

A network diagram background consisting of various sized orange circles (nodes) connected by thin orange lines (edges). The nodes are scattered across the page, with some larger nodes and some smaller ones, creating a complex web-like structure.

OBSESSIVE COMPULSIVE DISORDER

CURRENT STATE OF THE RESEARCH FIELD
& OPPORTUNITIES FOR PHILANTHROPY



RODAN FAMILY
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Rodan Family Foundation

The Rodan Family Foundation aims to invest significantly in the OCD research field with the goal of eliminating symptoms for those with treatment-resistant OCD, freeing them to lead fully functional, meaningful and happy lives.

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INTRODUCTION

Approximately two percent of adults in the United States are diagnosed with obsessive compulsive disorder (OCD) in their lifetimes. While seemingly a small number, the condition is vastly under- and mis-diagnosed, leaving millions of Americans suffering with unexplained symptoms. Good, effective treatments exist that help some people reduce symptoms and lead functional lives; however, there are a good number of people—30 to 50 percent of those diagnosed—for whom current treatments do not work. The field has been working for the past 30 years to address the needs of that population through research, treatment development, awareness, and advocacy. Due to a number of barriers, however, progress has been slow and many people continue to suffer from the symptoms of the disorder.

This report provides a snapshot of the current state of OCD research and the treatments based on that research, using a philanthropic lens to identify opportunities that will move the field forward at a faster pace to effectively treat more people. This report includes an overview of the current state of the field, relevant stakeholders, a list of leading OCD research centers, a description of emerging research, promising efforts focused on moving the field forward, and initial considerations for philanthropic investment opportunities.

Written as a practical guide for those seeking more information on OCD and for those with philanthropic resources available to support the field, this report will be useful for anyone seeking to better understand the disorder and the latest developments in research and treatment. While it aims to objectively cover all key areas relating to OCD research as of July 2019, this is not an exhaustive report.

The Rodan Family Foundation, a family foundation based outside of San Francisco, California, and deeply interested in advancements made in OCD research, commissioned the report from Rockefeller Philanthropy Advisors (RPA) as part of its learning agenda to inform its philanthropic strategy in the OCD field.



METHODOLOGY

Research and analysis for this report focused on: i) the current state of OCD treatment and research ii) the funding landscape for OCD treatment and research; and iii) the best opportunities to move the field forward in treating more people effectively.

To uncover information about the above, RPA:

- *Interviewed field experts:* RPA conducted hour-long phone interviews with 21 experts in OCD research, treatment, and funding. This represents approximately 20 percent of the active research field in the United States.
- *Conducted a literature review:* RPA conducted a literature review of leading medical journals and publications to gather the most recently published research relevant to OCD.
- *Gathered information from leading centers of research:* RPA solicited written descriptions from the ten OCD research centers that emerged as leaders in the field during research and interviews. The purpose of this aspect of the research was to better understand the respective backgrounds, histories and approaches of the research centers.
- *Leveraged existing institutional knowledge:* RPA used resources from its own experience as the philanthropy advisor to a leading grantmaker in the OCD field.

RPA analyzed the findings and synthesized them into the key themes presented in this report, which includes the current state of the field; an overview of stakeholders; challenges to the field; emerging research; and future opportunities.

EXECUTIVE SUMMARY

CURRENT STATE OF THE OCD RESEARCH FIELD

Approximately two percent of adults in the United States are diagnosed with obsessive compulsive disorder (OCD) in their lifetimes. However, this number doesn't represent the full extent of the disorder given the recognition among experts that it is under- and mis-diagnosed. First-line treatments for OCD include cognitive behavioral therapy (CBT)—exposure response prevention therapy (ERP) in particular—and selective serotonin reuptake inhibitors (SSRIs). These treatments were developed 30 years ago and effectively treat only 50 to 70 percent of those diagnosed with OCD. Second-line treatments include other antipsychotic medications, brain stimulation therapies, and alternative methods for delivering psychotherapy.

CURRENT CHALLENGES


The OCD field faces a number of challenges that have slowed the progress of research and prevented more people with OCD from receiving effective treatment. Leading challenges include:

- Low awareness and high stigma of the disorder.
- Lack of effective treatments.
- Limited access to providers.
- Sluggish research progress due to the complexity of the disorder, poor understanding of the disorder's biological origins, small sample sizes, lack of funding, weak pipeline of researchers entering the field, and lack of collaboration.

ECOSYSTEM OF RESEARCH STAKEHOLDERS

There are three major players in the OCD ecosystem.

- *Government:* The U.S. National Institute of Mental Health (NIMH) funded \$27 million in 2018 (as of September 2018) for 72 OCD research projects.
- *Philanthropy:* The International OCD Foundation has provided \$3.5 million in OCD research funding since 1994; the Brain & Behavior Research Foundation has provided \$4 million to OCD research funding since 1987; and private families and individuals have also provided funding.



▪ *Research and treatment institutions:* Several institutions conduct OCD research. Those noted below were included in the research for this report.

- Baylor College of Medicine
- Brown University—Butler Hospital and Bradley Hospital
- Columbia University
- Johns Hopkins Medical Institutions
- Massachusetts General Hospital/Harvard Medical School
- The McLean Hospital Corporation
- Rogers Behavioral Health
- Stanford University
- University of California Los Angeles Semel Institute of Neuroscience and Human Behavior
- University of California San Francisco
- University of Florida
- University of Pennsylvania
- University of Pittsburgh
- Yale University

EMERGING RESEARCH

The field is making advances in discoveries related to neural circuits, neurotransmitters, genetics, and immunology. Treatment advances include drug development targeting glutamate modulation, alternative methods of psychotherapy (e.g., intensive CBT, family therapy, acceptance & commitment therapy, inhibitory learning, attention bias modification, and the use of technology), and new methods of invasive and non-invasive brain stimulation (e.g., transcranial magnetic stimulation and deep brain stimulation).

MOST PROMISING AVENUES FOR MOVING THE FIELD FORWARD

Experts recommend the following as the most promising ways to influence the trajectory of OCD research to enable more people to live symptom-free lives.

- *Short-term approach:* Better disseminate existing treatments and increase access to care.
- *Medium-term approach:* Find better ways to diagnose and treat people.
- *Long-term approach:* Understand the causes of the disorder through basic science research that develops a deeper understanding of the neurocircuit level functioning and the suite of genes implicated.

PHILANTHROPIC OPPORTUNITIES

Philanthropy can play specific roles in the effort to improve OCD outcomes, using defined strategies and approaches recommended by experts. Those roles include that of a connector, a sustainer, or a catalyst.

- *Connectors* connect stakeholders across the field (researchers, clinicians, advocates, funders) toward common, ambitious goals.
- *Sustainers* provide sustained research funding to: alleviate the pressure of chasing grant funding; allow more ambitious projects; promote collaboration; and encourage new researchers to enter the field.
- *Catalysts* attract additional funding from government and other sources, fund innovative research that could lead to larger government grants, and enhance efforts around advocacy and awareness, which could further increase government spending allocations for OCD.

Strategies that philanthropists might use to move the field forward can include:

- Funding basic research, translational research, and treatment development.
- Funding training for psychiatrists and psychologists.
- Funding treatment dissemination.
- Supporting advocacy and awareness.

For all of these strategies, experts recommend facilitating collaboration in the field through data sharing, supporting multi-disciplinary teams, and investing across multiple sites.

These strategies to move the OCD field forward can be implemented through various funding approaches, including:

- Donor collaboratives.
- “Big bets,” utilizing a large scale, multi-disciplinary, university-based approach.
- Multi-pronged grantmaking that focuses on short-, medium-, and long-term outcomes.
- The “prize” approach, using the power of competition to achieve significant advances in therapeutics.
- High-risk, high reward grantmaking with a focus on funding innovation.

PART ONE: CURRENT STATE OF THE OCD FIELD

To lay the groundwork for understanding the role philanthropy can play, it is important to understand the disorder, how it is diagnosed, the overall state of the field, barriers and opportunities.

DEFINITION AND DIAGNOSIS

Obsessive compulsive disorder is a common psychiatric disorder characterized by recurring and uncontrollable thoughts and behaviors that a person feels compelled to repeat. These obsessions and compulsions are time consuming and cause significant distress, often interfering with work, school, and personal relationships.¹

Until 2013, OCD was considered an anxiety disorder. With the publication of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) that year, the diagnostic criteria were revised to focus on obsessions and compulsions.² While OCD is no longer considered an anxiety disorder, anxiety disorders and major depression are both more common in people with OCD than they are in the general population.³

OCD often goes undiagnosed for a number of reasons. One of those reasons is its high rate of comorbidity, often presenting with anxiety, attention deficit hyperactivity disorder (ADHD), Tourette syndrome, depression, and other disorders. Another reason is the stigma and lack of understanding of the disorder among the public and medical professionals. Commonly diagnosed in childhood or adolescence, OCD can also begin later in life.⁶

About 2 percent of adults in the United States are officially diagnosed with OCD in their lifetimes, and about half of these cases are considered severe.⁴ The actual prevalence of the disorder is slightly higher at 2.5 percent, with an estimated 1 in 40 people in the U.S. having OCD during their lifetime. To put this in context, an estimated 18 percent of Americans have mental illness, and 4.2 percent of Americans have serious mental illness. The most common disorder is anxiety, which affects 7.7 percent of people. Schizophrenia affects 1 percent of the population, and post-traumatic stress disorder affects 3.5 percent of the population annually.⁵

TREATMENT

First-line treatments for OCD include cognitive behavioral therapy (CBT)—exposure response prevention therapy (ERP) in particular—and selective serotonin reuptake inhibitors (SSRIs). These treatments reduce symptoms for many patients, but rarely eliminate them entirely. Experts estimate 50 to 70 percent of people with OCD could be helped by current first-line treatments if applied appropriately.

However, appropriate application of these first-line treatments remains a challenge. SSRIs can take months to take effect, and patients may have to try several drugs before finding one that works for them.⁷ CBT is a very effective treatment when applied appropriately, but few providers are trained properly to administer treatment. Moreover, these first-line treatments were developed 30 years ago, and there have been very few breakthroughs in highly effective treatments since.

Second-line treatments include brain stimulation therapies. Approximately 60 percent of people with treatment-resistant OCD respond to deep brain stimulation. Thus, these second-line treatments appear to benefit some individuals with OCD, but need more thorough clinical testing to establish their safety and to determine how they can be used most effectively.⁸

About one-third of patients with OCD do not experience a significant reduction in symptoms from either first-line or established second-line treatments.⁹

The field is developing several new treatments, which are explored in more detail in Part Four of this paper.

- *Medication:* A new class of medications for treating OCD may be on the horizon. Recent research has suggested a role for neurotransmitters other than serotonin, such as glutamate, in OCD. Drugs that modulate glutamate signaling are now being evaluated¹⁰ as potential treatments¹¹ for the disorder.
- *Brain stimulation:* In 2018, the U.S. Federal Drug Administration (FDA) approved the first medical device for transcranial magnetic stimulation (TMS) for use in OCD. TMS is a noninvasive alternative to deep brain stimulation (DBS).
- *Psychotherapy:* Alternative methods for delivering CBT are under investigation and in use across the country, including intensive, short-term therapy; use of technology to deliver or augment therapy; and alternatives to ERP, such as acceptance & commitment therapy (ACT), inhibitory learning, and attention bias modification.

Still, the development of new, targeted treatments for OCD has been hampered by a poor understanding of the disorder's biological origins. While genetics clearly

influence who develops OCD, no single genetic factor has been found to confer a strong risk of developing the disorder.¹² Neuroimaging studies, however, have provided compelling evidence of which brain circuits are impaired¹³ in OCD. Researchers are beginning to refine their view of how these circuits are dysregulated in OCD, although more detailed knowledge is still being developed.

CURRENT CHALLENGES IN ACCESS TO CARE

The OCD field faces a number of challenges that have slowed the progress of research and prevented more people with OCD from accessing and receiving effective treatment. Indeed, experts describe access to effective treatment for patients with OCD as the leading challenge in the field. It is a multi-dimensional challenge with a variety of contributing factors, including low awareness and high stigma, a lack of effective treatments, and a lack of access to qualified providers.

LOW AWARENESS AND HIGH STIGMA

The first of these factors is the low awareness and high stigma associated with the disorder. OCD is described as a hidden disorder and is less understood by the public and many medical professionals than other psychiatric illnesses. Amongst the public, OCD is often used colloquially, undermining an understanding of the level of disability it can cause in the lives of people who suffer from it. Experts believe that lack of awareness about the disorder negatively impacts the field in a number of ways:

- People with OCD often suffer from symptoms for a long time before seeking treatment.
- Medical and mental health providers do not know enough to properly diagnose OCD when a person presents with symptoms.
- Low awareness and trivialization of the disorder have contributed to limited government funding for OCD research. This contrasts with other conditions that have been successful in raising public awareness and building strong lobbies, such as autism, breast cancer, and HIV / AIDS, which have generated large allocations of research funding by the U.S. government.

LACK OF EFFECTIVE TREATMENTS

Current psychiatric treatments for OCD are considered very good. Experts estimate 50 to 70 percent of those with OCD could be helped by current first-line treatments if applied appropriately. However, that leaves 30 to 50 percent for whom there are no effective treatments. And, current treatments also pose some challenges as noted below.

- Though considered effective, ERP is a very structured therapy that requires specific training for providers, and high levels of compliance from patients. There is a challenge getting people into treatment—both because of access and willingness to commit—and once in treatment, keeping them compliant.
- Improvement is slow with current treatments. SSRIs and CBT/ERP take weeks or months to result in a reduction of symptoms. And because the OCD field lacks treatment predictors, clinicians are unable to observe a diagnosis or set of symptoms and know what treatment combination will be most effective.

Very little has changed with the first-line treatments for OCD since they were established 30 years ago. Because first-line treatments are slow to cause improvement in people suffering from OCD, faster treatments are under investigation, though there are currently no quick fixes to relieve symptoms. Most innovations to date have been around second-line treatments to enhance or augment the effectiveness of current protocols.

LIMITED ACCESS TO FULLY TRAINED PROVIDERS

Current treatments could be more effective for more people with OCD, but many patients do not have access to care that includes proper treatment protocols.

One significant factor in this lack of access is that there is a dearth of trained professionals who can accurately and fully diagnose and treat OCD. Experts estimate that one-third of patients presenting with OCD are misdiagnosed because front-line medical providers (e.g., primary care doctors, emergency room doctors, nurses) and mental health professionals so often misunderstand the disorder. From there, the challenges continue along the spectrum of clinical care. As noted earlier, most medical providers do not have the proper training to effectively deliver CBT/ERP or prescribe SSRIs for OCD, which leaves patients under served when they could be helped by these treatments under the right circumstances.

Those who are properly diagnosed enter a healthcare system that often funnels them to the least qualified, least expensive providers who are even less likely to have the right training. Most evidence-based clinical training takes place in academic doctoral programs, which each graduate only ten to fifteen people per year. Consequently, the majority of people available to treat patients with OCD are graduates of Master's

level programs, and thus have less rigorous training. Experts estimate that there are only 1,500 properly trained providers in the United States, which is not nearly enough to treat the two million people diagnosed with OCD.

A second major restriction on access to the right providers and protocols is a lack of insurance coverage. Most insurance companies do not reimburse providers for an adequate number of sessions to effectively administer CBT/ERP therapy. Additionally, reimbursement rates in psychiatry do not follow the medical model, which reimburses specialists at higher rates. Therefore, those providers who are specially trained to properly administer ERP therapy most often do not take insurance. Demand for services is high enough and incentives from insurance companies are low enough to avoid the insurance system all together, thereby further restricting access.

LOW BAR FOR SUCCESS

An additional limitation on adequate treatment is the low bar for success. Within the field, treatment is considered successful with as little as a 25 percent reduction in symptoms. Experts argue that this bar is too low and treatment standards should be raised to move more people to experiencing fewer symptoms.

SLOW PROGRESS ON RESEARCH

A second highly significant challenge in furthering the field of OCD is the state of research. A number of factors contribute to the slow pace of progress toward effectively treating more people with OCD; and these barriers also keep the field micro-focused on disparate angles of investigation, with very little incentive to look at the big picture across the field.

COMPLEXITY OF THE DISORDER

First of these barriers is the complexity of the disorder. The biological and physiological complexity of OCD creates obstacles to the discovery of new treatments that will work across wide swaths of people with the disorder. The OCD field is behind many other mental health fields in terms of its human evidence base. Though researchers have made strides in recent years related to the genes and brain circuitry associated with OCD, there is still a long way to go.

Researchers have not yet discovered the exact brain circuitry implicated in the disorder, and research is hampered by a lack of access to the human brain. Technology does not yet exist that provides sophisticated data on the brain or

effectively studies the brain in real time, leaving researchers to rely on neuroimaging, post-mortem brain research (which is minimal), and imperfect animal models.

Moreover, while OCD is a genetic disease, the field has yet to identify genetic markers for OCD. Two genome-wide association studies (GWAS) have compared the DNA sequences of people with and without OCD in search of variants that associate with the disorder, and their findings were inconsistent. A later meta-analysis pooled from both studies included 2,688 individuals with OCD and 7,037 controls. In this meta-analysis, some variants showed minimally significant associations with OCD (variants located in or near the genes *ASB13*, *RSP04*, *DLGAP1*, *PTPRD*, *GRIK2*, *FAIM2* and *CDH20*),¹⁴ but because the genetic factors that contribute to OCD are likely to be of small effect individually, much larger studies may be needed to find them.¹⁵ In other fields (e.g., schizophrenia, autism, bipolar, and depression), researchers have made advances by identifying families with single gene mutations causing large effect sizes, which has allowed them to create better animal models to study. Publications on this kind of work are very limited in the field of OCD.

SMALL SAMPLE SIZES

In order to make breakthroughs in understanding the basic biology and physiology of OCD, researchers require much larger sample sizes than have been available. As discussed above, advances in understanding the brain circuitry of OCD are hampered by limited access to the human brain and by small post-mortem brain studies. To move the field further faster, much larger samples sizes for neuroimaging and postmortem studies would be beneficial. For genetics research, because so many genes are implicated in OCD, extremely large sample sizes are necessary in order to see large effect sizes.

Getting the necessary sample sizes is difficult because researchers often lack access to enough people with the disorder. Researchers may have sophisticated labs, but they lack direct access to clinics and people. Additionally, the lack of collaboration across sites prevents researchers from accessing patients in multiple locations. The comorbidity of OCD also makes it more difficult to find “clean” samples for studies. Experts note that if the field finds better ways of studying the disorder in typical patients who present with multiple diagnoses, they would most likely have access to much larger sample sizes.

FUNDING

Experts observe that lack of access to funding is one of the largest barriers in the OCD research field. As explored more fully in Part Three of this report, NIMH is the leading funder of OCD research in the United States. While NIMH does not officially categorize funds for OCD in their database, an unofficial search conducted by NIMH shows that research funding going toward OCD increased from \$19 million in 2008 to \$28.1 million in 2018. However, the experience of researchers in the field is that NIMH funding, specifically, has become harder to get and more restrictive.

Experts further note the following challenges presented by the current state of NIMH funding:

- NIMH tends to fund low-risk research.
- NIMH grants are not big enough to support multi-site collaboration, limiting the scale and scope of studies.
- For animal studies, NIMH prefers to fund research targeting specific genetic markers. However, because genetic markers haven't been identified for OCD, funding is more difficult to secure.
- NIMH funding priorities often change, forcing researchers to adapt their proposals to match new priorities as they arise.
- NIMH funding is very slow. It typically takes more than one year from grant submission to receive funding.
- NIMH grants often do not cover the full breadth of proposed studies, forcing researchers to piece together multiple funding sources or to scale back studies.

Researchers conclude that the lack of funding keeps them in a constant search for new funding, moving from grant to grant, rather than being able to fully explore big picture ideas over time. Competition for limited funding also keeps researchers from collaborating more often and more effectively, especially on cross-discipline research.

INSUFFICIENT PIPELINE OF RESEARCHERS

Many of the factors outlined above contribute to a weak pipeline of researchers entering the OCD field. Experts estimate that perhaps a dozen new researchers enter the field in the United States annually, which is smaller than the numbers for other psychiatric fields. The lack of available funding disincentivizes people from choosing to build a career in the field, though smaller grant programs for young investigators through the International OCD Foundation and the Brain and Behavior Research Foundation have been somewhat successful in helping those researchers who do decide to enter the field, to get started.

LOW COLLABORATION

The OCD research field is small, with experts estimating fewer than 100 leading researchers in the United States. Experts characterize themselves as very collegial and willing to collaborate, but point out that actual collaboration is not common. Small NIMH grant sizes make multi-site collaboration difficult, and competition for funding from NIMH and other sources keeps researchers from actively pursuing collaboration. Experts believe that with funding barriers removed, collaboration would be much more common and would significantly benefit the field.

Experts note that genetics researchers actively collaborate the most, likely due to the need for larger sample sizes, which requires access to data and patients across sites. Collaboration and information sharing between researchers to clinicians happens at the highest levels, with senior clinicians well aware of recent research discoveries and implications for clinical practice. Beyond that, there is a major disconnect between research findings and clinical care.

Despite this general consensus regarding collaboration, there are several notable platforms promoting collaboration in the field:

ENIGMA OCD Working Group¹⁶

- *Background and goal:* This international, Amsterdam-based group was founded in 2010 to address the challenge of small study populations for OCD resulting in unreliable findings. ENIGMA has the goal of bringing OCD research groups together to share neuroimaging and genetic databases.
- *Membership:* ENIGMA currently includes 200 researchers, representing 32 research groups from 16 countries. The group is currently chaired by Dr. Odile A. van den Heuvel of the Amsterdam University Medical Center.
- *Activities:* All sites contribute data to the collaborative studies, and the group largely collaborates virtually through email and teleconferencing. The group has published three major publications on brain abnormalities associated with OCD.
- *Funding:* In 2014, Dr. Paul Thompson received four years of NIH funding for ENIGMA, which enabled it to grow its annual budget to \$70,000, to professionalize, and to hire a staff member.¹⁷ The NIH grant funds ran out in 2018, and the group is currently in search of funding so that it may convene an in-person conference and pay staff, who are now volunteering.

International OCD Foundation (IOCDF) Research Symposium¹⁸

- *Background and goal:* Based in the U.S., the IOCDF Research Symposium is an annual one-day symposium, held in conjunction with a four-day OCD Conference. The

goal is for researchers to discuss their findings with one another, to network, and to “foster increased collaboration.” The Symposium is chaired by Christopher Pittenger, MD, PhD (Yale) and Carolyn Rodriguez, MD, PhD (Stanford). The attendant OCD Conference marked its 25th year in 2018, and the Symposium has been running for the past three years.

- *Attendance:* The Symposium attracted 50 participants in 2016 and 2017 respectively, and 100 participants in 2018. IOCDF is planning for 125 to 150 participants in 2019. For context, the OCD Conference had nearly 2,000 attendees in 2018 (including mental health professionals, researchers, people living with OCD or a related disorder, and friends/ family members).
- *Activities:* The majority of the day consists of numerous 10 to 20 minute presentations, followed by a moderated discussion among researchers and attendees led by a senior researcher. Presentations are organized by topic (e.g., “factors affecting OCD presentation and treatment outcomes”), providing researchers the opportunity to connect on related initiatives. IOCDF’s primary approach to collaboration is to provide opportunities to network (formally and informally through poster Q&A, a speaker reception, mentoring/ professional/ trainee meet-ups, and social gatherings). An additional approach to foster collaboration includes encouraging participants to join the Scientific and Clinical Advisory Board (50 members) and special interest groups (e.g., the Genetics Collaborative).

International College of Obsessive Compulsive Spectrum Disorders (ICOCS)¹⁹

- *Background and goal:* Based in the U.K. near London, the ICOCS is an international member organization created to stimulate and coordinate research projects among members, and to increase public health awareness of OCD. Annual meetings have been held since 2006.
- *Attendance:* In 2018, ICOCS had 45 participants at its conference.
- *Activities:* Undertakings include collaborative research (conducted virtually across sites), publications in primarily European and American journals, convenings (North America and Europe), the building and maintenance of an international database of patient data (clinical and demographic data from across 11 countries), and managing a European College of Neuropsychopharmacology (ECNP) network

focused on OCD.²⁰ The ECNP is a scientific multi-disciplinary pan-European platform for research collaboration that is primarily focused on data collection related to specific diseases.

- *Funding:* The organizational budget is supported primarily by membership fees, with additional grant funding.

PART TWO: ECOSYSTEM OF RESEARCH STAKEHOLDERS

The diverse stakeholder groups comprise a robust ecosystem of players with an interest in advancing knowledge and practice within the OCD field. Stakeholder groups include government, philanthropy, research institutions, mental health care providers, community groups, patients, families, advocates, and educators. This section focuses on three major stakeholder groups currently in a prime position for moving the research field forward: government, philanthropy, and research institutions.

GOVERNMENT

In the field of mental health and disorders, NIMH, the U.S. National Institute of Mental Health, is the largest funder of research in the world.

FUNDING AMOUNTS

In FY 2018, NIMH operated with a budget of \$1.6 billion.²¹ Even with such a large budget, NIMH can only fund a portion of research projects that request funding. Since 1988, the number of applications for NIMH funding increased by 75 percent—and only 20 percent of applications are funded.²² In 2018 (as of September), NIMH funded 72 projects related to OCD for a total of \$27 million.²⁴ Funding for OCD is significantly less than that for other disorders or conditions.

GRANTMAKING STRUCTURES

At NIMH, grants are either “investigator initiated”, or by requests for proposals. Below are the current options (or “series”) for investigator-initiated grants, which fall into categories of: research grants (R series); career awards (K series); fellowships and training grants (F and T series); research program project and center grants (P series).

TABLE 1. Types of Investigator Initiated Research Grants at NIMH

TYPE OF GRANT	\$ AMOUNT	DESCRIPTION
Research Project Grant (Parent R01)	Up to \$250,000 per year for up to five years	<ul style="list-style-type: none"> Provides support for health-related research Supports grants for a project performed by one or more named investigator(s) Longer-term award
Collaborative Grants for Clinical and Services Studies of Mental Disorders and AIDS (Collaborative R01)	\$500,000+ across 2+ sites per year	<ul style="list-style-type: none"> Collaborative intervention trials in the treatment, prevention or rehabilitation of those with mental disorders and comorbid mental disorders Mental health services research, AIDS, genetics, and psychopathology Two or more sites needed to complete the study
Small Research Grant (R03)	Up to \$50,000 per year	<ul style="list-style-type: none"> Pilot or feasibility studies Secondary analysis of existing data Small, self-contained research projects Development of research methodology Development of new research technology
Academic Research Enhancement Award (R15)	\$300,000 for up to three years (not per year)	<ul style="list-style-type: none"> AREA grants create opportunities for scientists and institutions, otherwise unlikely to participate extensively in NIH research programs, to contribute to the nation's biomedical and behavioral research effort
NIH Exploratory/ Developmental Research Grant Program (Parent R21)	\$275,000 over 2 years, with no single year exceeding \$200,000	<ul style="list-style-type: none"> Encourages exploratory and developmental research projects in all NIMH-relevant scientific areas by providing support for the early and conceptual stages of these projects
NIMH Research Infrastructure Support Program (R24)	Case-by-case	<ul style="list-style-type: none"> Supports strengthening research environments and/or expanding existing capacities for conducting research in all fields related to mental health
NIMH Research Education Grants (R25)	Case-by-case	<ul style="list-style-type: none"> Fosters the development of mental health researchers via creative and innovative research educational programs including regional and national programs as well as programs involving a single institution Short courses for mental health-related research education Research education programs supporting psychiatric residents Mentoring networks for mental health research education Research education mentoring programs for HIV/ AIDS

TYPE OF GRANT	\$ AMOUNT	DESCRIPTION
Exploratory Clinical Research Grants (R34)	Case-by-case	<ul style="list-style-type: none"> ▪ Resources for evaluating the feasibility, tolerability, acceptability and safety of novel approaches to improving mental health and modifying health risk behavior ▪ Resources for obtaining the preliminary data needed as a prerequisite to a larger-scale (efficacy or effectiveness) intervention or services study ▪ Collaborative grants for pilot study of innovative treatments in mental health disorders
Research Career Development Grants (K)	Grant calculated based on salary; maximum award size is \$300,000 for direct faculty	<ul style="list-style-type: none"> ▪ Grants to individual researchers for research training and career development, from predoctoral to mid-career in the areas of (1) programs to enhance workforce diversity; (2) programs for physician-scientists and other clinician-scientists; (3) institutional programs, and loan repayment
Small Business Grants (R)	Up to \$150,000 for concept development (phase 1), up to \$1 million for prototype development (phase 2)	<ul style="list-style-type: none"> ▪ Support small businesses to develop technologies that can advance the mission of NIMH ▪ Can include basic neuroscience research, translational and clinical research, clinical diagnosis and treatment, and dissemination and implementation of evidence-based research on mental disorders ▪ Includes a three phase process ▪ One of the largest sources of early-stage capital for technology commercialization in the United States
Training-Individual Fellowships (F)	Case-by-case	<ul style="list-style-type: none"> ▪ Same as K grants above
Training-Institutional Fellowships (T)	Case-by-case	<ul style="list-style-type: none"> ▪ Support research training programs within the research areas and research priorities supported by NIMH ▪ Offsets the cost of stipends, tuition and fees, and training-related expenses including health insurance for the appointed trainees
Program Project Grants/Center Grants (P) (these currently exist only for study of HIV/AIDS)	<p>Up to \$675,000 annually for up to 5 years (P01)</p> <p>Up to \$1.75M (P30)</p> <p>Up to \$2M per year for 5 years (P50)</p>	<ul style="list-style-type: none"> ▪ Research Program Projects (P01): Supports a multi-disciplinary long-term research program ▪ Center Core Grants (P30): Supports shared resources and facilities for categorical research by a number of investigators from different disciplines who provide a multidisciplinary approach to a joint research effort or from the same discipline who focus on a common research problem ▪ Specialized Center (P50): Supports any part of the full range of research and development from very basic, to clinical

CURRENT OCD-RELATED NIMH GRANTS

In general, NIMH RFP grants are dictated by “the needs of the field,” and NIMH has never issued an RFP for OCD grants. NIMH interviewees noted that they are most likely to fund treatment over other research for OCD—and have previously funded ERP studies (specifically, whether individuals could reduce medications while participating in ERP treatment). NIMH does not code its grants as specifically focused on OCD, though a search of its database for active grants with “OCD” as a keyword returns 110 results for grants made in 2017 and 2018. NIMH is currently funding two DBS trial studies on OCD. Although not all OCD specific, 51 of NIMH’s current projects are focused on neural circuits and brain networks, and include research on topics such as the modulation of NDMA receptors, regulation of serotonin transporters, and brain functions in pediatric OCD cases. While many of these studies may not be counted toward the total amount of funding toward OCD, they may contribute to advances in the field.

PHILANTHROPY

In 2016, approximately eight percent of all philanthropic giving in the United States (\$33.1 billion) went toward health-related causes.²⁵ This amount includes support of health care services and facilities, mental health and crisis intervention, diseases and disorders, and medical research. Historically, the mental health field has not attracted the same kinds of large philanthropic gifts as other health-related causes, and OCD remains relatively underfunded. This section outlines some of the leading philanthropic entities working specifically within the OCD field.

INTERNATIONAL OCD FOUNDATION (IOCDF)

Founded in 1986 “to help everyone affected by OCD and related disorders to live full and productive lives,” IOCDF aims to increase access to effective treatment, end the stigma associated with mental health issues, and foster a community for those affected by OCD and the professionals who treat them. IOCDF is based in the U.S. and has affiliates in 25 states and territories, in addition to global partnerships.

IOCDF’s activities are varied and include:

- Educational resources in the forms of newsletters, fact sheets, handouts, brochures, and websites.
- Community events and programs such as an annual OCD Conference, OCD Awareness Week, OCD Walks, and an OCDvocates program (ambassadors for IOCDF).

- A training institute that provides a curriculum of professional training opportunities for mental health professionals treating people with OCD. The flagship program is the Behavior Therapy Training Institute (BTTI), which trains clinicians in CBT for adult and pediatric patients. Online courses are also offered.
- Pediatric outreach programs aimed at raising awareness and providing general education around OCD.
- A genetics collaborative, which is an international group of 50 genetics investigators who convene annually to foster collaboration and share findings and DNA samples, with the ultimate goal of identifying the genetic causes of OCD.

Research Grants

As of 1994, IOCDF has awarded \$3.5 million total in research grants. It operates a tiered research award program, as outlined below.

TYPE	AMOUNT	DESCRIPTION
Young Investigator Award	Up to \$50,000 for one year	<ul style="list-style-type: none"> ▪ For researchers in graduate school or with up to five years of research experience ▪ Focus on OCD, PANS/PANDAS, hoarding disorder, body dysmorphic disorder
Innovator Award	\$300,000	<ul style="list-style-type: none"> ▪ New award as of 2019 ▪ For researchers with at least five years of experience ▪ Focus on finding a cure for OCD; could include prevention and treatment
Breakthrough Award	\$500,000	<ul style="list-style-type: none"> ▪ New award as of 2018 ▪ For researchers with at least five years of experience ▪ Focus on finding a cure for OCD; could include prevention and treatment

Recent grantees have focused across approaches, including genetics, ERP therapy, new technology treatments, and diversity (OCD symptoms in African Americans, for example). The first Breakthrough Award, the largest grant ever from IOCDF, recently was awarded to Susanne Ahmari from the University of Pittsburgh. The award will support her study of molecular changes in a rare sample of post-mortem brain tissue from patients with OCD. The goal is to pave the way for development of new, more effective pharmacological treatments for OCD.

BRAIN & BEHAVIOR RESEARCH FOUNDATION (BBRF)

BBRF's mission is to alleviate the suffering caused by mental illness by awarding grants that will lead to advances and breakthroughs in scientific research. It is the nation's top non-governmental funder of mental health grants. Founded in 1987, BBRF funds 11 illnesses, one of which is OCD, and has awarded more than \$394

million to fund more than 5,700 grants. BBRF funds “the most innovative ideas in neuroscience and psychiatry to better understand the causes and develop new ways to treat brain and behavior disorders.” BBRF is formerly known as National Association for Research on Schizophrenia and Depression (NARSAD).

Research Grants

Rather than issuing RFPs, BBRF uses its internal scientists and its scientific council to select grantees. Research award categories include:

- basic research;
- new technologies;
- early interventions / diagnostic tools; and
- next generation therapies to help reduce symptoms of mental illness and work towards prevention.

The types and amounts of grants are:

- Young Investigator: Two-year award of up to \$70,000 total.
- Independent Investigator: Two-year award of up to \$100,000 total.
- Distinguished Investigator: One-year award of \$100,000.

Since 1987, BBRF has awarded \$4 million to OCD. One recent study focused on the neurocircuitry of people with OCD; another examined differences in the cortex between people with and without OCD.²⁶ BBRF’s featured OCD researchers include several of those interviewed during the research for this publication:

- Dr. Carolyn Rodriguez (Stanford University), who won Young Investigator grants in 2009 and 2014 for her studies on rapid-acting treatments.
- Dr. H. Blair Simpson (Columbia University), who serves as an expert on OCD to the organization and won two awards for her work on a clinical trial to test whether motivational interviewing could increase adherence to CBT and an imaging study to measure glutamate in a part of the brain called the stratum.
- Dr. Susanne Ahmari (University of Pittsburgh), who won a Young Investigator award in 2012 for her studies on the use of deep brain stimulation on mouse models.

OTHER FUNDERS

There are several other funding sources available for OCD, though determining total funding amounts going toward OCD is difficult. In reporting, OCD is often categorized as a subset of another condition (e.g., anxiety) and research is conducted under the auspices of larger studies. Those sources include private funding, global funding, and other funders.

Private family philanthropic dollars towards OCD tend to come from families with an affected family member. In this circumstance, funders often fund a researcher or an institution that they personally connect to (e.g. because their family member was treated there).

Globally, research institutes such as the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) in Brazil and Fondation FondaMental (FFM) in France fund research for OCD, but the amount that goes towards OCD is unknown.²⁷

Other foundations include the Henry L. Hillman Foundation, which granted \$600,000 to the University of Pittsburgh Brain Institute to launch numerous studies researching brain functions and several disorders, including OCD.²⁸ This is an example of how funding towards OCD may be subsumed within larger research efforts.



INSTITUTIONS

There are many universities, hospitals, and other mental health care facilities working to diagnose, treat, and innovate within the OCD field. The following institutions are considered leaders in OCD research and treatment in the United States and were included in analysis for this report.

TABLE 2. Leading US OCD Research & Treatment Institutions

INSTITUTION	NAME OF OCD CENTER(S)	FOUNDING YEAR	DIRECTOR(S)	PHILOSOPHY
Baylor College of Medicine	BCM OCD Program	2016	Wayne Goodman, MD and Eric Storch, PhD	To provide state-of-the-art care for OCD today and develop the treatments of tomorrow using a two-pronged research approach that combines molecular/genetic/immunological and circuit/network science to develop new and better drug, behavioral and device based interventions for OCD.
Brown University, Butler Hospital, Bradley Hospital	Butler Hospital/ Brown University OCD Research Program	1983	Benjamin Greenberg, MD PhD (Butler) and Jennifer Freeman PhD (Bradley Hospital, pediatric OCD)	Apply improving understanding of OCD phenotypes and neurocircuitry to treatment and research.
Johns Hopkins Medical Institution	Johns Hopkins OCD Clinic	1986	Gerald Nestadt, MBCh MPH	“We believe in the integration of research, clinical care and education, with many faculty being active in all these spheres. Our current treatments are ameliorative, however, more needs to be learned to provide the treatment and prevention that our patients need.”
Massachusetts General Hospital/ Harvard Medical School	OCD and Related Disorders Program	1980	Sabine Wilhelm, PhD	“Our program’s ultimate goal is remission and recovery from OCD. The program integrates genetics, neuroscience, neurophysiology, technology, and clinical research to understand, assess, and treat OCD and related disorders.”

INSTITUTION	NAME OF OCD CENTER(S)	FOUNDING YEAR	DIRECTOR(S)	PHILOSOPHY
The McLean Hospital Corporation	<i>Basic research:</i> Center of Excellence for Depression and Anxiety Disorders	1997 (residential OCD program);	Kerry Ressler, MD, PhD, Chief Scientific Officer and Chief, CoE for Depression and Anxiety Disorders	“We have a broad team of basic neuroscience and genetic researchers focusing on OCD, as well as neural circuits and genetic mechanisms related to OCD-related behaviors. Our work combines cell and molecular biology, neural circuit and neuroimaging, and genetic and epigenetic approaches across a variety of complementary experts.”
	Center of Excellence in Basic Neuroscience	2015 (pediatric OCD program)		
	<i>Clinical research and treatment:</i> OCD Institute (OCIDI)		Diane Davey, RN, MBA, Program Director, OCIDI	
	Child and Adolescent OCIDI		Mark Picciotto, PhD, Program Director, OCIDI Junior	
	Center for Depression, Anxiety and Stress Disorders Research Center		Kathryn Boger, PhD, Program Director, McLean Anxiety Mastery Program (MAMP)	
	McLean Anxiety Mastery Program (MAMP)		Mona Potter, MD, Medical Director, MAMP	

INSTITUTION	NAME OF OCD CENTER(S)	FOUNDING YEAR	DIRECTOR(S)	PHILOSOPHY
Stanford University	Stanford Translational OCD Research Program	2015	Dr. Carolyn Rodriguez	Stanford's Department of Psychiatry and Behavioral Sciences aims to cure mental illness. Its OCD research and clinical programs aim to transform the diagnosis and treatment of people with OCD by catalyzing translation of neuroscience research into evidence-based, novel therapeutics.
	Stanford OCD Clinic	1989	Dr. Elias Aboujaoude	
	Stanford Brain Stimulation Lab	2015	Dr. Nolan Williams	
	Stanford Mood Disorders Clinic	2008	Dr. Alan Schatzberg	
University of California Los Angeles. Semel Institute of Neuroscience and Human Behavior	UCLA Anxiety and Related Disorders Program	1986	Alexander Bystritsky, MD, PhD	Combining medication CBT, non-invasive brain stimulation (magnetic and ultrasonic) for treatment resistant patients. Intensive inpatient and day treatment (CB) and eventually DBS for non-responders.
	UCLA OCD Program		Jamie Feusner, MD	
	UCLA Anxiety Behavioral Research Center		Michelle Craske, PhD	
	UCLA Child OCD and Anxiety Program		John Piacentini, Ph.D.	
University of California San Francisco (UCSF)	N/A	N/A	N/A	"UCSF does not currently have an OCD center, but we are poised to pursue, simultaneously, a bottom-up approach focused on discovery of rare large-effect de novo genetic mutations as well as a top-down approach focused on enhanced, closed loop DBS."

INSTITUTION	NAME OF OCD CENTER(S)	FOUNDING YEAR	DIRECTOR(S)	PHILOSOPHY
University of Pennsylvania	Center for the Treatment and Study of Anxiety (CTSA)	1979	Edna B. Foa, PhD	“Our philosophy and mission is to provide evidence-based treatment for OCD, which is structured and manualized, but also flexible to accommodate for individual differences during their recovery towards wellness. Additionally, we conduct studies aimed at increasing the efficacy and effectiveness of treatment.”
University of Pittsburgh	OCD Intensive Outpatient Program	1998	Bob Hudak, MD	“Although clinical excellence in the treatment of OCD is a longstanding tradition at the University of Pittsburgh, the OCD research program at Pitt is relatively new but rapidly expanding due to key faculty recruitments in the past 5 years. Because our program is young, nimble, and still relatively small, we have a tightly-knit and collaborative community that is creatively thinking outside of the box to try to develop new treatment approaches for OCD, capitalizing on unique strengths in bidirectional translation between humans and animal models, invasive and non-invasive neuromodulation treatment approaches, and human post-mortem research.”
	Translational OCD Laboratory	2014	Susanne Ahmari, MD, PhD	
	Brain Modulation Laboratory	2013	Mark Richardson, MD, PhD*	
Yale University	Yale OCD Research Clinic	1984	Christopher Pittenger	“We simultaneously pursue short-, medium-, and long-term goals: short term entails getting today’s treatments out with fidelity; medium is using today’s understanding to develop new treatments; and long is developing new insights into genetics, neurobiology, and psychology to pave the way for the treatments of tomorrow.”
	Yale Child Study Center Tic/OCD Clinic	1990	Michael Bloch Tom Fernandez	
	Pittenger Basic Science Laboratory	2007	Christopher Pittenger	

*Mark Richardson, MD, PhD was previously a member of the OCD team the University of Pittsburgh at the time of this report, but he has since moved to MGH.

RESEARCHERS

RPA interviewed the following top researchers throughout the field, selected based on their emergence as leading researchers during the course of our research. Their top OCD areas of expertise are highlighted, though each may also do work in other specialties.

TABLE 3. Top OCD Researchers and Their Specialties

NAME	INSTITUTION	AREA(S) OF EXPERTISE								
		ANIMAL MODELS	NEUROIMAGING	NEURAL CIRCUITS	GENETICS	TREATMENT (GENERAL)	PSYCHOTHERAPY	MEDICATION	BRAIN STIMULATION	PEDIATRICS
Susanne Ahmari, MD, PhD	University of Pittsburgh	✓	✓							
Helen Blair Simpson, MD, PhD	Columbia University Center for Obsessive Compulsive Treatment and Related Disorders		✓	✓	✓	✓	✓	✓		
Alex Bystritsky, MD, PhD	University of California, Los Angeles		✓						✓	
Darin Dougherty, MD, MMSc	Massachusetts General Hospital		✓						✓	
Jamie D. Feusner, MD	University of California, Los Angeles		✓	✓					✓	
Edna Foa, PhD	University of Pennsylvania					✓	✓			
Wayne Goodman, MD	Baylor College		✓			✓		✓	✓	
Carol Mathews, MD	University of Florida		✓	✓	✓	✓				
Gerald Nestadt, MBBCh, MPH	Johns Hopkins				✓					
John Piacentini, PhD	University of California, Los Angeles		✓			✓	✓			✓
Christopher Pittenger, MD, PhD	Yale University	✓	✓			✓		✓		
Bradley C. Riemann, PhD	Rogers Behavioral Health					✓	✓			
Carolyn Rodriguez, MD, PhD	Stanford University		✓			✓		✓		
Jeremiah Scharf, MD, PhD	Massachusetts General Hospital and Harvard University				✓					
Matthew State, MD, PhD	University of California, San Francisco				✓	✓				✓
Eric Alan Storch, PhD	Baylor College		✓			✓	✓			✓
Sabine Wilhelm, PhD	Massachusetts General Hospital and Harvard University		✓			✓		✓		

PART THREE: EMERGING RESEARCH

While the exact origins of OCD have not been confirmed, scientific research has pointed to differences in the genes and brains of those affected. The following section maps what we know, recent findings, and what's next in research and treatment discoveries throughout the field.

SCIENCE

NEURAL CIRCUITS

What We Know

Most neuroimaging studies examining the brain's structure and function in people with OCD have pointed toward impaired cognitive and emotional processing within cortico-striatal-thalamic-cortico (CSTC) circuits. These circuits carry information in a loop that begins and ends in the cortex, where most higher cognitive processes take place. Abnormal patterns of activity within CSTC circuits have been observed in people with OCD while the brain is in a resting state, as well as when affected individuals perform cognitive tasks or are exposed to stimuli that activate the circuits, including those known to trigger OCD symptoms.

Recent findings

Magnetic resonance imaging (MRI) and computed tomography (CT) scans have indicated a variety of structural abnormalities between the brains of people with OCD and healthy controls, but findings have been inconsistent among studies.

- The ENIGMA OCD Working Group conducted the largest analysis of brain structure in OCD to date, comparing MRI scans of 1,905 OCD patients and 1,760 healthy controls collected at multiple sites. The study concluded that the most significant abnormalities in both adults and children occurred in the parietal cortex, a region in the back of the brain.²⁹
- Smaller studies have found the caudate nucleus, a structure in the striatum of the basal ganglia that is involved in the acquisition of habits, to be smaller in people with OCD than in healthy controls. Other structural abnormalities in the cortex and thalamus have also been reported.³⁰

- Beyond CSTC circuits, structural abnormalities have been observed in the hippocampus and amygdala,³¹ parts of the brain involved in memory and emotion. With a newer method of MRI called diffusion tensor imaging, researchers have also detected widespread small-scale defects (known as microstructural abnormalities) that may affect how information passes between different areas of the brain in people with OCD.³²
- Functional imaging studies have consistently reported that patients with OCD have unusually high levels of activity in two regions of the brain's cortex, the orbitofrontal cortex and the anterior cingulate cortex.³³ Circuits involving the orbitofrontal cortex are thought to be involved in context-related processing and response inhibition, whereas the anterior cingulate has been more closely tied to emotion and reward processing.³⁴ Some, but not all, studies have also found elevated resting activity in the basal ganglia, another component of CSTC circuits.^{35,36} Elevated activity in these regions has been found to decrease after treatment for OCD, supporting the idea that these circuits mediate patients' symptoms.³⁷
- Functional MRI during symptom provocation also indicates abnormalities within the orbitofrontal cortex in patients with OCD.³⁸ Based on neuroimaging findings, it has been proposed that dysfunction within CSTC circuits in people with OCD arises from an imbalance between two pathways through which information passes from the thalamus to the brain's frontal cortex: a direct, excitatory pathway and an indirect, inhibitory pathway.³⁹

What's Next

Researchers are now taking advantage of new tools for manipulating neuronal activity in animal models to explore in more depth how activity within specific connections within CSTC circuits might trigger or prevent compulsive behaviors. In one set of experiments, researchers simulated a type of cortico-striatal hyperactivity that has been observed in the brains of patients, and found that repeated activation over several days caused mice to increase grooming. The animals' OCD-like behavior persisted for weeks and could be reversed with SSRI treatment.⁴⁰ Conversely, other researchers have found they can successfully suppress excessive grooming in a mouse model of OCD by activating specific inhibitory connections within the CSTC circuitry.⁴¹ These experiments suggest potential therapeutic strategies for overcoming functional abnormalities in CTSC circuits.

NEUROTRANSMITTERS

What We Know

- Because treatment with SSRI medications successfully reduces symptoms for many patients with OCD, the brain's serotonin system has been assumed to play an important role in the disorder. Genetic studies have suggested that certain serotonin receptors and transporters may be altered in people with OCD.⁴² These molecules are found at high levels within certain regions of the basal ganglia, implicating serotonin in CSTC circuit function.⁴³

Recent findings

- Evidence of a role for dopamine signaling comes from clinical studies that found that certain antipsychotic medications that block dopamine signaling⁴⁴ reduce the intensity of obsessions and compulsions when combined with SSRIs.⁴⁵ What's more, medications that activate dopamine receptors can provoke side effects that mimic symptoms of OCD.⁴⁶ Different dopamine receptors are predominant in the excitatory and inhibitory (direct and indirect) pathways between the thalamus and the cortex, suggesting dopamine signaling may be critical for balancing signaling and regulating information flow between the two pathways.⁴⁷
- Glutamate is the most abundant excitatory neurotransmitter in the brain, and the driving force for CSTC circuits. Individuals with OCD were found to have higher levels of glutamate in their cerebrospinal fluid, the fluid that bathes the brain, than healthy controls.⁴⁸ Imaging studies have also found evidence of high levels of glutamate and related compounds in the brains of patients with OCD,⁴⁹ and demonstrate that these levels change when patients undergo and respond to cognitive behavioral therapy.⁵⁰ Glutamate signaling has been further implicated in OCD through genetic studies, which have linked the disorder to variations in SLC1A1, a gene that encodes a glutamate transporter.⁵¹ When the SLC1A1 gene is switched off in a mouse model of OCD, OCD-like symptoms such as excessive grooming are reduced.⁵² Other genetic changes that alter glutamate signaling in the brains of mice can provoke OCD-like symptoms.⁵³

What's Next

Studies continue to increase the understanding of the role of glutamate in OCD.

GENETICS

What We Know

A role for genetics in OCD has been well established through twin and family studies.⁵⁴ Some studies have also examined the heritability of OCD traits independent of an OCD diagnosis. These studies confirm a role of genetics in influencing these traits, and suggest that different types of OCD thoughts and behaviors (such as cleaning, forbidden thoughts, ordering, and hoarding) may have overlapping but distinct genetic and biological origins.^{55, 56, 57}

This heterogeneity may be part of the reason that genetic studies have yielded few definitive associations with OCD. Variations in numerous genes have been linked to OCD with varying degrees of support, but so far there is insufficient evidence to implicate any single gene or combination of genes as a definitive risk factor for the disorder.⁵⁸

Recent findings

Several genetic studies have searched for associations among sets of genes hypothesized to be associated with OCD. These studies have largely focused on genes associated with serotonin, glutamate, and dopamine signaling. Several such studies have found an association with the *SLC1A1* gene, which encodes a glutamate transporter,⁵⁹ although variations in this gene were not linked to OCD in genome-wide association studies.

Another gene implicated in multiple studies is *GRIN2B*, which encodes a glutamate receptor subunit that is important for synaptic plasticity.⁶⁰ Studies investigating genes encoding serotonin receptors and transporters and dopamine receptors have also found some positive associations with OCD.⁶¹

A small study that compared all of the protein-coding genes in 20 children with OCD to the genes of their unaffected parents—a strategy aimed at identifying rare mutations associated with the disorder that are not inherited—found mutations in genes involved in developmental and immunological pathways.⁶²

Two genome-wide association studies have compared the DNA sequences of people with and without OCD in search of variants that associate with the disorder, and their findings were inconsistent, albeit promising.⁶³

What's Next

Since the biological origins of OCD remain largely unknown, the genetic factors associated with the disorder may lie beyond those that have so far been considered candidate genes. In addition, because the genetic factors that contribute to OCD are likely to be of small effect individually, much larger studies may be needed to find them.⁶⁴

IMMUNOLOGY

What We Know

Recently, the immune system has drawn the attention of researchers interested in OCD. Certain infections can lead to a rapid onset of obsessive compulsive behavior in some individuals. The best studied example is pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), which is thought to be caused by an overactive immune system triggering inflammation in the brain's basal ganglia.⁶⁵

Recent findings

These cases have led researchers to investigate the role of inflammation in cases of OCD that are not clearly associated with infection.

- Using positron emission tomography (PET) imaging, researchers found evidence that unmedicated adults with OCD had higher levels of inflammation within the brain regions that comprise CSTC circuits than healthy controls.⁶⁶
- Another study examined blood samples from pediatric patients with OCD and found elevated levels of proinflammatory cells and markers compared to healthy controls.⁶⁷ A similar study also found elevated levels of proinflammatory molecules in unmedicated adults with OCD.⁶⁸

What's Next

Recent studies suggest that anti-inflammatory or other immune-modulating treatments may be beneficial for people with OCD.

TREATMENT

DRUG DEVELOPMENT

What We Know

Serotonin reuptake inhibitors (SRIs) and selective serotonin reuptake inhibitors (SSRIs) are commonly used in all of psychiatry, and have been proven effective in treating OCD.⁶⁹ SSRIs directly affect serotonin, a neurotransmitter in the brain. An SRI known as Anafranil has been available the longest, and is the best studied medicine for OCD. Four SSRIs have been FDA approved for OCD.

- sertraline (brand name Zoloft);
- fluoxetine (brand name Prozac);
- fluvoxamine (brand name Luvox); and
- paroxetine (brand name Paxil).⁷⁰

Recent findings

Researchers have been studying alternative medications to SSRIs, with much of the current developments focusing on treatments that modulate glutamate signaling in the brain. Several glutamate-modulating drugs have been FDA-approved for treating other conditions are under clinical evaluation in OCD.

- Memantine, a drug approved for the treatment of Alzheimer's disease, has been found in small randomized trials to have a positive effect on OCD treatments when added to standard medications.^{71,72}
- Riluzole, which is currently used to treat ALS, and the anti-convulsant drugs lamotrigine and topiramate^{73,74} have shown positive effects.
- Ketamine is an FDA-approved glutamate-modulating drug that has long been used as an anesthetic. It has been found to have fast-acting antidepressant effects, and in a small trial the drug rapidly reduced obsessions in patients with OCD symptoms.⁷⁵ When combined with CBT, a single dose of ketamine reduced OCD symptoms for weeks.⁷⁶ Although ketamine may be unsuitable for widespread use due to its undesirable side effects and potential for abuse, researchers are exploring related glutamate-modulating molecules as potential fast-acting treatments for OCD.
- Rapastinel, an alternative medication to ketamine that targets NMDA receptors in the brain, in a small pilot study decreased symptoms of OCD, anxiety, and depression within hours without causing the side effects associated with ketamine.⁷⁷

What's Next

Additional medications that have shown some promise in small, single studies include stimulants such as amphetamine and caffeine, opiates such as morphine and buprenorphine, and ondansetron, a drug used to treat nausea.⁷⁸ Larger studies would be needed for more conclusive results.

PSYCHOTHERAPY

Psychotherapy, paired with medication(s), is a first-line treatment for OCD. The following section details psychotherapy treatments and emerging research related to commonly used and emerging therapies.

Cognitive Behavioral Therapy (CBT)

CBT includes a structured approach towards increasing an individual's awareness of his or her own inaccurate or negative thinking. Through this, he or she can view challenging situations more clearly, respond in a more effective manner, and learn how to better manage stressful life situations. CBT focuses on solutions and rests on the idea that thoughts and perceptions influence behavior. The individual works with a mental health counselor (therapist or psychotherapist) in a limited number of sessions. Research indicates that CBT can be delivered effectively online, in addition to face-to-face sessions. Evidence shows that CBT can benefit numerous conditions, including anxiety disorders, PTSD, eating disorders, and others.^{79, 80}

Recent findings relating to intensive CBT treatment and the use of CBT to prevent the onset of symptoms show promise.

- **Intensive CBT treatment:** Studies have shown that several days of intensive CBT treatment can have a long-term effect. A study out of Norway recently made popular news headlines⁸¹ for treating patients in just four days. Of the 1,200 people who have gone through the treatment, 70 percent remain in remission four years later.
- **Using CBT to prevent the onset of symptoms:** A study has shown that treating children of mothers with anxiety disorders with CBT can prevent anxiety symptoms from occurring in those children.⁸² Researchers posit that early intervention with CBT in OCD might have a similar effect.

Looking forward, studies on the effects of CBT in the brain are ongoing. Imaging studies are being used to predict how the brain reacts to CBT, which can help predict which people will respond to which combinations of CBT and medications. In particular, researchers are looking at glutamate and its impact on the brain in combination with CBT. Stanford and UCLA both have related studies.

Exposure Response Prevention Therapy (ERP)

ERP is a type of CBT, and the one most commonly used to treat OCD. Through this treatment, individuals are exposed to the thoughts, images, objects and situations that lead to anxiety or initiate obsessions. Through response prevention, individuals work with a therapist to learn to not enact a compulsive behavior once the anxiety or obsessions have been triggered.⁸³

There is a commonly held belief that ERP drop-out rates are quite high at 25 percent. One study examined this belief and actually found it to be untrue.⁸⁴ In fact, ERP has relatively low drop-out rates that are on par with drop-out rates for other mental disorders.

Family Therapy

Family members may play an important role in an individual's OCD and are often involved in a patient's rituals and related behaviors. To address this, there are numerous strategies that involve family members in behavioral treatments. For a child, for example, a parent may act as a coach during exposure homework (as part of ERP treatment). Another option is the multifamily behavioral treatment, which combines elements of family support groups and family-assisted behavioral therapy.⁸⁵

In terms of recent findings, family therapy has been shown to have a positive effect on family members. Studies show that participation in family treatment can help parents deal with their own anxiety. UCLA engaged in a recent study in this approach,⁸⁶ and Yale in 2012 developed a "Family Accommodation Scale for OCD" to measure impact/role of family members on OCD behaviors.⁸⁷ In addition, a University of Pennsylvania study found that family-based CBT was more effective than other types of CBT for young children.⁸⁸

Acceptance & Commitment Therapy (ACT)

ACT is an intervention that uses acceptance and mindfulness strategies, together with commitment and behavior change strategies, to help patients accept what is out of their control and commit to actions that can improve and enrich their lives. The intervention uses six core processes: acceptance, cognitive defusion, being present, self as context, values, and committed action.⁸⁹ Experts believe ACT may help patients get into and remain compliant with ERP treatment, and ACT was recently found to be an effective intervention. A recent Utah State University study investigated how ACT activates the brain for both obsessions and perfectionism, and, using a control group, found treatment to be slightly effective.

Inhibitory Learning

Inhibitory learning is an approach to ERP treatment that helps maximize the treatment. This model is a way to understand and optimize how ERP reduces (or “extinguishes”) obsessional fear. To be effective, ERP needs to help people learn that something is “safe” in such a way that is strong enough to block out (“inhibit”) the original fear.⁹⁰ Traditional ERP uses an extinction model that helps people break the link between an obsession and a compulsion in order to make the compulsion go away. However, over time, the compulsion may come back. In the inhibitory learning model, people learn to take the fear away from the obsession, which potentially makes its effects last longer.

The use of an inhibitory learning approach with CBT was found to benefit youth with OCD, according to a 2016 study conducted across several sites, including UCLA, Johns Hopkins and Baylor.⁹¹ While potentially promising, inhibitory learning requires empirical testing in OCD in a controlled clinical trial for more conclusive results.

Attention Bias Modification (ABM)

ABM is based on the view that anxious individuals have a bias towards threats: they see the world as more threatening and frequently sense danger in their environment. ABM aims to reduce anxiety by reducing this bias towards threat. This treatment tends to be multi-session and can be delivered by computer. For example, a computerized program could present an image on a screen rapidly, so that a patient reacts by pressing a button left or right subconsciously. The patient can be trained to always respond to the anxiety-provoking image, which can correct the threat bias, teaching them to respond rather than avoid.⁹²

A study of ABM treatment for youth with clinical anxiety (not OCD specific) took place at UCLA in 2013.⁹³ Further testing is required for more conclusive results.

Therapy Powered by Technology

New technologies are on the rise for mobile OCD treatment options. These include smartphone-based applications (“apps”), as well as internet and computer-based software programs. One advantage to these therapies is that apps and computer programs are widely accessible and provide lower cost alternatives to traditional therapy. Studies have found that software programs using CBT principles can be effective in treating OCD. For many, these programs must be used in conjunction with ongoing in-person treatment, rather than as a replacement. The programs enable users to practice CBT skills on their own in between sessions, or after treatment has ended.

Apps are primarily developed by private companies. NOCD, a smartphone-based tool to help those with OCD, was developed by a Chicago-based startup (founded in 2014) and received \$1 million in venture seed funding in early 2018. The app is free and includes access to educational material, ERP therapy “guidance,” and customizable treatment plans.

As of the time of this writing, Dr. Sabine Wilhelm at Massachusetts General Hospital (MGH) was developing a smartphone CBT therapy app with an emphasis on inhibitory learning. MGH seeks to develop the first app that connects users to live therapists, and hopes to obtain FDA approval. The project received an initial grant of \$725,000 in early 2018. Since apps for OCD are still relatively new, there have yet to be large-scale scientific studies on the long-term impacts of app usage among individuals with OCD. Further studies are needed.⁹⁴

BRAIN STIMULATION

Brain stimulation therapies, including deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS), have shown some efficacy in treating patients whose OCD symptoms do not adequately respond to medication or psychotherapy.

Deep Brain Stimulation

DBS, in which electrodes are implanted in the brain to stimulate targeted areas, is an FDA-approved treatment for treatment-resistant OCD. The number of patients who have received deep brain stimulation is small, and different regions of the brain have been targeted.

A recent comparison of 25 studies involving deep brain stimulation for OCD found little difference in response rates between five different anatomical targets.⁹⁵ The next generation of DBS research will involve closed-loop DBS, which provides much more precise stimulation that is only in response to brain activity related to identified biomarkers, as opposed to DBS which provides continuous stimulation. Closed-loop DBS in OCD is currently being studied with NIMH Brain Initiative funding by Wayne Goodman at Baylor University and Darin Dougherty at MGH/McLean (see case study on pp. 38-39).

Transcranial Magnetic Stimulation

A deep transcranial magnetic stimulation (TMS) device was approved by the FDA in 2018 for use in OCD.⁹⁶ TMS is a noninvasive procedure that uses magnetic fields

to stimulate nerve cells in particular regions of the brain for treatment of OCD.⁹⁷ Transcranial magnetic stimulation is currently used to target superficial parts of the brain, though an ongoing clinical trial is evaluating its potential for targeting deeper structures in patients with OCD.⁹⁸ To date, approximately 20 locations across the country have access to the FDA-approved TMS device, though experts anticipate it will become more readily available over the next few years.

Recently, a meta-analysis of 15 studies found the therapy to be more effective at reducing OCD symptoms in treatment-resistant patients than a placebo.⁹⁹ Experts report that the next area of research for TMS is to develop new coils, which deliver the current, and to identify targets in the brain to make it more precise. Transcranial direct current stimulation, which uses constant, low direct current delivered via electrodes on the head, has shown some promise for use in depression and, through further research, may also be useful in OCD. In addition, low-intensity focused ultrasound has the potential to be more specific in targeting circuits in the brain than is possible through TMS.

CASE STUDY

NIH'S THE BRAIN INITIATIVE—NEUROSTIMULATION

The U.S. National Institutes of Health (NIH) funds “The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative,” aimed at revolutionizing our understanding of the human brain. Through this initiative, two prominent OCD researchers have grants to study closed-loop deep brain stimulation—the next generation of more precise DBS treatment:

- Dr. Wayne Goodman, MD, Chair of the Menninger Department of Psychiatry and Behavioral Sciences at Baylor College of Medicine, received a \$1.5 million grant in 2018.

Dr. Goodman and his colleagues recently received three prestigious grants from the NIH BRAIN Initiative to develop next generation “closed loop” DBS devices. Unlike currently available systems, these devices can record local field potentials (LFPs) from the brain as well as deliver stimulation. This feature will allow scientists and clinicians to learn more about the disease and to further refine

and adjust treatment. This technology is expected to lead to the development of a “smart device” informed by machine learning to automatically adjust stimulation according to the patient’s clinical state based on direct brain recordings. In addition, such a device might be used to monitor the fluctuations in a dynamic disease so that DBS stimulation can be automatically adjusted before symptoms become unmanageable. Dr. Goodman is working in partnership with Medtronic, a medical device manufacturer, for this study. Meeting all study milestones would result in a prototype-adaptive DBS system that would manage fluctuations in OCD symptoms and device-related side effects automatically.

- Dr. Darin Dougherty, MD, MMSc, Psychiatrist, McLean OCD Institute and Director of the Division of Neurotherapeutics at Massachusetts General Hospital, received a \$625,000 grant in 2016.

In an effort to improve DBS for OCD, this project will develop and test in a small early feasibility study a next-generation, brain circuit-oriented DBS treatment for drug-refractory OCD. The main objective is to test a stimulator that affects the deep brain and the cortex (brain surface) at once and tries to break the abnormal CSTC synchrony. It drives two brain areas at slightly different frequencies, keeping them out of sync. The second objective is to test whether activity in the CSTC loop correlates to the symptoms of OCD. No study has proven that these two are linked in humans because it is difficult to record from the human brain, especially over long periods of time and from deep brain areas. The study will use a novel technology, the Medtronic PC+S “sensing DBS,” to record the brain’s activity while delivering the stimulation treatment. This study leverages a broad interdisciplinary team of psychiatrists, statisticians, a neurosurgeon, and electrophysiologists, all with experience in OCD and brain stimulation.

PART FOUR: MOVING THE FIELD FORWARD

Analysis of the history and current state of the OCD research field along with expert input from researchers and clinicians surfaced a number of approaches to help the field eventually treat more people, more effectively. The following section outlines these approaches, including short-, medium- and long-term opportunities.

Most experts agree the ultimate goal of OCD research is to support more people to live functional lives with minimal to no disruptive symptoms. Given the complexity of the disorder and what is known about how it affects people differently, experts do not believe eradication of OCD altogether is a reasonable expectation.

With this definition in mind, experts have varying opinions on the most promising avenues for advancing the field. They note that approaches will vary depending on the level of funding available and the desired time frame for results, as outlined below. About one-third of the experts interviewed noted the need to support all three strategies.

SHORT-TERM APPROACH

BETTER DISSEMINATE CURRENT TREATMENTS AND INCREASE ACCESS TO CARE

Because current treatments are effective and would be effective for more people if they had access, more than half of the experts interviewed recommend that an immediate goal should be to get more people into treatment. This would help the broadest number of people in the short term, moving many more people toward living fully functional lives.

The most promising approaches for increasing access to care include:

- Instituting better and more training on effective treatments for clinicians.
- Leveraging alternative models for treatment delivery (e.g., telehealth, computer-based or app-based delivery).
- Focusing on early recognition and prevention.

- Building advocacy and awareness to reduce stigma and address the hidden nature of the disorder.
- Increasing advocacy and lobbying to demand more government investment in OCD-related research.

MEDIUM-TERM APPROACH

FIND BETTER WAYS TO DIAGNOSE AND TREAT PEOPLE

Thirty to fifty percent of people with OCD do not respond to current treatments. Half of the experts interviewed recommend that a good medium-term approach to moving more people toward living fully functional lives is to develop new treatments to reach those who do not respond to current offerings.

The most promising approaches are noted below.

- Develop a precision medicine approach (note: there was the most consensus about this approach) by:
 - studying predictors and how people respond to treatments (e.g., understanding what treatments will work for which patients based on symptoms, brain scans, and other factors); this would require strong translational research between clinics, labs, and imaging experts;
 - improving neuromodulation (DBS and TMS) and developing new noninvasive ways to stimulate the brain; and
 - combining the understanding of neurobiology and psychotherapy to develop more precise treatments (e.g., combining brain stimulation with psychotherapy).
- Develop new psychotherapy treatments.
- Discover new medications for use in OCD. Most experts do not recommend developing entirely new medications, but discovering new uses for existing medications that might be useful for OCD.

LONG-TERM APPROACH

UNDERSTAND THE CAUSES OF THE DISORDER THROUGH BASIC SCIENCE RESEARCH

The longest-term approach to move the field significantly forward is to make new discoveries about the biology and physiology of the disorder. About one-third of experts interviewed believe basic science discoveries are critical to advancing the field. Experts estimate the field is ten to twenty years away from making significant

breakthroughs in understanding the causes of OCD, with the most promising approaches being in neuroscience, and to a lesser degree, genetics research.

In terms of neuroscience, the goal is to understand the circuit level functioning of the disorder through:

- animal models;
- neuroimaging studies;
- neuromodulation studies; and
- post-mortem brain studies to understand the circuits and cell types that may be abnormal in people with OCD. Such research has yielded enormous insight into pathology in other fields (e.g., Tourette syndrome and schizophrenia), and it is a glaring gap that the OCD field needs to fill.

The genetics approach would include gaining an understanding of the suite of genes implicated in the disorder. The genetics field is at an inflection point where it has discovered that OCD is not caused by a single gene mutation or alteration, but rather many genes working together to influence brain circuit development. Now the field needs to conduct large-scale genetic studies with large sample sizes to identify the suite of genes responsible. Breakthroughs in understanding the genetics of OCD could lead to developing more perfect animal models for conducting further studies.

While some experts believe discoveries in basic science will move the field the furthest ahead, they provide several cautions. Experts note that basic science research will have the least effect on people who currently live with the disorder, and some believe there is no “silver bullet” to be discovered through research that would be applicable to every case of OCD. To keep the research relevant and applicable in the nearer-term, they believe any basic science research should incorporate clinical perspectives.

PART FIVE: RECOMMENDATIONS FOR PHILANTHROPY

The following section provides insight on how philanthropic resources can most significantly influence the trajectory of OCD research. Since mental health funding from government sources specifically earmarked for OCD is limited and often slow and bureaucratic, philanthropy can have significant impact on the field of OCD as a nimble, adaptive funding source. Philanthropy can serve the role as catalyst, convener, and instigator, and can create opportunities to forge new relationships among researchers, academic institutions, funders and policymakers. While this section relates to large, transformational gifts to catalyze change, individual donors can also read it with an eye toward understanding the kinds of activities that, with additional philanthropic dollars, would support the field's growth and forward trajectory.

PHILANTHROPIC OPPORTUNITIES

ROLES

Philanthropy can play a unique role in the OCD research field going forward, especially given its modest role to date. With increased investment, experts noted the following roles as best suited for philanthropy.

- *Connector.* In order to connect stakeholders throughout the field, philanthropic actors can:
 - Connect researchers across disciplines.
 - Connect researchers within disciplines by encouraging and requiring data sharing.
 - Help connect research findings to clinical practice through dissemination.
 - Connect research efforts across multiple sites to increase sample sizes.
 - Connect stakeholders (researchers, funders, advocates) with adjacent interests (e.g., brain research, other psychiatric disorders) to efforts in OCD.
- *Sustainer.* Sustained funding would benefit the field by:
 - Alleviating the pressure researchers feel to chase funding from grant to grant.
 - Allowing researchers to think bigger, more creatively, and longer-term. Many researchers currently feel constrained by available dollars and funding priorities and practices of NIMH.

- Encouraging new researchers to enter the field.
 - Reducing competition for funding.
 - Promoting collaboration across sites and disciplines.
- *Catalyst.* An influential funder in the OCD field could serve as a catalyst, attracting additional funding from government and other sources. New funding could support innovative research that could lead to larger government grants, and an influential funder voice could enhance efforts around advocacy and awareness, which could increase government-spending allocations for OCD. For example:
- NIMH has never issued an RFP related to OCD research. With more public and Congressional pressure, it might be inclined to do so.
 - With increased awareness around OCD, funders who support related causes such as brain research or other related disorders, could be inspired to contribute toward the OCD field.

STRATEGIES

Experts recommend several strategies that philanthropists might use to move the field forward. Experts have varying opinions about where philanthropic dollars would have the greatest impact, and many advocate for a multi-pronged approach that covers all the areas outlined below.

Basic Research

There are mixed opinions on whether basic research is best left to government funding or whether it is a good target for additional funding from philanthropy. About one-third of experts interviewed believe basic research is underfunded generally, and as a long-term approach, philanthropic investment in research to better understand the brain circuitry and genetics of OCD could move the field ahead. In genetics specifically, experts note the field is underpopulated with good researchers and a few million dollars could make a big impact. Others caution against investing heavily in basic and animal model research, believing it is currently well-funded by NSF, NIH, and NIMH. This group also believes that basic research has been incredibly slow and unproductive across the field of psychiatry, leading to very few breakthroughs that make it into the lives of people with OCD.

Translational Research and Treatment Development

The majority of experts emphasized the tremendous opportunity and potential impact that philanthropists could make by helping the field develop better treatments for OCD. Specific recommendations include supporting the following categories.

- Translational research that fills the gap between basic science and clinical practice. This could help the field move toward a precision and personalized medicine approach.
- Research to better connect what is happening in the brain to enhance therapy. Experts note this is a good niche for philanthropy since it is not an area where industry would be likely to provide capital (as pharmaceutical and device companies are not already in this space), and NIMH funds very limited psychosocial research or treatment studies.
- Phase 2 proof of concept studies for potential new drugs to treat OCD. Pharmaceutical companies conduct Phase 3 trials, the precursor to FDA approval, but philanthropy could play a role in discovering new uses for existing drugs through Phase 2 trials.

Treatment Dissemination

Some experts believe supporting treatment dissemination will produce the largest return on investment for philanthropy. Potential roles for philanthropy include supporting the development of novel treatment delivery mechanisms, such as telehealth or mobile apps, and increasing the supply and quality of providers trained to deliver treatment appropriately.

Advocacy and Awareness

Philanthropic investments in advocacy and awareness can help build the field in terms of public interest, potential government investment, and pipeline of talent entering the field. Experts recommend:

- Partnering with institutions such as IOCDF and Peace of Mind Foundation to help support greater public understanding of OCD. This could lead to reduced stigma, better community support, and more frequent and accurate diagnoses.
- Lobbying Congress to allocate dedicated funding toward OCD research, which has been successful for other fields such as autism, breast cancer, and AIDS. Several experts note this is the best way to approach basic research for the field, since government coffers are far vaster than those of philanthropy.

Across all of the above strategies, experts recommend facilitating collaboration in the field through data sharing, supporting multi-disciplinary teams (e.g., including the clinical perspective), and investing across multiple sites.

PHILANTHROPIC APPROACHES

Below are several funding approaches illustrated by case studies featuring philanthropic entities working to make transformational discoveries in science and medicine.

DONOR COLLABORATIVES¹⁰⁰

When trying to address large-scale challenges, such as curing a mental health disorder, it can be greatly beneficial to join forces with other interested parties. A formal structure like a donor collaborative enables funders to pool funds, leverage one another's resources, and join forces towards creating strategic partnerships.

CASE STUDY

THE END FUND: A DONOR COLLABORATIVE SEEKING TO CONTROL & ELIMINATE NEGLECTED TROPICAL DISEASES

The End Fund's goal is to "ensure people at risk of neglected tropical diseases (NTDs) can live healthy and prosperous lives." The Fund plans to end the most prevalent NTDs by 2030. This is the only private philanthropic initiative solely dedicated to ending the most common neglected tropical diseases.

The fund was created in 2012 by a private investment firm and its philanthropic advisors. Additional funders across philanthropy, business, government, medicine, education and local communities have since joined the effort by contributing both dollars and expertise. Within its first six years, the fund raised \$118 million.

Grantmaking	Fundraise and distribute grants to aligned non-profits
Investment	Raise and allocate capital; manage a portfolio of high-impact investments that work on scaling treatment and reaching disease elimination goals
Platform	Serves as a platform across efforts to coordinate donors and increase collaboration
Outreach	Partner with government, local and international NGOs, academic institutions, pharmaceutical companies, funders, and private sector leaders
Technology	Fast-track deployment of new tools and technology that treat NTDs
Advocacy & Awareness	Lead advocacy and awareness efforts towards ending NTDs
Monitoring & Evaluation	Conduct ongoing monitoring & evaluation of investees and grantees to track progress

BIG BETS: LARGE SCALE, MULTI-DISCIPLINARY, UNIVERSITY-BASED APPROACH

Experts agree that a major challenge to OCD research is small sample sizes. An approach to address this might be investing in a large-scale study that would work across several sites to gather sufficient data. It could be beneficial to base a study at a university, and to provide treatment to participants alongside the data collection.

CASE STUDY

UCLA DEPRESSION CHALLENGE

In 2012, UCLA launched a series of “grand challenges,” which are ambitious multi-disciplinary, collaborative research projects that work towards one goal. One of the challenges is the Depression Grand Challenge, which has the goal to cut the burden of depression in half by the year 2050, and to eliminate it by the end of the century. As part of the challenge, UCLA embarked on the largest depression study in history: enrolling 100,000 participants over ten years to identify genetic, biological, cognitive, social and environmental factors associated with depression.

As part of the study, UCLA students and staff fill out an online screen of depressive symptoms. Those that show depressive symptoms have the opportunity to enroll in the study, and to be treated. Those with mild depression are offered an online program, and those with severe depression are connected to the university’s counseling system. Smartphone apps are used to collect participant data.

A neuroscientist, clinical researcher and genetics researcher are leading the study, which enables UCLA to address depression holistically. The estimated budget to complete the study is \$500 million, and initial funds came out of traditional operating dollars and private donors.

MULTI-PRONGED GRANTMAKING THAT FOCUSES ON SHORT-, MEDIUM-, AND LONG-TERM OUTCOMES

Many experts advocate for an approach that accounts for short-term wins while investing in long-term breakthroughs. Several recommended supporting education, awareness and treatment in the short- and medium-terms, while working long-term towards the bigger goals. This could be done through grantmaking across several portfolios in parallel.

CASE STUDY

BONNIE J. ADDARIO LUNG CANCER FOUNDATION

The Bonnie J. Addario Lung Cancer Foundation is a grantmaking public charity that was established in 2006 with the goal of turning lung cancer into a chronically managed disease by 2023, and ultimately eradicating the disease. The foundation has raised more than \$30 million for lung cancer research and related activities.

Strategies include research, education, and treatment.

In terms of research, the foundation supports clinical research related to early detection, diagnostic/prognostic biomarkers, small cell lung cancer, and underlying causes of lung cancer in particular populations.

- Young Innovator Team Awards support transdisciplinary and translational team research with potential of high clinical impact, and provide \$500,000 over two to three years.
- Fellowships support young researchers to study early detection, providing \$300,000 over two years.

For its education initiative, the foundation provides resources for people with lung cancer, including educational resources, support groups, a patient handbook to navigate treatment options, and other resources.

The foundation also supports the development of a patient-centric, collaborative model of treatment that can be provided at community hospitals to give all patients—no matter where they live—access to the most effective treatments.

“PRIZE” APPROACH: COMPETITION TOWARDS BETTER THERAPEUTICS

Given how few grants there are for OCD researchers, establishing a prize could incentivize new people to enter the field. Many interviewees mentioned machine learning as a path towards discovering better therapeutics, and a prize might appeal to engineers, designers, and others outside of the traditional sciences.

CASE STUDY

DATA SCIENCE CHALLENGE

The Bonnie J. Addario Lung Cancer Foundation put out a global call to scientists, engineers, designers, and researchers to develop open source software that brings advances from machine learning into the clinic. There are no restrictions on age, country of origin, gender, educational accomplishment, etc. for eligibility, and top contributors are eligible for a share of a \$100,000-\$180,000 prize. In 2016, the foundation published the criteria matrix,¹⁰¹ which includes factors such as solution design, innovation, viability, scalability, implementation plan, impact, and cost.

Challenge History

YEAR	TOTAL PRIZE AVAILABLE	CHALLENGE TOPIC	INDIVIDUAL PRIZE AMOUNTS
2015	\$30,000 <i>“Phase 1”</i>	“Double Participation in Cancer Clinical Trials: Ideation Phase”	First Prize: \$20,000 Second Prize: \$5,000 People’s Choice Award: \$5,000
2016	\$150,000 <i>“Phase 2”</i>	“Double Participation in Cancer Clinical Trials: Implementation/ Proof of Concept Phase”	First Prize: \$100,000 Second Prize: \$50,000
2017	\$180,000	Crowdsourcing Challenge to Increase Patient Enrollment in Oncology Trials	First Prize: \$100,000 Second Prize: \$80,000
2018	\$100,000	Lung Cancer Early Detection Challenge: Concept to Clinic	Top three winners were awarded: \$30,840; \$26,250; and \$15,989

The prizes are judged by a panel of experts using a points system. The foundation administers the prize through partners that specialize in managing competitions such as HeroX and DrivenData.

HIGH-RISK, HIGH REWARD GRANTMAKING WITH A FOCUS ON FUNDING INNOVATION

A key challenge of NIMH funding is that it is low-risk: a model often has to be proven before NIMH will award funds—and those funds are often primarily used to scale up. This leaves a key gap when it comes to funding innovative, early-stage, riskier ideas. This is a critical role for philanthropy, and a foundation could fill this gap in the field. Below are two case studies that show award strategies foundations have used for other mental and physical health research initiatives.

CASE STUDY

SIMONS FOUNDATION

The Simons Foundation is a private foundation based in New York City that funds research in mathematics and basic science. The foundation makes grants in math & physical sciences, life sciences, autism research, and education & research. Its Autism Research Initiative (SFARI) has the mission of improving the understanding, diagnosis and treatment of autism spectrum disorders by funding innovative research of the highest quality and relevance.

SFARI’s strategy is to support diverse scientific disciplines within a broader framework that emphasizes connecting genes to molecular mechanisms, to neural circuits, to behavior, and to therapeutic interventions. The goals are to seed exploratory hypotheses, and to provide substantial support for high-priority topics through the following awards:

- Pilot Awards provide up to \$300,000 for up to 2 years as early support for high-risk, exploratory ideas, particularly those with novel hypotheses.
- Research Awards provide up to \$1.3 million for up to 4 years for high-priority topics in autism, with a lower requirement for conceptual novelty.

With a budget of approximately \$78 million per year, SFARI supports over 250 investigators. Since its launch, it has provided or committed more than \$480 million in external research support to more than 480 investigators in the U.S. and abroad.

CASE STUDY

THE KENNETH RAININ FOUNDATION

A family foundation based in Oakland, California, the Kenneth Rainin Foundation's mission is to enhance the quality of life by championing the arts, promoting early childhood literacy, and supporting research to cure chronic disease. Collaboration and innovation are at the heart of all its programs.

The foundation's health program seeks to improve the prevention, diagnosis, and treatment of inflammatory bowel disease (IBD). Its strategy is to provide early support for high-risk, innovative ideas and to facilitate collaboration through an annual symposium that brings together scientific leaders, researchers, trainees and clinicians from around the world to promote cutting-edge and creative thinking about IBD. In doing so, the foundation helps encourage new and seasoned researchers to push boundaries and test ideas. The foundation provides this funding through Innovator Awards and Synergy Awards.

- **Innovator Awards:** To support new and veteran IBD researchers in embracing novel, untested ideas spanning the spectrum of basic, translational and clinical science, these awards provide up to \$200,000 for one year, with potential to extend for two additional years.
- **Synergy Awards:** To encourage collaboration among health researchers from across disciplines to advance the study of IBD, these awards support groundbreaking or unconventional methodologies, whose risky outlook is justified by the possibility of a major breakthrough. Grants are awarded across basic, translational, and clinical science. This award provides \$100,000 per investigator, up to a maximum of \$300,000.

MEASURING PROGRESS

Measuring progress in medical research can be complex. FasterCures, a center of the Milken Institute, is interested in the unique role philanthropy can play in jump-starting innovation in medical research and development. It developed a framework for foundations to assess and improve their organizational effectiveness based on best practices in the field.¹⁰² Its assessment framework recommendations include both internal measures of operational performance and external measures of the foundation’s contribution to the field.

OPERATIONAL PERFORMANCE	FIELD CONTRIBUTION
<p>Accountability</p> <ul style="list-style-type: none"> ▪ Strategy Planning ▪ Milestones & Monitoring ▪ Management ▪ Financial Sustainability ▪ Technology Transfer & Commercialization ▪ Community Engagement 	<p>Research Effectiveness</p> <ul style="list-style-type: none"> ▪ Strategic Achievements ▪ Portfolio Congruence ▪ Scientific Advancement
<p>Collaboration</p> <ul style="list-style-type: none"> ▪ Knowledge Sharing ▪ Cooperative Research ▪ Strategic Partnerships ▪ Global Research 	<p>Resource Building</p> <ul style="list-style-type: none"> ▪ Tool & Resource Development ▪ Training & Career Development

Figure 2. Source: “Measuring and Improving Impact: A Toolkit for Nonprofit Funders of Medical Research.” FasterCures: A Center of the Milken Institute.

The framework recommends a few key questions to guide in developing an understanding of a foundation’s contribution to scientific advancement:

- What are our most important scientific milestones? Do outside experts consider these to be significant contributions to moving the field forward?
- Can we quantify the scientific deliverables from the research we have sponsored?
- What is the rate of projects moving through the R&D pipeline? Is this faster or slower than we anticipated? How many projects have advanced, and how many have been terminated? At what stage?
- How many annual presentations, publications, and citations have resulted from the research we have funded?



CONCLUSION

There is enormous potential for philanthropy to influence the OCD field in a significant way over the next 10 to 20 years, and make a meaningful difference for hundreds of thousands, if not millions, of people. By building on the findings and research in progress, and leveraging the cited strategies, approaches, and examples, philanthropy can play a key role in moving the field forward.

If you or your foundation are interested in learning more about OCD, including currently available treatments, access to treatments, support for those affected by OCD and advocacy programs, please contact the International OCD Foundation at iocdf.org. If you are a funder interested in investing in the development of new therapeutics designed to eliminate OCD symptoms, contact the Rodan Family Foundation at RFF_Team@jpmorgan.com.

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