THE CARLAT REPORT PSYCHIATRY

A CME Publication

Subscribe today! Call 866-348-9279

AN UNBIASED MONTHLY COVERING ALL THINGS PSYCHIATRIC

Chris Aiken, MD
Editor-in-Chief

Volume 20, Issue 9
September 2022
www.thecarlatreport.com

IN THIS ISSUE

Focus of the Month:
College Mental Health

Learning Objectives

After reading these articles, you should be able to:

1. Identify the potential role for lithium in patients at risk for dementia.
2. List the strengths and weaknesses of the olanzapine-samidorphan combination (Lybalvi) to treat antipsychotic-related weight gain.
3. Develop a plan for students attending college to have continuity of care in their transition from home.
4. Summarize some of the current research findings on psychiatric treatment.

Low-Dose Lithium to Delay Dementia?

James Phelps, MD. Psychiatrist Emeritus, Samaritan Mental Health, Corvallis, OR. Medical Director, PsychEducation.org.

Dr. Phelps, author of this educational activity, has no relevant financial relationship(s) with ineligible companies to disclose.

Your 65-year-old patient Mr. Hoffman recently saw his father through a devastating course of Alzheimer's disease. Mr. Hoffman had his own risk assessed with ApoE genotyping, and the result—E4/E4—indicates a high risk. He comes to your office after reading an online article about low-dose lithium for dementia prevention and asks if you can prescribe it.

Dementia is a disaster for patients and their families. Current treatments can only temporarily slow the decline, but new evidence suggests that tiny doses of lithium can significantly delay the onset of dementia. Is it enough evidence to support prescribing 150 mg of lithium for patients like Mr. Hoffman?

Highlights From This Issue

Feature article
Low-dose lithium showed preventive effects against dementia in several trials, and Dr. James Phelps looks at whether it is ready for practice.

Q&A
With rising rates of pandemic-related anxiety and suicide in young people, Dr. Michelle Riba explores ways to support the unique needs of students transitioning from home to college life.

On page 5
Dr. Brian Miller examines how Lybalvi compares with other treatments for antipsychotic-induced weight gain, which is often the culprit behind decreasing medication adherence.

Continued on page 4

Q&A With the Expert

Advances in College Mental Health
Michelle B. Riba, MD, MS

Professor, Department of Psychiatry; Co-Director, Workplace Mental Health Solutions, Eisenberg Family Depression Center; Director, PsychOncology Program, University of Michigan Rogel Cancer Center. Editor, College Psychiatry: Strategies to Improve Access to Mental Health *(co-editor: Meera Menon, MD).*

Interview by Garrett Rossi, MD. Inpatient/consult attending psychiatrist, AtlantiCare Regional Medical Center, Pomona, NJ.

Dr. Riba, expert of this educational activity, has disclosed that she receives book royalties from Springer, Wiley, and APA Publishing. Dr. Aiken has reviewed this educational activity and has determined that there is no commercial bias as a result of this financial relationship. Dr. Rossi has no relevant financial relationship(s) with ineligible companies to disclose.

TCPR: What are the most common psychiatric conditions in the college mental health setting?

Dr. Riba: Anxiety and depression are the most common psychiatric conditions. It is very difficult to get timely psychiatric evaluations and evidence-based treatment. It has been especially difficult during the last two years during COVID, but telehealth has certainly helped. Substance use disorders are also quite prevalent among college students. A lot of students are exposed to these substances for the first time during college, where there is no shortage of opportunities to use alcohol and other substances. Marijuana use is on the rise, in part because of the loosening of state restrictions.

Continued on page 2

Expert Interview

Continued from page 1

TCPR: How does marijuana affect students?

Dr. Riba: In the 18- to 19-year-old developing brain, the impact of cannabis use can be profound. Recent studies on the long-term use of cannabis are now starting to show the cognitive issues that can develop because of early use (Scott JC et al, *JAMA Psychiatry* 2018;75(6):585–595). I've seen young college students coming in looking psychotic, and it's related to marijuana use. There's cause for alarm for those who are overusing marijuana. Students are also getting stimulant medications like amphetamines on the black market, and many of these are laced with drugs like fentanyl and methamphetamine, contributing to very dangerous situations, such as unintentional overdose (www.tinyurl.com/2nn88up4).

TCPR: How do you handle stimulant medications for students with ADHD?

Dr. Riba: We require neuropsychiatric testing before prescribing. We do this because it's easy for someone to read the DSM criteria and endorse the necessary symptoms to meet criteria. Prescribing stimulants can be harmful if students are taking other medications such as benzodiazepines or are using substances. We do not liberally give out stimulant medications for these reasons.

TCPR: Is there anything we should be mindful of when making a diagnosis or prescribing medications to college students?

Dr. Riba: You need to make sure they have the right diagnosis. Many students have been taking psychotropic medications for years, sometimes for incorrect diagnoses or for conditions that have resolved and no longer require medication treatment. The bright side is more people are able to go to college who have major mental health problems, including schizophrenia. Improved access, early evaluation, treatment, medications, and therapy have made this possible.

TCPR: How has COVID-19 impacted the mental health of college students?

Dr. Riba: Many students have lost the first two years of college life. Compared to 2017–2019, many more students worldwide, not just in the United States, have been depressed and anxious. Suicidal ideation has also increased among college students (Wang C et al, *J Am Coll Health* 2021:1–8; Gratz KL et al, *Psychiatry Res* 2021;302:114034). What's less clear is how long these problems will last and what the best practices will be to handle the consequences of this pandemic on mental health.

TCPR: Any insights on the rise in suicide?

Dr. Riba: An alarming number of college students have had suicidal thoughts or ideation, and it is very frightening. The pandemic has contributed, as have the changes to the college experience during the last few years, including isolation, social media, depression, and loss. We are also seeing the "contagion effect" where suicidal ideation spreads among people who learn of someone's suicidal ideation or behavior. The effects on the second victims—the friends and classmates of students who died by suicide—are terrible. They feel grief, loss, and self-doubt, wondering if there were clues they missed. It's very demoralizing and tragic.

TCPR: How is access to mental health care on college campuses?

Dr. Riba: There are campuses where the college mental health service is not located in a place that is easily accessible to students. In some cases, services are too expensive. Telehealth has helped, but some state licensing laws make it very difficult or illegal for mental health professionals at a university or college to continue to care for a student once the student returns home to another state or country.

TCPR: How has telehealth impacted access to services?

Dr. Riba: I think telehealth works best when you already have an established relationship with the patient. You get a lot of valuable information from in-person contact with the student. One solution is to make the first visit in person and transition to telehealth appointments after that. It's been very promising for people in certain geographic regions and for people with certain disabilities where transportation is an issue to increase access to care (Li Z et al, *BMC Psychiatry* 2021;21(1):182; Annaswamy TM et al, *Disabil Health J* 2020;13(4):100973).

TCPR: Do you think social media has a positive or negative impact on college mental health?

Dr. Riba: This generation of students grew up with it, so it's part of their world. They don't go anywhere without their phones, and they rarely put their devices down. The problems come up with how people don't talk to one another in person—instead, their relationships are often just by text or email. Important social cues such as eye contact or body language are lost in the relationship.

Continued on page 3

Mailing Information

The Carlat Psychiatry Report (ISSN 2473-4128) is published monthly, excluding July and Dec., by Carlat Publishing, LLC; 2 Prince Place, Newburyport, MA 01950. Periodicals Postage Paid at Newburyport, MA and at additional mailing offices.

POSTMASTER: Send address changes to *The Carlat Psychiatry Report*, P.O. Box 626, Newburyport, MA 01950.

Expert Interview
Continued from page 2

Social media has helped in a lot of ways, but it can't be the only form of interaction. And of course, social media can have negative effects, leading to people being bullied or made fun of or unfriended. There was a case in New Jersey several years ago where a college student was outed as gay by his roommate on social media and committed suicide as a result. That was one of the terrible consequences.

TCPR: There was one viral post that I wanted to ask about. A psychiatry resident took a photo of himself taking his psychotropic medication. Do you think this is helpful in reducing stigma?

Dr. Riba: It has positives and negatives. I don't think being a good doctor means that the doctor must have a psychiatric disorder. We go to a doctor because of their expertise, not necessarily because they have the same problem. A post like this also takes the focus of treatment away from the patient and places it on the physician. Patients need to focus on themselves and their treatment, not that of the person providing the treatment.

TCPR: The trend among the younger generation of physicians seems to be "I'm more relatable to the patient if I've experienced similar things." What are your thoughts on this?

Dr. Riba: As physicians, it is important to have a strong alliance with our patients. Patients are more and more interested in working with physicians who are of the same gender, race, or cultural background as themselves. It is important for patients to be able to choose the clinicians they want to work with and to attain a strong doctor-patient relationship.

TCPR: Is there anything that you recommend for students who are preparing for college that can help build resiliency or prepare them for campus life?

Dr. Riba: I think it's important for students and families to sit down and talk about the challenges of being away from home and starting college. A lot of students are in treatment prior to starting college and think they can make it back home during breaks to get refills or receive psychotherapy. That's usually not feasible. For a successful transition to college life, it's essential to be prepared for all the potential pitfalls and have a plan to deal with them. It is helpful for the student to make an appointment with a mental health professional before they leave home. Further, the medical records should be sent ahead of time, and permission given for the involved clinicians to "hand off" and discuss important information. This will help facilitate excellent care for the student and allow for any needed changes in the treatment in between holidays, breaks, etc.

> **"Many students have been taking psychotropic medications for years. The bright side is more people are able to go to college who have major mental health problems, including schizophrenia. Improved access, early evaluation, treatment, medications, and therapy have made this possible."**
>
> Michelle B. Riba, MD, MS

TCPR: So, there are many aspects to getting prepared to leave for school.

Dr. Riba: Getting prepared to establish treatment and ensure the continuation of psychiatric medications is no different than making sure you have enough insulin if you have diabetes, or speaking with a clinician to see if you need your high blood pressure checked. It's important to prepare ahead of time and make sure options are available should a crisis occur. Substance use and peer pressure should be discussed as well, given their high prevalence on college campuses. Having a routine, sleeping and eating properly, and getting exercise can go a long way toward building resiliency. Many students are living on their own for the first time, with roommates and with class schedules that change from day to day, so new routines need to be created.

TCPR: How do student loans affect college stress?

Dr. Riba: They are a big problem. We have students graduating with $100,000 or more in student loan debt. This is why community college is a great option. It gives you a place to start without accruing that huge debt (Pisaniello MS et al, *BMJ Open* 2019;9(7):e029980).

TCPR: Are the mental health issues different for two-year students?

Dr. Riba: Two-year students are generally much more thoughtful about why they're going to college. They are aware of the financial aspect and take education seriously. The mental health resources available at a two-year college are often not as substantial as a four-year school or university, though. Students in a two-year school may be working during the day and going to school at night, and they usually don't live in a dorm. These students may not have the resources or time to get proper mental health treatment.

TCPR: What about graduate students? What types of challenges are they facing?

Dr. Riba: Graduate students have always had difficulty adjusting because many are from foreign countries or are enrolled in small programs that lack the resources and time to identify mental health problems. The students also have a lot of pressure to succeed in these programs, coping with demanding work hours and the added fear of returning home ashamed or embarrassed. Some come from cultures that don't accept mental health as a reason for problems. The price of failure is often much higher for these students, as their livelihood and that of their family may depend on that graduate degree. Graduate students are older and often have families, so studying, working, and family care, including financial pressures, often create additional stresses when compared to undergraduate students.

TCPR: Thank you for your time, Dr. Riba.

Low-Dose Lithium to Delay Dementia?

Continued from page 1

Evidence for low-dose lithium

Several studies have found that patients with mood disorders who took lithium had a lower incidence of dementia than similar patients who were not prescribed lithium. This finding held up in three of four epidemiologic studies and five of six clinical studies (Ishii N et al, *Int J Environ Res Public Health* 2021;18(15):7756).

Another line of evidence is more indirect. Multiple studies have found an inverse relationship between lithium concentrations in drinking water and suicide rates. Those findings prompted studies of trace lithium exposure and incidence of dementia. Of these three epidemiologic studies, two found a correlation in support of lithium's preventive effects. In the one negative study, average lithium exposures were unusually low.

Lacking industry support, randomized trials of lithium for the prevention of dementia are few and small. Of six studies reviewed in 2014 by Mauer et al, one was negative, one was positive, one used trace lithium (300 mcg/day) but was positive for preservation of cognitive function, and the rest examined only indirect outcome measures (Mauer S et al, *Aust N Z J Psychiatry* 2014;48(9):809–818).

Then came a 2019 continuation of the positive low-dose study by Forlenza and colleagues. All patients began the trial with mild cognitive impairment. The average serum lithium level was 0.4 mEq/L. At two- to three-year follow-up, cognition had declined in the placebo group but not in the lithium group (p=0.05). Unfortunately, nearly half the sample was lost to attrition (illness, medical complications, withdrawal from the study—not lithium-related problems) for a final N of only 34 participants, making it difficult to generalize these results (Forlenza OV et al, *Br J Psychiatry* 2019;215(5):668–674).

To sum up, the existing empirical evidence is suggestive of an antidementia effect with low-dose lithium, but we need more studies before drawing definitive conclusions. A larger randomized trial using full-dose lithium (serum levels of 0.6–0.8 mEq/L) is scheduled for completion in 2023 (the LATTICE trial).

Risks of low-dose lithium

What are the potential risks of low-dose lithium? Renal impairment is rare and is mainly a risk in patients on relatively high lifelong cumulative doses, especially when there are spikes above 0.8 mEq/L (Clos S et al, *Lancet Psychiatry* 2015;2(12):1075–1083). Lithium at low serum levels presents no significant renal risk if creatinine is monitored, as suggested by a two-year controlled trial that found no changes in renal function with low-dose lithium in the elderly (Aprahamian I et al, *J Clin Psychiatry* 2014 Jul;75(7):e672–678).

On the other hand, thyroid suppression by therapeutic doses of lithium is very common, affecting roughly 10% of patients who start standard doses of lithium (Kirov G et al, *J Affect Disord* 2005;87(2-3):313–317). Two sources of data suggest that even tiny doses of lithium can lower thyroid hormone. First, in the high Andes, some villages have as much as 1000 mcg/L of lithium in their water supply. In this region, urinary lithium concentrations are inversely correlated with free T4 (p=0.007). Second, in a small primary care study, 12% of patients given low-dose lithium (average level 0.43 mEq/L) had a TSH increase >4.2 mIU/L during follow-up. Thus it appears that low lithium doses, perhaps even less than 1 mg/day, may suppress thyroid function.

What about lithium orotate?

Lithium orotate is a salt of lithium and orotic acid. It is available in health food stores and via the internet, in doses closer to the lithium concentrations found in drinking water in some regions. For example, the common 5 mg pill contains 220 mcg of elemental lithium. However, low doses might not translate to low tissue levels. A 1978 study in rats found that brain lithium concentrations were three times higher with lithium orotate than regular lithium. Unfortunately, further research on lithium orotate was abandoned in 1979 when another rat study found greater renal toxicity with lithium orotate than with lithium carbonate.

Should you prescribe low-dose lithium?

The LATTICE study will substantially advance our understanding of lithium's putative benefit for the prevention of dementia, but while awaiting those results in the next two to three years, are there some patients for whom lithium should be considered now?

Current evidence does not support widespread recommendation of low-dose lithium, but we can help patients who inquire about it. Lithium may be considered if a patient is seriously concerned about their risk of dementia for a variety of reasons: a strong family history, positive ApoE testing, mild cognitive impairment, or simply an acute awareness of the disastrous personal and family consequences of the illness. Cardiovascular disease, diabetes, obesity, sleep apnea, a history of substance abuse, recurrent depression, or schizophrenia also raise the risk.

Of course, first steps include behavioral risk reduction: regular physical activity, cognitive and social engagement, and a lipid-lowering, heart-healthy diet (van den Brink AC et al, *Adv Nutr* 2019;10(6):1040–1065). *(Editor's note: Both the Mediterranean and DASH diets have epidemiologic evidence to prevent dementia, and these approaches are very similar to the diet we presented for depression in the May 2019 and Nov/Dec 2021 issues of* The Carlat Psychiatry Report*.)*

When those steps are in place, a highly motivated patient with no relative contraindications to lithium (eg, cardiac arrhythmias, psoriasis, renal impairment) could be offered low-dose lithium. Until further data are available to establish the safety of lithium orotate, the simplest practical dose to prescribe is 150 mg of lithium carbonate. Titration to higher doses could be considered for patients who already have minimal cognitive impairment, if fully tolerable (as treatment may go on for years), up to a serum level of 0.6–0.8 as per the LATTICE study.

CARLAT VERDICT

Accumulating evidence supports low-dose lithium to delay the onset of dementia. Until further data arrive, low-dose lithium could be considered for patients at high risk of dementia, with monitoring of creatinine and TSH.

Treatment of Antipsychotic-Induced Weight Gain

Brian Miller, MD, PhD, MPH. Professor of Psychiatry at the Medical College of Georgia, Augusta, and President of the Georgia Psychiatric Physicians Association.

Dr. Miller, author of this educational activity, receives research support from Augusta University; the National Institute of Mental Health; the Brain and Behavior Research Foundation; and the Stanley Medical Research Institute. Relevant financial relationships listed for the author have been mitigated.

Antipsychotic-induced weight gain can decrease medication adherence, with a domino effect of negative consequences on the psychiatric illness. Recently the FDA approved the first therapy to address this problem: Lybalvi, a combination of olanzapine and samidorphan. In this article, I'll look at how it compares with other treatments for antipsychotic-induced weight gain.

An ounce of prevention

Prevention starts before prescribing an antipsychotic. When taking a medical history, check baseline weight/BMI and look for metabolic risk factors, including hypertension, hyperlipidemia, and a family history of diabetes—this confers a fourfold increased odds of the patient having diabetes (Chung J and Miller BJ, *Schizophr Res* 2020;216:41–47). Genetic factors influence the risk of metabolic side effects, so ask if the patient or their family members have diabetes or other metabolic problems. Younger patients and those starting an antipsychotic for the first time are also at greater risk for weight gain.

When possible, choose antipsychotics with a favorable weight/metabolic profile, such as aripiprazole, brexpiprazole, lumateperone, lurasidone, or ziprasidone. When starting an antipsychotic, especially one with greater weight/metabolic liability, I give patients the option either to start an adjunctive treatment to help mitigate risk, or to closely monitor the effects of the antipsychotic on their weight.

Switching

When weight gain develops, the most common treatment approach is to switch to a different agent with a more favorable weight/metabolic profile. However, my adage is, "The best antipsychotic is the one that the patient will take and that controls their symptoms." If the patient is willing to continue the current medication and is clinically stable, then I generally prefer to continue their current antipsychotic and use an adjunctive treatment for weight gain, although I make this decision collaboratively with the patient.

Olanzapine-samidorphan

Olanzapine is an efficacious antipsychotic in schizophrenia based on head-to-head comparisons with other agents (Leucht S et al, *Lancet* 2013;382(9896):951–962), but its use is limited by its high risk of weight gain and metabolic problems. The opioid system plays a role in that weight gain, as antipsychotics increase the rewarding effects of high-calorie foods. Lybalvi offers a novel solution by combining olanzapine with the opioid receptor antagonist samidorphan.

Three randomized controlled trials (lasting up to six months) compared olanzapine-samidorphan versus olanzapine alone in 1,116 patients with schizophrenia (Srisurapanont M et al, *Sci Rep* 2021;11(1):7583). Patients still gained weight on both treatments but had statistically significant less weight gain on olanzapine-samidorphan versus olanzapine (6.9 versus 10.7 lb), especially in patients with lower BMI. Both olanzapine-samidorphan and olanzapine were associated with similar improvements in symptom ratings and adverse effect profiles. Although samidorphan curbed some of the weight gain, it did not protect against elevations in glucose or lipids.

These trials tested the preventive effects of samidorphan, enrolling only non-obese patients (mean BMI 25.7). We don't know if samidorphan will work in those who have already gained significant weight, which unfortunately is the population most likely to get this $1,300/month drug authorized by their insurer. Most insurers require significant weight gain on an antipsychotic or clinical failure of two generic antipsychotics before they will cover Lybalvi.

Lybalvi should not be started within seven days of taking a short-acting or 14 days of taking a long-acting opioid.

Other pharmacologic treatments

Lybalvi may hold FDA approval, but metformin and topiramate have better evidence to reduce both weight gain and metabolic problems on antipsychotics. The antidiabetic agent metformin may reduce weight by both decreasing insulin resistance and suppressing appetite. In a meta-analysis of 10 studies involving 681 adults on second-generation antipsychotics, most of which lasted three months, adjunctive metformin was associated with a 7.1-lb weight *decrease* versus placebo. That sounds like a bigger effect than Lybalvi, but the figures can't be easily compared because the metformin studies enrolled patients who were already obese.

What sets metformin apart from Lybalvi is metformin's ability to improve not just weight but also the patient's metabolic profile. Insulin resistance, fasting glucose, triglycerides, and even hyperprolactinemia improved when metformin was added to an antipsychotic. There was no evidence of worsening psychopathology with metformin. The average metformin dose was 1000 mg (500 mg twice daily), although doses ranged from 750 to 2500 mg/day. In these trials, the most common adverse effects were nausea, vomiting, and diarrhea. Contraindications to metformin use include severe kidney disease (GFR <30) and metabolic acidosis.

Compared to metformin, topiramate has similar effects on weight reduction, with an average weight reduction of 6.8 lb versus placebo in seven studies of 439 adults taking second-generation antipsychotics. An extra benefit of topiramate is that in trials of its weight benefits, it also improved positive and negative symptoms of schizophrenia with a medium effect size (0.6). Only one of the seven trials reported on blood glucose and lipids, with results favoring topiramate. Most of the trials lasted three to four months. The average dose was about 200 mg/day, although doses ranged from 50 to 400 mg/day.

Topiramate also has some evidence of efficacy in many common psychiatric disorders, including PTSD, OCD, and bulimia, as well as alcohol, cocaine, and methamphetamine use disorders. Its main risk is renal stones, and most of its side effects—cognitive problems, imbalance, and paresthesias—are dose related.

Other second-line options for patients who cannot tolerate or fail to respond

Continued on page 7

Research Update IN PSYCHIATRY

TRAUMA

Does Childhood Maltreatment Reduce Response to Antidepressant Treatment?

Brian Miller, MD, PhD, MPH. Dr. Miller, author of this educational activity, receives research support from Augusta University; the National Institute of Mental Health; the Brain and Behavior Research Foundation; and the Stanley Medical Research Institute. Relevant financial relationships listed for the author have been mitigated.

REVIEW OF: Medeiros GC et al, *J Affect Disord* 2021;291:39–45

STUDY TYPE: Longitudinal study

A history of childhood maltreatment (which includes abuse and neglect) is common in people with major depressive disorder and is associated with worse severity, chronicity, and recurrence of depression. What we don't know is whether childhood maltreatment affects antidepressant response. Some studies show it reduces response rates, while others show it does not, and this study aimed to investigate this association.

This was a secondary analysis of the COMED trial, a large (n=663) randomized trial that compared escitalopram monotherapy with two antidepressant-combination groups (escitalopram plus bupropion and venlafaxine plus mirtazapine) in major depression over 12 weeks. Patients were not receiving depression-specific psychotherapy. Most were female (68%), mean age was 43, and 50% had a history of childhood maltreatment (based on a four-item self-report questionnaire). Depressive symptoms were evaluated with the clinician-rated Quick Inventory of Depressive Symptomatology.

After 12 weeks, patients with a history of childhood maltreatment had nonsignificantly greater reduction in depressive symptoms on antidepressants compared to those with more stable upbringings (-9.6 vs -8.2, p=0.20). However, patients subject to childhood maltreatment had significantly greater total side effect burden (p=0.01) throughout the trial. Patients with and without childhood maltreatment responded similarly to the three treatment arms (p=0.30). Dropout rates were similar in patients with and without childhood maltreatment (21% vs 19%). Response rates did not differ between patients with early maltreatment (before age 7) compared to later maltreatment. (Other studies have identified maltreatment before age 7 as a major risk factor for depression.)

As a secondary analysis, the trial was not designed to test the hypothesis in question, which is the main limitation here. Also, the analysis lacked detail about the intensity or duration of trauma, and about specific antidepressant-related side effects.

CARLAT TAKE

This study offers hope that patients with a history of childhood maltreatment can still respond to antidepressants, although they may experience more side effects on these medications.

In Brief: Sexual Activity on the Decline

Alfred Kinsey caused widespread shock in 1948 when his surveys of sexual behavior revealed what was happening behind bedroom doors. This year, researchers from Kinsey's institution (Indiana University) updated his work, and this time the surprise is about what is *not* happening.

The new survey asked over 4,000 US adolescents and adults about their sexual behavior in 2009 and polled them again in 2018. Nearly all forms of sexual activity declined over the intervening decade, particularly among adolescents and young adults: penile-vaginal intercourse, oral sex, anal sex, and mutual masturbation. Only solo masturbation held steady, and only among adults (ages 18–49), three out of four of whom had masturbated alone in the past year. Adolescents (ages 14–17) reported a steep decline in solo masturbation: 61% had not masturbated in the past year in 2018, compared to 44% in 2009. The percentage of adolescents who reported no sexual activity (including no masturbation) rose from 29% to 43% among young men and from 50% to 74% among young women (Herbenick D et al, *Arch Sex Behav* 2022,51(3):1419–1433).

The decline has been documented by similar surveys in the US, UK, Australia, Germany, and Japan, and seems to have begun in the early 1990s. What's new in the current data is the drop in adolescent masturbation, suggesting that sexual desire itself may be waning. In line with that, most teens and adults who are not having sex feel no discontent about their situation, even if they had been sexually active in years past, according to a UK study (Ueda P and Mercer CH, *BMJ Open* 2019;9(10):e030708).

As to the cause of these trends, we can only speculate. Gender identities have expanded and more adolescents identify as asexual. Alcohol use is on the decline in youth and respect for sexual consent is on the rise. Young adults are less likely to marry and less likely to seek romantic relationships than they were in the past. Screen time, social media, and serotonin reuptake inhibitors have increased in parallel with these trends, as has exposure to endocrine-disrupting chemicals from pesticides, cosmetics, and processed foods.

The Kinsey Report helped normalize behaviors that were previously taboo, including masturbation, homosexuality, and extramarital sex. Therapists often quoted those surveys to reassure patients who were anxious that their sexual practices were a form of mental illness. As asexuality moves closer to the center, today's surveys may offer solace to patients who feel alone in their lack of sex. At the very least, they can help us better understand our patients.

—Chris Aiken, MD. Editor-in-Chief, The Carlat Psychiatry Report

CME Post-Test

To earn CME or CE credit, log on to www.TheCarlatReport.com to take the post-test. You will be given two attempts to pass the test. You must answer 75% of the questions correctly to earn credit. 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. Carlat CME Institute maintains responsibility for this program and its content. Carlat CME Institute designates this enduring material educational activity for a maximum of one (1) *AMA PRA Category 1 Credit*™. Physicians or psychologists should claim credit commensurate only with the extent of their participation in the activity. This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Learning Objectives are listed on page 1.

1. According to a 2015 study of lithium therapy on renal function, what doses of lithium raise the risk of renal impairment (LO #1)?
   [ ] a. High, temporary cumulative doses
   [ ] b. Low, temporary cumulative doses
   [ ] c. High, lifelong cumulative doses
   [ ] d. Low, lifelong cumulative doses

2. What benefit does liraglutide have for patients who fail to respond to metformin and topiramate (LO #2)?
   [ ] a. It is inexpensive
   [ ] b. It is associated with improvements of visceral fat
   [ ] c. It can be used for mild, moderate, and severe cases of weight gain
   [ ] d. It has no associated risks of nausea

3. In recent studies of young adults, what has been concluded about the effects of long-term cannabis use (LO #3)?
   [ ] a. Long-term use has no negative effects on cognition
   [ ] b. Long-term and short-term use have similar positive effects on cognition
   [ ] c. Long-term use is associated with the development of cognitive problems
   [ ] d. No conclusions can be drawn due to insufficient evidence and methodological limitations

4. What was the main limitation of a 2021 study that found antidepressants may cause a greater side effect burden in patients with a history of childhood maltreatment (LO #4)?
   [ ] a. The sample size was small
   [ ] b. The study was not designed to test this hypothesis
   [ ] c. Patients received depression-specific psychotherapy
   [ ] d. There was no randomization

5. Thyroid suppression by therapeutic doses of lithium affects what percentage of patients who start standard lithium doses (LO #1)?
   [ ] a. 2% [ ] b. 10% [ ] c. 35% [ ] d. 27%

Treatment of Antipsychotic-Induced Weight Gain

Continued from page 5

Antipsychotic-Induced Weight Gain Management

Medication	Starting Dose	Notes
Liraglutide	0.6 mg SC QD	• Can increase by 0.6 mg/day weekly up to max dose of 3.0 mg/day • Decreases weight and improves glucose tolerance • Retail cost $1,300/month
Metformin	500 mg BID	• Contraindicated in chronic renal disease and metabolic acidosis • Decreases weight and improves insulin resistance • Retail cost $4/month
Olanzapine-samidorphan	10/10, 15/10, or 20/10 mg/day	• Should not be started within seven days of taking a short-acting opioid or 14 days of taking a long-acting opioid • Less weight gain versus olanzapine monotherapy • No significant effects on glucose lipids • Retail cost $1,300/month
Topiramate	25 mg BID	• Can increase by 50 mg/day weekly up to max dose of 400 mg/day • Decreases weight and improves symptoms • Low-cost options (<$10/month) at goodrx.com if not covered by insurance
Additional Considerations		
Switching	Agents with a more favorable weight/metabolic profile: generic aripiprazole or ziprasidone; or brexpiprazole (Rexulti), lumateperone (Caplyta), or lurasidone (Latuda)	
Lifestyle	Exercise, nutrition, sleep hygiene, and smoking reduction/cessation	

to metformin and topiramate are the glucagon-like peptide-1 (GLP-1) receptor agonists. Liraglutide (Victoza, Saxenda), which is FDA approved in diabetes and obesity, currently has the most evidence. In a 16-week study of 103 patients treated with clozapine or olanzapine, the GLP-1 agonist liraglutide was associated with an average weight reduction of 11.7 lb versus placebo, as well as improvements in glucose tolerance, blood pressure, cholesterol, and visceral fat (Larsen JR et al, *JAMA Psychiatry* 2017;74(7):719–728). Similarly, a six-month study of 790 overweight or obese antipsychotic-treated patients found an average weight reduction of 13.2 lb with liraglutide versus placebo and reduced HbA1c (Whicher CA et al, *Diabetes Obes Metab* 2021;23(6):1262–1271).

Liraglutide requires slow titration due to risk of nausea and is administered as a subcutaneous injection (see table). It is also costly and—pending further evidence—should be reserved for severe cases.

Lifestyle modification

Regardless of the pharmacologic approach, lifestyle modification is important for every patient. I discuss physical activity, nutrition, sleep hygiene, and tobacco smoking cessation, then work with the patient to set realistic, incremental, achievable goals. If they don't exercise, a five-minute daily walk is a good starting point. Small dietary changes like cutting back on sodas, increasing fruits and vegetables, and shifting to baked instead of fried foods can also add up.

So how best to proceed?

Use the psychiatric and medical history as a "risk assessment" to guide

Continued on page 8

THE CARLAT REPORT
PSYCHIATRY
P.O. Box 626
Newburyport, MA 01950

This Issue:
College Mental Health
September 2022

Next Issue:
Depression
October/November 2022

Your subscription expires:

Renew or extend online at
www.thecarlatreport.com
or by check using the order form below.

Treatment of Antipsychotic-Induced Weight Gain

Continued from page 7

antipsychotic selection and collaborate with the patient on adjunctive treatment. Younger patients and those starting an antipsychotic for the first time are at particularly heightened risk for weight gain. In obese patients, I favor adjunctive treatments if they are clinically stable. My first-line choices for antipsychotic-induced weight gain are either metformin or topiramate. Consider metformin if there is a family history of diabetes or if using medications with greater weight gain liability, and consider topiramate if there are residual symptoms of psychosis. I typically say, "We can try metformin or topiramate, and if it's not helpful or you have side effects, we can try the other one." Lybalvi is a second-line option, as patients do not lose weight on this medication (only experience less weight gain) and there is no evidence for improvements in glucose, lipids, or symptoms.

CARLAT VERDICT

Perform a baseline "risk assessment" for antipsychotic-induced weight gain and discuss lifestyle modifications with every patient. To treat weight gain, first decide whether or not to switch agents. If using adjunctive treatments, either metformin or topiramate are good options for weight loss that may also benefit metabolic parameters (glucose/insulin, lipids) or symptoms, respectively.

To learn more and earn additional CMEs, search for "Carlat" in your favorite podcast store and subscribe to our weekly podcast.