The Treatment of Psychotic Depression

William Coryell, M.D.

Psychotic depression is marked by increased severity, longer episodes, greater incapacity, and a lower likelihood of placebo response. Psychotic features often recur in subsequent episodes and interepisode intervals are shorter when psychotic features have been previously present. Among the treatment options for psychotic depression, electroconvulsive therapy is particularly effective. Conventional pharmacotherapy consists of tricyclic antidepressants combined with antipsychotics; recovery with tricyclic antidepressant monotherapy is less likely. Serotonin selective reuptake inhibitors may prove useful but the relevant literature is scant. Pharmacokinetic interactions are likely in combination treatment, as are side effects that may mimic the underlying condition. Little is known regarding the importance of antipsychotics to maintenance therapy.

(J Clin Psychiatry 1998;59[suppl 1]:22–27)

The presence of psychotic features within major depressive syndromes has implications both for immediate treatment selection and for long-term management. The following will begin with a review of the phenomenology and natural history of psychotic depression to establish the particular importance of acute and prophylactic treatment in this disorder. Subsequent sections will describe data underlying recommendations for the use of tricyclic antidepressants, monoamine oxidase inhibitors, serotonin selective reuptake inhibitors, electroconvulsive therapy, and antipsychotics, both traditional and atypical.

PHENOMENOLOGY AND COURSE

The distinction between psychotic affective disorder and schizophrenia is a common, often difficult, but important clinical judgment. In the DSM-IV, the separation of these disorders turns on the temporal relationship of psychotic features and affective symptoms. If mood episodes have been brief relative to the duration of active and residual schizophrenia-like symptoms, schizophrenia may be the appropriate diagnosis. If an affective syndrome has been present for a substantial portion of the total duration of the active and residual periods of the (schizophrenia-like) illness, but psychotic features have, at some point, been present for at least 2 weeks in the absence of prominent mood symptoms, then schizoaffective disorder is the appropriate diagnosis. Thus, in psychotic depression, the psychotic features appear only in the context of a full depressive syndrome. Obviously, this critical distinction is based on history rather than cross-sectional appraisal. The evaluation should therefore include interviews with family members and a careful review of clinical records.

Though rarely discussed in the literature, the boundaries between psychotic features and nonpsychotic clinical phenomena are also often unclear. This is particularly true in the appraisal of hallucinations. When they are encountered in the context of somatization disorder, reports of visions, voices, or tactile experiences are more appropriately viewed as conversion symptoms than as psychotic features.[1] Quasi-psychotic experiences are, likewise, a component of borderline personality disorder.[2] Patients with these disorders often present with superimposed major depressive disorder, and many such patients are vigorously, but inappropriately, treated for psychotic depression, typically with highly unsatisfactory results. In fact, true hallucinations rarely exist in major depressive disorder unless delusions are also present (Table 1).[3] Thus, in the absence of clear delusions, the presence of somatization disorder or borderline personality disorder should be carefully considered in the evaluation of depressed patients who appear to describe hallucinations.

A variety of findings associate psychotic features and episode severity. First, individual depressive symptoms are typically more severe when psychotic features are present.[4–8] This is especially true of those symptoms which comprise criteria for endogenous or melancholic subtypes.[5,6,8]

From the Department of Psychiatry, University of Iowa College of Medicine, Iowa City, Iowa.

Presented at the closed symposium "Clinical Outcomes in the Treatment of Schizophrenia," April 12, 1996, held in New Orleans, Louisiana, and sponsored by an unrestricted educational grant from Janssen Pharmaceutica, Inc.

Reprint requests to: William Coryell, M.D., Department of Psychiatry, University of Iowa College of Medicine, Psychiatry Research—MEB, Iowa City, IA 52242.

Table 1. Hallucinations as the Sole Psychotic Feature in Psychotic Major Depressive Disorder (MDD)

	Number of Patients With Psychotic MDD	Patients With Hallucinations Only	
		N	%
Lykouras et al (1986)[7]	22	0	…
Parker er al (1991)[8]	35	1	3
Anton and Burch (1993)[47]	37	2	5
Coryell and Zimmerman (Unpublished data)[a]	58	3	5

[a]Derived from database described in reference 3.

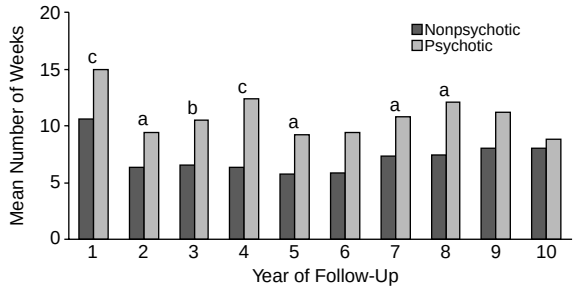
Second, psychotic episodes are more likely to be incapacitating,[9] to feature unvarying dysphoria,[8] and to persist for longer periods.[10] The likelihood of placebo response in depression generally correlates inversely with severity[11] and, accordingly, depressed patients with psychotic features are much less likely to respond to placebo than are other depressed patients.[12,13]

Finally, psychotically depressed patients are much more likely to exhibit an abnormal plasma cortisol escape from dexamethasone suppression. A recent meta-analysis[14] showed the presence or absence of psychotic features to be a much more consistent predictor of dexamethasone nonsuppression than endogenous or melancholic subtyping.

Follow-up studies show that the presence of psychotic features has a significance that extends well beyond a given episode. This is most clearly shown by the high likelihood that psychotic features will recur in new episodes.[15–18] The tendency is sustained across multiple episodes, making psychotic depression the most stable of the phenomenologically based subtypes.[18] Thus, the psychotic-nonpsychotic distinction appears to be more consistent across episodes than is the endogenous-nonendogenous distinction.

Patients with psychotic depression experience a shorter time to recurrence than do those with nonpsychotic depression,[10,19] regardless of whether the immediately preceding episode includes psychotic features. The presence of psychotic features in any episode therefore indicates an illness with a persistently high risk of recurrence. The higher number of recurrences and the likelihood that many of these recurrences will involve psychosis with longer durations combine to produce a persistently greater depressive morbidity. Figure 1 uses data from a study by the National Institute of Mental Health Collaborative Depression Study (Clinical Branch) to show that patients who began this prospective follow-up with psychotic major depressive disorder experienced a higher likelihood of a full depressive syndrome throughout 10 years of follow-up.[10] The substantial short- and long-term morbidity experienced by patients with psychotic depression, together with their failure to show placebo responses, underscores the importance of optimal treatment selection.

Figure 1. Number of Weeks With Full Major Depressive Syndrome by Year of Follow-Up*



*Data from reference 10.
[a]$p < 0.1$.
[b]$p < 0.05$.
[c]$p < 0.01$.

ACUTE TREATMENT

Tricyclic Antidepressants With and Without Antipsychotics

Research interest in psychotic depression as a distinct subgroup originated with the observation that psychotic features predicted poor outcome in antidepressant trials of conventional length.[20–26] It is now broadly accepted that the short-term effectiveness of tricyclic antidepressants (TCAs) combined with antipsychotics exceeds that of TCAs alone,[27] although a meta-analysis has failed to show this difference to be statistically significant across studies.[28]

Psychotic features also predict a poorer short-term outcome with monoamine oxidase inhibitor (MAOI) therapy. Janicak et al. (1988)[29] assigned 52 depressed inpatients to a 4-week trial of phenelzine. Twenty-one (68%) of those with nonpsychotic depression (N = 31), but only 3 (21%) of those with definite psychotic features (N = 14) were considered responders at the end of the trial.

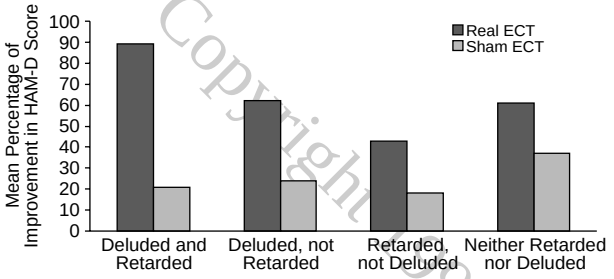
Although many studies support this conclusion, few have employed a prospective design to compare combination treatment to TCAs used alone. Of the three available studies,[30–32] one[30] included fewer than five subjects in each cell and another[31] was restricted to patients with schizoaffective disorder as defined by the authors. That sample was comprised exclusively of patients with Schneiderian first-rank symptoms and included an unquantified portion with DSM-IV schizoaffective disorder. Nevertheless, results agree closely with those of the remaining study[32,33] (Table 2). In both studies, three quarters of those given combination therapy, but slightly less than half given TCA monotherapy, responded.

Clinicians undertaking combination therapy should remember that conventional antipsychotics may interfere with the metabolism of TCAs, substantially raise plasma levels,[34,35] and lengthen the time needed to reach steady state.[35] Because toxicity resulting from excessive TCA

Table 2. Prospective Studies of Tricyclic Antidepressant (TCA) Monotherapy Versus TCA-Antipsychotic Combinations in Psychotic Depression

	Duration of Active Treatment (wk)	TCA Alone			TCA and Antipsychotic		
			Responders			Responders	
		Completers (N)	N	%	Completers (N)	N	%
Brockington et al (1978)[31]	4	13	6	46	12	9	75
Spiker et al (1985)[32]	5	17	7	41	18	14	78

Figure 2. Improvement with Sham Versus Real ECT by Depressive Subtype: Leicester Study*



*Data from reference 44. Abbreviation: HAM-D = Hamilton Rating Scale for Depression.

levels may be confused with the signs and symptoms of depression or psychosis,[36] TCA plasma level monitoring is warranted at both 1 to 2 weeks and at 4 to 6 weeks of combination treatment.

The treating physician should also carefully monitor extrapyramidal symptoms. Stiffness and akathisia can be easily confused with psychomotor retardation and akathisia closely resembles psychomotor agitation.

Potential side effects and the feasibility of blood level monitoring should determine the choice of medicines used in combination treatment. Antipsychotics with prominent anticholinergic effects (i.e., thioridazine, mesoridazine, or chlorpromazine) are poor choices because such effects, as well as orthostatic blood pressure changes, are additive to those of TCAs.

Studies have shown only that TCA monotherapy is relatively ineffective. Two have described placebo response rates of zero for delusional depression. If the 30% placebo response rate generally assumed for nonpsychotic depression is subtracted from the 65%–75% recovery rate associated with active drug treatment, the figure approximates the 40% response rate typically seen for TCA monotherapy in psychotic depression. Thus, true responses to TCA monotherapy may be equally likely in psychotic and nonpsychotic depression. Spiker and Kupfer (1988),[12] in fact, demonstrated statistically significant drug effects for amitriptyline monotherapy in psychotic depression. Moreover, Nelson et al. (1986)[37] described a statistically significant relationship between plasma desipramine levels and response in delusional depression.

Electroconvulsive Therapy

In contrast to TCA or MAOI monotherapy, psychotic features have not been associated with poorer electroconvulsive therapy (ECT) outcomes. Rather, some studies have found that psychotic features are a positive predictor of ECT response.[38–41] Particularly noteworthy are two sham-controlled trials of ECT.[42–44] In these, the procedure for simulated ECT was identical to that for real ECT except that current was not applied. This allowed for double-blind outcome assessments and for control of the potentially powerful placebo effects of the ECT procedure. In both trials, clear outcome differences between real and simulated ECT emerged for delusional depressives. Statistically significant differences were absent for those who lacked both delusions and psychomotor retardation[43] (Figure 2).

Such studies avoid the confounds of simple response predictor studies in which the features associated with placebo response are indistinguishable from those associated with true treatment effects. The association of delusions with a low placebo response would tend to cancel an association with specific responses to treatment. Sham control studies, though, indicate that psychotic depression is a particularly robust indicator for ECT.

The results from the few direct comparisons of ECT and TCA-antipsychotic combination therapy have been inconsistent.[30,45,46] A meta-analysis of physical treatment trials in psychotic depression, however, revealed a strong trend toward a higher effect-size (ES) for ECT (ES = 2.3) than for combination therapy (ES = 1.6).[28] This analysis also noted a higher effect-size for bilateral than for unilateral electrode placement. Findings of Pande et al. (1990)[41] echo this; the superiority of bilateral over unilateral electrode placement was much more obvious for delusional than for nondelusional patients.

While ECT may be particularly efficacious for psychotic depression, the diagnostic caveats mentioned earlier are quite important when ECT is being considered. Both pseudohallucinations and a prior history of unsatisfactory responses to antidepressant treatment are common among patients with somatization disorder or with borderline personality disorder. Because antidepressant nonresponse is a widely accepted indication for ECT, such patients are frequently referred to this modality. While there are no formal studies of ECT in these disorders, in this author's experience any improvements are quite transient

and these patients are much overrepresented among those who claim long-lasting and disabling memory deficits consequent to ECT.

Newer Antidepressants and Antipsychotics

A direct comparison of amoxapine monotherapy and the combination of amitriptyline and perphenazine[47] showed the two treatments to be equally effective. Amoxapine, however, has potent dopamine-receptor blocking properties,[48] and its use entails all of the potential side effects associated with conventional antipsychotics. The advantages of monotherapy are offset by the loss of dosing flexibility.

There has been very little effort to determine the effectiveness of serotonin selective reuptake inhibitor (SSRI) monotherapy in psychotic depression. Recently, though, a four-cell comparison of fluvoxamine plus placebo, fluvoxamine plus haloperidol, desipramine plus placebo, and desipramine plus haloperidol, given to inpatients with psychotic depression over a 6-week trial, showed fluvoxamine alone to be as effective as the combination of desipramine and haloperidol.[49] Surprisingly, fluvoxamine given with haloperidol was only as effective as desipramine alone and was less effective than fluvoxamine alone. The same investigators followed this with a larger, open trial of fluvoxamine monotherapy. In that study, 84% of 57 patients with psychotic depression met response criteria (a final 21-item HAM-D score less than 8) after 6 weeks of treatment with fluvoxamine.[50] Six weeks is longer than the 4 or 5 weeks typical of acute treatment trials, and the authors did not describe time-to-recovery. Nevertheless, dropout rates were quite low (2 of 59 or 3%) and the recovery rate compared favorably with that typically reported for ECT.

At least one group has described a combined SSRI and antipsychotic trial.[51] In this, 73% of 30 patients with mood-congruent psychotic features met the response criteria (50% or greater reduction in HAM-D scores) after 4 weeks of treatment with fluoxetine and perphenazine. There appear to be no other published comparisons of SSRI and TCA therapies, nor of SSRI therapy with and without antipsychotics.

SSRI effects on the dopamine system are apparently complex,[52] and evidence is accumulating that these effects may be clinically important. Reports of akathisia during SSRI therapy[53–55] indicate clinically manifest dopamine blockade in at least some areas, though SSRI-induced akathisia is not accompanied by extrapyramidal symptoms. On the other hand are reports of patients treated with fluoxetine who developed delusions which resolved promptly on discontinuation.[56,57] It is therefore difficult to predict whether additional studies will confirm the efficacy of SSRI monotherapy in psychotic depression. Such trials are clearly warranted, though.

Caveats pertain to the coadministration of SSRIs and antipsychotics as they do to the combination of TCA and antipsychotics. While pharmacokinetic interactions between antipsychotics and SSRIs are not as well characterized as are those between TCAs and SSRIs, such interactions do occur,[58] and antipsychotic levels may be increased by the coadministration of SSRIs. A recent review mentioned, in particular, the potential interactions between conventional antipsychotics and fluoxetine, paroxetine and sertraline, and between clozapine and fluvoxamine.[59]

Atypical Antipsychotics

A number of cases published in the last 5 years have suggested a role for atypical antipsychotics in the management of psychotic depression. The large majority of patients in these reports had bipolar affective disorder with psychotic features. Dwight et al. (1994)[60] used risperidone as the sole treatment for six patients with DSM-III-R schizoaffective disorder, of whom four had a bipolar subtype; risperidone was added to a thymoleptic regimen in two other patients with bipolar schizoaffective disorder. The six with substantial depressive symptoms at the outset experienced reductions in depressive symptoms, but all of the bipolar patients had at least some increase in manic symptoms while taking risperidone. Hillert et al. (1992)[61] successfully treated seven patients with psychotic depressive disorder but those were apparently all unipolar. In contrast, McElroy et al. (1991)[62] included 14 patients with psychotic bipolar disorder in their series of patients treated with clozapine. They specifically mentioned neither antidepressant effects nor any tendency for mania to emerge or worsen. Dassa et al. (1993)[63] presented a single patient with psychotic depression refractory to a variety of drug treatments and to ECT. Discharge took place 2 months after clozapine therapy was begun, and the HAM-D score at that point was 15. Thus, the scant literature so far developed suggests little role for clozapine as an antidepressant, but a possible one for risperidone. The use of risperidone in bipolar illness, though, may be problematic.

Other Therapies

Though lithium enhancement of ongoing antidepressant therapy is perhaps the best studied of the pharmacologic options for treatment-resistant depression, few have described its use in psychotic depression. Nelson and Mazure (1986)[64] reviewed the records of psychotically depressed patients who received ECT or the addition of lithium following unsuccessful treatment with desipramine and a neuroleptic. Eight of 9 bipolar patients, but only 3 of 12 unipolar patients, recovered with lithium enhancement ($p = .003$, Fisher's exact test). Among those with unipolar depression who were given ECT, 9 (60%) of 15 responded, as did 3 (50%) of the 6 unipolar patients who failed to respond to lithium enhancement. These findings suggest that the unipolar/bipolar distinction should be strongly considered in treatment selection when psychotic depression fails to improve with the conventional antidepressant/

antipsychotic regimen. However, other researchers at the same center described lithium enhancement without ongoing antipsychotic therapy.[65] Only 6 (24%) of the 25 patients with psychotic depression had a "marked response" and bipolar patients fared as poorly as unipolar ones.

A high proportion of patients with psychotic depression exhibit hypercortisolemia.[14] High corticosteroid levels have adverse effects on cognitive performance[66] and are suspected to play a key role in the long-term morbidity of psychotic depression.[51,67–69] Several researchers have tested the antidepressant effects of corticosteroid suppression with some success.[70–72] Optimal doses and safeguards have yet to be established, nor have controlled studies been accomplished.

Maintenance Treatment

Intervals between episodes appear to be shorter for patients with psychotic depression.[10,19] This, combined with the likelihood that psychotic features will redevelop in subsequent episodes, makes prophylaxis particularly important. There are no published, controlled trials of prophylaxis in psychotic depression, however. This leaves unanswered the important question of when antipsychotics should be discontinued after symptom resolution. On the one hand, risks for tardive dyskinesia increase substantially with as little as 3 months of lifetime exposure to conventional antipsychotics.[73] On the other hand is the observation of several naturalistic follow-up studies that risks for relapse seem to increase after the elimination of antipsychotics, despite the continuation of antidepressants.[74,75]

One solution to this dilemma is the gradual tapering of antipsychotic during the maintenance of full-dose antidepressant. Family members should be recruited to monitor the early reemergence of depressive symptoms or psychotic features typical of that patient's illness. Early signs are often easily reversed by a return to higher antipsychotic doses. If several trials of discontinuation are unsuccessful, at least the minimum effective dose can be established and cumulative neuroleptic exposure minimized.

Maintenance ECT should be considered when repeated prophylactic efforts fail. Preliminary results from an ongoing study suggest that this approach should come into wider use.[76] Of 7 patients randomly assigned to receive continuation pharmacotherapy after ECT, 3 have relapsed. Of the 12 assigned to ECT, only 1 has relapsed. Maintenance ECT typically begins with weekly treatments. Intervals can be gradually increased, but, as with the downward titration of medications, this should be done only with careful surveillance and the readiness to introduce an additional ECT treatment on short notice.

SUMMARY

Severity, long episodes, and high recurrence all characterize psychotic depression and make treatment selection critical. Two modalities, ECT and the combination of an antipsychotic and a tricyclic antidepressant, have the best documented efficacy, though SSRIs, with or without antipsychotics, show promise. Diagnostic alternatives to psychotic depression should be carefully considered before ECT or combination therapy is undertaken. Also, pharmacokinetic interactions are likely in combination treatment and side effects may be confused with symptoms of psychotic depression. The necessity of antipsychotic therapy in maintenance has not been formally established and must be determined on a case-by-case basis.

Drug names: amitriptyline (Elavil and others), amoxapine (Asendin), chlorpromazine (Thorazine and others), clozapine (Clozaril), desipramine (Norpramin and others), fluoxetine (Prozac), fluvoxamine (Luvox), haloperidol (Haldol and others), mesoridazine (Serentil), paroxetine (Paxil), phenelzine (Nardil), perphenazine (Trilafon), risperidone (Risperdal), sertraline (Zoloft), thioridazine (Mellaril and others).

REFERENCES

1. Perley M, Guze S. Hysteria: the stability and usefulness of clinical criteria. N Engl J Med 1962;266:421–426
2. Zanarini M, Gunderson J, Frankenburg F. Cognitive features of borderline personality disorder. Am J Psychiatry 1990;147:57–63
3. Coryell W, Zimmerman M. Demographic, historical and symptomatic features of the nonmanic psychoses. J Nerv Ment Dis 1986;174:585–592
4. Frances A, Brown R, Kocsis J, et al. Psychotic depression: a separate entity? Am J Psychiatry 1981;138:831–833
5. Coryell W, Pfohl B, Zimmerman M. The clinical and neuroendocrine features of psychotic depression. J Nerv Ment Dis 1984;172:521–528
6. Coryell W, Tsuang M. Major depression with mood-congruent or mood-incongruent psychotic features: outcome after 40 years. Am J Psychiatry 1985;142:479–482
7. Lykouras E, Malliaras D, Christodoulou G, et al. Delusional depression: phenomenology in response to treatment. Acta Psychiatr Scand 1986;73: 324–329
8. Parker G, Hadzi-Pavlovic D, Hickie I, et al. Distinguishing psychotic and nonpsychotic melancholia. J Affect Disord 1991;22:135–148
9. Coryell W, Endicott J, Keller M. The importance of psychotic features to major depression: course and outcome during a 2-year follow-up. Acta Psychiatr Scand 1987;75:78–85
10. Coryell W, Leon A, Winokur G, et al. The importance of psychotic features to long-term course in major depressive disorder. Am J Psychiatry. 1996;153:483–489
11. Brown W, Johnson M, Chen M. Clinical features of depressed patients who do and do not improve with placebo. Psychiatry Res 1992;41:203–214
12. Spiker D, Kupfer D. Placebo response rates in psychotic and nonpsychotic depression. J Affect Disord 1988;14:21–23
13. Glassman A, Roose S. Delusional depression. Arch Gen Psychiatry 1981; 38:424–427
14. Nelson J, Davis J. DST studies in psychotic depression: a meta-analysis. Biol Psychiatry. In press
15. Charney E, Nelson J. Delusional and non-delusional unipolar depression: further evidence for distinct subtypes. Am J Psychiatry 1981;138:328–333
16. Helms P, Smith R. Recurrent psychotic depression. J Affect Disord 1983;5: 51–54
17. Lykouras L, Christodoulou G, Malliaras D, et al. The prognostic importance of delusions in depression: a 6-year prospective follow-up study. J Affect Disord 1994;32:233–238
18. Coryell W, Winokur G, Shea T, et al. The long-term stability of depressive subtypes. Am J Psychiatry 1994;151:199–204
19. Leyton M, Corin E, Martial J, et al. Psychotic symptoms and vulnerability to recurrent major depression. J Affect Disord 1995;33:107–115
20. Hordern A, Holt N, Burt C, et al. Amitriptyline in depressive states. Br J Psychiatry 1963;109:815–825
21. Hordern A, Burt C, Holt N, et al. Depressive States: A Pharmacotherapeutic Study, Springfield, Ill: Charles C. Thomas; 1965:110–112
22. Glassman A, Kantor S, Shostak M. Depression, delusions and drug

response. Am J Psychiatry 1975;132:716–718
23. Nelson J, Bowers M. Delusional unipolar depression: description of drug response. Arch Gen Psychiatry 1978;35:1321–1328
24. Avery D, Lubrano A. Depression treated with imipramine and ECT: the DeCarolis study reconsidered. Am J Psychiatry 1979;136:559–562
25. Chan C, Janicak P, David J, et al. Response of psychotic and nonpsychotic depressed patients to tricyclic antidepressants. J Clin Psychiatry 1987;48: 197–200
26. Kocsis J, Croghan J, Katz M, et al. Response to treatment with antidepressants of patients with severe or moderate nonpsychotic depression and of patients with psychotic depression. Am J Psychiatry 1990;147:621–624
27. Kroessler D. Relative efficacy rates for therapies of delusional depression. Convuls Ther 1985;1:173–182
28. Parker G, Roy K, Hadzi-Pavlovic D, et al. Psychotic (delusional) depression: a meta-analysis of physical treatment. J Affect Disord 1992;24:17–24
29. Janicak PG, Pandey GN, Davis JM, et al. Response of psychotic and nonpsychotic depression to phenelzine. Am J Psychiatry 1988;145:93–95
30. Minter R, Mandel M. The treatment of psychotic major depressive disorder with drugs and electroconvulsive therapy. J Nerv Ment Dis 1979;167: 726–733
31. Brockington I, Kendell R, Tellett M, et al. Trials of lithium, chlorpromazine and amitriptyline in schizoaffective patients. Br J Psychiatry 1978;133: 162–168
32. Spiker DG, Weiss J, Dealy R, et al. The pharmacological treatment of delusional depression. Am J Psychiatry 1985;142:430–436
33. Spiker DG, Perel JM, Hanin I, et al. The pharmacological treatment of delusional depression: Part II. J Clin Psychopharmacol 1986;6:339–342
34. Gram L, Overo K. Drug interaction: inhibitory effect of neuroleptics on metabolism of tricyclic antidepressants in man. BMJ 1972;1:463–465
35. Oliver-Martin R, Marzin D, Buschsenschutz K, et al. Concentrations plasmatiques de l'imipramine et de la desmethylimipramine et effet antidepresseur au cours d'un traitement controls. Psychopharmacologia 1975; 41:187–195
36. Preskorn S, Jerkovich G. Central nervous system toxicity of tricyclic antidepressants: phenomenology, course, risk factors and role of therapeutic drug monitoring. J Clin Psychopharmacol 1990;10:88–95
37. Nelson J, Price L, Jatlow P. Neuroleptic dose and desipramine concentrations during combined treatment of unipolar delusional depression. Am J Psychiatry 1986;143:1151–1154
38. Carney M, Sheffield B. The effects of pulse ECT in neurotic and endogenous depression. Br J Psychiatry 1974;125:91–94
39. Coryell W, Zimmerman M. Outcome following ECT for primary unipolar depression: a test of newly proposed response predictors. Am J Psychiatry 1984;141:862–867
40. Pande A, Krugler T, Haskett R, et al. Predictors of response to electroconvulsive therapy in major depressive disorder. Biol Psychiatry 1988;24: 91–93
41. Pande A, Grunhaus L, Haskett R, et al. Electroconvulsive therapy in delusional and nondelusional depressive disorder. J Affect Disord 1990;19: 215–219
42. Crow T, Deakin J, Johnstone E, et al. Mechanism of action of ECT: relevance of clinical evidence. In: Proceedings of the 13th Collegium Internationale Neuro-Psychopharmacologicum; June 1982; Jerusalem, Israel
43. Brandon S, Cowley P, McDonald C, et al. Electroconvulsive therapy: results in depressive illness from the Liecestershire trial. Br J Med 1984;288: 22–25
44. Buchan H, Johnstone E, McPherson K, et al. Who benefits from electroconvulsive therapy? combined results of the Leicester and Northwick Park Trials. Br J Psychiatry 1992;160:355–359
45. Perry P, Morgan D, Smith R, et al. Treatment of unipolar depression accompanied by delusions. J Affect Disord 1982;4:195–200
46. Khan A, Cohen S, Stowell M, et al. Treatment options in severe psychotic depression. Convuls Ther 1987;3:93–99
47. Anton R, Burch E. Response of psychotic depression subtypes to pharmacotherapy. J Affect Disord 1993;28:125–131
48. Rudorfer M, Golden R, Potter W. Second generation antidepressants. Psychiatr Clin North Am 1984;7:519–535
49. Bellini L, Gasperini M, Gatti F, et al. A double blind study with fluvoxamine vs. desipramine combined with placebo or haloperidol in delusional depression. In: Langer S, Brunello NR, Racagni G, et al, eds. Critical Issues in the Treatment of Affective Disorders. Basel, Switzerland: Karger; 1994
50. Gatti F, Bellini L, Gasperini M, et al. Fluvoxamine alone in the treatment of delusional depression. Am J Psychiatry 1996;153:414–416
51. Rothschild A, Samson J, Bessette M, et al. Efficacy of the combination of fluoxetine and perphenazine in the treatment of psychotic depression. J Clin Psychiatry 1993;54:338–342
52. Arnt J, Overo K, Hyttel J, et al. Changes in rat dopamine and serotonin function in vivo after prolonged administration of the specific 5HT uptake inhibitor, citalopram. Psychopharmacology (Berl) 1984;84:457–465
53. Altshuler L, Pierre J, Wirshing W, et al. Sertraline and akathisia. J Clin Psychopharmacol 1994;14:278–279
54. Rothschild A, Locke C. Reexposure to fluoxetine after serious suicide attempts by three patients: the role of akathisia. J Clin Psychiatry 1991;52: 491–493
55. Lipinski J, Mallya G, Zimmerman P, et al. Fluoxetine induced akathisia: Clinical and theoretical implications. J Clin Psychiatry 1989;50:339–342
56. Mandalos G, Szarek B. Dose–related paranoid reaction associated with fluoxetine. J Nerv Ment Dis 1990;178:57–58
57. Narayan M, Meckler L, Nelson J. Fluoxetine-induced delusions in psychotic depression [letter]. J Clin Psychiatry 1995;56:329
58. Goff D, Midha K, Brotmann A, et al. Elevation of plasma concentrations of haloperidol after the addition of fluoxetine. Am J Psychiatry 1991;148: 790–792
59. Nemeroff C, Lindsay C, Pollock B. Newer antidepressants and the cytochrome P450 system. Am J Psychiatry 1996;153:311–320
60. Dwight M, Keck P, Stanton S, et al. Antidepressant activity and mania associated with risperidone treatment of affective disorder. Lancet 1994;344: 554–555
61. Hillert A, Maier W, Wetzel H, et al. Risperidone in the treatment of disorders with a combined psychotic and depressive syndrome: a functional approach. Pharmacopsychiatry 1992;25:213–217
62. McElroy S, Dessain E, Pope H, et al. Clozapine in the treatment of psychotic mood disorders, schizoaffective disorder, and schizophrenia. J Clin Psychiatry 1991;52:411–414
63. Dassa D, Kaladjian A, Azorin J, et al. Clozapine and the treatment of psychotic refractory depression. Br J Psychiatry 1993;163:822–824
64. Nelson J, Mazure C. Lithium augmentation in psychotic depression refractory to combined drug treatment. Am J Psychiatry 1986;143:363–366
65. Price L, Charney D, Heninger G. Variability of response to lithium augmentation in refractory depression. Am J Psychiatry 1986;143:1387–1392
66. Wolkowitz O, Rus V, Weingartner H, et al. Cognitive effects of corticosteroids. Am J Psychiatry 1990;147:1297–1303
67. Schatzberg A, Rothschild A, Langlais P, et al. A corticosteroid/dopamine hypotheses for psychotic depression and related states. J Psychiatr Res 1985;19:57–64
68. Schatzberg A, Rothschild A. Psychotic (delusional) major depression: should it be included as a distinct syndrome in DSM–IV? Am J Psychiatry 1992;149:773–745
69. Rothschild A, Benes F, Hebben N, et al. Relationships between CT-scanned findings and cortisol in psychotic and nonpsychotic depressed patients. Biol Psychiatry 1989;26:565–575
70. Wolkowitz O, Reus V, Manfredi F, et al. Ketoconazole administration in hypercortisolemic depression. Am J Psychiatry 1993;150:810–812
71. Murphy B, Dahr V, Ghadirian A, et al. Response to steroid suppression in major depression resistant to antidepressant therapy. J Clin Psychopharmacol 1991;11:121–126
72. Thakore J, Dinan T. Cortisol synthesis inhibition: a new treatment strategy for the clinical and endocrine manifestations of depression. Biol Psychiatry 1995;37:364–368
73. Sweet R, Mulsant B, Gupta B, et al. Duration of neurolyptic treatment and prevalence of tardive dyskinesia in late life. Arch Gen Psychiatry 1995;52: 478–486
74. Aronson T, Shukla S, Hoff A. Continuation therapy after ECT for delusional depression: a naturalistic study of prophylactic treatments and relapse. Convuls Ther 1987;3:251–259
75. Lykouras L, Markianos M, Hatzimanolis J, et al. Biogenic amine metabolites in delusional (psychotic) depression and melancholia subtypes of major depression in progress. Neuropsychopharmacology and Biological Psychiatry 1994;18:1261–1271
76. Figiel G, McDonald W, Nemoroff C. A study of continuation ECT versus continuation pharmacotherapy on relapse rates in the depressed elderly following a therapeutic trial of ECT. In: Proceedings of the 34th American College of Neuropsychopharmacology Annual Meeting; Dec 11–15, 1995; San Juan, Puerto Rico