



Pioneering Solutions for Depression and Bipolar Disorder

The Stanford Mood Disorders Center



We are all part of the equation.

“Never before have we been so close to breakthroughs that will transform our approach to mood disorders, delivering advanced solutions for sufferers, their families, their friends, and their communities. Stanford is leading the way in understanding brain processes and transforming new knowledge, rapidly and efficiently, into new therapies and technologies.”

Alan F. Schatzberg, MD

THE KENNETH T. NORRIS, JR. PROFESSOR AND CHAIR EMERITUS, STANFORD DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

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One out of five Americans will experience some form of mood disorder in their lifetime—such as depression or bipolar disorder. Despite their prevalence, mood disorders remain one of the most widespread, misunderstood, and stigmatized health issues we face. Their impact reverberates far beyond an individual’s life. Families, friends, communities, economies—all are affected by these diseases. By 2020, depression will rank second in morbidity among all illnesses worldwide; bipolar disorder will rank fifth. Tragically, suicide, often triggered by a mood disorder, takes more than one million lives worldwide every year.

Although the incidence and impact of mood disorders are undeniably on the rise, hope for solutions has never been higher. Through the Stanford Mood Disorders Center and Research Program, scientists and physicians are building on Stanford’s traditions of excellence, healing, and innovation. They are leveraging new knowledge of genetics and the brain’s molecular processes, and drawing on new techniques for imaging and healing the brain. Merging Stanford’s expertise across disciplines—psychiatry, biology, engineering, and myriad other fields—they are streamlining the process of translating laboratory discoveries into breakthrough treatments.

For the past 20 years, Stanford has led the quest for new knowledge and therapies for mood disorders. Today, the center is expanding its reach and mobilizing Stanford’s diverse expertise toward a powerful shared mission: to overcome mood disorders through innovation and compassion.



MARK ESTES

STANFORD MOOD DISORDERS CENTER AT A GLANCE

- 900 inpatients per year
- 8,000 total patients annually
- 45 clinical trials completed since 2003
- 750 undergraduates and 120 postdoctoral fellows trained between 2004 and 2012
- 250 medical students per year
- 200 leading-edge interdisciplinary research projects under way

Alan F. Schatzberg, MD, the Kenneth T. Norris, Jr. Professor and chair emeritus of the Stanford Department of Psychiatry and Behavioral Sciences, heads the Stanford Mood Disorders Center.

THE STANFORD ADVANTAGE: AN INTERDISCIPLINARY APPROACH

Stanford's comprehensive, interdisciplinary approach to mood disorders integrates significant basic science research with innovative clinical care and training for future physician-scientists.

More than 30 senior faculty members from eight Stanford departments, including some of the most respected basic scientists in the world, take part in research, clinical care, and educational programs in:

- **BIOENGINEERING**
- **BIOLOGY**
- **GENETICS**
- **NEUROLOGY**
- **NEUROSURGERY**
- **PSYCHOLOGY**
- **PSYCHIATRY**
- **RADIOLOGY**

The Mood Disorders Center leverages this interdisciplinary strength to:

- Understand disease mechanisms through genetics, genomics, and proteomics
- Improve imaging techniques that enhance understanding of disease by “looking into the brain” and monitoring and measuring its functions
- Pioneer a holistic approach beyond traditional psychiatry—integrating social factors, a deeper understanding of brain mechanisms, and a diverse range of diagnostic and treatment techniques, including genetics, imaging, psychotherapy, acupuncture, and behavioral therapy
- Leverage pharmacological, pharmacogenetics, and other approaches to improve outcomes for today's patients
- Create new therapies using innovative techniques, including next-generation drugs, targeted brain stimulation, minimally invasive surgery, and computer-based brain training



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Trisha Suppes, MD, PhD, professor of psychiatry and behavioral sciences, is director of the Bipolar and Depression Research Program at the VA Palo Alto Health Care System. A recognized expert in biology and treatment of bipolar disorder, her clinical research focuses on developing optimal treatment approaches for bipolar disorders, including strategies for patients with complex exacerbating conditions, such as anxiety, substance use, or brain injury.

Using the latest in genetic analysis techniques, **Kiki Chang, MD, (R)** professor of psychiatry and behavioral sciences, is collecting data from families in which both children and adults suffer from bipolar disorder. His studies promise to yield crucial information about which genes indicate risk of developing a mood disorder. He is collaborating with **Terence Ketter, MD, (L)** professor of psychiatry and behavioral sciences, who is also studying bipolar disorder in adults and their children.

DEFINING DEPRESSION AND BIPOLAR DISORDER

Cutting a wide swath across all communities and cultures, major depression is more common in women and is characterized by a variety of psychic and physical signs that persist over several weeks or longer, including lowered mood, decreased energy, sleep disturbances, anxiety, self-destructive thoughts, poor concentration, and chronic pain. Bipolar disorder affects men and women equally and is characterized by episodes of mood highs and lows, each lasting at least one week. Although the onset of both disorders tends to be in adulthood, children can also be affected.

TRACING GENETIC ROOTS

What causes mood disorders? Scientists now understand that these illnesses occur when biological or genetic vulnerability intersects with environmental stress. Stanford experts are in the process of unraveling these interactions using unprecedented discovery techniques made possible by the mapping of the human genome over the past decade.

Since 1996, Stanford has been an institutional leader in the Pritzker Network for the Study of Depression, a collaborative forum established by the Pritzker family to study the root causes of depression and to improve treatment of the disorder. Now known as the Pritzker Consortium, Stanford—in partnership with investigators from the University of Michigan, Cornell University, and the University of California—is focused on identifying genes that contribute to bipolar disorder and depression and on the development of new treatments for patients with major mood disorders.

Scientists once thought they would be able to attribute mood disorders to a single genetic alteration in a single neurotransmitter system. They now know that the genetics of these disorders is complex. Genes may have an impact on many different functions that can all feed into depression or bipolar disorder—for example, by affecting how our brains respond to stress, modulate mood, or maintain cognitive performance. One Stanford effort enables scientists to look at a large number of genes simultaneously in specific regions and circuits of the brain. Combined with similar preclinical examinations, these studies will determine which circuits and structures in the brain play key roles in mood disorders—the first step in developing novel, better-directed, more effective treatments.



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Ian Gotlib, PhD, professor of psychology, is using functional magnetic resonance imaging (fMRI) to explore emotional processing in children of mothers with depression, who are thought to be at increased risk of developing the disorder. His studies combine genetic characterization with innovative brain imaging techniques and are testing methods to prevent depression in children at risk.



MARK TUSCHMAN

Natalie Rasgon, MD, PhD, professor of psychiatry and behavioral sciences, directs the Stanford Center for Neuroscience in Women's Health, which studies the connections among women's reproductive hormones, mood disorders, and cognitive health. Rasgon remains at the forefront of the effort to uncover the links between hormones and brain function.

To explore the genetic origins of mood disorders, Stanford is also investigating these diseases across generations—collecting data on families in which both adults and children have depression or bipolar disorder. Using the latest in genetic analytic technologies, these studies promise to reveal which genes connote increased risk for developing one or more mood disorders.

SEEING AND HEALING THE BRAIN

Can stress damage the brain and make it more vulnerable to mood disorders? What portions of the brain are affected by depression and bipolar disorder? How do antidepressants affect the brain? To answer these questions, scientists must be able to study the living brain in real time. And scientists at Stanford are internationally renowned for exploring and developing innovative technologies that reveal mood disorders at the biological level and promise to transform the way brain disorders are diagnosed and treated.

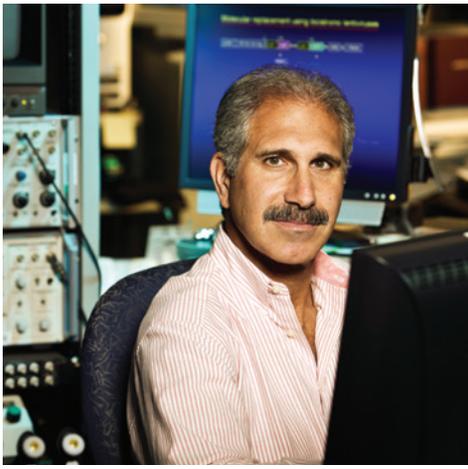
Among the advanced technologies developed by Stanford scientists is a new form of functional magnetic resonance imaging (fMRI) technology that can monitor activity in a difficult-to-image brain region—the subgenual cortex—thought to be associated with deep depression. Other researchers are looking at high-risk children of women with depression and are combining fMRI explorations with genetic studies to determine how particular genes and the neuronal circuits they affect might influence emotional regulation.

Several teams are using fMRI to explore how changes in emotion are associated with the activation of neuronal circuits in various parts of the brain. Some are investigating how neurotransmitters respond to current therapies. Others are looking at how certain hormones affect parts of the brain associated with severe depression.

Another novel investigation images, precisely and in real time, the brain's response to antidepressants. This landmark work will test promising new compounds before exposing humans to them.

NEXT-GENERATION TRAINING

With its highly regarded undergraduate, graduate, and postgraduate programs, Stanford is well positioned to prepare tomorrow's psychologists and neuroscientists to continue the Mood Disorders Center's innovative, collaborative work. Center faculty teach undergraduates in human biology as well as honors students in multiple majors, including psychology. The mentorship continues among medical students. Psychiatry residents rotate through the center's inpatient units and specialty clinics, and postdoctoral fellows, including those in psychology, are trained in programs funded by the National Institute of Mental Health. Students and fellows from diverse disciplines—basic neuroscience, cognitive neuroscience, bioengineering, physics, endocrinology, and experimental psychology—also receive training through the center.

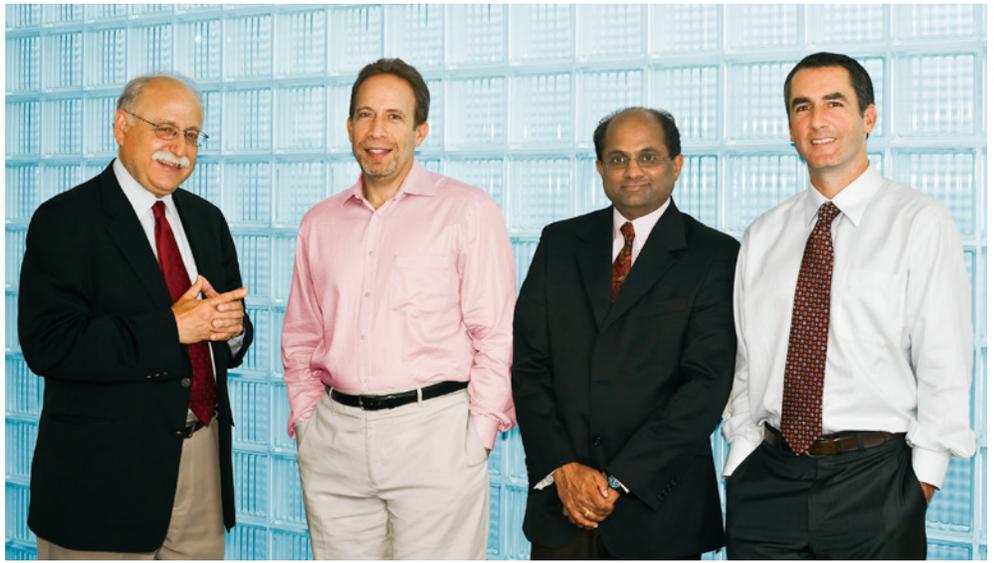


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Modifications in the brain's reward circuitry play a critical role in both the development and treatment of depression. **Robert Malenka, MD, PhD**, the Nancy Friend Pritzker Professor of Psychiatry and Behavioral Sciences, is a world leader in studying the molecular mechanisms by which stressful events or drug use modifies the function of key brain synapses. His studies have identified a potential target for treating a major symptom of depression—anhedonia, the inability to experience pleasure.

LEADING CLINICAL CARE

Stanford Hospital & Clinics has developed one of the premier clinical programs in psychiatry, ranked by *U.S. News & World Report* in the top 12 programs in the country. Delivering the highest standard of clinical care, the Mood Disorders Center offers inpatient and outpatient services, and operates both adult and child outpatient clinics for depression and bipolar disorder.



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Mood Center Director **Alan Schatzberg, MD**, and **Allan Reiss, MD**, the Howard C. Robbins Professor of Psychiatry and Behavioral Sciences, are using imaging technology to study the relationship between cortisol, a stress-marker hormone, and a key area of the brain that is associated with increased stress responses and increased risk of developing psychotic thinking. **Vinod Menon, PhD**, professor of psychiatry and behavioral sciences, and **Michael Greicius, MD, MPH**, assistant professor of neurology and neurological sciences, have developed new fMRI technology that can image brain circuits at rest, allowing scientists to study the subgenual cortex, an area of the brain where activity is increased in depressed patients.

IMPROVING OUTCOMES FOR TODAY'S PATIENTS

Psychiatrists today rely on a combination of pharmacologic agents and psychotherapy to treat patients with depression or bipolar disorder. Stanford scientists are actively exploring which strategies, based on existing drugs and psychotherapeutic techniques, are most successful. At the same time, they are developing new approaches to boost the effectiveness of these therapies.

One team is investigating whether a specific form of psychotherapy in combination with medication is more effective than aggressive pharmacologic treatment in patients with chronic depression. The team led by Rachel Manber, PhD, professor of psychiatry and behavioral sciences, is studying optimal psychosocial treatments for reducing insomnia in major depression and exploring whether these treatments can alleviate depression as well.

Other researchers, looking at recurrent depression, are comparing the long-term effectiveness of serotonin-based drugs to that of therapies that combine serotonin with norepinephrine, a type of stress hormone. One novel study, conducted across three medical centers, is looking at how a dopamine-based agent now used for restless leg syndrome might improve a patient's response to antidepressants and whether improvement can be visualized through brain imaging.

Stanford scientists are also assessing whether genetic variations can predict which of today's antidepressants will work best on specific patients. Over time, it may be possible to develop a series of genetic markers to help doctors identify the most promising treatment for each patient.

Bipolar disorder often requires a combination of mood stabilizers and antidepressants to bring relief to patients. However, some commonly used medications are associated with insulin resistance and diabetes. In collaboration with a national research network, one Stanford team is combining novel brain imaging and endocrinology techniques to explore risk factors for the development of these complications and to reduce the risk of side effects.



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Depression Research Center co-directors **Brent Solvason, MD, PhD**, (L) associate professor of psychiatry and behavioral sciences, and **Charles DeBattista, MD, DMH**, (R) professor of psychiatry and behavioral sciences, apply repetitive transcranial magnetic stimulation (rTMS), a new treatment option that uses an electromagnet to stimulate levels of the brain, providing relief to patients with severe mood disorders who do not respond to traditional therapy.

CREATING NEW THERAPIES

Although most people with mood disorders eventually respond to treatment, many must try several therapies before they find one (or a combination) that works. And some therapies are associated with considerable side effects. To usher in a new era of mood disorder care—more effective, faster acting, better tolerated—Stanford is taking the lead in developing groundbreaking treatment approaches.

One of the most severe forms of depression, delusional depression, has a high mortality rate due to physical causes or suicide. People with the disorder often receive electroconvulsive therapy, one of the most effective treatments available. Researchers at Stanford are working to reduce and in some cases eliminate the memory loss that can be a side effect of this treatment. Following up on a number of studies that reveal elevated cortisol as an indicator of delusional depression, Stanford research has led to the use of a fast-acting alternative medication that blocks a specific cortisol receptor in the brain.

Other Stanford teams are investigating which areas or circuits of the brain are potentially overactive in depression to develop new treatments that provide electrical stimulation to targeted areas of the brain through the scalp. Since some key areas associated with mood disorders lie deep within the brain, Stanford specialists are exploring deep brain stimulation—implanting electrodes into specific regions, such as the subgenual cortex, guided by imaging—as part of a national multicenter project.

Stanford is also pursuing alternative strategies to stimulate deep brain regions. One approach focuses stimulation on these regions using 3-D telemetry and magnetic or radiosurgical stimulatory techniques. Other Stanford researchers are exploring acupuncture—a safer alternative for pregnant women with depression—mindfulness techniques, and dialectic behavioral therapy.



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Karl Deisseroth, MD, PhD, the D.H. Chen Professor and professor of bioengineering and of psychiatry and behavioral sciences, both treats patients and develops molecular and cellular tools to reengineer brain circuits. His lab developed a novel technique to directly control brain cell activity by turning particular neural cells on and off with millisecond pulses of light. The technique may lead to targeted therapies for brain disorders.

A NATIONAL NETWORK OF EXCELLENCE

Bringing leaders together in breakthrough collaboration, Stanford has worked to develop a network of national designated depression centers in cooperation with the original center at the University of Michigan. The effort seeks to establish centers of excellence in treatment, research, and training related to depression and bipolar disorder. These centers promise to improve the productivity and efficiency of mood disorder research, speed the development of new therapies, and share new treatment guidelines widely—an important step in removing the stigma associated with depression and bipolar disorder.



TERRENCE MCCARTHY



COURTESY OF RACHEL MANBER

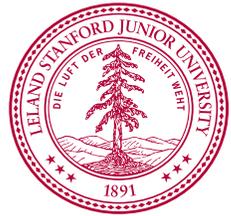


ALEX JOHNSON

Jaimie Henderson, MD, associate professor of neurosurgery and director of the stereotactic and functional neurosurgery program at Stanford, is a world expert in using deep brain stimulation and other minimally invasive surgical techniques to treat depression.

Integrating her clinical and research expertise in mood and sleep disorders, **Rachel Manber, PhD**, professor of psychiatry and behavioral Sciences, is working on improving the treatment of depression by simultaneously treating depression and insomnia.

Amit Etkin, MD, PhD, assistant professor of psychiatry and behavioral sciences, is a pioneer in the use of fMRI to reveal how brain activity differs in healthy people compared with those suffering from mood and anxiety disorders. He is developing novel treatments for correcting neural circuit dysfunctions in patients with these disorders.



RALLYING THE RESOURCES TO LEAD

What will it take to usher in a new era in the treatment of mood disorders—an era of deeper understanding of the biological and genetic roots of depression and bipolar disorder, wield technologies that enable physician-scientists to see and heal the brain in real time, optimize the effectiveness of current tools, and turn next-frontier ideas into high-impact therapies? It will take innovation and compassion, proven expertise and a constant hunger for new knowledge, and groundbreaking ideas and collaborative spirit. Inspired by the Campaign for Stanford Medicine—and by the enormous potential of research now under way at Stanford—the Stanford Mood Disorders Center is poised to achieve its mission: delivering solutions, cultivating understanding, and transforming lives.

PATIENT INQUIRIES

Please call 650.498.9111.

PHILANTHROPY

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