

Research

Nutrients as Adjunctive Treatment for Schizophrenia

The Psychotic Disorders Research Program's project director, Dr. Radhika Natarajan, has spent nearly a decade devoted to the field of nutrition and public health. Dr. Natarajan received her Master's degree in Nutrition Science in 2008 and her PhD in Public Health in 2015, both from the University of Massachusetts. Her expertise in dietary factors, such as vitamin D and B-vitamins, and their role in human health is especially useful in the present-day for biological treatment of severe mental illnesses such as schizophrenia.



Currently available medications are inadequate in treating patients with schizophrenia. About one third of them that are being treated with antipsychotics today still experience refractory symptoms and those medications also cause significant metabolic and extrapyramidal side-effects. When taking into consideration the high cost of antipsychotic medications, there is a need for safe and affordable adjunctive treatment options.

To address this need Dr. Natarajan and Sumedha Mitra, a former high school intern at the Psychotic Disorder Research Program and current undergraduate student at John Hopkins University, took the lead in writing a review paper on the topic

titled, "Anti-oxidant and Anti-inflammatory Nutrient Status, Supplementation, and Mechanisms in Patients with Schizophrenia". This paper was recently published in the journal *Progress in Neuro-Psychopharmacology & Biological Psychiatry*.

Up-regulated inflammation and oxidative stress have been found in schizophrenia patients indicating that they may play a role in the etiology of the disease. Nutrients with anti-inflammation, anti-oxidative stress and neuroprotective properties may be a promising adjunctive treatment for lingering symptoms of schizophrenia, offering patients the possibility for recovery.

This comprehensive review paper covers B vitamins, omega 3 fatty acids, vitamin D, and more nutrients in their potentially disease reversing benefits to patients. As the review paper notes, omega-3 polyunsaturated fatty acids (PUFAs) may be an effective supplement in ultra-high risk populations, but not helpful for chronic schizophrenia patients. Vitamin E is a lipid soluble antioxidant that might actually enhance the potency of other nutrients, like vitamin C and PUFAs; it protects cell membranes from lipid peroxidation by scavenging for oxidative stress-causing free radicals.

Telmisartan: A Medication for Hypertension... and Schizophrenia Too!

The Psychotic Disorders Program is pleased to share our recent research findings, which will be published in the journal *Acta Psychiatrica Scandinavica*, regarding the effect of adjunctive telmisartan treatment on psychopathology and cognition in patients with schizophrenia treated with olanzapine or clozapine.

Our group and others have previously reported immune dysfunction and sub-clinical inflammation in patients with schizophrenia suggesting that the regulation of inflammatory and immunological processes may be related to the manifestation of symptoms and treatment response. Furthermore, an accumulating body of evidence indicates that inflammation may contribute to the development of cognitive impairments in patients with schizophrenia. This patient

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population often shows significant deficits in attention, verbal memory, and executive function. Cognition is an important focus for research as the severity of cognitive impairment is highly correlated with real-life functioning in patients with schizophrenia.

Telmisartan, an angiotension II type 1 receptor blocker (ARB), is currently FDA approved for the treatment of hypertension. Studies have shown that telmisartan has significant anti-inflammation properties, and it is involved in the modulation of brain development, cognition, emotional regulation, as well as other neurological functions.

In our 12-week, double-blind, randomized, placebo controlled trial, patients diagnosed with schizophrenia or schizoaffective disorder treated with clozapine or olanzapine received either telmisartan or placebo as adjunctive therapy. The telmisartan group had a significant improvement in severity of schizophrenia symptoms compared to the placebo group, but there was no statistically significant difference in measures of cognition. This preliminary study provides support for the development of a novel treatment strategy for individuals with schizophrenia. The funding support for the study was from the National Institute of Mental Health and the Brain & Behavior Research Foundation.

Putting a Stop to Addiction: A New Study Targeting Substance Use

The Psychotic Disorders Research Program is excited to announce that a new multi-site, investigator initiated study led by the University of Massachusetts Medical School will be launched soon! This study will evaluate the efficacy of brexpiprazole for co-occurring substance use in individuals with schizophrenia. Substance abuse disorder is significantly more common in individuals with schizophrenia than in health individuals, but the treatment options are limited. There is an urgent need for effective treatments as studies have shown that moderate to heavy users have significantly poorer outcomes in the long-term. Although clozapine has been used to decrease alcohol and cannabis use, it has major side effects supporting the need for a more effective treatment.

Dopamine receptor partial agonists have been promising in reducing drug addiction in animal models, possibly by causing a release of dopamine in the prefrontal cortex. This is thought to balance dysfunctional brain reward circuits which may underlie the co-occurring alcohol or substance use. Brexpiprazole is a newly approved dopamine D₂ receptor partial agonist, and it may be even more effective in reducing

substance cravings with less adverse side effects in comparison to other similar treatment options.

This proof of concept study will follow 80 patients with schizophrenia and co-occurring substance use disorder over 12-weeks. Patients will be randomly assigned to the “brexpiprazole switch” group or the “treatment as usual” group. We hypothesize that brexpiprazole will reduce the use of substances, reduce cravings, and improve quality of life.

The trial is the first of its kind, and it is a much needed treatment, if proven to be effective, due to the high prevalence of dual diagnoses of schizophrenia and substance use disorder. Substance use adds greatly to the emotional toll that schizophrenia places on patients, families, and the mental health system.

The other participating study sites include University of North Carolina at Chapel Hill and Harvard Medical School’s Massachusetts General Hospital. The funding support for this investigator initiated study is from Otsuka.

Clinical Care

Teamwork Makes the Dream Work: DMH Grant for the STEP Clinic

The Screening and Treatment of Early Psychosis (STEP) clinic was established through the partnership between the UMass Psychotic Disorders Program and Community Health link. Recently, the STEP clinic became one of the four sites in Massachusetts to receive a DMH grant. The STEP team is working to implement a Multi-Component First Episode Psychosis treatment program utilizing a coordinated specialty care model. This multifaceted approach includes interventions

such as case management, psychotherapy, supported employment and education, family education and support, and antipsychotic medications. The evidence-based approach was developed as part of the Recovery After an Initial Schizophrenia Episode (RAISE) initiative, launched by the National Institute of Mental Health back in 2008.

There has been extensive research showing that early intervention is a determining factor of long-term outcomes, so

it is important to develop an effective system. The coordinated specialty care model is designed for early psychosis patients, hopefully offering them the best chance of recovery. This will soon become the standard of care for psychosis patients!

The STEP clinic is located at Community Healthlink. The clinic provides a thorough assessment of the patient's history, medication management, psychotherapy, family therapy and education, and substance abuse screening and treatment.

Community Healthlink offers primary care service, which is co-located with the STEP clinic; so our patients are able to keep track of health indicators such as blood pressure, cholesterol, and weight. This behavioral health-primary care integration helps us provide more comprehensive care to the patients we serve. For more information about the STEP clinic or potential patient referral, please contact us by phone at 508-856-MIND, or by email at MIND@umassmed.edu.

Community

Early Psychosis Enlightenment for Healthcare Professionals



On April 12th, the Psychotic Disorders Program hosted the Early Psychosis Professional Education Event. This event featured a wide range of topics, presented by experts in the field. Our program director, Dr.

Xiaoduo Fan, spoke about metabolic problems in patients with early psychosis, a common side effect of antipsychotic medications. Another member of the Psychotic Disorders program, Dr. Amy Harrington, gave a presentation on the co-occurring substance abuse.

Other UMass faculty members also presented: Dr. Sarah Langenfeld spoke about the Screening and Treatment for

Early Psychosis Clinic. Dr. Yael Dvir, from the Center for Autism and Neurodevelopmental Disorders at UMass, discussed psychosis with comorbid developmental concerns. Dr. Irene Colestos introduced psychosocial interventions in early psychosis. Invited speakers also included Dr. Oliver Freudenreich from Massachusetts General Hospital and Dr. Larry Siedman from Massachusetts Mental Health Center. Several representatives from various academic institutions, government agencies, community based mental health organizations, and patient advocacy groups from the greater Boston area also presented during the event.

This collaborative experience allowed individuals from a broad variety of settings to come together and promote the shared goal of providing the best possible care for patients with early psychosis. Thank you to all those who attended, as well as the speakers who shared their knowledge.

Introducing the Central Massachusetts Psychosis Network

The Psychotic Disorders Research Program has recently begun the Central Massachusetts Psychosis Network, an online community intended to bring together all those who share interests in psychosis and mental illness, including mental health professionals, patients, families, advocacy groups, and other partners and stakeholders in central Massachusetts and beyond. We hope that this can be a platform for us to share resources and build knowledge.

Our goals are for this network to ultimately help patients and their families overcome the emotional challenges brought on by mental illness, as well as to proactively work with other local support and advocacy groups in order to fight the stigma which continues to pervade popular perceptions of mental

illnesses such as schizophrenia, and improve the overall quality of life for the patients.

So far, the network has featured local resources, upcoming events, and even a patient's story. To read our recent network newsletters, please click [here](#). Our greatest asset as a community will always be our members; if you would like to be featured in our future newsletters, do not hesitate to send us information that you feel is relevant such as patient resources, upcoming events, research updates, and inspiring stories! If you know of anyone who is interested in joining this network, please share our contact information (Phone: 508-856-MIND; email MIND@umassmed.edu) with them, or let us know, and we will be happy to add them to the group.

Global Initiatives

An Exchange of Ideas with China

As a national leader in public sector psychiatric, the UMass Psychiatry Department developed the China Mental Health Program directed by Dr. Xiaoduo Fan, MD, MPH, MS. The UMass China Mental Health Program has led to collaborative relationships with multiple leading academic mental health institutions in China and is still growing! We are eager to introduce our two current visiting scholars.

Dr. Jiang Du, MD, PhD, is an associate professor of Psychiatry at Shanghai Mental Health Center and Shanghai Jiaotong University. Dr. Du is also the Director of the Shanghai Drug Addiction Treatment Center. Her expertise lies in intervention for patients with dual diagnoses of mental illness and substance use disorders. In collaboration with the UMass Psychotic Disorders Program, Dr. Du is currently working on two research projects. The first examines the causes for the decline in heroin users who received methadone maintenance treatment (MMT) in Shanghai, China over the past 10 years. Several important factors have been identified, such as limited knowledge on behalf of both patients and



MMT staff as well as inconvenient program procedures. Dr. Du's other research study is on naltrexone and bupropion combination treatment for smoking cessation and weight control in patients with schizophrenia. This is an important study to undertake as the rates of obesity and cigarette smoking are much higher in patients with schizophrenia compared to the general population.

Dr. Fang Liu, MD, PhD, is currently with the UMass Psychotic Disorders Program as a visiting scholar as well. She is an associate professor at the 1st Affiliated Hospital of Kunming Medical University in China. While at UMass, she has also conducted multiple research studies. One such study evaluates the relationship between serum levels of nitric oxide metabolites and negative symptoms in patients with schizophrenia.

Fostering Unity and Inclusivity throughout UMass and the World

Developed in 2014 by the Psychotic Disorders Program and the China Mental Health Program, the Global Mental Health Case Conference Series has been initiating discussion amongst healthcare professionals regarding mental illness in populations from diverse backgrounds.

The live-video conference series aims to enhance cultural competency, dispel stigma, and advocate for patients throughout Massachusetts and the world through their unique presentations of patients of various cultures. Examples of previous and upcoming discussion topics include the interplay of Chinese and American culture, influence of cultural beliefs in the presentation of psychosis, biopsychosocial case formulation, integrative treatment approaches, laws and ethics.

The Global Mental Health Case Conference Series recently



won the Briscoli Award for Resident-Faculty Collaboration. The series, led by two UMass psychiatry residents Dr. Kathy Niu and Dr. Jingjing Cui, features a real-time, interactive and critical discussion of interesting psychiatric case presentations among patients from different cultures.

The program initially started with psychiatry residents and attendings, but it grew to include medical students, physicians from other disciplines, researchers and psychologists.

The Global Mental Health Case Conference Series emerged through the collaboration between UMass Memorial Medical Center and Shanghai Mental Health Center, but now also includes the Tianjin Mental Health Center. In the upcoming years, the conference series hopes to continue to grow and flourish, increasing its involvement including other institutions and participants around the world.

Welcoming New Members

Stephen McElroy is Clinical Research Assistant. He received a Bachelor's degree in Psychology with a concentration in Mental Health Services from Worcester State University. He spent 14 months as a volunteer intern co-facilitating Cognitive Enhancement and Restructuring Therapy (CERT) and other groups at the Worcester Recovery Center and Hospital. Stephen's interests include studying the efficacy of treatment interventions for psychosis in both early and advanced stages.

Maya Duffy is a research intern and an undergraduate student at Clark University majoring in psychology with a minor in chemistry. Her research interests include examining health care disparities amongst vulnerable populations and cultural barriers to intervention and treatment outcomes. She aspires to attend medical school to pursue a career centered on patient care, specifically addressing medical comorbidity in mentally ill populations.

Rachel Madhur is a research intern. She is a rising senior at UMass Lowell majoring in Public Health, and she hopes to attend medical school after graduating. Her current research interests focus on pharmacological and psychosocial approaches to understand the various factors that play a role in mental illness. She is also interested in disparities in community healthcare and ways to reduce this gap in services.

Zain Raza is a summer intern working towards a high school diploma in the Greater Worcester area. His skills involve writing, growing digital marketing expertise. He is interested in pursuing either business or a medical degree after school.

We would also like to say a warm farewell to **Sarah Hopkins** who was our research coordinator. She will be going to Suffolk University to pursue a PhD in Clinical Psychology. We wish you the best of luck Sarah!

Editors

Rachel Madhur

Maya Duffy

Zain Raza

Dr. Radhika Natarajan

Dr. Xiaoduo Fan

For more information on our ongoing research studies, please visit [our website](#).

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

PHONE: 508-856-MIND (6463)

EMAIL: MIND@umassmed.edu