New ideas and expressions emerge frequently in health care, and recently there has been discussion around the concept of 'expert by lived experience.' As the expression implies, there is expertise gained from living through experiences and learning from these encounters with the life circumstances associated with the phenomenon. The experience could be an illness. The longer a person living with diabetes works with the treatment team, the better they become at figuring out how to work the routines associated with diabetes care into their daily habits. They become expert at it. Likewise, lived experience helps with becoming a better gardener, or pretty much most things that are practiced on a regular basis.

In working with those who live with bipolar disorder, I have learned so very much about how people manage their routines, lifestyle issues, and anticipate and manage challenges. **A major source of my continuing education is from those I have the privilege of caring for in the clinics.** We teach our trainees to listen and learn from those under their care. We emphasize that the management of bipolar disorder is a collaboration between those living with the disorder and the treatment teams. When we work together, so much more is possible.

"A major source of my continuing education is from those I have the privilege of caring for in the clinics. When we work together, so much more is possible."

-Melvin McInnis, M.D., FRCPsych
EXPERT BY LIVED EXPERIENCE
A Letter From Our Director: Melvin McInnis, M.D., FRCPsych
... continued from cover

The Prechter Program has embarked on an initiative that is nothing short of a health care paradigm shift that has been taking root globally — the Learning Health System. The key feature of the Learning Health System is the engagement of stakeholders; the primary stakeholders are those who live with the illness on a daily basis. These people are the experts by lived experience.

Now, an expert by lived experience is just that — learning by living with the experience. Expertise comes with time, focus, learning, evaluating, and implementing what has been learned. Think about gardening; one learns from one year to the next, and each year something different (often unexpected) comes up and requires evaluation and reconsideration based on what has been learned. This is what I often hear from those with bipolar disorder. Each new experience, such as going to college or a family wedding, brings its own challenges and ideas as to how to succeed.

Those with lived experience are helping us immensely. We have begun a series of public engagements focused on living well and learning from shared experiences. We are learning about the priorities of people living with bipolar disorder and have set in motion a number of projects based on what we have learned.

Partnerships are the essence of success and we are simply thrilled to partner with some of the many dedicated individuals that work on making each day count as they learn to navigate and share their knowledge about the bipolar life.
Knowledge Builds On Knowledge: Snapshot of the Last Year

The spark of a new idea, that “eureka” moment, a path forward on the journey of discovery: sharing the results of research can generate all of these and is a vital step in the scientific process that leads to new research and new discoveries. Every study builds upon previous learning and moves us toward more effective personalized treatments and best practices for wellness. This year, the Prechter team attended conferences, presented posters, participated on panels, contributed to workgroups, gave talks and wrote papers sharing our knowledge.

Over the last year, Prechter Program researchers presented posters and scientific talks at:

- American College of Neuropsychopharmacology meeting
- Society for Research in Psychopathology meeting
- 33rd Albert J. Silverman Research Conference
- Society For Ambulatory Assessment Conference
- Society for Affective Science Conference
- 25th International Society for Bipolar Disorders Conference
- SLEEP annual meeting
- Global Bipolar Cohort and Human Phenotype Ontology Summit
- 23rd World Psychiatric Association World Congress of Psychiatry

Awards

Bronya Sandorffy was awarded the U-M Library Student Mini Grant ($700) for her project in the EmoTe Lab. “The HAPPI Study: Emotion Regulation, Extreme Appraisals, and Mania Risk,” in October 2022. michmed.org/7NwAx

Victoria Murphy won first place in the undergraduate category at the 33rd Albert J. Silverman Research Conference at the University of Michigan for her poster, “Examining the interplay between sleep, emotion regulation, and mania risk.”

Audrey Stromberg won the Travel Award for runner-up best poster at the Society for Research in Psychopathology conference in Philadelphia, PA, in September 2022. She presented her research, “Alcohol use predicts domain specific life functioning in a longitudinal study of bipolar spectrum disorders” both as a poster and a flash talk.

Sarah Sperry, Ph.D., won the Samuel Gershon Young Investigator Award from the International Society for Bipolar Disorders. She received her award at the annual conference in Chicago, IL, in June 2023 and presented her work, “Longitudinal interplay between co-occurring alcohol use, mood, and functioning in bipolar spectrum disorders,” during the award ceremony.

Hanjoo Kim, Ph.D., won the Society for Research in Psychopathology (SRP) President’s Award. The award encourages and facilitates young scholars from diverse backgrounds and from groups that are traditionally underrepresented in the Society to join the organization and to participate in and present at the SRP’s annual convention. Dr. Kim presented his winning work, “Longitudinal dynamics between anxiety and depression in bipolar spectrum disorders,” at the annual convention in St. Louis, MO, this September.

Articles and Posters

- **Article:** “Low rate of performance validity failures among individuals with bipolar disorder.” Published in Journal of the International Neuropsychological Society
- **Poster:** “Examining the bidirectional relationship between anxiety and depression in bipolar spectrum disorders: A longitudinal study.” Presented at the 33rd Albert J. Silverman Conference
- **Article:** “Heightened inflammation in bipolar disorder occurs independent of symptom severity and is explained by body mass index.” Published in Brain, Behavior, & Immunity - Health
- **Poster:** “Alcohol impairs life functioning over and above other substances in a longitudinal sample of bipolar spectrum disorders.” Presented at the 25th International Society for Bipolar Disorders Conference
- **Article:** “Childhood trauma relates to worse memory functioning in bipolar disorder.” Published in Journal of Affective Disorders
- **Poster:** “Differentiation and Dynamics: An examination of emotion differentiation and intensity, variability, and reactivity of positive and negative emotion in daily life.” Presented at the Society for Affective Science Conference
- **Article:** “Longitudinal dynamics between anxiety and depression in bipolar spectrum disorders.” In revision in the Journal of Psychopathology and Clinical Science
- **Poster:** “Impact of marijuana legislation on marijuana and cannabidiol related perceptions and behaviors among adolescents receiving mood disorder treatment in the US and their parents.” Presented at the American Academy of Child and Adolescent Psychiatry annual meeting
- **Article:** “Extensive evidence for the impact of personality styles on disease course in two bipolar disorder cohorts.” In review in the Journal of Psychopathology and Clinical Science

Please visit our research publications web page at michmed.org/YlYja for more information and links to the articles.
A phenotype is a set of behaviors that can be observed by others. When we talk about human phenotypes, we’re talking about behaviors like sleep, eating, activity level, and mood. The Human Phenotype Ontology (HPO) Collaborative is a group of researchers working together to develop a common set of terms when describing symptoms found in human diseases. The Global Bipolar Cohort (GBC) team has formed a partnership with this collaborative to specifically improve and expand terms related to bipolar disorder (BD). This will provide a powerful tool in bipolar disorder research, unlocking data that holds great potential for informing care in BD, data that is currently underutilized, poorly organized, and largely inaccessible for analysis. Researchers across the world will be able to search medical records, national databases, and research datasets for sets of symptoms that may define and predict bipolar disorder and outcomes.

This partnership spurred the idea of the GBC Summit meeting. Sponsored collectively by the Heinz C. Prechter Bipolar Program with the generous support of Gil Leaf and the Human Phenotype Ontology Collaborative, the GBC met in late June 2023 to catalyze the development of a phenotype ontology platform to support further research in BD and to serve as a catalyst for better diagnostics and treatment options for the disease.

The Summit was a day and a half of meetings in Chicago, IL. The meetings focused on topics such as:

- Enriching the HPO system by developing terms that describe observable traits and unique characteristics in psychiatric illnesses, with a focus on bipolar disorder.
- Helping provide psychiatrists, psychologists, mental health providers, and advocates with a common and precise vocabulary to describe and compare phenotypes for psychiatric illnesses. This will lead to more accurate communication and better efficiency in discussing patient symptoms.
- Supporting data integration from different sources. Clinicians and researchers can use HPO terms to annotate, organize, and harmonize datasets from various research studies, medical records, or national databases.

With guidance from leaders of the HPO, the meeting brought together leaders from diverse medical and scientific disciplines to begin the painstaking task of establishing this essential resource for the global community of BD researchers. The group of 45 psychiatrists, psychologists, biomedical informatics specialists, clinical epidemiologists, computational biologists, and mental health advocates created over 100 terms that met HPO guidelines.

This group also undertook topics involving data harmonization, sharing data across international borders, and developing tools to enhance clinical and research communication for patients and research participants. In addition, they discussed supporting the next generation of bipolar disorder investigators and ways the GBC collaborative incorporates investigators from underrepresented countries.

The GBC-HPO partnership focuses on an ontological framework to organize, conceptualize, and identify clinical features so they can be integrated with biological data for analyses.

The collective efforts of these incredible individuals have the potential to reshape the landscape of mental health, revolutionizing how we approach diagnosis, treatment, and research.
Why do you do all the things that you do, choose to say this rather than that, look here rather than there, move toward something rather than away? It is because you are constantly making decisions to do all these things. We sometimes use the term “decision” to refer to something that unfolds over a long time, like deciding what to study in college. But in the study of the mind and brain, decision refers to rapid choice, which typically takes under a second. Your mind is engaged in these "speeded decisions" constantly.

According to leading models, speeded decisions involve both quick impulses as well as slower “executive” processes that help the person make future-oriented, more adaptive choices. The balance between these processes is likely altered in bipolar disorder. **Diminished executive input into speeded decisions contributes to impulsivity, racing thoughts, and mood variability — all hallmarks of the disorder.**

To improve diagnosis and treatment of bipolar disorder, we need to better understand what happens at these speeded decisions, and in particular the brain mechanisms that underpin them. Thus, we are excited to announce that the Sripada Lab, directed by Chandra Sripada, M.D., Ph.D., in collaboration with Melvin McInnis, M.D., director of the Prechter Program, received a five-year NIH R01 grant ($2.6 million) to address these questions.

This project combines two advanced methods: computational modeling and network neuroscience.

To better understand the psychological processes that unfold during speeded decisions, we designed a new battery of behavioral tasks. We then use sophisticated computational models to uncover the hidden internal processes that give rise to participants’ task responses.

To better understand the neural processes that underpin speeded decisions, the study participants also complete a set of tasks during functional magnetic resonance imaging (fMRI). The human brain is a complex interconnected network that dynamically changes in response to task demands. We will use the methods of network neuroscience to quantify how these brain networks change during speeded decisions.

**This work could lead to new objective methods to identify youth at high risk for developing bipolar spectrum disorders.** It could also spur the development of interventions, such as cognitive training regimens, that directly target dysfunction in speeded decisions in bipolar disorder.
1. Tell us about research and clinic work in Nigeria at the University of Port Harcourt.

To start, I’d like to give a background into psychiatry practice in Nigeria. Psychiatry typically carries a negative undertone in Nigeria. The discipline and its patients are typically stigmatized, very few doctors go into psychiatry residency training — and many fewer nurses and psychologists as well. Psychiatry departments and institutions generally are not as well funded as their clinical counterparts, and research is underfunded and not prioritized for funding. Yet, it is estimated that one in four Nigerians will require the services of a psychiatrist in their lifetime. However, with increased awareness and education of the population, more people are accessing psychiatric care and a wide array of conditions are now being seen clinically. This allows for clinical research in psychiatry to understand psychiatry in our environment and not just translate studies from Western countries and high-income countries to our low-income and culturally diverse setting. There is a lot we can do for our patients clinically. Our ability to utilize modern pharmacotherapy to alleviate psychopathology and improve the quality of life of people living with mental health disorders for many is a breath of fresh air, as mental illnesses are given a spiritual undertone with patients suffering for long periods before getting appropriate care. Carrying out research in Nigeria is exciting because we are contributing to large gaps in research knowledge. However, it has its challenges in terms of difficulty in getting funding, recruiting research participants, etc.

2. What does an average clinic day look like for you? What are some of the main challenges that your patients face?

An average clinic day starts at 8 a.m. with the arrival of patients and patient education by the clinic nurses on the causes of mental health disorders, the need for treatment compliance, and linkages to other services that may be required after seeing the doctor. We typically see about 25 patients a clinic day. Every clinic day, we offer general adult psychiatric services, attending to patients with schizophrenia, bipolar disorder, major depressive disorder, and anxiety disorders. Alongside the general adult psychiatry clinics, we also provide subspecialty psychiatric care in liaison psychiatry on Tuesdays, drug and substance abuse on Mondays and Wednesdays, child and adolescent clinics on Thursdays, and geriatric psychiatry clinics on Fridays. The clinics run this way because there is generally a shortage of psychiatrists, psychiatry residents, psychiatric nurses, and psychologists. Patients are thus faced with the challenge of long clinic waiting times. Patients also pay for psychiatric services out-of-pocket. Considering that most psychiatric conditions require a long duration of treatment, this added economic burden hurts the treatment compliance rate. During our outpatient clinics, patients are seen by the resident doctors, reviewed by consultant psychiatrists, and then prescribed pharmacotherapy and/or psychotherapy and may be referred to other members of the multidisciplinary team as the need arises. Sometimes we attend to acutely psychotic patients at the clinics. Although this is not the norm — as acutely ill patients are to come in via the accident and emergency department of the hospital — when they present at the clinic we have to pause or tone down regular clinic activities and attend to them immediately. If we refer them back emergency, they might change their minds and not return. If this happens, we lose them to traditional healers and others who might exploit their circumstances.
3. Could you discuss the prevalence of bipolar disorder in Nigeria and how it compares to the U.S.? Are there any cultural or societal factors that may influence the diagnosis and treatment of bipolar disorder in Nigeria?

The lifetime prevalence of bipolar disorder in Nigeria is said to be 0.1%. This was from a community-based study carried out in 2008 by Gureje and colleagues. The United States has a much higher prevalence than what has been reported in Nigeria. There are disagreements concerning this prevalence rate in Nigeria as it does not fully match what is being seen clinically. However, no other study has been carried out with as much rigor as the Gureje study to dispute it. As I mentioned earlier, mental illnesses are highly stigmatized in Nigeria, and getting people to enroll in studies is difficult. Bipolar disorder, in particular, is seen as a spiritual disorder due to its relapsing and remitting course and is managed traditionally. It is thought to be a possession by an evil spirit and some traditional ways of ‘treating’ it violate basic human rights, such as flogging, starvation, chaining to trees, etc. As such, a lot of people do not present to hospitals for care as they would rather go the traditional route where they get sympathy rather than the hospital route where they would be stigmatized. Bipolar disorder is thus underdiagnosed and orthodox treatment is not readily welcomed by society. Referral to the psychiatry department tends to be informal, by word of mouth from someone whose relative received treatment and was doing well.

4. Could you elaborate on your interest in the interplay of family dynamics and bipolar disorder? What are your plans for investigating this topic during your time with the Prechter Program at the University of Michigan?

In Nigeria, a family member is anyone related by blood or marriage. Very distant relatives all take part in family decisions. The family system tends to be connected, bordering on enmeshed, and this tends to work. Family members play an integral part when it comes to health care decisions. This led me to question other potential impacts of family dynamics. I wondered, ‘What other influence does the family structure and functioning have on mental health outcomes in people living with bipolar disorder?’ My clinical experience has shown that when patients relapse due to poor medication adherence, there would have been a family discussion on the need to halt medication and treatment for various reasons. This ignited my curiosity about the interplay between family dynamics and bipolar disorder. Is it a societal thing or is it a global phenomenon? During my time at the Prechter Program, I hope to answer this question. I would be using the data from the Prechter Program to look at the effect of family functioning on the quality of life of patients with bipolar disorder as well the bidirectional effect between family dynamics and bipolar disorder. Ultimately, the plan is to compare my findings in Michigan with the findings from the cohort in Nigeria to see if culture affects family dynamics and illness outcomes in bipolar disorder.

5. How do you anticipate using the Prechter Longitudinal Study of Bipolar Disorder as a model for your cohort in Nigeria, and what insights do you hope to gain from the Prechter Longitudinal Study?

There is a lot not known about the etiology and course of bipolar disorder generally. In Nigeria, very little research is done on bipolar disorder. In order for us to study the disorder, we needed to take a pluralistic approach as the etiologic and modifying factors of bipolar disorder are numerous. Also, we need to study the disorder in a longitudinal manner to look at the effect these factors have on the individuals during the course of the illness. The Prechter Longitudinal Study’s focus on the seven phenotypic classes of the observed phenotype provided us with a model we were able to design our study around. I believe that in using this model for our cohort in Nigeria, we will be able to gain more insight into the very nature of bipolar disorder and the influences our biological and social environments have on the illness onset and course.

It also allows us to be rigorous in our approach to studying the disorder and provides us with a basis to compare cultural differences in our findings. It allows us to contribute data from Nigeria on various aspects that concern bipolar disorder — from cognition to family dynamics and genetic variability. This is an exciting opportunity for me and my research team. We envision a very long and rewarding career in bipolar disorder.

6. You’re coming to Michigan during the most beautiful time of year. What are you most looking forward to during your time living in Michigan?

I think I am most looking forward to changes in seasons. I believe this would be magical. I am also looking forward to experiencing a different academic environment and fitting into the general way of life. I would also love to visit the University of Michigan library. Hopefully, when I get back to Nigeria I can pass on some of what I have learned to my colleagues.

Dr. Frances Adiukwu’s research team: Dr. Frances Adiukwu (principal investigator), Dr. Fisayo Adesokun (site coordinator), Drs. Izuchukwu Metu and Isoboye Jack (residents in psychiatry) and Allwell Opusunju (research assistant).
Bipolar Disorder Learning Community

Many factors contribute to living well with bipolar disorder. Some of these factors are individual, such as finding the ideal combination of treatments and the right group of providers, and some are systemic, like having access to high-quality medical care and insurance to help cover costs. Sometimes it can take awhile for individuals with bipolar disorder to overcome individual and systemic barriers to living well, which can lead to delays in diagnosis, care, and life stability. But patients and their loved ones shouldn’t have to navigate these barriers alone. Health care improvement initiatives in the Prechter Program are beginning to look at the interplay of individual and systemic factors to smooth the path for people with bipolar disorder — and those with lived experience are instrumental in driving these efforts.

Improving health care is a continuous process of identifying needs, trying to improve the health care system to resolve these needs, and learning from the process of improvement. This learning cycle is formed by a group of people who are dedicated to changing the status quo: a Learning Community.

Learning Communities are dynamic and inclusive multi-stakeholder groups that unite patients, family members, clinicians, researchers, data scientists, quality improvement specialists, and any other important stakeholders to collaborate on health care improvement initiatives. Learning Communities can be formed to tackle any problem and the problem they work on can evolve over time. When a Learning Community supports ongoing cycles of learning, it evolves into a Learning Health System.

While the individuals who are part of the Learning Community gain a deeper understanding of the problems in health care systems, the ultimate goal of their work is to make the health care system “learn” by changing its infrastructure and organizational processes. This could be something as simple as streamlining how forms are filled out before a health care visit or something as complicated as implementing new evidence-based treatment protocols in a clinic.

Learning Communities are starting to spring up across health care specialties and are improving the lives of patients with conditions as diverse as inflammatory bowel disease, epilepsy, asthma, arthritis, and more. These improvement initiatives work by tracking patient-level data, learning about what causes variation in health outcomes, and optimizing clinic workflows and treatment processes to improve care and health.

“As someone with a loved one who has a bipolar diagnosis, being a member of the [Bipolar Disorder Learning Community] has allowed me to connect with and learn from people who have all sorts of different ties to life with bipolar disorder. From members with lived experience to clinicians to social workers to statisticians and other family members, this group is a powerful coalition with the knowledge, drive, and influence to engineer important changes in the health care system. It is extremely rewarding to be a resource for others via the community events, to share my own lessons learned from navigating the mental health care system, to further my own understanding of bipolar disorder as an advocate, and to transform painful experiences into constructive change to make living with bipolar disorder safer and more manageable for all stakeholders involved.”

- Sarah Adams, member of the Bipolar Disorder Learning Community
In August 2022, the Prechter Program founded our own Learning Community to focus on improving care for individuals with bipolar disorder. Thanks to a generous gift from Raymond and Jane Cracchiolo, the development of the Bipolar Disorder Learning Community (BDLC) is possible. Alexandra Vinson, Ph.D., and Claudia Diaz-Byrd, M.S., co-lead the BDLC. Monthly meetings of our core team of 19 stakeholders facilitate idea-sharing, relationship-building, and design and execution of health care improvement initiatives.

Guided by values like “all teach, all learn” and “experience counts as expertise,” we seek to amplify the voices of people with lived experience and to support collaboration among Learning Community members. Our shared goal is to address the challenges and frustrations many people with bipolar disorder face in the current health care system and to work toward practical solutions that can improve their experiences and outcomes.

The BDLC has begun its first health care improvement initiatives. We developed a website for the Bipolar Clinic (michmed.org/2Vjjj) so people know how to access care at the University of Michigan. Our website also contains a compilation of educational and support resources (michmed.org/vJXXn) for individuals with bipolar disorder and their loved ones. The members of the BDLC have also identified well-being as a key area of interest. We have been working to develop a novel, strengths-based measure of well-being that can be tailored to each individual and taken periodically to help that individual keep track of whether they are participating in activities and hobbies that help them live well. We are currently working to validate our wellness measure to be used in both clinical and research settings.

Through our Learning Community, we aim to drive positive change for individuals with bipolar disorder, their families, and the health care system that serves them. As we approach the end of our first year of collaboration, the Bipolar Disorder Learning Community celebrates its accomplishments and looks forward to a strong second year.

“The Learning Cycle,” a diagram originally created by Charles Friedman, Ph.D., chair of the Department of Learning Health Sciences. Learn more about the Department of Learning Health Sciences at michmed.org/BAeD5.

“Having a Learning Community dedicated to bipolar disorder helps educate, advocate for, and support those with a mental health condition. It is so meaningful for this group to continue its work to reduce stigma and focus on really helping those that are disadvantaged.”
- Mike Buatti, member of the Bipolar Disorder Learning Community

“I think [the Bipolar Disorder Learning Community] is important because it demonstrates that U-M values the importance of innovative ways to treat bipolar disorder, a complex illness. It’s meaningful that people with lived experiences are valued and appreciated for their contributions to this learning community.”
- Wendy Ascione-Juska, member of the Bipolar Disorder Learning Community
The Prechter Program kicked off 2023 with a webinar, Living Well with Bipolar Disorder, where Dr. Melvin McInnis, Dr. Sarah Sperry, and four lived-experience individuals explored what it means to live well with bipolar disorder. Dr. Sperry began the webinar with a provocative statement: “Health is more than the absence of disease.” The speakers discussed the ways in which clinical and research settings currently measure wellness, how individuals with bipolar disorder define their own wellness, and what the Prechter Program is doing to make these changes by working side-by-side with lived-experience experts. The webinar also featured the four lived-experience individuals during a panel discussion where audience members heard methods for establishing and maintaining wellness when living with bipolar disorder, how to be a supportive family member or caretaker, and learning to accept a bipolar disorder diagnosis. Read more about the webinar at michmed.org/GyzZz.

In June, the Prechter Program in collaboration with Gesher Human Services hosted Living Well with Bipolar Disorder: Creative Expressions. The event featured two Prechter Program research participants who are artists and spoke about how their creative outlets play an integral role in their well-being. Gesher’s Creative Expressions Program Manager Craig Nowak spoke about the program’s positive impact on the lives of individuals living with mental health conditions and how it provided a space for all types of creativity and people to flourish.

The Prechter Program Highlights Lived Experiences at Living Well with Bipolar Disorder Events

The Prechter Program recently reached an enrollment milestone of 1,500 participants. This impressive number represents partnership in research with individuals across the country who are dedicated to improving the lives of those with bipolar disorder. We value and treasure this partnership. People participate in research for many reasons: to help themselves, to help others, and sometimes just because they’re asked. Our Longitudinal Study participants often cite a single word as to why they participate: hope. They willingly give their time and share their lives because they hope for a better future for themselves and for future generations.

We are continuing to grow the Longitudinal Study and to move in exciting new directions. Together we will unlock the mechanisms driving the condition and improve quality of life for everyone living with bipolar disorder!

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I have been a part of the Prechter Longitudinal Study of Bipolar Disorder since 2006. At the beginning it was a way to learn more about my recent diagnosis and to contribute to researchers and practitioners learning more about bipolar and how to help. Over the years, though, it has grown to mean something bigger to me. It means that I am complex, legitimate, and worthwhile, just like every other person on Earth. It means there are so many others out there who understand some of the ways I interface with the world, and yet we are also very different from each other. It means that what I experience is real and observable and explainable, and not just ‘in my head.’ It means that I am a conduit for understanding the human experience in richer and more nuanced ways. The study is a gift because it makes me feel like a gift.” [Rachel Rennie Klingelhofer, Ph.D.]

“I like knowing I am helping research efforts, I really like all aspects of this program. The yearly check-ins make me feel quite close to the team, as I have been doing this now for 11 years, and they know me well by now and often suggest other research opportunities I would be good for and would enjoy. It is like home for me.” [Anonymous participant]

“I like knowing I am helping research efforts, I really like all aspects of this program. The yearly check-ins make me feel quite close to the team, as I have been doing this now for 11 years, and they know me well by now and often suggest other research opportunities I would be good for and would enjoy. It is like home for me.” [Anonymous participant]

“Being a part of this study for so long has truly meant a lot to me. I hope that I can continue to be a useful participant for as long as they need me. The study has been so much more to me than questionnaires on a monthly basis.” [Dave Merchant, participant since 2006]

“The part I like best about the study is being part of advancing knowledge about bipolar disorder and reading about research studies I know I’m a subject in.” [Anonymous participant]

Panelists from the Prechter Program June 2023 event, Living Well with Bipolar Disorder: Creative Expressions.

Members of the Gesher Human Services team, who co-hosted Living Well with Bipolar Disorder: Creative Expressions with the Prechter Program.
Organoids are three dimensional miniaturized and simplified versions of organs, produced in the laboratory, that mimic the complexity of that organ in the human body. To study bipolar disorder (BD), we are using organoids that show us how the human brain develops. One of the key limitations in understanding bipolar disorder has been the lack of living brain cells (neurons and glia) to study, and much research to date has employed brain cells from cadavers. With the ability to derive human stem cells (induced pluripotent stem cells or iPSCs) from small samples of skin taken from individuals with and without bipolar disorder, we can now compare gene expression and behavior of neurons and glia from both groups.

**How We Grow Our Brain Organoids:** As in the early embryo, neurons grown in the bottom of a culture dish form a 2D layer of cells like the early neural plate — the embryonic precursor of the central nervous system. In the human embryo the flat neural plate then rolls up forming a long cylinder with the expanded brain at one end. Cells grown in 2D mature slowly, unlike cells in the developing brain or when stem cells are grown as 3D aggregates (a). Durga Attiti, Ph.D., the 2023 Clyde Bartter Scholar, has developed brain organoids by growing stem cell derived neurons and glia in suspension — or floating — culture. Neural cells aggregate, forming cylinders similar to the embryonic neural tube (a). Neuronal cells can then be identified using cell type-specific antibodies (b).

Dr. Attiti has grown brain organoids for sequential periods of development (less than 175 days), analyzed their gene and protein expression patterns, their functional properties, and whether stimulation/inhibition of the WNT signaling pathway found to be altered in BD cells could rescue the changes in gene expression and behavior observed in BD organoids. Finally, we have carried out single cell RNA sequences to determine if particular types of cells, genes, or proteins are altered in BD brains.

This approach provides an important opportunity to study differentiation and signaling pathways suggested to be involved in BD. Human development and disease, drug discovery and testing, cell therapy, and tissue engineering approaches will also be facilitated using organoids. We’re working to publish these studies now.

This work was made possible by a generous grant from the Hazel Ruby McQuain Charitable Trust (HRMCT) given to honor Clyde Bartter, trustee emeritus of the HRMCT and current member of the Prechter Advisory Board.
Can Brain Stimulation Boost Cognitive Training?

Cognitive difficulties are very common among people with mental health conditions like bipolar disorder and schizophrenia. They often interfere with work, school, or relationships, and aren’t usually improved with medication. So, what kinds of treatment might be helpful? ‘Brain training’ interventions have certainly received a lot of attention in the popular media, though their scientific support is more limited. There is some evidence that computerized cognitive training (CCT) might improve cognitive skills like attention or working memory, and separately there is some support for non-invasive brain stimulation as a productive therapy. Could the effects be enhanced if these treatments were combined? That is the aim of the Brain Stimulation and Cognitive Training Research Study.

The study recently wrapped up enrollment and the data analyses are underway. Adult participants with diagnoses of bipolar disorder, schizophrenia, or schizoaffective disorder completed the first phase, where all participants received 10 sessions of standard transcranial direct current stimulation (tDCS) while they completed CCT using an online program called BrainHQ. Because the treatment was well-tolerated and seemed feasible for participants, we then completed a randomized, controlled trial where everyone used BrainHQ but half of the participants received active high-definition tDCS and the other half received inactive tDCS for 10 sessions. All participants completed paper-and-pencil cognitive tasks and symptom interviews before and after treatment, and at a follow-up visit.

The main analyses will help us determine whether there is an additional benefit of tDCS brain stimulation on working memory, beyond any improvement with CCT alone. We hope the results will guide cognitive interventions and ultimately improve everyday function among people with serious mental health conditions. In the meantime, we know that the treatments are safe, well-tolerated, and generally positively received by participants, though the study schedule was demanding — 13 clinic visits — and many people experienced barriers like limited time or transportation. Future research will help us identify what dose of treatment is most beneficial and what frequency/intensity is ideal to balance benefit and burden. Advances in technology may also allow remote or at-home stimulation, which would reduce some of the geographic and transportation barriers.

Stay tuned for final results in the coming months.

What am I feeling and why? The HAPPI Study

Dr. Sarah Sperry and her team are embarking on an international collaboration to develop a measurement tool that can help us understand risk for mood instability in bipolar disorder.

Dr. Sperry is working with Dr. Alyson Dodd at Northumbria University in the United Kingdom and Dr. Tamsyn Van Rheenen at University of Melbourne in Australia to create and validate a new version of the Hypomanic Attitudes and Positive Predictions Inventory (HAPPI). The HAPPI measure is developed based on theories that suggest that individuals vulnerable to mood instability appraise changes in internal states, such as increased or decreased energy, and feeling happier or sadder, in ways that drive attempts to change such internal states. For example, a positive appraisal such as, “When I feel full of energy, the world is full of unlimited opportunities for me,” might lead to attempts to upregulate energy levels, whereas negative appraisals like, “When I feel full of energy, this means I’m about to become manic and have a breakdown,” might lead to attempts to downregulate energy levels. If successful, this measure could be deployed to identify both risk for development of bipolar disorder or impending mood instability in those with the disorder.

Drs. Sperry, Dodd, and Van Rheenen have completed data collection. Using the online research platform Prolific, 1,164 individuals — 730 from North America, 209 from the United Kingdom, and 225 from Australia — were recruited to complete questionnaire measures assessing mania risk, cognitive appraisals, energy, mood, and behavior. Next, the data will be combined from across the globe and analyzed at the University of Michigan, the data coordinating center for the project.
Rhythm and Blues: Changing the Clock to Breakthrough in Bipolar Disorder

It is increasingly recognized that many individuals with bipolar disorder have disrupted circadian rhythms. Circadian rhythms can be thought of as the body’s internal clock — it helps us to know when to go to bed and wake up by controlling various biological processes in the body that promote energy or sleepiness. Researchers with the Prechter Program have found that a high proportion of individuals with bipolar disorder are characterized by a delayed sleep phase. People with a delayed sleep phase tend to have difficulty falling asleep, often not until 2 or 3 a.m. or later, and have difficulty waking up at the times required for work or school, which can cause disruption to their lives. Their sleep-wake cycle is essentially shifted to undesirable times. Individuals with bipolar disorder and a delayed sleep phase are at greater risk for experiencing depressive episodes and day-to-day mood instability.

Drs. Leslie Swanson, Sarah Sperry, Helen Burgess, and Melvin McInnis recently won third place ($50,000) at the inaugural Psych Tank Funding Competition launched by the Eisenberg Family Depression Center to conduct a pilot project, “Rhythm and Blues: Changing the Clock to Breakthrough in Bipolar Disorder.” The goal of this project is to test whether a strategic intervention that targets delayed sleep phase will improve depression and mood instability in bipolar disorder. The intervention involves taking a low dose of a safe and affordable supplement, melatonin, in the afternoon alongside a prescribed bedtime schedule. Drs. Swanson and Sperry have been working over the last three months to develop the pilot project, which will enroll participants in the intervention for approximately one month. Participants will meet with study clinicians virtually to monitor progress and adjust the time that they take their melatonin and get in bed. During the intervention, they will answer daily questionnaires about their sleep and mood on a smartphone app. They will also provide saliva samples so that the researchers can determine whether the circadian rhythm is actually shifting biologically. Drs. Swanson and Sperry began recruitment of participants in August 2023.
Anxiety and depression are common emotional symptoms experienced by people with bipolar disorder. The coexistence of anxiety and bipolar disorder is estimated at 74.9%. Long-term studies have shown that individuals with bipolar disorder experience depressive symptoms about three times more frequently than manic symptoms throughout their illness.

Anxiety and depression can be associated with lower functioning, earlier onset of symptoms, reduced response to treatment, and an increased risk of suicide. It is important to understand how anxiety and depression interact with each other and which influences the other. However, we still have more to learn about the specific timing and relationship between anxiety and depression in bipolar disorder.

In light of this, Drs. Hanjoo Kim, Melvin McInnis, and Sarah Sperry analyzed data from 651 participants with various forms of bipolar disorder who had been assessed for at least five years in the Heinz C. Prechter Longitudinal Study of Bipolar Disorder. The researchers used an advanced statistical method called dynamic structural equation modeling (DSEM) which helps accurately study how things change over time.

The study results showed that people with bipolar disorder experience significant ups and downs in anxiety and depression over time, and these two symptoms affect each other. Interestingly, anxiety tends to increase the likelihood of subsequent depression more than the other way around. It is worth noting that in some individuals, like those who are older or have experienced the loss of a spouse or divorce, depression has a stronger influence on subsequent anxiety compared to younger participants or those who are single or married.

These findings suggest that reducing anxiety could potentially help prevent episodes of depression in individuals with bipolar disorder. This intervention might be particularly important for patients who do not respond well to antidepressant medications. Additionally, early interventions for depression could be beneficial for older patients and individuals who have experienced stress in their marriages.

The research team is deeply grateful to the participants of the Prechter Longitudinal Study of Bipolar Disorder. Without their invaluable contributions, these important insights would not have been uncovered.
A Letter from the Prechters

We are excited to see an important shift in our research as we move in the direction of the Learning Health Systems Model (LHSM). As a matter of fact, the University of Michigan is one of a few universities in the country with a focus on Learning Health Sciences. We see this as a paradigm change in that it promotes a model of care with built-in accountability and a strong emphasis on those with lived experience and their needs. Throughout this newsletter, you’ll read about the LHSM and the steps being taken to introduce a systems change and involve community stakeholders.

A key concept within the LHSM is the principle of collaboration with a shared commitment to quality care. We know this work will take a long time to implement as the learning cycle is an iterative practice. It is our hope that these cycles lead to a more comprehensive infrastructure connecting research to care, thereby making treatment more accessible.

For example, as it stands now, there is a significant time lag between the publication of a biomedical journal and the application of this knowledge to improve care. Quickly expanding knowledge, technology, and data systems will have to adapt at a more rapid rate to achieve wellness. Our work with the LHSM will facilitate this process.

Moving forward, we will have to emphasize partnerships with the community and engage in collaborative efforts locally, nationally, and internationally. This type of integrated clinical care will require extensive philanthropic efforts to ensure long-term sustainability.

We are grateful to see the spirit of collaboration in motion and the voices of those with lived experiences as an integral piece of the puzzle. We appreciate your generous support and your continued partnership.

Waltraud “Wally” Prechter
Founder, Heinz C. Prechter Bipolar Research Program
Prechter Advisory Board Chair

Stephanie Prechter
Prechter Advisory Board Member

YOU CAN HELP

You can help improve the lives of people living with bipolar disorder. There are many ways to support the bipolar disorder cause, both in your own community and through the Prechter Program. By making a donation, volunteering your time, or sharing your story with others, you are personally helping to ease the burden of bipolar disorder.

Volunteer to be a research participant.
Join the Prechter Program in the search for solutions! Contact our research team by phone or email. In order to determine your eligibility, we will conduct a 15 minute phone interview with you. Any information shared with our research staff will remain confidential.

Contact a Prechter research associate at: Phone: 877-UM-GENES (877-864-3637) Email: PResearch@umich.edu

Become a monthly donor.
Sometimes people worry that their contribution is too small to matter. The Prechter Program has achieved its leadership role in the field because of broad support and gifts of all sizes. They all add up. Some of our supporters set up a modest monthly gift and feel great knowing that they are helping provide a steady stream of resources that assist the continuation of the Longitudinal Study and pilot research dollars for new ideas from our students and faculty.

Host a jewelry party.
Hosting an ELLA Designs party is an opportunity for a fun gathering and adding to your jewelry collection while supporting the U-M Heinz C. Prechter Bipolar Research Program. As the host, you receive 15% of the day’s sales in retail jewelry.

ELLA Designs Jewelry began when Liz Guz and her daughter Lauren decided to create a business making beautiful jewelry while raising awareness and money for bipolar research. The company donates 100% of all proceeds to the endowed Michael Guz Bipolar Cell Biology Research Fund (michmed.org/XwZVx) at the U-M Prechter Program in memory of Liz’s son and Lauren’s brother, Michael, who passed away in 2009 at age 17. Through 2022 ELLA Designs Jewelry has donated over $340,000 to Prechter bipolar research.

Contact Liz at lcguz13@gmail.com to learn more.

Celebrate a milestone with a major gift.
Everyone who has bipolar disorder or loves someone who does knows that better treatments and understanding of how best to manage the illness are greatly needed. That is why the Prechter Program was founded. Few families have the resources to make major gifts — those large gifts that can truly transform a research project, test a new clinical idea, or help bring a valuable expert in bipolar disorder to the U-M faculty. If you have the financial capacity and commitment to elevate bipolar research, we invite you to meet with us and consider celebrating your success with this type of gift. Your contribution of $25,000, $50,000, or even $1 million may be the key to the next breakthrough.

Please contact Lisa Fabian at fabiani@umich.edu or leave a message at 734-763-4895 to discuss giving opportunities. She would be glad to hear from you.
If you would like to talk with a lab specialist about taking part in research, please email BPResearch@med.umich.edu.

OUR MISSION
The mission of the Heinz C. Prechter Bipolar Research Program is to discover the mechanisms that contribute to bipolar disorder, predict and improve outcomes, and develop effective, innovative treatments.

OUR VISION
We are building a future where personalized and evidence-based treatments for bipolar disorder will enable every individual with the illness to lead a healthy and productive life.

If you are interested in making a donation or a bequest to support the Prechter Bipolar Research Program, please email Lisa Fabian at fabianl@umich.edu or call 734-763-4895.

If you would like to talk with a lab specialist about taking part in research, please email BPResearch@med.umich.edu.

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