Treating Sexual Side Effects

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

Sexual side effects on SSRIs are so common that psychiatrist David Healy once argued these drugs more reliably lower libido than treat depression. Yet the problem isn’t limited to SSRIs, and it’s not unmanageable. In this article, I’ll look at some useful strategies to manage sexual dysfunction on antidepressants, antipsychotics, and mood stabilizers.

Gather the history
Sexual dysfunction is a classic “chicken and egg” problem. It can be a symptom of mental illness or a side effect of medication. It helps to get an idea of the patient’s baseline sexual function before starting medication.

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In Summary
• Serotonergic antidepressants have the highest rates of sexual dysfunction, but antipsychotics are not far behind, particularly when they elevate prolactin.
• Phosphodiesterase inhibitors like sildenafil (Viagra) have the best evidence to treat sexual side effects on SSRIs in men as well as in women.
• Among other antidotes for sexual side effects, bupropion and buspirone have mixed evidence, and new research supports CAM therapies like saffron and SAMe.

An Antidepressant Diet
Felice Jacka, MD
Professor at Deakin University, Geelong, Victoria, Australia. Director, Food and Mood Centre. Founder and President, International Society for Nutritional Psychiatry Research (http://www.isnpr.org).

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

TCPR: A few years ago, your group conducted the first clinical trial of diet on depression. Where did you get the idea for that?
Dr. Jacka: We had a decade of observational evidence linking the quality of people’s diets to their risk for depression. Those findings were pretty consistent across countries, cultures, and age groups: A healthy diet is associated with an approximately 30% reduction in the risk for depression and a 40% improvement in cognition. That’s after controlling for education, income, other health behaviors, and body weight. What we didn’t know was whether diet could also work as an intervention for active depression, so we set out to test that in a controlled trial. Honestly, we didn’t expect to see the kind of results we did.

TCPR: What did you find?
Dr. Jacka: The effect size for this diet was large: 1.2. (Editor’s note: The effect size for antidepressants ranges from 0.3 to 0.6.) We randomly assigned people to either dietary counseling with a clinical dietitian or social support with
Treating Sexual Side Effects
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Patients rarely volunteer a sexual history, so I make a habit of asking about it. Be culturally sensitive, but direct. Try saying, “These meds may affect sexual function, so I need to check in with you on this. How often are you having sex, and what problems have you noticed?” Alternatively, if directly approaching the topic of sex feels awkward, you can rephrase it along the lines of, “Have you noticed any problems in your sexual functioning?”

One thing to watch for is a midlife decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels peak at age 16, and after that they fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido. Testosterone is the key hormone in sex drive for both men and women. For women, testosterone levels fall during menopause. For men, the levels decline in libido.

Which med is responsible?
Even when they aren’t the sole cause of sexual dysfunction, most psychiatric medications have a good chance of contributing to the problem. There are a few exceptions, which I’ve listed in the table below. The rates are highest with serotonergic antidepressants: SSRIs, SNRIs, and clomipramine. Among the SSRIs, fluvoxamine has the lowest rate; for SNRIs, it’s duloxetine; and for tricyclics, it’s desipramine and nortriptyline.

Antipsychotics are almost as guilty, with rates (40%–70%) that approach those of SSRIs (60%–80%). Mechanisms range from anticholinergic to antipodalminergic, but one that’s useful to look for is elevated prolactin. In general, the problem is worse with prolactin-raising antipsychotics like paliperdone, risperidone, and haloperidol (La Torre A et al, Pharmacopsych 2013;46(6):201–208).

Hyperprolactinemia also has medical risks, such as osteopenia and galactorrhea, so a blood level is worth checking. When it’s high, I’ll switch to a prolactin-sparing antipsychotic like aripiprazole, ziprasidone, or olanzapine, or add an antidote to lower prolactin. Amantadine is my first choice (100 mg BID). Theoretically, psychosis is a potential side effect with amantadine, but I have not seen this in practice, and amantadine has the additional benefit of aiding weight loss on atypicals (Graham K et al, Am J Psych 2005, 162(9):1744–1746).

Data are scarce with mood stabilizers. Most mood stabilizers cause some sexual side effects, with the possible exception of lamotrigine. For anticonvulsants, reduction of free testosterone is a possible mechanism. Anticonvulsants that induce hepatic metabolism also increase the production of sex hormone–binding globulin (SHBG), and this SHBG then binds up free testosterone, effectively lowering its levels. An interesting theory, but does it fit the data? It turns out that enzyme-inducing anticonvulsants like carbamazepine and oxcarbazepine do have higher rates of sexual side effects than their non-enzyme-inducing cousins like valproate (La Torre A et al, Pharmacopsych 2014;47(1):1–6).

Management
Once I have an idea of the cause, I’ll move on to management. Many of the strategies are similar regardless of which medication is responsible:

• Watchful waiting. This works in 10%–20% of patients, but it can take several months.
• Lower the dose. Sexual side effects can sometimes be dose dependent.
• Change the timing. Ask, “What time of day is your sex drive the best?” Then, align the dose so the lowest blood level coincides with the optimal time for intercourse. Scheduling sex at the time of peak performance can also work, though at the cost of spontaneity.
• Take drug holidays. For example,

<table>
<thead>
<tr>
<th>Medications With a Low Risk of Sexual Side Effects</th>
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<tbody>
<tr>
<td><strong>Antidepressants</strong></td>
</tr>
<tr>
<td>Best: Bupropion, nefazodone, trazodone, vortioxetine</td>
</tr>
<tr>
<td>Second best: Mirtazapine, vilazodone, MAOIs</td>
</tr>
<tr>
<td>Off label: Pramipexole (1–2 mg/night), SAmE (800–1600 mg/day)</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
</tr>
<tr>
<td>Best: Aripiprazole</td>
</tr>
<tr>
<td>Second best: Ziprasidone, quetiapine</td>
</tr>
<tr>
<td><strong>Mood stabilizers</strong></td>
</tr>
<tr>
<td>Lamotrigine</td>
</tr>
<tr>
<td><strong>Anxiolytics</strong></td>
</tr>
<tr>
<td>Buspirone</td>
</tr>
</tbody>
</table>

Source: La Torre A et al, Pharmacopsych 2013;46(5):191–199
skip the dose on Friday or Saturday and resume it on Sunday or Monday. As long as there’s not a strong discontinuation syndrome or a long half-life, this strategy can work well. It’s not without risks, however, and I don’t use it when psychosis, mania, or severe depression are potential consequences.

**Switch treatments.** Treatments with a lower rate of sexual side effects, including psychotherapy, may be helpful.

### Antidotes

When it comes to antidotes, many have been tested, but few have passed muster in a randomized controlled trial. Most of those were tested in SSRI-induced sexual dysfunction (see the table on this page). Among them, phosphodiesterase inhibitors (PDEs) like sildenafil (Viagra) have the best support. Though usually thought of for erectile dysfunction, they actually increase both penile and clitoral blood flow and can work in both genders. In women on SSRIs, PDEs improved orgasmic function in a well-designed, industry-funded study. The benefits of PDEs may also derive from CNS effects by enhancing dopaminergic activity in areas involved in sexual arousal, like the nucleus accumbens (Kyratsas C et al, *J Sex Med* 2013;10(3):719–729).

Although sildenafil is the best studied of the PDEs, tadalafil (Cialis) is often my first choice. Why? Its effects last up to 36 hours, allowing for a needed dose of spontaneity. Now that all 3 of the PDEs have gone generic, price doesn’t have to be a decision-maker, and tadalafil can be purchased at the pharmacy for as low as $1.00 a pill (goodrx.com). When patients pay out of pocket, I write for the maximum dose and have them break it up.

Among complementary and alternative (CAM) therapies, saffron and SAMe stand out. They are relatively safe, relieve sexual side effects on SSRIs, and have antidepressant properties of their own. Both improve erectile dysfunction in men, while saffron also helps arousal, lubrication, and dyspareunia in women (Kashani L et al, *Hum Psychopharmacol* 2013;28(1):54–60). Maca root, which has testosterone-like effects, is particularly effective in postmenopausal women (Dording CM et al, *Evid Based Complement Alternat Med* 2015;2015:949036). The “Antidotes for Sexual Dysfunction on Serotonergic Antidepressants” table above lists products certified by Consumer Labs—a designation worth paying attention to with maca root, which has had problems with lead-contaminated products.

One medication I haven’t mentioned is mirtazapine. Unlike the antidotes in the table, its support is limited to open-label trials, but I’ve found it (at 15–45 mg/night) helpful in patients who can’t achieve orgasm on an SSRI. Mirtazapine antagonizes the descending 5-HT2 serotonergic fibers that are thought responsible for SSRI-induced anorgasmia (Atmaca M et al, *Psychiatry Investig* 2011;8(1):55–57).

Antidotes are understudied in psychosis and bipolar disorder. For lithium-induced erectile dysfunction, NSAIDs can help through effects on nitric oxide. Most NSAIDs interact with lithium, but aspirin does not, and it did indeed improve this side effect in a 6-week randomized placebo-controlled trial of men (aspirin 80 mg TID) (Saroukhani S et al, *Bipolar Disord* 2013;15(6):650–656).

### Antidotes for Sexual Dysfunction on Serotonergic Antidepressants

<table>
<thead>
<tr>
<th>Antidote</th>
<th>Dose</th>
<th>Gender</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tadalafil (Cialis)</td>
<td>Tadalafil 5–20 mg, 30 min to 36 hrs before sex</td>
<td>F &amp; M</td>
<td>Avoid in patients who take nitrates or cannot tolerate hypotension</td>
</tr>
<tr>
<td>Sildenafil (Viagra)</td>
<td>Sildenafil 50–100 mg, 30 min to 4 hrs before sex</td>
<td>F &amp; M</td>
<td></td>
</tr>
<tr>
<td>Bupropion (Wellbutrin)</td>
<td>75–300 mg daily</td>
<td>F &gt; M</td>
<td>Benefits are modest, studies are mixed</td>
</tr>
<tr>
<td>Buspirone (Buspar)</td>
<td>15–60 mg divided BID to TID</td>
<td>F &gt; M</td>
<td>Good products: Swanson Superior Herbs, Elixir, and BCN Saffron Ultra ($10–20/month)</td>
</tr>
<tr>
<td>Saffron</td>
<td>15 mg BID</td>
<td>F &amp; M</td>
<td>Good products: Nutrigold Maca Gold capsules, Maca Magic powder, Gaia Herbs Gelatinized Maca powder ($3–10/month)</td>
</tr>
<tr>
<td>SAMe</td>
<td>400 mg BID</td>
<td>M</td>
<td>Good products: Doctor’s Best, Swanson High-Potency, VitaCost ($30–50/month)</td>
</tr>
<tr>
<td>Maca root</td>
<td>3,000 mg daily</td>
<td>F &gt; M</td>
<td></td>
</tr>
</tbody>
</table>

All treatments above are supported by at least one randomized clinical trial.

**Correction:** In the QA interview covering choline supplementation in the March 2019 issue, Dr. Freedman reported that the minimum daily recommended intake of choline is 650 mg; it is actually 550 mg by current FDA recommendations. We apologize for the error.
what we call a befriending protocol, which we already know is helpful in depression. Both groups had the same face-to-face time in sessions, and after 3 months the depressive symptoms in the dietary group were significantly improved, more so than in the social support group (Jacka FN et al, *BMC Med* 2017;15(1):23). This was followed by a similar study that also found a large effect size for diet as a treatment for depression. This second study taught the diet in a group format and compared it to a social support group where people got together for activities like playing games and discussing books (Parletta N et al, *Nutr Neurosci* 2017:1–14; doi:10.1080/1028415X.2017.1411320). Now, this is only 2 studies, with a total of 219 subjects, and it will take more research to see if that large effect size holds up.

**TCPR: Tell us about the diet.**

**Dr. Jacka:** It's a modified version of the Mediterranean diet. No foods are prohibited, and there is no calorie counting. Patients were encouraged to eat more foods that we know are healthy for the brain: whole grains, beans, nuts and seeds, fish, extra virgin olive oil, and of course fruits and vegetables. At the same time, they reduced their intake of things that are particularly noxious to brain health: ultra-processed foods, fried or fast foods, sugary drinks and desserts, and refined flours like white bread. They were supported to make these changes in a way that was achievable, that was in line with their goals and wasn’t too costly or time-consuming. In fact, the patients in the dietary group spent less on food even as they ate more healthy meals. Of course, you can spend a lot at Whole Foods, but a healthy diet can also be achieved with beans, canned fish, and seasonal or frozen fruits and vegetables (See “The MediMod Diet” table on page 5).

**TCPR: How sure are we that the improvement was due to the food itself?**

**Dr. Jacka:** That's a good question. We controlled for other changes that might explain these results, like weight loss, exercise, and sense of self-efficacy. We also measured how well people followed the diet. The more they improved their diet, the more their depression improved, which suggests a real effect of the food.

**TCPR: What were some of the weaknesses in the study?**

**Ask the Editor**

**Can Antipsychotics Enhance Cognition?**

**Dear Dr. Aiken:** The article on Trintellix and cognition (TCPR, February 2019) reminded me of another industry claim: that atypical antipsychotics improve cognition. Any truth to that one?

**Dr. Aiken:** I’ve also heard this whispering campaign, and there is reason to doubt it. The logic goes like this: Unlike the typical antipsychotics, atypicals improve both cognitive and psychotic symptoms of schizophrenia, so they must have pro-cognitive effects of their own that can be harnessed in mood disorders, ADHD, and even dementia. The problem is that the data show the opposite.

Atypicals tend to worsen cognition in mood disorders, and the problem is more pronounced as the dose goes up. Most of this research was done in bipolar disorder, where atypicals came out behind on cognitive measures in head-to-head comparisons with anticonvulsants and lithium (Daglas R et al, *Eur Psych* 2016;31:20–28; Cankorur V et al, *Noro Psikiyat Ars* 2017;54:244–250). Lurasidone (Latuda) may be an exception. This atypical actually improved cognition independently of mood in stable bipolar I patients with cognitive problems in a 6-week, randomized, open-label, industry-funded trial (dose 20–80 mg/day) (Yatham L et al, *Lancet Psych* 2017;4(5):208–217).

One antipsychotic, aripiprazole (Abilify), is rumored to have specific benefits in ADHD through its unique partial dopamine agonism. This theory has been discredited, but not completely quieted, by two negative randomized controlled trials (Ghanizadeh A et al, *Neurosciences* 2013;18(4):323–329).

The cognitive benefits of atypicals don't translate from schizophrenia to other disorders, but how well do they hold up in schizophrenia? Cognition definitely improves when schizophrenia is treated with atypicals, but that improvement appears due to the resolution of psychosis rather than direct cognitive effects of the atypicals. Early studies did find superior cognitive outcomes when atypicals were compared to typical antipsychotics, but that research was stacked in favor of the newer drugs (for example, the typical antipsychotics were dosed higher and often used with anticholinergics). In the larger, NIH-funded CATIE trial, cognition improved equally well with either class.

On the other hand, there are concerns that atypicals may impair cognition over the long term, such as through their effects on metabolism, frontal lobe functioning, or cholinergic transmission (MacKenzie NE et al, *Front Psych* 2018;9:622).

There are many reasons to use atypicals, but cognition is not one of them. When a patient complains of feeling cloudy headed on an atypical antipsychotic, consider a lower dose, particularly if the patient has a mood disorder.
Dr. Jacka: We weren't able to blind people to the interventions, which is true of both studies. So it's possible that the subjects expected the diet to work, which may have exaggerated their response to it. Both studies were also relatively small, but they were backed up by controlled trials of dietary interventions in non-psychiatric patients. These include studies in obesity, diabetes, and normal subjects who had subsyndromal depressive symptoms. This body of evidence is much larger—45,000 subjects across 15 trials—and it confirmed our finding that depressive symptoms improve with a change to a healthy diet (Firth J et al, *Psychosom Med* 2019;81(3):265–280).

**TCPR: How long does the diet take to work?**

Dr. Jacka: In the 2 depression studies, we measured outcomes at 3 months. It may work faster than that, but we don't know. In some of the non-psychiatric studies, they saw differences in the gut microbiome and markers of gut health as early as 2–3 weeks, which is likely to be of relevance to mental health.

**TCPR: What do we know about the effects of diet on the brain?**

Dr. Jacka: We don't know exactly how the diet works, but there are several possibilities. Healthy diets are anti-inflammatory, and inflammation is both a cause and consequence of depression. These foods are also rich in nutrients that are essential to brain function, like magnesium, folate, and B-vitamins. They also improve brain plasticity. For example, brain-derived neuroprotective factor (BDNF) levels rise with a healthy diet, an effect that we also see with antidepressants and aerobic exercise.

Diet has well-documented effects on the hippocampus, which is involved in memory and depression. High-fat and high-sugar diets can impair hippocampal-dependent memory in as little as 5 days. The hippocampus shrinks with age, but according to our human study, as much as 60% of that atrophy may be related to the quality of one's diet (Jacka FN et al, *Psychosom Med* 2019;81(3):265–280).

**TCPR: Are there risks with the Mediterranean diet?**

Dr. Jacka: No. The Mediterranean diet is consistently associated with reduced risks of stroke, cardiovascular disease, diabetes, Alzheimer's disease, and all-cause mortality.

**TCPR: How would you introduce this diet to a patient with depression?**

Dr. Jacka: Start with simple questions. "What do you eat? What do you have for breakfast? For lunch? What are your snacks? What do you like? What do you not like?" And then you start to swap out. So if people eat processed cereal for breakfast, instead have oats, homemade muesli, or Greek yogurt with berries and nuts. Swap white bread for 100% whole-grain bread. Instead of chips, try snacking on nuts, hummus and veggies, or home-cooked popcorn, which is a whole grain.

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**The MediMod Diet**

<table>
<thead>
<tr>
<th>Food</th>
<th>Recommended servings</th>
<th>One serving equivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetables</td>
<td>6 servings/day.</td>
<td>Leafy vegetables: ½ cup cooked or 1 cup raw; other vegetables: ½ cup raw or cooked.</td>
</tr>
<tr>
<td></td>
<td>Include green leafy vegetables or tomatoes in at least one of those servings. Mushrooms count, but minimize potatoes to one serving a day unless it's a sweet potato.</td>
<td></td>
</tr>
<tr>
<td>Fruit</td>
<td>3 servings/day.</td>
<td>½ cup fresh, frozen, canned, or cooked fruit; 1½ tablespoons dried fruit. Juice counts but should be limited to ½ cup per day because of the sugar content.</td>
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<tr>
<td></td>
<td>Include berries in at least one of those servings.</td>
<td></td>
</tr>
<tr>
<td>Nuts, seeds, olives</td>
<td>1 serving/day.</td>
<td>1 ounce/day of nuts, seeds (about ¼ cup), and/or 3 ounces of olives (about ½ cup).</td>
</tr>
<tr>
<td>100% whole grains</td>
<td>5–8 servings/day (eat closer to 8 if you're physically active).</td>
<td>1 slice bread; ½ cup cooked grains, like brown rice or whole wheat pasta; ¼ cup oats or muesli; ½ cup breakfast cereal; 2–3 crisp bread crackers.</td>
</tr>
<tr>
<td>Fish</td>
<td>At least 2 servings/week. At least one of those should be an oily fish like salmon.</td>
<td>3 ounces cooked.</td>
</tr>
<tr>
<td>Beans</td>
<td>3–4 servings/week.</td>
<td>½ cup beans, or ½ cup hummus or tofu.</td>
</tr>
<tr>
<td>Extra virgin olive oil</td>
<td>3 tablespoons/day.</td>
<td></td>
</tr>
<tr>
<td>Red meat</td>
<td>3–4 servings/week.</td>
<td>3–4 ounces cooked. Use lean red meats.</td>
</tr>
<tr>
<td>Poultry</td>
<td>2–3 servings/week.</td>
<td>3 ounces cooked (= one breast or a leg + thigh).</td>
</tr>
<tr>
<td>Dairy</td>
<td>3 servings/day of milk, cheese, or yogurt.</td>
<td>1 metric cup milk or yogurt. For cheese: 1.5 ounces hard cheese or feta; 4–5 ounces soft cheese like ricotta or cream cheese.</td>
</tr>
<tr>
<td>Eggs</td>
<td>6 eggs/week.</td>
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<tr>
<td>Eat less of...</td>
<td></td>
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<tr>
<td>Fried, fast, sweet,</td>
<td>Maximum of 3 servings per week. A serving is 120 calories of: Sweets, sodas, snacks, and white bread. Fast, processed, or fried foods. Beef jerky, bacon, and deli meats.</td>
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<tr>
<td>processed foods</td>
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<tr>
<td>Alcohol</td>
<td>Maximum 1.5 standard drinks/day. Red wine is preferred. 1.5 standard drinks = 6.8 ounces wine, 2 bottles beer (1 bottle if it's high gravity), 2 ounces spirits, or 5 ounces sherry or port.</td>
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</tbody>
</table>

**DEMENTIA**

**Antidepressants Don’t Raise Depression Risk, With One Exception**


**TYPE OF STUDY:** Prospective cohort study

Depression is a risk factor for dementia, but can antidepressants change that risk? Some, like paroxetine (Paxil), have anticholinergic properties that can impair cognition. This study looked at what that means for the risk of dementia.

This was a prospective cohort study of 3,049 patients without dementia in the Kaiser Permanente Washington system. All subjects were over 65 (average age 75); the majority were white, and 60% were female. Patients were screened for dementia at baseline and evaluated with the Cognitive Abilities Screening Instrument every 2 years. Average follow-up was 8 years. The outcome—a diagnosis of dementia—was assessed by clinical evaluation, objective testing, and multidisciplinary conferences.

Half of the patients filled an antidepressant prescription, as assessed by the system’s pharmacy database. By the end of the study, 25% had developed dementia, the majority of whom (85%) were thought to have Alzheimer’s disease. Nonparoxetine SSRIs and tricyclics did not increase the dementia risk. The serotonin antagonist and reuptake inhibitors (trazodone and nefazodone) were associated with a lower risk of dementia, but this may have been due to the tendency to prescribe trazodone to non-depressed patients with insomnia.

The big story here, though, was paroxetine. It was associated with a higher risk of dementia in a non-dose-dependent manner (hazard ratio 1.7–2.1). This association held up after controlling for other factors such as anxiety, insomnia, and cerebrovascular disease.

This is not the first study to look at the association between antidepressants and dementia, but it is one of only 2 studies that has controlled for depression, which itself is a risk factor. The other, a case-control study comparing anticholinergic drugs in 40,000 patients, also implicated paroxetine, as well as the tricyclic amitriptyline (Richardson K et al, *BMJ* 2018;361:k1315).

**TCPR’S TAKE**

Anticholinergic antidepressants can cause a number of problems in the elderly, including urinary retention, constipation, temperature imbalance, confusion, blurry vision, and tachycardia. Dementia may be added to that list, at least with paroxetine and possibly the tricyclics. However, more data are needed. As for other antidepressants, it was refreshing to learn they didn’t increase dementia risk.

—Rehan Aziz, MD. Dr. Aziz has disclosed that he has no relevant financial or other interests in any commercial companies pertaining to this educational activity.

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**Expert Interview**

Continued from page 5

Swap sodas for sparkling water or unsweetened tea. Aim for diversity, particularly with fruits and vegetables. The more diverse the plant foods, the more diverse your gut microbiome. And try not to peel the skin. The skin has lots of fiber, antioxidants, and healthy bacteria in it. Diversity is also important with beans, nuts, seeds, and whole grains. Next is oily fish, which includes salmon but also sardines, mussels, tuna, and mackerel. Swap oil and butter out for extra virgin olive oil.

**TCPR: Why not regular olive oil?**

**Dr. Jacka:** Extra virgin olive oil has a far higher antioxidant count. There's a myth that you can't cook with extra virgin olive oil, but the antioxidants counteract the detrimental effects of heat so it doesn't produce toxic compounds even at high temperatures.

**TCPR: Your study recommended 100% whole-grain breads. How do you find those?**

**Dr. Jacka:** Whole grains are the natural form of the grain before it is “refined” and stripped of its nutrients. Whole wheat is the most common, but variety is also important, and there's also buckwheat, oat, barley, millet, freekeh, and rye. For rice, brown or black rice is the whole form. Couscous and quinoa also count. For pasta, look for 100% whole wheat on the label. For breads, look for the word “whole” on the ingredient panel or “100% whole grain” on the label. It's not enough to say “multigrain” or “made with whole grains”; that often just means the manufacturer sprinkled a few in. With commercially baked breads, look for options that don't have a lot of salt and sugar or chemical ingredients. Sourdough bread is also a good option.

**TCPR: What is sourdough?**

**Dr. Jacka:** Sourdough is made from a fermented starter, similar to yogurt. These breads are better for health and easier to digest.

**TCPR: How do fermented foods improve health?**

**Dr. Jacka:** Fermentation is how people preserved foods before they invented fridges. Fermented foods include good-quality, non-processed cheeses; quality yogurts like Greek and Icelandic without a lot of sugar or flavorings; kefir, kombucha, kimchi, tempeh, miso, soy sauce, and sauerkraut. Fermented foods have *prebiotics*, which is the food that the healthy bacteria like to eat. They have *probiotics*, which are the healthy bacteria that promote diversity of the gut. They also have biogeneetics, which are metabolites that are produced by the bacteria. These include short-chain fatty acids, long-chain fatty acids, and neurotransmitters that affect physiological processes throughout the body.

**TCPR: Why is red meat an important part of this diet?**

**Dr. Jacka:** We recommended 3–4 servings of lean (grass-fed) red meat a week based on a study we did in 2012. We found that women who consumed lower or higher amounts of red meat had double the risk of depression.
CME Post-Test

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Below are the questions for this month's CME/CE post-test. This page is intended as a study guide. Please complete the test online at www.TheCarlatReport.com. Note: Learning Objectives (LO) are listed on page 1.

1. Which of the following SSRIs is least likely to cause sexual side effects? (LO #1)
   - [ ] a. Citalopram
   - [ ] b. Paroxetine
   - [ ] c. Fluvoxamine
   - [ ] d. Fluoxetine

2. One characteristic of the MediMod diet includes: (LO #2)
   - [ ] a. Eating less than 50 grams of total carbs per day
   - [ ] b. Consuming no more than 2000 calories per day
   - [ ] c. Consuming a maximum of 3 servings per week of processed or sugary foods
   - [ ] d. Limiting alcohol to 1 drink per week of beer, wine, or spirits

3. According to a 2018 study, subjects over the age of 65 taking paroxetine had a similar increased risk of developing dementia as those taking other SSRIs or tricyclics. (LO #3)
   - [ ] a. True
   - [ ] b. False

4. A 55-year-old woman is experiencing sexual dysfunction on sertraline and would like an antidote that can be taken as needed and will last for the whole day so she can have sex spontaneously. Which is the best choice? (LO #1)
   - [ ] a. Buspirone
   - [ ] b. Tadalafil
   - [ ] c. Sildenafil
   - [ ] d. Bupropion

5. Prolactin-raising antipsychotics, such as paliperidone or risperidone, are less likely to cause sexual side effects than other antipsychotics. (LO #1)
   - [ ] a. True
   - [ ] b. False

Expert Interview

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and anxiety, and other research has backed that up. Grass-fed beef is important because it has a healthier lipid profile. It's also best to avoid processed meats like sausages, deli meats, hot dogs, and pepperoni—these are discouraged in the diet.

TCPR: What about nut butters: peanut butter and almond butter?
Dr. Jacka: Well, as long as they don't have huge amounts of added salt and sugar, they are wonderful.

TCPR: The diet discourages fried, fast, sugary, and ultraprocessed foods. How are they harmful to the brain?
Dr. Jacka: There are so many ways! Based on animal and human research, these types of foods seem to impair brain plasticity and cause weight gain and inflammation. Chronic inflammation raises cytokines that increase the risk of depression as well as a host of physical illnesses. Poor diet, obesity, low vitamin D, insufficient physical activity, smoking, insomnia, and stress are all pro-inflammatory, and they all contribute to depression.

TCPR: How can a patient identify processed foods in the grocery store?
Dr. Jacka: If it's got a long list of ingredients, especially one that contains a lot of chemical names you don't recognize, stay away. Likewise, avoid it if it comes in a package, unless it is a single-item thing like canned tomatoes or frozen vegetables. Shop from around the edge of the supermarket, not from the center.

TCPR: Are there other diets that are good for depression?
Dr. Jacka: We used the Mediterranean diet because that's where the weight of evidence is—both for physical and mental health. But there are other diets that seem to reduce the risk of depression, like Norwegian and Japanese diets. In one study of 90,000 Japanese adults, those following a healthy Japanese diet were half as likely to commit suicide over 10 years.

TCPR: What about a ketogenic diet?
Dr. Jacka: The ketogenic diet has good evidence in epilepsy and has been used since the 1920s...
for that indication. There is some emerging evidence that it might be helpful in Alzheimer's disease, and evidence suggests it may improve psychotic symptoms in animal models of schizophrenia. However, this diet is high in fats and animal products and low in dietary fiber, which is not as sound for overall health as the Mediterranean diet.

**TCPR: And gluten-free diets?**

**Dr. Jacka:** Gluten is a problem for a small number of people with celiac disease and possibly irritable bowel syndrome. In those populations, gluten consumption may raise depressive symptoms, but the effect is small and the studies sparse. People with celiac disease can still follow the Mediterranean diet. They'd just need to avoid grains with gluten in them, like wheat, rye, and barley.

**TCPR: And what about dark chocolate?**

**Dr. Jacka:** Yum. Dark chocolate has a lot of polyphenols, which are antioxidants that have brain-protective effects. We're also learning that polyphenols can protect against weight gain through interactions with the gut microbiome. Polyphenols are also found in berries, red wine, and green tea. So in small amounts, like 1-3 ounces a day, dark chocolate is really good for you.

**TCPR: Thank you for your time, Dr. Jacka.**

*Editor’s note: See [http://www.thecarlatreport.com/nutrition for a copy of the cookbook and patient handouts used in the diet.](http://www.thecarlatreport.com/nutrition)*

For further reading, see Dr. Jacka’s book: *Brain Changer: The Good Mental Health Diet* (Macmillan Australia, 2019).