

# Anxiety Disorders Research



At the National Institute of Mental Health

## FACT SHEET

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More than 19 million adult Americans ages 18 to 54 have anxiety disorders. The National Institute of Mental Health (NIMH) supports research into the causes, diagnosis, prevention, and treatment of anxiety disorders and other mental illnesses. This research is conducted both in the Institute's intramural laboratories and in biomedical research institutions across the country. Studies examine the genetic and environmental risks for major anxiety disorders, their course, both alone and when they co-occur with other illnesses such as heart disease or depression, and their treatment. Scientists seek to discover the basis of anxiety disorders in the brain and their effects on the functioning of the brain and other organs. The ultimate goal is to be able to cure, and perhaps even to prevent, anxiety disorders.

### Types of Anxiety Disorders

The term anxiety disorders encompasses several clinical conditions:

- *panic disorder*, in which feelings of extreme fear and dread strike unexpectedly and repeatedly for no apparent reason, accompanied by intense physical symptoms
- *obsessive-compulsive disorder (OCD)*, characterized by intrusive, unwanted, repetitive thoughts and rituals performed out of a feeling of urgent need
- *post-traumatic stress disorder (PTSD)*, a reaction to a terrifying event that keeps returning in the form of frightening, intru-

sive memories and brings on hypervigilance and deadening of normal emotions

- *phobias*, including specific phobia – a fear of an object or situation – and social phobia – a fear of extreme embarrassment
- *generalized anxiety disorder (GAD)*, exaggerated worry and tension over everyday events and decisions

### An NIMH Snapshot

The National Institute of Mental Health (NIMH) is one of 25 components of the National Institutes of Health (NIH), the Government's principal biomedical and behavioral research agency. NIH is part of the U.S. Department of Health and Human Services. The actual total fiscal year 1999 NIMH budget was \$859 million.

### NIMH Mission

To reduce the burden of mental illness through research on mind, brain, and behavior.

### How Does the Institute Carry Out Its Mission?

- NIMH conducts research on mental disorders and the underlying basic science of brain and behavior.
- NIMH supports research on these topics at universities and hospitals around the United States.
- NIMH collects, analyzes, and disseminates information on the causes, occurrence, and treatment of mental illnesses.
- NIMH supports the training of more than 1,000 scientists to carry out basic and clinical research.
- NIMH communicates information to scientists, the public, the news media, and primary care and mental health professionals about mental illnesses, the brain, mental health, and research in these areas.

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## Research Progress

NIMH research has led to advances in understanding the causes of these disorders and how to treat them. Today, the majority of people with panic disorder and OCD improve significantly within weeks or months of getting proper treatment. The same is true for people with phobias. And many people with PTSD and generalized anxiety disorder also make substantial improvement with treatment.

As the search continues for better treatments, NIMH is harnessing the most sophisticated scientific tools available to determine the causes of anxiety disorders. Like heart disease and diabetes, these brain disorders are complex and probably result from the interplay of genetic, behavioral, developmental, and other factors. Scientists in a number of disciplines are trying to identify risk factors that make certain people prone to these conditions.

## Studies of the Brain and Anxiety Disorders

Studies in animals and humans have focused on pinpointing the specific brain areas and circuits involved in anxiety and fear, which underlie anxiety disorders. Fear, an emotion that evolved to deal with danger, causes an automatic, rapid protective response that occurs without the need for conscious thought. It has been found that the body's fear response is coordinated by a small structure deep inside the brain, called the amygdala.

Neuroscientists have shown that when confronted with danger, the body's senses launch two sets of signals to different parts of the brain. One set of signals, which takes a more roundabout route, relays information to the cerebral cortex, the cognitive part of the brain that

## What Are the Treatments for Anxiety Disorders?

Treatments have been largely developed through research conducted by NIMH and other research institutions. They are extremely effective and often combine medication and specific types of psychotherapy.

More medications are available than ever before to effectively treat anxiety disorders. These include antidepressants and benzodiazepines. If one medication is not effective, others can be tried. New medications are currently being tested or are under development to treat anxiety symptoms.

The two most effective forms of psychotherapy used to treat anxiety disorders are behavioral therapy and cognitive-behavioral therapy. Behavioral therapy tries to change actions through techniques such as diaphragmatic breathing or through gradual exposure to what is frightening. In addition to these techniques, cognitive-behavioral therapy teaches patients to understand their thinking patterns so they can react differently to the situations that cause them anxiety.

explains in detail the threatening object or situation – such as a big black car heading for you as you cross the street. The other set of signals shoots straight to the amygdala, which sets the fear response in motion, readying the body for quick action – before the cognitive part of the brain comprehends just what is wrong. The heart starts to pound and diverts blood from the digestive system to the muscles for quick action. Stress hormones and glucose flood the blood stream to provide the energy to fight or flee. The immune system and the pain response are suppressed to prevent swelling and discomfort, which could interfere with a quick escape. And, as a preventive measure for similar confrontations in the future, the learned fear response is etched on the amygdala.

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## How Does This Learned Fear Response Turn into an Anxiety Disorder?

One or more fearful experiences can prime a person to respond excessively to situations where most people would experience no fear – such as in the supermarket – or only moderate nervousness – such as giving a speech. In anxiety disorders, the deeply etched memory can result in hypervigilance, making it hard to focus on other things, and leading to feelings of anxiety in many situations. In people who have survived overwhelming trauma and developed PTSD, for example, even mild reminders of the trauma may initiate the fear response. People with specific or social phobia often completely avoid their feared situation. In panic disorder the chronic worry about having another attack may lead to stress-related conditions such as heart problems and irritable bowel syndrome. In people with generalized anxiety disorder, the chronic anxiety may prevent them from focusing on even the simplest tasks. The amygdala, although relatively small, is a very complicated structure, and recent research with animals suggests that different anxiety disorders may be associated with activation in different parts of the amygdala.

## Brain Findings Point the Way to New Approaches

The amygdala findings may have important implications for treating people who suffer from anxiety disorders. If, as studies suggest, the memories stored in the amygdala are relatively indelible, one aim of research is to develop therapies for anxiety disorders that increase cognitive control over the amygdala so that the “act now, think later” response can be interrupted.

## Clinical Trials of New Treatments

Anxiety disorder treatment studies have been designed so that pharmacological and cognitive or behavioral therapies can be tested head-to-head. In one clinical trial, two separate centers are examining how well drug and behavioral therapies work separately and together in the treatment of OCD. Data collected from this study should help scientists determine if one of the treatments works better than the other in decreasing obsessions and compulsions.

In addition, the direct comparison of the combined treatment with the medication will provide much needed information on whether the high relapse rate associated with stopping the drug can be reduced. The comparison should also help determine if the medication can enhance compliance with the behavioral treatment.

Many of the current medications for anxiety disorders affect the neurotransmitter serotonin. New treatment approaches are examining drugs that affect other neurotransmitters and brain chemicals such as GABA, gamma-aminobutyric acid, and Substance P. A new research tool, magnetic resonance spectroscopy, will help scientists measure brain levels of GABA and other substances.

Researchers are also looking at combinations of medications that may have a synergistic effect – in panic disorder, for example, studies are underway to determine if an antidepressant medication that affects serotonin works better when used with the new anti-anxiety drug buspirone.

## The Role of Cognitive Factors

Cognitive factors play a significant role in the onset of anxiety disorders. People at risk for these disorders tend to be overly responsive to potentially threatening stimuli. Studies are underway to look at how people with anxiety disorders process

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information. The goal is to see which cognitive capabilities are affected by anxiety and which are free to handle other information. Data collected from the studies should help researchers determine more about the brain pathology associated with anxiety disorders.

## Early Life Stress May Play a Role

In animals, NIMH-funded researchers are studying how stress, especially when it occurs in early life, affects how adverse events are handled later in life. Rat pups who are subjected to the stress of being separated from their mothers for several minutes early in life have, months later, a much greater startle reaction to a stressful event than pups who were never separated. This line of research may help scientists learn how genes and experience affect who is vulnerable and who is resistant to anxiety disorders.

## Anxiety Disorders and Hormones

Another area of research has led to the discovery that anxiety disorders are associated with abnormal levels of certain hormones. People with PTSD, for example, tend to be low on the stress hormone cortisol, but have an overabundance of epinephrine and norepinephrine, which could be why they continue to feel anxious after the trauma. In addition, they tend to have higher-than-usual levels of corticotropin releasing factor (CRF), which switches on the stress response and may explain why people with PTSD startle so easily. Scientists are researching ways to correct hormonal imbalances and bring symptoms under control.

## The Importance of Imaging Tools

Scientists may be closer than ever before to creating therapies that are specifically targeted. NIMH studies use imaging tools to allow researchers to peer into the living

brain and watch the amygdala, the cortex, and other areas of the brain at work. They can identify abnormal activity when a person has an anxiety disorder and determine if medication or cognitive and behavioral therapies help to correct it.

Recent studies of the brain using magnetic resonance imaging showed that people with OCD had significantly less white matter than did control subjects, suggesting a widely distributed brain abnormality in OCD.

Imaging studies are also looking at how brain structure may be related to PTSD. A part of the brain involved in emotion, called the hippocampus, tends to be smaller in some people with PTSD. NIMH-funded researchers are trying to decipher whether that is a result of extreme stress responses related to the trauma or whether people who already have a smaller hippocampus are more prone to PTSD.

## NIMH Anxiety Research and Genetics

Research evidence points to genetics as a factor in the origin of anxiety disorders. Scientists have recently discovered a gene that influences fearfulness in mice. And NIMH-supported studies of twins have found that genes play a role in panic disorder and social phobia. Although genes help determine whether someone will develop an anxiety disorder, heredity alone can't explain what goes awry. Experience also plays a part. In PTSD, for example, the trauma is the experience that triggers the anxiety disorder; genetic factors may help explain why only certain individuals exposed to similar traumatic events develop full-blown PTSD. Researchers are honing in on the degree of influence that genetics and experience exert in each of the anxiety disorders – information they hope will yield clues to prevention and treatment.

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## The NIMH Anxiety Disorders Education Program

People with an anxiety disorder frequently attempt to hide their disorder rather than seek help. Often they are successful in concealing their symptoms from family, friends, and coworkers. An unfortunate consequence of this secrecy is that people with an anxiety disorder usually do not receive professional help until years after the onset of their disease. By that time, the illness is so entrenched it may be difficult to treat.

NIMH has developed the Anxiety Disorders Education Program in its Office of Communications and Public Liaison to increase awareness among the public and health care professionals that anxiety disorders are real medical illnesses that can be effectively diagnosed and treated. A primary goal of the education program is to put research into action, thus improving the lives of people with these often debilitating disorders. NIMH communicates with the public about anxiety disorders through a wide range of activities and materials including:

- Toll-free information line (1-88-88-ANXIETY) that provides callers with free printed materials
- Web site – <http://www.nimh.nih.gov/anxiety> – devoted to anxiety disorders
- Radio and television public service announcements
- Brochures and other print and audiovisual materials for the public, health care providers, and mental health professionals on diagnosis, treatment, and referral of patients with anxiety disorders
- Media outreach
- Partnerships with community mental health, health, and civic organizations that conduct public and professional education and research activities at the local level

## Some Cases of OCD Linked to Earlier Infection

NIMH studies of obsessive-compulsive disorder in young people have shown that the experience of having a streptococcal bacterial infection may lead to the development of crippling obsessions and compulsions. It appears that a genetic vulnerability, coupled with rheumatic fever, is associated with some cases of OCD. Preliminary evidence indicates that special treatment for the infection improves or cures the OCD.

## The Broad NIMH Research Program

In addition to studying anxiety disorders, NIMH supports and conducts a broad based, multidisciplinary program of scientific inquiry aimed at improving the diagnosis, prevention, and treatment of other mental disorders. These conditions include bipolar disorder, clinical depression, and schizo-

phrenia.

Increasingly, the public as well as health care professionals are recognizing these disorders as real and treatable medical illnesses of the brain. Still, more research is needed to examine in greater depth the relationships among genetic, behavioral, developmental, social and other factors to find the causes of these illnesses. NIMH is meeting this need through a series of research initiatives.

### ▪ NIMH Human Genetics Initiative

This project has compiled the world's largest registry of families affected by schizophrenia, bipolar disorder, and Alzheimer's disease. Scientists are able to examine the genetic material of these family members with the aim of pinpointing genes involved in the diseases.

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## ▪ **Human Brain Project**

This multi-agency effort is using state-of-the-art computer science technologies to organize the immense amount of data being generated through neuroscience and related disciplines, and to make this information readily accessible for simultaneous study by interested researchers.

## ▪ **Prevention Research Initiative**

Prevention efforts seek to understand the development and expression of mental illness throughout life so that appropriate interventions can be found and applied at multiple points during the course of illness. Recent advances in biomedical, behavioral, and cognitive sciences have led NIMH to formulate a new plan that marries these sciences to prevention efforts.

While the definition of prevention will broaden, the aims of research will become more precise and targeted.

## **More Than 2,000 Grants and Contracts**

In total, NIMH supports more than 2,000 research grants and contracts at universities and other institutions across the nation and overseas. It also conducts basic research and clinical studies involving 9,000 patient visits per year at its own facilities on the National Institutes of Health campus in Bethesda, MD, and elsewhere. NIMH research projects focus on:

- basic research on behavior, emotion, and cognition to provide a knowledge base for a better understanding of mental illnesses
- basic sciences, including cellular and molecular biology, developmental neurobiology, neurochemistry, neurogenetics, and neuropharmacology, to provide essential information about the anatomical and chemical basis of brain function and brain disorders

## **Training Future Researchers**

The Institute maintains a substantial investment in training and career development for researchers in fields related to mental health. NIMH is particularly interested in recruiting clinical investigators trained in cross-disciplinary areas such as molecular genetics and psychiatry. The integration of genetics, behavior, and neuroscience will facilitate the understanding of how the nervous system produces behavior and how behavior maps onto the brain.

- neuroscience and behavioral aspects of acquired immune deficiency syndrome (AIDS) and behavioral strategies to reduce the spread of HIV (human immunodeficiency virus)
- interventions to treat, prevent, and reduce the frequency of mental disorders and their disabling consequences
- mental health services research, including mental health economics and improved methods of services delivery
- co-morbidity among mental disorders and with substance abuse and other medical conditions, such as depression and heart disease
- the prevalence of mental disorders
- risk factors for mental disorders
- differences in mental health and mental illness among special populations
- children and adolescents who suffer from or who are at risk for serious mental disorders and learning disabilities
- psychotherapies and pharmacotherapies for specific disorders

At the beginning of the 21st century, NIMH stands poised to surmount the burden, loss, and tragedy of mental illnesses that afflict millions of Americans.

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## For More Information About NIMH

- The Office of Communication and Public Liaison carries out educational activities and publishes and distributes research reports, press releases, fact sheets, and publications intended for researchers, health care providers, and the general public. A publications list may be obtained on the web at <http://www.nimh.nih.gov/publist/puborder.cfm> or by contacting:

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<http://www.nimh.nih.gov>

Anxiety Disorders Information:  
1-88-88-ANXIETY (1-888-826-9438)  
Depression Information: 1-800-421-4211

- Information about research opportunities at the NIMH Intramural Research Program may be obtained from:

Office of the Scientific Director, NIMH  
9000 Rockville Pike  
Building 10, Room 4N224, MSC 1381  
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- Information for scientists on NIMH grants and contracts programs, including grant application and review, Requests for Applications, Requests for Proposals, program announcements, research training and career development, small business programs, program analyses of NIMH extramural research grants and applications, access to NIH Grants policy, and other material may be obtained from the NIMH home page: <http://www.nimh.nih.gov>
- Information about NIMH clinical studies can be obtained by accessing the NIMH home page at [www.nimh.nih.gov](http://www.nimh.nih.gov) or the National Library of Medicine clinical trials database at [www.clinicaltrials.gov](http://www.clinicaltrials.gov)

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