Letters to the Editor

Risperidone for Exclusively Negative Symptoms

TO THE EDITOR: Risperidone is a serotonin-2/dopamine-2 ($5\text{-}HT_2/D_2$) receptor antagonist with demonstrated efficacy in the treatment of both positive and negative symptoms of schizophrenia (1). However, it has been suggested that the improvement in negative symptoms might be associated with changes in positive symptoms, extrapyramidal side effects, or depression (2, 3). Therefore, such symptoms could be considered to be secondary negative symptoms (2). In addition, whether risperidone is superior to classical antipsychotics in reducing negative symptoms remains controversial (3). We here report a schizophrenic patient whose prodromal negative symptoms were not ameliorated by low-dose thioridazine, chlorpromazine, or sulpiride. Furthermore, following his first acute exacerbation, the residual negative symptoms persisted for 4 years, even though he was treated with 5 mg/day of haloperidol (alone or plus 20 mg/day of fluoxetine). Finally, risperidone monotherapy (3 mg/day) brought a substantial improvement in the exclusively negative symptoms. Depressive or manic symptoms were absent throughout his history.

Mr. A, a 31-year-old Chinese man, was physically healthy and devoid of any seizure or substance abuse history. Nine years ago, his drive began to decrease insidiously. Affective flattening, alogia, and anhedonia also evolved. Major areas of functioning, e.g., interpersonal relations, academic/occupational performance, and self-care, progressively and markedly deteriorated. Seven years ago, he started to receive a sequence of pharmacologic regimens: thioridazine (up to 200 mg/day for 6 months), chlorpromazine (up to 200 mg/day for 6 months), and sulpiride (up to 300 mg/day for 10 months). These strategies did not cause parkinsonian side effects, but all failed to curtail the negative symptoms. Positive psychotic symptoms (referential delusions, persecutory delusions, and thought broadcasting) also emerged 5 years ago. Physical examinations, ECG, chest X-ray, urinalysis, hematology, serum chemistry, and serology all produced negative findings. Haloperidol, 10 mg/day, was prescribed and produced a full remission of the positive symptoms in 4 weeks but induced moderate tremor over the lower extremities. Hence, the dose was tapered to 5 mg/day over another 12 weeks. The motor side effects vanished, while the negative symptoms continued. Thereafter, 5 mg/day of haloperidol plus 20 mg/day of fluoxetine for 16 weeks and then 5 mg/day of haloperidol alone for 45 months still left the negative symptoms unchanged. No positive symptoms ever recurred. Compliance was carefully monitored by a key relative.

Six months ago, Mr. A gave written informed consent to receive risperidone monotherapy. After a 3-day drug-free period, the dose was titrated to 1.5 mg b.i.d. over 1 week. After 2 weeks of therapy, his negative symptoms started to recede. He no longer lay in bed all day long, and he gradually regained his drive, appropriate affect, recreational and social interests, and fluidity and productivity of the verbal process. After 6 weeks of therapy, he made new friendships and began seeking a job. Four more weeks later, he obtained an unskilled job following 8 years of unemployment. He has now kept the position for 4 months. All the negative symptoms have become negligible. Neither adverse drug reactions nor positive symptoms appeared after the initiation of risperidone treatment.

To our knowledge, this is the first report of treatment of solely negative symptoms (not associated with positive symptoms, depression, or extrapyramidal symptoms) of schizophrenia with risperidone alone. The observations should be considered preliminary. Undoubtedly, risperidone benefited from a halo effect of the enthusiasm associated with using a new medication. However, the present patient had previously failed to improve in multiple trials for the treatment of negative symptoms. A 6-week open pilot study (4) has indicated that the addition of fluoxetine to antipsychotics can improve both positive and negative symptoms in some schizophrenic patients. On the other hand, an 8-week double-blind, placebo-controlled study (5) has demonstrated that adjunctive fluoxetine is not effective in alleviating positive or negative symptoms in clozapine-treated schizophrenic patients. In addition, our patient with merely negative symptoms did not profit from 16-week coadministration of haloperidol and fluoxetine. It has been suggested (3) that low doses of risperidone are better than high doses in reducing secondary negative symptoms. A small dose (3 mg/day) was effective in the present case. Rigorous studies to assess the impact of risperidone treatment (especially at various doses) on primary negative symptoms are urgently needed. Risperidone's preferential $5\text{-}HT_2$ antagonism and the resulting serotonin-dopamine interaction might contribute to its potential efficacy in the treatment of negative symptoms (2, 3). However, since risperidone also exhibits high affinity for dopamine D_4, histamine H_1, and adrenergic α_1 receptors (3), the various neurotransmitter effects on negative symptoms should be clarified (2, 3).

REFERENCES

1. Marder SR, Meibach RC: Risperidone in the treatment of schizophrenia. Am J Psychiatry 1994; 151:825–835
2. Kane JM: Risperidone (editorial). Am J Psychiatry 1994; 151: 802–803
3. Kapur S, Remington G: Serotonin-dopamine interaction and its relevance to schizophrenia. Am J Psychiatry 1996; 153: 466–476
4. Goff DC, Brotman AW, Waites M, McCormick S: Trial of fluoxetine added to neuroleptics for treatment-resistant schizophrenic patients. Am J Psychiatry 1990; 147:492–494
5. Buchanan RW, Kirkpatrick B, Bryant N, Ball P, Breier A: Fluoxetine augmentation of clozapine treatment in patients with schizophrenia. Am J Psychiatry 1996; 153:1625–1627

HSIEN-YUAN LANE, M.D.
CHIA-CHANG LIU, M.D.
WEN-HO CHANG, M.D.
Taipei, Taiwan

There Is Nothing New Under the Sun

TO THE EDITOR: A 1986 letter to the Editor (1) aptly suggested that in 1898 the polar explorer Dr. Frederick A. Cook conducted a natural "experiment" demonstrating the beneficial effects of light therapy for winter seasonal depression (2). The letter quotes Cook—apparently alluding to the cosmos—writing that the result of Antarctic winter darkness was to leave people "in a condition similar to that of a planet deprived of direct sunlight."

In view of a novel theoretical model suggesting that human chronobiological sensitivity to light may share behavioral and molecular properties with the plant kingdom (3, 4), it becomes reasonable to consider the possibility that the preceding Cook quotation represents a century-old typographical error and that Cook had intended to write that winter darkness left people in a condition similar to a *plant* deprived of direct sunlight. In support of this proposition, Cook's own writing elsewhere records that the depression induced by long polar nights implies "that the presence of the sun is essential to animal as it is to vegetable life" (5).

At the least, Cook's long-forgotten insight makes one wonder what other clinically and biochemically relevant treasures from past scholarship might productively inform the future.

REFERENCES

1. Jefferson JW: An early "study" of seasonal depression (letter). Am J Psychiatry 1986; 143:261–262
2. Rosenthal NE, Sack DA, Gillin JC, Lewy AJ, Goodwin FK, Davenport Y, Mueller PS, Newsome DA, Wehr TA: Seasonal affective disorder: a description of the syndrome and preliminary findings with light therapy. Arch Gen Psychiatry 1984; 41: 72–80
3. Oren DA: Humoral phototransduction: blood is a messenger. Neuroscientist 1996; 2:207–210
4. Oren DA, Terman M: Tweaking the human circadian clock with light. Science 1998; 279:333–334
5. Cook FA: Medical observations among the Esquimaux. New York J Gynecology and Obstetrics 1894; 4:282–286

DAN A. OREN, M.D.
West Haven, Conn.

Smoking Cessation and Anxiety

TO THE EDITOR: In their article, Robert West, Ph.D., and Peter Hajek, Ph.D. (1), concluded that their results weaken the view that increased anxiety is a central element of the nicotine withdrawal syndrome and suggested that giving up smoking is quite rapidly followed by a reduction in anxiety. Unfortunately, the frequency of assessments chosen by the authors may have confounded their results. Their data included measurements of anxiety 2 weeks and 1 week before smoking cessation, immediately before cessation, 24 hours after cessation, and 1, 2, 3, and 4 weeks after cessation.

According to DSM-IV, nicotine withdrawal symptoms typically peak in 1 to 4 days and last for 3 to 4 weeks. Since this study had only one assessment during the first 4 days after cessation, the true peak of anxiety symptoms from nicotine withdrawal may have been missed. Daily assessments would seem indicated, at least for the first 4 days after cessation, to clarify the role of anxiety symptoms in nicotine withdrawal.

Regarding the finding that levels of anxiety were lower after smoking cessation than at baseline, it would be interesting to know the reasons for smoking perceived by these subjects. Russell (2) speculated that stimulation and sedation were separate reasons for smoking. Perhaps the subjects in this study smoked for stimulation and, therefore, experienced reduced anxiety after smoking cessation. Different results might be obtained among those who smoke for the perceived sedating effects of cigarettes.

REFERENCES

1. West R, Hajek P: What happens to anxiety levels on giving up smoking? Am J Psychiatry 1997; 154:1589–1592
2. Russell MA: Subjective and behavioral effects of nicotine in humans: some sources of individual variation, in Progress in Brain Research. Edited by Nordberg A, Fuxe K, Holmstedt B, Sundwall A. New York, Elsevier, 1989, pp 289–302

EVE J. WISEMAN, M.D.
Little Rock, Ark.

Dr. West Replies

TO THE EDITOR: Dr. Wiseman comments that we may have failed to find an increase in anxiety following cessation of smoking because we looked at it after 24 hours and then again after 1 week. It is conceivable that anxiety as a symptom of withdrawal from smoking peaks on the second or third day and then decreases and that our measure after 24 hours was too early and our measure after 7 days was too late, but I think this is highly unlikely. No other DSM-IV nicotine withdrawal symptoms failed to be picked up by our methods, and I know of no other studies that have shown anxiety to peak specifically on day 2, 3, or 4. In addition, it is worth remembering that the ratings that smokers made after 1 week were in relation to the time since the last session and should have included all the days intervening.

Dr. Wiseman also suggests that our subjects may have for some reason smoked primarily for stimulation and that another group of subjects who smoked primarily for sedation might have experienced increased anxiety on stopping smoking. In fact, the distinction between stimulant and sedative smokers is artificial in that there is now good evidence that there is a positive correlation between smoking for stimulation and for sedation, rather than these being features of different categories of smokers. Also, it is highly implausible that by chance our heavy smokers happened to be those who smoked primarily for stimulation rather than sedation.

ROBERT WEST, PH.D.
London, U.K.

Managed Care and Psychotherapy for Schizophrenia

TO THE EDITOR: The article by Gerard E. Hogarty, M.S.W., and colleagues (1) and the accompanying editorial (2) continue the valuable debate about the clinical and economic value of psychotherapy as an adjunct to medication and case management in the treatment of schizophrenia (3–5). It is reasonable to expect that availability of individual psychotherapy for persons with schizophrenia (many of whom receive Medicaid) will be further affected by the recent trend in many states toward mandatory assignment of the care of outpatients receiving Medicaid to behavioral managed care companies.

In April 1996, following approval from Medicaid, our outpatient system serving 1,814 persons with severe mental illness was converted into a partially capitated prepaid mental health plan. The plan received a fixed annual amount per enrolled patient instead of payment per patient visit. The ba-

sic benefit package included medication monitoring and case management, with additional services such as individual psychotherapy available as clinically needed. Individual psychotherapy was defined as weekly individual therapeutic sessions lasting 30 or more minutes with a clear therapeutic goal mutually agreed on by therapist and patient and provided by a Ph.D. psychologist, master's-level social worker, or nurse with a bachelor's degree. For the purposes of resource allocation, we asked physicians and clinicians to complete a form providing justification for individual psychotherapy for any patient with schizophrenia who requests individual therapy or agrees to receive individual psychotherapy at the recommendation of his or her physician.

In our prepaid plan, 1,036 outpatients carry the DSM-IV diagnosis of schizophrenia and, of this group, 180 (17.4%) patients were identified by physicians and clinical staff as being in need of individual psychotherapy and having adequate justification in the completed review forms. We noted that symptom management was the leading goal (N=94), followed by psychoeducation (N=55) and supportive therapy (N=31). We suspect that the higher rate for symptom management (52.2%) is related to an increase in the number of outpatients with active symptoms due to shortened hospital stays. There were no significant differences by gender, either in the need for or in the goals of individual psychotherapy. In our plan, it is difficult to determine the exact costs incurred in providing individual psychotherapy to this small subgroup of patients, but we estimate that when the cost is distributed to all patients with schizophrenia, it may add as much as $231 to the annual cost of treating each patient with the diagnosis of schizophrenia. It is logical to assume that continuation of additional services such as individual psychotherapy depends on research results demonstrating that such services will reduce overall costs of treating patients with schizophrenia.

REFERENCES

1. Hogarty GE, Kornblith SJ, Greenwald D, DiBarry AL, Cooley S, Ulrich RF, Carter M, Flesher S: Three-year trials of personal therapy among schizophrenic patients living with or independent of family, I: description of study and effects on relapse rates. Am J Psychiatry 1997; 154:1504–1513
2. Fenton WS, McGlashan TH: We can talk: individual psychotherapy for schizophrenia (editorial). Am J Psychiatry 1997; 154:1493–1495
3. Borenstein BB: Does managed care permit appropriate use of psychotherapy? Psychiatr Serv 1996; 47:971–974
4. Bennett MJ: Is psychotherapy ever medically necessary? Psychiatr Serv 1996; 47:966–970
5. Gabbard GO, Lazar SG, Hornberger J, Spiegel D: The economic impact of psychotherapy: a review. Am J Psychiatry 1997; 154:147–155

HASSAN S. DINAKAR, M.D.
ROBERT N. SOBEL, M.D.
Orangeburg, N.Y.

Mr. Hogarty Replies

TO THE EDITOR: Drs. Dinakar and Sobel offer interesting survey results regarding the provision of psychotherapy to schizophrenic patients in a managed care program, but it is unclear what inferences they wish to have drawn. At first glance, it appears that only 17% of 1,036 schizophrenic patients enrolled in a partially capitated managed care plan either wanted individual psychotherapy or were judged by their treating physicians to need it. If the need or desire for psychotherapy is so circumscribed, do we and others waste our time and resources developing and testing more effective forms of psychotherapeutic intervention? Or is there a problem with the *method* used to estimate the need and desire for psychotherapy?

Asking physicians whether their schizophrenic patients need "psychotherapy" might well have implied insight-oriented, uncovering, investigative, or other psychoanalytically based approaches that might have led to a low rate of endorsement, at least among those who have read reports of the better-designed empirical studies of dynamic psychotherapy that were conducted over the past 30 years (1). Soliciting the schizophrenic patients' desire for psychotherapy might also predictably yield a similar response, when the majority of patients appear to have little or no insight into their illness (2).

But what would happen if both groups were asked their preference for a nonsomatic, disorder-relevant intervention that would 1) greatly reduce the risk for psychotic relapse and other poor outcomes, 2) teach patients about their unique prodromes and effective ways to manage them according to their clinical state and preference, 3) prepare patients to form and maintain important human relationships, and 4) increase the potential for vocational success and independent functioning (3, 4)? Whatever one might call this intervention (psychotherapy, psychosocial treatment, or mental health service), it is entirely possible that only 17% of patients or their psychiatrists would *decline* the invitation!

Further, what Drs. Dinakar and Sobel define as "psychotherapy" (symptom management, psychoeducation, and supportive therapy offered in the context of case management and medication monitoring), we have called "supportive therapy" in our studies. Our results suggest that significant symptom improvement and minor gains in social adjustment do occur during the first year of supportive therapy, but little or no continuing improvement is to be found in subsequent years. Personal therapy, on the other hand, significantly grows in efficacy with the passage of time (4). It is difficult to conclude that 83% of recovering schizophrenic patients would not need or desire such an intervention. While it is unlikely that personal therapy could be offered for $231 annually for each patient, it could prove to be cost-effective over time, once the savings from reduced inpatient use and increased social and vocational functioning entered the equation.

REFERENCES

1. Mueser KT, Berenbaum H: Psychodynamic treatment of schizophrenia: is there a future? Psychol Med 1990; 20:253–262
2. Cuester MJ, Peralta V: Lack of insight in schizophrenia. Schizophr Bull 1994; 20:359–366
3. Hogarty GE, Kornblith SJ, Greenwald D, DiBarry AL, Cooley S, Ulrich RF, Carter M, Flesher S: Three-year trials of personal therapy among schizophrenic patients living with or independent of family, I: description of study and effects on relapse rates. Am J Psychiatry 1997; 154:1504–1513
4. Hogarty GE, Greenwald D, Ulrich RF, Kornblith SJ, DiBarry AL, Cooley S, Carter M, Flesher S: Three-year trials of personal therapy among schizophrenic patients living with or independent of family, II: effects on adjustment of patients. Am J Psychiatry 1997; 154:1514–1524

GERARD E. HOGARTY, M.S.W.
Pittsburgh, Pa.

Reprints of letters to the Editor are not available.