



## HEINZ C. PRECHTER BIPOLAR RESEARCH PROGRAM MICHIGAN MEDICINE

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### Studying the Bipolar Brain

A LETTER FROM OUR DIRECTOR  
MELVIN MCINNIS, M.D., FRCPsych

Every year brings growth and innovation! This past year has been like no other and we are thrilled to share the progress and growth in the program, despite having to adapt to a new normal. The Prechter Bipolar Research Program is thriving in every way — celebrating the 15th year of our longitudinal study, seeing new advances in several of our labs, and driving new and meaningful collaborations in the international community of bipolar researchers.

**2021 marks 20 years since the death of Heinz Prechter.** Heinz had bipolar disorder. Upon his tragic death the family decided that they would do something to bring this dangerous illness into the light; they bravely refused to keep his illness and his suicide quiet and created what is now the **Heinz C. Prechter Bipolar Research Program.**

The legacy of Heinz lives in so many places throughout Michigan and in the hearts of so many people. I have often been in conversation with someone, and upon the mention of the Prechter Program, a fond personal memory or a second-hand anecdote about Heinz's warmth is shared. **So often I have heard "I knew Heinz,"**

**"I worked for him," or "I have never met anyone else like him."** The humanity of Heinz Prechter is an inspiration to all. In our work, we honor and celebrate his memory and the memories of the others who have died from bipolar illness.

Yet in our programs and projects we also celebrate the lives of the many who are finding ways to flourish while living with the bipolar condition. We recently hosted a virtual opening night for the art exhibit **ENERGY: Brain Health Arts.** This exhibit highlighted the creativity of those in our program who use art to express themselves, channel their energies, frustrations, and daily experiences. The common refrain from the artists is: "I work hard at this, and art helps me a lot!"

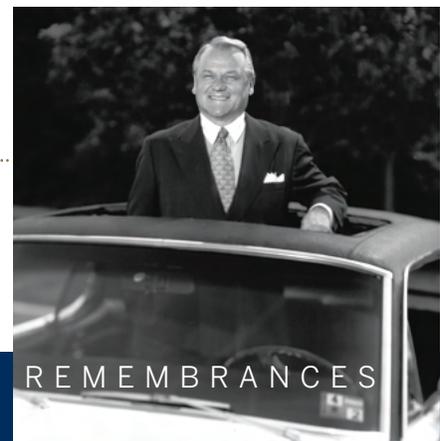
A consistent finding has emerged over the years that has become central to our current research. **The "bipolar brain" works differently compared to the brain of a non-bipolar individual.** How do we know this? We find evidence across the spectrum of our projects. **Ivy Tso, Ph.D.,** Associate Professor of Psychiatry, is

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20 YEARS  
Remembering  
Heinz Prechter

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MILESTONES and REMEMBRANCES

## Studying the Bipolar Brain

A LETTER FROM OUR DIRECTOR  
MELVIN MCINNIS, M.D., FRCPsych



Melvin G. McInnis, M.D., FRCPsych

Thomas B. and Nancy Upjohn Woodworth  
Professor of Bipolar Disorder and  
Depression

Professor of Psychiatry

Director, Heinz C. Prechter  
Bipolar Research Program

finding evidence of different patterns of electrical impulses on electroencephalogram (EEG) and brain activity on neuroimaging in those with bipolar. Dr. Tso can see that the “bipolar brain” reacts differently to social cues on the computer screen during tasks that require a withholding of response. Even when well, not manic or depressed, individuals with bipolar often show altered reactivity and response intensity to daily events. (See article on page 9).

The lab team, led by **Sue O’Shea, Ph.D.**, Professor of Cell and Developmental Biology, has found that the brain cells derived from samples of people with bipolar are also more reactive and send impulses with greater intensity and duration. Their research involves a constellation of cells in the brain, and they are working to pinpoint the fundamental mechanisms of the heightened cellular reactivity. (See article on page 10).

In a third example, we continue to research the differences in the context of a fundamental human activity — speech. We are learning how speech and communication are complicated by and dependent on context. This team formed 9 years ago to study speech and bipolar and is led by **Emily Mower Provost, Ph.D.**, Associate Professor of Computer Science and Engineering. We are thrilled to announce that this summer, **Sarah Sperry, Ph.D.**, has joined the Prechter Program as an Assistant Professor to team up with Dr. Mower Provost and study the complex patterns of emotional expression and speech. The “bipolar brain” communicates differently, and moods and

emotions vary in complex ways. Our understanding of the components of speech continue to progress which, in turn, results in improving the predictability of our models.

**The reach of the Prechter Program is expanding, and we stand united behind the vision of empowering people with bipolar disorder to achieve fulfillment personally, socially, and vocationally.** Thanks to the terrific work of the data management team, led by **Anastasia Yocum, Ph.D.**, our ability to share data with collaborators is now routine. Teams of national and international collaborators are actively working on projects using the extensive data gathered through our longitudinal study. In fact, just this year, the team filled 35 distinct data requests from bipolar investigators.

Our faculty are leading international collaborations to study questions central to understanding the course of illness like the importance of sleep (**Helen Burgess, Ph.D.**) and the effect of traumatic events (**Liz Duval, Ph.D.**). The Tam Foundation supports our internal (U-M focused) collaboration with **Precision Health** and facilitates integrating the rich clinical data with data collected by researchers.

Thank you for your kind and generous support of the Heinz C. Prechter Bipolar Research Program. We are energized by the many partnerships that include our participants, the community of supporters, the research teams, and of course the University of Michigan community.

“The reach of the Prechter Program is expanding, and we stand united behind the vision of empowering people with bipolar disorder to achieve fulfillment personally, socially, and vocationally.”

# 2021 Highlights and Progress

Chandra Sripada, Ph.D. collaborates with the Prechter team on **new research into how bipolar brains differ in cognition and impulsivity.** *see page 4*

The Global Bipolar Cohort, initiated by U-M and Harvard researchers, aligns with Center for Strategic Philanthropy at the Milken Institute in **stimulating international collaboration and funding strategies** in bipolar research. *see page 4*

The Prechter Program shines at the 2021 International Society for Bipolar Disorders (ISBD) Conference, **leading sessions and winning awards.** *see page 5*

The ENERGY: Brain Health Arts virtual art exhibit **celebrates the value of art in wellness** with **11 artists from the Longitudinal Study!** *see page 6*

The Michigan Social Cognitive and Affective Neuroscience (MiSCAN) Lab **investigates how bipolar brains respond in social situations.** *see page 9*

The O'Shea lab is making great progress identifying markers through **4 different studies to narrow the causes for bipolar disorder markers in brain cells.** *see page 10*

The PRIORI program **samples ambient sound to advance accuracy of models designed to detect mood changes.** *see page 11*

The Prechter Program currently has **36 active research studies.** *see page 12*

The Longitudinal study is in its **15th** year following **1,389 research participants.** *see page 12*

A new partnership with the University of Michigan **Learning Health System will improve the quality-of-care** bipolar patients receive. *see page 13*

The Prechter Program is expanding its reach with **22 collaborators from all around the world** and filled **35 data requests this year.** *see page 13*

It has been **20** years since the world lost Heinz C. Prechter. In remembrance of Heinz, researchers **strive to build a better understanding** of bipolar disorder through research and improving care. *see page 14*

There were **18 scientific publications** in 2020 — view them on the Prechter Website: [michmed.org/YIYja](http://michmed.org/YIYja)

## FROM OUR RESEARCH PARTICIPANTS:

*“I like it all because I like contributing to research which might help with the treatment of this condition.”*

—Thomas

*“I feel like I am a part of something bigger than me that is helping people.”*

—Trevor

*“It feels like they really want to get to know me and understand me.”*

—Myra

*“I feel like compiling this type of data from many subjects over a long period of time can be very helpful to recognize trends common to many bipolar patients.”*

—Vicki

## Investigating the Bipolar Brain

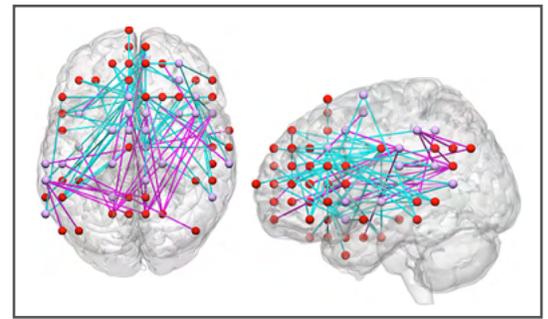
## SRIPADA LAB UPDATE



Chandra Sripada, M.D., Ph.D.

The Sripada Lab, directed by Chandra Sripada, M.D., Ph.D., is now partnering with the Heinz C. Prechter Bipolar Research Program to better understand brain mechanisms which contribute to symptoms in bipolar disorder by using both computational psychiatry and network neuroscience. **This study focuses on a specific brain process called Efficiency of Evidence Accumulation (EEA)**, the ability to gather relevant information needed to make decisions. EEA measures the ability of the brain to gather information in noisy background conditions and to select appropriate responses. EEA is altered in people with bipolar disorder, and this contributes to impulsive behaviors and choices. Currently, very little is known about the brain mechanisms behind reduced EEA in bipolar disorder or in any other psychiatric disorder.

Findings in the Sripada Lab support a flexible network reconfiguration model of EEA, meaning the brain has the ability to adapt and reconfigure connectivity patterns of brain networks across different task contexts. Patterns of reactions are molded and adapted in different ways according to place and purpose.



**DIAGRAM:** The connections shown here are important for paying attention to the environment and avoiding distractions.

Dr. Sripada is testing a **novel hypothesis: reduced EEA in bipolar disorder arises from decreased flexibility in brain network reconfiguration.** The “bipolar brain” may be challenged when there is a need to be flexible and adapt quickly. This will be tested using a selection of behavioral tasks to measure EEA and complete neuroimaging tasks that measure flexibility of brain network reconfiguration. **This project will provide critical insight about how changes in brain networks contribute to cognition differences and impulsivity in bipolar disorder.** This may lead to new points of interventions and training strategies to increase the ability of the “bipolar brain” to be flexible and adapt to an ever-changing world.

## MILKEN LED GLOBAL COLLABORATION

An exciting collaboration with the Milken Institute, Center for Strategic Philanthropy (CSP) has emerged over the past year. Efforts spearheaded by **Melvin McInnis, M.D., FRCPsych**, from University of Michigan, **Andrew Nierenberg, M.D.**, from Massachusetts General Hospital, Harvard and **Kate Burdick, Ph.D.**, from Brigham and Women’s Hospital, Harvard — in partnership with the Milken Institute — have the potential for **expanding bipolar research beyond borders, bringing together the world’s top researchers in bipolar disorder.**

Following the 2019 inaugural international bipolar disorder research meeting in Ann Arbor, Drs. McInnis, Nierenberg, and Burdick continued meeting with the leadership of the CSP team. The CSP has facilitated several brainstorming workshops, bringing the voices of a wide range of perspectives to the table. An emphasis on inclusion of ideas and cultures along with a collaborative

spirit has led to a strong partnership focused on defining a strategy for researching this chronic illness and setting goals for improving outcomes. In this past year, the team has had several milestones:

- An Executive Advisory Board was formed to determine the scientific goals and objectives in current bipolar research. A major focus has emerged: an integrated model that embraces a combined learning health system for bipolar alongside a longitudinal study.
- A team of dedicated program managers came together to work alongside Drs. McInnis, Nierenberg, and Burdick and the CSP’s team.

■ The CSP has brought together potential funders that are dedicated to bipolar research and share the vision of a game-changing approach to research and care of those living with bipolar.

A dynamic group of multidisciplinary researchers has been assembled to serve on the Scientific Planning Committee (SPC) that will review and develop materials to guide the study. The success of this venture is underwritten by the collaborative experience of the leadership team (Drs. McInnis, Nierenberg, and Burdick have collaborated internationally for over a decade), the institutional expertise of the Milken Inst. CSP (they have been the catalyst for several successful ventures, including bringing the Michael J. Fox Foundation together with dedicated supporters in the field of Parkinson’s research), and the determination of philanthropic minded individuals supporting bipolar research.





## Contributing to Research

## International Society for Bipolar Disorders (ISBD) Conference Highlights and Awards

The **International Society of Bipolar Disorders (ISBD)** held a virtual interactive conference this year that brought together bipolar disorder researchers from around the world. Sharing research findings, developing ideas for new research, and forming collaborations are critical steps on the road to improving the lives of individuals with bipolar disorder. **The Heinz C. Prechter Bipolar Research Program was well represented at the conference and made quite an impact, with three posters winning awards.**

Prechter Program director, Melvin G. McInnis, M.D., FRCPsych, chaired two panels:

- 1 A Global Bipolar Cohort: Premise and Strategies:** an open discussion on the planning and organization of a longitudinal cohort of individuals with bipolar disorder. This program was coordinated with the Milken Institute Center for Strategic Philanthropy. Presented by: Melvin G. McInnis, M.D., FRCPsych
- 2 Mood and Emotional Outcomes Trajectory and Patterns in Bipolar Disorder Offer Treatment and Interventional Targets: Integrating Mobile Technology with Clinical and Self-Assessments: Three Presentations on Monitoring Bipolar Disorder:** Presenters: Melvin G. McInnis, M.D., FRCPsych, Maria Faurholt-Jepsen, Ph.D. (University of Copenhagen), Amy Cochran, Ph.D. (University of Wisconsin), Sarah Sperry, Ph.D. (Vanderbilt University). Dr. Cochran is a former post-doc with the Prechter Program and remains a close collaborator.

The Prechter Program’s researchers submitted **7 POSTERS THAT WERE ACCEPTED** for the ISBD poster presentation. The posters and presenters who represented the Prechter Program this year were:

- Migraine History and Lithium Response in Bipolar Disorder**  
*Presented by:* Nicole M. Sekula, BS, et al.
- Life Goals Self-management Mobile Application for Bipolar Disorder: Consumer Acceptability and Perceptions**  
*Presented by:* Isabel Carley, BS, et al.
- Predictors of Employment Stability Over 10 Years in Bipolar Disorder**  
*Presented by:* Shamara Williams, BA, et al.
- Longitudinal Improvement of Executive Functioning in those with Low Baseline Executive Functioning in Bipolar Disorder**  
*Presented by:* Tobin Ehrlich, Ph.D., et al.
- Maladaptive Personality Styles Using the NEO-PI-R can Predict Future Depression and Anxiety in Bipolar Disorder**  
*Presented by:* Ellie Ahearn, BS, et al.
- Suicide Ideation, Attempts and Death by Suicide Have Not Increased in a Longitudinal Study of Bipolar Disorder Population During the COVID-19 Pandemic**  
*Presented by:* Ellie Ahearn, BS, et al.
- Dynamics of Data-driven Microstates in Bipolar Disorder**  
*Presented by:* Michael Yee, Ph.D., et al.

### 2021 BEST POSTER AWARDS

Congratulations to these **3 WINNERS OF THE BEST POSTER AWARDS!** The Prechter Program, representing the University of Michigan, was the only institution to win 3 awards.



You can watch videos of the Prechter Program presentations at the 2021 ISBD conference by visiting: [michmed.org/Pq2pv](https://michmed.org/Pq2pv)



# Celebrating the Health and Creativity of Artists with Bipolar



**ENERGY: Brain Health Arts** is an online exhibit centered around the power of art as a part of the process in healing and recovery, with a focus on the bipolar diagnosis. Artists explore the concept of energy and the impact of creative expression on their overall brain health.

The artists featured in this collection are also participants in the Heinz C. Prechter Bipolar Research Program's Longitudinal Study of Bipolar Disorder.

This is the second year for ENERGY and the 2021 exhibit is entirely virtual. The first year was a collaboration with Metropolitan Museum of Design Detroit and Collected Detroit. The exhibit was initially planned as a physical exhibit but given the circumstances around COVID-19, the event went virtual.

## What inspired you to put together this exhibit?

The driving force of inspiration is my experience with the bipolar diagnosis and the critical role the arts have played throughout my journey. Having the arts as an outlet has enhanced my concepts of self-awareness, compassion, and resilience. I figured that if it did that for me, then I'd be curious to see how other artists with this diagnosis feel.

It seemed like a natural fit to partner with the Prechter Program and recruit participants from the study to join this initiative. The research is filled with people coming from a vast array of perspectives and experience. It's inspiring for me

to channel our collective energy and highlight the ways in which we've been able to navigate through life's twists and turns.

## Can you explain the importance of art to help people with bipolar?

I can share my experience with photography and the way in which the highlights and shadows in every image serve as a range of emotion. Making pictures empowers me to reframe my reality and gives me agency to create meditative landscapes. That becomes my focus and influences my mood state in a positive way. It also addresses the entire gamut of human experience, making me curious about every bit of it with the urge to embrace the highs and the lows.

In more general terms, art encourages imagination and stimulates neuropathways to take a different route. The act of art-making solicits open-mindedness and curiosity, thereby freeing us from hazardous conditioning and giving way to new ways of thinking. I believe the arts to be a key to unlocking the world around us.

**The function of art is an extension of the function of the brain, the seeking of knowledge in an ever-changing world.**  
—Semir Zeki

## What has the experience of working with the featured artists been like for you?

For the most part, it was a fun experience! I think it helped for us to meet via Zoom and have a chance to get to know each other. It was a bit more challenging given that everything was virtual. I especially enjoyed

hearing about the wide range of work and the mediums used and I think it helped for the artists to meet each other and share their stories.

The challenging part for me was the fact that I put a ton of pressure on myself to present the work and the artists in the best way possible. This work means a great deal to me, and I sometimes feel overwhelmed by the nature of it.

## What did you learn from the artists?

I learned a tremendous amount from the 11 artists involved, namely that we all have our own unique way as to how we process the world around us, and that art allows for us to channel beauty and power in the face of adversity. I'm impressed by the artists' ability to transform pain and struggle into creative expression and inspiration.

It was especially refreshing to see the artists relate with each other and feel as if they have a shared experience in their relationship with the arts. All of them consider this to be a lifeline giving them a toolbox to draw from.

## What was the experience of doing this exhibit virtually like?

The virtual format has its costs and benefits. I prefer to have a physical space with the work because it offers a tangible experience for the audience, and it gives the artists a chance to interact with viewers opening opportunities for conversations and connection.

The major benefit with going virtual is the amount of people we were able to reach geographically. It makes sense for us to entertain a hybrid model as we move forward.

## STEPHANIE PRECHTER,

BSBA, Georgetown University  
AAS in Photography,  
Washtenaw Community College  
MFA Candidate, fall 2024,  
Maine Media College

The curator of ENERGY: Brain Health Arts answered some questions about this endeavor:

**What do you hope people will take away from ENERGY: Brain Health Arts?**

At the very least, I hope people walk away from the experience with a deeper appreciation for the arts and the urge to incorporate creativity in their every day.

I encourage people to get out of their comfort zone and explore the arts on their own terms. Take time with it and give it space. It may help to start out small. Pick up a journal and start writing, visit a museum and do some research on an artist, dive into a conversation related to brain health and the arts, explore different mediums, strike a balance between analog and digital, and again go at your own pace with it. The idea is that this will spark a fire within. It will become habit and you will see the arts as a part of your wellness.

I also hope that this work encourages research in the arts! It is critical for us to integrate forms of creative expression to better understand ourselves and each other and give the arts the weight they deserve.

**Do you plan to do another exhibit next year?**

I am taking some time to think about next steps, but my hope is that we can coordinate a physical exhibit and continue our partnership with The Heinz C. Prechter Bipolar Research Program to further integrate the arts.

For now, the current exhibit is on view at: [www.energybrainhealtharts.com](http://www.energybrainhealtharts.com)

Please take time to visit, thank you for your interest, and keep the energy moving!

**TO CREATE THE "NEXT THING" IS MY OBSESSION. IF I AM IN A CREATIVE LULL, I FEEL EMPTY.**  
-BEN MILLER



**ART IS FREEDOM. IT IS INESCAPABLE AND COMMUNICATES TO EVERYONE. ART IS POWER.**  
-VALENNA MALONE



**MY ARTISTIC EXPRESSION IS ROOTED IN EVERYDAY EXPERIENCES AND LIFE STORY.**  
-WENDY ASCIONE-JUSKA



**I WOULD BE LOST WITHOUT THE ABILITY TO EASILY EXPRESS MYSELF IN SONG, COLOR, AND PERFORMANCE. I SOMETIMES WISH I HAD A CHOICE.**  
-LAURENCE MILLER



**BEING CREATIVE IS A WAY TO FOCUS LIFE'S SQUEEZING AND SHAKING. WE ENDURE BEING PRESSED INTO OIL OR CRUSHED LIKE A DIAMOND, TO MAKE BEAUTIFUL ART WORTH SHARING.**  
-SANDY DODES



**ART IS A REFLECTION OF CONSCIOUSNESS, A PORTAL FOR CREATING AWARENESS AND DIALOGUE WITH THE WORLD AROUND ME.**  
-TREVOR MCCAULEY



**WHEN I CREATE ART, IT IS TO TURN THE PRESENT MOMENT OF WHO I AM INTO A PRESENT OR GIFT FOR ANOTHER.**  
-ELISABETH MADDIX

## MEET OUR NEW FACULTY & POST DOCS



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Sarah Sperry, Ph.D.

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Sarah Sperry, Ph.D. recently joined the Prechter Program as an Assistant Professor of Psychiatry. Her passion for bipolar disorder research developed during her BS at Tufts University and postbaccalaureate research at McLean Hospital. She went on to receive her Ph.D. in Clinical Psychology from the University of Illinois at Urbana-Champaign.

As part of her doctorate, Dr. Sperry completed a clinical internship at the Medical University of South Carolina where she focused on co-occurring bipolar disorder, substance use, and sleep disorders. She completed her postdoctoral fellowship in the Department of Psychiatry and Behavioral Sciences at Vanderbilt University Medical Center where she helped lead a large clinical study to better understand severe mental illness.

Dr. Sperry's work has significantly contributed to the understanding and measurement of emotion in bipolar disorder. **She is recognized as an expert in the use of smartphone and wearable devices to study changes in emotions in daily life.**

At U-M, she will start the **Emotion and Temporal Dynamics (EmoTe) Lab**. The mission of her research is to improve early detection and predict the course of illness in bipolar disorder. **The goal of her work is to improve treatments for individuals living with bipolar disorder using a person-centered, measurement approach.** Projects in the EmoTe lab will seamlessly integrate with the Prechter Program and the hallmark Longitudinal Study of Bipolar Disorder. Dr. Sperry has already begun working with key members of the Prechter team including Emily Mower Provost, Ph.D., and Ivy Tso, Ph.D., to submit grants that aim to identify key mechanisms underlying emotion instability in bipolar disorder using innovative technology and computational approaches.

Dr. Sperry is thrilled to be moving to Ann Arbor and looking forward to playing an integral role with the Prechter Program.



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Tobin Ehrlich, Ph.D.

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For Tobin Ehrlich, Ph.D., joining the University of Michigan and the Prechter Program in the Fall of 2020 as a postdoctoral fellow in neuropsychology has been an exciting and rewarding experience. He receives clinical training through the Neuropsychology Section of the Department of Psychiatry and is involved with research through the Prechter Program. This balance of clinical and research training has deepened **his interest in the intersection of mental health and cognitive functioning.**

As a clinical neuropsychologist, Dr. Ehrlich provides evaluations for a variety of individuals who present with cognitive difficulties. **His goal as a neuropsychologist is to understand what cognitive difficulties people are experiencing and how to help mitigate these difficulties.** His interest in cognition is further explored in his research with the Prechter Program. In addition to being an interviewer for the Prechter Longitudinal Study of Bipolar Disorder, Dr. Ehrlich works on several projects utilizing the cognitive data associated with this study.

With his interest in the intersection of mental health and cognition, he has been looking at what factors associated with bipolar disorder contribute to divergent cognitive functioning. **His goal is to help identify risk and protective factors to help promote cognitive health.**

During his free time Dr. Ehrlich enjoys reading, hiking, cooking, and spending time with his pup, Sierra. He has particularly been enjoying exploring the mountain biking trails here in Michigan. He is also looking forward getting to see football and basketball games once the U-M seasons start.



## Michigan Social Cognitive and Affective Neuroscience (MiSCAN) Lab



Ivy Tso, Ph.D.

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This line of investigation is expected to advance understanding of what adds to impulsivity in bipolar disorder and lead to new targeted treatments.

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The MiSCAN Lab, directed by Ivy F. Tso, Ph.D., investigates the thinking and brain-related basis of the ways in which people and groups interact and establish relationships that interfere with social functioning in psychiatric disorders, including bipolar disorder. The goal is to develop new and interesting brain-based ways to improve social interactions and quality of life of people living with psychiatric illnesses.

The MiSCAN lab, in partnership with the Prechter Program, uses a diverse organization of thinking and brain-based methods to identify the interaction of behavior and body processes in bipolar disorder. Work from the lab has shown multiple biological and psychological events (endophenotypes) that may show the differences in bipolar disorder from other psychotic disorders, like schizophrenia.

### THESE INCLUDE:

- Predicting how people living with bipolar will react to social rewards and goals
- The spike in activity during an electroencephalogram (EEG) when someone stops an inappropriate action in pursuit of a goal
- The way the brain processes faces when looking at another person
- Activation of the social thinking areas of the brain

Recent work in the lab includes application of cutting-edge time-frequency analysis — or studying a signal in both time and frequency areas of thinking at the same time in EEG bipolar brain signals. Results — in Hertz (Hz) — showed that changes in face processing

and stopping responses in bipolar disorder may be due to reduced (4-8 Hz) oscillation and lessened simultaneous high-frequency (30-60 Hz) brain activities.

These findings have strong treatment implications.

**Dr. Tso is planning to investigate a new treatment option using non-invasive technology that acts directly upon nerves. This new treatment is called transcranial alternating current stimulation (tACS). This can be programmed to imitate natural brain oscillations and synchronicity at each person's peak frequencies.** If successful, this would provide an innovative, personalized treatment that can improve thinking and daily life for people with bipolar disorder.

Another new line of research in the lab is using mathematical modeling to separate, analyze, and estimate psychological processes behind behavior in bipolar disorder. A recently completed study using this approach showed that risk-taking behavior in bipolar disorder is driven by increased reward sensitivity — but only in those with a history of substance abuse.

The results suggest that substance use in bipolar disorder likely reflects vulnerabilities that add to risky behavior, even when mood symptoms and substance use are in remission. **Dr. Tso and her team plan to develop this work into a unifying computational model explaining behavioral and brain responses in the context of stopping an emotional response.**

This line of investigation is expected to advance understanding of what adds to impulsivity in bipolar disorder and lead to new targeted treatments.





Sue O'Shea, Ph.D.

Better drugs to treat bipolar disorder (BP) are lacking, in part because there have been no living brain cells to study to understand its cellular origins. New research has made it possible to obtain stem cells from patient skin cells. Then, those stem cells are coaxed into forming living brain cells for scientific study. The O'Shea lab used this technique to form astrocytes called glial cells (a type of non-neuron brain cell that protects and supports neuronal cells). One way that glial cells perform their supportive role is by releasing packets of growth factors (exosomes) that are taken up by neurons (**Figure 1**).

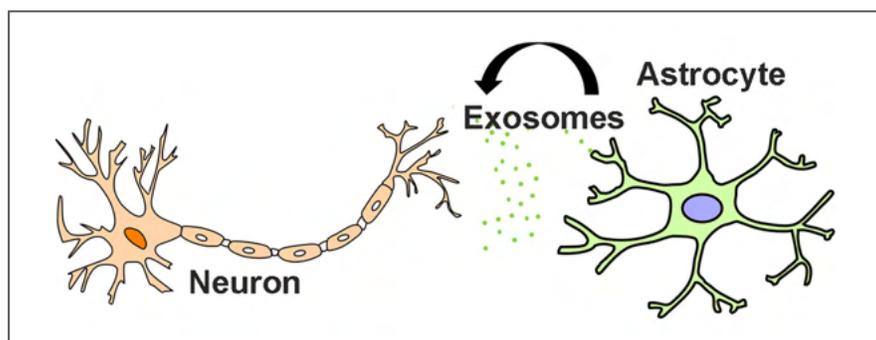


FIGURE 1: Astrocyte, Exomes, and Neuron Cells

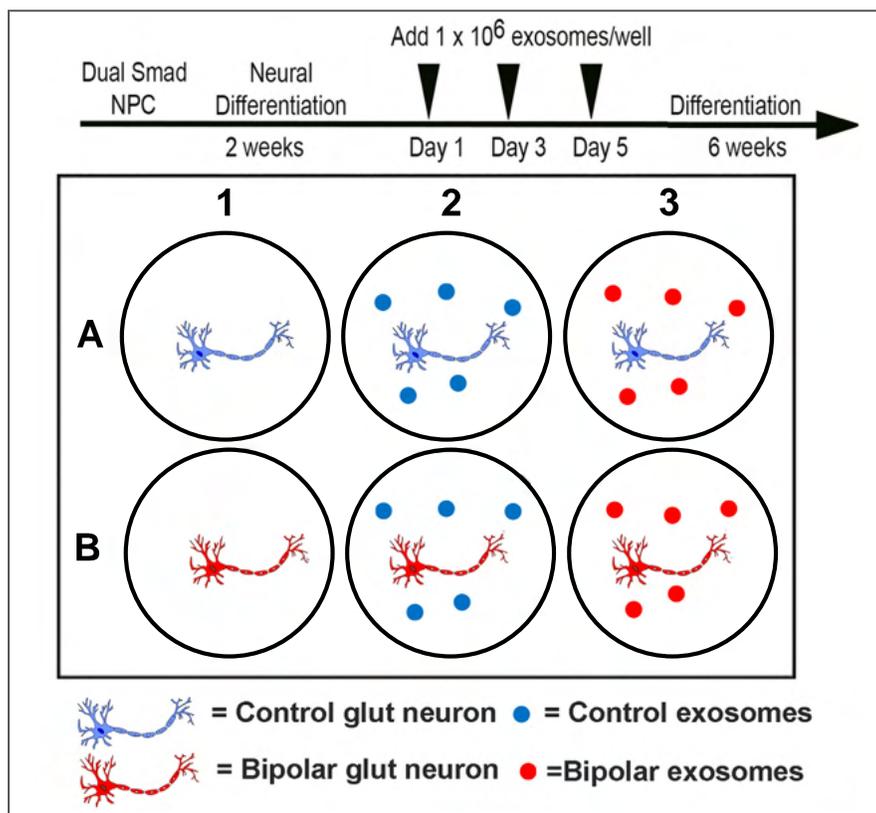


FIGURE 2: Tissue Culture Dish diagram

The O'Shea Lab is optimistic about new findings from several recent studies in which they have investigated the effects of exosomes on brain function. In the first, they obtained exosomes from the culture medium of BP and Control (C) astrocytes and added them to brain cells as illustrated in the diagram of a tissue culture dish (**Figure 2**).

**STUDY 1. (Figure 2)** The lab found that untreated C neurons (A1 left) had more electrical connections than untreated BP neurons (B1). If C exosomes were added to BP neurons (B2), the BP neurons were healthier and had more connections, while adding exosomes from BP astrocytes to C neurons (A3) damaged the control neurons. **This strongly suggests that BP astrocytes may produce toxic factors while C astrocytes produce protective factors.**

**STUDY 2.** Finally, to begin to identify the specific factor(s) responsible for the differences between the C and BP exosomes, the lab collected BP and C exosomes and studied what proteins were in each sample. 399 different proteins were identified. Many of the distinguishing proteins were found to be associated with psychiatric disorders. Additionally, some of the proteins are known to be associated with cellular communication and movement. Finally, several proteins connected to neurodevelopmental and neurodegenerative diseases were identified in the BP samples.

**Overall, this work indicates that:**

- Exosomes derived from C astrocytes contain factors that promote neuronal development and function.
- Exosomes derived from BP astrocytes contain factors that impair neuronal function and development.
- The lab now has several valid tests to identify specific proteins that may cause these effects.

In the coming year, the lab will investigate the blood of individuals who gave skin samples to obtain the iPSC brain cells to see if the same proteins are present. If so, the proteins could serve as early markers of bipolar disorder, helping with diagnosis and earlier treatment interventions.

**The O'Shea lab is open now – please don't hesitate to call and arrange a visit!**

## Using Cell Phones to Identify Mood Changes

## PRIORI PROGRAM UPDATE

The Predicting Individual Outcomes for Rapid Intervention (PRIORI) project is entering a new phase! As with most research projects, The Prechter Program has learned that things are more complicated than initially thought. The initial strategy was based on what has been learned from people who live with bipolar disorder. Many times, family members say: "something is wrong – I can hear it in his/her voice." Over the past several years, the Prechter Program has searched for patterns in speech that associate with mood states.

Several features of speech are associated with the mood of an individual when speech is sampled during mood assessments given by the research team. **The challenge is finding a pattern over time that can be used to predict with reasonable accuracy whether a person is headed for an episode.**

What happens when a close family member picks up on a cue from someone in difficulty? When asked, the family member often notes that it was the way the person responded to a particular theme in a discussion or argument – or the way they spoke when reflecting on a specific event. People with the bipolar condition have moods and emotions that can be unpredictable and reactive. In many cases, it is a stressful moment that triggers the expression of moods and emotions. Speech is the conduit.

The PRIORI program has learned that speech and expressions vary considerably, and the context of the interaction is important, if not critical. How one talks with a trusted loved one is often significantly different from a

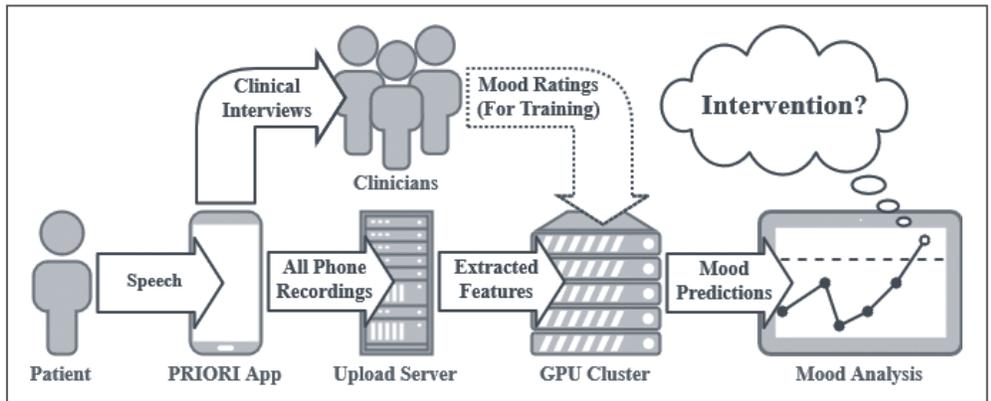


DIAGRAM: The PRIORI app and mood prediction pipeline

conversation with a repairman. What is going on in a person's environment influences how someone reacts.

**Over the past year PRIORI has made significant changes to gauge this critical context thanks to generous support by the Baszucki Brain Research Foundation.**

The PRIORI app has been adapted to sample the ambient audio around the person and process the features of the person's speech.

This is in relation to the quality and character of the prevailing features of the audio/noise in the background. Processing is streamlined and only the relevant statistical measures are stored for further analysis. Rigorous security measures are in place and, as always, the program is only operating with the patient's consent. The goal is to determine the minimal set of features, relevant to bipolar, that will serve as a measure of risk for an episode of mania or depression.

## Prechter-Tam Bipolar Seminar Series

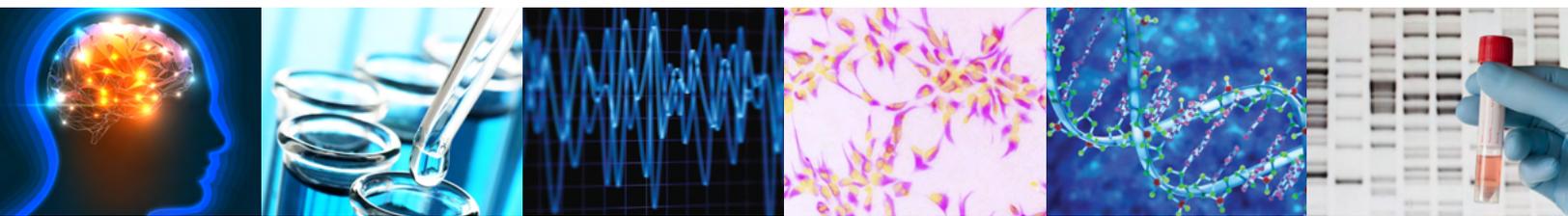


The Prechter Program now has **a new research science series – The Prechter-Tam Bipolar Seminars.** The seminars will give Prechter faculty and staff a space to share their research with peers and gain new perspectives to help guide their work.

The first seminar, "Characterization of Stem Cell-Derived Exosomes and Their Impact on Recipient Cells," was held on May 20, 2021. **The launch was a success with 60 attendees from 5 different countries, including the U.S.**

The name of the seminar honors the extraordinary commitment of the family of Heinz Prechter and of the Richard Tam Foundation to a shared goal of personalized and evidence-based treatments for bipolar disorder that will enable every individual with the illness to lead a healthy and productive life.

You can watch the recording of this seminar by visiting [michmed.org/axDbA](http://michmed.org/axDbA)



## Current Heinz C. Prechter Bipolar Research Program Studies

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Longitudinal Study of Bipolar Disorder

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Identifying Subtypes of Bipolar Disorder Using Longitudinal Mood Trajectories

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Bipolar Longitudinal Outcomes Measures Study (BLOOM)

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Electrophysiological Signature of Affective Response Inhibition in Bipolar Disorder: Development of a Biomarker

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Sleep Across Seasons Study (SASS)

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Mood Lifters for Bipolar Disorders

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Longitudinal Voice Patterns in Bipolar Disorder (PRIORI)

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Predicting Suicide: A longitudinal Analysis of Speech Patterns in a High-risk Sample

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Mining Social Media Data: Automated Timeline Extraction

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Integrated Apps for Medicaid Consumers (PRIORI and LIFE GOALS)

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Modeling Mood Course to Detect Markers for Effective Adaptive Interventions

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Dynamics of Data Driven States in Bipolar Disorder

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Biological Rhythms in Bipolar Disorder

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Offspring of Parents with Bipolar Disorder

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Multi-Modal Assessment of Gamma-aminobutyric Acid (GABA) Function in Psychosis (GABAmech)

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Neuromodulation Plus Cognitive Training to Improve Working Memory Among Individuals with Serious Mental Illness

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Phenotypes of Executive Functioning and Their Longitudinal Trajectories in Bipolar Disorder

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Low Rate of Performance Validity Failures During Cognitive Testing Among Individuals with Bipolar Disorder

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History of Migraines and Lithium Response in Bipolar Disorder I

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Impact of Cannabis and Alcohol Use Disorders on Clinical and Cognitive Outcomes in Bipolar Disorder

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Personality Traits and Dimensions in Bipolar Disorder

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Clinical and Personality Characteristics of Neuropsychological Clusters in Bipolar Disorder

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Employment Stability in Bipolar Disorder

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Neuropsychological Trajectories Over Ten Years in Bipolar Disorder

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Sleep Quality and Neuropsychological Functioning in Bipolar Disorder

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Cellular and Molecular Neurobiology of Mental Health—Induced Pluripotent Stem Cell (iPSC) Modeling

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The Function of Supporting Cells in the Nervous System in Bipolar Disorder

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The Balance Between Excitatory Signaling and Inhibitory Signaling in the Brain in Bipolar Disorder

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Differentiating Excitatory (Glutamatergic) Forebrain Neurons from Individuals with Bipolar and Controls

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Brain Organoids: Study of the Bipolar Brain

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Astrocytes in the Bipolar Brain

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Developing a Neural Network Model of Altered Reward Processing in Bipolar Disorder

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Neural Oscillatory Basis of Altered Gaze Processing in Bipolar Disorder

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A Bayesian Computational Model of Risk-Taking in Bipolar Disorder

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Neural Mechanisms of Eye Gaze Perception in Bipolar Disorder

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The Ank3 Variant in Bipolar Disorder

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Amy Kilbourne, Ph.D.

## Life Goals Collaborative Care for Bipolar Disorder

For the past 20 years, Amy Kilbourne, Ph.D., Celeste Liebrecht, LMSW and Mark Bauer, M.D., of Harvard Medical School, have implemented innovative models of care for bipolar and other mood disorders, especially in underserved communities.

**This work is now informing the next generation of evidence-based care implementation through Learning Health Systems (LHS).** Despite the availability of treatments, few with bipolar disorder receive adequate quality of care.

This leads to substantial functional impairment and premature mortality — especially from suicide and cardiovascular disease. LHS helps patients, providers and health systems improve outcomes through formation of a learning community that generates comprehensive data to gather knowledge and implement care improvements. This will ultimately inform ongoing inquiry and discovery that moves the needle on high-quality, equitable, patient-centered care.



Celeste Liebrecht, LMSW

## Building a Learning Health System

**Dr. Kilbourne's Life Goals Collaborative Care (LGCC) model aligns care management with self-management and clinical decision support to create an LHS.** Several randomized trials showed that LGCC improves both physical and mental health outcomes in persons with mood disorders. Groundbreaking research on LGCC in the U.S. Department of Veterans Affairs led to the Life Goals toolkit and mobile app. Currently, Dr. Kilbourne is implementing LGCC across Michigan and Maryland with Gail Daumit, Ph.D. (Johns Hopkins University) funded by the NIH. The Michigan collaborative team includes Celeste Liebrecht, LMSW, Brianna Osorio, MS, Department of Learning Health Sciences (DLHS), Shawna Smith, Ph.D., School of Public Health, and Daniel Almirall, Ph.D., Institute for Social Research. Dr. Kilbourne is working closely with the Prechter Program to integrate a learning health systems approach.

## Expanding the Reach of the Prechter Program

## INTERNATIONAL COLLABORATIONS

It has been said that no country controls ideas and this is especially true within academic research. New ideas come when one interacts with people from diverse backgrounds. It is through diversity of thought that one begins to see connections never seen before. Such has been the case within the Prechter Bipolar Research Program this past year as three large international collaborations have started in earnest. The goal of these collaborations is the advancement of global science in bipolar disorder and creating long-lasting collaboration networks for Prechter Program members.

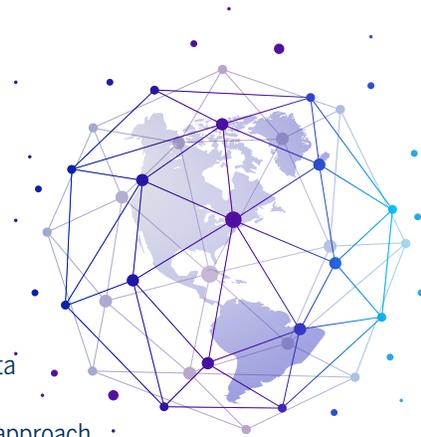
Most notably, the **Global Bipolar Cohort (GBC)** — a collaborative where researchers from 13 institutions in 9 countries have continued to participate monthly in discussions since October 2019. These monthly discussions have led to several manuscripts and grant applications. The first research project they worked on shows depression severity in those with bipolar can predict cognitive functioning. This finding was almost universal over the participating sites. The second, using longitudinal trajectories of functioning in individuals with bipolar aims to provide insight into social and occupational impairment. **Both studies creatively use data in the collective aggregate eliminating long and arduous data sharing regulatory approvals. Despite this, these studies are still able to**

**cross cultural boundaries to understand the disorder from a human perspective.**

Integration of this international data is key to research aims and is only reached by taking this large-scale approach.

Two additional international collaborations have developed: The **Bipolar Research in Sleep and Circadian Rhythms Collaborative (BRSCr)** and the **Trauma Research in Bipolar Disorder (TRiBe)**. These two areas have significant effect on a person's life story and daily functioning. Each of these studies have international members who will creatively analyze data across borders. Throughout, the collaboration has maintained and delivered upon the vision to engage early to mid-stage investigators.

GBC, TRiBe and BRSCr collaboratives bring together international researchers who share a passion for science in psychiatry. Members share ideas and experiences and combine perspectives to understand the complexities of bipolar disorder in a cross-disciplinary manner. Working in these groups will provide findings beyond what one team could achieve alone.



## 20 YEARS Building Bipolar Research



JULY 6, 2001

Heinz C. Prechter falls victim to suicide at age 59.

*I feel that I have made a little bit of a difference, and when it really comes down to it, that's what we live for — to make a difference in this world."*

NOVEMBER 2001

Waltraud "Wally" Prechter and her children establish the **Heinz C. Prechter Fund for Manic Depression** to promote scientific collaboration and medical research focused on the genetics and the intricacies of bipolar disorder.

APRIL 2002—JULY 2003

President George W. Bush appoints **Wally Prechter** to serve on the **New Freedom Commission on Mental Health** to help improve the mental health care system for all Americans.

MAY 2002

**Wally Prechter** provides testimony before **U.S. Congress** urging a 5% increase in federal funding for the **National Institute of Mental Health** and bipolar research.

MAY 2003

**Wally Prechter** testifies before the **Michigan Senate Health Policy Committee** seeking parity in **health insurance coverage for mental illness**.

JUNE 2003

**Wally Prechter** receives the highest honor in bipolar research, the **Mogens Schou Award from the International Society for Bipolar Disorders (ISBD)**, for her efforts to advance breakthrough medical research and for her work to combat the stigma of mental illness.

DECEMBER 2003—OCTOBER 2004

**Wally Prechter** serves as **Co-chair of the Michigan Mental Health Commission** with Pat Babcock under Governor Jennifer Granholm.

MAY 2004

**Heinz C. Prechter Fund for Manic Depression** transfers to the **University of Michigan Health System** and becomes the **Heinz C. Prechter Bipolar Research Fund** at the **University of Michigan Depression Center**.

JULY 2005

Launch of the **Prechter Bipolar Genetics Repository**, the first of its kind in the nation. Searching for the **genetic underpinnings of bipolar disorder**, the repository is a **collaborative effort** between the University of Michigan, Weill Cornell, and Stanford.

FEBRUARY 2006

**First research participant** enrolled in the flagship **Longitudinal Study of Bipolar Disorder** (study of many individuals over many years).

JUNE 2009

New **collaboration** with the **U-M Department of Psychology on ERP** (Event-Related Brain Potential) to examine the relationship between levels of impulse control and suicidal behavior.

FEBRUARY 2011

**First research participant** to complete 5-year follow-up in the flagship **Longitudinal Study of Bipolar Disorder**.

MARCH 2011

Launch of the stem cell project "**Cellular and Molecular Neurobiology of Mood Disorders**," whose goal it is to establish **stem cell lines from skin cells** taken from **individuals with bipolar disorder** and study details of molecular mechanisms. See more information about this project on page 10.

JUNE 2011

**PGBD project** (Pharmacogenomics of Mood Stabilizer Response in Bipolar Disorder) launched to **identify genes associated with good response to two commonly used mood stabilizing agents — lithium and valproate**.

MARCH 2014

**Prechter stem cell lab** uses skin from **people with bipolar disorder** to derive the **first-ever stem cell lines specific to the condition** and finds specific differences from cells derived from people without bipolar.

MAY 2014

**1,000th participant** registers for the **Heinz C. Prechter Longitudinal Study of Bipolar Disorder**.

MARCH 2016

PBS documentary about bipolar disorder "**Ride the Tiger, — A Guide Through the Bipolar Brain**" is released on Detroit Public Television, featuring many Prechter Program experts.

JULY 2016

Prechter Program **participates for the first time** at the **NAMI National Convention** — as speakers and exhibitors.

## 20 YEARS Remembering Heinz

Dear friends:

It has been 20 years since Heinz passed.

The Heinz C. Prechter Fund for Manic Depression was founded in November 2001. Our initial mission was the gathering and distribution of funds for bipolar research. We are now so much more! In 2004, we became the Heinz C. Prechter Bipolar Research Program at the University of Michigan Eisenberg Family Depression Center, the largest program of its kind in the nation.

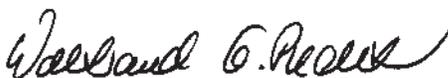
Today, we have many reasons to celebrate: Our flagship longitudinal study with close to 1,400 participants, 36 distinct and unique investigative studies using multi-disciplinary approaches to more accurately predict the course of bipolar illness, as well as best treatment options, the pluripotent stem cell work, which helps us better understand how development in utero can result in bipolar disorder, the PRIORI app study, which analyzes an individual's voice patterns in order to detect early-warning signs in upcoming changes in mood — to name just a few.

I salute our teams, working diligently under the great leadership of Melvin McInnis, M.D., FRCPsych, for their participation on a national level, as well as internationally, to establish a world-wide research collaborative. These invaluable efforts have resulted in the creation of large data sets that will lead to new findings!

So much has been accomplished over these last twenty years. So much more is yet to be discovered to “make a difference in people's lives.” This was Heinz's motto. He would have wanted us to continue to be fearless, think outside the box, and maintain a sense of urgency in attacking this illness from all directions.

Thank you from the bottom of my heart to our dedicated team of researchers and research participants and to all our contributors for your support.

In gratitude,



Waltraud E. Prechter  
BA, Ed, U-M School of Education



SEPTEMBER 2017

**“The S Word” suicide documentary is screened on U-M campus** with the filmmaker present in a panel discussion with Prechter Program researchers.

OCTOBER 2018

**Prechter Program experts and a research participant lead a Q&A** after the performance of the hit musical **“Next to Normal”** at the Crosswell Opera House in Adrian, Michigan.

MARCH 2019

**Wally Prechter** recognized as **Special Honoree at the 2019 NAMI Michigan Honors Gala.**

OCTOBER 2019

Inaugural gathering of the **Global Bipolar Cohort**

AUGUST 2020

**National Alliance on Mental Illness (NAMI)** partner with the Prechter Program to support **international collaboration.**

February 2021

The **first participant** reaches **15-year milestone** in the **Longitudinal Study.**

MAY 2021

**Prechter-Tam Seminars** series is inaugurated.

JUNE 2021

Prechter Program hosts the virtual opening night of **ENERGY: Brain Health Arts.**

20 YEARS

15th Annual

# Prechter Lecture

*Reforming and Transforming Our Broken System on Serious Mental Illness*

## Virtual Event

Wednesday, October 27

7:00 P.M. – 8:30 P.M.

## Featuring Norman J. Ornstein

Political scientist, contributing author for  
*The Atlantic* magazine



"We now know that there are many ways of providing wraparound services for people in an outpatient setting that can help get their lives back on track, it is not perfect, but it works. We need to be putting more investment into these kinds of services."

Visit [michmed.org/R1R9z](https://michmed.org/R1R9z) for more information & to register!

Featured talk by Norman J. Ornstein

Panel discussion about the present & future of mental health policy

Q&A with the keynote speaker & panelists

1.5 Continuing Education Credits for Social Workers are available

Questions? Contact Amanda at [alhudeck@umich.edu](mailto:alhudeck@umich.edu)

For information about supporting the Prechter Program or to make a gift, please contact: Lisa Fabian, Senior Associate Director, Mental Health Programs at [fabianl@umich.edu](mailto:fabianl@umich.edu) or 734-763-4895.

### 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.

### HEINZ C. PRECHTER BIPOLAR RESEARCH PROGRAM ADVISORY BOARD

|                             |                       |
|-----------------------------|-----------------------|
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[PrechterProgram.org](https://PrechterProgram.org)

**f** PRECHTERBIPOLARRESEARCH

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To sign up to receive our yearly printed newsletter or our quarterly E-newsletter, please contact: Amanda Hudeck at [alhudeck@med.umich.edu](mailto:alhudeck@med.umich.edu) or 734-232-0456.

If you or anyone you know are experiencing thoughts of **suicide**, contact the **Crisis Text Line** [Text HOME to 741741 to connect with a Crisis Counselor] or call the **National Suicide Prevention Lifeline** [1-800-273-TALK (8255)].

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