Yale
Center for Brain & Mind Health

Annual Report 2024

Contents

Mission Statement

The Yale Center for Brain and Mind Health strives to be a beacon of innovation, championing transformative clinical and translational neuroscience research for the betterment of society. We cultivate inclusivity and collaboration, uniting faculty and trainees across disciplines to passionately pursue scientific discovery. Rooted in community, we actively forge connections with the health system, academia, and the public to identify pressing needs and catalyze real-world change. We address today's urgent challenges and envision and shape a healthier tomorrow for all.

Message from the Directors

Dear Colleagues,

Earlier this year, we witnessed a solar eclipse crossing the contiguous United States. As we all looked to the sky at this as tronomical wonder, it was a powerful reminder that even though we looked through different filters, we all face a shared future together.

As we mark the second anniversary of the Yale Center for Brain and Mind Health (CBMH), we also look together at a shared future, one in which clinical and translational neuroscience research has direct impact on patient care. We believe that CBMH's mission of advancing clinical and translational neuroscience is an investment that will lead to ground-breaking sci entific discoveries. We have been empowered by the unwavering support of Yale's leadership, as our work is considered a key component of the University Science Strategy's investment in neuroscience. We know that the diverse strengths of our members will help us achieve our collective goals.

This year's annual report focuses on the work that you have done. Together, teams of researchers made strides to uncover the secrets of the brain, from understanding the basic mechanisms of depression to using focused ultrasound to restore human consciousness. In the stories compiled in this report, you will read in detail about work done by our members who are expanding our understanding of neurodegenerative disease, about community-level stroke prevention, about CBMH's support for a rising generation of scientists who will one day lead the field, and much more.

One of our most important achievements in 2024 was hiring a new faculty member who will enhance research in child and adolescent suicide prevention. At CBMH, we are taking an upstream view of this devastating national crisis. We recognize the ongoing investment from Dean Nancy Brown and the School of Medicine, who have made a commitment to support interdisciplinary research focused on preventing and easing the suffering associated with neurological and psychiatric conditions.

We're thrilled to share more about our work with you. Together, we're dedicated to making clinical and translational neu roscience research a leading initiative at Yale University and an essential resource for our nation. Working alongside the members of CBMH, we are continually inspired by your expertise and passion, and we are deeply grateful for your enthusi astic engagement. We welcome your insights and encourage you to share your feedback and ideas.

Best wishes for a healthy and productive academic year.

CBMH directors: Eyiyemisi Damisah, MD, Assistant Professor of Neurosurgery and Neuroscience; James McPartland, PhD, Harris Professor in the Child Study Center and Psychology; Christopher Pittenger, MD, PhD, Elizabeth Mears and House Jameson Professor of Psychiatry; Kevin Sheth, MD, Professor of Neurology and Neurosurgery; Serena Spudich, MD, Gilbert H. Glaser Professor of Neurology

CBMH Community Page

Member News: Celebrating the Accomplishments of the CBMH Members

CBMH recently surveyed members regarding their activities in the past year; below is some of what we learned from the responses that we received.

Publications

Amy Arnsten, Neuroscience *"Evidence of interneuronal traf ficking and early-stage neurodegeneration" Alzheimer's & Dementia*

Helene Benveniste, Anesthesiology *"VEGF-C prophylaxis favors lymphatic drainage and modulates neuroinflammation in a stroke model" Journal of Experimental Medicine*

Angelique Bordey, Neurosurgery and Cellular & Molec ular Physiology *"Reducing filamin A restores cortical synaptic connectivity and early social communication following cellular mo saicism in ASD pathways" Journal of Neuroscience*

Richard Carson, Radiology & Biomedical Engineering *"Synaptic density patterns in early Alzheimer's disease assessed by Independent Component Analysis are related to diminished cogni tive performance" Brain Communications*

Amanda M. Dettmer, Child Study Center *"Nonverbal Face-To-Face Interactions in Macaques and Humans: A Translational Pilot Study" Developmental Psychobiology*

Thomas Fernandez, Child Study Center & Psychiatry *"Rare de novo damaging DNA variants are enriched in atten tion-deficit/hyperactivity disorder and implicate risk genes" Nature Communications*

Adam de Havenon, Neurology *"Endovascular Treatment of Acute Ischemic Stroke After Cardiac Interventions in the United States" JAMA Neurology*

Ilan Harpaz-Rotem, Psychiatry *"Unveiling the Structure in Mental Disorder Presentations" JAMA Psychiatry*

Walter Kernan, Medicine *"Impaired mobility and MRI mark ers of vascular brain injury: Atherosclerosis Risk in Communities and UK Biobank Studies" BMJ Neurology Open*

Renato Polimanti, Psychiatry *"Gene Discovery and Biologi cal Insights into Anxiety Disorders from a Multi-Ancestry Large-Scale Genome-wide Association Study" Nature Genetics*

Dustin Scheinost, Radiology & Biomedical Imaging *"The brain structure, inflammatory, and genetic mechanisms mediate the association between physical frailty and depression" Nature Communications*

Steven Schiff, Neurosurgery *"Paenibacillus infection among infants with post-infectious hydrocephalus in Uganda: a case-con trol study" The Lancet Microbe*

Awards and Honors

2024 IEEE Marie Skłodowska-Curie Award, IEEE Nuclear and Plasma Sciences Society *Richard Carson, Radiology & Biomedical Engineering*

2024 Mood Disorders Award, American College of Psychi atrists *– Hilary Blumberg, Psychiatry*

American Society of Clinical Investigators (ASCI), Young Physician-Scientist Award *Youngsun Cho, Child Study Center & Psychiatry*

Harvey and Kate Cushing Professor of Neurosurgery *Steven Schiff, Neurosurgery*

Burroughs Wellcome Fund NextGen Pregnancy Initiative Awardee *Kieran O'Donnell, Child Study Center & Department of OBGYN*

Election to Association of American Physicians *David Fiellin, Internal Medicine*

Election to the Association of American Physicians *Flora Vaccarino, Child Study Center*

Neuroscience Research Fund (FRN) Project: Neurovascu lar monitoring *– Jean Leon Thomas, Neurology*

Steven M. Southwick Professor of Psychiatry *Marc Poten za, Psychiatry, Child Study Center, Neuroscience*

Targeted Genome Editor Delivery (TARGETED) Phase 1 Challenge Award, National Center for Advancing Trans lational Sciences, NIH *– Jiangbing Zhou, Neurosurgery*

Yale Anthony N. Brady Professorship of Anesthesiology *Helene Benveniste, Anesthesiology*

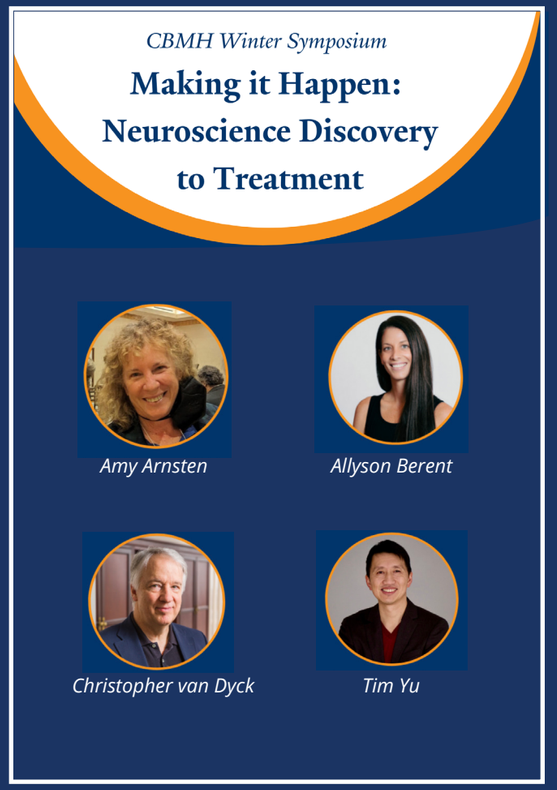
Membership Feedback

Our survey also requested suggestions of how CBMH can best foster high impact clinical and translational neuro science among our members. We heard that CBMH mem bers appreciate the chance to connect with others, whether through in-person meetings, small group sessions, or social events that promote informal discussions and networking. Expanding opportunities for collaboration in fields such as neuroimaging and biobehavioral pain management is con sidered highly valuable. Continued institutional backing as well as securing support from donors, especially for high-risk ideas, is considered vital. Increasing grant opportunities for collaborative projects, including support specifically aimed at pilot funding for junior faculty. Members also suggest developing co-mentorship for graduate students and post docs, creating disease-focused discussions, and facilitating interdisciplinary connections which will benefit both trainees and their PIs.

Highlights of the Year

Winter Symposium

In December we held the first annual CBMH Winter Sympo sium, entitled "Making it Happen: Neuroscience Discovery to Treatment." The symposium showcased impactful work that successfully bridged the gap between neuroscience discovery and meaningful patient outcomes. The event featured two scientific leaders from the Yale community, Drs. Amy Arnsten and Christopher van Dyck. Additionally, we were honored to host two visiting colleagues. Dr. Tim othy Yu, an interventional geneticist at Boston Children's hospital, delivered a keynote address on the "N of 1" trial concept, which has gained global attention. We also wel comed Dr. Allyson Berent, the Chief Scientific Officer for the Foundation for Angelman Syndrome Therapeutics. Her compelling story provided an inspirational model for trans lational research.



CBMH Monthly Conversations

In December 2023 we began a new monthly discussion series, the CBMH Conversations. Each month we pick a topic that is of interest to multiple research groups across campus and gath er to discuss it. We seek topics that are narrow enough for a coherent Conversation, but broad enough that different re searchers in our community may not be aware of each others' work. These discussions are opportunities for us to educate one another and to form new partnerships and collaborations. We aim to seed each Conversation with local experts who can bring deep knowledge to the discussion, but all are welcome.

We didn't know if this was going to work we're all busy people, after all, and carving out an hour for unstructured discussion about a broad topic that may be outside our primary area of interest can feel like a big ask. But the response has been en thusiastic, attendance has been great, and discussion has been vigorous. At least one of these Conversation led to an ongoing discussion series, and a number of new potential collabora tions have been created. We are excited to continue this series in the coming year.

CBMH Conversation topics during 2023-2024 are listed below. We welcome suggestions for new topics for the coming year, and any other ideas you may have about how to further enrich such collaborative interactions in our community.

Topic	Date
Social Neuroscience	Dec 2023
Polygenic Risk Scores	Jan 2024
Synaptic Density Imaging	Feb 2024
Developmental Stress	March 2024
Consciousness and the Self	May 2024
Microglia	June 2024

Highlights of the Year

Major New Grants

CBMH seeks to enhance clinical and translational neuroscience across our community. And as we all know, research takes money! A key metric of success is the ability of our members to secure new grants to support their work – in particular, the development of new large, collaborative projects that grow out of CBMH initiatives. We are pleased to announce early successes of this effort.

A new grant from the Wellcome Trust brings together investigators from Neurosurgery and Psychiatry to probe how the brain encodes anxiety, and how this encoding is dysregulated in individuals with anxiety disorders. Dr. Eyiyemisi Damisah will record from the amygdalae and connected cortical structures in patients with epilepsy, about 30% of whom suffer from comorbid anxiety disorders. Dr. Alfred Kaye will model this anxiety circuitry in mice and probe causal relationships within it. Dr. Matthew Girgenti will molecularly profile human and mouse amygdalae, characterizing the cellular constituents of the implicated circuitry. Drs. Ilan Harpaz-Rotem and Robert Pietrzak will support clinical and statistical aspects of the work, respectively. The whole project is headed by Dr. John Krystal, Chair of Psychiatry. This project grew out of a 2023 CBMH Pilot Grant to members of the same group. We are excited to see this work progress.

The Yale IMPACT-MH project, a large new contract from the National Institute of Mental Health, is led by CBMH members Drs. Sarah Yip, Godfrey Pearlson, and Chris Pittenger. It will bring together a team of 20 collaborators from Psychiatry, the Child Study Center, Psychology, and Biostatistics to recruit a large cohort of patients with a wide range of mental health symptoms. These participants will be characterized using both conventional and novel strategies incorporating computational methods and AI analysis of their own descriptions of their symptoms and their lives, and will then be followed over two years. The project seeks to identify new ways to categorize mental illness and to identify predictors of which patients are going to do well, and which will require intensive support. The IMPACT-MH project brings together Yale investigators focused on a wide range of diagnoses for the first time and is sure to generate a wealth of new collaborations.

Back row to front row, left to right: Drs. Robert Pietrzak, Matthew Girgenti, Alfred Kaye, Drs. Ilan Harpaz-Rotem, John Krystal, Eyiyemisi Damisah

Godfrey Pearlson

Christopher Pittenger

Sarah Yip

Impact MH Project Lead Directors

Yale Meets with Senator Blumenthal

Sen. Richard Blumenthal (D-CT) visited the Yale School of Medicine (YSM) on June 26, to engage in discussion and better understand the impact and importance of neuroscience research at Yale as Congress starts deliberating the FY 2025 budget. He toured neuroscience labs and participated in a roundtable with YSM researchers.

The visit came a day before the House Appropriations Committee's subcommittee approved a preliminary bill to provide level funding for NIH but cut $1 billion from ARPA-H, possibly reallocating it among NIH institutes. This reallocation could impact the BRAIN initiative, which has already seen a $278 million decrease in funding from FY 2023, affecting both new and existing grants at Yale.

Michael Crair, PhD, Vice Provost for Research at Yale University, emphasized the critical state of neuroscience research, highlighting the potential setback if NIH funding is reduced. During his visit, Blumenthal toured the shared lab of Michael Higley, MD, PhD, and Jessica Cardin, PhD, at the Wu Tsai Institute.

Blumenthal then joined Nancy J. Brown, Dean of YSM, and other neuroscience faculty for a discussion on NIH funding's importance. Participants included CBMH directors Serena Spudich, Kevin Sheth, and Christopher Pittenger, together with Lauren Sansing, Nenad Sestan, Anthony Koleske, Stephen Strittmatter, and David Hafler. They discussed their NIH-funded projects and the potential impact of budget cuts.

Blumenthal stressed the importance of sustaining NIH funding to avoid missing significant opportunities in health advancements, committing to advocate for increased federal investment inspired by his visit to Yale.

Pictured: Dean Nancy Brown, Senator Blumental, and CBMH Co-Director Serena Spudich

CBMH Faculty Hire

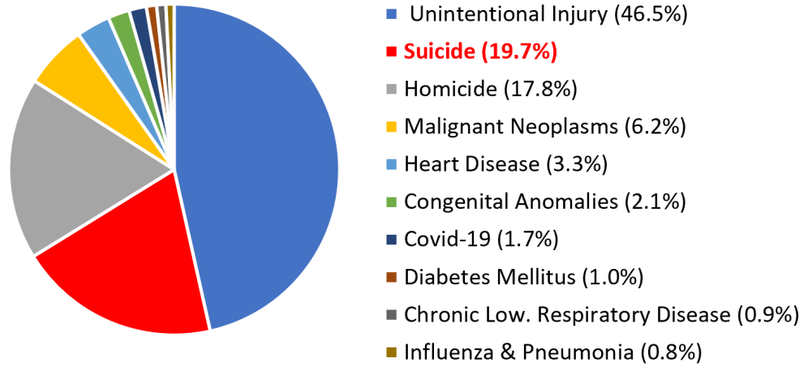
Dr. Christine Cha is an incoming Associate Professor at the Yale Child Study Center and an inaugural CBMH core faculty member. She previously held a tenured Associate Professor position in the Clinical Psychology program at Teachers College, Columbia University, and brings more than 18 years of experience studying youth suicide risk and prevention. Her research program focuses on ways to assess, predict, and prevent suicide and self-harm early in life and has been funded by the National Institute of Mental Health, the Department of Defense, and the American Foundation for Suicide Pre vention. Her lab uses behavioral and self-report mea sures across settings ranging from the laboratory to the emergency department to adolescents' everyday lives via ecological momentary assessment. Her projects have introduced novel tools (e.g., reaction times, facial action) intended to help clinicians identify high-risk patients. Dr. Cha's work has also begun to clarify the cognitive profile of suicidal youth (e.g., mental representation of future life and death) to uncover modifiable cognitive intervention targets. She is eager to forge collaborations across Yale University to pursue future research that improves suicide assessments for clinical use; creates new and augments existing interventions; identifies optimal intervention win dows; and informs population-level suicide prevention strategies. As a firm believer that multidisciplinary research yields impactful innovation, Dr. Cha is thrilled to join CBMH and help accelerate the pace and scale at which health solutions can reach suicidal youth.

To learn more:
https://medicine.yale.edu/brain-mind-health/news-article/youth-suicide-is-on-the-rise-yale-aims-to-save-lives/

The Center for Brain & Mind Health (CBMH) is grateful for the expertise of the Yale faculty who served on the search committee. Their knowledge and deep understanding of population-level mental health in youths and young adults were highly relevant to this effort. They conducted a broad, open, and equitable search to ensure the best possible outcome.

The Center conducted an open faculty search, and the committee's involvement was crucial in identifying the best candidate. As part of the search process, committee members reviewed applications and participated in interviews.

Leading Causes of Death in US-Based Youth



Note. Based on CDC data from youth (5-25 years) in the United States between 2018-2022. Citation: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Web-based Injury Statistics Query and Reporting System (WISQARS) [online]) August 13, 2024. Available from URL: www.wisqars.cdc.gov

Search Committee	
Nii Addy	Psychiatry and Cellular & Molecular Physiology
Uche Aneni	Child Study Center & Biomedical Informatics & Data Science
Deepa Camenga	Emergency Medicine & Pediatrics
Derrick Gordon	Psychiatry and Public Health
Kimberly Hieftje	Pediatrics
Joy Kaufman	Psychiatry
Terika McCall	Public Health and Biomedical Informatics & Data Science
James McPartland	Child Study Center & Psychology
John Pachankis	Public Health & Psychiatry
Kim Smolderen	Cardiology & Psychiatry
Kevin Sheth	Neurology & Neurosurgery
Sam Wilkinson	Psychiatry

CBMH Post-Doctoral Fellows Corner

Cellular and Molecular Mechanisms and Novel Therapy in Porcine Stroke

Post Doc: Martina Glavan

Mentors: Drs. Nenad Sestan, Jiangbing Zhou

Departments of Psychiatry, Neuroscience, Pharmacology, and the Child Study Center

Martina is dedicated to developing more effective treatments for ischemic stroke, a leading cause of disability worldwide. Despite the critical need, there have been no new pharmacological treatments approved for stroke in nearly 3 decades. She works with Professors Sestan and Zhou using a porcine model that mimics human stroke. Her project involves advanced imaging and molecular techniques to understand stroke's impact on the brain over time. In her first year, Martina focused on identifying spatial cellular and molecular changes during stroke. She analyzed MRI data to locate injured areas and track ischemic lesion progression, guiding subsequent histopathological and multiomic analyses. This multidisciplinary approach aims to pinpoint key targets for potential therapies. Martina's research seeks to uncover novel insights into stroke biology, potentially laying the groundwork for innovative therapies and significantly enhancing stroke treatment options.

Comprehensive Functional Analysis of Copy Number Variants in Major Depressive Disorder

Post Doc: Diana Nuñez-Rios

Mentors: Drs. Janitza Montalvo-Ortiz, Thomas Fernandez

Departments of Psychiatry, Neuroscience, Pharmacology, and the Child Study Center

Diana, a postdoctoral associate in the Montalvo-Ortiz Lab, investigates copy number variants (CNVs) in Latin American populations. CNVs are changes in the DNA that can lead to the loss or gain of genetic material, contributing to diversity among populations and potentially increasing the risk of diseases like depression. Existing genetic research is predominantly Eurocentric, necessitating studies in Latin American groups. Diana's project targets two areas: CNV differences across ancestries and rare CNVs linked to depression. Through the Latin American Genomics Consortium, Diana collaborates with Mexican, Puerto Rican, Brazilian, and Colombian researchers, amassing 8,000 samples for depression studies and 150,000 for genetic diversity. Utilizing tools like PennCNV and GENESIS, she has identified and filtered CNVs related to depression. Future work includes case-control analyses in Latin American cohorts and meta-analyses with PGC-MDD and PGC-CNV to elucidate MDD's genetic architecture.

Interrogation of the Causal Genes and Disease Mechanisms for Major Depressive Disorder

Post Docs: Davide Capauto & Tracy Warren

Mentors: Drs. Kristen Brennand and Marina Piccioto

Departments of Psychiatry, Neuroscience, Pharmacology, and the Child Study Center

Drs. Brennand and Piccioto are using the CBMH Postdoctoral award to mentor two different trainees over the two year period to initiate and then expand upon a novel project using genetic approaches to study depression. In the first year, Davide has been developing a comprehensive library of neurodevelopmental and psychiatric risk variants. These will be evaluated in vivo in mice and in vitro in human neurons. Tracy, who completed her PhD at UC Davis, joined Yale in September 2024 to contribute to this interdisciplinary project. She specializes in in vivo massively parallel reporter assays (MPRAs), which link genomic sequences to tissue-specific regulatory functions, and has designed an innovative project to enhance the original proposal using MPRA techniques.

Natural Language Processing and Neuroimaging of Addiction

Post Doc: Marzieh Babaeianjelodar

Mentors: Drs. Sarah Yip, Rajita Sinha, Arman Cohan

Departments of Psychiatry, Neuroscience, Pharmacology, and the Child Study Center

Marzy is working with mentors with expertise in addiction neuroscience and artificial intelligence bridging the realms of computational network neuroscience and subjective patient experiences as assessed via natural language processing (NLP). Her work aims to elucidate individual differences influencing clinical outcomes in addiction. In her initial project, she links semantic content in craving narratives to brain functional connectivity, utilizing Rajita Sinha's data. In the first year, Marzy, with mentors Sarah Yip and Arman Cohan, has processed narrative data through tokenization, lemmatization, punctuation removal, and NLTK tools, analyzed via BERTopic. She will next correlate narrative data with neuroimaging. Additionally, Marzy has started collecting spoken narrative data from participants in combined PrEP-focused HIV prevention and opioid use disorder treatment.

A Conversation with CBMH Collaborators

Al Powers, MD, PhD, and Carolyn Fredericks, MD, are collaborators whose shared work embodies the interdis ciplinary ideals of CBMH. Here, they reflect on the nature of their team science approach and how CBMH has facili tated their progress.

Drs. Al Powers and Carolyn Fredericks

What are your academic and clinical backgrounds?
Al: I became fascinated with how the brain encodes sensory information from as early as high school in North Branford. My early research experiences focused on perception and multisensory integration.
Carolyn: Also as a high school student, in New Canaan, I de veloped an interest in the brain circuitry underlying affective and misattributive states such as the switch between mood states in bipolar disorder, and the parietal underpinnings of delusions of alien control.
Al: Having been the Student Interest Group in Neurology leader for 6 years in medical school, I was surprised to find I was a psychiatrist at heart, fascinated and moved by the struggles of people with psychosis. Back at Yale for residency, I studied perception in this context, under the mentorship of Phil Corlett, John Krystal, Scott Woods, and others. I started my own lab in 2018 focused on understanding the emergence of psychotic symptoms.
Carolyn: I ultimately found my niche in behavioral neurology under the mentorship of Bruce Miller & Bill Seeley at UCSF. Neurodegenerative diseases are essentially circuitopathies, and offer a unique window into how the breakdown of a spe cific circuit gives rise to symptoms and compensatory responses. I came to Yale in Fall 2019 to start a lab dedicated to understanding these relationships.

What are you working on together?
It's hard to answer this question without smiling because this project has always spilled around the edges of our attempts to contain it. Basically, we're taking a perceptual inference-based model that Al has developed in hallucinations, and applying it to alpha-synucleinopathies including dementia with Lewy bodies, which features early, vivid visual hallucinations. There are so many interesting questions we can ask using this model, spanning emergence, pathophysiology, and pharmacology.

Have you had a collaboration of this interdisciplinary nature previously? How did you come to be collaborators?
We've both worked across disciplines before, but this collaboration feels very different. The ideas we are playing with are a deep integration of Al's approach to understanding hallucinations, Carolyn's approach to alpha-synucleinopathy, and the questions that arise in thinking about them side by side. This work arose organically after we started talking at an early CBMH event in 2022 and remains exciting to us and those we share it with. This includes a very talented graduate student, Raina Vin, whom we co-mentor and whose dissertation will be based on this work.

What do you see as the benefit of this type of team science approach?
It's creative. We have complementary approaches to the questions that need to be asked, which means we can often elabo rate upon the models in our own minds just by asking each other questions and build something together that neither of us would have been able to create alone. It's too easy in a specialized field of study to get stuck in the ideas and approaches that are circulating within that field and go for the next incremental step rather than looking sideways. This collaboration takes us out of that siloed mentality.

How has CBMH supported your work, as individuals and as a team?
Al: CBMH supports conversations across the broader medical school community, among people who think deeply about how disorders of the brain manifest. This–and the financial support needed to test these ideas–have been world-expanding for me.
Carolyn: The sense of community the CBMH creates is really palpable, and we've felt so welcomed into that community. We were both humbled and honored to lead the review of the inaugural CBMH postdoc awards, for instance. There's a joyful ness in the leadership's approach to community-building and boosting these kinds of collaborative projects.

Pilot Award Symposium

Our 2024 CBMH Pilot Award Symposium invited eight applicant teams selected as finalists for the CBMH Pilot Award Program. To foster interdisciplinary collab oration, we mandated that applications feature at least two Co-Principal Investi gators from different departments or disciplines, propose novel initiatives, and demonstrate potential for near-term impact on patient or community health. We were pleased to receive 26 applications in response to this request, reflecting numerous cross disciplinary and cross department projects.

The review process was a rigorous three-stage evaluation led by Sarah Yip, Ph.D., and Adam de Havenon, M.D. (pictured). A committee of 22 CBMH members as sessed the proposals using an NIH scoring system. The top eight scoring applica tions advanced to present their ideas at the symposium held on May 23, 2024. Audience feedback played a crucial role in the final selection, and CBMH Direc tors and review committee chairs chose four recipients based on scores and this input.

The CBMH Pilot Award Program has been generously supported by the Dean of the School of Medicine and the Provost's Office at Yale University. Our sincere thanks to Dean Brown for championing these transformative early-stage cross disciplinary clinical and translational research projects in areas of brain and mind health. This year, we awarded a total of $500,000 to support these promising projects.

Adam de Havenon, MD, MSCI
Sarah Yip, PhD; Psychiatry

CBMH Pilot Grant Recipients

Functional mapping of the primary motor cortex in Parkinson's disease: Effector and inter-effector circuits.

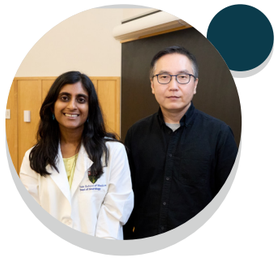
Team : Drs. Michelle Hampson and Sule Tinaz

By 2040, Parkinson's Disease (PD) is projected to affect over 12 million people worldwide, posing a significant individual and public health burden. A recent functional MRI study challenges the traditional view of the primary motor cortex (M1) as a continuous homunculus, revealing that foot, hand, and mouth regions in M1 are interleaved with regions connected to the cingulo-opercular network involved in intentional action - circuitry that likely influences PD motor symptoms. We will characterize this circuitry using the Parkinson's Progression Markers Initiative's clinical and resting-state functional MRI data, the largest longitudinal PD database. Understanding this circuitry's role in PD's motor symptoms will inform network-based therapeutics, such as deep brain stimulation used in advanced PD stages, as well as future brain-based therapies like neurofeedback and non-invasive neuromodulation.

Low-intensity MR-guided focused ultrasound to restore consciousness in coma and related states

Team : Drs. Hal Blumenfeld and Zion Zibly

Normal consciousness relies on multiple arousal systems ensuring brain alertness. Traumatic brain injury or severe neurological disorders can lead to impaired consciousness, such as coma and vegetative states. Deep brain stimulation (DBS) benefits these patients but requires invasive neurosurgery. Our objective is to use high-precision, low-intensity focused ultrasound (LIFU) to noninvasively stimulate deep brain arousal structures. Ultrasound modulates brain function and promises to restore consciousness in comatose patients. This technique offers non-invasiveness and precision, targeting deep brain structures without surgery. Utilizing clinically established high-precision ultrasound technology with over 1,000 transducer elements, we ensure millimeter-precision regional targeting. MRI thermography ensures safe, low-intensity stimulation, avoiding tissue injury. This method surpasses existing neuromodulation techniques in precision and safety, promising substantial clinical impact by improving quality-of-life for patients and reducing long-term care burden.



Multi-Modal Phenotyping of Patients with Acute Ischemic Stroke To Inform Precision-Driven Secondary Stroke Prevention Treatment Implementation.

Team : Drs. Ho-Joon Lee, Srikant Rangaraju, Richa Sharma, and Hongyu Zhao

Accurate stroke etiology diagnosis is unknown in up to 30% of the 77 million annual global stroke cases due to data complexity, insufficient information, expert shortages, and human error. We will quantify 11,000 proteins in plasma samples from 71 acute ischemic stroke patients at Yale to develop precision-driven diagnostic approaches. Using the SomaScan assay (SomaLogic), combined with protein data from 60 Emory patients, we will generate computational signatures for each known etiology. By incorporating clinical and radiographic data, we will optimize the model to identify underlying causes in cryptogenic stroke patients. The outcome will be an AI-based, multi-modal diagnostic tool for stroke etiology, supporting future post-stroke studies and potentially leading to scalable, plasma-based biomarker panels for precise secondary stroke prevention treatments.

Targeting fronto-striatal neural circuitry using repetitive transcranial magnetic stimulation to reduce irritability.

Team : Drs. Vaughn Steele and Wan-Ling Tseng

Irritability, common in psychiatric disorders, causes adverse outcomes in youth, including anxiety, depression, low socioeconomic status, and high suicidality. Despite this, evidence-based treatments are scarce. Frustration from withheld rewards is central to irritability's pathophysiology. Our research shows frontostriatal circuitry (dorsal lateral prefrontal cortex (dlPFC), dorsal anterior cingulate cortex (dACC), striatum) abnormalities during frustration in youth with irritability, notably reduced dACC-striatum connectivity, and increased connectivity post-rTMS to dlPFC. We will use rTMS to modulate this circuitry, reducing frustration in irritability via an rTMS (active/sham) study on 20 young adults (18-25 years) with high irritability. Our study aims to establish this circuitry's role in frustration and evaluate changes in connectivity, motor activity, and self-reported frustration pre- and post-rTMS. This research supports future advancements and trials in psychiatric disorder interventions.

Looking Ahead

Recruitment of New Core Faculty to Yale and the CBMH

Building on the successful recruitment of Dr. Christine Cha, CBMH continues to expand its Core Faculty. After a broad and engaging search, the Search for Network Therapeutics is in advanced discussions with a promising candidate who we hope to announce in the coming weeks. Next, in concert with Yale University initiatives to invest in artificial intelligence, CBMH is collaborating with Dr. Lucila Ohno-Machado and others in the newly formed Department of Biomedical Informatics and Data Science to initiate a search for colleagues with a track record and interest in applying 21st century methods in advanced data science to mind and brain applications. A cross-cutting theme in CBMH recruitments is a commitment to collaborative science that interweaves multiple traditional disciplines and research approaches. These and future searches will bring new CBMH colleagues to Yale who will enhance the environment for clinical and translational neuroscience that will ultimately benefit patients
and populations.

CBMH Winter Research Symposium

This year's winter symposium is titled: "Rewiring Reality: How Brain Research is Reshaping Our Understanding of Self". We will welcome Helen Mayberg, a leading neurologist and pioneer of deep brain stimulation across a range of brain and mind disorders. She will be joined by leading Yale experts including Abhishek Bhattacharjee from the Yale School of Engineering & Applied Sciences and Laurie Paul from the Department of Philosophy in the Faculty of Arts & Sciences. Formal presentations and an informal panel discussion, as well as a post-symposium reception, will facilitate engagement with the presenters.

CBMH Community Engagement Core

CBMH aims to nurture neuroscience investigation that improves the lives of individuals and impacts communities. We are fortunate to have many members who direct leading programs in the community and many more who aim to do so. In partnership with the Office of Health Equity Research, CBMH will explore the creation of a community engagement core to serve as a resource and bridge for faculty and trainees who currently do or aspire to work in this setting.

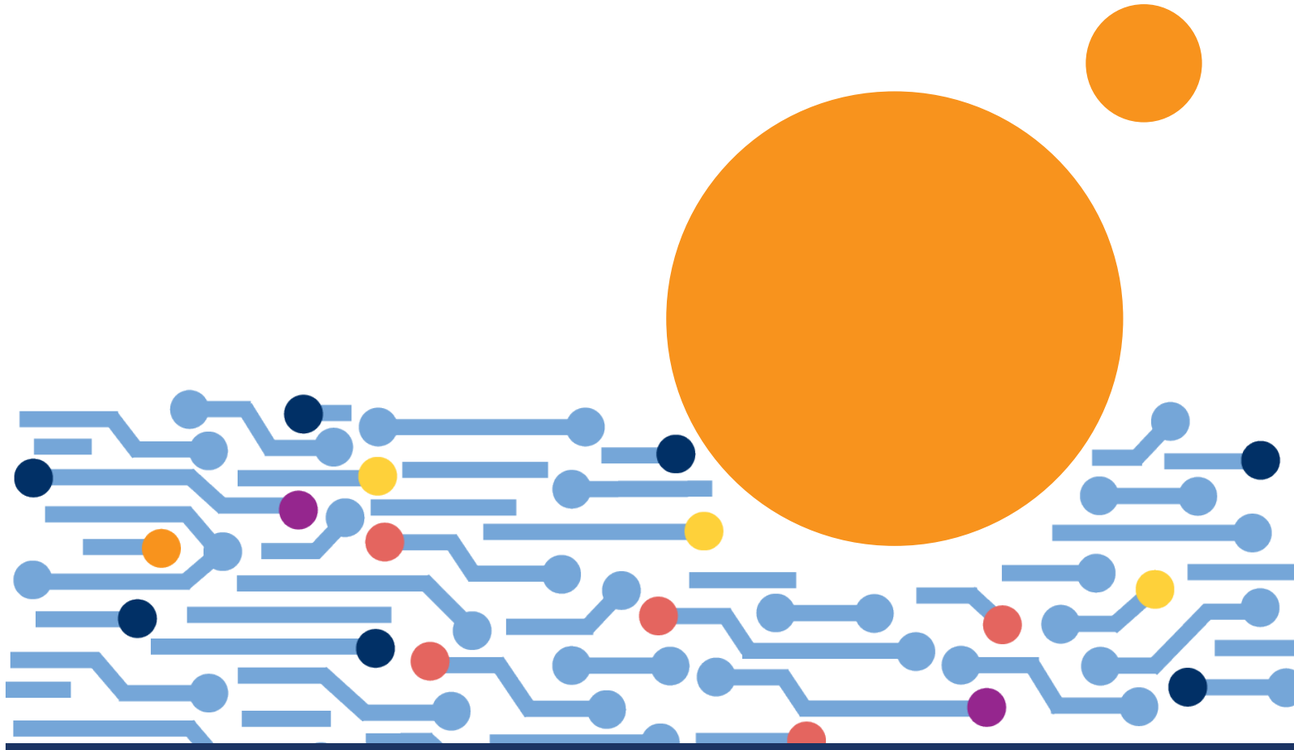
Interdisciplinary Team Science and Thinking Big

This past year witnessed the receipt of CBMH inspired large grant awards from federal agencies and international foundations. We will continue to identify similar opportunities and catalyze teams that may be interested in responding to program announcements that are aimed at clinical and translational neuroscience investigation.

The CBMH Ecosystem

CBMH will continue to foster intellectual exchange through our ongoing Conversations and community building events, which have been key to cultivating a collaborative culture. Our successful grant programs will remain central in supporting innovative research, and we will actively create opportunities for trainees to engage with these initiatives, ensuring that they benefit from the multidisciplinary environment that defines our center. These efforts will be pivotal in driving further advancements in neuroscience and expanding the reach of our mission.

Yale Center for Brain & Mind Health



https://medicine.yale.edu/brain-mind-health/

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