Letters to the Editor

Weight Gain and Antipsychotic Medications

Sir: Your recent publication (*JCP Visuals*, January 1999[1]) unfairly characterizes some atypical antipsychotics as more likely to produce weight gain than risperidone.

Weight gain is a side effect of the atypicals, but our work with olanzapine, clozapine, and risperidone demonstrates that a patient's diet is a better predictor of weight gain than a physician's selection of a particular atypical antipsychotic medication.

Contrary to the view expressed in *JCP Visuals*—that weight gain is unmanageable—our work tells quite the opposite story. With nutritional counseling and dietary changes, patients in our study who gained weight were able to shed that weight and keep it off.[2] This was true for each drug and contradicts *JCP Visuals*, which infers that once weight is added (my receptors made me eat it!), it never comes off. Having followed the individuals in our study for 2 years, we conclude that while symptoms and medications can complicate the process of weight management, the critical variables are more likely to be healthy eating habits and dietary education.

Interestingly, prior to starting atypical medications in our study, patients who were apathetic, with little or no motivation to attend programs or work outside the residence, gained the most weight. We attribute the atypicals' efficacy in treating negative symptoms to successful weight management in these patients.

As evidence continues to mount that atypicals can lead to higher productivity[3] and greater self-sufficiency, we regard the *JCP Visuals* publication on weight gain to be misleading and an impediment to greater prescription of these newer agents.

References

1. Masand PS, ed. Weight gain and antipsychotic medications. J Clin Psychiatry JCP Visuals; January 1999
2. Emanuel M, Dalheim L, Aquila R, et al. Weight gain and atypical antipsychotics. Presented at the 38th annual meeting of the New Clinical Drug Evaluation Unit; June 10–11, 1998; Boca Raton, Fla
3. Tollefson GD, Beasley CM Jr, Tran PV, et al. Olanzapine versus haloperidol in the treatment of schizophrenia and schizoaffective and schizophreniform disorders: results of an international collaborative trial. Am J Psychiatry 1997;154:457–465

Ralph Aquila, M.D.
Marianne Emanuel, R.N.
New York, New York

Dr. Masand Replies

Sir: First, there is no question that some antipsychotic agents are associated with greater weight gain than other agents. For example, in the Allison et al. meta-analysis[1] of data from 73 trials, mean weight increases after 10 weeks of treatment were as follows: 9.8 lb (4.5 kg) with clozapine, 9.1 lb (4.1 kg) with olanzapine, 4.6 lb (2.1 kg) with risperidone, 2.3 lb (1.0 kg) with haloperidol, and 1.9 lb (0.9 kg) with ziprasidone. In 1997, a researcher from Eli Lilly reported that the mean increase in weight after 1 year in patients receiving 15 ± 2.5 mg/day of olanzapine was 26 lb (11.8 kg).[2] It is not only the atypical agents that differ in their propensity to result in weight changes. In 1979, Doss[3] reported that, in 78 randomly assigned patients, weight changes after 36 weeks of treatment were +13.2 lb (+6.0 kg) with thiothixene, +8.8 lb (+4.0 kg) with fluphenazine, +6.5 lb (+3.0 kg) with haloperidol, –3.4 lb (–1.5 kg) with thioridazine, and –9.1 lb (–4.1 kg) with molindone.

Second, there is no question that weight gain is associated with increased morbidity and mortality. The following is from the recent National Institutes of Health (NIH) *Evidence Report*[4(p12)]: "Higher morbidity in association with overweight and obesity has been observed for hypertension, type 2 diabetes, coronary heart disease (CHD), stroke, gallbladder disease, osteoarthritis, sleep apnea and respiratory problems, and some types of cancer." A possible link between diabetes and exposure to antipsychotics has recently been reported.[5] Among 396 outpatients treated at the Pittsburgh Schizophrenia Treatment and Research Center, type 2 diabetes was diagnosed in 15.5% of patients treated with clozapine, 11.0% of patients treated with olanzapine, 6.6% of patients treated with haloperidol, 6.0% of patients treated with risperidone, and 4.5% of patients treated with fluphenazine.

The same NIH report[4] describes the enormous difficulties people have in losing weight. Even cognitively sound, nonpsychotic people find it a problem. How much more difficult it must be for cognitively impaired patients with schizophrenia who see their lifesaving medication making them obese.

In my clinical experience, and in that of many colleagues with whom I have discussed this, patients treated with clozapine and olanzapine gain more weight than patients receiving other antipsychotic agents. Moreover, patients who put on weight with olanzapine and who are then switched to another antipsychotic find it difficult to lose the weight they have gained.

I agree with Dr. Aquila and Ms. Emanuel that the keys to weight stabilization and weight loss (for everyone) include healthy eating habits and dietary education. But we also need to recognize that, if a medication is an important contributor to the weight gain experienced by one of our patients, we should consider switching the patient to an effective medication that is not so strongly associated with gaining weight.

References

1. Allison DB, Mentore JL, Heo M, et al. Weight gain associated with conventional and newer antipsychotics. Eur Neuropsychopharmacol 1998;8(suppl 2):S216–S217
2. Beasley CM. The safety of olanzapine. J Clin Psychiatry Monogr 1997;15(2):19–21
3. Doss FW. The effect of antipsychotic drugs on body weight: a retrospective review. J Clin Psychiatry 1979;40:528–530
4. National Institutes of Health. National Heart, Lung, and Blood Institute. Clinical Guidelines on the Identification, Evaluation, and Treat-

ment of Overweight and Obesity in Adults: The Evidence Report. Bethesda, Md: NHLBI; 1998
5. Zoler ML. Antipsychotics linked to weight gain, diabetes. Clin Psychiatr News 1999;27:20

Prakash S. Masand, M.D.
Syracuse, New York

Ileus as a Possible Result of Bupropion in an Elderly Woman

Sir: Although constipation has been reported as a side effect associated with bupropion, no cases of bupropion-associated ileus have been cited. The following case report describes an elderly patient in whom the addition of bupropion to lithium appeared to induce ileus.

Case report. Ms. A, an 80-year-old woman with a history of recurrent major depression, had an episode of hypomania while off treatment with antidepressants. From further history obtained, this hypomania appeared recurrent. She was placed on treatment with lithium, which was titrated to 450 mg daily (serum level = 0.67 mEq/L). Ms. A developed polyuria, and the dosage was reduced to 300 mg/day (serum level = 0.4 mEq/L). Concurrently, she developed depressive symptoms. Bupropion was added and titrated over 3 weeks to a maximum of 150 mg daily (in divided dosage). After 1 week at this dose, Ms. A complained of constipation, contrasting with her usual regularity. It was recommended that she drink fluids, consume dietary fiber, and take psyllium preparations as needed. Several days later, she contacted her psychiatrist, now complaining of nausea, vomiting, and abdominal pain. Bupropion and lithium were discontinued, and she was sent to the emergency room. There, her serum lithium level was measured at 0.52 mEq/L (< 12 hours after last dose). Ms. A was noted to be impacted, and she was manually disimpacted and discharged.

Although Ms. A remained off treatment with psychotropic medications, the next day she continued to experience abdominal discomfort, nausea, and vomiting. She was then admitted to the medical service. The initial differential diagnosis included adynamic ileus versus a mechanical obstruction (given a history of a sigmoid colectomy for diverticulitis 8 years earlier). Medications upon admission included diltiazem, ranitidine, aspirin, and calcium. No metabolic-electrolyte abnormalities were found except elevated serum urea nitrogen (42 mg/dL) and serum creatinine (1.1 mg/dL) levels thought secondary to vomiting and poor oral intake prior to admission. She was kept n.p.o. and given i.v. hydration and magnesium hydroxide and psyllium preparations. The radiologist felt that the series of abdominal x-rays obtained during Ms. A's stay were consistent with acute paralytic ileus. After 5 days, she resumed normal bowel movements, tolerated diet advancement, and was discharged. After discharge, she underwent outpatient colonoscopy, which yielded no significant pathology. Subsequently, she was placed on treatment with valproic acid as a mood stabilizer. In the 6 months after discharge, she has maintained bowel regularity.

To our knowledge, this is the first report of ileus possibly associated with bupropion. Ileus can occur with tricyclic antidepressants,[1,2] presumably secondary to anticholinergic effects. Bupropion, while low in anticholinergic effects, is commonly associated with constipation.[2] Although the ileus reported here may have been due to a bupropion-lithium interaction, there was no significant change in serum lithium level with combined treatment.[3] It is also possible that the patient may have been more vulnerable to this side effect given her history of colon surgery. The patient was also taking diltiazem (stopped during the hospital stay) and ranitidine (which was continued) at the time of admission, both of which can cause constipation.[4] However, she had taken these for 4 years without difficulties. Thus, the recent addition of bupropion to her regimen was felt to be a more proximate, likely cause of the ileus. Even though bupropion is generally a well-tolerated antidepressant in the elderly, clinicians should be aware of the possibility of the development of ileus in patients treated with this drug.

References

1. Milner G, Hills NF. Adynamic ileus and nortriptyline [letter]. BMJ 1966;5500:1421
2. Rudorfer MV, Manji HK, Potter WZ. Comparative tolerability profiles of the newer versus older antidepressants. Drug Saf 1994;10: 18–46
3. Goodnick PJ. Pharmacokinetics of second generation antidepressants: bupropion. Psychopharmacol Bull 1991;27:513–519
4. Physicians' Desk Reference. Montvale, NJ: Medical Economics; 1997

Helen C. Kales, M.D.
Alan M. Mellow, M.D., Ph.D.
Ann Arbor, Michigan

Methamphetamine-Associated Obsessional Symptoms and Effective Risperidone Treatment: A Case Report

Sir: Methamphetamine psychosis is induced by long-term use of methamphetamine and easily reactivated by reuse of the drug or under stress.[1] For the last 2 decades, anxiety disorder–like symptoms have emerged as one of methamphetamine-associated mental problems.[2] However, treatment strategies for these symptoms have yet to be established. We describe a patient with a history of methamphetamine psychosis, who, after a drug-free interval of 1½ years, developed persistent obsessive-compulsive symptoms without a recurrence of psychosis. These obsessive-compulsive disorder (OCD)–like symptoms responded well to risperidone, a serotonin-dopamine antagonist.

Case report. Mr. A, a 24-year-old single man, started abuse of methamphetamine by intravenous injection twice or more a week at the age of 19. About 1½ years later, psychotic symptoms, such as auditory hallucinations and persecutive delusions, emerged. He also experienced the intrusion of odd ideas into his mind, for instance, "this tea consists of urine," or "this meat is human flesh." He had no insight into the symptoms. He began treatment with neuroleptics (haloperidol and levomepromazine); after 4 months of treatment, the symptoms disappeared. Thereafter, he stopped use of methamphetamine.

One and a half years later, the ideas described above suddenly recurred without any symptoms of psychosis, and Mr. A became obsessed with the ideas. On this recurrent occasion, he had insight and described them as absurd ideas. He became anxious lest the ideas continue for life. Mr. A then visited a local hospital and began treatment with bromperidol, one of the butyrophenones, at 9 mg/day. He received this treatment for 6 months; however, the odd ideas persisted.

Mr. A was then referred and admitted to our hospital at age 24. He was in an anxious-restless state with odd thoughts frequently intruding in his mind and met criteria for OCD accord-

ing to DSM-IV. Neither compulsive behaviors nor obsessive rituals were noted. There also were no marked signs or symptoms suggestive of tic disorders or major depression. Routine laboratory examinations on admission revealed no abnormalities. No abused substances, including methamphetamine, were identified in urine by a drug screening test.

We initiated risperidone treatment at 2 mg/day and increased dosage to 5 mg/day. In the following 3 weeks, the intrusive thoughts and symptoms of an anxious-restless state gradually subsided and eventually disappeared. Mr. A then stopped use of risperidone, and the symptoms came back within a week. When risperidone, 5 mg/day, was restarted, these symptoms resolved again.

Butyrophenones, such as haloperidol and bromperidol, are known to be effective against methamphetamine psychosis,[3] probably through blocking dopamine-2 (D_2) receptors, but in the present case, these agents did not ameliorate the OCD-like symptoms. There is evidence to suggest long-lasting imbalance between D_2 and serotonin-2A (5-HT_{2A}) receptors in methamphetamine abusers with a history of psychosis,[4] and effectiveness of risperidone treatment for methamphetamine psychosis has also been reported.[5] Furthermore, the augmentation of risperidone has been indicated to be effective in OCD patients who are resistant to SSRIs.[6] On this basis, we used risperidone for the treatment in the current case, and the patient responded well. Therefore, we conclude that the blockade of both D_2 and 5-HT_{2A} receptors by risperidone may have played a role in the improvement of symptoms in the present case.

Transient OCD-like symptoms following stimulant therapy (*d*-amphetamine, or dextroamphetamine) for hyperactive children[7] and an elevated risk for OCD in active users of cocaine and other substances[8] have been reported. However, to our knowledge, this is the first report of successful treatment with risperidone of persistent OCD-like symptoms in a patient who had a history of methamphetamine psychosis. The present case report prompts the necessity of further investigation into methamphetamine-associated mental problems including anxiety disorder–like symptoms, particularly in view of a worldwide increase in the number of methamphetamine abusers. This report also suggests the possibility that the alteration of the central serotonergic system may be involved in the mechanisms of OCD.

References

1. Sato M, Numachi Y, Hamamura T. Relapse of paranoid psychotic state in methamphetamine model of schizophrenia. Schizophr Bull 1992;18:115–122
2. Fukui S, Wada K, Iyo M. Epidemiology and amphetamine abuse in Japan and its social implication. In: Cho AK, Segal DS, eds. Amphetamine and Its Analogs. San Diego, Calif: Academic Press; 1994: 459–478
3. Konuma K, Hirai S, Kasahara M. Use and abuse of amphetamines in Japan. In: Cho AK, Segal DS, eds. Amphetamine and Its Analogs. San Diego, Calif: Academic Press; 1994:347–364
4. Iyo M, Nishio M, Itoh T, et al. Dopamine D2 and serotonin S2 receptors in susceptibility to methamphetamine psychosis detected by PET. Psychiatry Res 1993;50:217–231
5. Misra L, Kofoed L. Risperidone treatment of methamphetamine psychosis [letter]. Am J Psychiatry 1997;54:1170
6. Stein DJ, Bouwer C, Hawkridge S, et al. Risperidone augmentation of serotonin reuptake inhibitors in obsessive-compulsive and related disorders. J Clin Psychiatry 1997;58:119–122
7. Borcherding BG, Keysor CS, Rapoport JL, et al. Motor/vocal tics and compulsive behaviors on stimulant drugs: is there a common vulnerability? Psychiatry Res 1990;33:83–94
8. Crum RM, Anthony JC. Cocaine use and other suspected risk factors for obsessive compulsive disorder: a prospective study with data from the Epidemiologic Catchment Area Surveys. Drug Alcohol Depend 1993;31:281–295

Masaomi Iyo, M.D., Ph.D.
Yoshimoto Sekine, M.D.
Tsutomu Matsunaga, M.D., Ph.D.
Toshio Tsukamoto, M.D.
Nori Takei, M.D., Ph.D., M.Sc.
Norio Mori, M.D., Ph.D.
Hamamatsu, Shizuoka, Japan

Comparing the Efficacy and Safety of Fluoxetine and Venlafaxine in Outpatient Depression

Sir: I read with interest the recent report comparing the efficacy and safety of fluoxetine and venlafaxine in outpatient depression.[1] However, the reporting of several aspects of the results as well as their interpretation was rather unusual and deserves comment.

First, the comparison of patients who had their dose increased at 3 weeks is statistically problematic, since patients were not randomly assigned to dosage increases or to continue at the initial dose. The unsuitability of the study design for this comparison is not mitigated by the fact that the groups are similar on a number of variables, because the hypothesis tested was that fluoxetine and venlafaxine responders are qualitatively different, and that selecting for nonresponse in each group is also likely to select for qualitatively different, statistically noncomparable populations.

Perhaps more troubling than the lack of statistical rigor, however, is the reporting of the results. The study found very similar outcomes among the groups as a whole, suggesting that, overall, patients responded to both medications equally well. The author then reports results for those patients whose antidepressant dosage was adjusted upward at 3 weeks and suggests that response was higher among venlafaxine-treated patients. Response among the subgroup of patients who did not have their dosage adjusted is not reported—despite the fact that, arithmetically, any differences in the increased-dosage subgroup must be balanced by reciprocal differences in the subgroup of patients who did not have their dosage increased. In other words, fluoxetine-treated patients still taking the initial dosage must have a greater response than venlafaxine-treated patients still taking the initial dosage. In this regard, the data could be interpreted to suggest that at the recommended starting dose, venlafaxine is less effective than fluoxetine.

Also remarkable for its absence is a paragraph discussing problems of the study and those factors that limit the interpretation of its results. With respect to the dosage increase at 3 weeks in particular, no mention is made of the likelihood of confounding dose and time effects with early titration designs. Failing to include such cautions, the author then speculates beyond the data, raising questions about the efficacy of selective serotonin reuptake inhibitors (SSRIs) in subpopulations of patients, particularly the severely ill, and implicitly suggesting that a mixed serotonin/norepinephrine mechanism is potentially superior—despite the fact that these data show no evidence for such a therapeutic advantage for venlafaxine.

It may be that there are differences in efficacy among different classes of medications, and that SSRIs differ from serotonin/norepinephrine reuptake inhibitors with respect to which patients are most likely to benefit from which medication. To date, however, no substantive evidence has been advanced to support

Table 1. Comparison of Most Common (≥ 5%) Treatment-Emergent Adverse Effects Occurring During the First Week of Treatment With Venlafaxine or Fluoxetine

	Data From Original Table 3[a]				
	Venlafaxine (N = 194)		Fluoxetine (N = 185)		p Value
Adverse Effect	N	%	N	%	(Pearson chi-square)
Nausea	56	28.9	35	18.9	.023
Headache	22	11.3	13	7.0	.147
Dizziness	16	8.3	6	3.2	.037
Somnolence	16	8.3	3	1.6	.003
Trembling	16	8.3	3	1.6	.003
Diaphoresis	15	7.7	2	1.1	.002
Anxiety	14	7.2	8	4.3	.229
Dry mouth	14	7.2	6	3.2	.084
Insomnia	12	6.2	15	8.1	.467

[a]From reference 1.

this hypothesis, and nothing in the data presented in this article changes this. Demonstrable differences among antidepressant drug classes have generally been limited to safety and tolerability, and it is in this context that the most serious misstatements in the article occur. The discussion of safety in the Results section reports that there were no significant differences in specific adverse events between the groups, and goes on to assert that all events decreased in the venlafaxine group but not the fluoxetine group over time, implying a safety advantage to venlafaxine. However, when the numbers given in Table 3 of Dr. Costa e Silva's article are used to compare adverse event frequencies using the Pearson chi-square test, a majority (Table 1) were statistically significantly more common in the venlafaxine group, while none of these events was significantly more common in the fluoxetine group. These results suggest that, contrary to the interpretation of data presented in the article, fluoxetine was safer and better tolerated during the initiation of therapy.

It is quite understandable that investigators who are close to the data may miss some of their limitations or bring a particular perspective to the data that shapes their interpretation of them. However, it is precisely to control for these issues and to bring independent judgment to bear that articles are subjected to the peer review process. Publication in a peer-reviewed journal imparts credibility and weight to the data published in it and influences the clinical judgments made by practitioners. This imposes a considerable responsibility on the peer reviewers. The number of errors of interpretation and presentation of the data in this article is significant and raises reasonable concerns about a potential breakdown of the process in this case.

Reference

1. Costa e Silva J. Randomized, double-blind comparison of venlafaxine and fluoxetine in outpatients with major depression. J Clin Psychiatry 1998;59:352–357

David Michelson, M.D.
Eli Lilly and Company
Indianapolis, Indiana

Dr. Costa e Silva Replies

Sir: In response to the letter from Dr. Michelson regarding the comparative study of venlafaxine and fluoxetine, although re-randomization after 3 weeks may have been ideal, the flexible-dose design of this study was selected to reflect clinical practice, where doses are adjusted based on patient response and tolerability. The hypothesis tested was not that responders are qualitatively different, but rather that patients requiring a higher dose of either drug for an insufficient response are qualitatively different from those responding at recommended initial doses of each drug.

Among patients who maintained their dose at 75 mg/day of venlafaxine or 20 mg/day of fluoxetine throughout the study, a Clinical Global Impressions-Improvement scale score of 1 was observed in 69.3% taking venlafaxine and 75.8% taking fluoxetine (NS). Differences in response between groups were 7% in favor of fluoxetine in the low-dose group and 23% in favor of venlafaxine in the high-dose group.

The selection of 3 weeks for a dosage increase was based on a previous study with fluoxetine.[1] Regarding superior efficacy of venlafaxine, the results of this study do suggest that venlafaxine is both statistically and clinically superior to fluoxetine among patients requiring higher doses. A substantial and growing body of literature suggests that venlafaxine and other drugs with combined action on more than one neurotransmitter are more effective than SSRIs, particularly in severely depressed patients.[2–8] Anderson and Tomenson,[9] in a meta-analysis of controlled clinical trials, reported that tricyclic antidepressants were more effective than SSRIs in severely depressed hospitalized patients.

Regarding comparisons of tolerability, the statistical analysis tested for the presence or absence of at least one study event over the entire 8 weeks of treatment using a chi-square test and found no significant differences. The results presented by Dr. Michelson report the incidence during week 1 only. Over time, the incidence of nausea, dizziness, insomnia, and somnolence decreased with venlafaxine. The incidence of nausea decreased over time with fluoxetine also, but the incidence of anxiety and headache remained constant or increased.

We quite agree with Dr. Michelson concerning the importance of the peer review process in establishing and maintaining credibility and the impact that this process has on influencing clinical judgment. We think that the data presented from our study appropriately reflect our findings.

References

1. Dornseif BE, Dunlop SR, Potvin JH, et al. Effect of dose escalation after low-dose fluoxetine therapy. Psychopharmacol Bull 1989;25: 71–79
2. Danish University Antidepressant Group. Citalopram: clinical effect profile in comparison with clomipramine: a controlled multicenter study. Psychopharmacology 1986;90:131–138
3. Danish University Antidepressant Group. Paroxetine: a selective serotonin reuptake inhibitor showing better tolerance, but weaker antidepressant effect than clomipramine in a controlled multicenter study. J Affect Disord 1990;18:289–299
4. Roose SP, Glassman AH, Attia E, et al. Comparative efficacy of selective serotonin reuptake inhibitors and tricyclics in the treatment of melancholia. Am J Psychiatry 1994;151:1735–1739
5. Clerc GE, Ruimy P, Verdeau-Pailles J, on behalf of the Venlafaxine French Inpatient Study Group. A double-blind comparison of venlafaxine and fluoxetine in patients hospitalized for major depression and melancholia. Int Clin Psychopharmacol 1994;9:139–143
6. Dierick M, Ravizza L, Realini R, et al. A double-blind comparison of venlafaxine and fluoxetine for treatment of major depression in outpatients. Prog Neuropsychopharmacology Biol Psychiatry 1996;20: 57–71
7. Schaeffer P, Poirier M-F, Boyer P. Double-blind trial of venlafaxine and paroxetine for treatment-resistant depression [abstract]. Eur Neuropsychopharmacol 1998;8(suppl 2):S159

8. Wheatley DP, van Moffaert M, Timmerman L, et al. Mirtazapine: efficacy and tolerability in comparison with fluoxetine in patients with moderate to severe major depressive disorder. J Clin Psychiatry 1998;59:306–312
9. Anderson IM, Tomenson BM. The efficacy of selective serotonin reuptake inhibitors in depression: a meta-analysis of studies against tricyclic antidepressants. J Psychopharmacol 1994;8:238–249

Jorge Costa e Silva, M.D.
Rio de Janeiro, Brazil

Relationship Between Antidepressant Treatment and Suicide

Sir: An inaccuracy in the opening sentence of the recent letter by Haffmans et al.[1] caused me to read closer. The inaccuracy is that Haffmans et al. state that 3 cases of suicide are described in the article by Praschak-Rieder et al.[2]; there were, in fact, no suicides described in the article by Praschak-Rieder et al.

What also concerns me, though, are some statements and conclusions that are made relative to the case described in the letter. As far as I am aware, there is no proof of the widespread belief that antidepressant treatment may energize (or activate) people with suicidal propensities, especially early in treatment, and thus result occasionally in suicide even though the individuals had appeared to be getting better otherwise. I know of only 1 study in which data were presented to challenge this clinical wisdom, however.[3]

Family members and other observers sometimes describe suicide victims as appearing more relaxed and even cheerful in the several days prior to death when no treatment is being given or taken. Some speculate this change in attitude reflects that an individual has already decided to commit suicide and has become at peace with the decision. For several reasons, such a speculation could also apply to a patient receiving drug treatment, including inadequate time for the antidepressant treatment to work, ineffective treatment, or noncompliance.

As someone who has studied a large number of suicides outside the clinical setting,[4] I favor this second hypothesis. However, as far as I am aware, it also lacks proof, and of course, neither hypothesis precludes other possible explanations.

Regardless of the outcome of this debate, the observation of apparent improvement in depression early (perhaps too early) in treatment needs to be viewed cautiously, particularly if hopelessness or overt suicidal ideation persists. Unfortunately, it is very difficult to justify a more vigorous and protective approach to treatment, e.g., hospitalization, at a point where the patient "looks" better. Even worse, a patient who has decided that "it is time to die" would probably not confide that decision to a clinician who would take steps to prevent it. So, in our current uncertain state of suicide prediction, we will probably continue to face such paradoxical bad outcomes as suicide following apparent improvement in depression. I think it would be an error, however, to conclude that successful treatment of depression can lead to greater likelihood of suicide.

References

1. Haffmans J, Lucius S, Ham N. Suicide after bright light treatment in seasonal affective disorder: a case report [letter]. J Clin Psychiatry 1998;59:478
2. Praschak-Rieder N, Neumeister A, Hesselmann B, et al. Suicidal tendencies as a complication of light therapy for seasonal affective disorder: a report of three cases. J Clin Psychiatry 1997;58:389–392
3. Rich CL, Spiker DG, Jewell SW, et al. Response of energy and suicidal ideation to ECT. J Clin Psychiatry 1986;47:31–32
4. Rich CL, Young D, Fowler RC. San Diego suicide study, I: young vs old subjects. Arch Gen Psychiatry 1986;43:577–582

Charles L. Rich, M.D.
Mobile, Alabama

Dr. Praschak-Rieder and Colleagues Reply

Sir: We were very pleased to read the letter by Dr. Rich. Suicide and suicidality are problems that clinicians have to face frequently in their daily work. We think that these phenomena need to be viewed in all their complexity and their manifold dimensions. We agree with Dr. Rich that our tools in the field of suicide prevention are very limited. Therefore, our intent in reporting suicidal tendencies in patients with seasonal affective disorder (SAD) was to point out the need for a careful evaluation of suicidal thoughts and intentions even in a patient collective where suicide seems to be infrequent.[1]

Therefore, probably the most important inaccuracy in the letter by Haffmans et al.[2] is their statement that no suicidal thoughts were found in our 3 patients with SAD before bright light therapy was started. On the contrary, all 3 patients who became suicidal in the early phase of bright light therapy had elevated pretreatment scores in item 3 (suicide) of the Hamilton Rating Scale for Depression (HAM-D). This was not the case in the other 30 patients with SAD who did not become suicidal. Moreover, 2 of the 3 patients who became suicidal while undergoing bright light therapy had a history of suicidality, and many stressors and precipitants, including chronic pain, the development of a mixed affective state in a bipolar II patient under light therapy, and, not least, partial noncompliance, were present in these 3 patients.

Considering the complexity of the phenomenon of suicide, it seems to be of great importance not to draw precocious causal conclusions. However, the occurrence of suicide attempts in the early antidepressant treatment phase has been observed by many clinicians. A possible medication- or light therapy–induced dissociation of mood and drive in the early treatment phase should therefore be considered as one of many potential hazards in the treatment of patients with suicidal tendencies.

References

1. Praschak-Rieder N, Neumeister A, Hesselmann B, et al. Suicidal tendencies as a complication of light therapy for seasonal affective disorder: a report of three cases. J Clin Psychiatry 1997;58:389–392
2. Haffmans J, Lucius S, Ham N. Suicide after bright light treatment in seasonal affective disorder: a case report [letter]. J Clin Psychiatry 1998;59:478

Nicole Praschak-Rieder, M.D.
Matthäus Willeit, M.D.
Alexander Neumeister, M.D.
Siegfried Kasper, M.D.
Vienna, Austria

Risperidone Treatment of Tardive Dyskinesia and Dystonia

Sir: Although more attention has been given to neuroleptic-induced tardive dyskinesia, tardive dystonia, characterized by local or general twisting and sustained muscle spasms, is also a

longer term complication of typical neuroleptic treatment. Reported here is a Chinese patient whose psychosis and tardive movements, both dyskinetic and dystonic, were effectively treated when low-dose risperidone was added to diazepam and trihexyphenidyl.

Case report. Mr. A, a 47-year-old Chinese man with a 17-year history of schizophrenia, had no significant medical history and no family history of dystonia. Despite the fact that he had received continuous treatment with various neuroleptics (fluphenazine decanoate, pipotiazine palmitate, chlorpromazine, trifluoperazine, haloperidol, and thioridazine), his psychotic symptoms (auditory hallucinations, bizarre behavior, social withdrawal, and volitional disturbances) remained prominent. Dosages of neuroleptics were increased steadily, reaching a maximum of pipotiazine palmitate, 75 mg every 3 weeks, in combination with trifluoperazine, 40 mg/day. He was also taking trihexyphenidyl, 8 mg/day, as well as diazepam, 15 mg/day.

After being on this drug regimen for 14 weeks, Mr. A was noted to have tardive dyskinesia involving his mouth, tongue, and face. About 6 weeks later, he also developed dystonic movements (spasmodic twisting of his trunk and torticollis). These tardive dyskinetic and dystonic movements were persistent and caused him considerable distress. A neurologic examination revealed no abnormalities other than these movements. An increase of diazepam to 19 mg/day brought no improvement. Because of the persistence and severity of his psychotic symptoms, his antipsychotic medications were not reduced.

Nine months after the tardive movements commenced, he was started on a trial of risperidone at an initial dose of 0.5 mg/day. His pre-risperidone Abnormal Involuntary Movement Scale (AIMS) score was 20. Previous neuroleptics (pipotiazine palmitate and trifluoperazine) were tapered gradually over the following months. There was steady improvement of the abnormal movements, and 1 year later he is maintained on risperidone, 1 mg/day, trihexyphenidyl, 6 mg/day, and diazepam, 12 mg/day—a regimen he has now been on for 7 months. No attempt has been made as yet to discontinue trihexyphenidyl, although this is planned as there is no indication of acute extrapyramidal side effects. His tardive dystonic and dyskinetic movements have resolved completely (AIMS score = 0 at the time of this report), and he experiences no more auditory hallucinations. He is more alert, interacts more with others, and shows greater interest in daily activities.

The resolution of this patient's tardive movements, including both dyskinesia and dystonia, might have been due to the withdrawal of typical neuroleptics; stopping or reducing the dosage of neuroleptics has been suggested to have a favorable outcome on tardive dyskinesia.[1] Wojcik et al.,[2] however, reported that tardive dystonia resolution that results from withdrawal of typical neuroleptics is rare (as is spontaneous remission of tardive dystonia).[3] Rangwani et al.[4] described a case of an elderly woman who showed significant improvement of her tardive dystonia following treatment with low-dose risperidone. It is not possible to attribute the resolution of our patient's tardive dystonia to risperidone alone, as he was also taking diazepam and trihexyphenidyl. These 2 agents, however, were ineffective while the patient was still taking typical neuroleptics. Although most studies have not shown any clear association between tardive dyskinesia and dosage of neuroleptics,[5] the low dose of risperidone may possibly account for the resolution of our patient's tardive dystonia. Kopala and Horner[6] postulated that risperidone may reduce tardive dyskinesia by changing the balance between dopamine and serotonin in the basal nuclei. The resolution of the tardive movements in this particular case suggests that risperidone, like clozapine, should be considered in patients with neuroleptic-induced tardive movements.

References

1. Casey DE. Spontaneous and tardive dyskinesias: clinical and laboratory studies. J Clin Psychiatry 1985;46(4, sec 2):42–47
2. Wojcik JD, Falk WE, Fink JS, et al. A review of 32 cases of tardive dystonia. Am J Psychiatry 1991;148:1055–1059
3. Burke RE, Fahn S, Jankovic J, et al. Tardive dystonia: late onset and persistent dystonia caused by antipsychotic drugs. Neurology 1982; 32:1335–1346
4. Rangwani SR, Gupta S, Burke WJ, et al. Improvement of debilitating tardive dyskinesia with risperidone. Ann Clin Psychiatry 1996;8: 27–29
5. Kane J. Tardive dyskinesia: epidemiological and clinical presentation. In: Bloom FE, Kupfer DJ, eds. Psychopharmacology: The Fourth Generation of Progress. New York, NY: Raven Press; 1995: 1485–1502
6. Kopala LC, Horner WG. Schizophrenia and severe tardive dyskinesia responsive to risperidone. J Clin Psychopharmacol 1994;14:430–431

Siow-Ann Chong, M.B.B.S., M.Med.(Psychiatry)
Gary Remington, M.D., Ph.D., F.R.C.P.C.
Toronto, Ontario, Canada
Chay-Hoon Tan, M.B.B.S., M.Med.(Psychiatry)
Singapore

Corrections

In the article "Clinical Practice Guidelines for Bipolar Disorder From the Department of Veterans Affairs" (January 1999 issue, pp. 9–21) by Mark S. Bauer, M.D., and colleagues, the "Go to" circle that follows item 11 in Module E on page 14 should read "Go to Box 16."

Evelyn Howanitz, M.D., has notified the *Journal* that Robert G. Stern, M.D., was an author on "The Efficacy and Safety of Clozapine Versus Chlorpromazine in Geriatric Schizophrenia" (January 1999 issue, pp. 41–44). The corrected byline is as follows: Evelyn Howanitz, Moris Pardo, David A. Smelson, Charles Engelhart, Norman Eisenstein, Robert G. Stern, and Miklos F. Losonczy. Dr. Stern is with the Schizophrenia and Treatment Research (STAR) Program, Bronx Veterans Administration Medical Center and the Department of Psychiatry, Mount Sinai School of Medicine, New York, N. Y.

Anne N. Nafziger, M.D., disclosed funding for the article "Incidence of Sexual Dysfunction in Healthy Volunteers on Fluvoxamine Therapy" (March 1999 issue, pp. 187–190) by the E. Donnall Thomas Resident Research Program in Internal Medicine and the American College of Clinical Pharmacists' Wyeth-Ayerst Laboratories Women's Healthcare Research Award. The editors regret our oversight in omitting this disclosure when the article was published.