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Psych-e News

DEPARTMENT OF PSYCHIATRY AND BEHAVIORAL NEUROSCIENCES

School of Medicine

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University Physician Group

Upcoming Events

DPBN Chairman's Grand Rounds

Chairman's Grand Rounds will resume September 16, 2015

I. Greetings from the Chair

Detroit Wayne Mental Health Authority's first interdisciplinary mental health conference was held at Wayne State University School of Medicine's Gordon Scott Hall on June 8th and 9th. Along with DWMHA, it was cohosted by WSU Department of Psychiatry and Behavioral Neurosciences, the Detroit Veterans Affairs Healthcare System and the Michigan Area Health Education Center. With its successful attendance of over 350 people and positive feedback, this conference will be one of many. http://prognosis.med.wayne.edu/article/detroit-wayne-mental-health-authority-hosts-first-interdisciplinary-conference-at-wayne-state

Also, on Monday, June 29th and Tuesday, June 30th, CARF surveyors were at Tolan Park and UPG Livonia for a reaccreditation audit. The mission of CARF is to promote the quality, value, and optimal outcomes of services through a consultative accreditation process and continuous improvement services that center on enhancing the lives of persons served. A sincere thank you goes to who participated in the 2015 CARF accreditation survey. Preliminary results show that we were successful in maintaining our 3-year accreditation status. Among the many strengths of our programs, specifically mentioned were: Our "Best Practice" and innovative approach to service delivery and strong leadership support. Special recognition goes to the individuals who worked "above and beyond" in preparation of the survey and those who worked "behind the scenes" during the 2-day survey: Ed Mischel, Suzanne Manji, Judy Vershave, Gary Rhodes, Celia Polich, Gwen DeWalt, Al Pizzuti, Julie Giroux, Sean Kelley, Valerie Felder, Leslie Alexander and Michelle Caton.

II. News from the Faculty

Eugene Schoener, PhD, received a grant award from the Children's Hospital of Michigan Foundation studying the effectiveness of motivational interviewing training of BCBAs for engagement and retention of families in the treatment of their children with behavior analysis. The Children's Hospital of Michigan Foundation represents a tremendous opportunity for funding for faculty in DPBN. Several have been quite successful. Dr. Schoener's grant is also a collaboration between the Department of Pediatrics (Dr. Diane Chugani) and Departments of Psychiatry and Pharmacology (Dr. Schoener). Please let the Office of the Chair know if you are interested in applying for funding from the Children's Hospital of Michigan Foundation.

David Rosenberg, M.D., and **Vaibhav Diwadkar, Ph.D.** received a National Institute of Mental Health (NIMH) Collaborative R01 grant award studying the genetic underpinnings and neural network functioning as measured by functional magnetic resonance imaging (fMRI) of children and adolescents with obsessive compulsive behaviors. Wayne State University is the lead coordinating center for this grant with the University of Michigan (Gregory Hanna, M.D., UM, PI) and University of Toronto (Paul Arnold, M.D., Ph.D., Toronto PI). All MRI scans are conducted at Wayne State University.

III. Research Activities

- Kudos and congratulations to **Eric Woodcock,** recipient of the DPBN 2015 Junior Investigator

Awards, for his project, “Neuropharmacological investigation of frontostriatal network function and nicotine seeking behavior in current smokers”. Mr. Woodcock is currently a PHD candidate in the Translational Neuroscience Program working in Dr. Mark Greenwald’s lab.

- The first fall symposium for Wayne State University’s new transdisciplinary initiative, Researchers of Biobehavioral Health in Urban Settings Today (RoBUST) will be held on Friday, October 9th, 2015, at the new WSU iBio building, which is devoted to team science initiatives. The RoBUST group consists of over 50 faculty across many different departments and disciplines around the Wayne State campus. They are soliciting paper submissions for both general oral (15 minute conference-style format) and poster sessions (due by 5 pm on July 30, 2015). Abstract submission form can be found on page 3. Topics of interest include health behavior, personality and social processes and health, urban and minority health, stress and disease, intervention and implementation science, and the science of biobehavioral team science. Young investigators, including graduate students and post-doctoral fellows, are especially encouraged to submit.

- After a dozen years of flat funding, the National Institutes of Health has become a top target on Capitol Hill — not for less money but more, potentially billions more by 2020.
  http://www.politico.com/story/2015/07/national-institutes-of-health-funding-119696.html#ixzz3fEgjiOiu

IV. Office of Education and Training

- Congratulations to **Drs. Sean Prabhu and Yedishtra Naidoo** who’s essays/blogs were published on the pages of Psychiatric times, reporting form the APA! Publications are attached.

- The Liaison Committee for Medical Education placed the Wayne State University School of Medicine “on probation (subject to reconsideration)” on June 15, 2015. The school remains fully accredited. The LCME decision is not final until after a reconsideration hearing. The dean and president of Wayne State University have determined that the school will seek reconsideration. The reconsideration hearing is scheduled for Oct. 13-15, 2015. At that hearing, LCME officials will determine whether to amend the organization’s findings or uphold probation status. The probation period is two years. If the probation status is upheld after the reconsideration hearing, the school will have two years to address the issues raised by the LCME. Probationary status may be lifted at any time before the two-year period. Members of the school’s administration have been assigned to develop action plans to address the issues raised by the LCME. This has already resulted in one report and recommendations to resolve one of the issues. Causes for this decision were; 1. Lack of Diversity - The LCME cited a lack of “under-represented populations” in medicine within the student body of the school of medicine. The Association of American Medical Colleges defines under-represented populations as African-Americans, Hispanics, Native Americans and socioeconomically disadvantaged students. 2. BASIC SCIENCES MEDICAL EDUCATION ISSUES - The LCME concerns in this area do not relate to the quality of medical education provided by the school of medicine. The findings of the LCME have more to do with system, monitoring and reporting issues internally. These concerns revolve around the manner in which students obtain and apply knowledge, not their actual success as demonstrated by performance on exams and other successes. The LCME also noted concerns about dedicating time for students to pursue “self-directed and lifelong learning,” and the size of the student lounge and lecture halls. The dean and administration are fully committed to addressing these issues and will resolve all areas of noncompliance with the LCME standards in a timely fashion. Along with the School of Medicine, the Department of Psychiatry and Behavioral Neurosciences is actively involved in trying to help and correct this. If you have any suggestions and/or advice please contact the Office of the Chair.

It is with great sadness to inform you all of the passing of Dr. Elliot Luby’s wife of 65 years, Ideane, on Wednesday July 1st. Services were held on Sunday, July 5th at The Davidson/Hermelin Chapel at Clover Hill Park. For guestbook and additional information, please click on the link below. http://www.irakaufman.com/funeral-details.php?id=5888

"It's never what you say, but how you make it sound sincere. - Marya Mannes"

RoBUST Fall Symposium Abstract Submission Form

1. Name and affiliation:

2. Phone and email address:

3. Author(s):

4. Title:

6. Preference (Check one):

Poster Session __
Paper Session __

5. Abstract (200 words)

Please submit this form to wsurobust@gmail.com by July 30, 2015.

Reflections From Toronto and APA 2015

PHOTO COURTESY OF SUSAN KWESKIN

The 168th Annual Meeting of the American Psychiatric Association, held on the banks of Lake Ontario, was a particularly well-attended and exciting conference that provided a broad range of educational opportunities, with presenters and attendees from all over the world. The conference theme this year—Integrating Body and Mind, Heart and Soul—served as background for a series of deep dives that probed the inner workings of the brain.

Psychiatric Times invited a small group of "roving reporters"—among them two young psychiatry residents, Sean Prabhu, MD, and Yedishtra Naidoo, MD; editorial board member H. Steven Moffic, MD; and neurobiologist Alisa G. Woods, PhD—to roam the halls and write up short reports for "readers back home" about new and exciting things happening at the conference. On the following pages—and also on our Web site (see conferences)—you'll find brief descriptions of what these reporters learned. We also asked Drs Louis Trevisan and Charles Nemeroff to review their presentations on geriatric depression and anxiety and the latest on treatment-resistant depression. Finally, Dr Sahana D'Silva writes on one of the hot topics at the conference—the new Cultural Formulation section in DSM-5. Read about it here and understand why it's the essential ingredient in patient care.

Tectonic Shift in My Conception of Bipolar Disorder

by Sean Prabhu, MD

As a fourth-year psychiatry resident, the thought of completing training and entering the "real world" can be quite daunting. For me, a symposium at APA 2015, "Evidence-Based Psychopharmacology: Algorithms to Guide Clinical Decisions for Treating Bipolar Disorder," translated into "if you're worried about making mistakes, follow these key points and you should at least be okay for treating patients with bipolar disorder."

Walking into the symposium, I figured we would simply be following along some type of flow diagram or decision tree. What I didn't see coming was a tectonic shift in my conception of the disorder—particularly the depressed phase.

From the first day of training, we are repeatedly cautioned about the use of antidepressants in patients with bipolar disorder and the risk of causing a switch from a depressed phase into a manic phase. The state of irritability, impulsivity, poor judgment, and potential compromise in reality testing is feared for its potential to bring harm to the patient and to others. While the manic phase is arguably the "sexier" of the two poles, we may not always focus closely enough on the target of euthymia instead of simply "getting out of mania." This may have been the first time I can recall being formerly cautioned about causing a switch from a manic to a depressed state.

Patients can be weighed down with the negative emotional and cognitive cloak of depressed mood while still having the leftover goal-directed and physical energy of the manic phase from which they came. This can be disastrous for obvious reasons. We may have helped our inpatients out of a manic phase before they are discharged. However, the stability we see at this time may be a temporary state and may herald a depressive episode. Thus, it is crucial to have a high level of vigilance for depressed features and to ensure follow-up within 7 days—at which time we can still intervene if needed.

On average, patients with bipolar disorder spend approximately two-thirds of their time in a depressed or euthymic state. Thus, effective treatment of depressive symptoms is paramount to preserving safety and quality of life. To this end, Drs Dana Wang, David Osser, Arash Ansari, and Othman Mohammad presented a beautifully detailed algorithm for treatment options—for the depressed phase of the illness as well as the manic phase.

The algorithms are available on the Psychopharmacology Algorithm Project Web site (http://psychopharm.mobi), and I highly recommend taking advantage of them.

Some of the key points discussed regarding treatment of bipolar depression:

1. Is there a clinical argument for ECT (are patients acutely suicidal)?

- In most cases, patients with bipolar depression require fewer treatments than those with unipolar depression.

2. What is the best option for the patient who demonstrates psychotic symptoms?

- An atypical antipsychotic is preferred for initial mood stabilization. Olanzapine is not the first choice, given its metabolic adverse effects. Typical antipsychotics can increase the risk of depressive symptoms.

3. Initiation of therapy with a mood stabilizer is recommended if the patient is not already taking a mood stabilizer.

- Lithium remains the first choice (barring any contraindications), given its proven efficacy (even as monotherapy) in reducing suicidality and its likely neuroprotective effects (thought

to reduce neuronal apoptosis and glutamate-mediated excitotoxicity). The number needed to harm for causing long-term renal impairment is about 300.
- Quetiapine is the next best choice (barring any contraindications) and is FDA-approved for bipolar depression. Evidence demonstrating its use as monotherapy for bipolar disorder is still lacking.
- Lamotrigine is not FDA-approved for acute bipolar depression but is approved for bipolar depression maintenance therapy. It has a more favorable adverse-effect profile than many other options and has been shown to increase the time between manic episodes.
- Lurasidone is also a valid option, and it enjoys a more reasonable adverse-effect profile. It has FDA approval for treating bipolar depression. Its relative novelty to many clinicians and fewer number of clinical trials are likely holding it back from receiving even higher recommendations for use.

These points are but a fraction of the suggestions and recommendations for treating this patient population. The speakers covered other topics—including possible treatment options for failed trials, when to augment with a second agent, and the lack of overall clinical evidence to support the use of adjunct antidepressants. These algorithms are wonderful tools for all clinicians because they are based on the scientific evidence available to date.

Dr Prabhu is Chief Resident in the department of psychiatry and neuroscience at Detroit Medical Center/Wayne State University ❒

Schizophrenic Disorders: Is There an Elephant?

by Yedishtra Naidoo, MD

In the Indian parable of the blind men and the elephant, a group of blind men touch various parts of an elephant to identify it. One man feels the beast's trunk and thinks it may be a hose. Another feels its body and thinks it is a wall. Yet another feels its tail and concludes it is snake.

This story may be interpreted as one person's truth not being a total truth—and that multiple perspectives are required to fully understand a concept. This seems to be the growing consensus with the schizophrenia spectrum disorders. At the APA 2015 conference, the theme of multiple perspectives was evident across the pathophysiology, diagnosis, and treatment of the psychotic disorders.

Schizophrenia is a highly heritable disorder, which suggests a major role for various alleles in its etiology. At the conference, Anil Malhotra, MD, discussed a recent multistage schizophrenia genome-wide association study published in the journal *Nature*.[1] In that study, all available schizophrenia samples with published or unpublished genome-wide association study genotypes (36,989 cases and 113,075 controls) were combined into a systematic analysis. The results were 108 conservatively defined loci that met genome-wide significance, which coded for approximately 341 different genes. The identified loci likely represented the low-hanging fruit, with larger effect sizes, and it is likely that many more loci—and therefore more functional units—exist with reduced relative impact.

What is fascinating is that when the group cross-referenced the genes in a drug target database, 20 drug targets were identified for which there are approved drugs. Calcium channel modifiers, NMDA antagonists, nicotine partial agonists, and the well-known *DRD2* receptor antagonists were identified. This indicates that even viewed through a strictly genetic lens, schizophrenia is not a single disorder, but rather a spectrum—some possibly channelopathies, some glutamatergic-related, some dopamine- and glutamate-related, and possibly other variants as well.

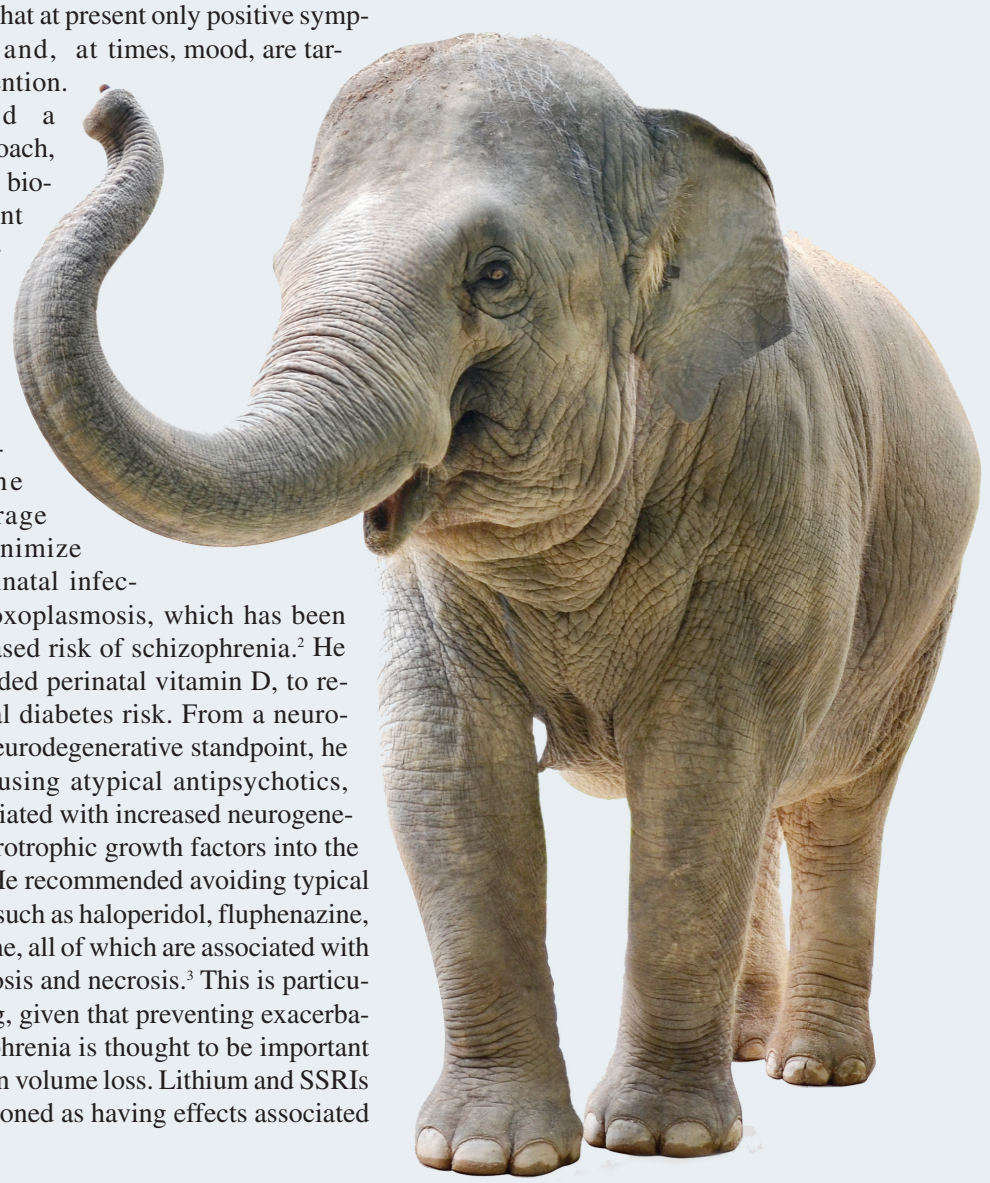
In an associated talk, Matcheri Keshavan, MD, noted that the 341 genes could be organized into functional gene networks, consisting of immunity-related genes and ones involved in the glutamate system.

Rajiv Tandon, MD, discussed the attempt of DSM-5 to embrace the heterogeneity of schizophrenia, through the new 0-4 subscale rating across 8 dimensions: hallucinations, delusions, disorganized speech, negative symptoms, disorganized behavior, mood, motor, and cognition. It is important to consider all 8 when constructing and monitoring a treatment plan.

Henry A. Nasrallah, MD, discussed treatment by considering that at present only positive symptoms, motor and, at times, mood, are targets for intervention. He suggested a 3-pronged approach, conceptualizing biological treatment from neurodevelopmental, neurochemical, and neurodegenerative viewpoints. Neurodevelopmentally, one should encourage patients to minimize the risk of perinatal infection, such as toxoplasmosis, which has been linked to increased risk of schizophrenia.[2] He also recommended perinatal vitamin D, to reduce gestational diabetes risk. From a neurochemical and neurodegenerative standpoint, he recommended using atypical antipsychotics, which are associated with increased neurogenesis through neurotrophic growth factors into the hippocampus. He recommended avoiding typical antipsychotics, such as haloperidol, fluphenazine, and perphenazine, all of which are associated with neuronal apoptosis and necrosis.[3] This is particularly concerning, given that preventing exacerbations of schizophrenia is thought to be important in reducing brain volume loss. Lithium and SSRIs were also mentioned as having effects associated with increased brain-derived neurotrophic factor in the brain.

The elephant parable can be interpreted as a metaphor for multiple perspectives to find total truth. Schizophrenia is now viewed as a spectrum with multiple parts to be examined by researchers. Given the above, it seems more likely that what we will find is that there is no elephant at all, but a collection of different parts, each with its own etiology and treatment.

Dr Naidoo is a fourth-year psychiatry resident in the department of psychiatry and behavioral neurosciences at Wayne State University in Detroit.



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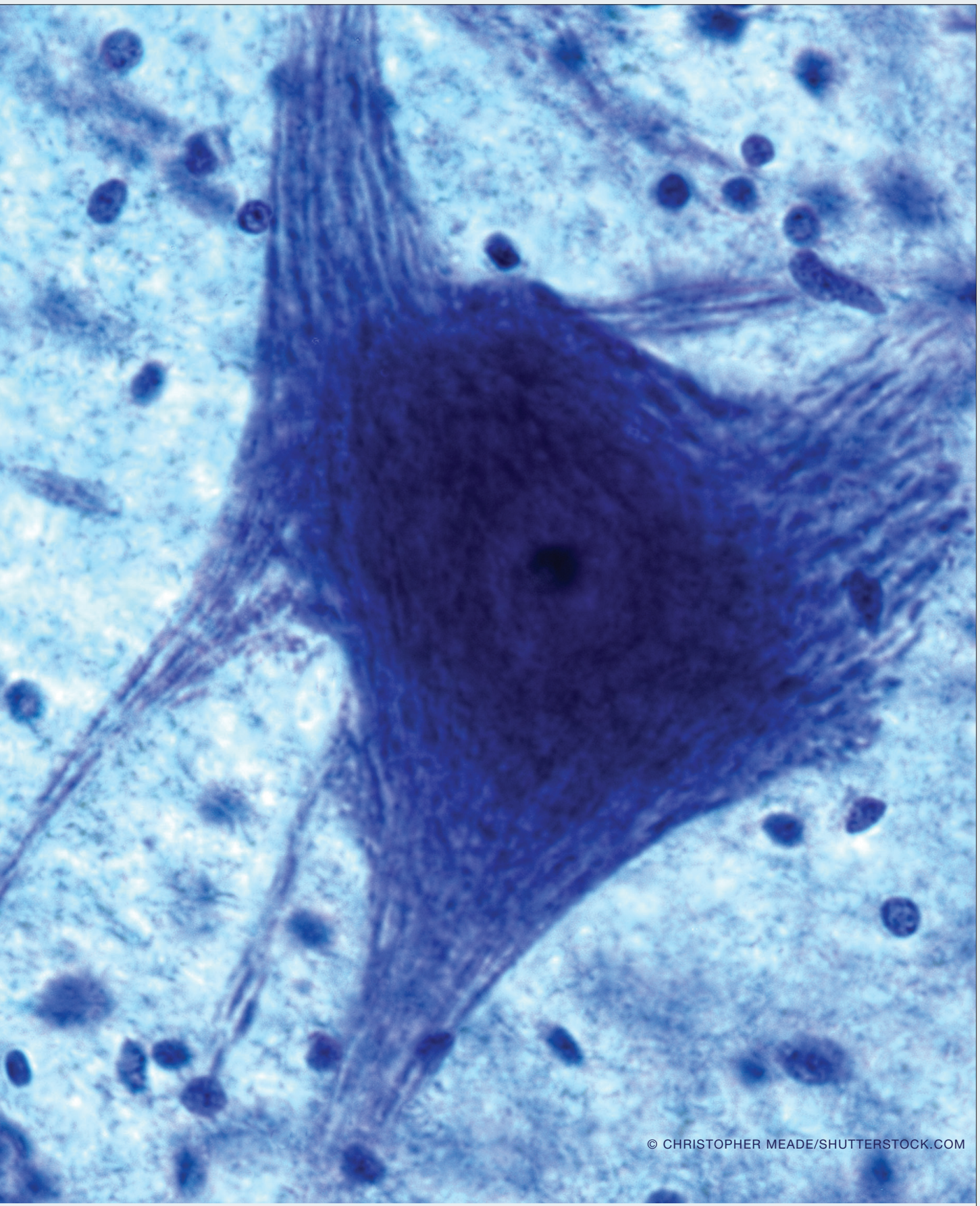
Schizophrenia: It's Not Just About Dopamine

by Alisa G. Woods, PhD

Physicians recognize many features of schizophrenia, including positive and negative symptoms, social/occupational effects, cognitive problems, comorbid substance abuse disorders, and mood changes. However, one neglected area is the common symptom of a poor self-other boundary—in fact, this has also been neglected as a criterion for DSM, despite the fact that it is a common symptom of schizophrenia and that there is a vast literature on the topic.[1]

In his talk, "Beyond Dopamine: the Evolving Therapeutics of Schizophrenia," at APA 2015, Henry A. Nasrallah, MD, Chair of the Department of Neurology and Psychiatry at the St Louis University School of Medicine, noted that 95% of patients with a first episode of psychosis have had contact with the health care system before the first psychotic episode. This makes recognition of prodromal symptoms and risk factors especially important.

Schizophrenia needs to be recognized, according to Nasrallah, as a disorder with a neurodevelopmental basis that is characterized by progressive brain atrophy. With increased psychotic episodes, the ventricular system of persons with schizophrenia enlarges. "Why can't we do something?" asked Nasrallah.



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In addition, gray matter is lost.[2] "The parietal lobe, temporal lobe, and prefrontal cortex take a huge loss," said Nasrallah. There is also a loss of dendritic spines,[3] the substrates of cognition and memory.

"But we focus on dopamine," Nasrallah noted, despite the evidence for neurodegeneration in schizophrenia.

In addition to the loss of global gray matter and dendritic spines, Nasrallah stated that glial cells die in schizophrenia—perhaps accounting for gray matter deficits rather than neuronal loss. "When the glial cells die during a psychotic episode, the neurons become helpless," observed Nasrallah. Effects on glia in schizophrenia remains a topic of much research, although controversy about the exact nature of glial effects might remain.[4]

To add further insult to injury, trophic factors—from which neurons derive their support and ability to differentiate, grow axons, and survive—are also affected, such as brain-derived neurotrophic factor.[5]

Researchers have conducted numerous studies of neurogenesis and antipsychotics, finding that atypical antipsychotics increase neurogenesis, but that haloperidol may be neurotoxic.[6,7] In addition, atypical antipsychotics appear to boost levels of neurotrophins in the brains of persons with schizophrenia.[8]

Given this evidence for numerous other processes, can the neurochemical model of schizophrenia go beyond dopamine? Nasrallah questioned the focus on that sole neurotransmitter system, asking "why aren't we using GABA agonists in conjunction with the dopamine antagonists?" He also mentioned that the antihypertensive agent nitroprus-

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Schizophrenia

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side could be effective for treating schizophrenia.[9] Oxytocin might also hold potential.

Glial cells die in schizophrenia—perhaps accounting for gray matter deficits rather than neuronal loss.

Nasrallah believes that therapeutic approaches should concentrate on the neurodevelopmental dimension of schizophrenia. Prevention might also help, for example, protect pregnant women from the risk factors associated with increased schizophrenia risk—such as maternal infections, toxoplasmosis, and gestational diabetes—and ensuring safe deliveries.

In addition, Nasrallah suggested that it might be possible to prevent neurodegeneration and minimize the risk of psychosis through the early use of long-acting atypical antipsychotics. In general, he advocated the urgent need for "therapeutic approaches and strategies that go beyond what we are doing now."

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Update on Geriatric Depression and Anxiety

by Louis A. Trevisan, MD

In the elderly, mood disorders often accompany substance use disorders and anxiety disorders. Moreover, they portend dementing illness and other medical problems of the elderly. It is estimated that the prevalence of major depression is 1% to 3% in the elderly population; it is higher (6% to 14.4%), however, in long-term–care facilities.[1] Some of the biological factors that contribute to risk of late-life depression include female sex, vascular changes, and comorbid medical illness. Significant psychosocial factors include disability and functional decline as well as loss of a spouse or other loved one.

Screening, recognition, and treatment of mood disorders in late life significantly decrease morbidity associated with many problems encountered by the elderly. The elderly completed 18% of all suicides in 2000, while individuals 65 years or older made up 13% of the population.[2]

Many older adults experience loneliness, profound psychosocial changes, loss of a spouse, and stresses associated with chronic medical problems, as well as the surreptitious, harmful, and often hazardous use of alcohol and prescription opioid medications. Prescription pain medications and sedative anxiolytics are regularly started by primary care physicians or general psychiatrists who treat patients with chronic pain and anxiety. These medications are often ineffective in the long run and become extremely difficult to terminate. They may, in fact, contribute to the depressive symptoms experienced by so many of the elderly.

Mood disorders in the elderly (eg, major depression) respond to several different approaches, such as antidepressants, psychotherapy, and ECT. Traditional antidepressant augmentation strategies as well as specialized evidence-based and supportive psychotherapy are widely used in late-life depression, and ECT has been found to be safe and effective in late-life treatment-resistant depression.

Treatment of late-life depression is important in terms of reducing caregiver burden. The elderly population is growing as is medical burden. We are keeping people alive longer and they often become sicker and more vulnerable to loneliness, substance misuse, and despair. Treatment of depression in later life offers remarkable opportunities to effect real change in people's lives. Treating depression and substance abuse in the elderly has the promise of not only helping the individual but also reducing the burden on caregivers.

Our ability to screen for substance use and psychiatric problems in the elderly has improved, but many problems still go undetected and undertreated. We are experiencing a rapid increase in the number of older adults with psychiatric problems and substance misuse that need informed/expert treatment. Currently, there are fewer than 1900 board-certified geriatric psychiatrists in the US.

Given our current educational models, it will be impossible to train adequate numbers of geriatric psychiatrists to meet the growing needs for clinical services for older adults with psychiatric illness. Because of the shortage of geriatric psychiatrists, general adult psychiatrists, primary care clinicians, advance practice nurses, and physician assistants will be expected to ease the burden and care for many of our older adults with psychiatric substance use problems.

The theme of depression in late life transcends all of the talks that were offered in course 0209 at APA 2015. The course on geriatric mood, anxiety, psychosis, and substance use disorders provided valuable updates on the epidemiology, signs, symptoms, assessment, and evidence-based treatment of these growing concerns. It is imperative that if we are to address the needs of the elderly, more general psychiatrists, primary care physicians, and advanced practice nurses have to learn to recognize and treat the problem as well as know when to refer to the geriatric or addiction psychiatrist for specialized treatment.

Dr Trevisan is Associate Clinical Professor in the department of psychiatry at the Yale School of Medicine in New Haven, Conn. He is the Acting Chief of Psychiatry at VA Connecticut Healthcare System. He is certified in addiction and geriatric psychiatry and teaches in both the addiction and geriatric psychiatry fellowships at Yale University.

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The Latest on Treatment-Resistant Depression

by Charles B. Nemeroff, MD, PhD

Depression is well established as a major cause of morbidity and mortality worldwide. It is associated with a markedly shorter life span and an increased risk for several major medical disorders, including cardiovascular disease, cerebrovascular disease, and diabetes. Moreover, depression is associated with a much worse outcome in terms of disease severity and mortality. These findings, the high suicide rate associated with mood disorders, and the disability also associated with this common disorder speak to the need for effective treatments for depression.

Unfortunately, studies such as Sequenced Treatment Alternatives to Relieve Depression (STAR*D) revealed remarkably low remission rates in patients who received monotherapy with an SSRI or citalopram. Although a variety of augmentation, switch, and combination strategies including CBT were used, remission rates were far from optimal. Two findings were especially concerning: the unusually low remission rate in depressed patients with high levels of anxiety and the high relapse rate in patients who had finally had symptom remission.

Subsequent studies have revealed similarly low remission rates in patients who received previously demonstrated effective evidence-based treatments, including CBT and antidepressants.[1,2] What is clearly lacking in our field, unlike for example, oncology or infectious disease, are predictors of antidepressant response to specific antidepressants or psychotherapy in individual patients. Hopefully, a combination of genetic, epigenetic, and functional imaging techniques will provide such a tool. The field is now plagued with a meager database to guide us in managing patients in whom an antidepressant trial has failed.

Here I describe assessment and treatment strategies for treatment-resistant depression (TRD).

Diagnosis

First and of foremost importance is to confirm the diagnosis—does the patient fulfill criteria for MDD? Is there any evidence of bipolarity? Is there a family history of unipolar or bipolar disorder? Does the patient fulfill diagnostic criteria for other psychiatric disorders, including (but not limited to) an anxiety disorder, eating disorder, late luteal phase dysphoric disorder? Has a major medical disorder been ruled out by laboratory testing, which should include thyroid function tests and measurements of testosterone and vitamins D and B12 levels?

Has a thorough neurological examination been performed to rule out early Parkinson disease, Lewy body disease, and frontotemporal degeneration? Has neuropsychological testing been obtained to assess cognitive function? Is the disorder being treated with any medication that is associated with depression as a known adverse effect, such as glucocorticoids or alpha interferon? If the patient has never had a structural brain imaging study done using MRI, it should be seriously considered to rule out any occult CNS disorders. Depending on presentation of symptoms, sleep polysomnography may be used to rule out sleep apnea and other sleep disorders, and an electroencephalogram should be considered to rule out various forms of epilepsy.

Treatments

Once major medical disorders are ruled out, the clinician must decide on a course of treatment. Treatments for which there is considerable evidence of efficacy include switch, combination, and augmentation strategies. If the patient is currently being treated with one of the SSRIs, as is most commonly the case, it is of paramount importance to determine whether he or she has had a partial response (improvement of 20% to 30%) or no response at all. If the former, a combination or augmentation strategy makes the most sense; if the latter, a switch to another antidepressant class (eg, SNRI, MAOI) should be considered.

There is some evidence that patients with atypical depression characterized by hypersomnia, reverse diurnal mood disorder, fatigue, and extreme rejection sensitivity respond well to MAOIs.[3] Patients with psychotic depression must receive either combination antipsychotic/antidepressant treatment or electroconvulsive therapy. For the remainder of TRD patients, there are many other potential treatments. One is to switch to another class of antidepressant. Switch studies have demonstrated that some patients in whom a trial with 1 antidepressant, at an adequate dose for an ample length of time, has failed will, in fact, respond to treatment with another antidepressant.

Common strategies include switching from an SSRI to an SNRI, bupropion, mirtazapine, an MAOI, or a TCA. A combination of an SSRI with either mirtazapine or bupropion has been reported to be effective. Augmentation with triiodothyronine (25 to 50 μg/d), lithium, or one of several atypical antipsychotics (aripiprazole, risperidone, quetiapine, or olanzapine) has also shown efficacy. Both lurasidone and quetiapine have been FDA-approved for the treatment of bipolar depression. There is substantial evidence that for both unipolar and bipolar depression, psychotherapy (CBT and interpersonal psychotherapy) combined with optimal pharmacotherapy is effective.

It is also of interest to include a brief consideration of nonpharmacological somatic treatments, including repetitive transcranial magnetic stimulation, FDA-approved for patients in whom 1 (but not more than 1) SSRI trial has failed; ECT, generally regarded as the most effective of all treatments; and deep brain stimulation, an experimental treatment available at a few academic centers for the most refractory patients. There is also considerable interest in ketamine in TRD, although concerns about substance abuse liability and long-term efficacy remain.

Dr Nemeroff is Professor and Chairman, department of psychiatry and behavioral sciences, Leonard M. Miller School of Medicine, University of Miami in Florida. This article is based on "Management of Treatment-Resistant Depression: The Art and the Science," an interactive session at APA 2015, chaired by Dr Nemeroff.

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Cultural Context: The Essential Ingredient for a Whole Formulation

by Sahana D'Silva, MD, MS

"Diagnose before you treat."
"Diagnose before you treat."
"Diagnose before you treat."

With a nod to Professor Strunk, of *Strunk and White* fame, when I see patients, I often think of this teaching pearl by one of my mentors in residency. He aimed to teach succinctly, with phrases that stick in your mind. And then like Professor Strunk did, he repeated them frequently, to emphasize their importance. Those pearls come from teachers who have crystallized learned wisdom.

In attending the APA symposium on the new section on Cultural Formulation in DSM-5, my mentor's line once again returned to my thoughts. The symposium was chaired and led by Dr Roberto Lewis-Fernández, with co-speakers Drs Neil Aggarwal, Devon Hinton, Ladson Hinton, Ravi DeSilva, and Laurence Kirmayer. Listening to them speak reminded me of the importance of truly understanding the whole picture that frames a patient's life. We need to get a sense of the social and cultural context of a patient's story before we attempt to formulate a diagnosis and determine a treatment plan. The Cultural Formulation gives us the tools to do just that, comprehensively. Using these tools, we can guide aspects of our interview with different kinds of patients and the people who might provide collateral information. It helps us incorporate the additional information into the usual history that we gather, which will sharpen our assessment and subsequent treatment.

The Cultural Formulation can be found in Section III of DSM-5, under Emerging Measures and Models. It begins by explaining that a clinician needs to keep 3 principles of cultural concepts in mind when taking a cultural history. The first is *"cultural syndromes":* what clusters of signs and symptoms do people within a culture seem to describe together. That clustered description might indicate a disorder within that culture that people are bothered by and might want addressed and treated. The second is *"cultural idioms of distress":* listening for the way a person within a certain culture describes his or her experience of a symptom or sign, almost at a metaphorical level. The third is *"cultural explanations of distress":* how a person within a culture explains how he understands the distressing experience, such as why it is occurring (ie, what meaning is ascribed to the experience).

The 4 parts of the Cultural Formulation section

The core Cultural Formulation Interview (CFI) contains 16 questions that the clinician can use to understand the social and cultural context for the individual patient. Those questions can be grouped into how one defines the problem and how one explains the problem:

- Stressor or source of support
- Background or one's identity in that context
- Ways of coping by oneself
- Past efforts and successes at seeking help
- Barriers to getting help

In planning for treatment with the interviewing clinician, these bulleted points will aid the clinician to understand the ways in which the patient seeks help: what his care preferences are and how he perceives the clinician-patient relationship.

The CFI-Informant section contains questions that the clinician can ask to get the informant's (ie, person accompanying the patient) perspectives on the situation. The questions in the Supplementary Modules help modify the CFI or CFI-Informant versions, when interviewing either caregivers of patients or special patient populations of school-age children or adolescents, older adults, or immigrants or refugees. Finally, the Glossary is a list of terms that help cross-reference culturally based information that the clinician gathers, with diagnostic frameworks from DSM-5.

During the symposium, the speakers discussed how, through this process of interviewing a patient using the cultural formulation tools, the clinician would aim to bridge explanatory models. Imagine 2 circles, which encompass information that you have elicited from the patient. One circle contains the patient's perceptions of the distress and explanations for it, as well as the cultural contextual information. The other circle contains the diagnostic framework in which Western psychiatrists are trained: to understand and diagnose a problem.

Assuming that you have ruled out a medical basis for symptoms and know them to be psychologically based, you might question the patient on how she understands what these symptoms mean, where they come from, how serious she perceives them to be, what has been helpful before, and what she thinks might help now. At the same time, you might frame a diagnosis of moderate depression, based on the sequence of events between her husband dying and her symptoms, her other descriptions of grief, and perhaps trouble sleeping. The aim is to "meld" the two circles into understanding this distress, perhaps building a treatment plan for moderate depression, but continuing to converse with the patient about her symptoms with language within her framework of reference.

Another important notion to keep in mind is, "What really is the "other"? We all hold a cultural framework, a way of seeing the world based on our upbringing and sociocultural background. We need to move toward a way of using the Cultural Formulation to inform our mental health work no matter what we perceive the culture of the individual patient before us to be—because it applies to all of us.

Ultimately, the use of the Cultural Formulation returns to applying patient-centered care. In doing so, we achieve 3 main outcomes: increased adherence, increased treatment satisfaction, and clearer diagnoses. For instance, the CFI can be used to explore further history with a patient who presents with symptoms that appear to indicate bipolar disorder. What if the patient offers information about war trauma as a child, that he lived in a refugee camp, and was raised by relatives when his parents were killed in the war? The clinician might better understand the patient's mood instability to be a traumatic stress reaction and not really bipolar disorder. This affects the treatment plan, both with psychopharmacology and psychotherapy.

The implementation of the Cultural Formulation into clinical practice and mental health training will, over time, promote organizational change through increased cultural and structural competence.

You may be concerned that incorporating the CFI and supplementary modules will take too much time during the patient interview. The speakers pointed out that part of getting comfortable with the CFI is to simply know its components, and then use them when you think they might be helpful. Over time, you might find yourself naturally folding it into your regular history-taking process.

Further research needs to be done in assessing barriers to implementation, cost-effectiveness, and perhaps thinking about how to measure outcome indicators—whether qualitative or quantitative.

The implementation of the Cultural Formulation into clinical practice and mental health training will, over time, promote organizational change through increased cultural and structural competence. Using CFI tools, we will be better able to see through our patients' eyes why illness happened, what they experience now, and what improvement they can expect. We will gain more perspective in understanding the nature of that illness and connect patients to treatment options that match their needs more closely. In essence, we will close the gap between how we as clinicians frame mental illness and how our patients give meaning to their experience of illness, thereby transforming their care through a cultural partnership.

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