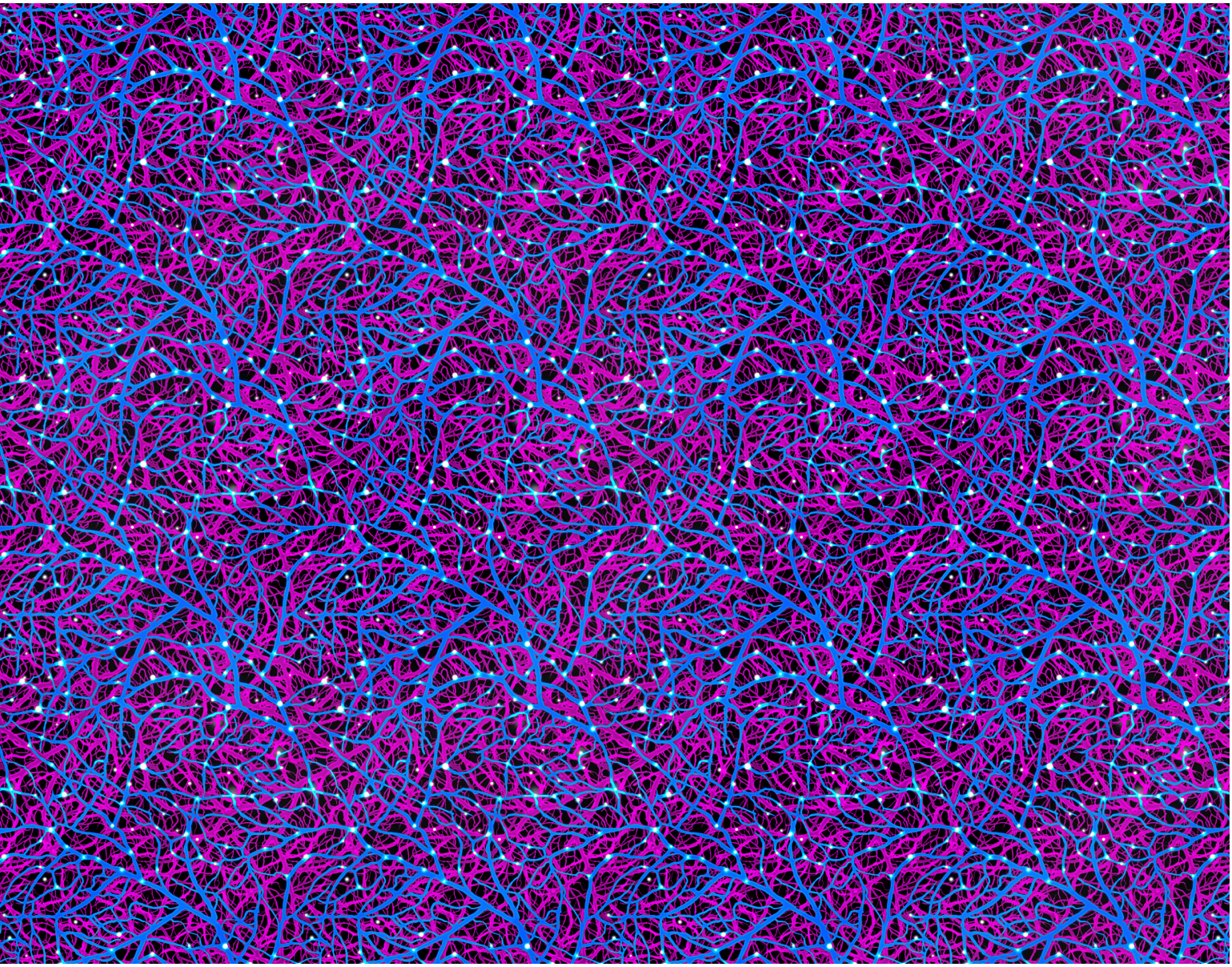
Stanford MEDICINE | Department of Psychiatry and Behavioral Sciences



Speaking the Language of the Brain

Nolan Williams, MD, Assistant Professor

A story of hope. *Deirdre had been managing her bipolar depression well with support from her family and psychiatrist. Then one morning she inexplicably awoke with suicidal thoughts. Deirdre's psychiatrist reached out to Stanford University, having heard of a revolutionary new treatment method achieving dramatic results against even the most unyielding forms of depression. Nolan Williams, MD, and his research team offered this promising treatment—that modulates brain circuits more precisely than other methods—to Deirdre in hopes of avoiding hospitalization.*

Incredibly, after one intense day of multiple treatment sessions, the thoughts of suicide relented. She went home, equipped with detailed plans for follow-up care. A year after treatment, she continued to do well.

While every patient's story and response is unique, this new treatment approach is seeding hope for those who have tried many other options.

"We were so fortunate to experience first-hand this innovative treatment approach that we deemed miraculous. We have committed to help advance this research through philanthropy so that this world-changing discovery can help as many people as possible."

—Clark and Deirdre Lehman

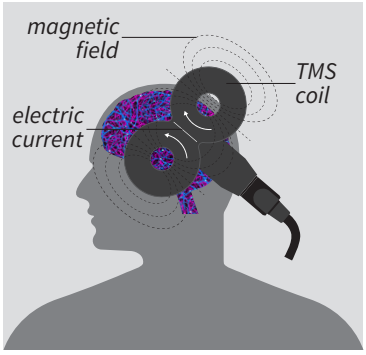
Every year, millions of patients seek treatment for depression, anxiety, and other psychiatric conditions. Existing therapies work for some, but over one-third exhaust treatment option after treatment option, with little or no relief. Life can become overwhelmingly frustrating. For some, this frustration can be life-threatening.

Lives are at stake. Globally, one in six people suffers from a mood or anxiety disorder, and roughly 75 percent do not receive treatment, with sometimes dire consequences. The World Health Organization estimates that suicide claims a life every 40 seconds, and it is believed that for every suicide, 20 more are attempted. Tragically, those numbers are projected to only increase. The economic toll is also significant. In the United States alone, annual costs related to treatment of depression, depression-related illnesses, and lost workplace productivity exceed $210 billion.

Losing self and meaning. Unlike temporary sadness that everyone occasionally experiences, clinical depression and anxiety are long-term illnesses that interfere with how the brain's networks connect and communicate. One may exhibit a lack of insight, or perceive little or no control over circumstances or situations. The ability to feel joy or take action might be diminished, leading to social isolation. Excessive, intrusive worrying about daily matters makes it challenging to concentrate and accomplish tasks. Impairment of working memory, planning, and attention can rob someone of vital familial, social, and professional roles that give their life meaning.

New treatments to modulate brain activity are needed now. Globally, prevalence of mood disorders is increasing across the age spectrum. In the United States, suicide rates are increasing at a time when the capacity of inpatient facilities is faltering. Finding fast-acting, effective interventions has never been more urgent. Clinicians and researchers at Stanford feel an imperative to improve upon existing neuromodulatory brain therapies, such as electro-convulsive therapy (ECT) and traditional transcranial magnetic stimulation.

Taking up the challenge. Psychiatrist and neurologist Dr. Nolan Williams believed that repetitive trans-cranial magnetic stimulation (rTMS) held greater potential for those who had not responded to other first-line treatments. He theorized the problem was one of dosage, lack of precision, and communication. Patients with depression, for example, exhibit hyperactivity in a region deep in their brains. To persuade the brain into reducing this hyperactivity, Dr. Williams developed tools to use brain stimulation to "speak to the brain using its own language." He developed tools to precisely target brain networks and designed brain stimulation patterns and dosing that mimics how the brain learns to rewire itself. The result is SAINT.



First-generation *transcranial magnetic stimulation was developed in the 1990s. Second-generation repetitive transcranial magnetic stimulation (rTMS) followed. Revolutionary for the time, rTMS (pictured above) delivers electromagnetic pulses to "rewire" brain circuitry and alleviate symptoms. Magnetic coils are gently placed on a patient's head and neurons in selected brain regions are stimulated. The traditional application takes between four and six weeks with multiple treatments per week. It's time for SAINT—the next generation rTMS method developed at Stanford.*

THE STORY IN NUMBERS

33 percent
of patients who seek care for depression are not helped by current treatments

70 percent
of patients who try traditional rTMS receive little benefit

90 percent
of patients in the pilot SAINT study met criteria for remission

Stanford Accelerated Intelligent Neuromodulation Therapy (SAINT) uses electromagnetic pulses to mimic the language of the brain. Matched with state-of-the-art imaging techniques to uncover each individual patient's unique brain networks, SAINT targets specific brain circuits and retrains the brain through a series of magnetic pulses that induce brain activity. The protocol uses higher doses than standard rTMS in shorter intervals. It also uses patterns of stimulation that provide time for the brain to build proteins needed for the brain to rewire itself, resulting in sustained changes in neural circuits. By speaking to the brain in its own language, the time commitment from the patient has been reduced from 6 weeks to 5 days and the effectiveness of TMS treatment is dramatically improved.

The results have been astonishing. A pilot study in treatment-resistant depression yielded tremendously exciting results. Analysis shows that 90 percent of the 31 patients enrolled in the study met remission criteria, using established depression scales. Not only did patients' symptoms improve, but they improved to the point that they are indistinguishable from individuals who have never suffered from depression. The risk of suicide in these patients all but vanished. Perhaps most intriguing, this patient group included those who had sought ECT and traditional TMS without relief. Encouragingly, the therapeutic effects for most of the patients continued weeks and even months after treatment ended. Some patients have remained well for over a year. A re-treatment protocol was offered to study participants if needed to sustain results.

Maintaining momentum is critical. A larger double-blind, placebo-controlled trial is underway for treatment-resistant depression to confirm the initial study's high response and remission rates. An inpatient treatment study for suicidality specifically is also underway. The research team believes the SAINT protocol is a robust platform that, with some modifications, could be applied to other brain disorders such as chronic pain, obsessive compulsive disorder (OCD), bipolar affective disorder, and addiction relapse. All of these studies require philanthropy through the first two phases. A specific pilot study for bipolar affective disorder is partially funded and underway, and a pilot study for OCD has been completed, with a larger trial in design.

Enabling hope around the world. When patients have tried everything medicine has to offer to no avail, they suffer and wait for something new to give them hope. SAINT is that something new. The culminating steps in fully realizing the potential of SAINT are a combination of donor and federally funded large multi-site clinical trials. SAINT will then be disseminated to other medical centers, enabling countless people around the globe to benefit from research taking place here at Stanford. Additionally, the SAINT platform will inform other efforts to develop new, alternative neuromodulation therapies at Stanford and beyond its walls.

OPPORTUNITIES FOR PARTNERSHIP

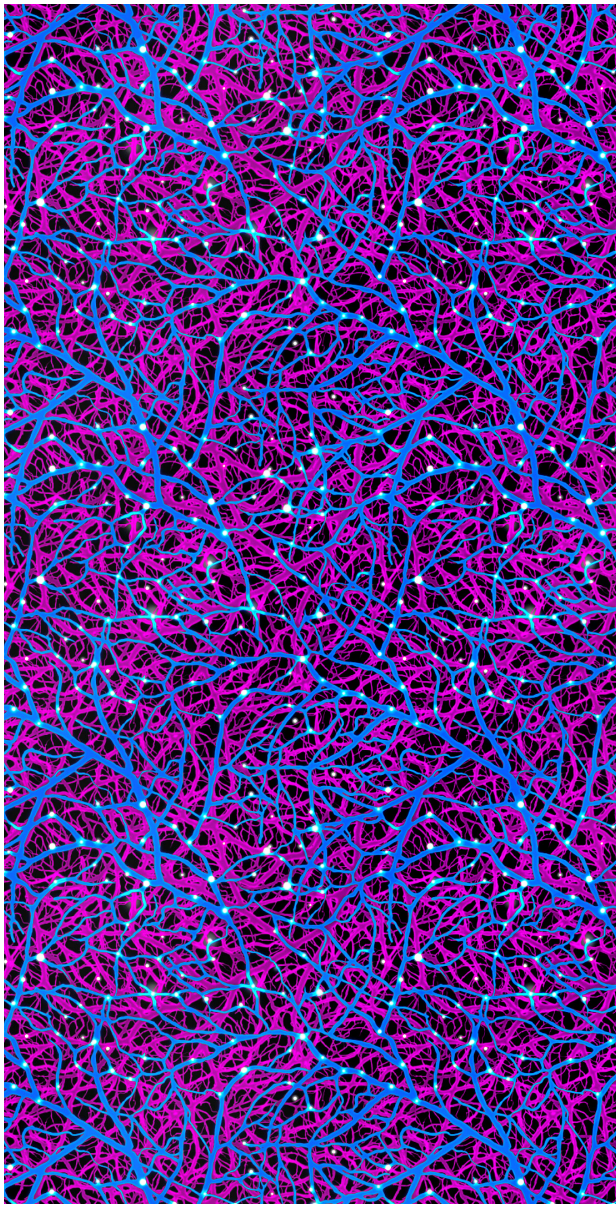
Join with others to help advance neuromodulation therapies. With your partnership, we will fundamentally transform the way that mental illness is treated and help millions of people around the world live happier, more fulfilling lives.

Phase 1 Pilot Studies for Neuropsychiatric Conditions
$250,000 estimated per study

Phase 2 Larger Double-Blind, Placebo-Controlled Trials
$1.2 million estimated per trial

Fully Funded Five-Year Plan Toward Multiple Phase 3 Multi-Site Trials
$7–$8 million estimated

Neuromodulation Research Pooled Fund
Gifts of any size



PRINCIPAL INVESTIGATOR

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