April is Sexual Assault Awareness Month. And while our society is well aware of female victims, often male victims of sexual assault are forgotten or neglected due to shame, stigma, and the like. Indeed, some may find it surprising that at least 1 in 6 boys is sexually abused before their 18th birthday. This number rises to 1 in 4 men who experience unwanted sexual events across their lifetime. To wrap your head around those numbers, picture a large college football stadium filled with 100,000 seats. If the audience was solely male, that would mean that at least 25,000 men have been or will be sexually assaulted. That number is staggering.

The public and some health care providers may hear the words men and sexual assault and automatically assume that men are the perpetrators. Somehow seeing men as the targets of sexual violence is difficult to comprehend. The truth is it is hard for most men to see themselves as victims.

Anxiety and Stress Disorders

The Other #MeToo: Male Sexual Abuse Survivors

Joan M. Cook, PhD, and Amy E. Ellis, PhD

At precisely 9:02 AM on the morning of April 19, 1995, a rental truck filled with explosives was detonated outside the Alfred P. Murrah Federal Building in Oklahoma City (OKC). One third of the building was reduced to rubble, nearby cars were incinerated, and more than 300 nearby buildings were damaged or destroyed. The act of domestic terrorism killed 168 people, including 19 children, and injured hundreds of others. A mere 90 minutes later, a key conspirator was pulled over by authorities, but by then the damage had been done. Until September 11th, this was the worst terrorist attack on US soil.

ISSUE HIGHLIGHTS

MOOD DISORDERS
What Is the Deal With Esketamine?
Samuel T. Wilkinson, MD

ADDITION & SUBSTANCE DISORDERS
Interpersonal Violence in the Context of Posttraumatic Stress and Substance Use Disorders
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Rajesh R. Tampi, MD, MS, and Deena J. Tampi, MSN, MBA-HCA, RN

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The future of psychiatry is evidence based
As I write this, the world is dealing with an unprecedented crisis. COVID-19 is not only affecting us in terms of our health, but it is also having a huge impact on the global economy and our everyday lives. Psychiatry is in a unique position to help the world navigate these times.

Psychiatry’s focus on recovery and resilience allows for a positive approach to challenges. Psychiatrists have been on the forefront of dealing with disasters and learning from them, so not only can they help their patients but also society as a whole. Along those lines, Phebe Tucker, MD, shares a poignant perspective on resilience in her article commemorating the Oklahoma City bombing.

Similarly, Harold J. Bursztajn, MD, shares stories of resilience during another tragic time in our history—the Holocaust. His reflections and commentary remind us that the right attitude sprinkled with hope can make a huge difference in our survival during the most horrific times. I concur that resilience, not panic, is key in this time of pandemic.

And so, we continue to march forward, meeting our daily challenges despite this new crisis. Your patients continue to need care, perhaps now more than ever, and Psychiatric Times is here to support you in that endeavor.

David Osser, MD, sheds light on the growing use and normalization of medical marijuana in patients with bipolar disorder. Did you know that 25% to 30% of patients with Parkinson disease have psychotic symptoms? Rajesh R. Tampi, MD, and Deena J. Tampi, RN, discuss the underlying pathophysiology, assessment, and management of these symptoms. Stephen A. Wyatt, DO, delves into world of benzodiazepines, exploring their mechanism of action and how to use them helpfully if used cautiously and appropriately.

You will also find our Special Report on Sleep Disorders and some of our regular features to support you in your practice. And, don’t forget to check out our special coverage of COVID-19 online at www.psychiatrictimes.com.

We hope you and yours remain safe, well, and resilient during these challenging times!
Drug Receptor Profiles Matter

John J. Miller, MD | Editor in Chief

The classifications of medications into various groups was a helpful organizer in the early years of psychiatry. Identifying a drug as an antidepressant versus an antipsychotic versus an anxiolytic helped us quickly access a medication from a large armamentarium of psychotropics. Established effectiveness allowed clinicians to target a patient’s specific symptoms. In those early days we knew very little about pharmacodynamics, brain circuits, drug metabolism, the possible benefit or harm of a drug’s metabolites, and a drug’s receptor binding profile. The good news is that we have made tremendous strides in understanding each of these drug characteristics. We are now able to make more informed decisions about which drug to use for each patient with a particular diagnosis and specific comorbidities who is being prescribed an array of other prescription medications.

Regrettably, this significant expansion of knowledge about medications gets lost in the continued grouping of drugs by their old classifications into various groups. To keep the discussion focused, I explore the class of drugs that we typically call antipsychotics. Significantly, all current FDA-approved medications for the treatment of schizophrenia antagonize dopamine type 2 receptors (DR2)—but that is where their similarity ends. The antipsychotics in this larger grouping have remarkably different, and commonly unique, properties that can provide benefits but may have adverse effects or contraindications. Each of these antipsychotic drugs has a remarkably unique set of receptor binding affinities at a wide range of possible receptors that can assist in making informed choices about which medication to start with, how it will be dosed, how it should be cross-titrated with another antipsychotic, and how to maximize success in managing adverse effects.

The following is a list of some of the receptor properties that differ significantly from one antipsychotic to another:

- Dopamine 2 receptor antagonist
- Dopamine 2 receptor antagonist/partial agonist
- Dopamine 3 receptor antagonist
- Dopamine 3 receptor antagonist/partial agonist
- Serotonin receptor antagonist (7 families of serotonin receptors with many subfamilies)
- Serotonin receptor antagonist/partial agonist
- Serotonin receptor agonist
- Muscarinic cholinergic antagonist
- Histamine 1 antagonist
- Noradrenergic alpha 1, 2 (with sub-receptors of each) antagonist or agonist
- Potency of each drug at each receptor: very potent, potent, moderate, weak, very weak

To be clear, we still do not understand all of the drug-receptor proper-
ties of any drug for the simple reason that we do not understand all of the receptor genes that reside in the human genome that have not yet been discovered or characterized. Additionally, as we see with the DR2, a gene product can be further processed by post-transcriptional editing (introns and exons) to provide a range of sub-sub-receptors with different binding affinities and circuitry locations (for example, the differing dopamine receptor 2 long [DR2L], which is postsynaptic, versus dopamine receptor 2 short [DR2S], which is presynaptic). To add an additional layer of complexity, each drug that is administered will likely be metabolized to chemically distinct molecules that will have their own unique set of receptor binding properties, which may contribute significantly or negligibly to the pharmacodynamics of the parent drug.

Chlorpromazine, discovered in France in 1950 as a derivative of an antihistamine, became the world’s first antipsychotic medication and was widely used in the 1950s. Interestingly, chlorpromazine has a diverse receptor profile, which includes activity at the dopamine 1, 2, 3, and 4 receptors, serotonin 2, 6, and 7 receptors, histamine 1 receptor, muscarinic acetylcholine 1 and 2 receptors, and the noradrenergic alpha 1 and 2 receptors. Subsequent members of this first-generation antipsychotic group included many drugs with variations of the chlorpromazine receptor profile—significantly all with activity antagonizing DR2s that surfaced as the mechanism necessary for these drugs to treat the positive symptoms of schizophrenia.

When clozapine was FDA approved in 1989, it became a paradigm changer, and it remains our most effective antipsychotic to date with the unique FDA indication for refractory schizophrenia. We still have no idea what receptor property or properties clozapine retains to provide this unique efficacy, but it ushered in a generation of novel medications—second-generation antipsychotics.

Honestly speaking, I disagree with this simplified nomenclature, as this descriptor suggests that all clozapine and post-clozapine drugs differentiate similarly from first-generation antipsychotics.

In my opinion, there are 3 post-clozapine families:

1. Apinones: Clozapine, olanzapine, quetiapine, and asenapine. All of these are more potent at the histamine 1 receptor than the D2 receptor, and all (with the exception of asenapine) have significant anticholinergic properties.

2. Idones: Risperidone, paliperidone, ziprasidone, lurasidone and iloperidone. All of these are potent at the D2 receptor, have a wide range of unique binding profiles to various serotonin receptors, and all have some degree of activity at the noradrenergic alpha 1 receptor.

3. Potent antagonists/partial agonists: Aripiprazole, brexipiprazole and cariprazine. All of these are extremely potent antagonists at the D2 receptor—all three are more potent at all of the other antipsychotics—but also have partial agonism at D2 that renders their pharmacology different than all of the other first- and second-generation antipsychotics, which are pure antagonists. Beyond that, all 3 molecules have very different receptor profiles at other significant receptors.

We cannot generalize antipsychotics into one class of drugs

With this background, I would like to turn your attention to a recent publication in the February 2020 online issue of JAMA Psychiatry: “Effects of Antipsychotic Medication on Brain Structure in Patients With Major Depressive Disorder and Psychotic Features.” Voineskos and colleagues analyzed the cortical thickness in gray matter of 72 patients with major depressive disorder with psychotic features. Patients were treated with the sertraline/olanzapine combination for 12 to 20 weeks, including an 8-week period of remission of psychosis, as well as remission or near remission of depression.

This cohort was then randomized in a double-blind fashion to continue the combination regimen or to be switched from olanzapine to placebo (and remain on sertraline) for an additional 36 weeks. For the patients with sustained symptom remission at 36 weeks compared with the placebo-sertraline group, the olanzapine-sertraline group demonstrated a significant decrease in cortical thickness. A decrease in cortical thickness was also seen in a post-hoc analysis of the patients who relapsed in the placebo-sertraline group compared with the group with sustained remission.

During the several weeks following its online publication, I have read many reviews of this article in various online psychiatric resources, all of which infer that the finding of this study is generalizable to all antipsychotics. Notably, and to the authors’ credit, they recognize a limitation to their study results:

Finally, our data were obtained with 1 specific antipsychotic, olanzapine, and it is possible they do not apply to other antipsychotics. However, based on the wealth of data demonstrating equivalent efficacy among antipsychotics and similar effects of different antipsychotics on brain structure in both animal and human studies, we speculate that our findings are likely to apply across all medications in this class.

The authors should have stopped after their first sentence. The second sentence, in my view, has no merit. “Equivalent efficacy” of olanzapine to other antipsychotics should not support a speculation about brain atrophy as an adverse effect. Moreover, their claim that the generalizability to all antipsychotics is further supported by “similar effects of different antipsychotics on brain structure in both animal and human studies” is also negated by their own claim that:

Concerning animal and uncontrolled human data suggest antipsychotics are associated with change in brain structure, but to our knowledge, there are no controlled human studies that have yet addressed this question.

Yes, they have now published the first controlled human study—but it is with a unique antipsychotic medication, which has a unique receptor profile that is not shared by most other antipsychotics. Hence, their study should pave the way for future studies that are randomized, double-blind, and placebo controlled, and which look at antipsychotics with different receptor profiles, or with receptor specific drugs to tease out which receptor(s) activity may be contributing to the decrease in human brain cortical thickness.

One possible explanation: anticholinergic receptor activity

Olanzapine contains anticholinergic receptor antagonism, which its FDA 2013 product insert lists as roughly 4 times weaker than its activity as a DR2 antagonist—relevant activity in the world of receptor binding properties. There is evidence showing that anticholinergic medication is correlated with increased brain atrophy. Risacher and colleagues’ evaluated data obtained from the Alzheimer’s Disease Neuroimaging Initiative of 402 cognitively healthy older adults divided into two groups: individuals taking drugs with medium to high anticholinergic effects (Ac+) compared with individuals taking drugs with low to no anticholinergic effects (Ac−). The researchers monitored cognition, brain metabolism, and brain atrophy over a mean follow-up period of 32 months.

They reported that: “Reduced total cortical volume and temporal lobe cortical thickness and greater lateral ventricle and inferior lateral ventricle volumes were seen in the Ac+ participants relative to the Ac− participants.”

Chuang and colleagues’ monitored 725 subjects with a mean baseline age of 52.3 years from the Baltimore Longitudinal Study of Aging for a mean follow-up period of 20.1 years. They looked at the impact of long-term anticholinergic drug exposure on brain atrophy in cognitively healthy older adults. They concluded: “Long-term exposure to medications with mild Ac (anticholinergic) activity during midlife is associated with increased risk of AD (Alzheimer disease) and accelerated brain atrophy.”

Conclusion

Clearly, much research remains to be done on many fronts. In my view, it is time to upgrade our nomenclature for drug classifications to a system more in line with the proposed neuroscience-based nomenclature (NNB). With this system, a drug’s unique molecular fingerprint would be apparent, and it would facilitate a well-needed transition to a more accurate nosology for drug classifications—one based on mechanism(s) of action rather than artificial and misleading categories.

REFERENCES


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US-LUM-1900014 12/19
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Sleep Disorders

A Wake-Up Call

Ruth Benca, MD, PhD

There is overwhelming evidence that sleep and circadian rhythm disturbances and disorders are prevalent in psychiatric patients and associated with worse outcomes. Nonetheless, the associations between sleep/rhythms and psychiatric disorders are not well understood, and additional research is necessary to mechanistically link sleep dysfunction to mental illness. Furthermore, despite the fact that there is evidence that treating sleep and behavioral rhythms improves psychiatric outcomes, training in sleep medicine for psychiatrists is often insufficient. As a result, sleep and rhythms are often not adequately assessed or appropriately targeted in the clinical practice of psychiatry.

The articles in this Special Report address key issues. While the association between insomnia and psychiatric disorders has long been recognized, more recent evidence demonstrated a strong relationship between insomnia and suicidal ideation and behaviors across the lifespan, as discussed by Wilfred R. Pigeon, PhD, and Todd M. Bishop, PhD. Thus, patients with insomnia, even in the absence of severe psychiatric symptomatology, should be screened for suicide, and treatment for insomnia should be considered to reduce suicidal ideation.

Circadian rhythm abnormalities are also prevalent in psychiatric patients, although they have received less attention than sleep problems. Practitioners may not always recognize circadian abnormalities in their patients and may lack the training and knowledge to provide adequate chronotherapy; for example, delayed onset due to a shifted circadian rhythm may be mistaken for sleep onset insomnia if a careful sleep history is not obtained. Helen J. Burgess, PhD, and Leslie M. Swanson, PhD, discuss the association between delayed sleep phase and mood, anxiety and substance abuse, as well as the increased risk of psychiatric illness related to irregular sleep timing. Their expert tips and guidance in screening patients for circadian rhythm abnormalities as well as stabilizing and entraining rhythms with light therapy, melatonin, and behavioral interventions is most useful.

Similarly, the article by Ellen E. Lee, MD, discusses how sleep can affect psychiatric disorders by increasing inflammation and oxidative stress. Her group has shown that patients with serious mental illnesses have increased levels of pro-inflammatory cytokines. Other studies have shown that sleep deprivation, insomnia, and obstructive sleep apnea are not only more common in patients with psychiatric disorders, but they are also associated with worse outcomes and contribute to inflammation. Conversely, treatments for insomnia and sleep apnea have been shown to have positive effects on psychiatric symptomatology. Taken together, these findings suggest mechanistic pathways by which sleep disorders, inflammation, and psychiatric illness are linked.

In summary, there is increasing evidence that disturbed sleep and circadian rhythms impact the risk for developing psychiatric disorders, and inflammatory processes are suggested as one possible mechanism of this well-established relationship. Sleep and circadian rhythm disturbances are modifiable factors, and while data on the effects of sleep disorder treatment on inflammatory processes is preliminary and limited, treating sleep and behavioral activity rhythms have consistently shown positive impact on mental health outcomes. Most importantly, treatment of sleep dysfunction may reduce suicide risk.

Future research is necessary to better understand the mechanistic pathways and to improve the availability of evidence-based treatments of sleep disorders in patients with mental health disturbances. Hopefully this Special Report will help you better understand some of these relationships and will lead to improved patient outcomes.

Dr Benca is Chair of Psychiatry & Human Behavior in the School of Medicine at University of California, Irvine. She reports that she has served as a consultant to Eisai, Genomind, Jazz, and Merck.
The Strong Relationship Between Sleep and Suicide

**SPECIAL REPORT**

Wilfred R. Pigeon, PhD, and Todd M. Bishop, PhD

The steadily rising rate of suicide in the US is a vexing public health crisis. Between 2007 and 2017, suicide was the 10th leading cause of death, claiming the lives of nearly half a million people. It is perhaps even more striking that suicide is the fourth leading cause of death for individuals aged 35 to 54 as well as the second leading cause for those aged 10 to 34. Based on 2018 epidemiologic data, 1.4 million adults per year make a non-fatal suicide attempt and 10.4 million have serious thoughts of suicide. Among the many risk factors for suicidal thoughts and behaviors, one that consistently emerges as an independent risk factor is sleep disturbance (broadly defined) along with the specific sleep disorders of insomnia, nightmares, and sleep apnea.

One reason that this sleep-suicide relationship is so important is that sleep disorders represent a modifiable risk factor. As noted a decade ago, several sleep medicine interventions can potentially make a difference in the lives of individuals who may be on a trajectory to suicide.

It has yet to be firmly established if improving sleep actually reduces suicidal risk. However, in a recent analysis of a large medical record study, it was observed that having a sleep medicine consultation was a protective factor for subsequent suicide attempts among those with a sleep disorder. There are also some indications that cognitive-behavioral therapy for insomnia (CBTI) reduces suicidal thoughts.

Mechanisms by which improved sleep may reduce risk are also putative. Indirectly, we can say with some certainty that sleep disorders (eg, insomnia, sleep apnea) are strongly related to the development and course of depression and their reversal improves mood. Other hypothesized mechanisms through which poor sleep may be associated with suicidal thought and behavior include increased impulsivity, emotional dysregulation, and impaired executive functioning, each of which may be reversed with improved sleep.

**Significance for Practicing Psychiatrists**

There is a strong relationship between sleep disturbances and suicidal thoughts and behaviors. Given the existence of several evidence-based interventions for common sleep disorders, the increased usage of sleep treatments can support suicide prevention.

What, then, are actionable items for the clinician wishing to address the sleep-suicide relationship? We present three focal areas:

- **Sleep disturbance screening**
- **Suicide assessment and safety planning**
- **Sleep treatment options in the suicidal patient**

Given the high prevalence of insomnia in psychiatric populations and the ability of psychiatrists to fully manage insomnia (as opposed to sleep apnea), the primary focus of treatment options is for insomnia disorder.

**Screening for sleep disorders**

Often a sleep disturbance is identified in an initial psychiatric evaluation or in the normal course of a treatment episode by either a general screening question, “Do you have trouble sleeping?” or a direct patient complaint “My sleep is terrible.” We strongly recommend leveraging the use of standard depression screening tools to identify sleep complaints. For example, item 3 of the Patient Health Questionnaire–9, which probes for insomnia and hypersomnia has been found to be a good screen for clinically meaningful insomnia. An endorsement of 1 or higher on this 0-3 Likert-type scale item can be followed with questions to quickly assess for the possible presence of either of the two most common sleep disorders (ie, insomnia and sleep apnea).

Alternatively, the 7-item Insomnia Severity Index and the 8-item Stop-Bang Questionnaire can be used to assess sleep problems. Both are efficient and well-validated instruments for detecting probable insomnia and apnea, respectively.

**Suicide/safety assessment**

Even among mental health providers a frequent barrier to reliable suicide risk assessment is the clinician’s comfort with asking the patient about suicide. It is, therefore, worth highlighting the importance of asking patients about all aspects of suicide risk. These inquiries range from asking whether the patient is thinking of killing themselves to inquiring whether they have made a plan or started gathering the means to attempt suicide.

For those involved in graduate medical education or residency training, the coupling of traditional didactic suicide prevention training with videotaped standardized patient interactions can optimize supervision around suicide assessment. Having a well-established safety protocol and clinical staff that are trained to use it will free you and your staff to conduct more thorough assessments with the confidence that a plan is in place to handle risk, should it emerge or worsen. For the same reason that we ask patients to write down their safety/crisis plan, it is best to have these safety protocols in writing so that they can be easily referred to when the situation to use them arises (see Table 1 for examples of protocol content).

Safety contracts or no-harm contacts between patient and provider, which were widely used, are of limited value. Instead, the use of a more involved safety planning or crisis response planning process is recommended. Safety planning and crisis response planning differ slightly but share many common features (Table 2).

**Treatment planning**

While the presence of a sleep complaint or sleep disorder may increase the risk of suicide compared with the absence of sleep disturbance in otherwise similar patients, it does not significantly change the approach to the treatment of suicidality. One important exception is that patients with current prescriptions for sedative-hypnotics have at their disposal a potential means of suicide (ie, overdose); this needs to be evaluated as part of safety or crisis planning. Otherwise, the recommended treatments for suicide prevention can be utilized for suicidal patients with sleep disorders.

Cognitive behavioral therapy for suicide prevention (CBT-SP) is the only intervention with enough empirical evidence to warrant a strong recommendation; no other nonpharmacologic or any pharmacologic treatment for suicide prevention has enough evidence to receive more than a weak recommendation for its use. In contrast, there are very well-supported, strongly recommended treatments for several sleep disorders.

Generally, standard sleep interventions can be delivered to patients endorsing suicidal thoughts with few modifications, provided that an office/clinic safety protocol and a patient-specific crisis plan are in place. For instance, suspicion of apnea would lead to a referral for a diagnostic evaluation at a sleep center. For nightmares, which can present as idiopathic nightmares but are more...
commonly associated with PTSD, two main nighttime interventions are considered to have the strongest evidence base: the use of the α₁-adrenergic agonist prazosin and imagery-therapy.

For insomnia disorder, CBT-I, is the recommended first-line treatment. CBT-I typically consists of 6 to 8 weekly individual or group sessions including sleep psychoeducation, stimulus control, sleep restriction, sleep hygiene, and cognitive therapy and tends to be more enduring than pharmacological interventions. It has been effectively delivered in numerous comorbid populations and can have positive effects on mood.

Numerous pharmacologic interventions for insomnia are recommended as second-line treatment when there is no response to CBT-I or it is contra-indicated. Despite clinical practice guidelines, pharmacotherapy for insomnia is far more common than CBT-I or related approaches and may be preferred by some patients. Hypnotics can be administered safely to suicidal patients with insomnia as has been done with zolpidem ER, which may reduce suicidal ideation.16,17 The prescribing physician must be cognizant that many hypnotics come with FDA black-box warnings; overdose is the most common means of suicide attempts, and off-label use of medications with sedating properties (eg, trazodone, tiagabine) have a significant harm-to-benefit profile.18 Psychiatrists are in an excellent position to manage deprescribing hypnوتics in the not uncommon presentation of persistent severe insomnia despite multiple sedating medications taken at night. We find many patients who present with major depressive disorder, insomnia disorder, CBT-I, however, the latter may be more advantageous.

In addition, when patients present with insomnia and a co-occurring condition (eg, depression, posttraumatic stress disorder, chronic pain) there is good evidence that CBT-I can be combined with psychological or pharmacologic therapy that targets the comorbid condition. For example, CBT-I can be combined with an antidepressant in depressed patients or with trauma-focused treatments for patients with PTSD. With appropriate safety planning, patients who also endorse suicidal thoughts can be similarly treated.

We recognize that a full course of CBT-I may not fit every psychiatrist’s clinic model and/or they have few appropriate referral options. In such cases, very viable alternatives exist. Shorter versions of CBT-I have been utilized with good effect, as have single components of CBT-I (eg, stimulus control, sleep restriction).19-20

Sleep hygiene, which is often delivered with minimal follow-up, is insufficient for many patients. If sleep hygiene is delivered as the primary method of addressing insomnia, it may be improved by systematically incorporating specific goals (eg, reduce caffeine intake, limit napping), daily tracking, and problem-solving during follow-up sessions.

Conclusion
Treatment outcomes for sleep disorders are enhanced by regular assessment, follow-up, and/or titration of treatment. For example, ask patients to complete a sleep diary each morning and to meet with you on a weekly or biweekly basis in order to interpret the results and adjust the sleep schedule accordingly. Likewise, patients starting positive airway pressure veterantraining.va.gov/insomnia/index.asp).

Although a myriad of pressing clinical issues face a patient with suicidal ideation, incorporating sleep assessments and interventions into the clinical care plan has multiple advantages. First, improving sleep not only provides immediate relief of sleep related symptoms, it may also lead to improvements in co-occurring pathologies such as depression. Second, sleep disorders represent a comparatively low stigma entry point into treatment, and a successful course of sleep-focused therapy can instill confidence in the patient that therapy works and is worth the investment. Finally, sleep disorders have been linked to increased suicide risk and, thus, their treatment may reduce risk and, therefore, improve overall outcomes.

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<th>Table 2. Components of a safety crisis plan</th>
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Patients may benefit from apps that aid in monitoring behavior and sleep diary data.

and suicidal ideation who have been prescribed a nightly antidepressant (eg, 40-mg fluoxetine) are also using a non-benzodiazepine receptor agonist (eg, 10-mg zolpidem) and 100-mg trazodone or 150-mg quetiapine fumarate while supplementing with an over-the-counter formulation at well-above the recommended dosage (eg, diphenhydramine, doxylamine, melatonin). Discontinuation plans may precede or be combined with (PAP) for sleep apnea will nonetheless benefit from psychiatric consultations early in the treatment process to encourage and support treatment adherence. Moreover, patients may benefit from the use of apps and web-based platforms that aid in monitoring behavior and logging sleep diary data as well as providing supplemental education (eg, CBT-I Coach: https://mobile.va.gov/app/cbt-i-coach; Path to Better Sleep: www.

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Circadian Rhythms Across the Lifespan
Impact on Sleep and Psychiatric Disorders

Significance for Practicing Psychiatrists
Strategically timed circadian treatments can improve patients’ mental and physical health.

Circadian health is a key pillar of well-being.

Disruptions in the circadian system and its alignment with the sleep-wake cycle can contribute to psychiatric illness.

Strategically timed light therapy and melatonin are first-line treatments for circadian disorders, but their timing is critically important to their success.

Circadian rhythms have a profound effect on our mental and physical health. This is not surprising due to our evolution under a 24-hour light/dark cycle. Almost every cell in the body contains a molecular circadian clock, which is influenced by the master circadian clock in the suprachiasmatic nucleus in the anterior hypothalamus. At least half of all genes in the genome oscillate with a circadian rhythm.1

There is growing recognition that circadian health, which is defined as robust 24-hour rhythms that are stably and appropriately timed with respect to both the external light-dark cycle and social rhythms (eg, sleep times), is a key pillar of health. This ensures that human behaviors and biological processes are optimized by occurring at biologically appropriate times. Indeed, mental health and circadian health are tightly entwined, and circadian interventions can improve mood and well-being, even in healthy people.

Infancy
The human suprachiasmatic nucleus starts oscillating in utero, in synchrony with time cues from the mother. With birth, newborns lose this time cue and have irregular sleep patterns, which begin to consolidate around 3 to 5 months. The emergence of a stable sleep-wake pattern is likely to reflect the development of the infant’s endogenous circadian system. Increased daily exposure to light is associated with a faster transition to a stable sleep-wake pattern, and a stronger, more well-defined circadian pattern in infant activity levels. This suggests the possibility that increasing daytime exposure to moderate light intensities and maximizing light-dark differences in the 24-hour day may promote circadian entrainment in infants.2

Needless to say, a consolidated sleep pattern in infants is associated with less sleep disruption and improved mood in caregivers.

Adolescence
With the onset of puberty, circadian rhythms shift later in time (phase delay). This is at least in part physiologically driven by sex hormones, as it is also observed in other mammals.3 Behaviors such as staying up later and the associated increased exposure to evening light also shifts the timing of the clock later.4 The increased use of blue-light-emitting electronic devices close to the face in the evening will phase delay the clock, as the circadian clock is maximally sensitive to blue light.5 Phase delays in circadian timing (a later circadian clock and more “eveningness”) are associated with increased incidence of depression, anxiety, and substance use, and may well be a transdiagnostic risk factor.6

When circadian phase delays lead to chronic complaints of difficulties in falling asleep and waking up at desired, often socially mandated earlier clock times, the patient may have delayed sleep-wake phase disorder (DSPD). DSPD affects approximately 7% to 16% of adolescents and young adults.7 Indeed, these later sleep onsets in combination with early school or work start times result in chronic sleep deprivation. Adolescents and young adults are arguably the most sleep-deprived segment of society. The major sleep and circadian disruption that occurs in adolescence and young adulthood likely contributes to the emergence of many psychiatric illnesses during this developmental stage.

Adulthood
Circadian rhythms drift back earlier with aging. Eveningness tends to peak in the late teens or earlier twenties, and thereafter there is a progressive drift towards earlier circadian rhythms—or more “morningness”—with aging.8 In general, females tend to have slightly earlier timed circadian rhythms than males. Most healthy adults (~70%), have an endogenous circadian period that is greater than 24 hours.9 This suggest that the majority of adults need to shift earlier (phase advance) to stay in synchrony with the external light-dark cycle. Despite increased time spent indoors, endogenous circadian timing in humans is still influenced by the external light-dark cycle. Later sunsets lead to later sleep onsets and, in the face of socially mandated fixed wake times, also to shorter sleep durations.

Historically, only adults engaged in shift work were considered to suffer from chronic circadian disruption. Rotating shift work or irregular shifts lead to a constantly changing light/dark cycle to which the circadian clock continually tries to adjust. Even stable permanent shifts, whether morning, evening, or night shifts, can be difficult, particularly as most shift workers prefer to sleep at socially normative night-time hours on days off. Thus, shift work is associated with sleep disruption and worse mental (particularly depressive symptoms) and physical health.10,11 If possible, shift work should be avoided, particularly in patients with or at risk for mental health conditions.

More recently, irregular sleep timing has been recognized as a subtle, but chronic form of circadian disruption. Irregular sleep timing in general is associated with poorer mental and physical health, which is likely to be due in part to the circadian shifting in response to the associated irregular light/dark cycle.12 A subtype of irregular sleep timing is known as “social jet lag,” which refers to shifts in sleep times from work or school days to free days.13 Typically, socially mandated work or school schedules push sleep to earlier clock times, while sleep drifts back to later more circadian appropriate clock times on free days.

Shifts of two hours or more in the midpoint of sleep between work days and free days is associated with depression, greater substance use, and worse physical health, and is estimated to occur in approximately 30% of the general population.13 Irregular sleep timing and social jet lag appear to be risk factors for psychiatric disorders, but longitudinal studies are needed.

Elderly
In the elderly, several factors can contribute to circadian disruption. Circadian rhythms continue to drift earlier in time. If this morningness leads to complaints of falling asleep too early in the evening and waking...
too early in the morning, the patient may have advanced sleep-wake phase disorder (ASWPD). Aging is also associated with reduced light exposure, as less time is spent outdoors and indoor lighting can be very dim. The lenses in the eyes yellow with aging; this reduces exposure to the most potent, blue wavelengths of light. In the extreme case of dementia, these factors, in addition to a potentially disintegrating suprachiasmatic nucleus, can result in irregular sleep-wake rhythm disorder (ISWRD). This consists of a less robust circadian rhythm with multiple episodes of sleep during the day and multiple periods of wake during the night.

Screening tools
Circadian timing is currently difficult to objectively measure outside of specialized sleep and circadian research laboratories. There are several approaches in development to address this problem. A home saliva collection kit to assess dim light melatonin onset, the current gold standard marker of circadian timing in humans, is in development. Blood-based transcriptomic biomarkers and algorithms to analyze data from wearables are starting to be validated against the dim light melatonin onset kit. Meanwhile, the Morningness-Eveningness Questionnaire (MEQ) asks people to consider their “feeling best” rhythms and indicate preferred clock times for sleep and engagement in various hypothetical situations (eg, physical exercise, exams, work). The questionnaire also assesses morning alertness, morning appetite, evening tiredness, and alarm clock dependency. Lower MEQ scores indicate more eveningness, and higher scores indicate greater morningness. Although morningness or eveningness correlates with dim light melatonin onset (r = -0.70) there can be up to a 4-hour range in dim light melatonin onset for a given MEQ score.

The Munich ChronoType Questionnaire (MCTQ) focuses on sleep timing and the regularity of one’s work schedule, number of workdays per week, and sleep timing and alarm clock use on workdays and free days. Sleep timing on free days can give a sense of endogenous circadian timing, although sleep on free days can also be influenced by alarm clock use, or by recovery from sleep deprivation that may have built up over the work/school week. More easily, the MCTQ can help assess for social jet lag as the difference between usual sleep timing on work/school days versus usual sleep timing on free days. Sleep timing and social jet lag can also be assessed over the short term with a 7-day sleep diary. For patients with shifting or irregular work schedules, a work diary (with commute times if they are long) can be also be useful. A more recent questionnaire, SATED (Satisfaction, Alertness, Timing, Efficiency and Duration) may be useful to assess sleep and circadian issues. This brief questionnaire may pinpoint the sleep and circadian factors most bothersome to the patient. In general, asking patients about daily routines, what changes they would like to make to their sleep schedule, and what social factors affect their sleep times will be useful.

“Melatonin use is contraindicated in the elderly as well as patients with epilepsy, those taking antihypertensive medications or blood-thinners, and women who are pregnant or breastfeeding.”

Circadian treatments
Overall, striving for bright light during daytime and minimizing nighttime light promotes wakefulness during the day and sleep at night and leads to a more robust circadian rhythm. Specific first-line treatments...
for circadian rhythm disorders include strategically timed light therapy and melatonin. Circadian treatments work best when they are integrated into the patient’s regular routine. A summary of circadian treatments and their effects is shown in Figure 1.

A first step in treatment is to stabilize sleep timing as much as possible and ensure that the patient has the opportunity to get 7 to 9 hours of sleep. It may also be necessary to slowly shift the sleep schedule in the desired direction (~15–30 min/d), as the associated changes in light/dark exposure will help shift the circadian clock.

Furthermore, light exposure across waking hours should be considered. If trying to shift rhythms earlier, evening light should be minimized; to shift rhythms later, morning light should be minimized. For example, older adults with ASWPD should be instructed to minimize light exposure prior to their desired wake time. Light exposure can be minimized by staying indoors, dimming room lights and light-emitting devices, wearing commercially available blue light blocking amber glasses, and of course by sleeping/keeping eyes closed.

Light therapy, which is indicated for ASWPD, DSWPD, and ISWRD in adults with dementia, is typically administered for 30 to 60 minutes using a bright light box or a wearable light device that permits ambulation during the light treatment (eg, Re-Timer). To shift circadian rhythms earlier (ie, for DSWPD treatment), light therapy should be administered in the morning, ideally at habitual wake time. Timing is adjusted as the wake time is advanced. To delay circadian rhythms (ie, for ASWPD treatment), light therapy should be used in the evening.

Contraindications for light therapy include eye disease, conditions that cause photosensitivity (eg, lupus), phototoxic medication use, and a history of hypomania/mania (unless patients are very carefully monitored).

Supplemental melatonin is available over the counter in the US and can be used to assist with phase shifting, particularly in DSWPD, although the phase shifts are smaller than those seen with light. Low doses (~0.5 mg) of melatonin are usually recommended to avoid the soporific effects seen with higher doses.20 Morning melatonin can shift rhythms later, whereas melatonin taken about 5 hours before usual sleep onset time can shift rhythms earlier.

Melatonin use is contraindicated in the elderly because of increased risk for falls and mood changes as well as patients with epilepsy, those taking anti-hippervigilant medications or blood-thinners, and women who are pregnant or breastfeeding.

Circadian treatments can be difficult to implement because the treatment needs to be timed according to the individual’s endogenous circadian timing. Incorrect timing of treatments can worsen circadian rhythm disturbances. For example, in an individual who habitually wakes around 7 AM, light exposure at 7 AM would be biologically interpreted as morning light, and result in phase advances. However, in an individual who habitually wakes at 11 AM, 7 AM light exposure could be biologically interpreted as late night light, and possibly result in phase delays. For this reason, we do not initiate morning light treatment any earlier than 1 hour before habitual wake time.

Physical activity may also shift circadian timing, although findings indicate that the effects of a 1-hour high-intensity exercise on subsequent circadian timing were small.21 While meal timing may not shift circadian timing, restricting eating to during the biological day can lead to weight loss.22 Social rhythms therapy, a treatment for mood disorders, focuses on regulating daily activities with potential impact on circadian timing such as closely scheduling the timing of bed/wake, meals, exercise, first social contact, and start of work so that these events occur at a consistent time and do not vary significantly day-to-day.23 The therapy is considered potentially effective, although more comparative efficacy trials are needed.

Conclusion
Circadian health is a key pillar of well-being. Exposure to bright light during the daytime and minimizing light during the night can help strengthen circadian rhythmicity. Circadian rhythms change across the lifespan; adolescents and young adults are more likely to experience circadian phase delays, whereas older adults are more vulnerable to circadian phase advances. Disruptions in the circadian system and its alignment with the sleep-wake cycle can contribute to psychiatric illness.

Treatment of circadian rhythm disorders can improve mental health. Treatments include bright light therapy and melatonin; however, the timing of such interventions is critically important to their success.

Dr Burgess is Professor, and Dr Swanson is Associate Professor, Sleep and Chronobiology Research Laboratory, Department of Psychiatry, University of Michigan, Ann Arbor, MI. Dr Burgess reports that she is a consultant for Natrol, LLC and MovingMindz, Pty Ltd. Dr Swanson reports no conflicts of interest concerning the subject matter of this article.

Acknowledgement—We thank Muneer Rizviyoon for his help with creating the figure.

REFERENCES
OKC Reflections

My story is only one among many accounts by individuals who were touched by the event. Most of us remember where we were when the OKC terrorist bomb shattered our sense of peace in this usually quiet community. The shockwave travelled for miles.

The tragedy unfolds

I recall being in my office less than 2 miles away, supervising a resident, when the entire building shook. Having grown up in the San Francisco Bay Area, my immediate thought was that it was an earthquake. But in Oklahoma, that didn’t make sense. More likely a natural gas explosion, I imagined. My resident, who had attended medical school in Kosovo, later told me that she knew exactly what it was.

We wandered to a room with a TV to see if anything unusual had been reported. A local news channel had their weather helicopter hovering over the downtown area. We watched in disbelief and horror. As the smoke parted, we saw the remains of what we later learned was the Alfred P. Murrah Federal Building, with a large section blown away. My thought at the time was that it would not be possible to survive in this structure, whatever had happened to it. As sometimes occurs, a bomb threat was apparently reported at our University of Oklahoma Health Sciences Center campus, and we dutifully left the building. My contact lenses were undamaged, free of invisible dust particles in the air.

Many of my memories from that time are spotty. Later in the day I tried to drive downtown to St Anthony’s Hospital, where many of the physically and emotionally wounded survivors were taken. Traffic leaving the city center was so heavy that I couldn’t proceed on the main route. I turned around, rationalizing that I would be of no help at the bombing site given my small stature, and later felt guilty.

Firefighters, police officers, military personnel, doctors and other volunteers reported to the site to search for survivors—grueling work in an unstable structure surrounded by massive debris. Some medical trainees without disaster experience helped the medical examiners sort out human remains. I went to the local Veterans Affairs Medical Center and met with civilians who had been close to the federal building. Countless community members reported to a local church to help—handling donations of food, bottled water, gloves, and other items to aid rescue and recovery workers. Many OKC residents with relatives and friends in the building and surrounding areas wandered around local hospitals to find loved ones.

Back at our outpatient clinic, we tried to reassure the patients who showed up for mental health care. Whatever problems they had were confounded by fear and sadness at the inexplicable loss of human life so close by. For the next days and weeks, we dealt with the additive effects of the bombing on our patients, and our doors and those of numerous mental health professionals were open to survivors, bereaved individuals, and others who were troubled.

Many of our health and mental health professionals were consumed with recovery work—attending to and doing surgeries on broken bones, head injuries, organ damage, and soft-tissue injuries; and assisting those with mental health sequelae. Psychiatrists and psychologists teamed up with clergy and medical examiners to meet with and notify family members of the deaths of their loved ones. In these sessions, the medical examiner started with a statement about identifying the remains of the loved ones, followed by the mental health care professional and clergy member processing the family members’ reactions. I recall feeling very grateful for the clergy, who had far more experience than I had in processing death and grief.

Media coverage of the bombing was intense, and reporters from across the country flooded the airport to chronicle the event. At some point President Clinton visited to express his condolences. Even actors and celebrities visited to show their support and perhaps boost publicity.

Our governor got tough with insurers when only mental health damage was covered. Unfortunately, federal workers’ compensation benefits covered survivors when only mental health diagnoses occurred due to work-related problems.

Beyond the first days

For weeks and years, we dealt with the aftermath of this event on our community, with people pitching in from all areas of expertise. We were all affected by the tragedy. In addition to the more than 800 injured by the explosion, another 12,000 individuals assisted in extensive rescue efforts, sifting through the destroyed building and surrounding areas for survivors and bodies, caring for those with physical and emotional injuries, transporting and identifying bodies, counseling the bereaved, and performing other duties, many of whom were donating their time. Sadly, there was one fatal injury during the search and rescue operations. In addition to sustaining emotional and physical injuries, many people dealt with unemployment and economic consequences because of barriers to insurance reimbursements and destroyed businesses.

The impact was felt by survivors (adults and children) of direct exposure as well as first responders and family and friends of victims via indirect exposure. Not surprisingly, in a study of 255 who were directly exposed to the blast, about one-third had a PTSD diagnosis.1 About 80% had witnessed death or injuries, and 77% required medical attention.

Seven years later, 26% still suffered from PTSD while many others had subclinical PTSD symptoms.2 Moreover, almost 19 years following the event, another study found that 23.2% of directly exposed survivors met threshold criteria for probable PTSD.3 The study also found that survivors had more anxiety and depression symptoms than controls, and higher symptoms were associated with heavy drinking and worse social functioning.

Children who lost close relatives had greater autonomic reactivity than those who lost more distant relatives, with higher levels of grief associated with more reactivity.1 Study findings suggest that the enduring physiological effects of trauma may be sepa-
rate from emotional symptoms in children indirectly exposed, rep-resenting a lasting footprint of disaster. For instance, seven years after the incident, children of survivors reported relatively low levels of posttraumatic stress and depressive symptoms, but they had more physiological reactivity than a community comparison group.7

First responders seemed to handle the stresses relatively well, which may be partially due to onsite brief-ings, use of healthy coping tech-niques (social support and positive reframing), onsite critical stress man-agement, a strong sense of purpose and sense of community, positive manage-ment style, a high educational level, medical experience, and as-sumption of a professional role.8

Learning from disaster

We, in the field of psychiatry, not only helped in the aftermath, but also used this unfortunate event as a learning opportunity. For instance, Art Rousseau, MD, was among several Oklahoma psychiatrists who took a leadership role in organizing mental health recovery efforts, and he was awarded the American Psy-chiatric Association’s Bruno Lima Award in Disaster Psychiatry for his work. Betty Pfefferbaum, MD, JD, immersed herself in research on ef-fects of the bombing and recovery efforts, especially among children. Her mentorship inspired me to conduct research on biological after-effects among survivors, and long-term health and mental health sequelae. The expertise and contributions of Carol North, MD, MPE, to disaster research have been invaluable. The Oklahoma State Department of Health worked with physicians and psychologists to study physical and emotional injuries. Our research is indebted to many of the survivors who pledged early on to participate in future research; they were passionate about promoting a better un-derstanding of the effects of terror-ism on those directly exposed, to help others in similar situations.

Increasingly our communities are affected by diverse disasters—acts of terrorism, mass shootings, destructive wildfires, colossal storms and other catastrophic events. As a global com-munity, it is essential that we share information about interventions that helped survivors, the bereaved, first responders, caregivers and others—and that we give our support. Healing may take many years.

Dr. Tucker is Professor, Arnold and Bess Underman Endowed Chair in Psychiatry, Vice Chair of Education, Department of Psychiatry, University of Oklahoma Health Sciences Center, Oklahoma City, OK.

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COMMENTARY
Resilience, Not Panic, in a Time of Pandemic

Harold J. Bursztajn, MD

As the pendulum has swung from denial to near-pandemonium about COVID-19, sensible public-health strategies to contain the spread of the virus must compete for attention with panic reactions like calling for quarantining people of a particular nationality. First it was the Chinese, next perhaps the Italians. As a psychiatrist, clinical ethicist, and citizen, I struggle with the reality that panic and hysteria spread more easily and quickly, covering more space in less time, than does hope. Instead, through solidarity, hu-manity, mutualism, and compassion, we can do likewise under much more benign—albeit unnerving—conditions. We need not assume that a catastrophic pandemic is at hand, and we must not resort to racist measures like demonizing and shaming an ethnic community. Such panic can easily become a self-fulfilling prophecy, with demoralization and economic chaos cascading into a life-threatening catastrophe. Far better to under-stand that life goes on and that hope and resilience can be nurtured, even amid cases of illness and death.

Fortunately, the internet can also convey practical preventive measures for individuals and communities, like those by the Centers for Disease Control and Prevention. For example, a blogpost by Ian M. Mackay, PhD, and Katherine E. Arden, PhD, titled “So you think you’re about to be in a pandemic?” on the website

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The feskalist women’s battalion Lodz 1944 with the author’s mother, Miriam Brikis Bursztajn, third from right.

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Virology Down Under shared useful recommendations, such as staying at least 2 meters away from visibly sick people, washing hands thoroughly, trying not to touch your face, and stocking up a 2-week supply of food and other essential household items. We can reasonably quarantine infected individuals, but we should not stigmatize our social and moral capital by automatically quarantining whole communities at random without weighing the risks that isolation, helplessness, demoralization, and despair bring in the longer term.

Dr. Bursztajn is Co-founder of the Program in Psychiatry and the Law at Harvard Medical School and President of the American Unit of the UNESCO Bioethics Chair (Haifa). He practices clinical and forensic psychiatry in Cambridge, MA.
The Other #MeToo

Continued from Cover

tims or as someone who has been abused. That is one of the reasons why we encourage the men with whom we work to see themselves as survivors—a small but important change in language that connotes resilience and empowerment.

**Trauma in men**

CASE VIGNETTE

“Bill” is 45 years old. Married for 20 years, he and his wife have two children. Bill reports that he and his wife are no longer intimate emotionally, and he finds it difficult to talk with his wife, be affectionate, and often finds himself zoning out when his wife is talking to him. Bill works as a retail supervisor; he noted difficulty holding onto jobs for longer than a year, often due to angry outbursts and irritability that are difficult to control.

When directly asked if he has experienced any traumatic events in his life, he reported none. In answering additional intake questions, he noted that some “funny business” had occurred when he was 14 years old when his next-door neighbor touched him inappropriately.

How and why is it so hard for men to recognize and acknowledge the occurrence of this type of trauma and subsequent mental health problems, and how can we help them?

While traumatic events are quite common in the general population, most people do not have long-standing negative mental health consequences as a result. However, with some traumatic events there is higher incidence mental health difficulties. Sexual trauma packs a huge wallop compared with other traumatic experiences. The probability of having negative consequences is much higher with sexual abuse compared with most other traumatic events. Individuals who experience sexual abuse or assault are at risk for a wide range of medical, psychological, behavioral, and sexual disorders.

Men who have experienced sexual abuse and assault may have very prominent psychological symptoms that are not easily captured in any one psychiatric diagnosis. For example, males who have been sexually assaulted often have buckets of seething anger. This never leaves them but especially comes out when they are feeling threatened or betrayed. Another example is difficulties with sexual functioning such as low sex drive or erectile problems, which not only affects self-esteem and sense of manhood but also interferes with intimate relationships. They may also feel unable to give or feel love or happiness, effects that reverberate into every aspect of their life.

Men who have been sexually assaulted may have concerns about their masculinity as well as their sexual orientation; they struggle intensely with shame and self-blame.” They are less likely to report sexual abuse, to identify experiences they have had as abusive, and to seek support or formal treatment for these experiences.

Boys and men are socialized to see themselves as strong, tough, and self-sufficient. Acknowledging feelings and disclosing vulnerabilities are in some ways antithetical to traditional masculine roles. Men also frequently wear thick coats of shame, having internalized the blame. When they do disclose, they are frequently met with disbelief, such as “That’s impossible. A man can’t be raped.” Or they are met with invalidation and victim-blaming such as, “How could you let that happen?”

**Barriers to treatment**

All kinds of male rape myths are responsible for delayed treatment seeking and perpetuating stigma (Table 1). The most prominent barriers to receiving mental health services in adult trauma survivors are concerns related to stigma, shame and rejection, low mental health literacy, lack of knowledge and treatment-related doubts, fear of negative social consequences, and limited resources. Male survivors typically do not disclose their histories of sexual abuse and assault for 20 to 25 years.

They may deny, minimize, or fail to see the connection between sexual abuse and subsequent mental health difficulties. Sometimes they dissociate and do not fully register or remember what happened.

Because many patients may not be completely forthcoming about their histories, patients should always be asked about exposure to traumatic events, including sexual abuse. It is also important to provide validation of the occurrence of the experience and to help the patient understand the connection between the trauma and consequent difficulties.

**Supporting male survivors**

It is important to offer male survivors a safe place where they are believed and accepted. Many male survivors with whom we have worked over the years tell us that having someone who listened and did not question the validity of their story was paramount to their healing.

The therapeutic alliance is predictive of, or associated with, a reduction in various symptoms. However, it is not enough to have a kind, caring, non-judgmental therapist. A mental health clinician who works with male sexual abuse survivors should have the knowledge and skills to understand and help patients who have been abused. For example, some well-intentioned providers may discourage their male patients from talking about their traumatic experiences. They may incorrectly think that talking about such experiences will open Pandora’s box or they themselves may be uncomfortable hearing details of the abuse.

While it may be upsetting for the patient, working through the trauma narrative in a process-oriented or more formalized exposure-based manner is tremendously helpful. Many patients tell us that the more they talk about it, the less impact the abuse has on them. And those discussions of the traumatic event, including details no matter how graphic, can allow survivors to understand and process what happened.

We have also worked with male survivors who have told us that their therapists seemed inappropriate, voicing explicit details of the abuses and appeared excited and eager to hear more, which felt like being abused all over again. Others have told us stories of therapists grimacing in disgust or pain or communicating an inability to hear the patients’ stories, all of which perpetuates shame and silence.

After disclosing the pain of their traumatic experiences, some survivors were met with insensitive, inaccurate, victim-blaming, and dismissive reactions. One patient told us that when he told his therapist that he needed to talk about the sexual abuse he had experienced, the response was, “I hope you are not one of those homosexuals who are going to waste my time telling me about imagined sexual abuse.” By reinforcing the patient’s belief that he was a severely flawed human being, the comment kept him from seeking help for many years.

<table>
<thead>
<tr>
<th>Myth</th>
<th>Fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men cannot be forced to have sex against their will.</td>
<td>Any individual can be forced to have sex against their will. If someone does not want to have sex, or is not able to give fully informed consent, they are being forced or coerced into unwanted sexual activity.</td>
</tr>
<tr>
<td>Men are less affected by sexual assault than women.</td>
<td>Men are just as affected by sexual assault as women, although it may be expressed differently.</td>
</tr>
<tr>
<td>Men who become sexually aroused or have an erection when assaulted must have wanted it or enjoyed it.</td>
<td>Many men have experienced unwanted or unintentional arousal during a sexual assault, as men often get erections in painful or traumatic situations. Arousal from abuse can be confusing for survivors of assault, but like our heartbeat, physiological reactions like erections are often outside our control.</td>
</tr>
<tr>
<td>A man cannot be raped by a woman.</td>
<td>Men can be raped by women. This type of crime is often underreported due to gender stereotypes. Any unwanted sexual contact is sexual assault regardless of gender. Men can, in fact, be made to penetrate and forced into oral sex, among other things.</td>
</tr>
<tr>
<td>People become LGBTQ+ when they are abused by someone of the same sex.</td>
<td>While abuse is prevalent in the sexual and gender minority community, it is most often the result of stigma and prejudice against a person who already identifies as or is labelled to be different than the accepted sexual orientation or assigned gender identity.</td>
</tr>
</tbody>
</table>

Anxiety & Stress Disorders
Treatments for adults

There are numerous guidelines that provide recommendations on psychological and pharmacological treatments for posttraumatic stress disorder in adults (Table 2).10,11 The American Psychiatric Association guidelines strongly recommend the use of cognitive behavioral therapy, cognitive processing therapy, cognitive therapy, and prolonged exposure therapy as part of treatment. The use of brief eclecticism, psychotherapy, eye movement desensitization and reprocessing, and narrative exposure therapy as well as pharmacotherapy with fluoxetine, paroxetine, sertraline, and venlafaxine are conditionally recommended for this patient population.12

The guidelines do not make recommendations for first-line treatment—psychotherapy first or instead of medications—because of insufficient evidence. The assignment of a strong recommendation is based primarily on a harm-to-benefit analysis, with more benefits seen as a result of psychological treatments for these patients.

In a meta-analysis of PTSD treatment for adults, trauma-focused psychotherapies were compared with selective serotonin reuptake inhibitors or serotonin and norepinephrine reuptake inhibitors.13 Only four studies met inclusion criteria; of those, two were deemed at high risk of bias. The unbiased studies showed no difference in PTSD symptom reduction but had wide confidence intervals. The authors concluded that there is insufficient evidence to determine whether medications or trauma-focused psychotherapies are more effective for PTSD symptom reduction.

Guidelines are intended to simplify treatment decision-making and as such, they are not rigid. While we celebrate several effective psychotherapies and pharmacotherapies for PTSD, it is possible that male survivors may refuse to participate or drop out before completing therapy. Moreover, they may engage in these therapies but not experience their full benefit and are thus in need of ongoing care. For example, in one study of interpersonal assault survivors who received an evidence-based psychotherapy for PTSD, women evidenced more rapid gains on global guilt, guilt cognitions, anger/irritability, and dissociation as compared with men.14

Shared decision-making that takes into account the values and preferences of patients is essential as is the consideration of benefits and harms of any intervention. Educating trauma survivors also allows shared decision making. Thus, clinicians should be ready to offer information about evidence-based options. They also should teach coping skills while being sensitive to cultural and socio-demographic differences.

**CASE VIGNETTE (CONT’D)**

What are Bill’s treatment options? During Bill’s appointment, the clinicians should elicit his treatment preferences and ask about his current functioning. Following a three-phase model, ensure Bill is safe, stable, and utilizing healthy coping skills before delving into trauma processing. Begin by providing psychoeducation about available treatments specific for trauma processing (eg, prolonged exposure and cognitive processing therapy), as well as treatments that are trauma-informed (eg, cognitive behavioral therapy, dialectical behavior therapy) that might help Bill with his impulsivity and anger. Since anger may be a symptom of depression, let Bill know that an SSR (eg, fluoxetine, paroxetine, sertraline, and venlafaxine) would be a useful adjunct to the psychotherapy.

**Conclusions**

The characteristics of the abuse as well as male survivors’ responses may be different, which can have an impact on assessment and treatment. For example, the assault may involve a single occurrence of penetration by several perpetrators (ie, a gang rape that occurs while a man is a young adult serving in the military or in a fraternity) or it may involved skilled grooming of a boy by an older and deceptively admirable figure such as a priest, coach, or teacher.

Of course, some men who have experienced sexual abuse or assault may not have significant sexual health difficulties or may recover on their own without professional intervention. Similarly, some male survivors may have difficulties that wax and wane across their lifespan, becoming particularly strong with certain triggers (eg, smells) or during particular times of the year (eg, anniversary of the abuse). Others, especially those with severe and prolonged abuse histories, may experience more profound or longer-term problems.

Some patients may prefer a support group rather than one-on-one counseling.15 Peer-based support lets survivors know that they are not alone and removes the element of a power hierarchy or judgment. Regardless of their treatment choice, it is our hope that survivors can work through their traumatic experience and live a healthy and meaningful life.

**Dr Cook is Associate Professor, Department of Psychiatry, Yale University School of Medicine, New Haven, CT; Dr Ellis is Assistant Director, Nova Southeastern University Trauma Resolution and Integration Program, Fort Lauderdale, FL. The authors report no conflicts of interest concerning the subject matter of this article.**

**REFERENCES**


**Table 2. Key considerations when working with male survivors of sexual trauma**

1. Assess for trauma and modify language when appropriate. Male survivors of sexual trauma may not present to treatment specifically for trauma-related issues. Psychiatrists should consider exploring previous or current sexual trauma by asking about any unwanted sexual experiences or events, rather than using the term trauma.

2. Work to reduce the power differential. Sexual trauma can result in feeling unsafe and mistrustful, particularly of authority figures. Clinicians can reduce this hierarchy by using less jargon, deferring to patients as experts in their own life, and approaching treatment in a collaborative way.

3. Avoid assumptions regarding masculine norms. Not all males assigned at birth desire to be masculine in traditionally defined terms. Explore your patient’s definition and expectations of masculinity.

4. Avoid terms like therapy. Replace with words like consultation, meeting, coaching, or discussion, all of which reduce some stigma and discomfort of mental health issues.

5. Respond sensitively, non-judgmentally, and compassionately. For example, “Thank you for sharing that with me. It must not have been easy to disclose, and I am honored that you trust me with this information.” “It sounds like it might be hard for you to acknowledge the impact these events had on you and your current functioning in life: let’s talk more about how this.” “It’s normal to feel ashamed, embarrassed, or guilty and it is important that you know that you’re not alone; that is a safe place for you to talk about those feelings.”

6. Integrate additional services and resources. Peer support is particularly useful for male survivors. Consider referring to free, informal, peer-based organizations such as Male Survivor (malesurvivor.org) and Men Healing (menhealing.org).
Integrating Deep Transcranial Magnetic Stimulation Into the OCD Treatment Algorithm

Ryan Vidrine, MD

In the US, obsessive-compulsive disorder affects about 4 million people.1 Compared with schizophrenia, which is notoriously disabling, obsessive-compulsive disorder causes similar degrees of serious impairment in social relationships and daily living. We often do not consider OCD in this same light because effective treatments are available. Yet, up to half of patients do not respond to first-line treatments and traditional pharmacological approaches are often associated with difficult adverse effects. In fact, even when patients do respond, it is rare to see true symptom remission.

Unlike depression studies, which often measure the percentage of responders and remitters, many OCD studies only measure responders and partial responders. For these reasons, it is essential to develop a more effective treatment algorithm that can help patients who do not respond to first-line options.

Current OCD treatment

OCD is characterized by uncontrollable, recurring thoughts or images (obsessions) accompanied by the urge to repeat specific behaviors (compulsions) to alleviate these intrusive thoughts. Effective treatments reduce symptoms and help patients cope with the anxiety surrounding these obsessions and compulsions. The American Psychiatric Association implemented an OCD treatment algorithm that designates a specific type of cognitive behavioral therapy (CBT)—exposure-response prevention (ERP)—and selective serotonin reuptake inhibitors as first-line treatments.

ERP involves patients working with their therapist to actively expose themselves in increasing degrees to the very things that elicit their fears. The process reduces anxiety surrounding the various triggers that induce the obsessive thoughts and compulsions. This form of CBT is effective in patients who complete a full course of treatment; however, some patients may have difficulty fully committing to the therapy as it can be extremely anxiety inducing. Ultimately, 45% of OCD patients either quit ERP because of the difficult treatment process or fail to respond to this treatment to a satisfactory degree.2 One option is to introduce a pharmacological treatment in parallel with ERP.

The first pharmacological option for patients with OCD is an SSRI. SSRIs are effective in about 50% to 70% of patients.3 However, because their effects are not localized only to OCD brain regions, they can have significant negative adverse effects in other parts of the body. Further exacerbating this issue is the fact that patients with OCD often require higher doses of SSRIs than those effective in treating depression. Research has shown that increasing the dose of SSRIs in this manner can lead to increased adverse effects, which can often be severe enough that patients choose to stop their medications.4,5 Moreover, because we do not fully understand how SSRIs work in the brain to reduce OCD symptoms, we have not yet found methods for predicting who will respond to the treatment in any reliable, affordable, or clinically feasible way.

Options after first-line

After non-response to ERP and/or initial doses of SSRIs, psychiatrists have only a few validated options. Clinicians will often escalate the dose of SSRIs, try multiple different SSRIs, or switch to or add clozapine, an older, but sometimes more effective SRI, but which unfortunately can often have more serious adverse effects. Next, atypical antipsychotics such as risperidone or aripiprazole are added to the patients’ treatment regimen. Again, the adverse effects associated with adding an antipsychotic are often worse than those associated with treatment with an SSRI alone. This process of escalating doses and testing different medications and combinations can often take several months to years.

When these options are exhausted, the next option in the treatment algorithm is surgical implantation of a deep brain stimulator (DBS) or a procedure known as a ventral capsulotomy, which creates a lesion in part of the brain implicated in OCD.6,7 While surgery has been proven effective in treatment-resistant patients, there are risks, costs, and complications associated with the procedures.8

Furthermore, brain surgery can be particularly anxiety-provoking for patients with severe OCD, and many...
Figure 3. Where dTMS should fit in the OCD treatment algorithm

Screen for OCD; if present assess severity and associated conditions

Mild to moderate OCD; patient has good insight

Begin ERP or SSRI

Improvement within 12 weeks?

Yes

Taper ERP with monthly “booster” sessions for 3 to 6 months

Minimal or none

Initiate SSRI

Improvement within 8 to 12 weeks?

Yes

Taper ERP with monthly “booster” sessions for 3 to 6 months

1. Consider referral to specialist for medication or behavioral management
2. Begin ERP and SSRI simultaneously

Severe OCD, or patient has poor insight or moderate to severe co-occurring hoardings, tics, depression, or anxiety disorder

1. Consider referral to specialist for medication or behavioral management
2. Begin ERP and SSRI simultaneously

1. Consider alternative diagnostic explanations for symptoms or presence of additional comorbidities

Minimal or none

Improvement within 12 weeks?

Yes

1. Taper ERP with monthly “booster” sessions for 3 to 6 months
2. Continue SSRI for 1 to 2 years before a gradual taper
3. Continue to regularly monitor for symptom exacerbation
4. Consider restarting ERP during medication tapering

Consider alternative approaches in the following order:
1. Intensify or restart ERP or refer to ERP therapist specialized in treatment of the OCD
2. Optimize SSRI dose to maximum tolerated dose
3. Cross-titrate to alternate SSRI and optimize dose
4. Switch from SSRI to clomipramine or augment SSRI with atypical neuroleptic drug
5. Augment SSRI with clomipramine

Address alternative diagnoses before proceeding with standard treatment algorithm

No

Minimal or no improvement or intolerable side effects

Intensive outpatient, partial hospitalization, or residential treatment

OR

dTMS

Improvement within 3 to 6 months?

Yes

1. Taper ERP with monthly “booster” sessions for 3 to 6 months
2. Continue SSRI for 1 to 2 years before a gradual taper
3. Continue to regularly monitor for symptom exacerbation
4. Consider restarting ERP during medication tapering

Consider alternative or experimental pharmacological neuromodulatory approaches:
1. SSRI augmentation or monotherapy with experimental agents, including riluzole, N-acetylcysteine, memantine, lamotrigine, calecixib, ondansetron
2. Experimental or novel rTMS or dTMS protocols
3. Ketamine

Minimal or no improvement or intolerable side effects

Consider:
1. DBS
2. Ablative surgery

*Given such low risk of side effects, dTMS may be included earlier in the algorithm to augment other treatment options in attempt to enhance or speed up recovery.
are not willing to proceed with surgery. This leaves clinicians in a difficult position, and other non-invasive treatment options are needed. Fortunately, a non-invasive treatment was cleared by the FDA, offering psychiatrists another neurocircuitry-based tool with far fewer risks compared with surgical options.

**dTMS as an option**

The FDA approved deep transcranial magnetic stimulation (dTMS); dTMS works by directing electromagnetic fields that generate excitation or inhibition of neurons deep inside the brain. It is completely noninvasive and performed in an outpatient setting, with no need for hospital gowns or anesthesia. Patients receive stimulation through a helmet with a built-in magnetic coil (Figure 1).

Treatment is well tolerated, usually with only mild discomfort due to sensations on the scalp sometimes described as feeling like a woodpecker tapping on the head; however, with increasing treatments, the scalp desensitizes to this sensation, and most patients report it to be less bothersome with each treatment.

Unlike SSRIs, this treatment is localized, more precisely targeting specific brain regions—the medial prefrontal cortex and the anterior cingulate cortex (Figure 2)—that play an essential role in regulating stress disorder: a pilot study. Eur Neuropsychopharmacol. 2012;26:800-809.

**References**

With the emergence of new therapeutic strategies, we now have more options for improving the quality of life for people diagnosed with psychiatric disorders. As the field continues to progress it is important for you and your colleagues to understand the current clinical data and best practices when caring for your patients.

The Annual Psychiatric Times® World CME Conference™ is an event specifically designed to help you apply new evidence-based clinical concepts in psychiatry to real-world clinical practice. This 3-day meeting will feature expert presentations and panel discussions addressing emerging psychiatric treatments and newest clinical trial data, and best practices for managing challenging psychiatric diagnoses including mood disorders, anxiety disorders, eating disorders, postpartum depression, substance abuse disorders, and more. This experience provides the ideal curriculum with a focus on challenging patient case scenarios, integrating relevant evidence into real-world patient management, and comparing your practices with those of experts and peers.

Benefits of Attending:

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- Hear about strategies for early diagnosis and intervention to improve outcomes
- Learn about how new therapies work to treat various psychiatric conditions
- Get a better understanding of the impact of psychiatric disorders for those affected
- Explore future directions for treating psychiatric disorders
- Earn CE credit while interacting with psychiatric experts and peers

Overview:

Agenda:

Thursday, October 15, 2020

12:00 pm Registration and Lunch
Sleep, Migraine, Psycho-Oncology
1:00 pm Interventions for Sleep Disturbances in Psychiatric Disorders
1:15 pm The Interplay of Migraines and Psychiatric Disorders: Treatment Implications
1:30 pm Panel Discussion, Q&A
1:45 pm Clinical Psycho-Oncology: Assessment and Management
2:15 pm Audience Q&A
2:30 pm BREAK
Hot Topics
3:00 pm Cannabis in Psychiatry: Clinical, Legal, and Ethical Issues
3:20 pm The New Role of Psychedelics
3:40 pm Panel Discussion, Q&A
Special Lectures, Giants in Psychiatry
4:00 pm Diagnosing and Treating PTSD
4:30 pm Special Guest Speaker
5:00 pm ADJOURN
5:00 pm Welcome Reception
Friday, October 16, 2020
7:00 AM  Registration and Breakfast
8:00 AM  Welcome, Introductions, and Presession Questions
Plenary Session: Special Report on Major Depressive Disorder
8:10 AM  Diagnostic Issues in Mood Disorders
8:35 AM  State-of-the-Art Treatment in Major Depressive Disorder
9:00 AM  Treatment-Resistant Depression
9:15 AM  Treating Major Depressive Disorder: Beyond MAOIs and SSRIs
9:30 AM  BREAK
Plenary Session: Special Report on Bipolar Disorder
10:00 AM  State-of-the-Art Treatment in Bipolar Disorder
10:30 AM  Medical Crossfire®: Should Bipolar Depression Be Treated With Antidepressants?
11:00 AM  Medical Crossfire®: Should Benzodiazepines and Opioids Be Used Concurrently?
11:15 AM  Postsession Questions
11:20 AM  Keynote Lecture
12:00 PM  Non-CME Lunch
Breakout Sessions
Specialist Track: Clinical Conundrums and Commentary
1:30 PM  Major Depressive Disorder
2:15 PM  Bipolar Disorder
Primary Care Track
1:30 PM  Treating Major Depressive Disorder in a Primary Care Setting
2:00 PM  Treating Anxiety in a Primary Care Setting
2:30 PM  Panel Discussion, Audience Q&A
3:00 PM  BREAK
Plenary Session: Hot Topics
3:30 PM  Presession Questions
3:35 PM  Treatment Strategies for Attention-Deficit/Hyperactivity Disorder
3:55 PM  Symposium: Causes, and Treatment of Binge-Eating Disorder
Plenary Session: Special Report on Psychiatry and Women’s Health
4:05 PM  Practical Psychoneuroendocrinology: How the Brain, Nervous System, and Endocrine System Interact
4:25 PM  Psychotomimetic and Psychopharmacological Options for Postpartum Depression
4:40 PM  Effective Strategies for Hypoactive Sexual Desire Disorder
4:55 PM  Postsession Questions
5:00 PM  ADJOURN
5:30 PM  RECEPTION

Saturday, October 17, 2020
7:00 AM  Registration and Breakfast
8:00 AM  Welcome, Introductions, and Presession Questions
Plenary Session: Special Report on Substance Abuse
8:10 AM  Treatment for Opioid Use Disorder
8:40 AM  Medication-Assisted Treatment and Alternative Therapies for Addressing Addiction
9:20 AM  Methamphetamine Abuse and Treatment Options
9:25 AM  Medical Crossfire®: Should Benzodiazepines and Opioids Be Used Concurrently?
9:35 AM  Audience Q&A
9:45 AM  BREAK
Plenary Session: Special Report on Schizophrenia
10:15 AM  Diagnosing Schizophrenia
10:35 AM  State-of-the-Art Treatment in Schizophrenia
10:55 AM  Long-Acting Injectables for Schizophrenia
11:15 AM  Postsession Questions
11:20 AM  Keynote Lecture
12:00 PM  Non-CME Lunch
Breakout Sessions
Specialist Track
1:30 PM  Clinical Conundrums and Commentary: Substance Abuse
2:15 PM  Clinical Conundrums and Commentary: Schizophrenia
Primary Care Track
1:30 PM  Addressing Opioid Use Disorder
2:00 PM  Practical Strategies for Addressing Sleep Disorders
2:30 PM  Panel Discussion, Audience Q&A
3:00 PM  BREAK
Hot Topics: Overcoming Challenges Associated With Antipsychotics
3:30 PM  Advances in Predicting and Treating Tardive Dyskinesia
3:45 PM  Diagnosis and Management of Metabolic Syndrome
4:00 PM  Genetics, Genomics, and Psychiatry: What Do We Know?
4:15 PM  Update on Neuroimaging for Psychiatric Disorders
4:30 PM  New Pharmacological Targets for Psychiatric Disorders
4:45 PM  Advances in Clinical Studies: Implications for Your Practice
5:00 PM  ADJOURN

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Consultation-Liaison Psychiatry
The Interface of Psychiatry and Other Medical Specialties

James A. Bourgeois, OD, MD, and Michael Sharpe, MD

Consultation-liaison (C-L) psychiatry is a major psychiatric subspecialty that, within general medical/surgical and academic medical and increasingly in primary care settings, serves as the “tip of the spear” for psychiatry. This metaphor reflects consultation-liaison’s place as the most forward clinical psychiatry service in the wider medical world and the opportunity to lead improvements in patient care in all medical services.

Who we are
Consultation-liaison psychiatrists specialize in the diagnosis and management of psychiatric disorders that are comorbid with general medical/surgical illness. Examples include the psychiatric comorbidity of neurological illnesses (eg, Parkinson disease, multiple sclerosis, cerebrovascular disease), endocrinological illness (eg, diabetes mellitus, hyper- or hypothyroidism), rheumatic illness (eg, systemic lupus erythematosus, giant cell arteritis), and cardiovascular illness (eg, heart disease, vascular disease). In addition to psychiatric comorbidity, there is a broad area of psychiatric adverse effects of systemically administered medications (eg, corticosteroids, other immunomodulators, CNS-active agents) and the often complicated systemic medical and psychiatric adverse effects of medications used for primary psychiatric illness (eg, anticonvulsants, lithium, antipsychotics, antidepressants)

The general medical context of consultation-liaison psychiatry practice means that the psychiatric illness profile differs from that of general psychiatry practice. The most common disorders in the general medical setting include dementia, delirium, other neurocognitive disorders (eg, the sequelae of traumatic brain injury), catatonia, substance use disorders, intoxication and withdrawal states, and medical complications of psychiatric interventions (eg, neuroleptic malignant syndrome, serotonin syndrome, medication toxicity states, adverse effects) as well as depressive, anxiety, and substance use disorders. The psychiatric illnesses that constitute much of general psychiatric practice are also seen by consultation-liaison psychiatrists when they are associated with a general medical illness (eg, melancholic/psychotic depressive disorders, acute manic states, acute psychotic states) and when they result from medical illness and the trauma of treatment (eg, acute stress disorder, PTSD following major surgery or intensive care).

Consultation-liaison psychiatrists are expert at the complex task of managing psychiatric illness in the context of the general hospital and the emergency department. The responsibility of the C-L psychiatrist is first to assure that the proper medical evaluation and management are accomplished for the medical stabilization of patients before providing the necessary psychiatric treatment in collaboration with the patient’s clinical team. The C-L psychiatrist then arranges for psychiatric disposition, if and when that is clinically indicated.

Current training models for C-L psychiatry include 2 or more months of core rotation in the standard psychiatry residency program. Following residency there is an additional full academic fellowship year for psychiatrists who wish to qualify for subspecialty board eligibility and certification in consultation-liaison psychiatry.

Where we have been
Modern C-L psychiatry has developed as a distinct model of psychiatric practice. Unlike the care of patients with serious mental illness in long-term inpatient psychiatric facilities or the care for high-functioning psychiatric outpatients with psychotherapy, the C-L model evolved from placing psychiatric services in general medical hospitals, which began in the mid-20th century. This innovation led to the development of the dual partner concepts of “consultation” and “liaison” functions in hospital-based psychiatric practice. The consultation role refers to the direct care of the medical inpatient on request from the admitting physician, with recommendations for direct care and brief, in-hospital follow-up. In contradistinction, the liaison function refers to the psychiatrist sharing their understanding and interpretation of behavioral manifestations of psychiatric illness in medical/surgical patients and direct advice to medical and nursing services to improve the care of medical/surgical patients with comorbid psychiatric conditions.

Until recently, with its inpatient medical/surgical hospital heritage, C-L psychiatry was primarily hospital-based subspecialty, with the development of one-year fellowships in C-L psychiatry that were primarily inpatient-based. However, in the past 20 years, there has been an accelerating development of outpatient C-L models. This movement involves placing psychiatrists in outpatient specialty medical settings and in primary care, where specialty physicians and primary care physicians work together with psychiatrists to care for patients.

The development of psychiatry in the general hospital led to a movement to establish C-L psychiatry as a specific and differentiated subspecialty of psychiatry. In the US, this happened in 2003 with the establishment of the subspecialty board in psychosomatic medicine (a synonym of consultation-liaison psychiatry) and with the first American Board of Psychiatry Neurology examinations offered in 2005. The subspecialty has thrived ever since.

New proactive and integrated models of inpatient C-L psychiatry are increasing the field’s reach and effectiveness.

Where we are now
We are now in a period of the rapid and robust development of C-L psychiatry, driven by an increasing awareness of the need to treat the whole patient as well as by increasing amounts of evidence that indicates the clinical and financial importance of better management of psychiatric illnesses in patients under general medical care. Two major medical journals, Psychosomatics and General Hospital
Psychiatry, are devoted specifically to C-L psychiatry scholarship.

There are a rapidly increasing number of C-L psychiatry fellowships. The leading national and international organization, the Academy of Consultation-Liaison Psychiatry (ACLP; www.aclppsychiatry.org) has almost 2000 members; the most recent annual meeting in San Diego, CA, attracted more than 1200 attendees—an all-time record. The next annual meeting is in Phoenix, AZ, in November 2020 (www.clp2020.org) and promises to be even larger. This spectacular growth largely reflects the expansion of C-L psychiatry beyond academic medical centers into hospitals.

Where we are going

There are many exciting opportunities for C-L psychiatry to improve patient care. It is now clear that all sizeable hospitals must have real-time access to psychiatric consultation (whether in-person or by telemedicine). New proactive and integrated models of inpatient C-L psychiatry are increasing the field’s reach and effectiveness. The incorporation of standard clinical approaches to psychiatric illnesses (e.g., dementia, delirium, catatonia, traumatic brain injury) commonly encountered in C-L practice into electronic health records is ensuring better and safer care for patients with these high-acuity psychiatric illnesses. Greater availability of psychiatric consultation for medical outpatients, with standardized pathways for patients with the common psychiatric comorbid illnesses in primary care, is extending consultation-liaison care outside the hospital setting.

Consultation-liaison psychiatrists have also been early adopters of innovative communication and other technology for advancing patient care. These technologies include the provision of psychiatric care by video communication (telemedicine or telepsychiatry) and the creative use of the electronic health record to enhance psychiatric care for medical patients (e.g., standardized clinical pathways, incorporation of outcome and rating measures).

As clinical science and technology advances at an extraordinary pace, the value of C-L psychiatry within academic departments of psychiatry, and, indeed, in medical centers and medical schools, is being reflected in increased leadership and academic opportunities as the tip of the spear in psychiatry’s reintegration into the house of medicine.

Dr Bourgeois is Chair, Department of Psychiatry, Baylor Scott & White Health, Central Texas Division, and Clinical Professor (Affiliated), College of Medicine, Texas A&M University Health Science Center, Temple, TX. Dr Sharpe is President, Academy of Consultation-Liaison Psychiatry and Professor of Psychological Medicine, University of Oxford, UK. They report no conflicts of interest concerning the subject matter of this article.

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Mood Disorders

RESEARCH UPDATE

What Is the Deal With Esketamine?

Samuel T. Wilkinson, MD

Major depressive disorder is the leading cause of disability worldwide. Esketamine’s approval by the US Food and Drug Administration as the first rapid-acting therapy for treatment-resistant depression (TRD) was welcome news to patients. But many doctors have questions and legitimate concerns. What is so special about esketamine? What type of patient should we consider for this treatment? Where do we send patients for treatment? What are the risks? Here, I try to answer some of these questions.

Why ‘S’ ketamine?

Esketamine is the S-enantiomer of ketamine, which is more potent at the N-methyl-D-aspartate (NMDA) glutamate receptor than its mirror image, R-ketamine. The traditional theory of how ketamine produces antidepressant effects is that it works through the NMDA receptor to lead to a growth of new nerve connection (synapses). This is one of the reasons why ketamine treatments provide a distinct mechanism of action and are an improvement on existing therapies.

Esketamine v R-ketamine

Many clinicians wonder how esketamine compares with racemic ketamine (comprised of a 50/50 mix of S- and R-ketamine) with respect to clinical effectiveness. The short answer: there is a lot we do not know.

One comparative effectiveness study by Correia-Melo and colleagues’ showed that intravenous esketamine is not inferior to intravenous ketamine in patients with TRD. However, this study was fairly small for a non-inferiority study (N = 63) and only evaluated patients at 24 hours after a single dose. At least in this context, it does not seem like there is a large difference between the two drugs when given intravenously.

Rapid improvement

Part of the excitement about ketamine and esketamine is that this approach has the potential to improve mood and other depressive symptoms in a much shorter time than classic antidepressants such as the selective serotonin reuptake inhibitors. In the early studies of ketamine, a substantial number of patients experienced dramatic improvement just 4 hours after dosing.

While some patients may need several treatments before effects are noticeable, the possibility of helping patients experience significant improvement after just one treatment—as seen in the following clinical vignette—is an important advancement over traditional antidepressants. Some experts question whether the effects of esketamine are as rapid as those of ketamine; nonetheless, these treatments provide a distinct mechanism of action and are an improvement on existing therapies.

CASE VIGNETTE

“John” is a 45-year-old single man with MDD who was referred to our depression clinic by his nurse practitioner for refractory symptoms. He reported a 5-year history of depressive symptoms that had only minimally abated in recent years with medication trials that included fluoxetine, bupropion, duloxetine, lithium augmentation, and brexpiprazole.

His work as a business manager was beginning to suffer because of the worsening depression. After a thorough consultation as well as physical examination and laboratory assessment, a treatment protocol commenced with 56-mg intranasal esketamine, twice weekly. His depression symptoms decreased significantly after the first treatment, and he is now in remission and receiving esketamine every other week as part of the maintenance phase of treatment.

Which patients benefit?

The patients who were enrolled in the esketamine trials for TRD had a specific profile. Generally, in clinical trials, patients with major medical problems or psychiatric comorbidities are excluded. In the clinical trials of esketamine that led to FDA approval for TRD MDD, key exclusion criteria included active substance use disorder (or any use within 6 months), current or past psychosis, and bipolar disorder.14 These patients were moderately to severely depressed, and in general had two or more adequate antidepressant courses that failed during the current episode but generally no more than 8 (different upper limits were used in different trials; most trials used 5) and had not failed electroconvulsive therapy (ECT) prior to participating in the trials.

In selecting patients for esketamine treatment, the Interventional Psychiatry Service at Yale strives to align with the key inclusion/exclusion criteria of the trials, with some exceptions. For instance, in clinical practice, there is no legitimate reason to exclude patients if they have 8 or more adequate antidepressant trials that have failed, or ECT that failed.

Of chief concern is to be cautious when the potential risk-to-benefit analysis is shifted by a clinical factor. For example, we generally do not treat TRD in patients who are active using illicit substances or missing habit-forming substances that are legal (ie, alcohol, cannabis). Other clinical and demographic factors (ie, presence of psychosis, older age) are also considered carefully.

Implementation challenges

Despite the excitement about esketamine, it has been a very difficult treatment for psychiatrists to implement. A lot of this has to do with a different routine of administration as compared with most of our treatments, which are pills. Patients who receive esketamine must be treated on-site, at a doctor’s office, or other health care facility. Patients must be observed for 2 hours following esketamine administration, which includes measuring vital signs. Most psychiatrists’ offices do not have the space or other resources needed for such. Furthermore, while it is easy...
to get insurance to pay for the cost of the drug, the reimbursement process and compensation for two hours of monitoring is unclear.

Exploring the risks

Despite the potential benefit of esketamine, there are several risks. The FDA label for esketamine includes a black box warning of the potential for misuse of esketamine. It is also important for clinicians to know that patients should not drive on the days they receive treatment. Cognition is impaired in the acute period following esketamine administration, but usual-ly resolves within 60 to 90 minutes.

The bottom line

Esketamine offers a novel treatment approach that can lead to rapid improvement in patients with depression. However, significant logistical barriers prevent the medicine from being implemented widely, and questions remain about the long-term approach to treating depression with esketamine.

Dr Wilkinson is Assistant Professor of Psychiatry; Assistant Director, Yale Depression Research Program, New Haven, CT. He reports that he has received research funding from Janssen (manufacturer of esketamine), Sage Therapeutics, LivnaNova, and Oui Therapeutics. He is a consultant for Janssen, Oui, and Biohaven, which have been subject to the consulting pol- icies of Yale University. Yale University holds a share of the patent of ketamine/ esketamine for depression; this patent does not include Dr Wilkinson.

REFERENCES


BIPOLAR UPD ate

Cannabis: Patients With Bipolar Should Avoid Use

David N. Osser, MD

We frequently encounter patients who use cannabis. More than 50 indications for medical marijuana are approved by various state governments, although no indications are FDA-approved. Marijuana is legal in 36 states—and 10 states allow recreational use—but regulation of the quality or purity of these products is minimal. Some patients are convinced that marijuana calms them, uplifts them, blunts their anxiety, enables them to sleep, and has calming effects. Some patients believe it is the only thing that is helpful for their neurological symptoms. Potentially, scores of nicotine users say the same thing: it is their coping strategy of choice. Patients frequently encounter pa- tients with cannabis who had never used cannabis and a group that continued to use. The total sample included 1922 patients. In a two-year period, the con- tinued use significantly lowered rates of recovery, greater work impair- ment, and fewer were living with a partner. The data were based on patient reports and self-report surveys. The data was likely under-reporting and probably an un- derestimate of the association between cannabis use and lives worsened. A systematic review of the effects of can- nabis on mood and anxiety disorders confirmed a negative association between cannabis use and long-term out- comes.¹

Some patients exhibit psychotic symp-toms after cannabis use. A recent study found that schizophrenia or bi- polar disorder developed in many of these patients.² This happened in 47% of patients who became psychotic on cannabis over the next four years. This was the highest incidence of conver-sion after initial psychosis following use of various substances: the second highest was with amphetamine, at 32%.³


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interpersonal violence is a global public health concern and a leading cause of injury, disability, and mortality worldwide. Although most individuals with psychiatric diagnoses do not engage in violent acts, existing evidence suggests that interpersonal violence is highly prevalent among individuals with psychiatric disorders. For example, individuals with serious mental illness incur approximately 2 to 3 times greater risk for interpersonal violence, while individuals with both serious mental illness and substance use disorders incur risk up to 10 times that of healthy individuals.1-3

Interpersonal violence in individuals with psychiatric conditions is not only a significant clinical concern for health care providers, caregivers, and loved ones, but also a substantial stigmatizing factor for mental health populations. While most individuals with psychiatric conditions will not use violence in their lifetime, the empirical link between interpersonal violence and mental illness perpetuates impairment associated with the condition and presents a barrier to treatment-seeking.

There is tremendous heterogeneity in the frequency, severity, and type of violent episodes with whom the violence occurs (ie, general aggression versus intimate partner violence or other family violence), as well as the etiology and course in both psychiatric and general populations. Thus, there is agreement in the literature that while developing screening and intervention approaches with a high degree of reach is useful, a one-size-fits-all approach to screening and intervention of interpersonal violence is inadequate.

Two psychiatric conditions have been identified as salient correlates of interpersonal violence perpetration and victimization. The following is a brief review of the literature on posttraumatic stress disorder and substance use disorders (SUD), as well as their co-occurrence with interpersonal violence. Screening tools and existing data regarding intervention strategies to prevent and reduce interpersonal violence in the context of PTSD and SUD are also briefly reviewed.

**Co-occurrence of PTSD and SUD**

PTSD and SUD, which commonly co-occur with one another, are among the most frequently identified psychiatric correlates of interpersonal violence. In the US, up to 40% of individuals with SUD also meet diagnostic criteria for PTSD.4 Individuals with co-occurring PTSD and SUD incur heightened risk for other psychiatric problems (eg, depression, anxiety), suicidality, neuropsychological impairment, increased morbidity and mortality, unemployment, and social impairment. Co-occurring PTSD and SUD also place a tremendous economic burden on the health care system, as individuals with this complex dual condition have poorer treatment outcomes on multiple indices of functioning, longer duration of substance use, and more treatment episodes.

**Interpersonal violence, PTSD, and SUD**

PTSD has been commonly and causally linked to use of interpersonal violence among a variety of populations, including men and women in civilian and military populations, students, and treatment-seeking patients.5-7 The association between PTSD and interpersonal violence has often been explained by social information processing theories positing that PTSD can predispose individuals to hostile attribution bias, increased perception of threat, and heightened stress reactivity, thereby precipitating a propensity toward maladaptive stress responding, including interpersonal violence.

Similarly, substance misuse and SUD are salient risk factors for interpersonal violence and victimization. Alcohol use has shown the most unequivocal causal effects. For example, rates of interpersonal violence perpetration are up to 8-fold higher among individuals with alcohol use disorder, as compared to those without.8 Moreover, interpersonal violence episodes are more frequent and severe in the presence of alcohol use.9 Findings suggest a dose-response effect between alcohol use and interpersonal violence severity.10

The association between alcohol use and interpersonal violence is most commonly explained by the alcohol myopia theory, which suggests that the pharmacological effects of alcohol simultaneously cause a reduction in the scope of one’s attentional focus to the most salient cues in the environment and reduce the capacity to engage adaptive cognitive abilities. Thus, under the context of acute intoxication, provocative cues such as interpersonal conflict instigate aggressive behavior.

The effects of drug use on interpersonal violence is less clear. Although drug use and drug-related problems are correlated with interpersonal violence, very little research has been done to examine casual links. Stimulants, such as cocaine and amphetamines, are the drugs most frequently linked to interpersonal violence. There is some evidence to
suggest that high doses of cocaine are associated with aggressive responses and cocaine use has an impact on same-day interpersonal violence.\textsuperscript{11}

Research examining associations between cannabis and interpersonal violence is mixed. Cannabis may decrease subjective feelings of aggression, while other data suggest it decreases the risk for interpersonal violence.\textsuperscript{12} The link between other drugs, such as opioids and benzodiazepines, and interpersonal violence is not strong. Opioid use has been positively associated with interpersonal violence while other research suggests that opioid use may have stronger associations with interpersonal violence victimization.\textsuperscript{13} There is a great deal more work to be done on the distinct and combined associations between different drugs and interpersonal violence, as well as the pharmacologic and behavioral mechanisms explaining their effects on aggressive behavior.

Several studies have examined the combined and relative associations of PTSD and substance use on interpersonal violence. While additional research is urgently needed in this area, findings consistently suggest that these disorders independently and collectively increase risk for interpersonal violence.

In an extension of the alcohol myopia model, the more complex I-cubed (instigation, impellance, inhibition) model posits that interpersonal violence might be potentiated by a combination of instigating stimuli paired with cognitive and contextual factors that compel and/or disinhibit one toward violence.\textsuperscript{13} Despite abundant evidence that PTSD and SUD commonly co-occur, and that these two diagnoses are among the most well-documented and salient risk factors for interpersonal violence, no studies have directly integrated PTSD diagnoses or symptom severity into an empirical examination of the alcohol myopia or I-cubed model. Closing this gap in the theoretical and empirical literature is a critical next step for the interpersonal violence field so that prevention and intervention efforts can be improved.

**Screening, referral, and intervention**

As the state of the science that links PTSD, SUD, and interpersonal violence evolves, the existing data afford mental health providers with clinical recommendations for screening, referral, and treatment. Some notable clinical considerations include the critical need for all patients to receive interpersonal violence screening at treatment entry and at least once then at least one additional time since interpersonal violence exposure fluctuates over the lifespan. It is particularly important to ensure screening of exposure to violence among commonly overlooked and high-risk populations, including women and girls, racial and ethnic minority populations, patients with limited English proficiency, LGBTQ patients, and individuals living with HIV/AIDS.

Another persistent limitation to interpersonal violence screening measures is the availability of validated measures that are demographically and culturally adapted to ensure rigorous measurement. For example, some measures have not demonstrated adequate validity to assess men’s interpersonal violence victimization, racial and ethnic minority populations, and sexual and gender minority populations.

Although providers commonly report feeling ill-equipped to assess and adequately respond to interpersonal violence disclosure, data suggest that it is important for mental health care providers to screen for interpersonal violence and provide relevant treatment referrals. Education for physicians in training as well as medical residents and fellows in available screening and referral methods is essential. A selection of widely available and validated interpersonal violence screening measures are described in the Table.

When it comes to interventions for interpersonal violence, treatments are still evolving. Cognitive behavioral therapy (CBT) is among the most widely studied approaches for interpersonal violence but evidence suggests that it remains somewhat limited in its efficacy.\textsuperscript{14,15} There is emerging evidence that brief motivational interviewing interventions prevent and reduce aggression in the context of substance use.\textsuperscript{16} The Strength at Home Couples program, a trauma-informed CBT intervention for veterans and their partners, has been shown to prevent physical violence and reduce psychological violence among couples.\textsuperscript{17} A single-session of emotion regulation skills training also holds potential to reduce aggression among veterans with PTSD.\textsuperscript{18}

Couples-based interventions might also be appropriate for reducing interpersonal violence among partners, particularly when violence is bidirectional between partners. To date, there is limited evidence that intervening with women survivors of interpersonal violence is effective in reducing subsequent episodes and there is a critical need for more research to examine effective intervention strategies to prevent revictimization. Interventions, like CBT, that are focused on improving the well-being of survivors, may help survivors reduce symptoms of depression and PTSD and feelings of guilt, provided the violence has ceased.

**Summary**

Individuals who present for mental health care are likely to be suffering from a mental disorder and substance use disorder. The most critical next step for the interpersonal violence field is to further develop the empirical examination of I-cubed model. Closing this gap in the theoretical and empirical literature is a critical next step for the interpersonal violence field so that prevention and intervention efforts can be improved.

**Table. Selected measures for interpersonal violence screening and assessment**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Items and type(s) of violence assessed</th>
</tr>
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<tbody>
<tr>
<td>Revised Conflict Tactics Scale (CTS-2)\textsuperscript{19}</td>
<td>78-items assessing perpetration and victimization of psychological, physical, and sexual violence between intimate partners; also assesses negotiation strategies between partners</td>
</tr>
<tr>
<td>Brief Conflict Tactics Scale (Brief CTS-2)\textsuperscript{20}</td>
<td>5-items assessing physical violence between intimate partners; also assesses negotiation strategies between partners</td>
</tr>
<tr>
<td>VIO-SCAN\textsuperscript{21}</td>
<td>5-items assessing risk of violence among veterans</td>
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<tr>
<td>Hurt Insult Threaten Screen (HITS)\textsuperscript{22}</td>
<td>4-items assessing frequency of intimate partner violence</td>
</tr>
<tr>
<td>Ongoing Abuse Screen\textsuperscript{23}</td>
<td>5-items assessing current emotional, physical, sexual violence and fear</td>
</tr>
<tr>
<td>Abuse Assessment Screen (AAS)\textsuperscript{24}</td>
<td>5-items assessing lifetime emotional, physical, sexual violence and fear</td>
</tr>
<tr>
<td>Partner Violence Screen (PVS)\textsuperscript{25}</td>
<td>3-items assessing physical violence and perceptions of safety</td>
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Note. A comprehensive collection of interpersonal violence screening measures for use in health care settings are openly available through the Centers for Disease Control.
health care, particularly those with PTSD and SUD, are at increased risk for interpersonal violence perpetration and victimization. While new and adapted interventions that target the prevention and reduction of interpersonal violence are under development, the limited availability of efficacious mainstream behavioral therapies and effective pharmacologic and combined treatment approaches is an urgent health priority. In the meantime, rigorous and repeated screening using validated tools is a critical strategy to identify interpersonal violence and make appropriate treatment referrals.

Dr Flanagan is Associate Professor, Medical University of South Carolina, Charleston, SC, and Staff Psychologist, Ralph H Johnson VAMC. Dr Jarnecke is Assistant Professor, Medical University of South Carolina, Charleston, SC. The authors report no conflicts of interest concerning the subject matter of this article.

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Table 1. Risk factors for psychosis in PD

- Older age
- Greater severity of illness
- Longer duration of illness
- Axial rigidity subtype of PD
- Idiopathic PD
- Underlying dementia, delirium or depression
- Presence of sleep disturbance
- Use of dopaminergic agents

Parkinson Disease: Psychosis

Rajesh R Tampi, MD, MS, DFAPA, DFAAGP and Deena J. Tampi, MSN, MBA-HCA, RN

Parkinson disease (PD) is the second-most common neurodegenerative disorder in the US after Alzheimer disease (AD).3 It is estimated that in the US alone approximately 630,000 individuals have a diagnosis of PD. The prevalence of PD increases with age and it is estimated that the prevalence will double by 2040.4 The disorder is significantly more common among individuals aged 80 years or older compared with those aged 40 to 49 years (1903 per 100,000 population versus 41 per 100,000 population, respectively). The overall cost of caring for individuals with PD is approximately $52 billion per year.2

Although not one of the cardinal features of PD, psychotic symptoms are seen in approximately 25% to 30% of individuals with PD.4 The risk factors for the development of psychotic symptoms in PD (ie, PD psychosis) include older age, greater severity of illness, longer duration of illness, the axial rigidity subtype of PD, idiopathic PD, underlying dementia, delirium or depression, the presence of sleep disturbance including REM behavior disorder, reduced vision, and the use of dopaminergic agents (Table).2-4 PD psychosis is also associated with worsening quality of life, greater caregiver distress, higher rates of institutionalization, increased mortality, and greater health care costs.2-4

Among individuals with PD, visual hallucinations are the most prevalent psychotic symptom (Table 2). Visual hallucinations are seen in approximately one-quarter to one-third of individuals with PD, with a lifetime prevalence of about 50%.2 Auditory hallucinations occur in approximately 20% of individuals with PD. Certain minor phenomenology such as the “sense of presence” and visual illusions can be seen among 17% to 72% of individuals with PD and these may progress to visual hallucinations as the illness progresses. Delusions are not very common with a prevalence of approximately 5%.

Diagnostic criteria

The work group of the National Institute of Neurological Disorders and Stroke (NINDS) and National Institute of Mental Health (NIMH) has proposed the following for the diagnosis of PD psychosis:1

- The presence of one or more of the following symptoms: illusions, false sense of presence, hallucinations, or delusions.
- The UK brain bank criteria for the diagnosis of PD is met;
- The symptoms occurred after the diagnosis of PD;
- The symptoms are recurrent or continuous for 1 month;
- The symptoms are not better accounted for by another cause of Parkinsonism (eg, dementia with Lewy bodies; psychiatric disorders such as schizophrenia, schizoaffective disorder; delusional disorder or mood disorder with psychotic features; a general medical condition including delirium);
- PD psychosis could be associated with or without insight, with or without dementia, and with or without treatment for PD.

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stem dysfunction all contribute to the psychosis. Frontal cognitive dysfunction, with pathologies in the hippocampus. Moreover, alterations in the visual pathways, often associated with PD psychosis. The exact pathophysiology of PD is not completely understood. Additionally, the involvement of neurochemical factors, such as dopamine, serotonin, and glutamate, is widely discussed. The pathophysiology of PD psychosis is complex and involves neuropathological, neurochemical, and genetic changes.

Pathophysiology

The exact pathophysiology of PD psychosis is unclear, but findings indicate that the cholecystokinin gene (CCK)-45C-T polymorphism is most often associated with PD psychosis. Moreover, alterations in the visual processing areas in the brain along with pathologies in the hippocampus and cholinergic brain structures are seen among individuals with PD psychosis. Frontal cognitive dysfunction, impaired visual processing, sleep-wake cycle dysregulation and brainstem dysfunction all contribute to the development of PD psychosis.

Assessment

When assessing patients, a thorough history assists in identifying risk and precipitating factors for PD psychosis. Precipitating factors include medical conditions such as dehydradation, infections, metabolic dysfunction, psychosocial factors include poor sleep and limited nutrition, psychological factors include stress and hospital admissions as well as the use of drugs like amantadine, anticholinergic drugs, dopaminergic drugs, and beta-blockers.

The Movement Disorder Society Task Force that evaluated the rating scales for assessing PD psychosis found that none of the currently available scales adequately captured its entire phenomenology. They recommend that the following be used as primary scales in clinical trials evaluating new treatments for patients with PD psychosis: the Neuropsychiatric Inventory (NPI) for the cognitively impaired population or when a caregiver is required; Schedule for Assessment of Positive Symptoms (SAPS), Positive and Negative Syndrome Scale (PANSS) or the Brief Psychiatric Rating Scale (BPRS) for the cognitively intact population or when the patient is the sole informant. The Clinical Global Impression Scale (CGIS) was suggested as a secondary outcome scale to measure change and response to treatment over time.

Management

The first step in the management of PD psychosis is to assess the severity of symptoms. For mild symptoms that are not bothersome, there is no need for specific intervention other than providing reassurance and close monitoring to evaluate the progression of symptoms. The next step is to identify and treat for secondary causes of PD psychosis including medical disorders. Medications that are used to treat the motor symptoms of PD may cause or worsen psychosis. A reduction or discontinuation of anticholinergics, monoamine oxidase inhibitors, levodopa, or dopamine agonists may result in the improvement of symptoms. If discontinuation of these agents is ineffective, psychotropic medications, may be indicated.

A systematic review of placebo-controlled trials by Wilby and colleagues demonstrated benefit for clozapine and pimavanserin for the treatment of PD psychosis. There were no definitive benefits noted for either quetiapine or olanzapine. The comparative studies showed improvement in PD psychosis symptoms when clozapine or comparator drugs were assessed alone, but the data did not suggest any superiority of one active drug over the other drugs.

Pimavanserin, a novel 5-HT2A inverse agonist is the first FDA-approved antipsychotic for the treatment of hallucinations and delusions associated with PD psychosis. Pimavanserin improves symptoms of PD psychosis when compared with placebo (P < .0014). The adverse effect profile of pimavanserin include urticarial reactions, falls, peripheral edema, hallucinations, confusion, nausea, and headaches. Electroconvulsive therapy (ECT) has also been found to be beneficial for refractory symptoms.

Conclusion

Psychotic symptoms are not uncommon among patients with PD, and psychosis is associated with worse outcomes. Risk factors for PD psychosis include advancing age, more severe disease stage, cognitive impairments, depression, and sleep disorders.

The pathogenesis of PD psychosis involves neuropathological, neurochemical, and genetic changes. Management of PD psychosis involves treatment of underlying medical disorders and discontinuing drugs that may precipitate or worsen symptoms. Findings also indicate efficacy for clozapine and pimavanserin for the treatment of symptoms of PD psychosis. Pimavanserin remains the only FDA-approved medication for the treatment of PD psychosis. ECT may be beneficial for refractory PD psychosis symptoms.

Dr Tampi is Chairman, Department of Psychiatry & Behavioral Sciences, Cleveland Clinic Akron General, Akron, OH, and Chief, Section of Geriatric Psychiatry, and Professor of Medicine, Cleveland Clinic Lerner College of Medicine, Case Western Reserve University, Cleveland, OH; Ms Tampi is Executive Vice President, Diamond Healthcare, Richmond, VA. The authors report no conflicts of interest concerning the subject matter of this article.

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Big Brother FDA Is Watching, Helping

Heidi Anne Duerr, MPH

Before the pandemic took front and center stage, the US Food and Drug Administration was busy in the field of psychiatry. With a number of medications in the pipeline, new indications for old familiar faces, and the industry’s desire to share information with clinicians and patients alike, the FDA will likely remain busy, both policing the field and making approvals.

Pharmaceutical company makes the FDA’s naughty list

A warning letter was sent from the FDA’s Office of Prescription Drug Promotion (OPDP) for misleading advertising for the drug ProCentra, an oral solution used to treat attention-deficit/hyperactivity disorder. The warning letter was in response to a sponsored link on Google.com that failed to include risk information and use the medication’s established name. The letter also noted that the FDA Bad Ad Program received complaints.

The OPDP explained that the ad suggested the drug’s efficacy and ease use by pointing out its “Bubblegum Flavor” and “Liquid Treatment Option,” all of which easily would appeal to parents as desirable for children, without including any risk information.

The OPDP noted:

These violations are especially concerning from a public health perspective because they create a misleading impression about the safety of ProCentra, a drug that is a schedule II controlled substance used in the vulnerable pediatric patient population, and bears a Boxed Warning that describes the high potential for abuse, that administration of amphetamines for prolonged periods of time may lead to drug dependence, and states that misuse may cause sudden death and serious cardiovascular adverse events.

The letter was sent to Stefan Antonsson, CEO of Outlook Pharmaceuticals, with specific corrective actions requested. For starters, the company was told to “immediately cease misbranding.” In addition, they must respond in a letter detailing not only how they will comply with this request, but, since the violations are deemed serious, they must include “a comprehensive plan of action to disseminate truthful, nonmisleading, and complete corrective messages about the issues discussed in this letter to the audience(s) that received the violative promotional materials.”

According to Regulatory Focus, the ad has been removed and the CEO will respond. Meanwhile, its likely Outlook is not alone in such missteps. According to AdComplyRx, more than 30 major prescription brands inadvertently ran non-compliant ads on Google and Bing. Nonetheless, the warning letter, which is the first of its kind for this calendar year, showed that the FDA is watching and will hold companies responsible for irresponsible action.

New hope for depression on the horizon

On a more positive note, the FDA reviewed and accepted the New Drug Application (NDA) for LY03005, a serotonin-norepinephrine-dopamine triple reuptake inhibitor (SNDRI). Developed under Luye Pharma’s New Chemical and Therapeutic Entities Research and Development platform, the company has obtained patents covering the chemical compound, crystal form, and formulation of LY03005.

“Compared with monoamine transporters, their broader spectrum inhibition would lead to enhanced efficacy and faster antidepressant response.”

REFERENCES

“Schizophrenia” Is Heard Worldwide

» Robert M. Kaplan, MBChB, FRANZCP MA (Journ), MPhil (Sc)

D r Eugen Bleuler became Director of the Burghölzli Hospital in 1898. He attracted outstanding psychiatrists—including Carl Jung, Herman Rorschach, Ludwig Binswanger, and Karl Abraham—encouraging them to try new methods and tests. Determined to regard his patients as individuals, Bleuler made prolific notes, taking as much time as necessary to understand his patients.

On April 24, 1908, at the German Psychiatric Association meeting, Bleuler delivered a lecture titled “Die Prognose der Dementia Praecox (Schizophreniegruppe).” Thus the world first heard the name schizophrenia defined as a disease “characterised by a specific type of alteration of thinking, feeling and relation to the external world.”

Bleuler wanted to widen Kraepelin’s characterization of dementia praecox. He conceived of schizophrenia as a genus, rather than a species. He listed secondary symptoms, largely derived from psychoanalysis, implied an etiology. This was the critical difference with Kraepelin’s view: a disturbance or exaggeration of normal psychic function was flight years away from his categorical distinction between psychosis and sanity.

The term schizophrenia came from classical Greek; schizein meant splitting; phren originally denoted the diaphragm and later soul, spirit, mind. It was capable of abstractivization and humanized the concept. The semantic distinction from Dementia Praecox was critical; Bleuler’s name derived from classical Greek with its focus on the nature of man.

However, the schizophrenia that Bleuler described was not free of problems. The secondary symptoms were difficult to define, open to misinterpretation, and fostered a purely psychological view of the condition. Bleuler saw schizophrenia as an extension of normal personality that could, with perseverance, be understood and ultimately provide an insight into human nature. His classification was optimistic and gradualist, maintaining the option that it was ultimately a manifestation of the human condition. Schizophrenia endures and will remain—in one form or another—as the urword for psychiatry. To quote Tim Crow, “Schizophrenia is not just an illness of humans, it may be THE illness of humanity.”

A century later, Bleuler would have good reason to be pleased with his creation.

Dr Robert M Kaplan is Clinical Associate Professor at the Graduate School of Medicine, Wollongong University and Research Fellow, History Department, Stellenbosch University. He wrote about Eugen Bleuler in his book The Exceptional Brain and How It Changed the World (2011).

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The Art of Self-Disclosure

» Carl A. Hammerschlag, MD

T he question of whether to self-disclose in my work as a community psychiatrist is a non-issue—it must be done. No matter how well-intentioned and well-trained you are, the community wants to know about what makes you “real.” If you want to hear their stories, you have to tell yours.

Neighborhoods, tribes, gangs—each has its own culture. Unless you have been raised in one of them, you come as a stranger. Your credentials may get you in the door, but to gain access to the heart and soul of a community, you must be willing to share something about your authentic self.

I joined the Indian Health Service within the Department of Health and Human Services in 1964, thinking I would fulfill my two-year military obligation and then move on. Those two years became 20 because I kept learning more and more about how people got sick and how they got well. It was in “Indian Country”—not in medical school—where I learned what it meant to be healthy.

School taught about pathology and treating illness, and health was a diagnosis by exclusion. If you weren’t sick, you were healthy.

Early on in my work with Native American patients, a woman sat down in my office and looked around at my diplomas. “You know, all those degrees don’t mean you have a higher education. Look up at the ceiling. There’s nothing hanging up there which doesn’t mean there isn’t anything to be learned by looking up.” In other words, she wanted to know whether I belonged to a tribe, prayed in my native language, and knew the songs of my father.

During morning rounds, I learned about an elderly man who had been admitted. “Santiago” wore a headband and turquoise earrings, his long hair tied in a traditional chignon. He asked, “You’re going to be my doctor?” I nodded, and then he asked, “Where did you learn how to heal?” I recited this litany of academic achievements and, when I finished, he asked, “Do you know how to dance?” I looked at him incredulously and repeated the question, “Do I know how to dance?” He said, “Yes, if you want to heal you have to be able to dance.”

I didn’t want to be caught short; after repeating, he motioned for me to show him. I did a little two-step shuffle at the bedside, and he approved. Then I asked him if he knew how to dance (at the time I did not know he was a traditional medicine man). He got out of bed slowly and did some corn-dance steps. I applauded him, and I asked him if he would teach me. He said, “I can teach you my steps, but you have to be able to hear your own music.” In Indian Country, the music expressed what it meant to be healthy.

The Navajo word for health is Hózhó, the same word for truth, beauty, balance, harmony, and the Great Spirit. Your health is measured by what you say with your lips, reveal by your actions, and feel in your heart. All tell the same story. If you keep saying things you don’t mean and doing things you don’t believe, you will get sick. This ancient wisdom of mind/body/spirit in balance as a prerequisite for health is now spoken in the language of the science of psychoneuroimmunology or mind/body/spirit medicine.

Psychiatry training focuses on not getting too personal because self-disclosure may impair clinical judgment, leading to misdiagnosis or mistreatment. I believe that maintaining a posture of dispassionate clinical objectivity, not connecting with people at a heartfelt level, can do the same.

Being real actually magnifies one’s therapeutic efficacy. Self-disclosure humanizes us, and that soulful connection is where the real healing takes place; it will also move you from being a doctor to becoming a healer.

A good doctor can make a diagnosis and prescribe the appropriate treatment; a great doctor can make the diagnosis, prescribe the treatment, and add a preventative module by teaching the patient/community how to take better care of themselves. A healer can do all that and is also an active participant in the entire process. The healer does not watch from the sidelines but is totally engaged in every aspect of the healing journey.

Now in my 80s, I still work and engage with people in body, mind, and spirit. I disclose and make relationships at the heartfelt level, which allows me to tell a healing story using symbols and metaphors that my patients understand. I light candles; induce trance; recite poetry; sing; prescribe rituals, and create healing ceremonies. My experience has taught me to trust my intuition in what I choose to disclose in sharing my landscape with new eyes.

Dr Hammerschlag is a practicing psychiatrist in Phoenix, AZ. Further examples of Dr Hammerschlag’s self-disclosures can be found on his blog site, Schlagbytes, located at www.healing-doc.com.
Understanding Benzodiazepines
Commonly Prescribed but Caution Advised

Stephen A. Wyatt, DO

CASE VIGNETTES

A 40-year-old patient with a known history of anxiety associated with depression currently treated with a selective serotonin reuptake inhibitor presents after a personal trauma that took place a week ago. She reports that she has less than 4 hours of inconsistent sleep per night. There is a tearful description of an existential dread and anxiety.

A 67-year-old patient that you have been seeing for 10 years has a history of anxiety and depression. In recent months, the anxiety has been manageable and the depression stable; neither problem is causing social impairment. You have been treating the anxiety and depression with an SSRI and a high potency short-acting benzodiazepine (BZD) for 10 years. The patient is scheduled for a total knee replacement in a month and it is anticipated that she will need opioid pain medication. A discussion ensues concerning the potential complications of the coadministration of a BZD and an opioid. The mere discussion of tapering, much less discontinuing the BZD, results in significant distress and resistance.

A little history
Chlordiazepoxide was synthesized in 1955 and the first BZD was brought to market in 1960 as chlordiazepoxide (Librium). Multiple other products with various molecular modifications followed. This class of medications quickly gained favor over the barbiturates because of their more favorable safety profile yet comparable efficacy as an anxiolytic and for reducing sleep onset latency.

ACTIVITY GOAL
The goal of this activity is to provide an understanding of the class of medications known as benzodiazepines as well as when and how they can be used as part of treatment.

LEARNING OBJECTIVES
After engaging with the content of this CME activity, you should be better prepared to:
- Discuss the mechanisms of action of the various benzodiazepines.
- Consider the utility of benzodiazepine treatment.
- Recognize the indications for benzodiazepines.

TARGET AUDIENCE
This continuing medical education (CME) activity is intended for psychiatrists, psychologists, primary care physicians, physician assistants, nurse practitioners, and other health care professionals who seek to improve their care for patients with mental health disorders.

ACCREDITATION/CREDIT DESIGNATION/FINANCIAL SUPPORT
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These are two relatively common scenarios with which psychiatrists and other clinicians are confronted. In the first vignette, there may be a need for acute medical management and psychotherapy in treating the symptoms of distress. A BZD may be considered because it can provide the most rapid and effective relief.

The second vignette is more complicated. The patient has been on chronic BZD therapy and there are now compensatory changes, making the management of anxiety much more difficult.

Many clinical problems can be managed with BZDs. This variety of problems, and the fact the problems are often complex, make it important to understand the limitations and appropriate use of BZDs. This article serves as a review of BZD pharmacology and examines the risks and benefits of prescribing these medications. By way of disclosure, I am an addiction psychiatrist and have been challenged with some frequency by patients physically dependent on and/or misusing these medications who need an alternative care plan.

Intravenous BZDs were also found to have other clinical applications (eg, as a muscle relaxant, an antispasmodic, a preanesthetic). By way of disclosure, I am an addicted addict, a preanesthetic. By way of disclosure, I am an addicted addict, a

Chlordiazepoxide was synthesized in 1955 and the first BZD was brought to market in 1960 as chlordiazepoxide (Librium). Multiple other products with various molecular modifications followed. This class of medications quickly gained favor over the barbiturates because of their more favorable safety profile yet comparable efficacy as an anxiolytic and for reducing sleep onset latency.

Compared with barbiturates, BZDs result in less respiratory depression and a higher therapeutic index. Moreover, BZDs were thought to have less potential for misuse and dependence. BZDs were also found to have other clinical applications (eg, as a muscle relaxant, an antispasmodic, a preanesthetic). By way of disclosure, I am an addicted addict, a preanesthetic. By way of disclosure, I am an addicted addict, a
scribed medications.

In the 1980s, the similar nonbenzodiazepines or “Z drugs” (eg, zolpidem) were marketed for insomnia. These have all but completely taken the place of the BZDs as the drugs of choice in treating sleep onset latency problems.

Mechanism of action

With similar mechanisms, BZDs and the Z drugs continue to play an important role in multiple areas of health care. However, there have been concerns for several years surrounding the overprescribing of these medications and their adverse effects.

The problems associated with both medications include misuse and dependence, worsening cognition, potential for tolerance, rebound anxiety, and difficulties associated with withdrawal. There can be significant disinhibition typically resulting from the misuse of these medications in a vulnerable population, which is made worse when co-administered with other sedatives (including alcohol).

Most recently there have been more isolated concerns for two vulnerable populations: the elderly and patients taking or misusing opioids. An improved understanding of the mechanism of action of these medications can aid in the selection of a specific BZD and appropriate dosing, resulting in greater efficacy and an improved safety profile.

The mechanism of action of BZDs is dependent on the availability of γ-aminobutyric acid (GABA). This is key to its safety profile and different than both barbiturates and alcohol that work independently of GABA as sedatives in a variety of ways. One of these is by direct dose-dependent, prolonged hyperpolarization of the GABA receptor neuron, which can result in toxic levels of inhibition seen with alcohol and barbiturates. The BZDs work instead by binding to the GABA-A receptor subunit sites, increasing the affinity and efficiency of GABA as an agonist. This results in an influx of negatively charged chloride ions and an increase in the frequency of the hyperpolarization of the calcium channel that leads to enhanced inhibition.

GABA receptors are found extensively and exclusively in the central nervous system. Clinically, we are most interested in the effects associated with the ε1 and ε2 subunits. The effect of agonist stimulation of the ε1 subunit results in the hypnotic, retrograde amnestic and, in part, the anticonvulsant effects of these medications. The Z drugs target this specific GABA-ε1 subunit, resulting in only the sedation and hypnotic effects, although their use at higher, typically nonclinical, doses can result in antegrade amnesia.

The adverse effects of the BZDs have a positive correlation to the lipophilicity of the medication associated with the speed in which the drug reaches the brain and GABA receptor. Greater lipophilicity, like that associated with midazolam, results in greater antegrade amnesia. Interestingly, it is the speed at which an individual gets intoxicated with alcohol that contributes to the potential for blackout. The combination of alcohol and benzodiazepines is associated with rapid intoxication and greater frequency of antegrade amnesia due to increased absorption of a BZD when taken with alcohol and the synergistic effects of the two drugs.

The ε2 subunit is primarily involved in the anxiolytic effects and can play a role in muscle relaxation. The affinity of BZD to ε2 receptors in the spinal cord and motor neurons is their primary role in muscle relaxation. Diazepam, typically at higher doses, is a good example of a muscle relaxant.

Treatment decisions

More than 21 different BZDs have been approved internationally with varying time to onset, action duration, and therapeutic effect. It should be noted that these medications are sedative hypnotics at certain dosages. The BZDs are all easily absorbed from the GI tract with high protein binding and lipid solubility; variations of absorption and lipid solubility influence the speed of onset.

Medications such as alprazolam and clonazepam are rapidly and efficiently absorbed resulting in a more rapid onset. Their comparatively higher affinity to the GABA receptor is associated with greater potency. The high lipophilic properties of midazolam, diazepam, and chlorzolazepoxide are associated with rapid onset in the brain.

All the BZDs are rapidly absorbed orally but some can be administered by injection, depending on the pharmacokinetics of the specific medication. Lorazepam and midazolam are water soluble, resulting in less irritation when delivered by injection and are rapidly absorbed by intramuscular or intravenous administration. The duration of action after acute administration is most prominently affected by lipophilicity and volume of distribution of the drug. Whereas the duration of action with chronic administration is increasingly influenced by elimination half-life and the existence of active metabolites. Active metabolites result in the prolonged activity of chlorzolazepoxide and diazepam. The health status of the patient (eg, underlying renal, hepatic disease), current tolerance to any BZD, and age also affect the dose response and are important to consider.

Because of the wide variability of potency and metabolites, the identification of these medications on urine toxicology screening is not straightforward. The primary metabolite identified by common immune assay point of care (POC) testing is oxazepam. Many of the benzodiazepines will be identified using point of care screening; however, some of the most commonly prescribed formulations will not.

Lorazepam is metabolized through glucuronidation. It is not metabolized hepatically, which is one of the reasons it is often used for alcohol withdrawal. Clonazepam and alprazolam are not metabolized to oxazepam and, as high potency BZDs, often fall under standard cut-off levels.

When using urine drug testing in clinical management, it is important to have working knowledge of the point of care test to know which BZD can be identified and use confirmatory testing—gas or liquid chromatography mass spectrometry—for greater specificity. Urine screening for BZDs can have both false positive and false negative results. In general, point of care testing should always be used in conjunction with clinical presentation and when the results are in conflict; use confirmatory testing before making a judgment.

Understanding the pharmacology and pharmacokinetics of the various benzodiazepines can help in choosing the appropriate medication for the treatment of sleep disorders, anxiety, and agitation (Table 1 and Table 2).

Specific indications

Sleep onset latency

The use of BZDs for reduction in sleep onset latency is very effective. All the GABA agonist medications can be effective in establishing sleep and for many patients will have excellent short-term utility. Initially the FDA only approved them for short-term use—7 to 14 days. However, in 2005 the recommendation was updated once it was recognized that patients can have chronic insomnia; if the medications are monitored appropriately there can be continued efficacy, better tolerance, easier withdrawal, and less misuse.

Z-drugs were considered to have less risk of dependency and misuse than standard BZDs, but unfortunately this has not always been the case. Another problem is that extended use can result in adverse effects on sleep architecture: affecting the quality of restorative sleep and being responsible for rebound sleep difficulties following withdrawal. Before prescribing Z-drugs, patients should be evaluated for the potential cause of sleep instability with attention paid to underlying physical and behavioral health disorders such as substance misuse, movement disorders, and parasomnias.

Both BZDs and Z drugs can result in slowing respiration and should be used cautiously if at all
in the elderly and in patients who have an underlying respiratory problem. Patients should also be encouraged to use healthy sleep hygiene before initiating these medications.

**Posttraumatic stress disorder**

Most frequently, BZDs are prescribed for their anxiolytic effects. They work rapidly and effectively in anxious patients. In patients with PTSD, BZDs can reduce anxiety and improve sleep. However, their efficacy in preventing PTSD or trauma-related anxiety on delayed administration. Therefore, clonazepam may have greater utility for this purpose because it is easily administered either orally or parenterally. However, there is no evidence for efficacy with BZD monotherapy; although they can be effective in treating some episodes of catatonia as monotherapy.9

**Anxiety and panic disorders**

The efficacy of SSRIs, serotonin-norepinephrine reuptake inhibitors, and tricyclics in the treatment of anxiety disorders is comparable to that of BZDs; as such, they are considered the medications of choice.5 The introduction of high potency, rapid onset formulations (eg, lorazepam, clonazepam, and alprazolam) have added to BZD utility in acute treatment. Choosing a medication is based on adverse effects and co-occurring disorders.

The precautions and complications of using BZDs long term for panic disorders are similar to those of other behavioral health problems. BZDs are most effectively used acutely, as needed for significant panic episodes in patients at low risk for misuse. Evidence suggests use of a BZD as an initial 2- to 3-week bridge to starting treatment with an SSRI or SNRI.5,6 When used this way, there is less potential for problems on discontinuation. Short-acting alprazolam requires redosing every 4 to 6 hours. And after regular daily dosing for 1 to 4 months, there is most often rebound anxiety. This rebound results in the patient's belief that the rebound anxiety is their baseline anxiety and they become reluctant to consider discontinuation. This scenario can contribute to the development of dependence.

The additive potential of a drug is positively correlated to the rate of onset of a positive effect. The rate of the positive effect is dependent on the pharmacokinetics of the drug and/or the route of administration. Alprazolam is rapidly and efficiently absorbed throughout the CNS, thus increasing its addictive potential. More dopamine is released with alprazolam than with other BZDs, thereby increasing the sense of pleasure on administration and potential for dependency. For these reasons, it is often difficult to switch from alprazolam to an alternative longer-acting BZD.7,8

Clonazepam, a longer-acting BZD with a wider dosing schedule. As such, there is less rebound anxiety on delayed administration. Therefore, clonazepam may have greater utility for a longer period of daily administration but is not as effective in the acute panic setting.

**Other indications**

Another area of important clinical use of BZDs is in the agitated patient with or without psychosis. In this case, BZDs are often used with an antipsychotic medication. Lorazepam is most often the drug of choice for this purpose because it is easily administered either orally or parenterally. However, there is no evidence for efficacy with BZD monotherapy; although they can be effective in treating some episodes of catatonia as monotherapy.9

**Precautions to consider**

BZDs continue to be one of the most commonly prescribed medications. Their long-term use has continued to rise even though the evidence for long-term efficacy has not been established.9 This has contributed to greater overall availability and nonprescription use (Figure 1). Although the recreational use of BZDs alone is not common, concurrent use with other prescribed and non-prescribed drugs is quite common.9 BZDs are used in conjunction with other drugs to augment euphoria, notably with opioids and alcohol, or reduce agitation or anxiety and promote sleep when using stimulants (eg, cocaine, methamphetamine, cannabis).

Using BZDs with alcohol can result in harmful disinhibition and retrograde amnesia. The combination of opioids and BZDs plays a significant role in the incidence of lethal overdose in the US (Figure 2). BZD-related overdose mortality has risen dramatically, from 0.6 per 100,000 adults in 1999 to 4.4 per 100,000 in 2016. Emergency department visits because of BZD effects has been estimated to have risen from 2.6% in 1990 to 7.4% in 2015.11

When considering tapering a patient, it is important to remember that significant symptoms associated with withdrawal are not typically seen unless the patient has been taking a BZD on a consistent basis for more than 1 to 4 months. There can often be significant withdrawal problems, primarily rebound anxiety, but may also include manifestations of seizure disorder. In a controlled setting, withdrawal can be more rapid, often with the use of phenobarbital or carbamazepine.13,14 For outpatients, a slow taper is best.

A short-acting BZD can be switched to a long-acting form at an equivalent dose. For example...
ple, patients on 6-mg alprazolam daily can be switched to an equivalent dose of 120-mg diaze-
pam over a few weeks. The long half-life of diaze-
pam and its active metabolites will vary depending
on the duration of time the patient has been on the
medication but will allow for a soft taper over many
weeks. However, keep in mind alprazolam is a
triazo-lo-benzodiazepine and is not fully covered by
non-triazo-lo-benzodiazepines such as diazepam, which might result in some rebound anxiety.

A conservative, widely used schedule, the Ash-
ton Protocol advocates for a diazepam taper at a
rate of 10 mg per week or longer, resulting in safe
and effective withdrawal. Withdrawal with other
long-acting BZDs can be achieved similarly.15,16

Conclusion
It is important to recognize that the disadvantages
associated with BZDs are most closely associated
with their long-term use. We should be sensitive to
prescribing BZDs to the elderly, who can experi-
ce more serious sedation due to a slower metabolism,
greater sensitivity to cognitive impairment, and
falls and fractures, as well as to patients with a
current or past history of a substance use disorder.

Because BZDs are primarily short-term acute
treatment modalities, it is important to consider
the use of a more definitive medication. Continu-
ous monitoring is needed to gauge the patient’s
need for a BZD while considering a switch to an
alternative evidence-based medication for long-
term treatment.

If the patient no longer needs or takes the BZD,
they should be advised to properly dispose of any
remaining medications. As seen with the recent
opioid epidemic, the number of pills in the commu-
nity drives misuse. Patients need to understand that
controlled substances are prescribed for a particu-
lar problem and their use for any other purpose is
misuse. Sharing BZDs can be dangerous and is il-
legal. As specialists, we can model the safe and
effective use of BZDs for other health care providers.

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Figure 2. Opioid Overdose Deaths Involving Benzodiazepines

Source: Centers for Disease Control and Prevention
(CDC). Multiple Cause of Death, 1999-2015.

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Medical Director (Emergency Mental Health, Consult Liaison, Worcester, MA)
Provide psychiatric and medical supervision. As well as consultation and liaison to our medical-surgical wards and emergency mental health department.

Medical Director (Adult Outpatient Psychiatry, Worcester, MA)
Clinical Academic oversight of new 3 8-office outpatient teaching clinic.

Medical Director (Adult Inpatient Psychiatry, PTRC, Worcester, MA)
Provide psychiatric and medical supervision and direction to a 22-bed behavioral health unit.

Adult Outpatient Attending Psychiatrist (Chelmsford, MA)
Outpatient clinic in Chelmsford serving a diverse population with mental health and substance use disorders.

Adult Inpatient Attending Psychiatrist (Chelmsford, MA)
Outpatient services while providing behavioral healthcare services.

Interested applicants should submit a letter of interest and curriculum vitae addressed to Sheldon Benjamin, M.D. at: Jessica Saintelus, Physician Recruiter Jessica.Saintelus@umassmemorial.org

http://jobs.jobvite.com/

As the leading employer in the Worcester area, we seek talented and ideas from individuals of varied backgrounds and viewpoints.
Inpatient Psychiatrist Opportunities
Cambridge Health Alliance (CHA)

Cambridge Health Alliance is a well-respected, nationally recognized and award-winning public healthcare system. CHA is a teaching affiliate of both Harvard Medical School (HMS) and Tufts University School of Medicine. Our system is comprised of three hospital campuses and an integrated network of both primary and specialty outpatient care practices in Cambridge, Somerville and Boston’s Metro North Region.

- Full-time and Part-time opportunities available at CHA Cambridge Hospital and CHA Everett Hospital
- Manageable call coverage
- Fully integrated electronic medical record (EPIC) is utilized
- Join a collegial group of multi-disciplinary staff of Psychiatrists, Psychologists, Social Workers, Nurses and Occupational Therapists
- Academic appointments at Harvard Medical School are available commensurate with medical school criteria.
- Opportunities to train medical students and psychiatry residents and fellows.

CHA offers competitive compensation and a comprehensive benefits package including health and dental insurance, 403b retirement accounts with matching, generous PTO, CME allotment (time and dollars) and much more.

Qualified candidates will be BC/BE in psychiatry and share CHA’s passion for providing the highest quality care to our underserved and diverse patient population. Please submit CV’s through our secure website at www.chaprotrec.org, or by email to Melissa Kelley at ProviderRecruitment@challiance.org. The Department of Provider Recruitment may be reached by phone at (617) 665-3555 or by fax (617) 665-3553.

CHA is an equal opportunity employer and all qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, disability status, protected veteran status, or any other characteristic protected by law.

In April, please watch your postal mail and e-mail for messages from us.

If you’re randomly selected to participate, please complete our survey and share your views with us.
CALIFORNIA

As the largest public health care system in northern California, we offer comprehensive healthcare resources to a large and diverse patient population. Psychiatrists are part of a robust team of staff that work in collaboration with other medical specialties to provide integrated health care to patients.

Psychiatrists are eligible for numerous benefits including 7 weeks of annual leave, 1 week of educational leave, 12 holidays, $4500 educational funds, health benefits, life insurance and CalPERS retirement plan.

If you are interested in working in a dynamic and collegial work environment, please submit a CV and letter of interest directly to:

Dr. Tiffany Ho
Behavioral Health Medical Director
tiffany.ho@hhs.sccgov.org
(408) 885-5767

The doctors of TRADITIONS BEHAVIORAL HEALTH are the largest provider of MD psychiatric services to adult populations all over California and also now in WA and NV! We provide services to the seriously and persistently mentally ill and have openings in the San Francisco Bay Area, Santa Barbara, San Diego, Los Angeles, Reno and Seattle.

We plan to add 50 more part-time psychiatrists to bring our medical staff team to 400 psychiatrists. Our packages vary from a minimum of $300,000 per year plus $10,000 in bonuses and a benefit package valued at approximately $90,000, up to $500,000, for the industrious physician. Our generous benefit package includes over 6 weeks paid time off per year. If you are creative and think outside the box, if you value diversity and cultural competency, if you like innovative programs that are better than illness model, if you want more time to work with patients, to get the best results, then TBH is the company for you. To learn more about the specific job openings and salary and benefit packages, check out our Website at:

www.tbhcare.com or Email your letter of interest and CV to our company VP of Recruitment, Derek Sawyer at: Derek@tbhcare.com

TBH is an equal opportunity employer

Outpatient Psychiatry Opportunity
San Joaquin County Behavioral Health Services is seeking to fill Outpatient Adult [General], and Sub-Specialty Psychiatry (Child Psychiatry, Geriatric, Forensic, Addiction and Psychosomatic Medicine) positions in a multidisciplinary, recovery-oriented clinical setting. Services are provided either on-site or using a hybrid model of on-site and tele-psychiatry practice. The positions offer a very competitive salary with a guaranteed base, plus incentive opportunities, board certified Psychiatrists have the potential to easily earn over 300K+ a year; comprehensive health insurance; up to three retirement and pension programs; 35 days of vacation and CME time that increase with tenure. Signing and moving bonuses are also available. Interested J-1 and H-1B candidates are welcome to apply.

Fax your CV to 209-468-2399 or email to BHSadmin@sjchbs.org. EOE

SANTA MARIA

New Mexico

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Top Leading Locum Psychiatrist Services

Please call to ask for details

California

California Correctional Facilities

$250 Plus/hr.

Department of the State Hospitals

$280 - $290/hr.

LA-DMH & LA County Jail

$185 – $265/hr.

Tulare County Adult Jail

$200/hr.

Tele-Psychiatry

$180-$225/hr.

Medical Doctors

$150-$255/hr.

NP / PA

$65-$110/hr.

New York

Psychiatrist

$200 - $350 Plus/hr.

All NYC & Upstate NY Locations Available

Ref. Bonus/Signing Bonus up to 2k/3k (Certain Rules Apply)

Free Direct Deposit

A+ Occurrence Malpractice Through PRMS

Phone: 559. 799. 8344 Fax: 888. 712. 2412

Email: imperiallocum@imperiallocum.com

Visit: www.imperiallocum.com

Psychiatrist Position

Excellen Opportunity in California

Imperial County Behavioral Health Services is currently recruiting for full-time or part-time psychiatrists. Imperial County, a rich farming area with a population of 180,000, is located 90 miles east of San Diego, 90 miles south of Palm Springs, 60 miles west of Yuma, Arizona, and just north of the cosmopolitan city of Mexicali, Mexico. And between them are two of the most popular vacation spots in the country.

The position pays a highly competitive salary, including health benefits for you and your family, requires no hospital work and minimal after-hours work, freeing you up for more leisurely activities. As a Psychiatrist with Imperial County Behavioral Health, you will be part of a multi-disciplinary treatment team that includes therapists, nurses and rehabilitation technicians that provide comprehensive support and resources to assist clients in achieving recovery.

J-1 and H-1B Applicants welcome. Our agency is experienced in successfully processing J-1 Waiver and H-1B Visa applicants.

Qualified candidates must have a CA medical license or ability to obtain. Send CV to Imperial County Behavioral Health Services, 2021 North 8th Street, El Centro, CA 92243.

For additional information, please contact:

Kristen Smith
(442)651-1606
kristensmith@co.imperial.ca.us

GREAT LOCATION IN CENTRAL CT

Only 19 miles from Hartford; 38 miles from New Haven; and only 2 hours from NYC and Boston. Three positions available at Bristol Hospital in Bristol, CT—an ANCC magnet recognized hospital that has been serving the greater Bristol area since 1921. They are seeking an additional FT Psychiatrist to work on small inpatient psychiatric unit and support crisis and consultation services. Also seeking FT Psychiatrists for Outpatient work: one position at a well-established community clinic providing care for mental health and substance abuse clients. The other position is in a BH office providing medication management and psychotherapy. Offering

Connecticut
a comprehensive array of benefits. Sign-on bonus available. JH/NI Visa applicants welcome. Be a part of an esteemed medical staff in an ideal location. The hospital is located in the family friendly community of Bristol which is the home of ESPN Sports network. Excellent public and private schools. It offers a great quality of life with easy access to urban areas. This is a must-see opportunity.

Please contact Terry Good at 804-684-5661; email: terry.good@horizonhealth.com; Fax: 1-804-684-5663. EOE

FRANKA

The University of Miami (UM) Miller
• Comprehensive benefits include: health/dental/vision, paid malpractice, 401(h) plan

School of Medicine is an academic medical center with extensive clinical facilities including the Sylvester Comprehensive Cancer Center (Sylvester). All Sylvester physicians are on the faculty of the Miller School of Medicine, South Florida’s only academic medical center.

CV’s and letter of interest can be directed to Maria Rueda-Lara, MD email: mrueda2@med.miami.edu

MASSACHUSETTS

Cape Cod Healthcare

Consultation/Liaison Psychiatrist

The Department of Psychiatry at the University of Miami and The Sylvester Comprehensive Cancer Center announces a search for an academic psychiatrist with interest and experience in psychosomatic medicine and psycho-oncology. Applicants can anticipate working collaboratively with fellow psycho-oncology providers including five psychologists, a psychiatrist and a team of oncology social workers.

JOY DESCRIPTION

Providing psychiatric consultation-liaison services in either inpatient, outpatient or both oncology settings across the oncology enterprise.

Participation as a member of the Department of Psychiatry and Behavioral Sciences

Participating in teaching activity for advanced trainees to ensure the highest level of educational excellence.

QUALIFICATIONS OF THE PSYCHIATRIST

• Board certification in Psychiatry.

• Board eligibility/certification in C-L Psychiatry would be preferred but experience will be considered.

COMPENSATION & BENEFITS

This dynamic position commands an extremely competitive salary enhanced by an attractive benefits package, including but not limited to:

• Competitive compensation including bonus programs, vacation

• Comprehensive benefits include: health/dental/vision, paid malpractice, 401(h) plan

The University of Miami (UM) Miller

University of Miami, Department of Psychiatry

SYLVESTER COMPREHENSIVE CANCER CENTER

EXCEPTIONAL PSYCHIATRY OPPORTUNITY

Consultation-Liaison Psychiatrist

Immediate full time opening for BC/BE psychiatrist. Responsibilities include evaluations and follow-up appointments for adult psychiatric patients requiring medication management.

40 hour-per-week position in our outpatient clinic in Hyannis, MA. Schedule is Monday through Friday. Must also work one weekend on-call. No weekend on-call duty is required but available if interested with extra compensation attached.

Consultation/collaboration with other clinical staff on shared cases as needed. This will be an employed position by Cape Cod Healthcare with a generous base salary, sign-on bonus, and relocation support.

Please take some time to look at the Cape Cod Healthcare website at www.capecodhealth.org/recruitment

Enjoy coastal living at its best! Miles of sandy beaches for your enjoyment, quaint villages, and beautiful sunsets over Cape Cod Bay make this a great place to practice medicine and enjoy the amenities the Cape has to offer. It is truly a wonderful place to live and work.

If you are interested in speaking further about our position, please email me your CV and the best day/time you are available to talk.

Jolia Georges
Director of Physician Recruitment
Phone: 508-862-5481
Email: jgeorges@capecodhealth.org

NEW HAMPSHIRE

South Oaks Hospital

We are seeking a full time attending psychiatrist (M-F: 12p-8p) to provide clinical leadership and direct care for our busy Evaluation and Admissions unit at South Oaks Hospital in Amityville, NY. The ideal candidate is an energetic leader with excellent clinical, teaching, supervisory and interpersonal skills who is comfortable leading a multidisciplinary team of clinicians. South Oaks Hospital is located on the Nassau/Suffolk border in NY and is a member of the Northwell Health system.

Job Requirements:

• NYS License to practice medicine, ACGME approved residency training with Board eligible in Psychiatry preferred. Excellent communication skills required. New graduates with leadership potential are welcome to apply.

• BC Candidates are eligible to apply for a faculty appointment with the Zucker School of Medicine at Hofstra/ Northwell.

• Additionally, Northwell encourages enrollment in any of the several faculty development opportunities that are offered by the system. Northwell health offers physicians an exceptional benefit package.

For more information, please call (631) 608-5102, or email your CV to yhassoun@northwell.edu or fax to (631) 264-5259.

NEW YORK

South Oaks Hospital

Northwell Health

We are seeking a full time attending psychiatrist (M-F: 12p-8p) to provide clinical leadership and direct care for our busy Evaluation and Admissions unit at South Oaks Hospital in Amityville, NY. The ideal candidate is an energetic leader with excellent clinical, teaching, supervisory and interpersonal skills who is comfortable leading a multidisciplinary team of clinicians. South Oaks Hospital is located on the Nassau/Suffolk border in NY and is a member of the Northwell Health system.

Job Requirements:

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For more information, please call (631) 608-5102, or email your CV to yhassoun@northwell.edu or fax to (631) 264-5259.

OHIO

Clinical Neuroscience of Mood Disorders Fellowship is looking to fill an available position.

Requirements for this position is to be a MD who has completed residency in psychiatry or related field or a PhD in Clinical Psychology. Candidate should be eligible for an Ohio Trainee License to conduct clinical work. This is a 1 - 2 year program and is accredited by the Cleveland Clinic. Position can be filled any time during the year on a rolling basis. The fellowship is designed to train fellows in clinical care and neurobiological basis of depression and bipolar disorder. Current research is focused on neurochemical, imaging and genetic biomarkers for diagnosis and treatment as well as on clinical trials of novel pharmacological agents and strategies.

Please contact Amit Anand, MD at ananda@ccf.org

PENNSYLVANIA

PSYCHIATRISTS & CHIEF OF PSYCHIATRY

AmeriCare Services, Inc. is pleased to announce three (3) excellent full time opportunities with our group in Danville and Clarks Summit, Pennsylvania. The first position is for a CHIEF OF PSYCHIATRY at Clarks Summit State Hospital and the compensation is $235.00 to $245.00 per hour. Staff Psychiatry positions are available at Danville and Clarks Summit State Hospital and the compensation is $210.00 to $220.00 per hour. The schedule is Monday – Friday with no on-call, evening, weekend or holiday coverage. For confidential consideration call 610.695.8521 or email: KGallagher@AmCareServices.com.

MISSOURI

Compass Health Network

PSYCHIATRIST

Provide full-time face-to-face psychiatric services to patients in Raymore, MO for a minimum of 40 hours a week. In addition, may provide services to patients in Royal Oak Hospital in Windsor, Missouri, as assigned. M.D. or professional equivalent degree, BC/BE in Psychiatry and Missouri medical license required. This position is eligible for the Employee Referral Program. Position is with Compass Health, Inc., dba Pathways Community Health in Clinton, MO.

Send CV to: Ms. Cathy Griggs, Director of Psychiatry Services at cgriggs@pbhc.org Fax: 417-532-6606.

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