THE STANFORD MOOD DISORDERS CENTER

Pioneering Solutions for Depression and Bipolar Disorders

Stanford MEDICINE

"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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Pioneering Solutions for Depression and Bipolar Disorders

MARK ESTES

Alan F. Schatzberg, MD, is founder-director of the Stanford Mood Disorders Center. His research focuses on the biological bases of depressive disorders, identification of biomarkers, and development of novel pharmacologic treatments. His team is exploring biomarkers for suicidal behavior, the role of stress hormones in delusional depression, and developing growth factor analogs as antidepressants. His group published seminal studies demonstrating that the acute antidepressant effects of ketamine are due to opioid effects, opening a search for similar agents with less potential risk of abuse.

An estimated 21.4 percent of American adults will experience some form of mood disorder—depression or a bipolar disorder—in their lifetime. The percentage of adolescents and young adults experiencing depression or anxiety in a given year is increasing dramatically. Yet, mood disorders remain one of the most 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. Depression is a leading cause of disability worldwide and bipolar disorders rank in the top 20. 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 to build a precision mental health approach to mood disorders.

We 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—we are accelerating the process of translating laboratory discoveries into breakthrough treatments.

Through the research programs at the center, Stanford is leading the quest for new knowledge and therapies, expanding and mobilizing diverse expertise toward a powerful, shared mission: to overcome mood disorders through innovation and compassion.

COURTESY OF MANPREET SINGH

NORBERT VON DER GROEBEN

COURTESY OF NOLAN WILLIAMS

Manpreet K. Singh, MD, MS, investigates the origins and pathways for mood disorders in childhood. Her science is anchored in understanding how young people adapt to stress in order to protect and preserve brain function. From socially engaged family-focused interventions to neuroscience-informed rTMS and digital therapeutics, her team strives to position youth to become thriving adults.

Leanne Williams, PhD, is developing a precision mental health model for understanding mood disorders and anxiety as disruptions within brain circuits. She has described new subtypes that translate to more precise diagnoses and treatment tailored to a person's experience. Her lab is also engaged in developing a wearable to characterize mental states quantitatively.

A dually trained psychiatrist and neurologist, **Nolan Williams, MD**, conducts studies that utilize novel brain stimulation techniques, psychopharmacological approaches, and neuroimaging methods to develop new models and treatments for neuropsychiatric disorders. Among these are major depressive disorder, bipolar disorder, addiction, obesity, pain, suicide, and obsessive-compulsive disorder.

THE STANFORD ADVANTAGE: AN INTERDISCIPLINARY APPROACH

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

Faculty members from departments across campus, including some of the most respected scientists in the world, take part in research, clinical care, and training programs:

- 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 approaches that integrate a deeper understanding of the brain with computational strategies, artificial intelligence, big data, and a diversity of diagnostic and treatment techniques
- Build, test, and scale evidence-based digital technology solutions
- Understand the interface of pain, depression, and opiates
- Leverage pharmacologic, pharmacogenetic, and proteomics approaches to improve outcomes
- Create new therapies using innovative techniques including next-generation drugs, targeted brain stimulation, minimally invasive surgery, and computer-based brain training

STANFORD MOOD DISORDERS CENTER AT A GLANCE

An estimated 21.4 percent of U.S. adults experience a mood disorder at some time in their lives. More than 14.3 percent of adolescents experience a mood disorder in any given year.

- Serving more than 8,000 patients of all ages annually
- 55-plus clinical trials completed since center launch
- More than 200 leading-edge research projects underway
- 250 medical students trained each year
- 230 postdoctoral fellows trained
- Undergraduate seminars and courses
- Mood Disorders Education Day—an annual community event with talks on the latest advances

MARK TUSCHMAN

Trisha Suppes, MD, PhD, is a recognized expert on the biology and treatment of bipolar disorder. Her clinical research focuses on developing optimal treatment approaches, including strategies for patients with complex, exacerbating conditions such as anxiety and substance use disorder. She has initiated a new line of research exploring the use of psychedelics for mood disorders.

ALEX JOHNSON

Amit Etkin, MD, PhD, is elucidating how the healthy brain works and how abnormal brain function causes psychiatric symptoms. He integrates large data sets using advanced custom-built artificial intelligence methods to understand how individuals respond to various treatments. This has revealed scalable insights for treatment personalization and prediction relevant to current and new therapeutics.

COURTESY OF CAROLYN RODRIGUEZ

Carolyn Rodriguez, MD, PhD, leads studies investigating the brain basis of ruminations, suicidal ideation, and other perseverative thoughts in mood and anxiety disorders. Her landmark clinical trials pioneer rapid-acting treatments for severe mental illnesses, including obsessive-compulsive disorder and depression.

COURTESY OF MICHAEL OSTACHER

Michael Ostacher, MD, MPH, MSSc, is medical director of the Bipolar Disorder and Depression Research Program. His primary research interest is large-scale clinical trials and implementation of evidence-based mental health practices including exploratory therapeutics, and device-based and web-based interventions.

DEFINING DEPRESSION AND BIPOLAR DISORDERS

Cutting a wide swath across all communities and cultures, major depression is characterized by a variety of psychological and physical signs and symptoms that persist over several weeks or longer, including lowered mood, decreased energy, sleep disturbances, anxiety, self-destructive thoughts, poor concentration, and chronic pain. Bipolar disorders are typically characterized by episodes of mood highs and lows of varying intensity and duration. Depression is more common in women while bipolar disorders affect men and women equally. Although the onset of the disorders tends to manifest most clearly 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 novel 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 Neuropsychiatric Disorders Research Consortium, a collaborative forum established to study the root causes of mood disorders and schizophrenia to improve treatment. In partnership with the University of Michigan, Cornell University, and the University of California at Irvine, investigators are focused on identifying genes that contribute to these disorders and on the development of new treatments.

It was once thought that a single genetic alteration in a single neurotransmitter system may be responsible. We now know that the genetics of these disorders is more complex. Genes may have an impact on many different functions that can all feed into depression or bipolar disorders—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 are unraveling which circuits and structures in the brain play key roles in mood disorders—the first step in developing novel, more precise, and more effective treatments.

MARK TUSCHMAN

COURTESY OF CASEY HALPERN

COURTESY OF MAHENDRA BAHTI

Natalie Rasgon, MD, PhD, remains at the forefront of efforts to uncover the links between hormones, stress, and brain function. She directs the Behavioral Neuroendocrinology Program and the Stanford Center for Neuroscience in Women's Health, where the team explores the relationship between reproductive hormones, mood disorders, and cognitive health.

Neurosurgeon **Casey Halpern, MD**, investigates the effects of deep brain stimulation and responsive neurostimulation in depression and various models of human behavior related to behavioral disinhibition. Disinhibition is a clinical feature in many conditions including obesity, traumatic brain injury, addiction, schizophrenia, and obsessive-compulsive disorder.

As section chief of interventional neuropsychiatry, **Mahendra Bhati, MD**, is building collaborations across many disciplines. He is active in a number of research trials including for post-traumatic stress disorder, closed-loop responsive neurostimulation for impulse and fear-related disorders, focused ultrasound, and augmented-reality TMS.

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 a bipolar disorder. The Biocollaborative Data Base of the center has genetic samples from more than 3,000 patients and controls. Using the latest in genetic analytic technologies, these studies are revealing clues as to 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. Stanford is internationally renowned for exploring and developing innovative technologies that reveal mood disorders at the biological level, promising to transform the way brain disorders are diagnosed and treated.

Among the advanced technologies developed at Stanford is a 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.

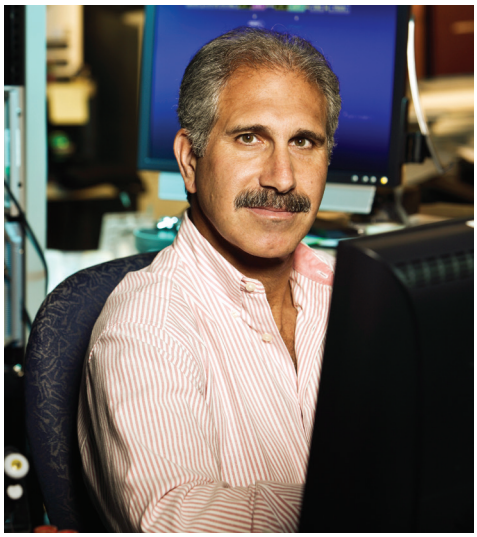
Several teams are using fMRI to explore how changes in emotion are associated with the activation of neuronal circuits in various parts of the brain. Others are investigating how neurotransmitters respond to current therapies. Still others are looking at how certain hormones affect parts of the brain associated with severe depression. Another novel investigation images, precisely and in real time, the brain's response to antidepressants. These and other landmark studies and tools enable scientists to test novel pharmacologic compounds in the laboratory before study in humans.

NEXT-GENERATION TRAINING

With its highly regarded undergraduate, graduate, and postgraduate programs, Stanford is well positioned to prepare tomorrow's psychologists, psychiatrists, and neuroscientists to continue the Mood Disorders Center's innovative, collaborative work. Center faculty teach undergraduates in multiple majors, including psychology.

The mentorship continues with medical students, fostering a career-long interest in psychiatric disorders. Residents and advanced clinical fellows rotate through the inpatient unit and specialty clinics. Postdoctoral fellows representing diverse disciplines—including basic neuroscience, cognitive neuroscience, bioengineering, data science, physics, endocrinology, and experimental psychology—all receive training through the center.

MARK ESTES

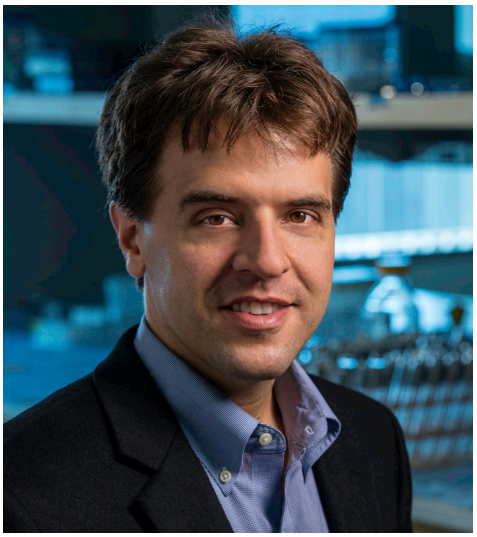


Modifications in the brain's reward circuitry play a critical role in the development and treatment of mood disorders. **Robert Malenka, MD, PhD**, is a world leader in studying the molecular mechanisms by which stressful events or drug use modify the function of brain synapses. He identified a potential target for treating a major symptom of depression—anhedonia, the inability to experience pleasure.

STEVE FISCH PHOTOGRAPHY

Joachim Hallmayer, MD, PhD, brings expertise in neurodevelopmental disorders, genetics, and ethics, exploring the reciprocal influences of social processes and biomedical research on the identity of neurobiological difference. He is helping to shape the center's BioCollaborative, a powerful pooled database to catalyze and increase the efficiency of clinical research and foster collaboration.

STEVE FISCH PHOTOGRAPHY



A psychiatrist and bioengineer, **Karl Deisseroth, MD, PhD**, brings both perspectives to his clinical work and his research innovations. His revolutionary molecular and cellular tools, including optogenetics, CLARITY, STARmap, and COSMOS, are revealing how brain circuits work. His lab trains scientists from around the world in these techniques, in service of the larger quest for targeted therapies for brain disorders.

LEADING CLINICAL CARE

The Stanford Department of Psychiatry and Behavioral Sciences with Stanford Health Care and Stanford Children's Health has developed one of the premier clinical programs in psychiatry. Delivering the highest standard of clinical care, we offer inpatient and outpatient services, and operate both adult and child outpatient clinics for depression and bipolar disorders.

IMPROVING OUTCOMES FOR TODAY'S PATIENTS

Psychiatrists today rely on pharmacologic agents, devices that modulate and stimulate the brain, and psychotherapy alone or in combination to treat patients with mood disorders. Stanford scientists actively explore which strategies are most successful and for which person, as well as develop new approaches to boost the effectiveness of these therapies. They are also developing new treatments that are more effective or better tolerated.

One group of investigators is applying a form of psychotherapy for insomnia to improve depression and to prevent suicide. Other researchers are exploring the potential properties of rapidly acting opioid agents such as ketamine. One novel study looked at how a dopamine-based agent now used for restless leg syndrome might improve a patient's response to antidepressants and whether improvement could be visualized through brain imaging.

Stanford scientists have described a number of genetic tests that can be used to predict responses to specific antidepressants and several of these have been incorporated into available genetic tests to select treatment. Our researchers continue to explore other genetic markers to guide treatment selection for individual patients.

Bipolar disorders often require 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 led by Natalie Rasgon, MD, PhD, the Rasgon 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.

Children with significant depression and who have a bipolar parent are at particular risk for developing a bipolar disorder. Antidepressants can be helpful but can also precipitate excited states. Manpreet Singh, MD, MS, is exploring the relative risk of converting to bipolar disorder in childhood and the optimal strategy for treating patients at risk.

COURTESY OF REBECCA BERNERT

COURTESY OF PO WANG

MARK ESTES

Rebecca Bernert, PhD, focuses on the identification of rapid, low-risk therapeutic targets for suicide prevention, including sleep, physical barriers, policy, and education. Her overarching goal is to harness new technologies within suicide prevention, including artificial intelligence and mobile health applications, to enhance risk detection.

Po Wang, MD, is chief of the Bipolar Clinic where he spearheads the clinical and research programs. The team focuses on the diagnosis and clinical management of bipolar disorders and co-occurring conditions, and managing a portfolio of clinical trials and neuroimaging studies that include longitudinal monitoring, novel treatments, and comparative effectiveness.

Depression Research Clinic Co-directors **Brent Solvason, MD, PhD**, (L) and **Charles DeBattista, MD, DMH**, (R) share research and clinical interests that include treatment of refractory depression, novel clinical and augmentation strategies, and the neurobiology of mood disorders. They explore strategies that augment treatment and apply exploratory therapeutics such as rTMS and psychedelic agents in severe mood disorders where traditional approaches alone are not sufficient. Dr. DeBattista is the Stanford lead investigator on a multi-site international study to assess the safety and efficacy of psilocybin in refractory depression.

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 disorders care—more effective, faster acting, better tolerated—Stanford is taking the lead in developing groundbreaking treatment approaches.

Stanford is a pioneer in the development of repetitive Transcranial Magnetic Brain Stimulation (rTMS) and has both active clinical and research programs. This noninvasive therapy is now being extended to studies in children and adolescents by Stanford researchers. Nolan Williams, MD, has developed a novel, more focused and intense form of accelerated theta burst rTMS to provide both more efficacy and more rapid response. Amit Etkin, MD, PhD, is exploring brain circuits using rTMS and other techniques to reveal the role specific brain circuits play in psychopathology and treatment response. Leanne Williams, PhD, is elucidating how patterns of brain activity, determined by using magnetic resonance imaging, can be used to subtype patients in order to guide clinicians in selecting optimal treatment more quickly.

Development of new drugs represents a challenging and important frontier in the treatment of mood disorders—an area Stanford is actively pioneering. For example, measurement of gene activation in the brain is laying the groundwork for new targets for medications that affect specific systems in the brain. A possible innovative drug treatment based on these studies has been identified and can now be studied in people. Researchers are attempting to understand ketamine's mechanism of action to design safer and more durable drug strategies. The Stanford Biocollaborative's repository of genetic data can help investigators understand how genetic variation relates to specific symptoms and provides clues for novel drug development.

These research examples represent just some of the strategies that Stanford clinicians and scientists are exploring.

A NATIONAL NETWORK OF EXCELLENCE

Advancing faster through breakthrough collaborations, our faculty are founders, leaders, and contributing members of a number of national networks including the National Network of Depression Centers, the Pritzker Consortium, the Mental Health Technology Transfer Center Network, and the international Psychopathology and Allostatic Load across the Life Span (PALS) Network. These networks share a commitment to propel and disseminate advances in treatment, research, and training related to depressive, bipolar, and related disorders.

MARK ESTES

Ian Gotlib, PhD, explores 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 brain imaging (fMRI) and testing methods with the goal to ultimately prevent depression in children at risk.

COURTESY OF RACHEL MANBER

Rachel Manber, PhD, is a behavioral sleep medicine scientist specializing in improving the treatment of depression by simultaneously treating depression and insomnia. She is a pioneer in cognitive behavioral therapy for insomnia and specializes in treating those who experience their sleep difficulties in the context of other disorders, including mood disorders.

COURTESY OF RUTH O'HARA

Ruth O'Hara, PhD, employs a life-span approach to the study of the relationship between cognitive abilities and depression. She uses neuroimaging, stem cell, and genetic approaches to investigate psychologic and physiologic stress and sleep dysfunction, in order to reduce the impact of cognitive impairment in late-life psychiatric disorders.

"People whose lives are governed by mood disorders need our most creative and valuable science, our most effective prevention and treatment interventions, and our finest education and policy efforts. We cannot turn away from this source of human suffering. Join with us to generate knowledge that leads to true solutions, cultivates understanding, and transforms lives."

Laura Roberts, MD, MA
KATHARINE DEXTER MCCORMICK AND STANLEY MCCORMICK MEMORIAL PROFESSOR

CHAIR, DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL SCIENCES

RALLYING THE RESOURCES TO LEAD

Leading a new era in the treatment of mood disorders takes a constant hunger for new knowledge and groundbreaking ideas, a collaborative and innovative spirit, and proven expertise mixed with compassion.

With your philanthropic support, we will achieve our mission to deliver solutions, cultivate understanding, and transform lives. Join with us and accelerate our efforts to:

- Secure and retain innovators and catalysts through endowed professorships and project- or investigator-specific funding
- Fund bold ventures that link basic, translational, and clinical sciences with new disciplines to rapidly improve the patient experience
- Fuel novel, potentially high-yield endeavors through innovation awards
- Recruit, train, and fund the next generation of clinicians and scientists
- Empower patients, families, and the public to create a better world for those with mood disorders

Make a difference in the lives of those with mood disorders.

CREATE IMPACT

PATIENT INQUIRIES | Please call 650.498.9111

PHILANTHROPY | For questions or a personalized conversation, contact:

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