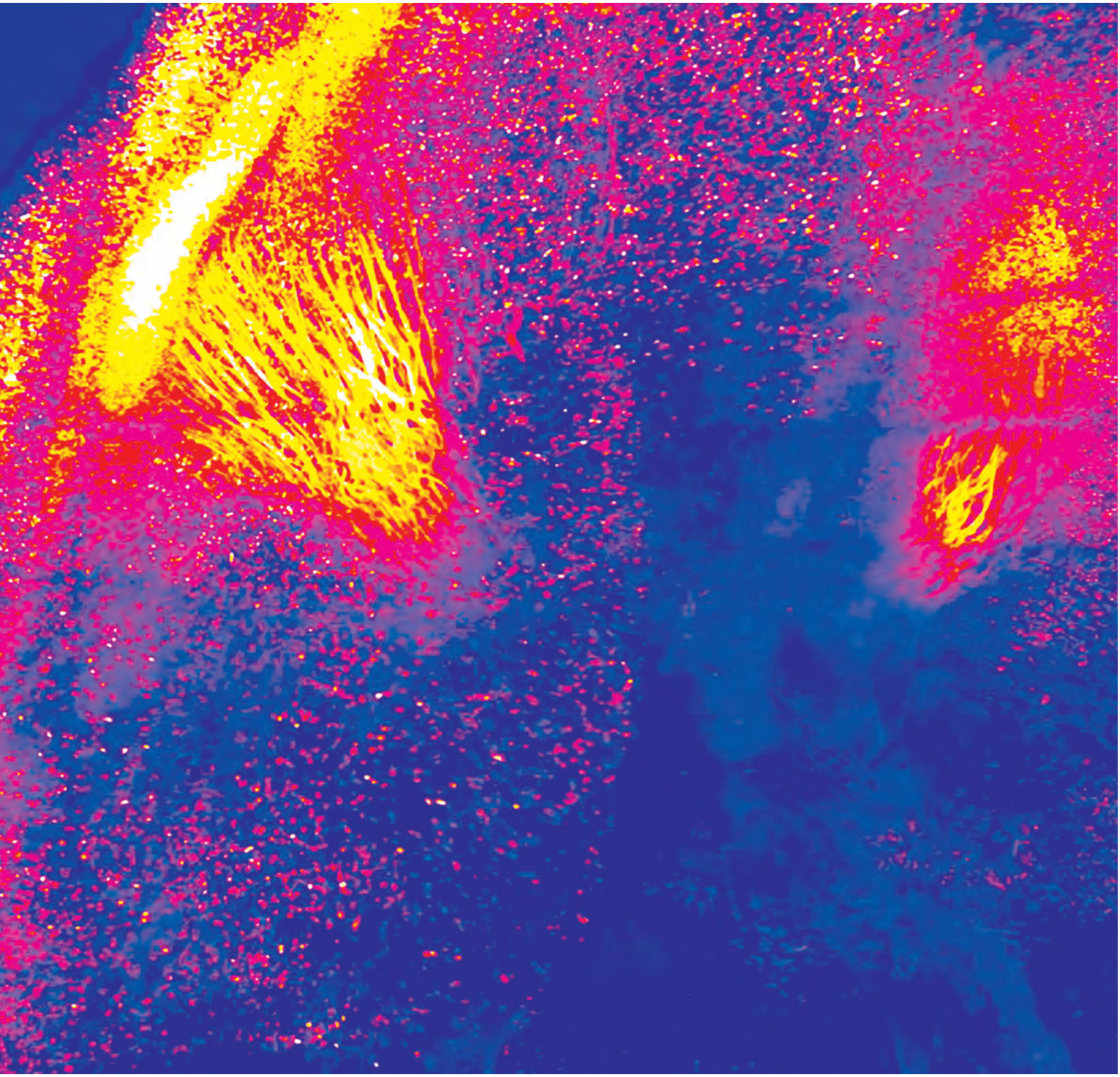


Addiction Medicine

Stanford MEDICINE | Department of Psychiatry and Behavioral Sciences

Substance use disorders know no boundaries, affecting individuals and families from all walks of life. In the United States alone, millions of lives are devastated by alcohol, tobacco, opioids and other prescription medications, electronic games, gambling, and illicit substances. Substance use disorders also result in an increased risk for more than 70 diseases, from lung cancer to diabetes, and those who experience addiction often also have other psychiatric conditions such as depression and bipolar disorder. Overdoses, the vast majority involving opioids, are the leading cause of accidental death, killing more Americans than car accidents.

More than $700 billion a year is spent on the downstream impact of addiction; a mere fraction of that sum is invested in preventing and treating substance use disorders. And yet, highly effective prevention programs and treatment options do exist—and many more are in development.

Robust, collaborative addiction medicine programs at Stanford—focused on research, treatment, education, and policymaking—are leading the way in restoring lives and reducing the devastating impact of addiction. We are linking the biology of substance use disorders and decision-making behavior to innovations in clinical care and public policy, and by doing so, have stepped forward to become a leading voice in the national conversation on addiction.

RISK FACTORS

During adolescence, the brain is best suited for learning new things. This is when the brain is most "plastic"—changing rapidly, growing connections, and pruning neurons. It is also the time when teenagers and young adults increasingly encounter opportunities to use potentially addictive substances.

Stanford faculty are working diligently in schools and policy making to emphasize prevention and the importance of reducing access to addictive substances to our youth.

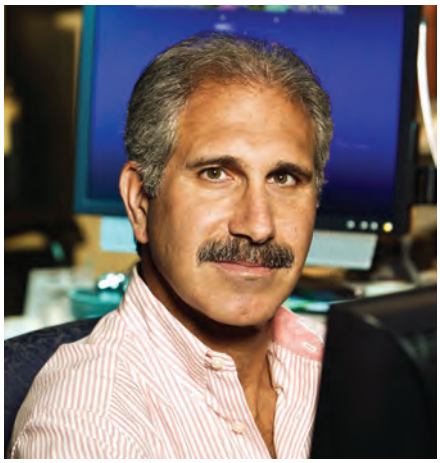
Other periods of potential risk can include unemployment, poor health, retirement, or other major life events. Injury or trauma also increases the risk of becoming addicted to opioid pain medications. In addition, genes influence how people respond to substances and alcohol, meaning that families across generations may be particularly vulnerable to substance use disorder-related complications.

SHIFTING OUR UNDERSTANDING

Neuroscience is shifting our understanding of addiction from a moral failing to a brain-based illness. Stanford scientist Rob Malenka, MD, PhD, was among the first to pinpoint the molecular mechanisms of addiction and identify their connection to memory and learning. Stanford studies have shown that drug and alcohol use alters the normal trajectory of brain structure and function in adolescents. Stanford researchers are delving deep into the brain's reward circuitry to understand the neural basis of decision-making, which may ultimately allow clinicians to predict individuals who might relapse so they can preemptively intervene.

Neuroscience reveals that the human brain has a built-in reward and learning system that has been critical to the survival of our species. Basic functions central to keeping us alive—including finding food, mates, or shelter—normally operate to reward behaviors that keep us safe and thriving. But when our brains

COVER: *High-resolution neural image showing how a mouse brain responds to cocaine addiction and fear. Produced using the CLARITY system developed by Karl Deisseroth, MD, PhD.*



For more than two decades, **Rob Malenka, MD, PhD**, has illuminated molecular mechanisms that underlie synaptic plasticity and learning in a number of different brain regions implicated in motivated behavior. His lab continues to innovate new combined techniques of molecular manipulations and cell biological and electrophysiological assays to investigate plasticity and its behavioral consequences.

Anna Lembke, MD, oversees clinical and training programs related to addiction. She was one of the first in the medical community to sound the alarm regarding opioid overprescribing and her work has had national impact in the wake of the ongoing opioid epidemic. She promotes a holistic, harm-reduction approach to each patient and encourages spiritual and alternative therapies in the process of healing.

Keith Humphreys, PhD, focuses on health services research and the larger mental health and addiction policy environment. His efforts are broad-ranging, including evaluations of psychotherapies, peer-operated mutual help groups, web and smartphone-based interventions, neurological predictors of treatment outcome, and national drug and mental health policy.

are repeatedly exposed to addictive substances or behaviors, this very same survival mechanism can cause us to believe that an addictive substance or behavior is needed for survival.

Addictive substances mimic natural rewards such as food and sex by activating the brain's reward circuitry responsible for enjoyment and our survival response. There is a corruption—or a hijacking—of these normal circuits and basic functions. The pull of the new "reward" is very intense. Self-control diminishes and urges to keep using grow. The drug becomes more and more important to the brain—and natural rewards pale by comparison.

THE TRANSFORMATIVE NATURE OF DISCOVERY

Through fundamental science and innovative clinical research, Stanford scientists are generating new, transformational knowledge about addiction. Innovations in neuroimaging technologies allow a clearer picture of the physiological underpinnings of addiction, a better understanding of brain development, and clues to how substance abuse alters the normal trajectory of brain structure and function. Our ongoing efforts to map the circuitry of the brain are yielding insights into the mechanisms that underlie tolerance, dependence, and decision-making. These insights are transforming strategies for treatment of substance use disorders.

Karl Deisseroth, MD, PhD, and Rob Malenka, MD, PhD, are focused on understanding addiction's root causes and discovering what drives development of evidence-based treatment interventions. They are breaking new ground in understanding how brain circuits increase vulnerability to developing an addiction and influence the consequences of addiction on decision-making and other behaviors. Dr. Deisseroth's revolutionary technologies—**optogenetics and CLARITY**—are now used by scientists around the world to study addiction and other brain-based disorders.

Through **human neuroimaging studies**, Edith Sullivan, PhD, has shown that there is a higher risk of brain deficits and accelerated aging in older people with alcohol use disorder. Her team has also shown that young people who drink

"From a normal, evolutionary point of view, it's inexplicable that a person would spend their last $10 on cocaine instead of food. Yet to that addicted person, the drug has become the object of survival."

Keith Humphreys, PhD
Esther Ting Memorial Professor

Karl Deisseroth, MD, PhD, develops revolutionary technology that allows researchers around the world to gain greater insight into psychiatric diseases, including depression and addiction. Focused on identifying specific links between circuitry and genetics, these links could allow us to identify the most vulnerable patients and intervene to halt the development of addictive and other behaviors.

By applying magnetic resonance imaging (MRI) and analyzing cognitive, sensory, and motor functions, **Edith Sullivan, PhD**, looks at brain mechanisms disrupted by alcoholism. Her team takes on challenges such as understanding the neural basis of alcoholism and identifying the scope and limits of recovery with sustained abstinence or responsible drinking.

Casey Halpern, MD, is a neurosurgeon whose lab is a collaborative effort with Rob Malenka, MD, PhD. They are investigating the effects of deep brain stimulation on impulse control behaviors, including binge eating and loss of control over eating. These disorders are a common clinical feature in countless neurologic and psychiatric conditions.

"Addictive substances do change the brain—hijack it—and youth are particularly vulnerable. The good news is that with early intervention, the brain can recover."

Anna Lembke, MD
Associate Professor of Psychiatry and Behavioral Sciences

Chief, Stanford Addiction Medicine Dual Diagnosis Clinic

moderately to heavily have smaller regional brain volumes, thinner cortices, and poor impulse control compared with youth who drink little or no alcohol, proving that alcohol can have drastic effects on the development of the still-maturing brain.

NeuroChoice, a Stanford interdisciplinary research initiative co-led by psychiatry faculty members Rob Malenka, MD, PhD, and Keith Humphreys, PhD, and psychology colleague Brian Knutson, PhD, explores the science of choice and the societal repercussions of those choices. By measuring the strength of reactions to cues associated with substance use, they identified a "brain signature" to predict which patients in addiction treatment are at the highest risk for relapse. One of the team's goals is to improve our ability to identify who is more likely to relapse so that clinical decisions, such as length of stay in treatment, can be based on brain science rather than arbitrary insurance guidelines and other non-evidence-based factors.

Deep brain stimulation (DBS) is an intervention where tiny implanted devices deliver electrical pulses to targeted regions of the brain. DBS is effective in treating Parkinson's disease and is in clinical trials for other disorders of the brain. In a recent preclinical study, Rob Malenka, MD, PhD, and neurosurgeon Casey Halpern, MD, explored DBS as an intervention for impulse control problems, including addiction. They identified a signature pattern of activity in a small but important deep brain region called the nucleus accumbens just a second or two before a burst of impulsive behavior. These findings may lead to a new treatment to deliver an immediate, measured dose of electrical stimulation to curb the impulsive behavior.

In the near future, we may be able to deploy **repetitive transcranial magnetic stimulation (rTMS)** to modulate the brain circuitry central to addiction. A medication-free, non-invasive treatment, rTMS has been successfully used for depression. In an investigation into forestalling relapse, a Stanford-Veterans Administration team led by Tim Durazzo, PhD, is conducting a clinical trial to see if rTMS could be an effective treatment for alcohol and tobacco use disorders.

Matt Kendra, MD, directs a comprehensive smoking cessation program incorporating mindfulness training, individual and group psychotherapy, motivation building, medications, and group support for people with substance use disorders or addiction. Dr. Kendra was featured in a national television media campaign calling out the tobacco industry for its targeting of people with mental illness.

J. Alexis Ortiz, PhD, treats high-acuity, psychiatrically complex, substance-using patients. Dr. Ortiz provides teaching, training, and supervision in a variety of evidence-based modalities, including specialty areas of Dialectical Behavior Therapy (DBT) for substance use disorders, motivational interviewing, and mindfulness-based interventions.

Kim Bullock, MD, directs the Virtual Reality Immersive Technology Clinic and hopes to bring her expertise in the treatment of anxiety and pain disorders to augment cognitive behavioral therapy for substance use disorders.

CLINICAL INNOVATION

As in many areas of medicine, there is no one solution that will work for all. Creative modes of inquiry and innovative treatment options are needed. At Stanford, we are bridging the gaps between neuroscience and the clinic, integrating traditional approaches with alternative therapies and technology to promote and sustain recovery.

Virtual reality may bring to mind video games. Yet, this third-generation cognitive behavioral therapy tool is a useful intervention for severe anxiety, chronic pain relief, and for teaching coping and psychological skills. A virtual-reality based environment provides a way to deliver repeated exposures to cues in a controlled, therapeutic environment. In the department's Virtual Reality Immersive Technology Clinic, Kim Bullock, MD, and colleagues are hoping to break new ground using this technology to help patients learn the "refusal skills" critical to achieving and sustaining recovery.

Hypnosis is the oldest Western form of psychotherapy. David Spiegel, MD, is a leading clinician-scientist in its use and is developing online tools and app-based interventions—straightforward self-hypnosis techniques—to help people access and utilize their abilities to control problems such as addiction, stress, anxiety, pain, phobias, and habit problems. Dr. Spiegel's first app for smoking cessation is in a clinical trial. Moving forward, he plans to develop and test software for pain management and addiction control.

The **Technology and Innovation Hub** brings together scientists, clinicians, computer scientists, and other collaborators to explore and address the immense possibilities and challenges associated with e-health and technological strategies to strengthen mental health. Elias Aboujaoude, MD, has commented that pathways in the brain that are activated in people with Internet addictions are similar to the brains of people with substance use disorders. Some users demonstrate classic patterns of behavior similar to other substance use disorders—intermittent to recreational use, progressing into daily use, and then into addictive use with dire consequences. Although it may seem paradoxical, technology itself may also hold one of the keys to addressing this challenge.

"We like building things in partnership. Our philanthropy launched a new era for addiction medicine at Stanford."

Liesl and Charles Moldow
Stanford Medicine benefactors

David Spiegel, MD, and colleagues saw altered brain areas and neural changes while scanning the brains of subjects in guided hypnosis sessions. With this knowledge, it may be possible to combine brain stimulation with hypnosis to improve analgesic effects, potentially replacing addictive painkillers and anti-anxiety drugs.

Elias Aboujaoude, MD, director of Stanford's Obsessive Compulsive Disorder Clinic, explores impulse control disorders and the intersection of psychology and technology. He has written extensively on the "e-personality" and digital addiction.

Tim Durazzo, PhD, studies the interplay between biomedical, psychological, and social factors that influence treatment outcomes in alcohol and substance use disorders. For example, one clinical trial is evaluating the effectiveness of a brain stimulation technique, rTMS, to reduce the high rate of relapse experienced by individuals with these disorders.

- More than 20 million U.S. citizens struggle with substance abuse.
- Only 10 percent of people with a substance use disorder receive treatment.
- About 15 percent of hospitalized patients have an active substance use disorder.
- Hospital admissions related to opioid overuse have increased 5 percent annually since 1993.
- The risk of death goes up nearly four-fold when benzodiazepines are combined with opioids.

The **Stanford Addiction Dual Diagnosis Clinic**, led by Anna Lembke, MD, uses an evidence-based, holistic, harm-reduction approach that addresses the complex needs of patients with substance use disorders, behavioral addictions, and co-occurring psychiatric disorders. The addiction care treatment model integrates newer approaches to medical therapy and physical, spiritual, and mental health care. Patients and their physicians, families, and personal support networks are all critical participants.

The **Ethics Laboratory** of Laura Roberts, MD, MA, advances the understanding of optimal ethical practices in research, clinical care, and policy related to vulnerable populations, including individuals living with or at risk for addiction and related conditions. The laboratory has generated new knowledge and valuable data to enrich appreciation of ethical issues in physical, mental illness, and addiction research, societal implications of genetic and brain investigations, the role of stigma in health disparities, and optimal approaches to professionalism in biomedical sciences and clinical medicine.

IMPLEMENTING WHAT WE KNOW TO SAVE LIVES

Despite the billions of dollars the biomedical research enterprise spends each year, estimates suggest only 14 percent of discoveries translate directly to patient care and those that do take on average 17 years to be implemented. By any account, this is a poor return on investment.

Political resistance and poor knowledge of science have made it challenging to develop effective policies surrounding addiction. By sharing our discoveries and advocating passionately for programs and policies that support early intervention and evidence-based care, we're advancing approaches to addiction that reflect its true nature.

Our department takes on the hardest problems so that we can make the biggest difference today and in the future. Our faculty engage in work across the continuum

With joint appointments at Stanford Medicine and the Veterans Administration – Palo Alto, **Steve Lindley, MD, PhD**, **Michael Ostacher, MD**, and **Jodie Trafton, PhD**, bring the resources of both institutions to bear on the treatment of substance use disorders. Collectively, they advance population health through investigating the neurological consequences of substance abuse, the intersection of addictions and mental health treatment, and implementation of innovations in care delivery to achieve large-scale transformation of mental and behavioral health-care delivery.

Mark McGovern, PhD, specializes in the treatment of patients with psychiatric and addictive disorders. As an implementation scientist, he focuses on integrating effective treatments into routine medical practice, primary care, and health-care systems. His work improves the return on investment in biomedical and psychosocial discoveries, benefitting patients, families, and communities far sooner than usual.

of mechanism to application, with discovery and impact at every level and every stage including public policy and transformation of health-care delivery.

Keith Humphreys, PhD, is an expert in innovative approaches to public policy that help improve health outcomes for people living with addiction. By addressing the socio-economic and cultural factors that drive addiction and working directly with public policy makers to advance evidence-based interventions, he is having a national impact.

Anna Lembke, MD, has traveled nationally, advocating for different ways to target the opioid epidemic, including congressional testimony and consulting with state governors, attorneys general, and lawmakers. Her approach is informed by evidence and insights from biomedical sciences, anthropology, sociology, and qualitative methods in the study of addiction.

Mark McGovern, PhD, focuses on scaling impact through implementation in health-care systems. He is leading Stanford Health Care's efforts to integrate behavioral health in primary care, consulting at the state and national level around implementing solutions for the opioid epidemic, and advising health-care systems on designing sustainable models of health-care delivery.

Through education and advocacy, we are working hard to influence key people in government to make sure that insurance plans cover substance use disorder treatment. Our efforts have illuminated the negative health and economic consequences of advertising to young people, which has spurred new legislation to change industry practices.

Moving forward, we are promoting the integration of behavioral health and addiction assessment and treatment into primary care. In addition, we are encouraging the utilization of the prescription drug-monitoring database, which allows prescribers to see all the prescriptions for a controlled addictive medication for a given patient in a given geographic region.

"New sustainable models of health-care delivery will allow those with substance use disorders access to the best care, when it's needed and wherever they need it—changing the trajectory of people's lives."

Mark McGovern, PhD
Professor of Psychiatry and Behavioral Sciences

Director, Integrated Behavioral Health, Primary Care and Population Health

EDUCATION—BUILDING CAPACITY AND ACCESS

Doctors and educators see addiction almost daily, yet there is a dire shortage of experienced specialists to consult and offer guidance. Due to the growing interest among medical students, residents, health-care professionals, and educators to gain skills to assess and intervene based on the latest science, we are developing programs to turn that interest into better access to care.

The **Stanford Addiction Medicine Fellowship** led by Anna Lembke, MD, gives clinicians from many disciplines vital expertise in recovery models and approaches to treatment, as well as the advanced skills necessary to provide consultations for other physicians. We have created a first-of-its kind addiction medicine curriculum for medical students, and free online medical education courses relevant to the opioid epidemic.

Beyond the clinic, we are providing school-based education and programs on Stanford's campus and in the community. Empowering parents, teachers, administrators, residence assistants, and students to understand the impact of substances on the brain, recognize warning signs of addiction, and navigate the treatment system leverages the expertise of our faculty to touch many more lives.

RALLYING THE RESOURCES TO LEAD

Leading the way in this new era in the treatment of substance use disorders requires a constant hunger for new knowledge, groundbreaking ideas, continual innovation, compassion, and a collaborative spirit.

At Stanford, we are drawing upon these powerful motivators to achieve deeper understanding of the biologic and genetic roots of addiction; to develop and implement technologies to see and heal the brain; to optimize the effectiveness of current treatments; and to turn next-frontier ideas into next-generation, personalized, high-impact therapies that can be scaled quickly and broadly.

With your philanthropic partnership, we can accelerate our efforts to:

- Secure and retain innovators and catalysts through endowed professorships and research funding
- Fuel bold ventures that link basic, translational, and clinical sciences to rapidly bring new treatments to patients
- Seed novel, high-yield endeavors that may otherwise go unexplored
- Educate the next generation of clinicians and scientists in neuroscience-based care strategies
- Empower patients, families, and the public to create a better future for those with substance use disorders

Join us in making a difference in creating a brighter future for all those touched by addiction.

CONTACT US

PATIENT INQUIRIES

Please call 650.498.9111

PHILANTHROPY

For questions or a personalized conversation, contact the philanthropic advisor for Psychiatry and Behavioral Sciences.

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medicalgiving.stanford.edu | med.stanford.edu/psychiatry.html

"People whose lives are governed by addiction need our most creative and valuable science, our most effective prevention and treatment interventions, and our finest education and policy efforts. They need our open hearts and minds, too. 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

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