# THE PRESENCE OF MIND

UMASS MIND CLINICAL AND RESEARCH PROGRAM

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UMASS MIND
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## THIS ISSUE:



## CLINICAL

### THE SILENT RISE OF METHAMPHETAMINE-INDUCED PSYCHOSIS

**By Lawrence Mendez and Anna Noroian**

Unlike many other parts of the world where methamphetamine (meth) makes headlines, the meth crisis in the U.S. has gone unnoticed. In 2023, 2.6 million people reported using meth, doubling the number since 2009. Overpowered by the opioid and fentanyl crisis, meth use has grown without much attention. As a stimulant, it accounts for over 25% of fatal drug overdoses. The co-occurrence of stimulants with opioids is called a "silent epidemic," emphasizing the increasing impact of meth in the illegal drug scene.

UMass Mind has published several papers on meth use in the past 1,2. Invited by the National Association of Mental Health Program Directors (NAMHPD) and the SAMHSA Serious Mental Illness Technical Assistance Center (SMI-TTAC), Xiaoduo Fan, MD, MPH, recently delivered a webinar titled "Intersections of methamphetamine-induced psychosis and schizophrenia spectrum disorders". The event was attended by hundreds of frontline service providers, administrators, policymakers, and researchers.

Like schizophrenia, symptoms of meth-induced psychosis (MIP) include delusions—beliefs not based in reality, such as being watched, poisoned food, or having magic powers—and auditory or visual hallucinations, which involve hearing or seeing things that are not there. However, negative symptoms—like loss of emotion, lack of pleasure, and decreased sociability—are less prominent in MIP than in a primary psychotic disorder such as schizophrenia. Studies show that 40% of meth users will experience MIP after stopping meth, and 16-25% will experience MIP beyond one month after stopping.

Existing research indicates that meth use might not cause schizophrenia, but it can "trigger" schizophrenia in individuals with a family history of psychosis. When psychotic symptoms persist without further links to drug use, a MIP diagnosis is reassessed as schizophrenia.

A common clinical situation is that substance use disorder (SUD) often co-occurs with schizophrenia. Research indicates a shared "neural overlap" between schizophrenia and SUD, helping to explain why these disorders frequently occur together. The brain chemicals involved in reward and motivation, triggered by meth, are also ones that people with schizophrenia may have imbalances or sensitivities to. This makes individuals with schizophrenia especially vulnerable to developing meth addiction, even if they understand the risks.

MIP can be frightening and have a significant impact on an individual. Currently, there are no FDA-approved medications for treating MIP. Non-drug approaches, such as contingency management, are the most effective treatment options available. Contingency management helps shift people's decision-making away from drug use and toward other rewards like social connection, consumer goods, and incentives (such as gift cards and vouchers for maintaining drug-free blood test results).

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Meth destroys and harms the lives of millions in the United States, where it has been overshadowed by the opioid and fentanyl crisis. Through better education, public health efforts, and community support, we can help those struggling with meth abuse live safer, more stable lives.

Next time you hear about substance abuse, consider what could be hidden underneath.

**References:**

1. Harrington A, Fan X. Methamphetamine-associated psychosis: what should clinicians know? *Psychiatric Times*, 2022.

2. Chiang M, Du J, Lombardi D, Harrington A, Shukair N, Zhao M, Fan X. Methamphetamine-associated psychosis: clinical presentation, biological basis and treatment options. *Human Psychopharmacology: Clinical and Experimental,* 2019.

# RESEARCH

## TWO BIRDS, ONE STONE—A POTENTIAL TREATMENT STRATEGY FOR SCHIZOPHRENIA AND CO-OCCURRING SUBSTANCE USE

**By Jazlynn Bailey and Madeleine Foard**

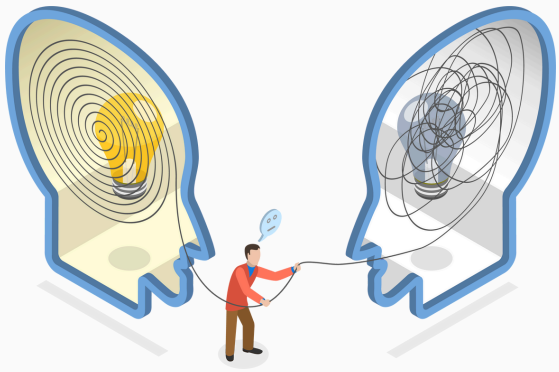
What if a single medication could treat two health conditions at once? A recent multi-site clinical trial, led by UMass Mind and involving three other academic centers—Massachusetts General Hospital, the University of North Carolina at Chapel Hill, and Augusta University— explored this idea. The study examined the potential benefits of brexpiprazole (Rexulti), an FDA-approved antipsychotic medication, in patients with both schizophrenia and active substance use.

People with schizophrenia often report high levels of substance use, which significantly affects their physical, mental, and social well-being. Many turn to drugs or alcohol for the same reasons as anyone else: to feel good, relax, or socialize. Substances can also temporarily mask or reduce schizophrenia symptoms, a pattern known as "self-medicating." The co-occurrence of schizophrenia and substance use, called "dual diagnosis," is associated with increased risks of relapse and hospitalization, increased support needs, and poorer quality of life[1].

In clinical settings, mental health care and substance treatment are often provided separately because there is no integrated care model to address these issues. Many patients receive treatment for only one condition, resulting in poor adherence to their treatment plans. Only about 12% of patients with dual diagnoses are treated for both conditions.

Brexpiprazole is a newer antipsychotic medication commonly prescribed for schizophrenia and major depressive disorder. It works by balancing dopamine and serotonin activity in the brain, which can help reduce paranoia and hallucinations, as well as stabilize mood. Since previous studies have linked similar medications to decreased substance use, we hypothesized that brexpiprazole may also help lower cravings and substance use behaviors, making it a potential treatment for both schizophrenia and drug addiction.

To assess this "two birds, one stone" concept, we conducted a randomized controlled trial to see if brexpiprazole could reduce both psychiatric symptoms and substance use.



Engaging patients with schizophrenia and active substance use in research was difficult, and the COVID-19 pandemic made recruitment even more challenging. We are very grateful for the help from many clinical colleagues at the UMass site who referred their patients to participate, including Sarah Langenfeld, MD, Madhusmita Dhakal, MD, Ursula Makrum, APRN, and Caitlin McElwee, APRN, among others.

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A total of 39 participants were randomly assigned to either continue their current antipsychotic medication ("treatment as usual") or switch to brexpiprazole for the 12-week study period. Substance use behavior data were collected during weekly check-in visits, while psychiatric assessments occurred at baseline, week 6, and week 12. As the first randomized, controlled pilot trial testing brexpiprazole in this dual-diagnosis population, the results were preliminary but promising. Patients on brexpiprazole reported using fewer substances, experienced fewer cravings, and by the end of the study, spent an average of $33 less per week on drugs and alcohol compared to those on standard treatment. Equally important, participants on brexpiprazole described noticeable improvements in their quality of life, along with a modest decrease in psychiatric symptoms.

While more research is necessary, this trial represents a significant step toward bridging the gap between mental health care and substance treatment. What started as the question "What if one treatment could address two conditions?" is now supported by some initial findings, which will be published in an upcoming issue of the *Journal of Clinical Psychiatry*[2].

**References:**

1. Ziedonis DM, Fan X, Bhatt S, Wyatt SA. Chapter 103: Co-occurring psychosis and substance use disorder. In: *The ASAM Principles of Addiction Medicine (7th ed).* American Society of Addiction Medicine, 2024.

2. Fan X, Freudenreich O, Jarskog F, McEvoy J, Harrington A. Brexpiprazole for the treatment of co-occurring schizophrenia and substance use disorder: a multi-site, randomized, controlled trial. *Journal of Clinical Psychiatry*, in press.

# COMMUNITY

## THE HEALING POWER OF PEER SUPPORT FOR INDIVIDUALS WITH SERIOUS MENTAL ILLNESS: AN INTERVIEW WITH SHERRY YUAN

**By Katie Lambert and Gregory Bourbeau**

People with serious mental illness (SMI), such as schizophrenia, should not face their mental health recovery journey alone. Common resources they can access include counseling and therapy, medications, and support groups. There is another often overlooked resource that can benefit them during their recovery: the help of a peer specialist.

Peer specialists engage patients by sharing their personal mental health experiences and demonstrating a genuine understanding of what patients are going through. Trained in care coordination and navigating healthcare systems, a peer specialist provides health education and encouragement, helping patients develop the skills they need to manage their own health.

While individuals in mental health recovery have been offering informal support to each other for decades, peer specialists have become a new and expanding part of the mental health workforce in the United States in recent years. The Massachusetts certified peer specialists' program, funded by the Massachusetts Department of Mental Health, is the only one in the country entirely operated by people with lived mental health experience. Today, there are over 1,600 certified peer specialists in the state, trained and certified to serve individuals in need.

Recently, the UMass Mind team met with Sherry Yuan, a certified peer specialist and a key member of the UMass Screening and Treatment of Early Psychosis (STEP) Clinic. She is also part of a collaborative research project led by McLean Hospital. Sherry highlighted the unique role a peer specialist plays in supporting patients during their recovery journeys. She explained, "While we work with clinicians and medical staff, the role is non-clinical."

Like many certified peer specialists in Massachusetts, Sherry has personal experience with mental health challenges. After her first nervous breakdown, she joined Genesis Club, a free community program that promotes mental health recovery.

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Sherry first learned about the importance of peer support at Genesis Club. When asked about her experience there, she said, "I received so much support from the staff and members through my good and bad days."

Inspired by how her peers helped her manage her recovery, Sherry decided to become a peer specialist herself. She explained her reason for taking this role: "I wanted to create a supportive space where anyone dealing with a mental health condition could come together and have a conversation."

Today, Sherry enjoys working at the STEP Clinic to support young people during the early stages of their mental health recovery. Many families often feel devastated and helpless when their loved ones are first diagnosed with psychosis. Sherry collaborates with patients and their families to navigate community resources and overcome obstacles, with the goal of helping patients return to school or work. Sherry understands that individuals diagnosed with SMI are not broken; they are like a jigsaw puzzle that may need some help to find the pieces and put them back together.

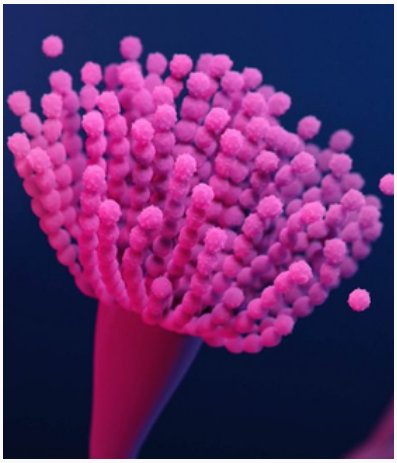
Not only does peer work benefit the SMI patients who use this resource, but it is also rewarding for the peer specialists themselves. For Sherry, "the most rewarding part of this role is learning from others and making a difference in patients' lives."

# GLOBAL

## THE GUT, BRAIN, AND SCHIZOPHRENIA

**By Angel Tang and Srika Raviraj**

Could clues to a schizophrenia patient's cognitive struggles be found in the brain – or even in the gut?



Cognitive impairment is one of the most disabling symptoms of schizophrenia, affecting memory, attention, problem-solving, and quality of life. Although these symptoms are well-known, they remain some of the most challenging to treat. Currently, there are no medications specifically aimed at addressing cognitive symptoms in patients with schizophrenia. However, recent research provides promising insights into their biological origins, suggesting two sources: brain structure and gut fungi.

Two recently published studies[1,2] from the First Affiliated Hospital of Zhengzhou University, China, led by Dr. Xueqin Song and in collaboration with UMass Mind, identified potential novel biomarkers linked to cognitive dysfunction in schizophrenia. Biomarkers are objective biological factors that help define or measure certain biological processes.

The brain structure studied is called white matter hyperintensities (WMHs). WMHs are bright spots seen on brain scans that indicate damage to white matter, the tissue responsible for communication between different brain regions. WMHs are commonly associated with the aging process, as they often occur in older adults. However, they are also connected to inflammation and reduced blood flow, which are believed to play key roles in their development. Inflammation damages blood vessels, which can worsen inflammation and create a harmful cycle that accelerates the growth of WMHs. The damage caused by inflammation, decreased blood flow, and WMHs has been associated with cognitive decline in various neurological conditions, such as dementia, as well as an increased risk of stroke and death. Dr. Song's research team found that drug-naive, first-episode schizophrenia patients had significantly more WMHs than healthy controls.

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These brain changes were closely linked to difficulties in memory, learning, and problem-solving tasks, further strengthening the connection between white matter integrity and cognitive performance.

Previous research found that imbalances in the gut microbiome are linked to inflammation and changes in the brains of patients with schizophrenia. In the second study, Dr. Song's team examined the role of gut fungi, specifically *Purpureocillium* and *Aspergillus*, in cognitive function in drug-naive, first-episode schizophrenia patients. It was found that *Purpureocillium* and *Aspergillus* have opposite effects on cognitive performance. Higher levels of *Purpureocillium* were linked to poorer performance across cognitive assessments, including attention, verbal learning, and working memory. Conversely, increased *Aspergillus* was associated with better cognitive outcomes, indicating it may play a protective role.

Together, the results from these two studies suggest that both brain-based and gut-based biological factors may influence cognitive function in people with schizophrenia. Identifying these biomarkers could pave the way for early detection and more targeted treatment of cognitive impairment in schizophrenia. Researchers caution that more longitudinal studies are needed to confirm these findings and to fully understand their clinical applications.

**References:**

1. Zhang Y, Yuan X, Zhang Y, Chen Y, Su K, Xue K, Ding S, Chen J, Fan X, Song X. White matter hyperintensity, inflammation, and cognitive impairment in drug-naive, first episode schizophrenia patients: a cross-sectional study. *BMC Psychiatry*, 2025.

2. Yuan X, X Li, Pang L, Kang Y, Hei G, Zhang X, Fan X, Song X. Association between *purpureocillium*, amino acid metabolism, and cognitive function in drug-naive, first episode schizophrenia. *BMC Psychiatry*, 2025.

## CURRENT STUDIES: ACTIVELY RECRUITING!

### Study #1: Metabolic Benefits of Lumateperone In Patients With Schizophrenia

The purpose of this study is to see whether determine whether adjunctive lumateperone (Caplyta®) might improve metabolic health in clozapine-treated individuals with schizophrenia. Lumateperone is an FDA-approved medication for adults with schizophrenia. Patients will receive lumateperone or placebo for 12 weeks and meet with the study team approximately 8 times. A variety of metabolic outcomes will be measured, including body fat distribution.

### Study #2: A Prospective Multi-center Study to Characterize the Natural History of Tardive Dyskinesia (TD) and Investigate the Real-world Effectiveness of Deutetrabenazine on the Multi-dimensional Impact of TD

The purpose of this study is to observe the real-world course of TD and evaluate the effectiveness of deutetrabenazine (AUSTEDO®), an FDA-approved medication, on TD. This is an observational study, meaning that the prescription of the medication will be by the patient's regular healthcare provider as part of their routine clinical treatment. Patients who experience at least mild TD symptoms and are planning to initiate AUSTEDO® are eligible for the study. Patients will meet with the study staff every 1-3 months over the course of 3 years. The study visits can be in-person or remote.

**Our studies are conducted at 26 Queen Street, Worcester, MA 01610. You will be compensated for your time being involved in any study. If you are interested or would like more information about any of our studies, please call 508-856-MIND (6463) or email mind@umassmed.edu**