of having a stroke.

Migraine in women often relates to changes in hormones. The headaches may begin at the start of the first menstrual cycle or during pregnancy. Most women see improvement after menopause, although surgical removal of the ovaries usually worsens migraines. Women with migraine who take oral contraceptives may experience changes in the frequency and severity of attacks, while women who do not suffer from headaches may develop migraines as a side effect of oral contraceptives.

**Phases of Migraine.** A migraine is divided into four phases, all of which may or may not be present during the attack:

- *Premonitory* symptoms occur up to 48 hours prior to developing a migraine. These include food cravings, unexplained mood changes (depression or euphoria), uncontrollable yawning, fluid retention, or increased urination.
- *Aura*. Some people will see flashing or bright lights or what looks like heat waves 10-12 minutes prior to or during the migraine, while others may experience muscle weakness or the sensation of being touched or grabbed.

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*The four phases of a migraine headache are premonitory, aura, headache, and postdrome. However, all of the phases may not be present during a migraine attack.*

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- **Headache.** Headache pain usually starts gradually and builds in intensity. It is associated with increased sensitivity to light and/or noise. It is possible, however, to have migraine without a headache.
- **Postdrome** (following the headache). Individuals are often exhausted or confused following a migraine. The postdrome period may last up to a day before people feel healthy.

**Types of Migraine.** The two major types of migraine are:

- **Migraine with aura**, previously called classic migraine, includes visual disturbances and other neurological symptoms that appear about 10 to 60 minutes before the actual headache and usually last no more than an hour. Individuals may temporarily lose part or all of their vision. Other classic symptoms include trouble speaking; an abnormal sensation, numbness, or muscle weakness on one side of the body; a tingling sensation in the hands or face, and confusion. Nausea, vertigo, loss of appetite, and increased sensitivity to light, sound, or noise may precede the headache.
- **Migraine without aura**, or common migraine, is the more frequent form of migraine. Symptoms include headache pain that occurs without warning and is usually felt on one side of the head, along with fatigue and associated symptoms seem in classic migraine.

Other types of migraine include:

- **Abdominal migraine** mostly affects young children and involves moderate to severe pain in the middle of the abdomen lasting 1 to 72 hours with little or no headache. Additional symptoms include nausea, vomiting, and loss of appetite. Many children who develop abdominal migraine will have migraine headaches later in life. Cyclic vomiting syndromes (CVS) also occur in children, half of whom develop migraine later in life. Children with CVS have attacks of vomiting that last hours to days.
- **Basilar-type migraine** mainly affects older children and adolescents. Symptoms include partial or total loss of vision or double vision, dizziness and loss of balance, poor muscle coordination, slurred speech, a ringing in the ears, and fainting. The throbbing pain may come on suddenly and is felt on both sides at the back of the head. Symptoms of basilar-type migraine are more frightening than harmful. There is no evidence that people with basilar-type migraine have a greater risk of stroke.
- **Hemiplegic migraine** is a rare but severe form of migraine that causes temporary paralysis—sometimes lasting several days—on one side of the body prior to or during a headache. Symptoms such as vertigo, a pricking or stabbing sensation, and problems seeing, speaking, or swallowing may begin prior to the headache pain and usually stop shortly thereafter. When it runs in families the disorder is called Familial Hemiplegic Migraine (FHM). Though rare, at least three distinct genetic forms of FHM have been identified. These genetic mutations make the brain more sensitive or excitable, most likely by increasing brain levels of a chemical called glutamate.

- ***Menstrually-related migraine*** affects women around the time of their period, although most women with menstrually-related migraine also have migraines at other times of the month. Symptoms may include migraine without aura (which is much more common during menses than migraine with aura), pulsing pain on one side of the head, nausea, vomiting, and increased sensitivity to sound and light.
- ***Migraine aura without headache*** is characterized by visual problems or other aura symptoms, nausea, vomiting, and constipation, but without head pain. Headache specialists have suggested that fever, dizziness, and/or unexplained pain in a particular part of the body could also be possible types of headache-free migraine.
- ***Retinal migraine*** is a condition characterized by attacks of visual loss or disturbances in one eye plus the pain phase of a migraine attack. The attacks are very similar in either eye. These attacks, like the more common visual auras, are usually associated with migraine headaches.
- ***Status migrainosus*** is a rare and severe type of acute migraine in which disabling pain and nausea can last 72 hours or longer. The pain and nausea may be so intense that sufferers need to be hospitalized.

**Migraine Treatment.** Migraine treatment is aimed at relieving symptoms and preventing additional attacks. Quick steps to ease symptoms may include napping or resting with eyes closed in a quiet, darkened room; placing a cool cloth or ice pack on the forehead, and drinking lots of fluid, particularly if the migraine is accompanied by vomiting. Small amounts of caffeine may help relieve symptoms during a migraine's early stages.

Drug therapy for migraine is divided into acute and preventive treatment. Acute or “abortive” medications can relieve pain and restore function when taken as soon as symptoms occur. Preventive treatment involves taking medicines daily to reduce the severity of future attacks or occurrence. The U.S. Food and Drug Administration (FDA) has approved a variety of drugs for these treatment methods. Headache drug use should be monitored by a physician, since some drugs may cause side effects.

Acute treatment for migraine may include any of the following drugs.

- *Triptan* drugs increase levels of the neurotransmitter *serotonin* in the brain. Serotonin causes blood vessels to constrict and lowers the pain threshold. Triptans—the preferred treatment for migraine—can ease moderate to severe migraine pain and are available as tablets, nasal sprays, and injections.
- *Ergot derivative drugs* bind to serotonin receptors on nerve cells and decrease the transmission of pain messages along nerve fibers. They are most effective during the early stages of migraine and are available as nasal sprays and injections.
- Non-prescription analgesics or over-the-counter drugs such as ibuprofen, aspirin, or acetaminophen can ease the pain of less severe migraine headache.
- Other non-prescription analgesics or over-the-counter drugs involve a mix of drugs such as acetaminophen plus caffeine and/or a narcotic for migraine that may be resistant to simple analgesics.
- Prescription or nonprescription nonsteroidal anti-inflammatory drugs (NSAIDS, including ibuprofen and naproxen) can reduce inflammation and alleviate pain.

- Nausea relief drugs can ease queasiness brought on by various types of headache.

Narcotics are prescribed briefly to relieve severe pain and should not be used to treat headaches.

Taking headache relief drugs more than three times a week may lead to **medication overuse headache** (previously called rebound headache), in which the initial headache is relieved temporarily. For example, taking triptan or analgesic drugs (including over the counter analgesics) too often can actually make your headache condition worse. Taking more of the drug to treat a new headache leads to progressively shorter periods of pain relief and results in a pattern of recurrent chronic headache. This kind of headache pain ranges from moderate to severe and may occur with nausea or irritability. It may take weeks for these medication overuse headaches to dissipate once the drug is stopped.

Preventive medications should be considered if migraines are frequent (occur two or more times weekly) or if migraines are disabling, regardless of frequency. Preventive medicines are also recommended for individuals who take symptomatic headache treatment more than three times a week. The doctor and patient will work together to find what type of preventive medicine works best (which means testing each medication for 2-3 months, unless intolerable side effects occur).



Quick steps to ease symptoms of a migraine include placing a cool cloth or ice pack on the forehead and drinking lots of fluids.

Several preventive medicines for migraine were initially marketed for conditions other than migraine.

- Anticonvulsants such as valproic acid and topiramate were originally developed for treating epilepsy, but these drugs can help prevent migraine because they increase levels of certain brain chemicals) and decrease the excitability of the brain. They may also be helpful for people with other types of headache.
- Beta-blockers are drugs used to treat high blood pressure and are often effective for preventing episodic migraine.
- Calcium channel blockers are medications that are also used to treat high blood pressure treatment and help to stabilize blood vessel walls. These drugs are often used to treat prolonged aura.
- Antidepressants may be helpful for individuals with other types of headaches because they increase the production of serotonin and may also affect levels of other chemicals, such as norepinephrine and dopamine. The effectiveness of antidepressants in treating migraine is not directly related to their effect on mood. The types of antidepressants used for migraine treatment include selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, and tricyclic antidepressants (which are also used to treat tension-type headaches). The effectiveness of antidepressants in treating migraine is not directly related to their effect on mood.

Natural treatments for migraine include riboflavin (vitamin B2), magnesium, and coenzyme Q10.

Non-drug therapy for migraine also includes biofeedback and relaxation training, both of which help individuals cope with or control the development of pain and the body's response to stress.

In March 2014 the FDA approved the Cefaly device—a battery-powered plastic headband worn across the forehead that uses a self-adhesive electrode to deliver a low electric current through the skin—for migraine prevention. The current stimulates the trigeminal nerves.

Lifestyle changes that reduce or prevent migraine attacks in some individuals include exercising, avoiding food and beverages that trigger headaches, eating regularly scheduled meals with adequate hydration, stopping certain medications, and establishing a consistent sleep schedule. Obesity increases the risk of developing chronic daily headache, so a weight loss program is recommended for obese individuals.

## Tension-Type Headache

Tension-type headache is the most common type of headache. Its name indicates the role of stress and mental or emotional conflict in triggering the pain and contracting muscles in the neck, face, scalp, and jaw. Tension-type headaches may also be caused by jaw clenching, intense work, missed meals, depression, anxiety, or too little sleep. Sleep apnea may cause tension-type headaches, especially in the morning. The pain is usually mild to moderate and feels as if constant pressure is being applied to the front of the face or to the head or neck. It also may feel as if a belt is being tightened around the head. Most often the pain is felt on both sides of the head. People who



Tension-type headaches—the most common type of headache—may feel as if a belt or “vice” is being tightened around the head.

suffer tension-type headaches may feel overly sensitive to light and sound but there is no pre-headache aura as with migraine. Typically, tension-type headaches usually disappear once the period of stress or related cause has ended.

Tension-type headaches affect women slightly more often than men. The headaches usually begin in adolescence and reach peak activity in the 30s. They have not been linked to hormones and do not have a strong hereditary connection.

There are two forms of tension-type headache: episodic tension-type headache and chronic tension-type headache. Episodic tension-type headaches occur between 10 and 15 days per month, with each attack lasting from 30 minutes to several days. Although the pain is not disabling, the severity of pain typically increases with the frequency of attacks. Chronic tension-type attacks usually occur more than 15 days per month over a 3-month period. The pain, which can be constant over a period of days or months, strikes both sides of the head and is more severe and disabling than episodic headache pain. Chronic tension headaches can cause sore scalps; even combing your hair can be painful. Most individuals will have had some form of episodic tension-type headache prior to onset of chronic tension-type headache.

Depression and anxiety can cause tension-type headaches. Headaches may appear in the early morning or evening, when conflicts in the office or at home are anticipated. Other causes include physical postures that strain head and neck muscles (such as holding your chin down while reading or holding a phone between your shoulder and ear), degenerative arthritis of the neck, and temporomandibular joint dysfunction (a disorder of the joints between the temporal bone located above the ear and the mandible, or lower jaw bone).

The first step in caring for a tension-type headache involves treating the cause. For example, arthritis of the neck is treated with anti-inflammatory medication and temporomandibular joint dysfunction may be helped by corrective devices for the mouth and jaw. A sleep study may be needed to detect and treat sleep apnea and should be considered when there is a history of snoring, daytime sleepiness, or obesity.

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A physician may suggest using analgesics, nonsteroidal anti-inflammatory drugs, or antidepressants to treat a tension-type headache that is not associated with a disease. Triptan drugs, barbiturates (drugs that have a relaxing or sedative effect), and ergot derivatives may provide relief to people who suffer from both migraine and tension-type headache.

Alternative therapies for chronic tension-type headaches include biofeedback, relaxation training, meditation, and cognitive-behavioral therapy to reduce stress. A hot shower or moist heat applied to the back of the neck may ease symptoms of infrequent tension headaches. Physical therapy, massage, and gentle exercise of the neck may also be helpful.

## Cluster Headache and Trigeminal Autonomic Cephalgias

Some primary headaches are characterized by severe pain in or around the eye on one side of the face and *autonomic* (or involuntary) features on the same side, such as red and teary eye, drooping eyelid, and runny nose. These disorders, called trigeminal autonomic cephalgias (*cephalgia* meaning head pain), differ in attack duration and frequency, and have episodic and chronic forms. Episodic attacks occur on a daily or near-daily basis for weeks or months with pain-free remissions. Chronic attacks occur on a daily or near-daily basis for a year or more with only brief remissions.

**Cluster headache**—the most severe form of primary headache—involves sudden, extremely painful headaches that occur in “clusters,” usually at the same time of the day and night for several weeks. They strike one side of the head, often behind or around one eye, and may be preceded by a migraine-like aura and nausea. The pain usually peaks 5 to 10 minutes after onset and continues at that intensity for up to 3

hours. The nose and the eye on the affected side of the face may get red, swollen, and teary. Some people will experience restlessness and agitation, changes in heart rate and blood pressure, and sensitivity to light, sound, or smell. Cluster headaches often wake people from sleep.



Cluster headaches involve sudden, extremely painful headaches that generally occur at the same time of the day or night. They can be provoked by alcohol, especially red wine, and smoking.

Cluster headaches generally begin between the ages of 20 and 50 but may start at any age, occur more often in men than in women, and are more common in smokers than in nonsmokers. The attacks are usually less frequent and shorter than migraines. It's common to have 1 to 3 cluster headaches a day with 2 cluster periods a year, separated by months of freedom from symptoms. The cluster periods often appear seasonally, usually in the spring and fall, and may be mistaken for allergies. A small group of people develop a chronic form of the disorder, which is characterized by bouts of headaches that can go on for years with only brief periods (1 month or less) of remission. Cluster headaches occur more often at night than during the day, suggesting they could be caused by irregularities in the body's sleep-wake cycle. Alcohol (especially red wine) and smoking can provoke attacks. Studies show a connection between cluster headache and prior head trauma. An increased familial risk of these headaches suggests that there may be a genetic cause.

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Treatment options include oxygen therapy—in which pure oxygen is breathed through a mask to reduce blood flow to the brain—and triptan drugs. Preventive treatment with certain calcium-channel blockers and lithium can reduce pain severity and frequency of attacks. In extreme cases, electrical stimulation of the occipital nerve to prevent nerve signaling may provide relief, as can surgical procedures that destroy or cut certain facial nerves.

***Paroxysmal hemicrania*** is a rare form of primary headache that usually begins in adulthood. Pain and related symptoms may be similar to those felt in cluster headaches, but with shorter duration. Attacks typically occur 5 to 40 times per day, with each attack lasting 2 to 45 minutes. Severe throbbing, claw-like, or piercing pain is felt in, around, or behind the eye on one side of

the face—and occasionally reaching to the back of the neck. Other symptoms may include red and watery eyes, a drooping or swollen eyelid on the affected side of the face, and nasal congestion. Individuals may also feel dull pain, soreness, or tenderness between attacks or increased sensitivity to light on the affected side of the face. Paroxysmal hemicrania has two forms: chronic, in which individuals experience attacks on a daily basis for a year or more, and episodic, in which the headaches may stop for months or years before recurring. Certain movements of the head or neck, external pressure to the neck, and alcohol use may trigger these headaches. Attacks occur more often in women than in men and have no familial pattern.

The nonsteroidal anti-inflammatory drug indomethacin can quickly halt the pain and related symptoms of paroxysmal hemicrania, but symptoms recur once the drug treatment is stopped. Non-prescription analgesics and calcium-channel blockers can ease discomfort, particularly if taken when symptoms first appear.

**SUNCT** (Short-lasting, Unilateral, Neuralgiform headache attacks with Conjunctival injection and Tearing) is a very rare type of headache with bursts of moderate to severe burning, piercing, or throbbing pain that is usually felt in the forehead, eye, or temple on one side of the head. The pain usually peaks within seconds of onset and may follow a pattern of increasing and decreasing intensity. Attacks typically occur during the day and last from 5 seconds to 4 minutes per episode. Individuals generally have five to six attacks per hour and are pain-free between attacks. This primary headache is slightly more common in men than in women, with onset usually after age 50. SUNCT may be episodic, occurring once or twice annually with headaches that remit and recur, or chronic, lasting more than 1 year. Occasionally SUNCT occurs as a headache disorder secondary to a brain lesion.

Symptoms include reddish or bloodshot eyes (conjunctival injection), watery eyes, stuffy or runny nose, sweaty forehead, puffy eyelids, increased pressure within the eye on the affected side of the head, and increased blood pressure.

SUNCT is very difficult to treat. The anticonvulsant drug lamotrigine may prevent attacks, while the intravenous anesthetic lidocaine and corticosteroid drugs can treat some of the severe pain felt during these attacks. Surgery and glycerol injections to block nerve signaling along the trigeminal nerve provide only temporary relief in severe cases. Doctors are beginning to use deep brain stimulation (involving a surgically implanted battery-powered electrode that emits pulses of energy to surrounding brain tissue) to reduce the frequency of attacks in severely affected individuals.

## Other Primary Headaches

Other headaches that are not caused by other disorders include:

***Chronic daily headache*** refers to a group of disorders that occur at least 15 days a month during a 3-month period. In addition to chronic tension-type headache, chronic migraine, and medication overuse headache (discussed above), these headaches include hemicrania continua and new daily persistent headache. Individuals feel constant, mostly moderate pain throughout the day on the sides or top of the head. They may also experience other types of headache. Adolescents and adults may experience chronic daily headaches. In children, stress from school and family activities may contribute to these headaches.

***Hemicrania continua*** is marked by continuous, fluctuating pain that always occurs on the same side of the face and head. The headache may last from minutes to days and is associated with symptoms including tearing, red and irritated eyes, sweating, stuffy or runny nose, and swollen and drooping eyelids. The pain may get worse as the headache progresses. Migraine-like symptoms include nausea, vomiting, and sensitivity to light and sound. Physical exertion and alcohol use may increase headache severity. The disorder is more common in women than in men and its cause is unknown. Hemicrania continua has two forms: chronic, with daily headaches, and remitting or episodic, in which headaches may occur over a period of 6 months and are followed by a pain-free period of weeks to months. Most individuals have attacks of increased pain three to five times per 24-hour cycle. The nonsteroidal anti-inflammatory drug indomethacin, the response to which is actually part of the diagnostic criteria, usually provides rapid relief from symptoms. Corticosteroids may also provide temporary relief.

***New daily persistent headache*** (NDPH), previously called chronic benign daily headache, is known for its constant daily pain that ranges from mild to severe. Individuals can often recount the exact date and time that the headache began. Daily headaches can occur for more than 3 months (and sometimes years) without lessening or ending. Symptoms include an abnormal sensitivity to light or sound, nausea, lightheadedness, and a pressing, throbbing, or tightening pain felt on both sides of the head. NDPH



Chronic daily headache occurs at least 15 days a month during a 3-month period.

occurs more often in women than in men and may occur spontaneously or following infection, medication use, head trauma, high spinal fluid pressure, or other condition. The disorder has two forms: one that usually ends on its own within several months and does not require treatment, and a longer-lasting form that is difficult to treat. Muscle relaxants, antidepressants, and anticonvulsants may provide some relief.

**Primary stabbing headache**, also known as “ice pick” or “jabs and jolts” headache, is characterized by intense piercing pain that strikes without warning and generally lasts 1 to 10 seconds. The stabbing pain usually occurs around the eye but may be felt in multiple sites along the trigeminal nerve. Onset typically occurs between 45 and 50 years of age. Some individuals may have only one headache per year while others may have multiple headaches daily. Most attacks are spontaneous but headaches may be triggered by sudden movement, bright lights, or emotional stress. Primary stabbing headache occurs most often in people who have migraine, hemicrania continua, tension-type, or cluster headaches. The disorder is hard to treat, because attacks are extremely short. Indomethacin and other headache preventive medications may relieve pain in some people.

**Primary exertional headache** may be brought on by coughing or sneezing or intense physical activity. Pain rarely lasts more than several minutes but can last up to 2 days. Symptoms may include nausea and vomiting. This type of headache is typically seen in individuals who have a family history of migraine. Warm-up exercises prior to the physical activity can help prevent the headache and indomethacin may relieve the headache pain.

**Hypnic headache**, previously called “alarm-clock” headache, awakens people mostly at night. Onset is usually after age 50. Hypnic headache may occur 15 or more times per month, with no known cause. Bouts of mild to moderate throbbing pain usually last from 15 minutes to 3 hours after waking and are most often felt on both sides of the head. Other symptoms include nausea or increased sensitivity to sound or light. Hypnic headache may be a disorder of rapid eye movement (REM) sleep as the attacks occur most often during dreaming. Both men and women are affected by this disorder, which is usually treated with caffeine, indomethacin, or lithium.

If you’ve ever eaten or inhaled a cold substance very fast, you may have had what’s called an **ice cream headache** (sometimes called “brain freeze”). This headache happens when cold materials such as chilled drinks or ice cream hit the warm roof of your mouth or back of your throat. Local blood vessels constrict to reduce the loss of body heat and then relax and allow the blood flow to increase. The resulting burst of pain

lasts for a few moments or even up to 5 minutes. Ice cream headache is more common in individuals who have migraine. The pain stops once the body adapts to the temperature change.

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*An “alarm clock” or hypnic headache generally awakens people at night.*

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## Secondary Headache Disorders

*Secondary headache* disorders are caused by an underlying illness or condition that causes pain-sensitive nerve endings to be pressed on or pulled or pushed out of place. Treatment depends on the primary disorder. Some examples of underlying conditions include fever, infection, medication overuse, stress or emotional conflict, high blood pressure, psychiatric disorders, head injury or trauma, stroke, tumors, and trigeminal neuralgia.

Some of the more serious causes of secondary headache include:

**Brain tumor.** Extremely few individuals with headache have a brain tumor. However, a tumor that is growing in the brain can press against nerve tissue and pain-sensitive blood vessel walls, disrupting communication between the brain and the nerves or restricting the supply of blood to the brain. Headaches may develop, worsen, become more frequent, or come and go, often at irregular periods. Headache pain may worsen when coughing, changing posture, or straining, and may be severe upon waking. Treatment options include surgery, radiation therapy, and chemotherapy.

**Disorders of blood vessels in the brain, including stroke.** Several disorders associated with blood vessel formation and activity can cause headache. Most notable among these conditions is stroke in both its hemorrhagic and ischemic forms. Headache itself can cause stroke or accompany a series of blood vessel disorders that can cause a stroke.

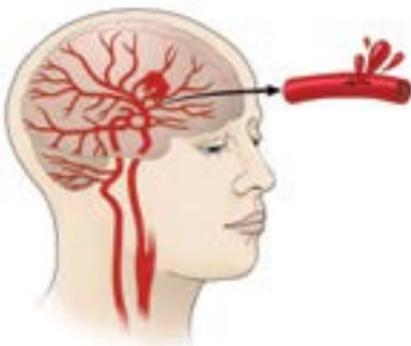
A **hemorrhagic stroke** occurs when an artery in the brain bursts, spilling blood into the surrounding tissue. Hemorrhagic stroke is typically associated with disturbed brain function and an extremely painful, sudden headache.

When the hemorrhage results from a rupture of a blood vessel located within the subarachnoid space—a fluid-filled space between layers of connective tissue (meninges) that surround the brain—the first sign of a subarachnoid hemorrhage is a severe headache with a split-second onset and no known cause. Neurologists call this a thunderclap headache. Pain may also be felt in the neck and lower back. This sudden flood of blood can contaminate the cerebrospinal fluid that flows within the spaces of the brain and cause extensive damage throughout the brain.

An intracerebral hemorrhage is also usually associated with severe headache. Several conditions can render blood vessels in the brain prone to rupture and hemorrhaging. Chronic hypertension can weaken the blood vessel wall. Poor blood clotting ability due to blood disorders or blood-thinning medications like warfarin further increase the risk of bleeding. And some venous strokes (caused by clots in the brain's veins) often cause bleeding into the brain. At risk for these strokes are mothers in the post-partum period and persons with dehydration, cancer, or infections.

An aneurysm is the abnormal ballooning of an artery that causes the artery wall to weaken. A ruptured cerebral aneurysm can cause subarachnoid hemorrhage and a sudden, incredibly painful headache that is generally different in severity and intensity from other headaches individuals may have experienced. Individuals usually describe the thunderclap-like headache as “the worst headache of my life.” There may be loss of consciousness and other neurological features that require emergency medical attention. “Sentinel” or sudden warning headaches sometimes occur from an aneurysm that leaks prior to rupture.

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Hemorrhagic stroke, which occurs when a brain artery bursts and spills blood into the surrounding tissue, is typically associated with an extremely painful, sudden headache.

*Arteriovenous malformation* (AVM), an abnormal tangle of arteries and veins in the brain, causes headaches that vary in frequency, duration, and intensity as vascular malformations press on and displace normal tissue or leak blood into surrounding tissue. A headache consistently affecting one side of the head may be closely linked to the site of an AVM (although most one-sided

headaches are caused by primary headache disorders). Symptoms may include seizures and hearing pulsating noises. Treatment options include blocking the blood vessel in the malformation by injecting particles or glue, or through focused radiotherapy or surgery.

An **ischemic stroke** occurs when an artery supplying the brain with blood becomes blocked, suddenly decreasing or stopping blood flow and causing brain cells to die. Headache that accompanies ischemic stroke can be caused by several problems with the brain's vascular system. Conditions of ischemic stroke that can cause headache include:

- An arterial dissection, which is a tear within an artery that supplies the brain with blood flow. The most common dissection occurs in the carotid artery in the neck, with head pain on the same side of the body (usually over the eyebrow) where the tear occurs. Vertebral artery dissection causes pain in the rear upper part of the neck. Cervical artery dissection can lead to stroke or transient ischemic attacks (strokes that last only a few minutes but signal a subsequent, more severe stroke). Dissections are usually caused by neck strain, i.e., trauma, an infrequent but reported complication of chiropractic manipulation, sports injuries, or even pronounced bending of the head backwards over a sink for hair washing (“beauty parlor stroke”). Immediate medical attention can be lifesaving.
- Cerebral vasculitis, an inflammation of the brain's blood vessel system that may cause headache, stroke, and/or progressive cognitive decline. Severe headache attributed to a chronic inflammatory disease of blood vessels on the outside of the head, called giant cell arteritis (previously known as temporal arteritis), usually affects people older than age 60.

Thunderclap headache can also be associated with *reversible cerebral vasoconstriction syndrome* (RCVS). It is more common in women. Blood vessels in the head show reversible narrowing sometimes leading to stroke. RCVS has been associated with pregnancy vasoconstriction drugs.

**Exposure to a substance or its withdrawal.**

Headaches may result from toxic states such as drinking alcohol, following carbon monoxide poisoning, or from exposure to toxic chemicals and metals, cleaning products or solvents, and pesticides. In the most severe cases, rising toxin levels can cause a pulsing, throbbing headache that, if left untreated, can lead to systemic poisoning, organ failure, and permanent neurological damage. These headaches are usually treated by identifying and removing the cause of the toxic buildup. The withdrawal from certain medicines or caffeine after frequent or excessive use can also cause headaches, as can overuse of medications to treat headache (medication overuse headache).



Arterial dissection—a tear within an artery that supplies blood to the brain—are usually caused by neck strain such as pronounced bending of the head backwards over a sink for hair washing. Dissections can cause lead to stroke and cause headache.

**Head injury.** Headaches are often a symptom of a concussion or other head injury. The headache may develop either immediately or months after a blow to the head, with pain felt at the injury site or throughout the head. In some rare cases, post-concussion or head trauma headaches may last for weeks to years. Emotional disturbances may worsen headache pain. In most cases, the cause of post-traumatic headache is unknown. Sometimes the cause is ruptured blood vessels, which result in an accumulation of blood called a hematoma—a mass of blood that displaces brain tissue and cause headaches as well as weakness, confusion, memory loss, and seizures. Hematomas can be drained surgically to produce rapid relief of symptoms. The most serious hematomas require immediate emergency treatment.

**Increased intracranial pressure.** A buildup or poor absorption of cerebrospinal fluid (CSF) in the brain can raise pressure in the brain and compress nerves and blood vessels, causing headaches. Two disorders that can lead to increased intracranial pressure are hydrocephalus and idiopathic intracranial hypertension. Hydrocephalus is an excess accumulation of CSF; Idiopathic intracranial hypertension, previously known as pseudotumor cerebri (meaning “false brain tumor”), is associated with severe headache and is most commonly seen in young, overweight females.

**Inflammation from meningitis, encephalitis, and other infections.** Inflammation from infections can harm or destroy nerve cells and cause dull to severe headache pain, along with other life-threatening conditions. Headaches may also occur with a fever or a flu-like infection but are not serious and generally do not require medical attention. A headache may accompany a bacterial infection of the upper respiratory tract that spreads to and inflames the lining of the sinus cavities.

**Seizures.** Migraine-like headache pain may occur after a seizure. Moderate to severe headache pain may last for several hours and worsen with sudden movements of the head or when sneezing, coughing, or bending. Other symptoms may include nausea, vomiting, fatigue, increased sensitivity to light or sound, and vision problems.

**Spinal fluid leak/low CSF pressure headache.**

About 10 to 25 percent of people who undergo a lumbar puncture (which involves a small sampling of the spinal fluid being removed for testing) develop a headache due to a leak of cerebrospinal fluid following the procedure. In other individuals, an internal spinal fluid leak also can cause the “Low CSF pressure headache.” Since the headache occurs only when the individual stands up, the “cure” is to lie down until the headache runs its course-anywhere from a few hours to several days. Persistent post-dural headaches may be treated by injecting a small amount of the individual’s own blood into the low back to stop the leak (called an epidural blood patch). Occasionally spinal fluid leaks spontaneously, causing this “low pressure headache.”

**Structural abnormalities of the head, neck and spine.** Headache pain and loss of function may be triggered by structural abnormalities in the head or spine, restricted blood flow through the neck, irritation to nerves anywhere along the path from the spinal cord to the brain, or stressful or awkward positions of the head and neck. Medications may ease the pain. *Cervicogenic* headaches are caused by structural irregularities in either the head or neck. In the Arnold-Chiari malformation, the back of the skull is too small for the brain. This forces a part of the brain to block the normal flow of spinal fluid and press on the brain stem. Chiari malformations are present at birth but may not cause symptoms until later in life, including headaches that worsen with coughing or straining.

Chiari malformations may be associated with syringomyelia, a fluid-filled cyst within the spinal cord, can cause pain, numbness, weakness, and headaches.

**Trigeminal neuralgia.** The trigeminal nerve conducts sensations to the brain from the upper, middle, and lower portions of the face, as well as inside the mouth. A potential cause of trigeminal neuralgia is a blood vessel pressing on the nerve as it exits the brain stem, but other causes have been described. Symptoms include headache and intense shock-like or stabbing pain that comes on suddenly and is typically felt on one side of the jaw or cheek.

## Children and Headache

Headaches are common in children. Headaches that begin early in life can develop into migraines as the child grows older. Migraines in children or adolescents can develop into tension-type headaches at any time. In contrast to adults with migraine, young children often feel migraine pain on both sides of the head and have headaches that usually last less than 2 hours. Children may look pale and appear restless or irritable before and during an attack. Other children may become nauseous, lose their appetite, or feel pain elsewhere in the body during the headache.

Headaches in children can be caused by a number of factors, including emotional problems such as tension between family members, stress from school activities, weather changes, irregular eating and sleep, dehydration, and certain foods and drinks. Of special concern



Headaches in children are common and can be caused by a number of triggers including emotional problems, stress, weather changes, irregular sleep and eating, dehydration, and certain foods and drinks.

among children are headaches that occur after head injury or those accompanied by rash, fever, or sleepiness.

It may be difficult to identify the type of headache because children often have problems describing where it hurts, how often the headaches occur, and how long they last. Asking a child with a headache to draw a picture of where the pain is and how it feels can make it easier for the doctor to determine the proper treatment.

Migraine in particular is often misdiagnosed in children. Parents and caretakers sometimes have to be detectives to help determine that a child has migraine. Clues to watch for include sensitivity to light and noise, which may be suspected when a child refuses to watch television or use the computer, or when the child stops playing to lie down in a dark room. Observe whether or not a child is able to eat during a headache. Very young children may seem cranky or irritable and complain of abdominal pain (abdominal migraine).

Headache treatment in children and teens usually includes rest, fluids, and over-the-counter pain relief medicines. The U.S. Food and Drug Administration has approved the drug almotriptan as a treatment for migraine pain in children age 12 and older, and the drug topiramate for migraine prevention in children ages 12 to 17. Always consult with a physician before giving headache medicines to a child. Most tension-type headaches in children can be treated with over-the-counter medicines that are marked for children with usage guidelines based on the child's age and weight. Headaches in some children may also be treated effectively using relaxation/behavioral therapy. Children with cluster headache may be treated with oxygen therapy early in the initial phase of the attacks.

A variety of headache education and drug and/or behavioral management approaches are now under development to improve headache treatment and prevention in children and adolescents. In 2015 the National Institute of Neurological Disorders and Stroke launched a project to develop a phone app to help pre-teen and adolescent children better manage their headaches by creating and following a headache log, monitoring medications, and noting changes they can share with their health care practitioner.

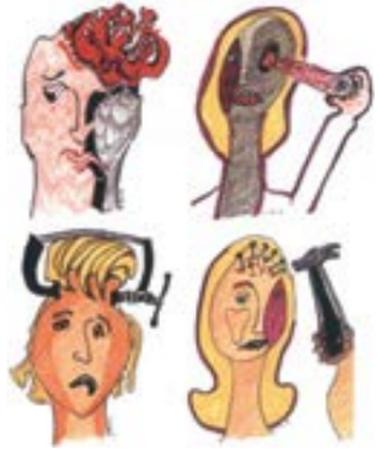
## Headache and Sleep Disorders

Headaches are often a secondary symptom of a sleep disorder but may also contribute to sleep disorders. For example, tension-type headache is regularly seen in persons with insomnia or sleep-wake cycle disorders. Nearly three-fourths of individuals who suffer from narcolepsy complain of either migraine or cluster headache. Migraines and cluster headaches appear to be related to the number of and transition between rapid eye movement (REM) and other sleep periods an individual has during sleep. Hypnic headache awakens individuals mainly at night but may also interrupt daytime naps. Reduced oxygen levels in people with sleep apnea may trigger early morning headaches.

Getting the proper amount of sleep can ease headache pain. Generally, too little or too much sleep can precipitate headaches, as can overuse of sleep medicines. Daytime naps often reduce deep sleep at night and can produce headaches in some adults. Some sleep disorders and secondary headache are treated using antidepressants. Check with a doctor before using over-the-counter medicines to ease sleep-associated headaches.

## Coping with Headache

Headache treatment is a partnership between an individual and his or her doctor, and honest communication is essential. Finding a quick fix to a headache may not be possible. It may take some time for a neurologist to determine the best course of treatment. Avoid using over-the-counter medicines more than twice a week, as they may actually lead to medication overuse headache with worsened headache pain and frequency of attacks. Visit a local headache support group meeting (if available) or join an online support group to learn how others with headache cope with their pain and discomfort. Relax whenever possible to ease stress and related symptoms, get enough sleep, regularly perform aerobic exercises, and eat a regularly scheduled and healthy diet that avoids food triggers. Gaining more control over your headache, stress, and emotions will make you feel better and let you embrace daily activities as much as possible.



Headache pain can range from mild to disabling. This drawing vividly illustrates how devastating headache pain can be. Learning to cope with headache pain and discomfort by gaining control over your headache, stress, and emotions will make you feel better and help you resume daily activities.

## What Research is Being Done by NINDS?

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. The NINDS is a component

of the National Institutes of Health, the leading supporter of biomedical research in the world.

The NINDS conducts and supports three types of research: *basic*—fundamental lab-based studies of how the nervous system works, *clinical*—the testing of treatment options for individuals with diseases, and *translational*—the creation of tools that speed the application of basic research discoveries into clinical practice. The goals of this research are to increase scientific understanding of the structure and function of the nervous system and nervous system disorders, and to find ways to prevent, treat, and cure these disorders.

NINDS-funded studies are revealing much about the difference between the brains of people who get frequent or chronic headaches and those who don't. In addition, ongoing studies of biomarkers (signs that may indicate risk of a disease) and associated symptoms of headache, beyond the pain symptoms, may lead to new treatments or perhaps ways to block some or all of the debilitating symptoms of headache. Studies by other investigators are adding insight to the causes and origins of headache and treatment.

Current NINDS research efforts include:

### **Understanding headache mechanisms and underlying causes**

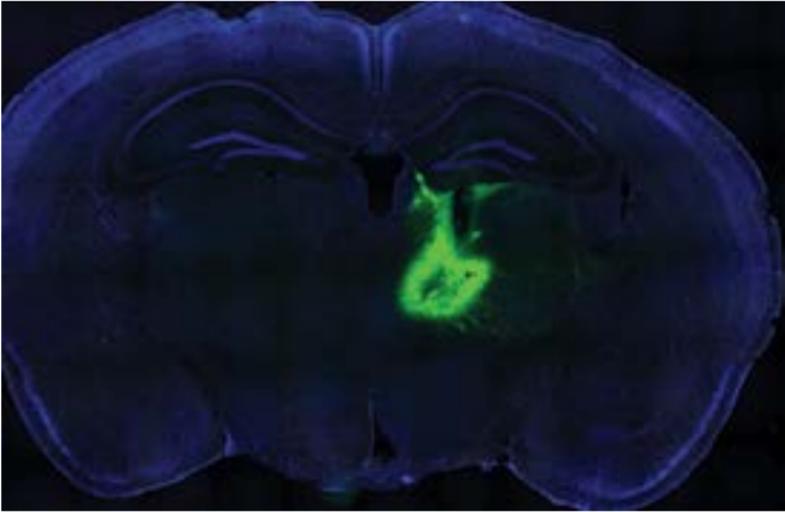
The neural mechanisms of photophobia—the abnormal sensitivity to light many individuals suffer immediately prior to or during a migraine—remain unclear.

Previous NINDS-funded research found that migraine photophobia occurs in blind persons that perceive light, but not in totally blind individuals who have migraines. Scientists are studying pain fibers in different parts of the brain and in the brain lining to identify any optic nerve and retinal involvement in

migraine pathophysiology. Related research hopes to identify the impact of light on sensory and other neurological functions during migraine and discover the neural pathways through which lights alter these functions. Other research on photophobia aims to test new hypotheses about how light modulates pain through interactions between neural circuits in pain and visual pathways.

Scientists are exploring the role of the molecule called calcitonin gene-related peptide (CGRP) in migraines. CGRP is thought to play a role in migraine due to blood vessel dilation in and around the brain, inflammatory substances released from mast cells, and activation of pain-sensitive nerve endings (nociceptors). Levels of the CGRP molecule, which is involved in sending signals between neurons, increase during migraine attacks and revert to normal when the pain resolves. Researchers using an animal model of migraine hope to identify mechanisms by which CGRP triggers photophobia.

Mast cells, which are part of the immune system and are involved in the inflammatory allergic response, are activated in some chronic pain conditions, including headache. Stress is common contributor to migraine. Researchers hope to better understand how stress may lead to mast cell activation in triggering photophobia and migraine. Additional research has shown that mast cells may release substances that activate nociceptive nerve cells that transmit signals from the linings of the skull and its blood vessels. Identifying biological pathways that link mast cell activation to headache pain may lead to new treatments for migraine and other cranial pain conditions.



**Shining a light on migraines.** Higher levels of calcitonin gene-related peptide (CGRP) are associated with light-avoiding behaviors in mice, which may serve as a model of a common symptom reported by people affected by migraines. Using optogenetics, a method of turning neurons on or off with a beam of light, scientists identified brain regions involved in this response. In this image, green fibers can be seen projecting from the posterior nuclei of the thalamus (a sensory processing area) up to the cortex (the outer layer of the brain). Surrounding brain cells are stained with a blue dye. The results from these experiments may help identify new therapeutic targets for the treatment of migraine.

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Researchers are also learning more about how nociceptors are activated to transmit pain signals. Many types of cell signaling are regulated through proteins called receptors, which reside in cell membranes and receive signals from outside the cell, triggering a cellular response. An NINDS-funded study on signaling pathways demonstrated that activation of a particular receptor in the brain, called transient receptor potential ankyrin-1 (TRPA1), may contribute to the development of pain associated with cluster headache and a variety of headache disorders. TRPA1 also may be involved in environmentally induced headaches, such as from exposure to chlorine or formaldehyde. Understanding the mechanisms of TRPA1 activation and related headache pain may offer new targets for headache treatment.

*Cortical spreading depression* (CSD) is a process in migraine with aura in which a wave of increased brain activity, followed by decreased activity, slowly spreads along the brain's surface. The wave of brain activity often travels across the part of the brain that processes vision and corresponds to the typical visual aura of migraine. Research has shown that migraines with aura may be associated with tiny areas of stroke-like brain damage caused by a short-term drop in oxygen levels (associated with the CSD) which disrupts normal cell function and causes swelling in the brain's nerve cells. Animal studies have shown that CSD also irritates the trigeminal nerve, causing it to transmit pain signals and trigger inflammation in the membranes that surround the brain. NINDS-funded researchers are studying vascular and metabolic events that may occur as a result of CSD and hope to determine their role in bringing about the persistent activation of sensory nerve cells in the membranes around the brain. Additionally, researchers are using animal and other models of CSD and migraine to create standardized screening tools for potential migraine drugs.

Genetics may contribute to a predisposition for migraine. Most migraine sufferers have a family member with migraine. Researchers have linked common forms of migraine to a specific gene location, and certain genes have been associated with rare types of migraine. One strategy is to test for a gene in several families having members with migraine and then determine if the gene is related to migraine in a broader population. NINDS-funded researchers are using genome-wide association studies (studies that look for common genetic variants) to determine if there are DNA sequence variations associated with migraine and with migraine accompanied by different co-occurring conditions such as asthma/allergy, cardiovascular disease, depression/anxiety, and epilepsy.

## Drug therapy and development

A major focus of headache research is the development of new drugs and other treatment options. Several NINDS-supported studies seek to develop and test new drugs to treat various headache disorders and to find safer, more effective doses for medications already being used.

Results of three randomized, placebo-controlled clinical trials show the drug topiramate is effective, safe, and generally well-tolerated for treating chronic migraine. Research on using a combination of more than one drug to treat migraine is ongoing. Nonetheless, a recent NINDS-funded clinical trial found no evidence that the addition of propranolol to topiramate added benefit to chronic migraine relief.

Migraine is often treated with triptan drugs, which cause blood vessels to constrict and inhibit the release of chemicals that lead to inflammation. However, overuse of these drugs to treat episodic migraine may lead to chronic migraine. The mechanisms of the transformation of episodic to chronic migraine are not known but may be related to changes in threshold for a response to migraine triggers. One NINDS-funded project is applying anatomical, molecular, and behavioral approaches to study how the drug sumatriptan modulates pain. Sumatriptan is used to treat migraine and cluster headache. Knowing more about how this drug works will increase our understanding of the disease process and aid in the design of new therapies. Understanding such mechanisms may reveal insight into changes



One area of migraine research focuses on genetics. Researchers have linked common forms of migraine to a specific gene location, and certain genes have been associated with rare types of migraine.

in the brain that trigger medication overuse headache and chronic migraine due to medication overuse, as well as into migraine mechanisms more broadly.

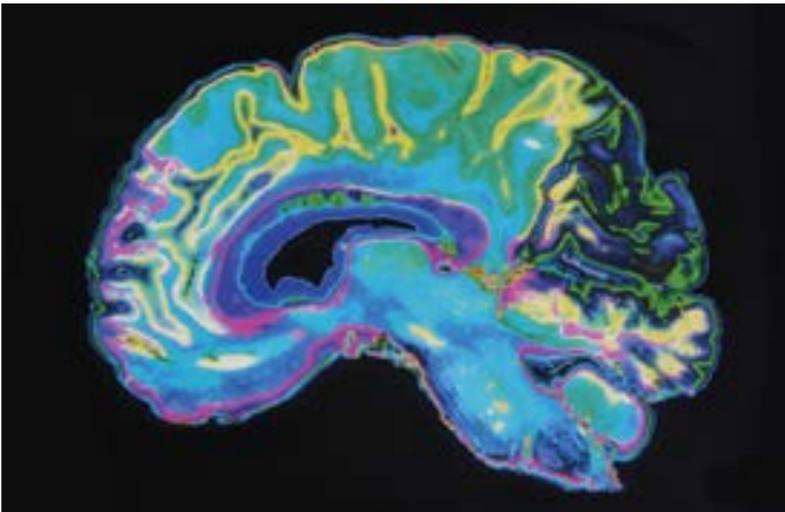
## **Brain imaging research**

Advanced brain imaging technologies are providing valuable insight into the pathophysiology of headache disorders. NINDS-funded researchers are using magnetic resonance imaging (MRI) to identify gender-related differences in brain structure and circuitry in people who experience migraines, suggesting the need for specific treatments for better results. Other NINDS-funded scientists are using advanced neuroimaging techniques such as functional MRI (fMRI, which measures changes in blood flow) to investigate networks in the brain that may explain the relationship between episodic and chronic migraine and hypersensitivities (such as to light, sound, or odors), as well as how environmental stimuli trigger an attack. The results of this research may lead to methods to normalize or block activation of these networks in order to prevent or reduce migraine symptoms.

The metabolic basis for migraine headaches and the aura associated with certain migraines is uncertain. NINDS-funded researchers hypothesize that cerebral blood flow and oxygen metabolism is abnormal in migraine, which affects the supply of oxygen to brain tissue. Researchers are using MRI to measure blood flow, oxygen metabolism, and tissue oxygenation in the brain to determine whether abnormalities in these measures are associated with migraine and if they remain abnormal following attacks. Results may help scientists assess the brain's physiological status during migraine and its response to therapy, with implications for migraine management and treatment.

Other research using neuroimaging techniques is evaluating and comparing the structure, chemistry, and function of brains of people with migraine who suffer frequent vs. infrequent attacks. A better understanding of the reasons for migraine progression may offer clues for novel therapeutic approaches and hope for preventing headaches. Researchers are evaluating and comparing the structure, chemistry, and function of brains of individuals who suffer from migraine at different ages. Researchers hope to demonstrate that males and females with migraine at different ages (pre-puberty, at puberty, and in adolescence) have significantly different brain processing as compared with people without migraine; and to identify changes in the female brain that may occur during puberty/adolescence. Measures of migraine's effect on the prepubescent brain may provide insights into brain changes involved in migraine independent of hormonal effects. Findings may show how brains are changed in different age groups and provide a basis for evaluation of medications to limit the progression of the disease.

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NINDS-funded scientists are using brain imaging technologies such as MRI to study gender-related differences in brain structure and circuitry in people with migraines.

## Behavior

Research shows a direct link between weight gain, obesity, chronic pain, and migraine. Behavioral weight loss programs are the “gold standard” treatment for obesity and consistently produce improvements in cardiovascular health, but their impact on migraine is unknown. A clinical study funded by the NINDS is testing the effectiveness of behavioral weight loss as a treatment for migraine in obese women aged 18 to 50 years. The primary aim is to examine whether participants assigned to a behavioral weight loss treatment program report fewer headaches than participants assigned to a migraine education condition.

## Sleep

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Sleep plays an important role in migraine. Sleep disturbance is a prominent risk factor in the progression from episodic to chronic migraine, yet very little is known about the mechanisms of sleep disturbance in migraine. NINDS-funded research is examining evidence for a pathway of sleep dysregulation in individuals with migraine, which may be characterized by instability in sleep behaviors and/or irregular circadian rhythm (the body’s clock that regulates the roughly 24-hour day-night cycle). Findings may help identify more precise ways to improve sleep for these individuals.

## NIH and NINDS—Expanding Pain Research

The NIH established a Pain Consortium to enhance pain research and promote collaboration among researchers across the many NIH Institutes and Centers that have programs and activities addressing pain. Among its goals, the Pain Consortium seeks to identify key opportunities in pain research (including those for headache), particularly those that provide for multidisciplinary and trans-NIH participation. NIH also works with patient advocacy groups and public-private partnerships to increase visibility for pain research.

The Interagency Pain Research Coordinating Committee (IPRCC) is a federal advisory committee created by the Department of Health and Human Services to enhance pain research efforts and promote collaboration across the government, with the ultimate goals of advancing fundamental understanding of pain and improving pain-related treatment strategies (including those related to headache). NIH is one of seven federal agencies represented on the Committee. Action items include the development of a summary of advances in pain care research supported or conducted by the federal agencies relevant to the diagnosis, prevention, and treatment of pain and diseases and disorders associated with pain. The committee also will identify critical gaps in basic and clinical research on the symptoms and causes of pain. The groups will make recommendations to ensure that the activities of the NIH and other federal agencies are free of unnecessary duplication of effort, and make recommendations on how to expand partnerships between public entities and private entities to expand collaborative, cross-cutting research.

Training the next generation of headache researchers is an important goal for NINDS and NIH. NINDS continues to fund training grants focused on headache disorders. Currently, several new or early stage headache researchers are funded through both career development awards intended to lead to independent research careers and through independent research awards.

## Where can I get more information?

For more information on neurological disorders (including other painful disorders) or research programs funded by the National Institute of Neurological Disorders and Stroke, contact 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](http://www.ninds.nih.gov)*

In addition to NINDS, several other NIH organizations also support research relevant to understanding, treating, or preventing headache. More information on headache research supported by the NINDS and other NIH components is available through the NIH RePORTER (*<http://projectreporter.nih.gov>*), a searchable database of current and previously funded research, as well as research results such as publications.

Information also is available from the following organizations:

**American Chronic Pain Association**

P.O. Box 850  
Rocklin, CA 95677-0850  
916-632-0922  
800-533-3231  
*www.theacpa.org*

**American Headache Society Committee for  
Headache Education (ACHE)**

19 Mantua Road  
Mt. Royal, NJ 08061  
856-423-0043  
*www.achenet.org*

**Migraine Research Foundation**

300 East 75<sup>th</sup> Street, Suite 3K  
New York, NY 10021  
212-249-5402  
*www.migraineresearchfoundation.org*

**National Headache Foundation**

820 North Orleans, Suite 411  
Chicago, IL 60610  
312-274-2650  
888-643-5552  
*www.headaches.org*

**NIH Pain Consortium**

*http://painconsortium.nih.gov/*

## Glossary

***abdominal migraine***—a type of migraine that mostly affects young children and involves moderate to severe abdominal pain, with little or no headache

***arteriovenous malformation***—a tangle of veins and arteries that can disrupt the normal flow of blood and are frequently associated with episodic headache. A catastrophic stroke may occur when an arteriovenous malformation in the skull bursts and bleeds into surrounding brain tissue.

***aura***—a warning of a migraine headache. Usually visual, it may appear as flashing lights, zigzag lines, or a temporary loss of vision, along with numbness or trouble speaking.

***autonomic***—occurring involuntary. The autonomic nervous system has many functions, including control of pupil size, eyelid droop, heart rate, breathing rate, digestion, perspiration, and elimination of body waste. Autonomic dysfunction is frequently associated with various types of migraine.

***basilar-type migraine***—a type of migraine, occurring primarily in young women, causing symptoms of abnormal brain stem functioning such as double vision, loss of peripheral vision, numbness, imbalance, or loss of consciousness

***benign intracranial hypertension***—increased pressure within the brain that causes severe headaches. It can be caused by being overweight, clotting in the major cerebral veins or from certain medications (including some antibiotics, human growth hormone replacement, and vitamin A and related compounds).

***cephalgia***—head pain

***cervicogenic headache***—a type of headache caused by structural irregularities in either the neck or head

**chronic headache**—headache that occurs 15 or more days a month over a 3-month period

**cluster headache**—sudden, extremely painful headaches that occur in a closely grouped pattern several times a day and at the same times over a period of weeks

**cortical spreading depression**—a wave of increased brain activity that slowly spreads from the back toward the front of the brain's surface and may be the basis for migraine aura

**electroencephalogram (EEG)**—a test to record electrical brain waves

**episodic**—comes and goes

**ergot derivative drugs**—drugs that bind to the neurotransmitter receptor for serotonin and help to decrease the transmission of pain messages along nerve fibers

**hemicrania continua**—one-sided headaches that are chronic or continuous and respond to indomethacin treatment

**hemiplegic migraine**—a type of migraine causing temporary paralysis on one side of the body

**hypnic headache**—a rare form of headache that awakens individuals at night (also called “alarm-clock headache”)

**ice cream headache**—a painful headache brought on by changes in blood flow that result from a sudden chilling of the roof of the mouth

**ischemic stroke**—stroke caused by a clot that blocks blood flow to the brain

**low CSF pressure headache**—a headache due to a leak of cerebrospinal fluid (CSF) following removal of a small sample of the fluid for testing, or caused by an internal spinal fluid leak

**medication overuse headache**—caused by the overuse of drugs (more than 3 times weekly) to treat headache. While the medication may help to relieve the headaches temporarily, over time the underlying headache becomes worse and occurs more frequently, creating a vicious cycle of medication use and head pain. The pain improves when the medication is stopped.

**meninges**—the three layers of membrane that cover the brain and spinal cord

**menstrually-related migraine**—a migraine that affects women around the time of their period

**migraine**—headaches that are usually pulsing or throbbing and occur on one or both sides of the head. They are moderate to severe in intensity, associated with nausea, vomiting, sensitivity to light and noise, and worsen with routine physical activity.

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**new daily persistent headache**—a type of treatment-resistant chronic headache marked by daily pain that can last for years

**nociceptors**—nerve fiber endings that receive and transmit pain signals

**paroxysmal hemicrania**—a rare form of headache that usually begins in adulthood and is marked by one-sided attacks that typically occur 5 to 40 times a day

**postdrome**—the period following the headache

**premonitory**—meaning before. Some individuals with migraine experience premonitory symptoms up to 24 hours prior to headache pain.

**primary exertional headache**—headache brought on by fits of coughing or sneezing, or by intense physical activity such as running or lifting

**primary headaches**—headaches that occurs on their own with no detectable underlying cause, such as migraine, tension-type headache, and the trigeminal autonomic cephalgias

**primary stabbing headache**—also called “ice pick headache” or “jabs and jolts” headache for its extremely intense pain that develops suddenly and generally lasts 1 to 10 seconds

**retinal migraine**—a type of migraine that is characterized by attacks of visual loss or disturbances in one eye

**reversible cerebral vasoconstriction syndrome**—a narrowing of the arteries in the brain that can be accompanied by sudden, “thunderclap” headache. It can occur during pregnancy and with the use of vasoactive drugs.

**secondary headaches**—headaches that are caused by an underlying condition or disease

**serotonin**—a neurotransmitter present throughout the body and brain that plays an important role in headache and migraine, mood disorders, regulating body temperature, sleep, vomiting, sexuality, and appetite

**status migrainosus**—migraine lasting more than 72 hours

**SUNCT (Short-lasting, Unilateral, Neuralgiform headache attacks with Conjunctival injection and Tearing)**—a rare form of headache marked by brief recurrent bursts of moderate to severe burning, stabbing, or throbbing pain, usually on one side of the head and around the eye or temple, accompanied by symptoms including watery, reddish eyes, and runny nose

***tension-type headache***—a primary headache that is band-like or squeezing and does not worsen with routine activity. It may be brought on by stress.

***trigeminal neuralgia***—a chronic pain condition that causes extreme, sporadic, sudden burning or shock-like face pain that lasts anywhere from a few seconds to as long as two minutes per episode

***trigger***—something that brings about a disease or condition.

***triptans***—a family of drugs used to treat migraines and cluster headaches by preventing or stopping nerve tissue inflammation and resulting changes in blood vessels

## **Credits**

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