UMassMemorial Health Care
University of Massachusetts Medical School
UMass Psychotic Disorders Clinical and Research Program
Beautiful Mind | Productive Life
Email: MIND@umassmed.edu
Phone: (508) 856-MIND (6463)

# Presence of Mind

**UMass Psychotic Disorders Clinical and Research Program**

**Summer 2019**

## Clinical Care

### Addressing Knowledge Gaps and Missing Links in Mental Health Care

On April 18, 2019, Dr. Xiaoduo Fan, Director of the UMass Psychotic Disorders Clinical and Research Program, was invited to give a presentation and interactive discussion to the Massachusetts Department of Mental Health (DMH) leaders and area medical directors at the University of Massachusetts Medical School campus.

The DMH leaders meet at the UMass campus every two months to discuss statewide initiatives to improve mental healthcare throughout the Commonwealth. They were excited to hear Dr. Fan's presentation, titled "From bench to trench: knowledge gaps and missing links in treating individuals with severe mental illness (SMI)", which addressed many challenges in treating the underserved and underprivileged SMI population.

The presentation honed in on where knowledge gaps exist in clinical and community settings and proposed feasible solutions for ameliorating these gaps. Specifically, Dr. Fan discussed the lack of integrated care in clinical settings, poor treatment compliance, and the use of community-based interventions

that address detrimental health behaviors, including poor diet, lack of exercise, smoking, and substance use. Community-based interventions stand important to strengthen relationships within the community, reduce rates of rehospitalization, increase treatment compliance, educate patients on healthy eating and exercise, and help them deal with everyday psychosocial challenges.

The UMass Psychotic Disorders Clinical and Research Program has already made significant effort in establishing successful community-based initiatives though long-term strategic partnerships with various stakeholders in central Massachusetts. The Community Intervention Program (CIP) initiative, launched by our program three years ago, has many branches of community outreach such as public education and intervention as well as professional education and training.

## Research

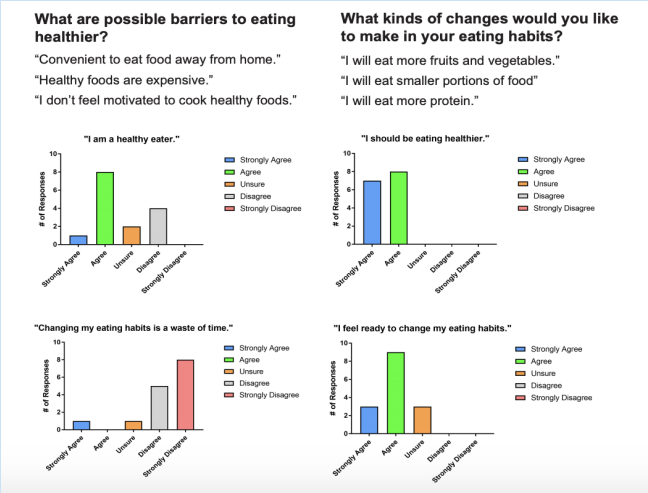
### Bringing CIP to the APA: Discussing the Impact of Healthy Living in Patients with Severe Mental Illness

Amy Cheung, a 5th year MD-PHD candidate at UMass Medical School, had the opportunity to attend the 2019 American Psychiatry Association Annual Meeting held in San Francisco to present on her involvement with the Community Intervention Program (CIP), part of the UMass Psychotic Disorders Clinical and Research Program. The American Psychiatric Association, celebrating its 175th anniversary, advocates and strives for the highest quality of care for all persons with mental illness. This year's theme was *Revitalize Psychiatry: Disrupt, Include, Engage & Innovate*, inspired by psychiatry's vital role in addressing and

proposing solutions to challenges facing our national and global communities.

Amy attended several sessions that increased her appreciation of the many different approaches currently being taken in psychiatry to improve patient health. Some of her favorite talks were *Hip-Hop: Cultural Touchstone, Social Commentary, Therapeutic Expression, and Poetic Intervention* in which the speakers used music videos- like "This is America" by Childish Gambino- to demonstrate how artists leverage this platform to make commentaries on mental wellbeing, substance use, racism, and poverty, and *Successfully Addressing Weight Gain in Patients With Serious Mental Illness* where a panel of mental health professionals presented different ways to deliver services targeting health behaviors through whole health management.

In the past year, Amy and other team members examined the impact of nutrition education and cooking demonstration among individuals living with severe mental illness. We hope this type of community-based intervention can promote healthy lifestyle, and reduce the risk of obesity and long-term cardiovascular consequences in this patient population. During the APA meeting, Amy shared the post-event survey results from two Healthy Living workshops UMass's CIP initiative organized in central Massachusetts recently (see figures below). Both events were rated highly by the participants. The meeting attendees shared ideas for resources used in psychosocial interventions such as food models provided for free by the National Dairy Council and promoting positive messages for patients working to achieve their weight (or general health) goals. Amy and the rest of the CIP team are excited to use these resources/messages in future Healthy Living events.

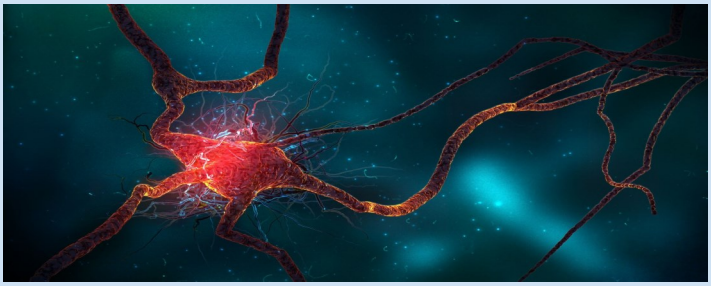



## New Clinical Trial on L-Arginine and BH4 for Treatment Resistant Schizophrenia

Treatment Resistant Schizophrenia (TRS) affects approximately one third of all individuals with schizophrenia. TRS is characterized by a lack of response to medication, even after taking two rounds of different medications at an adequate dosage. Currently available medications for schizophrenia target the dopamine system in the brain. However, in individuals with TRS, other chemical imbalances may exist. Hence, novel medications targeting alternative chemical pathways other than the dopamine system have been suggested for better treatment of TRS.

One possible alternative pathway present in TRS is abnormal glutamate signaling, which is thought to contribute to symptoms such as delusions, hallucinations and cognitive impairment. The abnormal glutamate signaling is possibly related to the malfunctioning of nitric oxide (NO), a chemical that plays an important role in the cell signaling pathway.

The Psychotic Disorders Program (PDP) at UMass previously participated in a clinical trial testing an injection of sodium nitroprusside, a compound known to promote NO production, in individuals with TRS. Unfortunately, the results of the study,



published in *JAMA Psychiatry*, were not convincing of NO's effect on restoring chemical imbalances in patients with TRS. Now, the Psychotic Disorders Program is piloting a novel approach to tackling TRS by launching a new study to examine the efficacy of combination treatment of L-arginine and tetrahydrobiopterin (BH4). Compared to previous NO donor sodium nitroprusside, L-arginine and BH4 are hypothesized to maximize NO induced neuroprotection and neuroplasticity, but at the same time minimize NO associated oxidative stress and neurotoxicity in the brain.

This pilot study will enroll up to ten patients for a 2-week trial of L-arginine and BH4 combination treatment. The trial will

measure the effect that short-term L-arginine and BH4 treatment has on patients with TRS by taking an image of the chemical levels in the brain associated with NO signaling and glutamate disfunction previously observed in individuals with TRS.

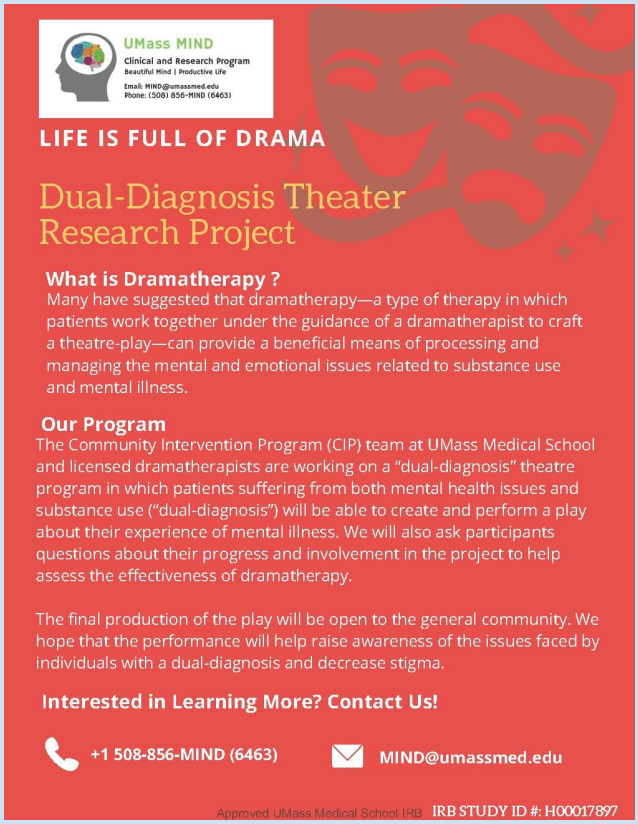
Through this trial, we hope to develop more effective treatment for TRS and have a deeper understanding on the biological differences between TRS and other types of schizophrenia.

## Community Engagement

### Dramatherapy for Individuals with a Dual-Diagnosis

Dramatherapy is a form of treatment that encourages spontaneity and creativity. It allows participants to share their stories, set goals, and solve problems. Through drama, the depth and breadth of inner experience can be actively explored, and interpersonal relationship skills can be enhanced. Participants can enjoy themselves on a journey of life-enhancing self-transformation in which they have the opportunity to work together under the guidance of a drama-therapist to map and share their stories with others in an effort to heal and affect their emotional well-being.

In collaboration with Lesley University, UMass MIND, the community identity of the Psychotic Disorders Program, launched a pilot project to assess the efficacy of drama therapy for individuals with a dual-diagnosis (severe mental illness and substance use). Rather than having these individuals participate in the traditional "talk therapy", the action and movement of dramatherapy may help them better experience reality and release emotions. In addition, dramatherapy may be used as a coping mechanism for those engaging in substances. The study will last for 10 weeks and participants will meet weekly to create a one-act drama related to issues relevant to their experiences and journeys with a dual-diagnosis. Participants will also have the opportunity to perform for the general Worcester community, redefining the public's understanding of mental illness.




If you are interested in learning more or possibly participating the program please contact us by phone or email at 508-856-6463 and MIND@umassmed.edu.

## Global Initiatives

### Novel Predictors of Schizophrenia Treatment Response

The UMass Psychotic Disorders Clinical and Research Program places a heavy emphasis on global collaboration in advancing mental health care and research. We frequently host leading mental health doctor-researchers from China as visiting scholars at UMass. Dr. Wenbin Guo, a professor of Psychiatry at the Second Xiangya Hospital and Central South University in China, was one of recent visiting scholars in our program. During his stay with us, Dr. Guo completed two brain imaging papers; both were published in *EBioMedicine*, a *Lancet* journal.

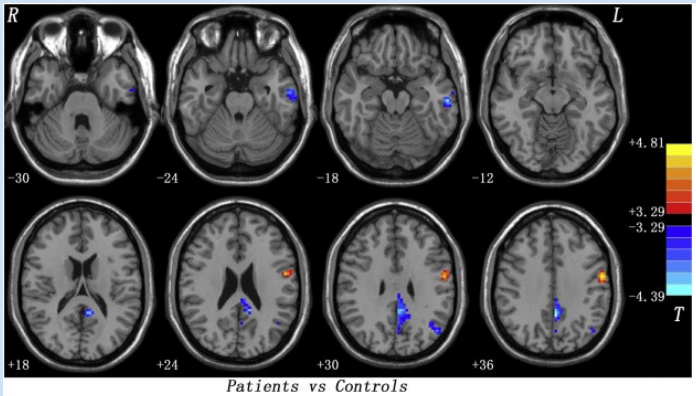
The first paper examined the asymmetry of functional connectivity in certain regions of the brain, and whether such an asymmetry could serve as a biomarker for schizophrenia. In

this study, drug-naïve patients with schizophrenia underwent an 8-week treatment of olanzapine, a commonly used medication for psychosis. Using MRI scan in both patients and unaffected relatives, the research team found that disrupted asymmetry within the left hemisphere of the brain was shared by both individuals with schizophrenia and their relatives (see figures below) . Further analysis also showed that such a reduced asymmetry may predict treatment response.

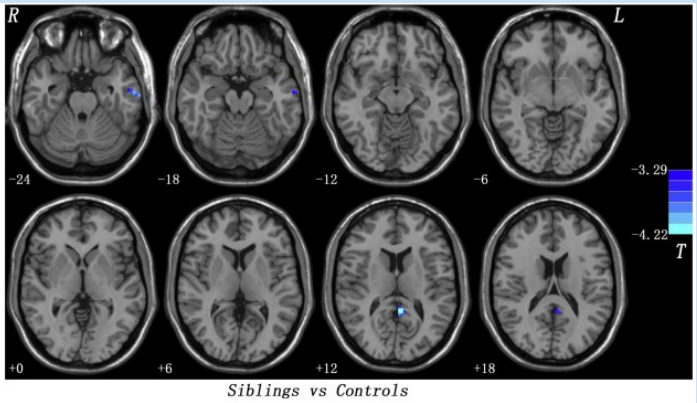
The second paper focused on putamen, a region of the brain critical to emotional and cognitive function, in drug-naïve patients with schizophrenia. Dr. Guo and his colleagues found that elevated pre-treatment putamen activity may predict individual therapeutic response to olanzapine treatment.

The novel imaging biomarkers reported in these two papers may potentially enable clinicians to predict a patient's response to treatment. However, future studies are needed to confirm whether these findings are generalizable to patients with schizophrenia treated with medications other than olanzapine.

*Dr. Wenbin Guo*




*Patients vs Controls*




*Siblings vs Controls*

## Ongoing Schizophrenia Studies Looking for Subjects

**The Refractory Symptom Study –** The purpose of this research is to see if daily 80mg of telmisartan changes brain chemistry in schizophrenia patients who have not experienced a significant relief of symptoms from current medication *as measured by MRI brain scans. (Docket #H00015574)*

**The Refractory Symptom Study 2** – The purpose of this research is to see if daily combination treatment of L-arginine and Kuvan changes brain chemistry in people experiencing schizophrenia as measured by MRS brain scans. (Docket #H00017202)

**The Substance Use Study** – The purpose of this study is to see whether Brexpiprazole, an investigational drug, can help reduce substance use in individuals with co-occurring schizophrenia and substance use disorders. (Docket #00014611)

**If you are someone you know is interested in participating in a research study or clinical service, please contact us at:**

**PHONE: 508-856-MIND (6463)**

**Editors**

Eric Hua, Kareem Hamada, Tao Xu, Amy Cheung, and Mathew Chiang