Pioneering Solutions for Depression and Bipolar Disorder

The Stanford Mood Disorders Center
“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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As many as 17 percent of 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. Depression now ranks first in rate of incidence among all illnesses worldwide; bipolar disorder ranks 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.

Through the research programs at the Stanford Mood Disorders Center, 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.

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 seven 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, pharmacogenetic, and proteomics 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
Such as anxiety, substance use, or brain injury. Patients with complex exacerbating conditions, for bipolar disorders, including strategies for management 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.

**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 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 disorder affects men and women equally and is characterized by episodes of mood swings, highs and lows, each lasting at least one week. Although the onset of both 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 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, anxiety, self-destructive thoughts, poor concentration, and chronic pain. Bipolar disorder affects men and women equally and is characterized by episodes of mood swings, highs and lows, each lasting at least one week. Although the onset of both disorders tends to manifest most clearly in adulthood, children can also be affected.

**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 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 neural 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 novel 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 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, experimental psychology—also receive training through the center.
inability to experience pleasure. Major symptom of depression—anhedonia, the have identified a potential target for treating a function of key brain synapses. His studies by which stressful events or drug use modifies the leader in studying the molecular mechanisms Psychiatry and Behavioral Sciences, is a world MD, PhD, the Nancy Friend Pritzker Professor of and treatment of depression. Modifications in the brain's reward circuitry operates both adult and child outpatient care, the Mood Disorders Center offers the premier clinical programs in psychiatry. LEADING CLINICAL CARE Stanford Health Care has developed one of the premier clinical programs in psychiatry. 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. IMPROVING OUTCOMES FOR TODAY'S PATIENTS Psychiatrists today rely on pharmacologic agents, brain stimulation devices, and psychotherapy alone or in combination to treat patients with depression or bipolar disorder. Stanford scientists not only actively explore which strategies are most successful, but at the same time, develop new approaches to boost the effectiveness of these therapies. Furthermore, they are 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, looking at recurrent depression, are comparing the long-term effectiveness of serotonin-biased drugs to that of therapies that combine serotonin with norepinephrine, a type of stress hormone. One novel study 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 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 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 reduce the risk of side effects. Children with significant depression and who have a bipolar parent are at particular risk for developing bipolar disorder. Antidepressants can be helpful but can also precipitate excited states. Manpreet Singh, MD, is investigating the relative risk of converting to bipolar disorder in childhood and who have a bipolar parent are at particular risk for developing bipolar disorder. A possible innovative drug treatment based on these studies has been identified and can now be studied in people. Ketamine, an anesthetic agent, produces rapid but not sustained antidepressant effects. Researchers are attempting to understand its mechanism of action to design safer and more durable drug strategies. Stanford researchers are also developing a biosilicobal collaborative repository of genetic data from subjects in studies to help investigators understand how genetic variation relates to specific symptoms and features of subjects with mood disorders. These research examples represent just some of the strategies that Stanford clinicians and scientists are exploring.

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.

Stanford was a pioneer in the development of repeated 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, is studying a more focused and intense form of rTMS that could provide both more efficacy and more rapid response. Arni Elkins, MD, PhD, is exploring stimulating specific brain circuits using TMS and understanding the role designated 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 and to select treatment. 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. Ketamine, an anesthetic agent, produces rapid but not sustained antidepressant effects. Researchers are attempting to understand its mechanism of action to design safer and more durable drug strategies.

Stanford researchers are also developing a biosilicobal collaborative repository of genetic data from subjects in studies to help investigators understand how genetic variation relates to specific symptoms and features of subjects with mood disorders. A National Network of Excellence bringing leaders together in breakthrough collaborations, Stanford has worked to develop a national network of 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—all important steps in removing the stigma associated with depression and bipolar disorder.
Ian Gotlib, PhD, 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 involve testing methods to prevent depression in children at risk.

Integrating her clinical and research expertise in mood and sleep disorders, Rachel Manber, PhD, is a behavioral sleep medicine scientist specializing in improving the treatment of depression by simultaneously treating depression and insomnia.

Ruth O’Hara, PhD, studies the physiologic markers of neurocognitive impairment in late-life disorders. 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 on late-life psychiatric disorders.

RALLYING THE RESOURCES TO LEAD
Leading this new era in the treatment of mood disorders takes innovation and compassion, proven expertise, and a constant hunger for new knowledge, groundbreaking ideas, and a collaborative spirit. Across the Stanford campus, scientists are drawing upon these powerful motivators to achieve deeper understanding of the biologic and genetic roots of mood disorders. Physician-scientists are utilizing this knowledge to develop and implement technologies to see and heal the brain in real time, personalize and optimize the effectiveness of current tools, and turn next-frontier ideas into next-generation, high-impact therapies.

With your philanthropic partnership, 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 programmatic endowment and project- or investigator-specific funding
- Fund bold ventures that link basic, translational, and clinical sciences with new disciplines to more rapidly improve the patient experience
- Fuel novel, potentially high-yield endeavors that may otherwise go unexplored
- Recruit and train the next generation of clinicians and scientists
- Empower patients, families, and the public to create a better world for those with mood disorders

Join us in making a difference in the lives of those with mood disorders.