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Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Therapy

Learning Objectives

After reading these articles, you should be able to:

1. Describe best practices for post-ECT maintenance treatment.
2. Assess and treat patients for nightmare disorder.
3. Summarize some of the current research findings on psychiatric treatment.

ECT Worked: Now What?

Michael Posternak, MD. Psychiatrist in private practice, Boston, MA.

Dr. Posternak has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Juan is a 72-year-old man with severe depression who has not responded to numerous antidepressant trials. He is reluctant to undergo a course of electroconvulsive therapy (ECT), but agrees to do so if one last medication trial doesn't work. After failing to respond to escitalopram augmented with aripiprazole, Juan receives a course of ECT and has a terrific response. Feeling better, he asks you what should be done next with his medications.

Patients frequently inquire whether any new treatments for depression have come to the market. But newer treatments, unlike new cars, aren't necessarily better; in fact, older treatments are better studied and are more battle-tested.

Highlights From This Issue

80% of patients relapse after successful ECT, but CBT, lithium augmentation, and maintenance ECT can increase their chance of success.

Nightmares darken people's moods, whether they have PTSD or not. Dr. Barry Krakow describes a simple intervention for nightmares that can be taught during a medication visit.

Hypnotics rarely improve sleep architecture. Lemborexant hopes to change that.

Nowhere is this more apparent than with ECT, whose treatment effect size (0.9) is one of the largest in psychiatry (Kho KH et al, *J ECT* 2003;19(3):139–147). But when patients do respond to ECT, we are inevitably confronted with a dilemma:

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Q&A With the Expert

Turning Nightmares Into Dreams
Barry Krakow, MD

Dr. Krakow is a board-certified sleep medicine specialist practicing in Savannah, GA following a 30-year research career that helped spearhead the movement to address sleep disorders in psychiatric patients.

Dr. Krakow has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

TCPR: What is nightmare disorder?
Dr. Krakow: This is a sleep disorder in DSM-5 characterized by repeated, distressing nightmares. Some patients awaken from the dreams and others do not, but either way they usually remember the dreams, sometimes vividly. These nightmares often involve themes of threat, fear, and other distressing emotions. An important element is that the nightmares cause impairment during the day—either from the dream content or the sleep disruption that goes along with it.
TCPR: Does it include sleep terrors?
Dr. Krakow: No. In sleep terrors (which used to be called "night terrors") the patient doesn't fully awaken, and they don't remember the dream material very well if at all.
TCPR: How is nightmare disorder different from PTSD?
Dr. Krakow: The way the DSM lays it out,

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ECT Worked: Now What?

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What do we do with their medications that had previously not worked?

Three main options exist: 1) Continue the current med regimen in hopes that it will prevent depression (even though it had not previously helped), 2) Switch medications, or 3) Begin maintenance ECT (m-ECT). Unfortunately, no studies have ever directly addressed what to do after a successful course of ECT. Therefore, we'll have to extrapolate from the current research to figure out what the most appropriate course of action might be.

Do patients who respond to ECT even need maintenance treatment?

Absolutely. Here, the data are unequivocal. Without treatment, around 80% of patients who recover with ECT will go right back into their depression within 6 months. In the most rigorous study, 21 of 25 patients (84%) who responded to ECT and were randomized to placebo relapsed within 6 months (Sackeim HA et al, *JAMA* 2001;285(10):1299–1307). That figure is backed up by a meta-analysis that found relapse rates on placebo of approximately 80% after 6 months (Jelovac A et al, *Neuropsychopharmacology* 2013;38(12):2467–2474). That's about twice the relapse rate seen with some of the preventative treatments I'll discuss below.

Do medications help reduce the risk of relapse?

Yes. A meta-analysis of seven studies (n = 402) found that medications cut the risk of relapse in half at the 6-month mark (Jelovac et al, 2013). The bad news is that even with treatment, about 50% of patients relapse within 6 months. One medication strategy stands out from the rest, however: lithium augmentation.

Lithium has long been touted as the best choice post-ECT. Is this just because it was the first treatment on the block, or is it truly better?

Lithium does have protective effects after ECT when used to augment an antidepressant. The landmark Sackeim study found relapse rates of 39% on nortriptyline with lithium, compared to 60% on nortriptyline alone (n = 55) (Sackeim et al, 2001). A naturalistic, retrospective study looking at a Swedish registry found that patients receiving lithium post-ECT had significantly lower relapse rates, while those receiving antipsychotic medications for depression had an elevated risk (n = 486) (Nordenskjöld A et al, *Depress Res Treat* 2011;2011:470985). Finally, a recent meta-analysis of 14 studies found that patients receiving lithium were about 50% less likely to relapse than patients receiving maintenance regimens that did not include lithium (n = 9748) (Lambrichts S et al, *Acta Psychiatr Scand* 2021;143(4):294–306).

Are some antidepressants better than others?

Tricyclic antidepressants (TCAs) have long been the gold standard, but unlike lithium, this appears to be more a function of being first on the block. Prudic and colleagues, for example, found that venlafaxine + lithium (n = 63) was just as effective for prevention of relapse post-ECT as nortriptyline + lithium (n = 59) (Prudic J et al, *J ECT* 2013;29(1):3–12). Although SSRIs have been much less studied than TCAs, the research to date suggests they are no less effective (Jelovac et al, 2013).

How does m-ECT compare with medications?

A meta-analysis across four studies (n = 146) showed that m-ECT clearly works, with reported relapse rates at 6 months of just under 40% (Jelovac et al, 2013). In comparing m-ECT to medications, Kellner and colleagues found no statistical difference in 6-month relapse rates between patients randomized to m-ECT (n = 89; 37%) and those randomized to maintenance antidepressant therapy (n = 95; 32%) (Kellner CH et al, *Arch Gen Psychiatry* 2006;63(12):1337–1344). Although no studies to date have ever found m-ECT inferior to pharmacotherapy, a recent meta-analysis concluded that "there is little evidence to support superior efficacy of m-ECT over maintenance pharmacotherapy" (Elias A et al, *J ECT* 2019;35(2):91–94).

Is the combination of medications and m-ECT better than either alone?

The combination appears to be better. Nordenskjöld and colleagues randomized 61 patients to receive m-ECT + pharmacotherapy or pharmacotherapy alone over the course of a year, and found that only 32% relapsed with combination treatment compared to 61% with medications alone (p = 0.04) (Nordenskjöld A et al, *J ECT* 2013;29(2):86–92). In a literature review on the topic, Brown and colleagues concluded that combination therapy has consistently outperformed medications alone, and a recent large-scale study by Kellner and colleagues further bolstered this conclusion

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ECT Worked: Now What?

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(Brown ED et al, *J ECT* 2014;30(3):195–202; Kellner CH et al, *Am J Psychiatry* 2016;173(11):1101–1109).

Can we expect ECT to work again if the patient responded to it in the past?

This is an important question since many patients would prefer to forgo m-ECT if they were confident that a second course of ECT, if needed, would work. Unfortunately, this question has never been studied. Lacking evidence, it would be a mistake to assume ECT will work again.

Can psychotherapy prevent post-ECT relapse?

Even if psychotherapy did not work during the acute phase of a severe depression, it might still help prevent relapse after a successful course of ECT. Brakemeier and colleagues randomized patients who had responded to ECT to receive either medications alone (n = 18), medications + m-ECT (n = 25), or medications + cognitive behavioral therapy (CBT; n = 17) (Brakemeier E et al, *Biol Psychiatry* 2014;76(3):194–202). The sustained response rate for the meds + CBT group was 65%—much higher than the response rates for meds alone (33%) or meds + m-ECT (28%).

Preventative Steps After Successful ECT

	Pros	Cons
Continue pre-ECT meds	• Avoids risk of new side effects • Some medications have preventative effects even if they did not work acutely (eg, lithium, lamotrigine)	• Generally less effective than other options
Lithium augmentation	• Lowers relapse risk by up to 50%, particularly when used with a tricyclic or SNRI	• Adds to side effect burden
Maintenance ECT	• Lowers relapse risk, particularly when combined with pharmacotherapy	• Side effects (eg, cognitive), cost, and inconvenience
Psychotherapy	• Has good evidence to prevent relapse into depression, including after ECT • May prevent depression even when it failed to treat depression	• Cost, time

Knowing the high rates of relapse, you discuss with Juan the post-ECT plans even before making the referral for ECT. You explain that the best option is the combination of m-ECT plus medications; over time, m-ECT can work even when given as infrequently as every 3 months. "Rescue" ECT can also be used if his mood starts to dip. Regarding Juan's specific medication regimen, you recommend staying on escitalopram but stopping the aripiprazole due to its lack of demonstrated efficacy and its risk of long-term side effects, many of which are worse for older patients like him. You recommend lithium as the best option if he wants additional medication protection. You also strongly encourage him to connect with a psychotherapist.

TCPR VERDICT: ECT works great for depression, but the relapse rates are high in the months following treatment. Start the preventative discussion before your patient undergoes ECT, and consider: 1) Maintenance ECT, 2) An antidepressant with lithium augmentation, and 3) Psychotherapy.

To learn more, listen to our 8/30/21 podcast, "How to Use Nortriptyline." Search for "Carlat" on your podcast store.

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Expert Interview

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nightmare disorder can't be diagnosed if the dreams occur during PTSD and reenact themes from a traumatic event. In practice, though, posttraumatic nightmares and nightmare disorder respond to the same therapy—imagery rehearsal therapy (IRT)—and in both disorders the patient's distress improves after eradication of nightmares. That's true in other psychiatric disorders as well where nightmare disorder can be diagnosed, like depression, anxiety, bipolar disorder, schizophrenia, and borderline personality disorder (Gieselmann A et al, *J Sleep Res* 2019;28(4):e12820). This is important to recognize, because treatment of nightmares decreases these other psychiatric symptoms, too.

TCPR: Interesting. Can you explain this further?

Dr. Krakow: In the past, it was thought that you had to treat the underlying disorder for the nightmares to get better, but two psychiatrists, my mentors Robert Kellner and Joseph Neidhardt, showed the reverse. Depression and anxiety symptoms got better when nightmares improved with a therapy they developed in 1987 called imagery rehearsal therapy (IRT). When we expanded our research program in the early 1990s, Dr. Kellner encouraged me to try it in PTSD. We did a study on 168 women who were survivors of sexual assault. It was a randomized controlled trial where they received three sessions of group treatment of IRT (7 total hours) or wait-list control. IRT improved nightmares and decreased PTSD symptoms as well. The effect sizes were in the large range for nightmares, sleep quality, and PTSD symptoms (Krakow B et al, *JAMA* 2001;286(5):537–545).

TCPR: Was the work more challenging in PTSD?

Dr. Krakow: We had to do more education and cognitive restructuring, as many of these patients had come to believe their nightmares were caused exclusively by their PTSD and would not improve unless the PTSD was treated. Indeed, they would debate this point with us in sessions and often declare, "My therapists said I needed to treat the trauma before my nightmares could resolve." The irony was not lost on them—seeking treatment for nightmares *after* years of psychotherapy, such as EMDR, exposure therapy, and medication, and most of all "talk therapy."

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Expert Interview

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TCPR: Psychiatrists are pretty good at recognizing nightmares in PTSD, but what should we look for in other disorders?

Dr. Krakow: Nightmares are very common in patients with depression, anxiety, and insomnia if you ask about them. They are more common in people who've been through lots of stress and have difficulty coping with stress. People don't bring them up because they don't know there is treatment for bad or disturbing dreams, or they presume that drugs or psychoanalysis are the only options, even though high-level evidence for these traditional approaches is sparse.

TCPR: Nightmares are also part of our normal experience, so how do we know when they need treatment?

Dr. Krakow: The answer is frequency and distress. Here's a pearl: If a patient has a bad dream at least once a week, the chance that it is bothering them is extraordinarily high. Maybe it's making them afraid to go to sleep and they have insomnia, or their sleep is fitful and they feel crappy in the morning. Or the nightmare comes back to them during the day and makes them feel sad or fearful. Ask the patient, "Do you think about your nightmare content at all during the day?" If they say "Yes," they would probably benefit from an intervention.

TCPR: What else do patients with nightmare disorder complain of?

Dr. Krakow: They have higher levels of anxiety, depression, somatization, and hostility (Kellner R et al, *Am J Psychiatry* 1992; 149(5):659–663). Their impairment in those respects is about equal to what you'd see for your average patient with anxiety or depression who comes to an outpatient psychiatric practice, so it is significant. But to reiterate, it is extremely rare for a patient to enter therapy requesting treatment for nightmares.

TCPR: Is this a vicious cycle where a negative mood sets them up for nightmares, those nightmares worsen their mood further, and it spirals from there?

Dr. Krakow: I think that cycle is part of it. I think almost all nightmare patients have something in their lives that is very difficult to cope with, to emotionally process, even if it is not a DSM trauma. But I think the larger part, from the vantage point of sleep medicine, is that disturbing dreams often seem to take on a life of their own to become an independent disorder that fuels or worsens insomnia.

TCPR: Is the idea that the nightmare was originally functional as a way to process the stressful event?

Dr. Krakow: Yes, it's likely that the dream started out that way. We don't know all the functions of dreams, but it seems dreams and REM sleep help people learn, remember, and process emotional events. In fact, we often wonder if REM sleep—where dreaming occurs most memorably—is a kind of psychotherapy while you're sleeping. So the question is, why do some trauma survivors suffer nightmares chronically? Most people have nightmares in the first month after a traumatic event, but for 80%–90% of them those nightmares go away 2–3 months later.

TCPR: IRT is based on a behavioral model of nightmares. Tell us about that.

Dr. Krakow: The idea is that nightmares become habitual, like any learned process. This is how we explain it to patients: "Maybe these nightmares keep happening because a habit forms in your brain where, when you are keyed into something during the daytime, your body says, 'Well, that was an anxiety-producing event, so I'm just going to have another nightmare tonight.'" And that is actually how we introduce IRT—as an idea that nightmares are a learned behavior. This concept can be a breath of fresh air for some or a deal-breaker for others. Unfortunately, conventional wisdom about nightmares has led most sufferers to imagine there cannot possibly be a learned-behavior model of nightmares. As such, the more entrenched they are in this view, the more education and restricting we need to work through.

TCPR: What happens in the therapy?

Dr. Krakow: The main technique is that patients take a nightmare and change it in some way—in any way they want. Then they'll rehearse the new dream in their imagination during the daytime.

TCPR: Can you walk us through the steps?

Dr. Krakow: We start with the education piece on nightmares as a learned behavior that originally served a purpose. Next we want the patient to become comfortable with imagery. It is much like guided imagery. We'll have them imagine a scene and engage their full senses in it: "Picture in your mind's eye how to drive from your house to your favorite restaurant," or "Picture going from the meadow down to the beach and listening to waves." This part may take longer in PTSD, because these patients are prone to flashbacks and intrusive memories when they allow their imagination to run far afield.

TCPR: What do you do when distressing thoughts intrude?

Dr. Krakow: You check for that. You want patients to be in control, so you have them stop and get grounded. Specifically, they stop the session, open their eyes, and take some relaxed breaths. Then they go back to the imagery when they are ready. When they become more accomplished with imagery, we want to encourage them to acknowledge a distressing image and then choose to move away from it and on to a new and pleasant image. Some patients learn this more advanced strategy very quickly, while others might need months and lots of coaching or counseling to achieve this aim.

TCPR: So first they practice imagery. What's next?

Dr. Krakow: That usually takes 2 sessions, so by the third session they are comfortable with imagery and have practiced it on their own. Then we say, "Okay, I want you to select a dream and write it down. Next I want you to change that dream 'any way you wish,' following Dr. Neidhardt's original instruction. And then I want you to rehearse the new dream you created in your mind's eye."

TCPR: Are they supposed to start with a repetitive nightmare?

Dr. Krakow: No. It can be any nightmare. Theoretically, they don't even have to choose a nightmare.

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Expert Interview

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We think the imagination process is where the action is. What matters is that they are engaging their imagination actively, instead of it taking hold of them and terrorizing them every night.

TCPR: Are you desensitizing them to the nightmare?

Dr. Krakow: No. This is not desensitization. This is new learning. In fact, I only have them write down the nightmare once, when they are first learning the therapy. I would never ask anyone to write a bad dream twice, because when they write down a nightmare it could overstimulate them. We don't want them to rehearse the nightmare.

TCPR: You ask patients to "change the nightmare." Do they ever have trouble coming up with new material?

Dr. Krakow: They may say, "Well, change what?" The best response we've found is very open: "Change the nightmare any way you wish." We want the ideas to come from the patient, not us. Once we adopted this instruction, we saw wild changes. One woman presented with a repetitive nightmare where she was chased to the edge of a cliff. What was the new ending she created? "I jumped off the cliff." Her nightmares cleared up fairly soon thereafter.

TCPR: So it's more important for them to take control and choose the ending than to create a happy ending?

Dr. Krakow: Exactly. It's empowering, but remember it's not about directing them to choose an ending. Changing it any way you wish means literally that. When most people hear that instruction, a lightbulb goes off and they run with it. There are a handful of patients who resist and say, "What do you mean, 'change it'? I can't change my dream. That's what happened to me." I say, "Well, then let's not pick that traumatic replay dream." And we may end up using a neutral dream or a fantasy if their nightmares trigger too much anxiety. In the end, we want them to have a "new dream," and that is what they rehearse outside of session. And this new dream need not be static. Its imagery may evolve as they practice it. That's good—we want to see change, because part of the patient's problem is that their dream life and their imagination have become stuck.

TCPR: Is it important to rehearse the dream just before bed?

Dr. Krakow: Not at all.

TCPR: Really?

Dr. Krakow: We don't tell patients when to rehearse the dream or for how long. If we do, they'll likely run into obstacles like "I didn't have time to do it." In the trials, the average patient rehearsed for less than 5 minutes every other day; many only rehearsed 1 minute every other day. We want to get them back in control of their imagination.

TCPR: What are some problems patients run into when they try this therapy?

Dr. Krakow: Some patients have trouble imagining anything. They say, "My screen is black." It may be they have so much anxiety they are just suppressing everything. I tell them, "What you need to do is just let your imagery session go longer. Just practice longer." But these patients might need more guided imagery sessions under the direction of a therapist.

"Here's a pearl: If a patient has a bad dream at least once a week, the chance that it is bothering them is extraordinarily high. Ask the patient, 'Do you think about your nightmare content at all during the day?' If they say 'Yes,' they would probably benefit from an intervention."

Barry Krakow, MD

TCPR: How widespread is IRT use?

Dr. Krakow: IRT has been declared the number one nonpharmacologic treatment for chronic nightmares for about a decade, and 99% of all research studies on IRT show decreases in nightmares and distress. Its use became fairly widespread in the US military after the war in Iraq, when soldiers were returning home complaining of PTSD, sleep disorders, and nightmares. We conducted 10 trainings at leading bases in the US in 2013 and 2014. In fact, I've got one coming up at Fort Campbell in August. But well before these trainings, VA medical centers frequently contacted me for trainings and use of our audio workbook, *Turning Nightmares Into Dreams*. European countries are very active in using IRT, in part because there are so many dream science research centers in Germany, the Netherlands, Switzerland, and England.

TCPR: Are there patients who are not appropriate for this therapy?

Dr. Krakow: I'd want to know that the patient can cope with the imagery work, so I may not do it with someone who is severely depressed or suicidal. I'd be careful in patients with unstable PTSD who are having flashbacks, dissociation, or panic attacks on a regular basis. Those cases are better managed by a therapist with expertise in PTSD. IRT has been most widely promulgated in sleep clinics in the US by clinicians with little training in psychotherapy, although mental health professionals have applied it successfully to more severe cases.

TCPR: Can you summarize the research benefits of IRT?

Dr. Krakow: IRT decreased nightmares in virtually all populations studied. After about 2 weeks, patients have fewer nightmares or less intense nightmares (usually both). Most of the benefits kick in between 2 weeks and 2 months. Their sleep also improves, and they have less depression, anxiety, somatization, and hostility (Krakow B et al, *Behav Res Ther* 1995;33(7):837–843). And in PTSD, there is decreased PTSD symptom severity; by comparison, the improvement in PTSD appears to be about the same magnitude of sertraline's impact on PTSD.

TCPR: Do patients continue the rehearsal technique on their own after they recover?

Dr. Krakow: Many do, particularly if the nightmares flare up again. But they also start using their

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Research Updates IN PSYCHIATRY

SLEEP

Lemborexant and Sleep Architecture in the Elderly

REVIEW OF: Moline M et al, *J Clin Sleep Med* 2021. Epub ahead of print.

TYPE OF STUDY: Randomized, double-blind, parallel-group study

As we age, sleep architecture worsens in ways that reduce sleep quality, particularly after age 55. Unfortunately, most hypnotics either do not improve sleep quality (eg, the z-hypnotics) or slightly worsen it (eg, the benzodiazepines). Specifically, benzodiazepines in higher doses can reduce stages of sleep that are critical for memory consolidation. Lemborexant (Dayvigo) was approved in 2019 for the treatment of insomnia in adults. Its effects are mediated by dual orexin receptor antagonism. Recently, researchers looked at how sleep architecture changed when older adults took this orexin antagonist.

The study was a secondary analysis of an industry-sponsored, randomized, double-blind trial of 1006 subjects known as SUNRISE 1. All subjects were over age 55 (average 63) and had primary insomnia; the majority were female (86%) and white (72%). The presence of sleep-maintenance insomnia was required; some subjects had sleep-onset insomnia as well. Patients with significant depression, anxiety, or substance use (including caffeine use after 6 pm) were excluded. Also excluded were patients with medical problems that could make hypnotic use unsafe, and those with comorbid sleep disorders (eg, sleep apnea, periodic limb movement disorder, restless legs syndrome, circadian rhythm sleep disorder, and narcolepsy).

Patients were randomly assigned to one of four conditions: lemborexant 5 mg, lemborexant 10 mg, zolpidem ER 6.25 mg, or placebo. Participants were treated for 30 nights followed by a follow-up period of 14 days before the end-of-study visit. The goal of this secondary analysis was to compare changes in sleep architecture (eg, total sleep time, non-REM sleep, and REM sleep) in older adults with insomnia disorder receiving lemborexant (5 or 10 mg), zolpidem, or placebo.

After a month of treatment, both doses of lemborexant outperformed placebo and zolpidem on measures of sleep architecture. Specific sleep architecture changes included increased total sleep time, non-REM sleep, and REM sleep, as well as reduced REM latency after the first 2 nights of treatment and again after a month of treatment. After 30 days, both doses of lemborexant increased total sleep time by about twice as much as placebo (total sleep increased by 30 minutes on placebo vs 64 minutes on lemborexant 5 mg and 69 minutes on 10 mg). Zolpidem, on the other hand, outperformed placebo in terms of total sleep time and non-REM sleep, but failed to reduce REM latency.

This study is weakened by being a secondary analysis, which makes it more prone to statistical error. Also, while lemborexant did improve sleep architecture, the changes were small and their clinical relevance is unclear. On the other hand, the changes in REM sleep seen here are relevant to age-related memory decline, and separate studies have found that lemborexant protects sleep-dependent memory consolidation in older adults with insomnia (Harand C et al, *Front Neurol* 2012;3:8).

The benefits seen in this study are consistent with prior research on another orexin antagonist, suvorexant, suggesting the orexin antagonists may have a beneficial class effect on sleep architecture (Snyder E et al, *Sleep Med* 2016;19:93–100).

TCPR'S TAKE

Quality is as important as quantity when it comes to sleep, particularly with older adults. Though this is only one study, it's encouraging to see a hypnotic that improves sleep architecture and may have a positive impact on memory. Lemborexant also belongs to a small group of hypnotics that are relatively safe in older adults (along with suvorexant, ramelteon, and melatonin). Unfortunately, these benefits come at a cost of $10 a pill.

—Garrett Rossi, MD. Dr. Rossi has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

SIDE EFFECTS

Comparison of GI Side Effects of Antidepressants

REVIEW OF: Oliva V et al, *Prog Neuropsychopharmacol Biol Psychiatry* 2021;109:110266

TYPE OF STUDY: Meta-analysis of placebo-controlled trials

Antidepressants often cause gastrointestinal (GI) side effects, but it's not clear which ones are the worst actors. A recent meta-analysis helps to clarify the picture.

The investigators searched the literature and located 304 randomized, placebo-controlled trials with information on GI side effects on 15 antidepressants (including SSRIs, SNRIs, bupropion, and mirtazapine). Nausea and vomiting was the most common side effect, with the worst five antidepressants being duloxetine (odds ratio [OR] 4.33), vortioxetine (OR 4.28), levomilnacipran (OR 3.81), venlafaxine (OR 3.52), and desvenlafaxine (OR 3.51). Only mirtazapine was not associated with nausea and vomiting, which is consistent with its mechanism of action. The risk of nausea and vomiting was dose dependent for citalopram and escitalopram and became more pronounced at dosages above 40 mg/day for citalopram and 10 mg/day for escitalopram.

Constipation occurred on 10 antidepressants, with levomilnacipran (OR 3.41), desvenlafaxine (OR 3.41), and duloxetine (OR 2.58) being the top three. Vortioxetine had a dose-dependent risk of constipation at dosages above 20 mg/day (which is also the maximum recommended dose). Only five antidepressants were associated with diarrhea: sertraline (OR 2.33), fluvoxamine (OR 2.29), escitalopram (OR 1.91), citalopram (OR 1.64), and duloxetine (OR 1.60).

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CME Post-Test

To earn CME or CE credit, log on to www.TheCarlatReport.com with your username and password to take the post-test. You must answer 75% of the questions correctly to earn credit. You will be given two attempts to pass the test. Tests must be completed within a year from each issue's publication date. The Carlat CME Institute is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians. The Carlat CME Institute is also approved by the American Psychological Association to sponsor continuing education for psychologists. Carlat CME Institute maintains responsibility for this program and its content. The Carlat CME Institute designates this enduring material educational activity for a maximum of one (1) *AMA PRA Category 1 Credit*™ or 1 CE credit for psychologists. Physicians or psychologists should claim credit commensurate only with the extent of their participation in the activity.

For those seeking ABPN Self-Assessment (MOC) credit, a pre- and post-test must be taken online at http://thecarlatcmeinstitute.com/self-assessment/

This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Learning Objectives (LO) are listed on page 1.

1. In patients with depression who respond to electroconvulsive therapy (ECT), which of the following post-ECT treatment plans is most likely to reduce the risk of depressive relapse (LO #1)?
   - [ ] a. Nortriptyline + antipsychotic
   - [ ] b. The patient's original antidepressant + antipsychotic
   - [ ] c. Ketamine, esketamine, or a glutamatergic medication
   - [ ] d. Nortriptyline + lithium

2. In a study of PTSD by Dr. Krakow, imagery rehearsal therapy (IRT) improved nightmares, sleep quality, and PTSD symptoms with effect sizes in what range (LO #2)?
   - [ ] a. Small
   - [ ] b. Small to moderate
   - [ ] c. Moderate
   - [ ] d. Large

3. In a recent study of primary insomnia, how did lemborexant, dosed at either 5 mg or 10 mg, perform on measures of sleep quality compared to zolpidem and placebo (LO #3)?
   - [ ] a. Lemborexant 5 mg outperformed placebo, but not zolpidem
   - [ ] b. Only lemborexant 10 mg outperformed zolpidem and placebo
   - [ ] c. Both doses of lemborexant outperformed zolpidem and placebo
   - [ ] d. Both doses of lemborexant outperformed placebo, but not zolpidem

4. Which of the following is true regarding the effects of tricyclic antidepressants (TCAs) + lithium versus SNRIs + lithium for preventing depressive relapse post-ECT (LO #1)?
   - [ ] a. SNRIs + lithium are equally as effective as TCAs + lithium
   - [ ] b. TCAs + lithium are significantly less effective than SSRIs alone
   - [ ] c. SNRIs + lithium are significantly more effective
   - [ ] d. TCAs + lithium are significantly more effective

5. According to Dr. Krakow, what's the best response to a patient with nightmare disorder who says, "Change what?" when instructed to change their selected dream during IRT (LO #2)?
   - [ ] a. "Change the ending in a way that evokes calm or positive emotions"
   - [ ] b. "Change the nightmare any way you wish"
   - [ ] c. "Change the nightmare so that you are embracing your fears rather than running from them"
   - [ ] d. "Picture yourself triumphing in your nightmare"

Research Updates

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Other GI side effects were also examined and are summarized in the table.

TCPR'S TAKE

While most antidepressants can cause GI side effects, it appears that SNRIs and vortioxetine are the most likely to cause both nausea and constipation. True to its reputation, sertraline caused the most diarrhea. Paroxetine was associated with anorexia, suggesting this medication may have opposite effects in different patients, as other studies have associated it with weight gain. Surprisingly, the two antidepressants associated with weight loss—bupropion and fluoxetine—did not decrease patients' appetite in this analysis.

—Jesus Ligot, MD. Dr. Ligot has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

To learn more, listen to our 8/9/21 podcast, "Treating Nausea on Psych Meds." Search for "Carlat" on your podcast store.

GI Side Effects on Modern Antidepressants

Side Effect (SE)	Antidepressants Likely to Cause SE (ordered from most to least)
Nausea/vomiting	Duloxetine, vortioxetine, levomilnacipran, venlafaxine, desvenlafaxine
Constipation	Levomilnacipran, desvenlafaxine, duloxetine
Diarrhea	Sertraline, fluvoxamine, escitalopram, citalopram, duloxetine
Abdominal pain	Escitalopram and citalopram
Anorexia	Fluvoxamine, desvenlafaxine, venlafaxine, paroxetine, duloxetine
Increased appetite	Mirtazapine

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daytime imagery to solve problems, which is exactly what most of us do in everyday life. For example, when you misplace something, you try to find it in your mind's eye: "Where was I when I lost it?" That's a good use of imagery, and patients have reported an increase in this activity after using IRT.

TCPR: Is it fair to say that you're teaching nightmare sufferers how to daydream?

Dr. Krakow: Absolutely. One of our patients came back a month after IRT and said, "It was amazing. I was in this conflict with my boss and I pictured ('daydreamed') having a better conversation with him. And then when I went and saw my boss, I had a better conversation with him." And she was ecstatic.

TCPR: Anything else we should know?

Dr. Krakow: Yes. Since starting this work, we were stunned to learn that nightmares are also a sign of sleep apnea in a very high proportion of cases, whether they occur during PTSD or nightmare disorder. The rate of sleep apnea is very high in PTSD, up to 80%. These patients don't look like they have sleep apnea—they are often young and thin—but you don't want to miss this diagnosis.

TCPR: Thank you, Dr. Krakow.

Editor's note: *To learn more about imagery rehearsal therapy, visit www.barrykrakowmd.com.*

To learn more, listen to our 8/23/21 podcast, "Why Nightmares Matter." Search for "Carlat" on your podcast store.