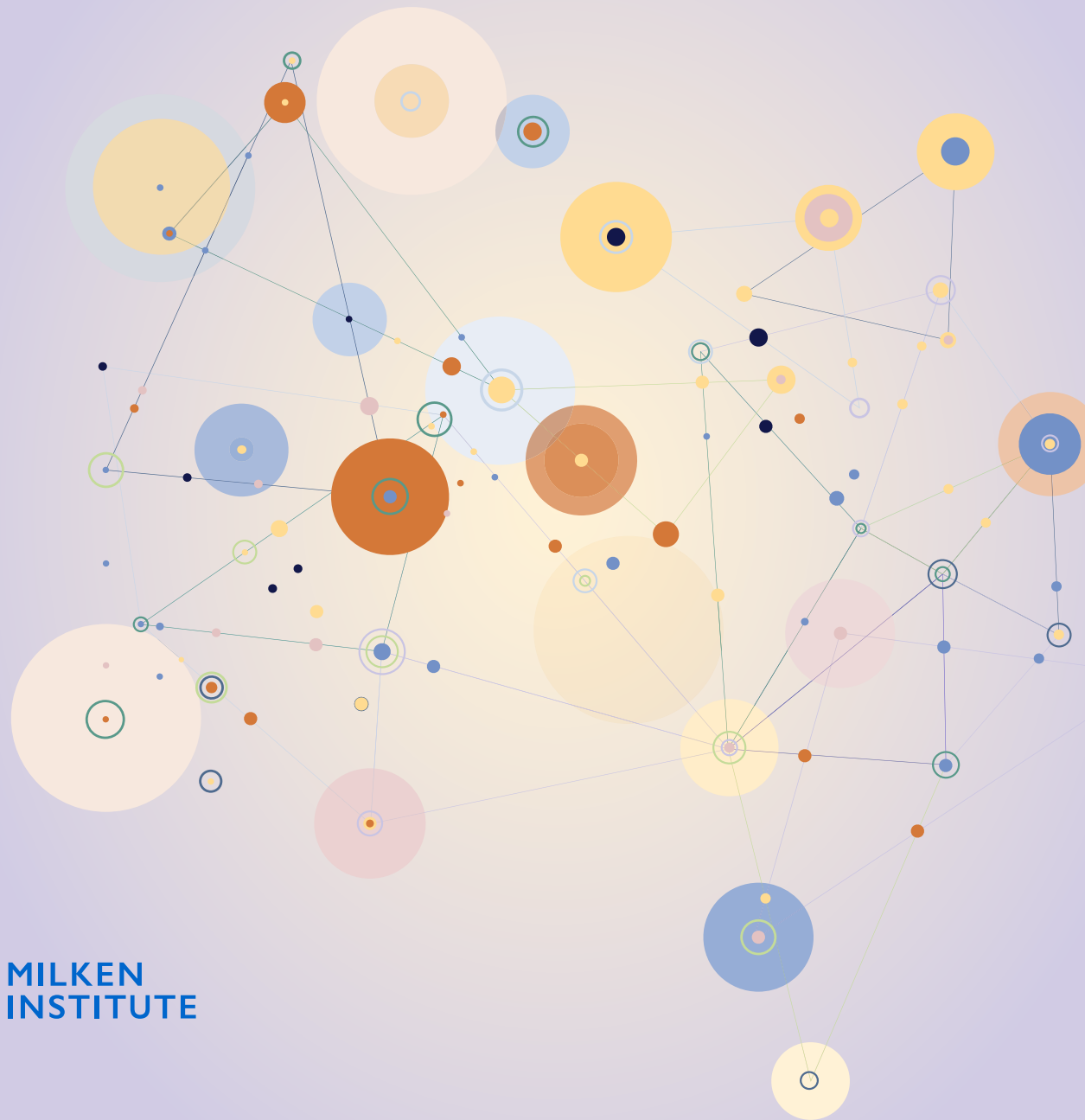




Neuromodulation in Psychiatry

A Giving Smarter Guide

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Foreword

Over the past 25 years, the world has witnessed incredible advances in biomedical science and technology. From gene-targeted therapies to bionic limbs controlled by brain-computer interfaces, what once seemed like science fiction has become reality. Families like ours, though, know there is still so much more to be done.

More than one billion people worldwide live with a psychiatric condition. Millions, including our daughter, still experience symptoms, even with the best available treatment. After years of trying therapy after therapy without success, we were finally able to make meaningful progress through an implanted neuromodulation device—but there is a vast difference between progress and a functional cure.

The Rodan Family Foundation has spent the past eight years supporting research on obsessive-compulsive disorder (OCD) because better treatments require a better understanding of biology. While our philanthropy has spanned multiple approaches (including genetics, animal models, and clinical studies), we have come to see neuromodulation as a uniquely powerful opportunity. Therapies like deep brain stimulation provide invaluable insights into the brain mechanisms that cause illness. Harnessing these rich, complex data can help us understand precisely what happens in the brain to cause psychiatric symptoms and how stimulation can reduce—or even reverse—the impacts.

Despite this promise, there is a notable lack of coordinated investment in advancing this field of research. We partnered with the Milken Institute Strategic Philanthropy's Science Philanthropy Accelerator for Research and Collaboration (SPARC) to engage leading experts from across the scientific, regulatory, and funding ecosystem and identify opportunities to accelerate progress. In June 2026, we convened a select group of these experts for two days of co-learning and discussion, clarifying the most pressing challenges and most promising avenues of future research.

While the gathering was a valuable first step, our work is far from over. With this report, we hope to increase awareness of the value of neuromodulation research, spark connection and collaboration among families like ours, and ultimately drive more strategic funding to high-impact research opportunities. Together, we can ensure that individuals like our daughter do not have to wait another 25 years to see a functional cure.

Katie Rodan, MD, and Amnon Rodan
Rodan Family Foundation

Executive Summary

More than one billion people worldwide live with one or more psychiatric conditions. In the United States, mental illness carries an estimated annual economic burden of \$282 billion, driven largely by lost productivity and reduced work capacity, not just treatment costs. Even with evidence-based psychotherapy and medication, many people with conditions such as depression and OCD do not achieve meaningful relief.

Neuromodulation offers a complementary approach: It uses precisely targeted electrical, magnetic, or acoustic energy to change the activity of brain cells and neural circuits that contribute to symptoms. Several neuromodulation therapies already have psychiatric indications approved or cleared by the US Food and Drug Administration (FDA) and are helping some patients who have not responded to standard care. Recent advances in neuroscience and engineering have made these therapies more precise, more responsive, and less invasive.

However, neuromodulation therapies have advanced more slowly for psychiatric conditions compared with other areas of brain health, largely because their use requires a clear understanding of the biological mechanisms of illness. Psychiatric conditions are incredibly complex, often involving alterations in the functionality of multiple brain regions, significantly increasing the difficulty of appropriately targeting therapeutic stimulation. OCD provides a compelling case study for how neuromodulation research can improve our understanding of these biological mechanisms and inform better treatment protocols. Its underlying circuitry is already comparatively well understood and can be further studied through both noninvasive and surgically implanted neuromodulation approaches. As many conditions (including depression, post-traumatic stress disorder [PTSD], and substance use disorders) feature shared symptoms and overlapping biology, findings from OCD research can be broadly applied to inform progress across the field of psychiatry.

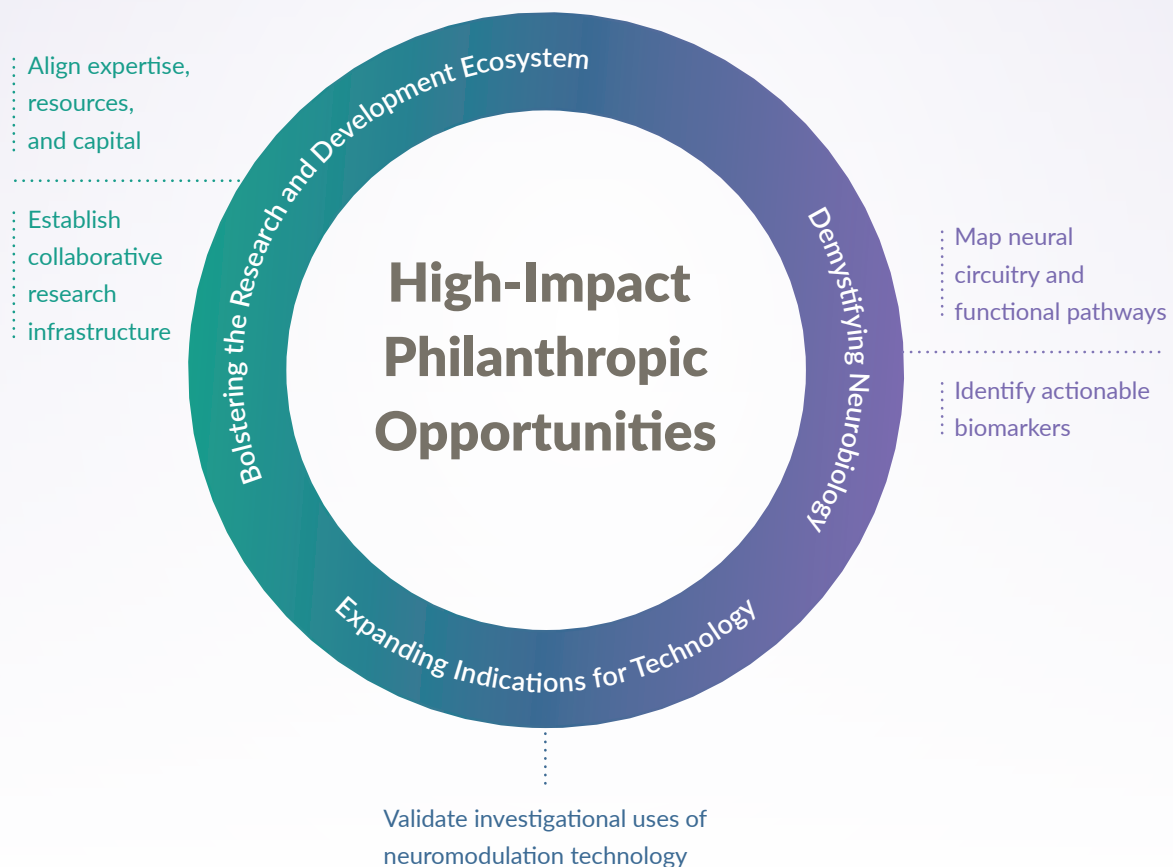
Despite the transformative potential of neuromodulation in psychiatric conditions, the current funding landscape is severely constrained. The National Institutes of Health (NIH) Brain Research through Advancing Innovative Neurotechnologies® (BRAIN) Initiative has driven innovation in brain science for over 10 years, with programmatic investments peaking at \$680 million in 2023. However, far-reaching changes in the availability and administration of public funding, including the expiration of BRAIN Initiative funding from the 21st Century Cures Act in 2026, have introduced significant uncertainty regarding the future of federally funded health research. Meanwhile, private investment in neurotechnology is increasing, but only a small fraction supports psychiatric applications. This gap presents a strategic opportunity for philanthropy to fund high-risk, high-impact projects that are too early for commercial investors to consider, too cross-disciplinary for traditional funding, or so diffusely impactful that no single funding institution should bear the risk alone.

In June 2026, SPARC, in partnership with the Rodan Family Foundation, convened the Neuromodulation in Psychiatry Stakeholders' Roundtable to identify the field's most pressing barriers and highest-leverage opportunities; this Giving Smarter Guide details the key learnings from that gathering of experts.

Drawing on SPARC analysis of scientific literature, public and private funding opportunities, and structured interviews with more than 70 leading experts from across the scientific, regulatory, and funding ecosystem, this guide outlines five areas in which philanthropy can strengthen the translational pipeline and accelerate progress toward more precise, accessible, and effective care (see **Figure E1**).

Every advancement in neuromodulation brings us closer to meeting the most critical needs of those living with severe psychiatric conditions, not just alleviating symptoms but achieving functional recovery and, ultimately, cures. With focused philanthropic investment, funders can transform scientific breakthroughs into lasting improvements for patients and their families.

Figure E1: High-Impact Philanthropic Opportunities



Source: Milken Institute (2026)

Overview of Psychiatric Conditions

Epidemiology

It is natural for an individual to experience periods of stress, low mood, or other disruptions to mental well-being. For many, however, these disruptions are more severe and less transient. Individuals who experience clinically significant disturbances in thinking, mood, or behavior that cause substantial distress and/or impair their ability to function in daily life may be diagnosed with a **mental illness**.¹ When these disturbances cause severe functional impairment, substantially limiting an individual's ability to be successful in one or more major areas of life, they are considered to constitute a **serious mental illness (SMI)**.² Collectively, these **psychiatric conditions** have far-reaching impacts for individuals, communities, and society at large.

More than one billion people worldwide live with one or more psychiatric conditions. Anxiety and depressive disorders are the most common, accounting for more than two-thirds of psychiatric diagnoses (**Box 1**).³

The prevalence and severity of these conditions can vary based on individual factors (e.g., age, sex, race/ethnicity) and societal factors (e.g., cultural background, socioeconomic status, and access to health care).

A growing body of research seeks to understand 1) the biological, environmental, and social factors that contribute to an individual's risk of developing a psychiatric condition and 2) the mechanisms by which these factors translate to specific symptoms. Although the role of environmental and social factors is significant, the remainder of this report will focus on the biological causes and mechanisms outlined in **Figure 1**.⁴

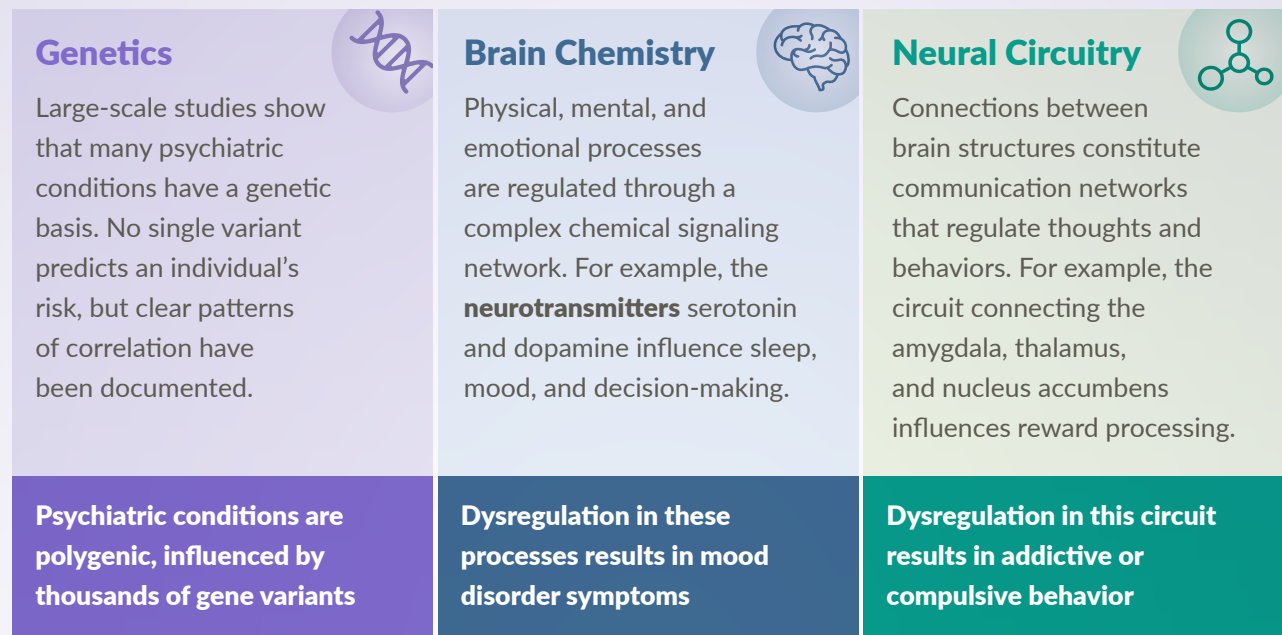
Given the complexity and diversity of psychiatric conditions, identification of a single causal mechanism, even within a single diagnosis, is unlikely. Further progress in understanding the risk factors and interrelated processes that contribute to psychiatric conditions is necessary to allow for earlier, more precise diagnosis and more effective treatment planning.

Box 1: Global Prevalence of Psychiatric Conditions

1 in 7 people live with a psychiatric condition.

- Any condition: **1+ billion**
- Anxiety disorders: **359 million**
- Depressive disorders: **332 million**
- Bipolar disorder: **37 million**
- Schizophrenia: **23 million**

Figure 1: Causes and Mechanisms of Psychiatric Conditions



Source: Milken Institute (2026)

Impact

Depending on the specific psychiatric condition, the timeliness and effectiveness of the intervention, and certain individual and societal factors (e.g., age, sex, race/ethnicity, socioeconomic status), an individual's health and well-being may be affected to various degrees. While some people experience temporary, moderate disruptions in their ability to function effectively in their daily lives, others face significant challenges, with wide-ranging effects on their physical health; personal, educational, and professional success; and overall livelihood. While individuals with SMIs often face the most challenging outcomes, it is important to note that any psychiatric condition can present complex difficulties and reduce quality of life—often requiring individuals to have lifelong treatment and support. **Figure 2** outlines examples of the diverse impacts of psychiatric conditions.⁵

Figure 2: Impacts of Psychiatric Conditions

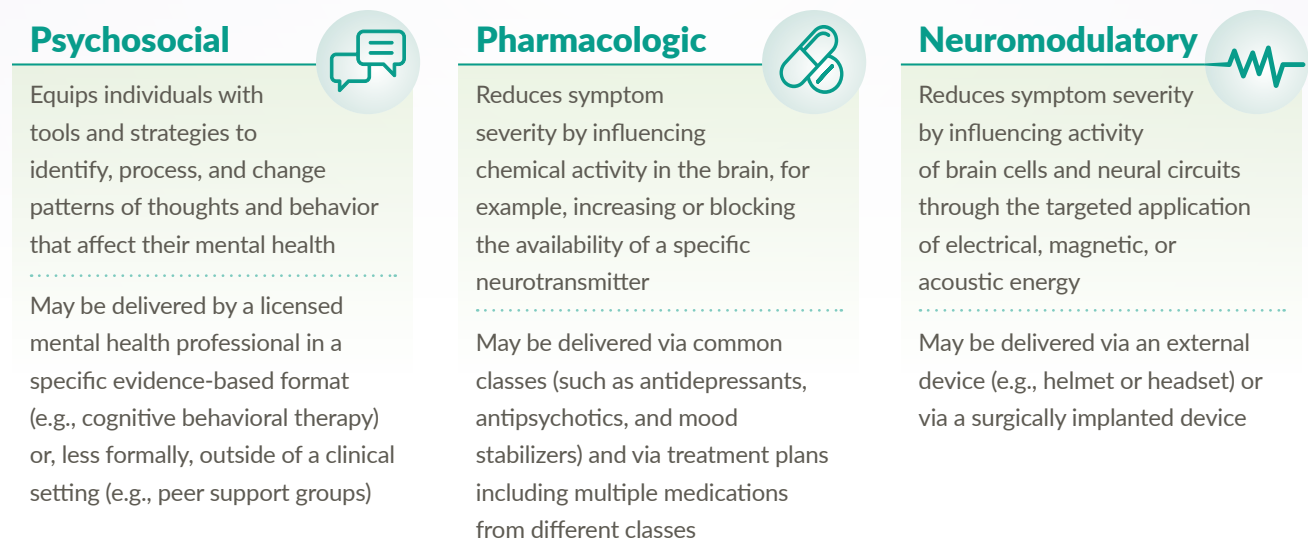


Source: Milken Institute (2026)

Treatment

A wide range of interventions may be used to treat psychiatric conditions, depending on the diagnosis, symptom severity, and individual patient characteristics. Treatment plans often require adjustments over time and, for many individuals, a combination of treatment modalities. **Figure 3** provides an overview of common treatment modalities.

Figure 3: Categories of Psychiatric Treatment



Source: Milken Institute (2026)

Despite their high prevalence and significant impacts, and the wide variety of treatment options available, psychiatric conditions remain overwhelmingly undertreated. In 2024, only half of US adults with a psychiatric condition received professional counseling, medication, or another treatment.⁶

Accessing treatment can be immensely challenging due to a range of individual and structural factors. Only 30 percent of the US population lives in an area with enough mental health professionals to meet their needs, and many clinicians do not accept either public or private insurance, leading to high out-of-pocket costs for patients.⁷

Additionally, many treatments can effectively reduce symptoms, but few are effective enough to support **functional recovery**—the ability to fully engage in all facets of daily life. Up to 60 percent of individuals with psychiatric conditions experience a **treatment-resistant** or **treatment-refractory** form of illness and do not reach a meaningful reduction in symptoms, even with an accurate diagnosis and evidence-based treatment.⁸

Meaningfully reducing the burden of psychiatric conditions for individuals, communities, and society at large necessitates not just increasing access to treatment but developing new and better treatment modalities.

Advancing Psychiatric Treatment

Biological Complexity as a Key Barrier

With a few notable exceptions in recent years, progress in developing new and more effective treatments for psychiatric conditions has been slow. In a clinical context, identifying the most effective treatment regimen for an individual patient is also exceedingly difficult. The primary impediment in both cases is the inherent biological complexity of these conditions.

Psychiatric conditions are generally understood to arise from pathological changes across multiple brain regions, particularly the alteration or dysregulation of **neural circuits**—interconnected groups of brain cells that transmit information through chemical and electrical signals. Viewing these conditions as brain disorders—functionally comparable to conditions like epilepsy or Parkinson’s disease—allows for a more objective, mechanistic lens in research and clinical practice. However, in contrast to other fields of medicine, psychiatry relies on self-reported experiences and observable behaviors rather than concrete, measurable biological characteristics.

As a consequence, an individual’s psychiatric diagnosis does not necessarily reflect the underlying biology of their condition. Individuals with similar symptom profiles may have very different neurobiology and therefore different responses to a particular treatment. In addition, individuals with similar neurobiology may experience and describe their symptoms differently, leading to different diagnoses. The lack of reliable methods for assessing an individual’s biology leaves researchers unable to effectively design and accurately interpret the outcomes of clinical trials, and clinicians in a position of prescribing treatments essentially through trial and error.

One promising avenue of research to address this issue is **brain mapping**—a method to measure the activity of neural circuits and the functional pathways connecting different areas of the brain. These maps may be used to guide individual treatment planning or aggregated into atlases for large-scale analyses. Visualizing the structural organization and activity within typically functioning brains and comparing them with those of individuals with different psychiatric conditions can provide valuable insights into the biological mechanisms of illness and opportunities for effective intervention.

The growing field of precision psychiatry has also made progress in addressing the challenge of biological complexity.⁹ Clinicians and researchers may use genetic tests to determine how a patient might metabolize a particular class of medications, neuroimaging to study or monitor brain function throughout treatment, or wearable sensors to collect data on metrics such as heart rate and sleep. However, collecting this information

is insufficient if the data are not actionable. Further research is necessary to determine which of the many possible measurable signals or indicators are validated **biomarkers** that can reliably indicate “normal biological processes, pathogenic processes, or responses to an exposure or intervention.”¹⁰

To advance the field as a whole—enabling earlier diagnosis, more precise treatment selection, and the development of more effective therapeutics—a more comprehensive understanding of the underlying biology of psychiatric conditions is needed.

Neuromodulation as a Key Opportunity

Neuromodulation therapies are interventions designed to produce specific changes in the activity of brain cells and neural circuits through the targeted application of electrical, magnetic, or acoustic energy. Compared with other classes of interventions, neuromodulation therapies can be particularly valuable as they are:

- **Nondestructive**—Stimulation influences neural structures and processes without damaging or removing brain tissue, so the intervention can be adapted as needed.
- **Targeted**—Stimulation can be precisely targeted to brain structures or pathways associated with symptoms, reducing unintended effects on other body systems.
- **Potentially Curative**—Stimulation may evoke neuroplastic changes in the brain structures and pathways that cause illness—potentially providing a functional cure, rather than merely reducing symptoms.

Neuromodulation therapies encompass a wide range of modalities, from surgically implanted devices (such as those used with deep brain stimulation [DBS]) to external stimulation devices (such as those used with transcranial magnetic stimulation [TMS]). Historically, these therapies have primarily been used to treat movement disorders and epilepsy. Such conditions are well suited to neuromodulation because of the clearly delineated connections between specific activity in defined brain areas and symptom expression. For example, clinicians can identify the precise location where abnormal electrical activity triggers a focal epileptic seizure, implant a depth electrode at that site, and program a responsive neurostimulation device to correct the electrical activity pattern.¹¹

For psychiatric treatment, neuromodulation therapies hold significant promise, as they can serve as both critical treatment options and powerful research tools. Innovation in neuromodulation has accelerated in recent years due to transformational advances in neuroscience, computer programming, and engineering.

For example, **invasive recording**—measuring brain activity at an anatomically precise level via surgically implanted electrodes—is currently the most direct method for collecting high-resolution brain activity data, the “ground truth” needed to map neural networks accurately.¹² Until recently, these recordings were possible only during surgical procedures. The introduction of **bidirectional interfaces**—devices capable of simultaneously providing neurostimulation and recording brain activity—enabled the capture of these data

longitudinally, as an individual's symptoms change over time.¹³ Multimodal studies that record brain activity while performing other types of monitoring (e.g., magnetic resonance imaging [MRI] mapping or wearable sensors) create an incredibly rich and detailed picture of the relationship between biology and symptoms, filling in critical knowledge gaps.

While most neuromodulation research and development efforts have historically focused on nonpsychiatric conditions such as Parkinson's disease or chronic pain, the opportunity to apply these technologies to psychiatric care is increasingly compelling. Neuromodulation can provide meaningful treatment options for individuals who do not respond to existing care while generating the high-resolution, longitudinal data needed to clarify the neural circuits and biomarkers underlying psychiatric symptoms. Strategic investment in this area could accelerate progress toward more precise, personalized, and effective treatments for psychiatric conditions.

Neuromodulation in Psychiatry

Current Utilization

Neuromodulation can provide potentially lifesaving relief for individuals who do not experience functional remission of their symptoms through first-line psychiatric treatments. Currently, **FDA-approved** or **FDA-cleared** neuromodulation indications are concentrated in a small number of psychiatric conditions, including major depressive disorder (MDD), bipolar disorder (BD), and OCD. **Table 1** provides an overview of these therapies,¹⁴ with further information on FDA regulatory categories in **Box 2**.¹⁵

Table 1: Neuromodulation Therapies Approved or Cleared by the FDA for Psychiatric Conditions

Therapy	Condition	Modality	Mechanism of Action
Deep Brain Stimulation*	OCD	Implanted: electrodes placed within brain tissue, battery implanted below clavicle	Continuous or intermittent electrical currents modulate activity in deep brain structures
Vagus Nerve Stimulation	MDD	Implanted: electrode wrapped around left cervical vagus nerve, battery implanted below clavicle	Intermittent electrical currents modulate activity in thalamocortical circuits (<i>precise mechanism unclear</i>)
Transcranial Magnetic Stimulation	OCD, MDD	External: stimulation coil placed against the head	Strong magnetic field generated by stimulation coil passes through the skull to modulate activity in cortical brain structures
Transcranial Direct Current Stimulation	MDD	External: electrodes placed on the scalp or embedded in a headset	Weak electrical currents pass through the skull to modulate activity in cortical brain structures
Electroconvulsive Therapy (ECT)†	MDD, BD	External: electrodes placed on the scalp	Weak electric currents pass through the skull to induce a brief, controlled seizure (<i>precise mechanism unclear</i>)

*Approved under a Humanitarian Device Exemption (HDE)

†Cleared for use in MDD and BD-associated depression

Source: Milken Institute (2026)

Box 2: FDA Regulatory Terminology

The FDA uses different criteria to evaluate medical devices, depending on the potential level of risk involved in their use.

Class II devices are considered to have a moderate risk and may be **FDA cleared** through a **510(k) premarket notification** demonstrating substantial equivalence to a previously cleared device.

Class III devices are considered to have the highest risk and must be **FDA approved** through a **Premarket Approval (PMA)** application process supported by clinical evidence of safety and effectiveness.

In rare cases, a Class III device may also be FDA approved through a **Humanitarian Device Exemption**, limited to devices for conditions affecting fewer than 8,000 people in the US each year. It requires evidence of safety and probable benefit rather than the full effectiveness data that a PMA demands.

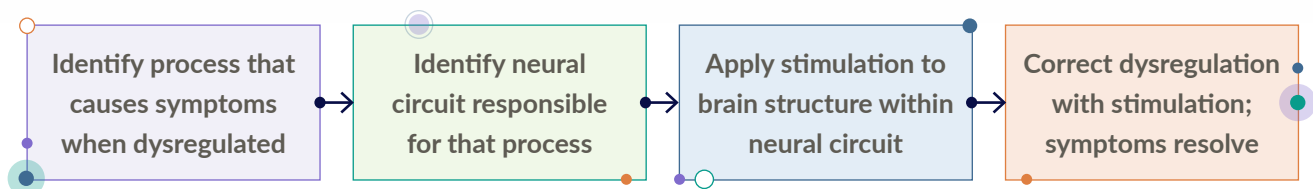
Biological Basis of Treatment

Neuromodulation therapies aim to modulate neural activity associated with symptom development by directly targeting specific brain structures or pathways.

Determining precisely where the stimulation should be applied, however, can be difficult in psychiatric conditions. In contrast to a condition like epilepsy, in which seizures are caused by an identifiable episode of abnormal activity at a discrete region, psychiatric symptoms are thought to reflect longer-term patterns of activity across multiple areas of the brain.

Mapping the brain's anatomical regions and the functional pathways that connect them is the first step in addressing this challenge. Interpreting these maps—understanding the functional role of different neural circuits and how they are connected to psychiatric symptoms—is the key to identifying where and how stimulation should be applied. **Figure 4** illustrates the fundamental steps to identifying stimulation targets.

Figure 4: Neuromodulation Targeting Process



Source: Milken Institute (2026)

Understanding the organization and functional roles of specific brain structures, as well as the pathways that connect them, are the foundation of effective neuromodulation therapy. The fact that many psychiatric conditions share certain symptoms—likely due to shared aspects of biology—can pose a challenge from a diagnostic perspective.

From a research perspective, however, this overlap presents an opportunity to apply learning across conditions.¹⁶ While there is no guarantee that a neuromodulation therapy that is effective for treating one psychiatric condition will be effective for treating another based solely on shared aspects of biology, such similarities can provide essential clues to guide research and treatment development. **Figure 5** demonstrates one example of this cross-applicability,¹⁷ in which the same brain structures are used as targets for neuromodulation therapy in multiple psychiatric conditions with shared symptom profiles.

Figure 5: Example of Shared Targets in Neuromodulation for Psychiatry

Many psychiatric conditions feature issues with **approach-avoidance conflict decision-making**—the inability to accurately judge whether one should approach a positive outcome or avoid a negative outcome.

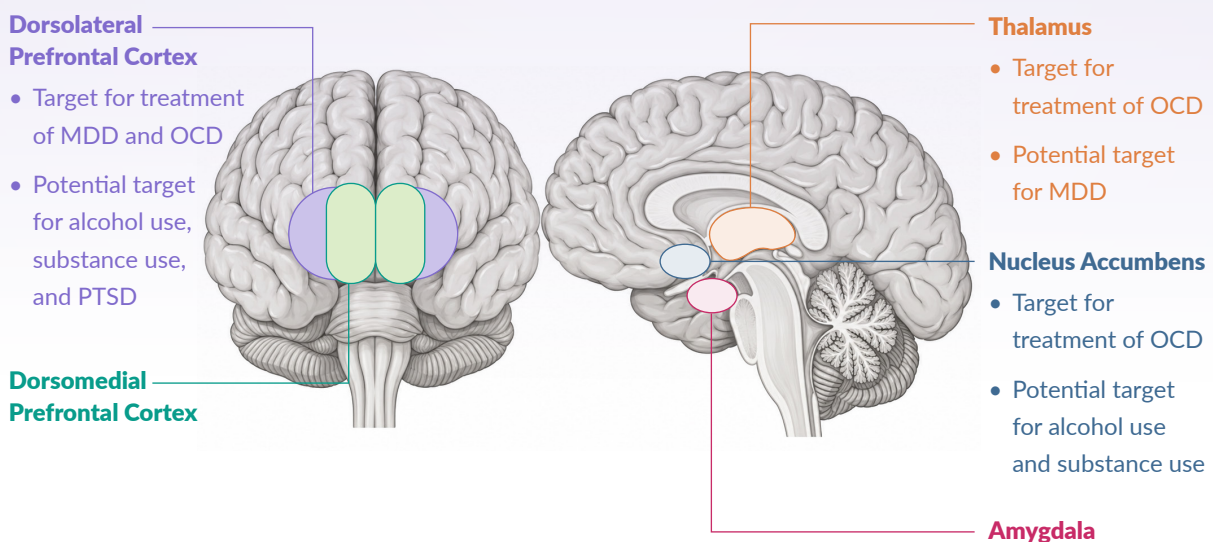
Symptoms: impulsivity/addiction (enhanced approach) or heightened fear response (enhanced avoidance)

Dysregulated Processes: reward processing, emotional regulation

Responsible Neural Circuits: dorsal cognitive, fronto-limbic, ventral affective

Brain Structures Within Circuits: prefrontal cortex, amygdala, thalamus, nucleus accumbens

Neuromodulation targeting these brain structures can restore typical functionality within the circuit, regulating reward and emotional response processes and reducing symptoms.



Sources: Milken Institute analysis (2026), BioRender

Priorities for Future Research

The field of research investigating the use of neuromodulation therapies in psychiatric conditions is diverse and continually expanding. Much of this research centers on the use of already approved therapies for additional indications, often based on shared biology and symptom profiles. There is also significant interest in the development and validation of alternative treatment modalities, particularly those that may be less invasive or otherwise more tolerable to patients.

The examples presented in this section reinforce the far-reaching potential of neuromodulation in psychiatry and the critical need to support continued research to clarify mechanisms, optimize targeting, and generate evidence for broader clinical adoption.

Expanding Indications Through Transdiagnostic Learnings

Current research assessing TMS as a treatment for PTSD is a prime example of neuromodulation's **transdiagnostic** potential (the opportunity to apply learnings from one condition to another). Since its approval for the treatment of MDD in 2008, TMS has been widely used to treat individuals with MDD and co-occurring conditions. When treated using standard TMS-MDD protocols, veterans with co-occurring MDD and PTSD can experience significant improvements in PTSD symptoms (**Box 3**).¹⁸



Box 3: Results of TMS-MDD Treatment in Veterans with Co-occurring PTSD

Response: **63%–78%**

Remission: **47%–49%**

Evidence also shows that this treatment could be further refined by modifying TMS-MDD protocols to focus more on regions connected to the amygdala, a structure critical for processing threats and regulating fear responses.¹⁹ This type of research can meaningfully accelerate the validation of additional therapeutic indications for neuromodulation therapies.

Improving Clinical Trial Design Through Patient Stratification

Research assessing DBS as a treatment for MDD clearly illustrates the challenges of studying neuromodulation therapies in highly **heterogeneous** conditions. Individuals with MDD may have very different symptom profiles, reflecting fundamental differences in their underlying biology. Grouping research participants without accounting for these biological differences makes it difficult to interpret the effectiveness of a particular treatment.²⁰

While small-scale studies of DBS-MDD have shown response rates of up to 70 percent, two industry-sponsored clinical trials failed to replicate these results in a larger population, leading to a reexamination of how participants and stimulation targets should be selected in depression research.²¹ The success of

ongoing efforts to validate DBS as a treatment for MDD, including through the currently enrolling Treatment Resistant Depression Subcallosal Cingulate Network DBS (TRANSCEND) study, will depend on appropriately interpreting treatment outcomes in the context of biological variation across the study population.²²

Validating Less-Invasive Technologies

Developing interventions that can provide meaningful, durable therapeutic effects with a minimal degree of invasiveness is a key lever to increase scalability and access. Focused ultrasound stimulation (FUS) has demonstrated significant potential to address this priority for neuromodulation in psychiatric conditions.

FUS is an externally delivered therapy that uses acoustic energy to achieve different effects depending on the frequency of the ultrasonic waves.

High-intensity focused ultrasound (HIFU) results in highly precise, targeted destruction of tissue and has long been used to treat glaucoma and certain cancers. More recently, MRI-guided HIFU was approved for the treatment of select movement disorder indications, including essential tremor and Parkinson's disease.²³ These conditions are commonly treated through surgical procedures to either remove or create a focal lesion on a structure in the deep brain; HIFU accomplishes this same effect nonsurgically.

Stimulation at lower frequencies does not result in tissue destruction and can be targeted to either deep or cortical brain structures, significantly broadening its potential therapeutic applications. Critically, low-intensity focused ultrasound (LIFU) enables noninvasive, nonpermanent modulation of neural activity in deep brain structures such as the amygdala, nucleus accumbens (NAcc), and thalamus—targets difficult to reach with surgically implanted neuromodulation devices.

Box 4: Response Rates in Preliminary Studies of LIFU in Psychiatric Conditions

OCD: **70%**

Generalized anxiety disorder: **64%**

Substance use disorders: **80%**

LIFU has not yet received FDA clearance or approval for use in any health condition, but an extensive body of evidence supports its use in a wide range of indications, including chronic pain, dementia, movement disorders, and multiple psychiatric conditions (**Box 4**).²⁴ While LIFU therapy has been proven safe under controlled conditions, further research is needed to establish optimal dosing and targeting protocols and to confirm the durability of treatment effect.

Ecosystem-Level Barriers to Progress

While there have been significant advances in the efficacy and availability of neuromodulation therapies for psychiatry in recent years, progress has been far slower and less consistent compared with other clinical indications, including movement disorders, epilepsy, and chronic pain. In addition to the greater degree of biological complexity in psychiatric conditions, multiple interrelated systemic factors have contributed to this disparity in momentum.

Limited Knowledge and Negative Perceptions

As in any healthcare context, individuals with psychiatric conditions often depend on their clinicians to inform them of alternative options when they do not see meaningful improvement from first-line treatments. However, clinicians are unlikely to integrate technology-based interventions in their practice if they are not convinced of their clinical utility.²⁵ Although the majority of psychiatric practitioners are aware of neuromodulation as a treatment option, referrals remain comparatively low, reflecting uncertainty about which patients benefit, how to fit therapies into standard care, and how to navigate access and reimbursement. Even for treatments that have been rigorously tested and approved by the FDA, a lack of knowledge about their safety and effectiveness remains a major barrier to adoption among clinicians and the general public alike (**Box 5**).²⁶

Progress in the field is also significantly hampered by the predominant negative perception of brain-based medical interventions for psychiatric conditions, a lasting legacy of the psychosurgery movement of the early 20th century. Procedures like prefrontal lobotomy were widely performed for a variety of psychiatric conditions beginning in the 1930s, often with devastating effects on patients' personalities, cognition, and physical function.

Despite dramatic improvements in the precision and efficacy of surgical interventions and the proliferation of nonpermanent, externally delivered therapeutic options, stigma and distrust of the field continue to influence patients, clinicians, and funders.

Box 5: Survey Results: Resident and Attending Psychiatrist Perspectives on Surgical Interventions (such as DBS)

87% were aware that surgical interventions could be used to treat psychiatric conditions

92% cited lack of knowledge about the procedures as a barrier to referral

35% believed the procedures were dangerous or unethical

Lack of Coordinated Investment

Human subjects research on neuromodulation therapies for psychiatric conditions is highly complex and resource-intensive in terms of expertise, infrastructure, and capital. Recruitment can be slow, particularly for invasive or intensive interventions that require assessments of risk and benefit and long-term monitoring. It may take years of effort to recruit a potential study participant, determine that the intervention will be safe and potentially effective for that individual, and ensure compliance with regulatory guidelines and eligibility for insurance coverage. The study itself then requires extensive collaboration across multiple medical specialties and long-term coordination of monitoring and follow-up visits.

Consequently, the majority of these studies are conducted at major academic medical centers, typically enrolling a limited number of participants. These limitations of scale are significant barriers to conducting research that is replicable, generalizable, and ultimately able to inform clinical practice.

In the commercial realm, a notable lack of coordinated investment exists for this field of research. The overall costs of medical device development can reach hundreds of millions of dollars over several years, and regulatory pathways are often uncertain. Major manufacturers have little incentive to invest in large-scale clinical trials for conditions with limited perceived commercial potential, and small- to medium-scale developers often struggle to secure the necessary resources. Many promising therapies fail to navigate the pathway from concept to commercialization because of insufficient access to capital at key stages of development, not a lack of scientific evidence.

Therapeutic device development can stall at two key transition points: first, from an academic research initiative to a start-up and then from a start-up to a commercially viable independent entity. Securing funding to traverse these “**valleys of death**” requires evidence of both clinical benefit and commercialization potential, typically in the form of data from human studies with validated biomarkers to demonstrate efficacy and generalizability.

Without funding to develop and test a prototype, however, this evidence may be impossible to supply. Thus, a self-reinforcing cycle is created in which capital is inaccessible without clinical data, yet those same data are inaccessible without capital.

In the current funding landscape, traditional funding strategies are insufficient to support the full life cycle of therapeutic device development. For example, philanthropic grants can be invaluable for early data collection but are rarely sufficient to support longer-term risk-bearing investments in efforts such as prototype development, the addressing of regulatory issues, and commercialization. Conversely, venture funding provides greater capital and higher risk tolerance but is ill-suited for earlier stages, when timelines are long and returns are uncertain.

Several federal, philanthropic, and public-private partnership mechanisms have been employed to address these challenges, matching promising research with the expertise and resources required to advance to the next stage of development (**Box 6**). Yet prominent pipeline gaps remain.

In this disconnected and precarious ecosystem, many potentially valuable interventions are stuck in limbo, unable to pursue FDA approval despite strong preliminary evidence. Disrupting this cycle requires 1) identifying which funding source is appropriate for each stage of research and development, based on the volume of capital and level of risk tolerance required, and 2) strategically sequencing and combining those funding streams.

Box 6: Examples of Mechanisms to Align Expertise and Resources

Advanced Research Projects Agency for Health: This funding agency within the US Department of Health and Human Services is designed to support high-impact research, including the development of breakthrough therapeutic technologies. Pivotal investments support work that cannot be accomplished in a traditional research or commercial context.

Blueprint MedTech: This is an incubator program within the NIH designed to accelerate the development of devices to diagnose and treat disorders of the brain and nervous system. Funding, design and testing services, and expert consultation on regulatory and commercialization issues support rapid translation from concept to first-in-human clinical studies.

One Mind Accelerator: This cohort-based accelerator program leverages philanthropic and corporate investment to support early-stage mental health start-ups. Leadership coaching, fundraising guidance, and facilitated networking provide founders with the resources and connections required to bring innovative products to market.



Case Study:

Obsessive-Compulsive Disorder

Obsessive-compulsive disorder (OCD) represents a particularly compelling case study on the value of advancing neuromodulation therapies for psychiatric conditions for three key reasons. There is a significant burden of unmet need, there is a strong understanding of its underlying biology, and it can be studied through external and surgically implanted neuromodulation technologies approved by the FDA. In addition to improving treatment options for individuals with treatment-refractory OCD, further research could create a road map for treating other complex psychiatric conditions for which shared neural pathways, overlapping symptoms, and similar barriers to adoption have slowed therapeutic innovation.

Overview and Burden of Illness

OCD is a chronic condition affecting approximately 2 percent of the global population.²⁷ Characteristic symptoms include persistent distressing thoughts or images (obsessions) and repetitive behaviors or mental rituals (compulsions), but the expression of these symptoms varies widely.²⁸ Any of OCD's diverse symptom profiles can result in serious and far-reaching impacts: 65 percent of individuals with OCD report a severe level of impairment in their ability to maintain relationships and be successful in home, work, and social settings. The condition is also associated with a higher risk of premature mortality, including an increased risk of suicide.²⁹

First-line treatments for OCD primarily consist of cognitive behavioral therapy (CBT) with exposure and response prevention (ERP) and **pharmacological treatments** including selective serotonin reuptake inhibitors (SSRIs). Up to 70 percent of individuals with OCD achieve meaningful reductions in symptoms with these evidence-based treatments, but as many as one in three patients continue to experience severe treatment-refractory symptoms. For individuals with treatment-refractory OCD, neuromodulation therapies may offer a meaningful option when standard treatments have failed.

Current Utilization of Neuromodulation Therapies

Two forms of neuromodulation therapy—deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS)—have authorized uses for OCD. Each of these therapies has potential benefits and significant challenges related to access, evidence, and implementation.

DBS has shown higher response rates in patients with treatment-refractory OCD, but the process of receiving treatment can be long and arduous. DBS therapy requires surgery to implant the device and, in some protocols, extensive mapping to determine the best target. Additionally, it may take several years for

a patient to meet eligibility requirements and secure approval from their insurer, due in part to DBS-OCD's Humanitarian Device Exemption (HDE) regulatory status set by the US Food and Drug Administration.

An HDE applies to medical devices intended to treat or diagnose rare diseases or conditions affecting small patient populations. Unlike full Premarket Approval, an HDE does not require the same level of evidence demonstrating effectiveness; instead, FDA approval is based on evidence that the device does not pose an unreasonable or significant risk and that its probable benefit outweighs the risk. While this pathway can allow individuals with severe or debilitating conditions, such as treatment-refractory OCD, to access potentially lifesaving therapies when stronger evidence is difficult to generate, it also carries restrictions that can limit uptake and commercialization.

Because TMS is delivered externally and is not subject to the same restrictions as an HDE-approved therapy, it can meaningfully lower barriers to access. However, the likelihood of a successful treatment response is also much lower. While efforts to improve the targeting range of TMS are ongoing, current devices primarily modulate the cortical, or surface, level of the brain. Therefore, this therapy cannot effectively access the deep brain structures implicated in OCD symptom development.³⁰

Underlying Biology

OCD is perhaps the best-characterized psychiatric condition in terms of its underlying neurocircuitry.³¹ Decades of neurophysiological and neuroimaging studies have contributed to identifying specific neural circuits that, when altered, cause dysregulation in cognitive and emotional processes, which are then expressed as OCD symptoms. **Table 2** provides an overview of five of these circuits.³²

Table 2: Select Neural Circuits Implicated in OCD

Circuit	Associated Processes	Symptoms of Dysregulation
Fronto-Limbic	Generation and evaluation of emotional responses, including fear and anxiety	Dysregulated fear response, intolerance of uncertainty
Sensorimotor	Generation and control of motor behaviors, integration of sensory information	Aversive or uncomfortable sensations that drive repetitive behaviors, altered habit formation
Ventral Cognitive	Control of self-regulatory behaviors	Altered response inhibition, inability to withhold inappropriate behaviors
Ventral Affective	Processing of and responses to reward	Altered reward response, compulsions either as reward or as a means to avoid anticipated punishment
Dorsal Cognitive	Executive functions required for effective goal-directed behavior, including working memory and planning; regulation of emotion	General impairments in executive function, emotional regulation

Source: Milken Institute (2026)

This circuit-level knowledge is critical to informing target selection for neuromodulation therapy. For example, the ventral affective circuit primarily comprises neural connections among the orbitofrontal cortex (OFC), thalamus, and NAcc. The OFC is commonly targeted for TMS-OCD, and the thalamus and NAcc for DBS-OCD.³³ While further research is required to fully understand the mechanisms behind OCD, our current level of understanding provides a valuable starting point for studying how neuromodulation can be used to refine treatment targets, test mechanistic hypotheses, and generate insights that may inform other psychiatric conditions.

Barriers to Progress

Although OCD is an excellent case study for the potential of neuromodulation therapies in psychiatric conditions, it is also subject to the same barriers facing the field overall.

- **Biological complexity:** OCD symptoms vary widely and may reflect different combinations of circuit alterations. This contributes to variability in treatment response, even when stimulation is delivered to recognized targets. Further research is needed to clarify the relationship across individual brain profiles, symptom expression, and optimal stimulation targets.
- **Limited knowledge and negative perceptions:** Stigma surrounding brain-based interventions, limited clinician familiarity, and the HDE status of DBS for OCD may contribute to uncertainty about its clinical utility and reduce patient referrals.
- **Lack of coordinated investment:** OCD places a significant burden on individuals and families, yet it is often not viewed by industry as a sizable or predictable market. Consequently, innovative neuromodulation approaches may struggle to secure the funding needed for large-scale trials, regulatory review, and broader clinical adoption.

Research Funding for Neuromodulation in Psychiatry

This section examines trends in US funding for neuromodulation research aimed at understanding and treating psychiatric conditions. Public investment has been the primary driver of research and development in the past decade, and funding for neuromodulation research continued to grow modestly in 2025. However, 2025 also brought destabilizing grant terminations and cuts to key initiatives, disrupting the research ecosystem. In contrast, commercial investment in the broader neurotechnology sector has grown substantially in recent years—but only a comparatively small proportion of this investment is directed specifically to psychiatric indications.

In this moment of significant momentum and possibility, yet increasingly uncertain funding, philanthropic and private investment could have an outsized impact by aligning and accelerating progress in the research and development of neuromodulation technologies in psychiatry.

Public Funding

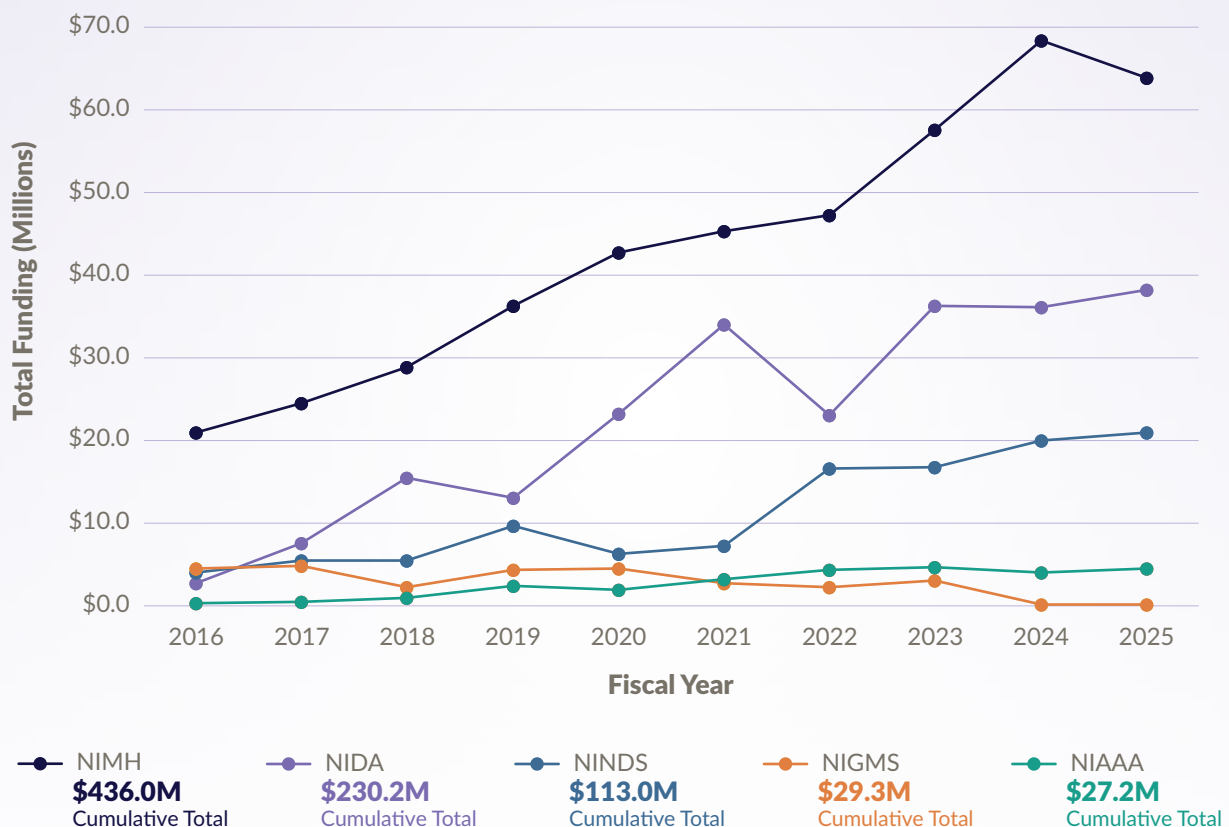
Over the past decade, the NIH has been the largest federal agency that promotes and funds research on the use of neuromodulation technologies for psychiatric indications. While funding has grown moderately at most institutes over the past few years, investment levels remain insufficient for breakthrough progress, and cuts to important programs have constrained promising research.

Significant 2016–2024 NIH Funding Increases, Followed by a 2025 Slowdown

From Fiscal Year (FY) 2016 through FY 2025, nearly all funding for research on the use of neuromodulation technologies for psychiatric indications was administered through five NIH institutes: the National Institute of Mental Health (NIMH), National Institute on Drug Abuse (NIDA), National Institute of Neurological Disorders and Stroke (NINDS), National Institute on Alcohol Abuse and Alcoholism (NIAAA), and National Institute of General Medical Sciences (NIGMS). Cumulative investment across these five institutes totaled approximately \$836 million throughout this period (see **Figure 6**).

Both NIMH and NIDA saw overall increases in funding between FY 2016 and FY 2024, though NIDA's growth was less consistent than NIMH's in this period for neuromodulation therapies. In FY 2025, NIDA funding rose slightly to its peak at \$38 million, while NIMH funding fell to \$64 million—the first time its annual spending declined in a 10-year period. From FY 2016 to FY 2021, funding from NINDS, NIAAA, and NIGMS was comparatively low, at less than \$10 million per year. While NIAAA and NIGMS funding have remained consistent at this level, NINDS funding increased from FY 2021 to FY 2025.

Figure 6: NIH Funding for Research on Neuromodulation for Psychiatric Indications, by Administering Institute and FY, 2016–2025

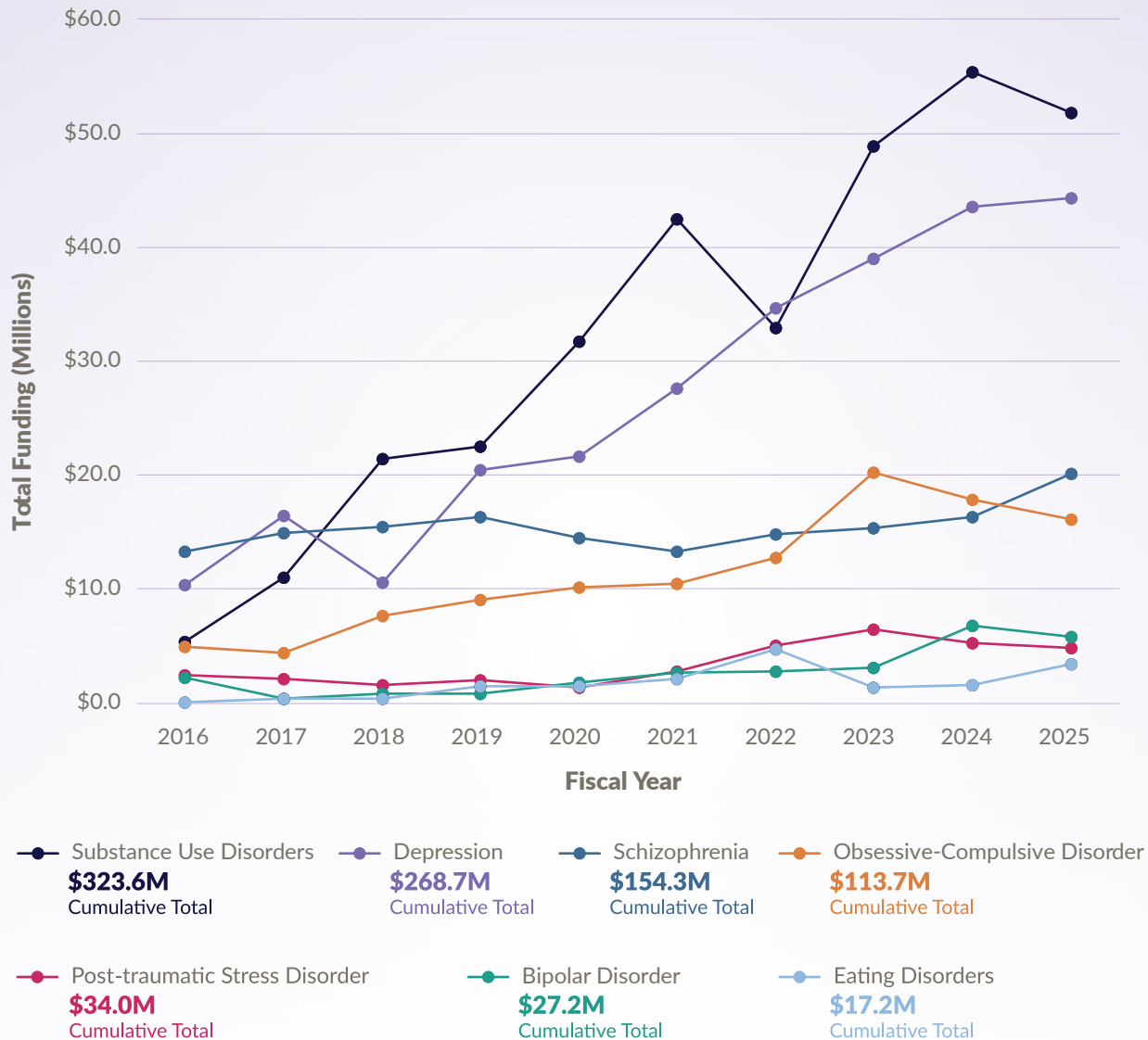


Source: Milken Institute (2026), analysis of funding data from NIH RePORTER (2026)

Level of NIH Funding Varies Significantly by Psychiatric Indication

For this report, seven psychiatric conditions with existing evidence of potential benefit from neuromodulation therapy were selected for additional analysis.³⁴ Funding data for research on the use of neuromodulation technologies for these indications, as administered by the five primary NIH institutes providing this type of funding from FY 2016 to FY 2025, are presented in **Figure 7**.

Figure 7: NIH Funding for Research on Neuromodulation for Psychiatric Indications, by Condition and FY, 2016–2025



Source: Milken Institute (2026), analysis of funding data from NIH RePORTER (2026)

Of the seven psychiatric conditions included in this analysis, NIH funding for research on neuromodulation technologies in depression and substance use disorders increased the most dramatically from 2016 to 2024, with funding for substance use disorders dropping slightly in 2025. OCD funding saw a slow but significant increase throughout this period, from \$4.9 million in 2016 to \$16.1 million in 2025. Funding for neuromodulation research in schizophrenia remained consistently modest (\$13–\$20 million per year), and in PTSD, BD, and eating disorders remained consistently low (less than \$10 million per year) throughout this period.

This variability in funding levels across conditions largely reflects strategic decisions by the NIH to focus research on conditions with the greatest impact in the United States. The estimated economic burden of MDD among US adults was \$236 billion in 2018, representing a more than 35 percent increase since 2010.³⁵ The estimated economic burden of opioid use disorder was \$1.02 trillion in 2017.³⁶ Given these substantial costs—let alone the high mortality rate and loss of quality of life associated with these conditions—the need to develop better treatment options is obvious.

Other Federal Agencies Provide Modest Levels of Funding

From 2016 to 2025, the Department of Defense (DOD) provided 31 grant awards totaling \$89.9 million for research on the use of neuromodulation technologies for psychiatric indications, primarily in PTSD and associated psychiatric health concerns related to traumatic brain injury (TBI).³⁷ In part because of the \$700 million in 2021–2024 congressional appropriations for TBI and psychological health, DOD funding for neuromodulation therapies increased rapidly from approximately \$4 million (awarded in 2021) to nearly \$16 million (in 2025).³⁸

From FY 2017 to FY 2025, the Department of Veterans Affairs (VA) supported 156 projects totaling \$40 million for research on the use of neuromodulation technologies for psychiatric indications relevant to the veteran population, primarily in PTSD, substance use, depression, and schizophrenia.³⁹ Notably, the VA emphasizes neuromodulation in both research and clinical care. VA-operated precision neuromodulation clinics offer TMS as a therapeutic option for patients with treatment-resistant depression, and key priorities for the VA's National Center for PTSD precision medicine initiative include research on the use of DBS, TMS, and cranial electrotherapy stimulation.⁴⁰ The number of VA-supported projects in this area increased from two projects in FY 2013 to a peak of 25 projects in FY 2023 but has subsequently declined.

NIH BRAIN Initiative, a Critical Driver of Research, Experiences Dramatic Decrease in Funding

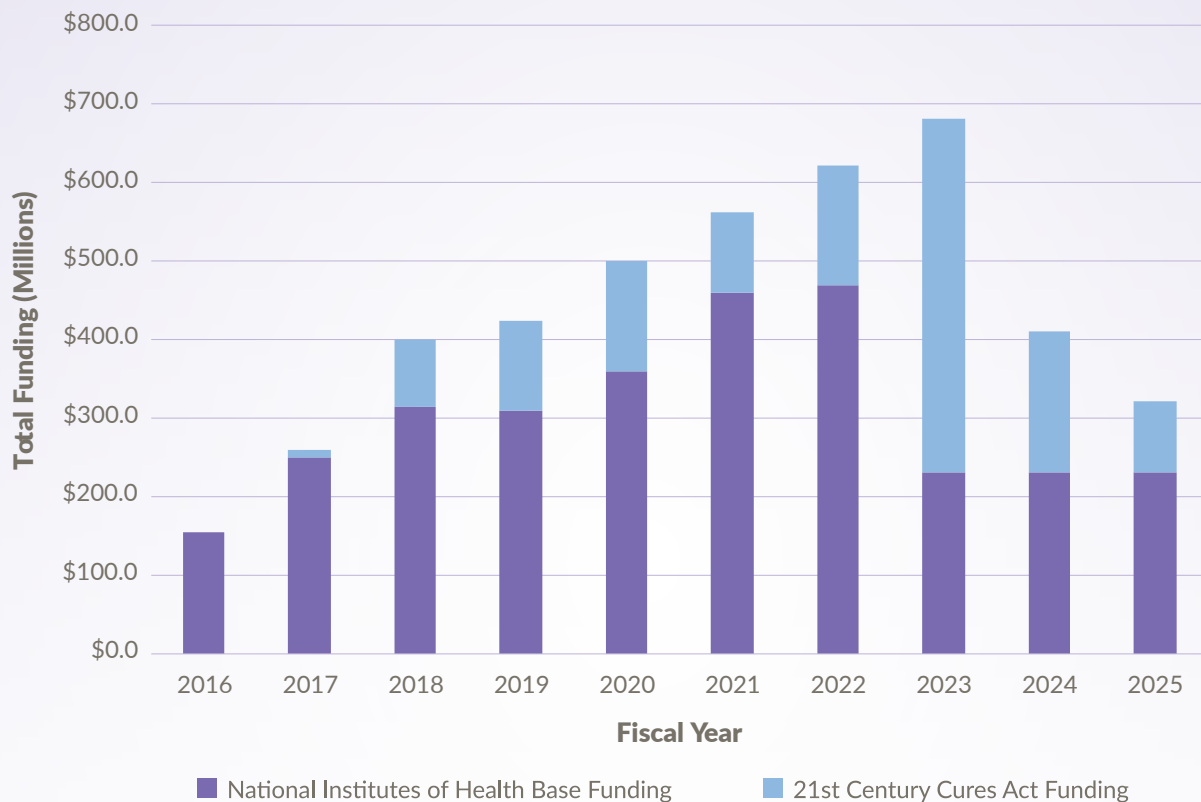
By leveraging a level of collaboration and investment beyond that of individual federal agencies, the BRAIN Initiative has been a critical driver of research into neuromodulation technologies for psychiatric indications since its launch in 2013.⁴¹ Led by the NIH, this ambitious initiative comprises work across multiple NIH institutes and centers, with federal partners (including the FDA and the Defense Advanced Research Projects Agency) and a network of federal and nonfederal members and affiliates through the BRAIN Initiative Alliance.⁴²

The research funded by the BRAIN Initiative provides a critical foundation for understanding mechanisms and treatments of psychiatric disorders. The initiative is guided by a mandate to “accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of the brain that show how individual brain cells and complex neural circuits interact at the speed of thought.”⁴³

From FY 2016 to FY 2025, cumulative funding for BRAIN Initiative research efforts totaled \$4.32 billion, with peak funding at \$680 million in 2023 (see **Figure 8**). Since that time, however, funding has sharply decreased. The base allocation for the initiative's budget comprises line items in the individual budgets of the 10 NIH

institutes and centers involved, with the remainder of funding allocated through the 21st Century Cures Act.⁴⁴ The act, signed into law in 2016, allocated varying predetermined annual funding amounts to support innovation programs like the BRAIN Initiative from FY 2017 through FY 2026.⁴⁵

Figure 8: NIH BRAIN Initiative Budget for FYs 2016–2025



Source: Milken Institute analysis (2026), reproduced from NIH BRAIN Initiative (2026)

As a result of reductions in both funding streams, the BRAIN Initiative’s overall budget decreased by 40 percent from its FY 2023 peak, to \$402 million in FY 2024 and then to \$321 million in FY 2025 (another 20 percent decrease). These funding cuts resulted in a 10 percent budget reduction for most active projects and the elimination of new funding opportunities in some NIH BRAIN Initiative programs.⁴⁶

Far-Reaching Changes in Public Funding Cast Uncertainty on Future Progress

In early 2025, a series of federal policy and administrative changes affected the availability and administration of public funding for health research through workforce reductions; changes to diversity, equity, and inclusion initiatives; and the suspension, termination, and withholding of support for nearly

6,000 NIH grants.⁴⁷ The immediate effects of these actions are evident in a notable reduction in the number of grants awarded by the NIH and the National Science Foundation in 2025, compared with prior years.⁴⁸

The NIMH, a major funder of research on neuromodulation in psychiatry, saw the largest number of terminated NIH-supported grants (128).⁴⁹ Though some of these grants have since been restored, the disruption to funding caused serious challenges, especially in projects that require continuous measurement in human and animal subjects. Funding interruptions can also disrupt careers, potentially causing promising talent to leave the field.⁵⁰

Taken together, federal policy and administrative changes have left public research funding volatile and unpredictable. However, this instability creates an opportunity for private investors and philanthropists to serve as reliable, consistent funders, filling gaps left by unsteady federal funding and enabling consequential research.

Commercial Investment

In the commercial context, the broader neurotechnology sector is experiencing unprecedented growth. Private investment in this sector totaled approximately \$4.8 billion in 2025, representing 109 percent growth over 2024 (\$2.3 billion) (see **Figure 9**).⁵¹ Investments were distributed across 140 firms, with the largest investments directed toward Neuralink (\$650 million) and Nalu (Boston Scientific, \$533 million).⁵²

Figure 9: Funding Snapshot of Commercial Investment in Neurotechnology, 2025

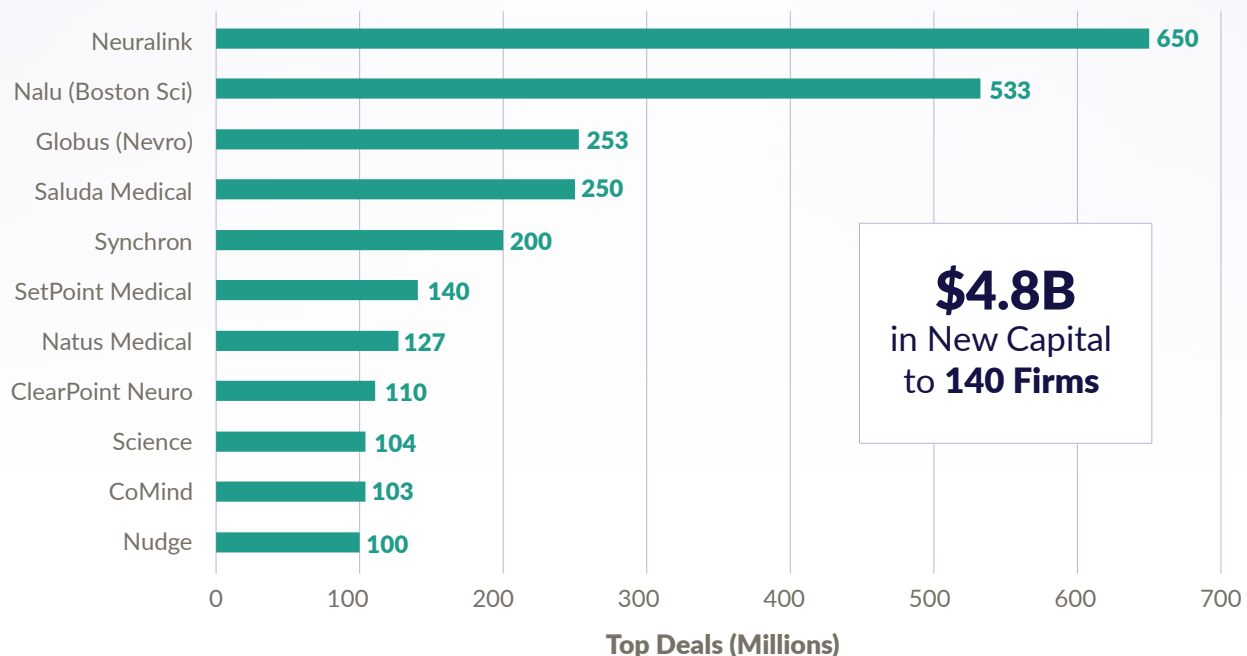


Figure 9: Funding Snapshot of Commercial Investment in Neurotechnology, 2025 (continued)



Source: Milken Institute (2026), figure reproduced from Neurotech Futures' Funding Snapshot (2025)

Investments were largely directed toward neurological and somatic indications, such as chronic pain and motor function, while a limited percentage focused on psychiatric indications. Commercial investment in neurotechnology for depression treatment totaled \$186 million in 2025, a 9 percent decrease from 2024. Sixty-three percent of the total investment was concentrated on brain-computer interfaces, peripheral nerve stimulation, and spinal cord stimulation.

In contrast to recent sharp reductions in public funding, these trends reflect strong and growing private investment in the neurotechnology sector, momentum that could translate into psychiatric applications if directed strategically.

Private Funding and Strategic Philanthropy

Research funding from philanthropic foundations and nonprofits is a vital component of the scientific landscape, often providing targeted investments in areas where government funding has been limited. In line with growing commercial investment in neurotechnology, expanding philanthropic and nonprofit engagement could prove catalytic for the field. **Table 3** details the select groups that have begun to lead the way through private funding and strategic philanthropy.

Table 3: Private Funders of Research on Neuromodulation for Psychiatric Conditions

Funder	Overview
Brain & Behavior Research Foundation (BBRF)	Since 1987, BBRF has distributed more than \$475 million in neuroscience and psychiatry research grants to scientists at various career stages. ⁵³ The focus areas of these grants include psychiatric conditions such as OCD, depression, BD, PTSD, and addiction. ⁵⁴
The Foundation for Neurofeedback and Neuromodulation Research (FNNR)	FNNR, part of the International Society for Neuroregulation & Research, supports research on neurofeedback and neuromodulation therapies across neurological and psychiatric conditions. ⁵⁵ The foundation awards mini-grants (\$2,500–\$3,000) to support projects that explore the mechanistic processes and clinical effects of neuromodulation, with a focus on underresearched disorders and populations.
Foundation for OCD Research (FFOR)	FFOR, an initiative sponsored by two family philanthropic organizations, supports basic, clinical, and translational research to identify the biological mechanisms underlying OCD and promote progress toward a functional cure. ⁵⁶ A core component of FFOR's strategy is strengthening the understanding of novel therapeutic targets for neuromodulation to advance more individualized treatment. To date, FFOR has raised over \$50 million toward its \$100 million goal to support moon-shot projects.
International OCD Foundation (IOCDF)	The IOCDF focuses on advancing research for, education about, and awareness of OCD and related conditions. Since 1994, the foundation has awarded over \$11 million in research funding, supporting investigators at all career stages. ⁵⁷ IOCDF has supported translational and clinical research to inform both invasive and noninvasive neuromodulation strategies for OCD.
One Mind	One Mind is a private funder accelerating breakthroughs in neuroscience and mental health research, integrating evidence-based research with lived-experience expertise. It has awarded over \$14 million to early-career investigators, prioritizing transdiagnostic research for precision psychiatry, through its Rising Star Awards. Further, the One Mind Accelerator supports mental health start-ups, investing about \$2 million across 21 start-ups in its first two years (2023–2024). ⁵⁸ The organization's 2025 cohort includes start-ups that are advancing brain stimulation technologies for mental health applications.
Wellcome Trust and Wellcome Leap	The Wellcome Trust is one of the world's largest charitable foundations dedicated to improving health through research, innovation, and advocacy. Founded in 1936, the London-based foundation manages an endowment of over £37 billion. The trust has pledged £16 billion toward science and health initiatives from 2022 to 2032, with a major mental health commitment, making it one of the largest funders in this area globally. ⁵⁹ In parallel, Wellcome Leap is a US-based nonprofit applying the trust's values through an accelerated innovation model. It supports neuromodulation research through Multi-Channel Psych, a \$50 million program focused on developing a mechanistic understanding of anhedonic depression.

Source: Milken Institute (2026)

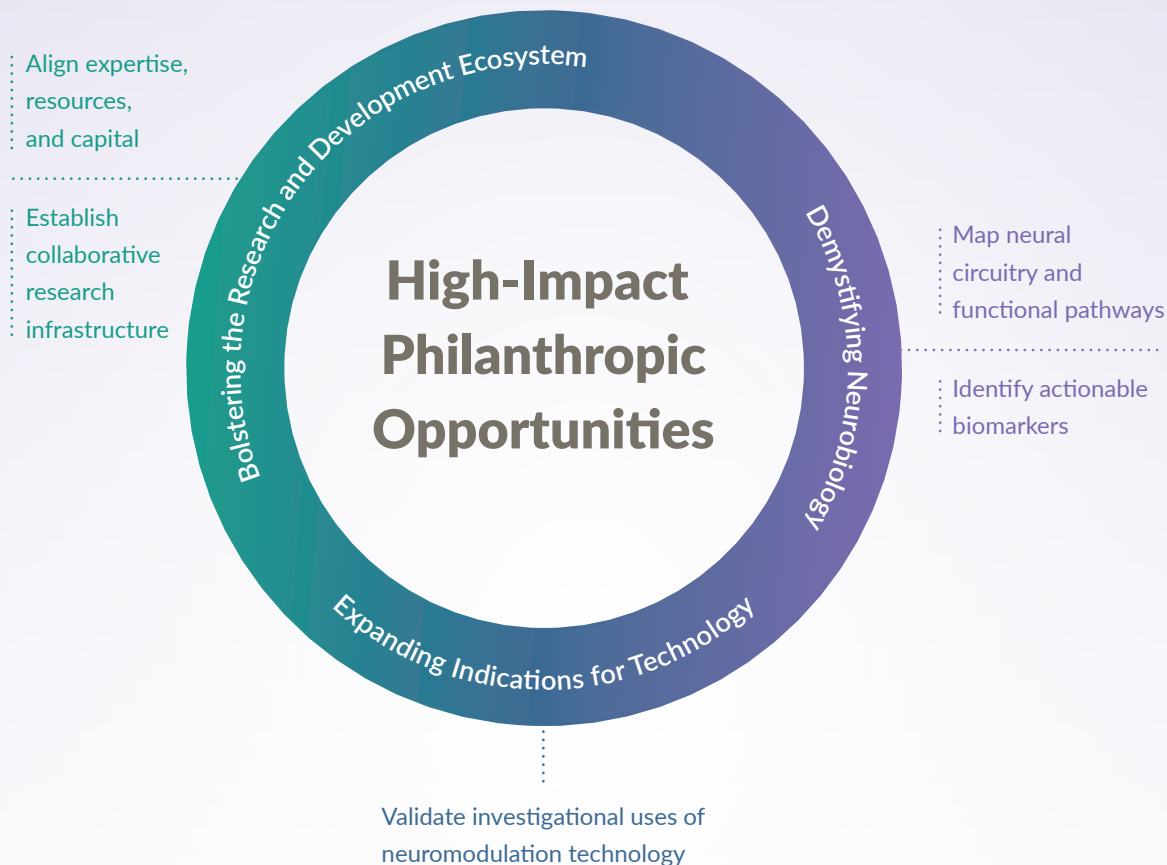
High-Impact Philanthropic Opportunities

Despite remarkable advancements in medical science in recent years, existing treatment options still fail a substantial proportion of people with psychiatric conditions. Moreover, success is generally defined in terms of reducing symptoms rather than eliminating the burden of illness. A true North Star for the field of psychiatric treatment—one that is ambitious, yet within reach, given sufficient commitment to advancing research—emphasizes providing functional recovery, improving independence, and restoring the ability to meaningfully participate in daily life.

Neuromodulation therapies are well positioned to serve the twin goals of improving clinical outcomes in the near term and accelerating future advancements, delivering meaningful relief to individuals who have exhausted first-line options while generating the circuit-level data needed to inform the next generation of therapeutics.

Given this North Star, SPARC has identified five opportunities through which thoughtful philanthropic investment could help overcome barriers to scientific progress in neuromodulation for psychiatric conditions (categorized in three areas) (see **Figure 10**). These opportunities span the research and development pipeline from basic neuroscience that establishes the foundation for future treatment to translational work that generates evidence for regulatory review and clinical adoption, all with an eye to the ecosystem conditions that determine the viability of commercializing and implementing new technologies. Supporting any of these opportunities will strengthen the field and accelerate progress toward more precise, more accessible, and more effective care.

Figure 10: High-Impact Philanthropic Opportunities



Source: Milken Institute (2026)

Demystifying Neurobiology

Significant gaps in our understanding of the underlying biological causes and mechanisms of psychiatric conditions present challenges in both research and clinical practice. Neuromodulation therapies are mechanistic interventions, and their successful application depends on a mechanistic understanding of the condition being treated. Meaningful progress in the field—enabling earlier diagnoses, more precise treatment selection, and the development of more effective therapeutics—requires developing a more comprehensive picture of the neurobiology of psychiatric conditions.

As public funding for this foundational work is increasingly unpredictable, and limited opportunities to commercialize the findings discourage traditional venture funders, philanthropic capital can be essential to catalyzing progress in two key areas of neurobiology research.

Opportunity 1:

Map Neural Circuitry and Functional Pathways

Understanding the organization and functional roles of specific brain structures and the pathways that connect them is the foundation of effective neuromodulation therapy. Considerable progress has been made in mapping anatomical regions and the circuits that link them, and a growing body of research connects those structures to specific psychiatric symptoms. But the overall picture remains incomplete.

Systematic, sequential investigation of the many interconnected circuits of the human brain is not feasible given the volume and complexity of the variables involved. This challenge may be somewhat alleviated through the use of aggregated maps intended to model the “average” expected functionality of the brain, but psychiatric conditions are poorly suited to this type of research. Because these conditions feature biological complexity and substantial person-to-person variation, a normative reference may obscure precisely the differences that matter for treatment selection.

In the absence of this mechanistic understanding, research remains largely confined to repeated assessment of stimulation targets implicated in prior studies. Dedicated funding for mapping studies conducted in psychiatric populations is needed to close this gap. Animal model studies may offer the most efficient route to rapidly assessing candidate targets for subsequent validation in human research.

Short-Term Impact



Candidate stimulation targets are assessed at a faster pace than is achievable through in-human studies alone, based on circuit-level maps that accurately represent psychiatric populations.

Long-Term Impact



Stimulation targets are selected based on an individual's neurobiology, increasing the precision and scalability of the therapy.

Opportunity 2:

Identify Actionable Biomarkers

Clinicians and researchers currently rely on a combination of observed changes in brain function (for example, measured by functional MRI) and patient-reported changes in symptoms to interpret the effects of stimulation. While these correlational data can be valuable in guiding an individual patient's treatment, they are insufficient in a research context.

Actionable biomarkers that provide objective data based on a mechanistic understanding of an illness are necessary for rapid, iterative investigation. Identifying these biomarkers will require analysis of large-scale, longitudinal, multimodal datasets that link brain activity, stimulation parameters, symptoms, and functional outcomes.

Two categories of biomarkers are particularly relevant in the field of neuromodulation for psychiatric conditions:

- **Predictive Biomarkers:** These provide objective evidence of how an individual is likely to respond to a specific intervention based on their unique biological profile. The inability to provide these data can be a significant barrier in a clinical context, potentially affecting clinicians' and patients' confidence in pursuing certain treatment options and reducing the likelihood that insurers will cover the costs of treatment. It also poses a specific challenge for clinical trial design, as enrollment based on diagnosis alone is likely to yield unpredictable variation in participant responses.
- **Response Biomarkers:** These provide objective evidence to interpret the effects of stimulation. These data can dramatically accelerate the pace of discovery and meaningfully improve the clinical care experience. Rather than waiting for symptom changes to emerge, often over several weeks, clinicians can watch for response biomarkers to rapidly confirm whether the correct target has been selected and the stimulation protocol is effective. These biomarkers also serve as the objective outcome measures needed to secure investment and support regulatory review.

Short-Term Impact



Candidate biomarkers are identified and prioritized for validation, and clinical trial enrollment is based on biological profile rather than diagnosis alone.

Long-Term Impact



Treatment selection is rapid and precise rather than iterative, strengthening the evidence base for regulatory approval and insurance coverage.

Expanding Indications for Technology

Despite compelling evidence supporting multiple investigational applications for neuromodulation in psychiatric conditions, few technologies are FDA cleared, FDA approved, or otherwise authorized for these indications. The prevailing view of psychiatric therapeutics as an uncertain or niche market discourages new

developers from entering the space, and there is little incentive for existing device manufacturers to pursue additional regulatory approvals for psychiatric indications.

While federal support for translational research in this space is comparatively strong, most public funding mechanisms are not designed to support clinical trials of sufficient scale to secure regulatory approval for a new device or therapeutic indication. Philanthropic investment can meaningfully address this gap by de-risking future clinical trials for later-stage funders.

Opportunity 3:

Validate Investigational Uses of Neuromodulation Technology

Given that recent clinical trials of DBS-MDD most likely failed due to the unknown effects of biological variation across the study population, attracting future industry investment will require evidence not just that a treatment is effective, but that critical aspects of study design—including target selection, patient stratification, and outcome measurement—are appropriate and likely to translate to success at a larger scale. Proof-of-concept studies can meet both of these needs, generating the preliminary data needed to justify large-scale investment. To advance the field of neuromodulation for psychiatric conditions, these studies may focus either on expanding indications for approved devices or validating the use of a new technology.

Efforts to expand indications benefit from the established safety profiles and regulatory precedent of the device's prior approval and, in the psychiatric context, may also benefit from the high degree of biological similarities across conditions. For example, TMS treatment protocols for MDD have been shown to be highly effective in the treatment of PTSD—likely due to the fact that these conditions arise from similar patterns of alterations in neural circuits. While larger controlled studies are needed to confirm this hypothesis, this evidence provides a strong argument for the transferability of neuromodulation therapies across psychiatric conditions.

Validation of new technologies is a more complex challenge but may represent even greater opportunity to advance the field. LIFU is a particularly compelling example; although it has not yet received FDA clearance or approval for use in any health condition, there is strong preliminary evidence for

its use in multiple psychiatric conditions. Critically, LIFU is capable of stimulating deep brain structures currently only accessible through surgically implanted modalities. Future research validating the strength and durability of this treatment could dramatically improve the scalability potential, and tolerability, of neuromodulation therapies in psychiatry.

Short-Term Impact



Proof-of-concept studies provide preliminary clinical data and confirm the appropriateness of study design, justifying investment in large-scale clinical trials.

Long-Term Impact



Additional modalities and indications reach approval, expanding treatment options for individuals with refractory illness.

Bolstering the Research and Development Ecosystem

Very few individual entities are capable of assembling the combination of risk-tolerant capital, engineering capability, clinical trial expertise, and commercial capacity required to develop a therapeutic device in any context, and this challenge is particularly relevant in the field of neuromodulation for psychiatric conditions. Industry interest is constrained by high costs of device development and low expected market penetration, traditional venture funding is ill-suited to long timelines and uncertain returns in the absence of objective outcome measures, and concerns about publicly disclosing a personal connection to a psychiatric condition may deter philanthropic funders. Multistakeholder efforts are often impeded by institutional silos and misaligned incentives, facing challenges ranging from inconsistent data collection protocols to conflicting reporting requirements from overlapping funding sources.

As a result of this fragmentation, there are very few active studies, with a limited number of enrolled participants at any given time—severely limiting the ability to generate data of sufficient scale to support clinical validation and regulatory approval. Furthermore, many promising initiatives stall not because the scientific evidence lacks promise, but because capital is insufficient at key stages of development. Strategic, intentional philanthropic investment is well positioned to address these challenges of scale and resource alignment, bridging gaps that neither the public nor commercial sector is structured to address.

Opportunity 4:

Establish a Collaborative Research Infrastructure

The most direct solution to the problem of scale is shared infrastructure, particularly in support of two key research functions: participant recruitment and data analysis. A centralized recruitment infrastructure addresses a primary constraint to study size, enabling standardized eligibility screening and long-term participant retention strategies while minimizing duplication of time, effort, and resources for individual study sites. Shared data platforms allow aggregation of findings from multiple studies, increasing the diversity of the sample size and the statistical power of the analysis. Critically, the ability to analyze a high volume of complex data is a precondition for the large-scale, longitudinal, multimodal datasets necessary for biomarker discovery.

While single-stakeholder approaches like using AI tools to retrospectively harmonize discrete datasets can begin to address this need for scale, precompetitive collaboration offers a more comprehensive approach to maximize the potential value of shared infrastructure.

Certain consortia models use contractual funding agreements as both an incentive and a governance mechanism, providing researchers with valuable datasets and analytical tools while ensuring meaningful contributions in return. Access is predicated on compliance with data standardization and information-sharing protocols, resulting in high-volume, high-quality, actionable pooled datasets. Particularly with the mediation

of a neutral “honest broker” to maintain focus on shared priorities, these precompetitive collaborations can allow stakeholders to address foundational challenges that market-driven approaches are unlikely to solve while unlocking downstream commercial potential for all contributors.

Short-Term Impact



Research initiatives are streamlined and accelerated through coordinated recruitment, harmonized protocols, and aggregated data.

Long-Term Impact



Studies achieve the scale required to generate replicable, generalizable findings sufficient to support clinical validation and regulatory approval.

Opportunity 5:

Align Expertise, Resources, and Capital

Successfully navigating the pathway from concept to commercialization requires a comprehensive long-term resourcing strategy. Mission-aligned networks and partnerships that bring together clinicians, engineers, regulatory specialists, and investors create the conditions for cross-sector work that no single institution can convene on its own. Beyond ensuring access to diverse types of expertise, these networks can also serve the critical function of enabling access to diverse sources of capital.

While some previously relied-upon funding sources remain relevant (e.g., philanthropic grants for proof-of-concept studies), they are generally insufficient to support long-term viability. For example, an initiative derived from intellectual property developed at an academic research center will likely require federal grant funding to develop a prototype. Once the prototype and preliminary proof-of-concept data are in hand, traditional venture capital may then fund the launch of a start-up. Each successive stage of development will require different levels of investment and entail different degrees of risk, so a comprehensive strategy depends on identifying the funding source most appropriate to each stage.

Nontraditional funding models like venture philanthropy may be particularly beneficial to advance research and development in the field of neuromodulation for psychiatric conditions. Similar to impact investing, venture philanthropy enables strategic investment in for-profit entities whose work is aligned with the stated mission of a philanthropic organization.

The key difference, however, is that financial returns from these investments flow back into the fund to finance additional research, providing a critical source to sustain capital for high-risk, high-impact areas of work that is unlikely to be supported by the traditional commercial sector.

Short-Term Impact

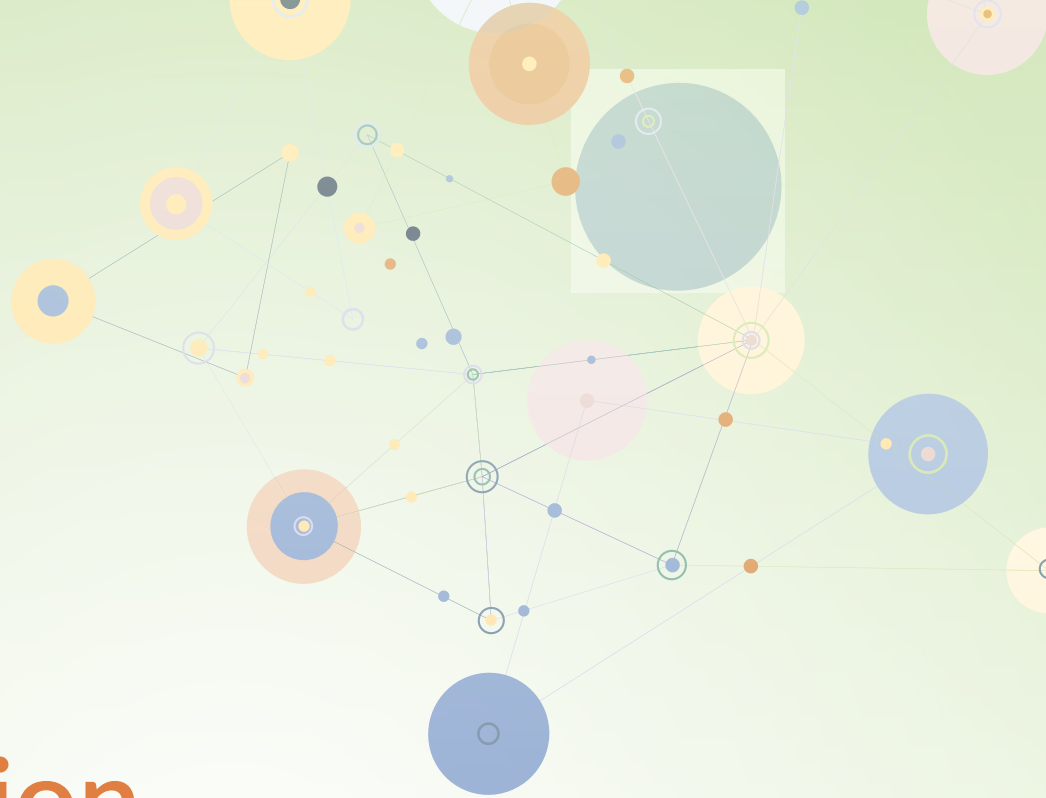


Cross-sector relationships form around shared priorities, enabling collaborative solutions to address critical gaps in expertise and capital.

Long-Term Impact



Promising interventions move from concept to commercialization rather than stalling due to a lack of appropriate capital at key stages of development.



Conclusion

Neuromodulation therapies are designed to modulate specific brain circuits implicated in psychiatric disorders by delivering electrical, magnetic, or acoustic stimulation. For patients with treatment-resistant conditions who have exhausted standard therapeutic options, these interventions may provide meaningful and, in some cases, transformative clinical benefit. By targeting defined neural circuits, neuromodulation also offers important mechanistic insights that have long been underdeveloped in psychiatry, helping to advance biological understanding beyond subjective symptom assessment and trial-and-error prescribing. This report examines the current and emerging applications of neuromodulation in psychiatric disorders, the barriers impeding progress, and the funding landscape shaping the field's development.

Despite its considerable potential, psychiatric neuromodulation remains substantially less developed than its application in movement disorders and epilepsy. Advancement in the field has been constrained by the biological complexity of psychiatric conditions, enduring stigma associated with the history of psychosurgery, and a fragmented research ecosystem concentrated within a limited number of academic centers that often lack shared infrastructure and sufficient capital. Although public funding has historically been a primary driver of progress, its future role is increasingly uncertain, particularly as recent reductions in funding for the NIH and the BRAIN Initiative have disrupted ongoing research. Commercial investment in neurotechnology is expanding rapidly, yet only a limited proportion is directed toward psychiatric applications.

As one of the best-characterized psychiatric conditions from a circuit perspective, OCD allows researchers to ask questions that are central to all of psychiatry: Which brain pathways drive symptoms? Which biomarkers predict or measure treatment response? Which patients are most likely to benefit? How can stimulation be optimized to support lasting functional recovery? In this sense, OCD is more than a single indication; it is a model system for learning how to translate circuit neuroscience into better psychiatric care.

Progress in OCD could create a road map for treating other complex psychiatric conditions for which shared neural pathways, overlapping symptoms, and similar barriers to adoption have slowed therapeutic innovation. With OCD's strong foundation of existing evidence, further strategic investment in neuromodulation therapies for that condition could have an outsized, catalytic impact on the overall field of neuromodulation for psychiatric conditions.

This context underscores a strategic opportunity for targeted philanthropic investment to advance neuromodulation for psychiatric indications by supporting the mapping of neural circuitry, identification of actionable biomarkers, validation of experimental neuromodulation applications, strengthening of a collaborative research infrastructure, and alignment of expertise, capital, and partnerships to facilitate the translation of therapies from laboratory research to clinical practice. By using OCD as a model while building infrastructure applicable across diagnoses, philanthropy can help accelerate the transition from promising neuromodulation interventions to a more precise, scalable, and patient-centered model of psychiatric care. Such investments could reposition neuromodulation not only as a treatment modality for symptom reduction but also as a pathway toward functional recovery for the many patients and families affected by psychiatric illness and in need of innovative therapeutic options.

Advancing neuromodulation in psychiatry will require more than scientific promise; it will require coordinated action. Philanthropy can help shape the field's trajectory by funding the studies, tools, data infrastructure, and partnerships that public and commercial systems are not yet positioned to sustain. With strategic investment now, funders can help ensure that neuromodulation becomes not only a last-resort option for the few, but a pathway toward better, more precise, and more accessible care for the many.

Appendix

Overview of Neuromodulation Therapies

Table A1: Overview of Neuromodulation Therapies

Therapy	Indications (Approval Year)	Modality	Mechanism of Action
Deep Brain Stimulation	Essential tremor (1997) Parkinson's disease (2002) Dystonia (2003) OCD (2009)* Epilepsy (2018)	Implanted: electrodes placed within brain tissue; battery implanted below clavicle	Continuous or intermittent electrical currents modulate activity in deep brain structures
Vagus Nerve Stimulation	Epilepsy (1997) MDD (2005)	Implanted: electrode wrapped around left cervical vagus nerve, battery implanted below clavicle	Intermittent electrical currents modulate activity in thalamocortical circuits (<i>precise mechanism unclear</i>)
Responsive Neurostimulation	Epilepsy (2013)	Implanted: electrodes placed either within brain tissue or under its surface membrane; battery implanted in the skull	Intermittent electrical currents disrupt progression of detected seizure activity
Electroconvulsive Therapy	Bipolar disorder-associated depression (2018) [†] Catatonia (2018) [†] MDD (2018) [†]	External: electrodes placed on the scalp	Weak electric currents pass through the skull to induce a brief, controlled seizure (<i>precise mechanism unclear</i>)
Focused Ultrasound Stimulation—High Intensity	Essential tremor (2016) [‡] Parkinson's disease (2018)	External: helmet placed on the head	Acoustic waves at high ultrasonic frequencies pass through the skull to create focal lesions in deep brain structures
Focused Ultrasound Stimulation—Low Intensity	None	External: helmet placed on the head	Acoustic waves at low ultrasonic frequencies pass through the skull to modulate activity throughout the brain

Table A1: Overview of Neuromodulation Therapies *(continued)*

Therapy	Indications (Approval Year)	Modality	Mechanism of Action
Transcranial Direct Current Stimulation	MDD (2025)	External: electrodes placed on the scalp or embedded in a headset	Weak electrical currents pass through the skull to modulate activity in cortical brain structures
Transcranial Magnetic Stimulation	MDD (2008) OCD (2017) Migraine (2019) Smoking cessation (2020)	External: stimulation coil placed against the head	Strong magnetic field generated by stimulation coil passes through the skull to modulate activity in cortical (traditional TMS) or deeper brain structures (deep TMS)

* Approved under an HDE
† ECT was widely used for a range of psychiatric conditions before its FDA reclassification in 2018. Previously covered conditions (including schizophrenia and BD-associated mania) are now Class III indications and not approved for ECT treatment without a new PMA application.
‡ First approval for a brain-based condition; FUS was originally used in treatment of glaucoma and certain cancers.
Source: Milken Institute (2026)

Funding Landscape: Method of Analysis

Public Funding

Data on public funding directed to research supporting the use of neuromodulatory approaches (see **Table A1**) to understand and treat psychiatric disorders were abstracted from NIH RePORTER and the Defense Technical Information Center's Grant Awards database.

Boolean search strings were used to combine relevant search terms (see **Table A2**) for each analysis. Search terms were identified through a literature review and refined through test searches and examination of NIH RePORTER results to ensure that the chosen search terms yielded projects relevant to this analysis.

The specific psychiatric disorders of focus were chosen based on existing evidence of potential benefit from neuromodulation. Results were limited to projects for which relevant search terms were included in the project title or project abstract, projects that received funding from 2016 to 2025, and projects with funding that was administered through the five major institutes that support neuromodulation and/or mental health research (NIMH, NIDA, NINDS, NIAAA, NIGMS).

It is important to note that for some projects, neuromodulation and/or psychiatric disorders may not be the primary research focus; relevant terms may appear in the project abstract as background, context, or potential downstream implications. Consequently, estimates should be interpreted as upper bounds on administered public funding for this area.

Data were exported and analyzed in Excel.

Table A2: Search Terms

Neuromodulation	"brain stimulation," "neural stimulation," "neurostimulation," "closed-loop stimulation," "adaptive stimulation," "vagus nerve stimulation," "high intensity focused ultrasound," "gamma knife," "focused ultrasound," "transcranial magnetic," "trans cranial magnetic," "electroconvulsive therapy," "transcranial direct current," "transcranial alternating current," "MR-guided focused ultrasound," "low intensity focused ultrasound," "transcutaneous vagus"
Psychiatric Disorders	"obsessive-compulsive," "obsessive compulsive," "obsessions," "compulsions," "treatment refractory depression," "treatment-refractory depression," "treatment resistant depression," "unipolar depression," "major depression," "major depressive," "depression disorder," "depression disorders," "depressive disorder," "depressive disorders," "substance-related," "substance use," "substance induced," "drug use," "alcohol," "tobacco," "cannabis," "cocaine," "methamphetamine," "opioid," "eating disorder," "eating disorders," "anorexia," "bulimia," "binge eating," "binge-eating," "food craving," "post-traumatic stress," "posttraumatic stress," "schizophrenia," "schizoaffective," "bipolar disorder," "bipolar disorders," "bipolar I," "bipolar 1," "bipolar II"

Source: Milken Institute (2026)

Commercial Investment and Private Funding

Sources of private funding were identified by searching existing funding and market research landscape analyses, acknowledged sources within primary publications on neuromodulation and mental health research, and input from experts familiar with the field. Private funding was estimated by reviewing annual fiscal reports, funding announcements, and lists of grantees on foundation websites.

Glossary

510(k) premarket notification: This is the FDA process of regulatory and scientific review to evaluate the equivalency of Class II (moderate-risk) devices to previously cleared devices.

Bidirectional interface: This is a device capable of simultaneously providing neurostimulation and recording brain activity, enabling a better understanding of the relationship between biology and symptoms.

Biomarker: This is a measurable indicator of biological processes, pathogenic processes, or responses to an exposure or intervention. Predictive biomarkers may be used to determine whether an individual is likely to respond to a specific treatment, and response biomarkers to confirm the effects of that treatment.

Brain mapping: This refers to the measurement of neural circuit activity and the charting of the functional pathways connecting different areas of the brain.

FDA approved: This status indicates that the FDA has reviewed the scientific evidence for a high-risk medical device and determined that it is safe and effective for use within a specific population.

FDA cleared: This status indicates that the FDA has reviewed the scientific evidence for a moderate-risk medical device and determined that it is substantially equivalent to a previously cleared device already in use within the US.

Functional recovery: This refers to the ability to fully engage in all facets of daily life following a mental health challenge.

Heterogeneous: This refers to individual psychiatric diagnoses that have very different symptoms and treatment responses between individuals.

Humanitarian Device Exemption (HDE): This is an FDA pathway for medical devices intended to treat or diagnose rare diseases or conditions, based on evidence that the device's probable benefit outweighs its risk when full Premarket Approval evidence is not available, allowing access for individuals with severe illnesses or debilitating conditions to potentially lifesaving interventions, but it also carries restrictions that can limit uptake and commercialization.

Invasive recording: This is a method used to measure brain activity at an anatomically precise level via surgically implanted electrodes.

Mental illness: Also called a psychiatric condition, this is a health condition that involves changes in emotion, thinking, or behavior, or a combination of these.

Neural circuit: This is an interconnected group of brain cells that transmit information through chemical and electrical signals.

Neuromodulation: This is a type of psychiatric treatment that influences the activity of brain cells and neural circuits through targeted application of electrical, magnetic, or acoustic energy. These treatments can be delivered through an external device or via a surgically implanted device.

Neurotransmitter: This is a class of molecules that enables neurons to communicate with one another and with other cells. Examples include serotonin, norepinephrine, and dopamine.

Pharmacologic treatment: This is a type of psychiatric treatment that influences chemical activity in the brain, for example, increasing or blocking the availability of a specific neurotransmitter. Common classes include antidepressants, antipsychotics, and mood stabilizers.

Premarket Approval (PMA): This is the FDA process of regulatory and scientific review to evaluate the effectiveness and safety of Class III devices.

Psychiatric condition: Also called a mental illness, this is a health condition that involves changes in emotion, thinking, or behavior, or a combination of these.

Psychosocial treatment: This is a type of psychiatric treatment that equips individuals with tools and strategies to identify, process, and change patterns of thoughts and behavior that affect their mental health. This may be delivered by a licensed mental health professional or through more informal contexts, such as peer support groups.

Serious mental illness (SMI): This is a mental illness that causes severe functional impairment, substantially limiting an individual's ability to be successful in one or more major areas of life.

Transdiagnostic research: This type of research seeks to understand mechanisms that are at play across multiple diagnoses, rather than focusing on a single disorder. It enables learnings from research on one condition to be applied to others.

Treatment resistant/treatment refractory: This refers to a form of illness wherein symptoms do not improve even with an accurate diagnosis and evidence-based treatment.

Valley of death: This refers to a period in the research and development pipeline when promising initiatives may stall due to scientific challenges or the inability to secure sufficient funding. In medical device development, two critical periods are the transition from academic initiative to start-up and the transition from start-up to a commercially viable independent entity.

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