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The Treatment of Psychotic Major Depression: Is There a Role for Adjunctive Psychotherapy?

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Abstract
Background: Psychotic depression is a relatively prevalent mood disorder associated with greater symptom severity, a poorer course of illness and higher levels of functional impairment compared with nonpsychotic depression. Separate lines of investigation suggest that various forms of cognitive-behavioral therapy are efficacious for treating severe forms of nonpsychotic depression as well as primary psychotic disorders. However, there currently are no empirically supported psychotherapies specifically designed for treating psychotic depression. ***Method:*** We review the efficacy of current somatic treatments for the disorder and discuss the limited data to date on potentially useful psychotherapeutic approaches. In particular, we describe the clinical improvement observed in a subgroup of hospitalized patients with psychotic depression treated with Acceptance and Commitment Therapy as part of a larger clinical trial. ***Results:*** Pilot results demonstrated that Acceptance and Commitment Therapy was associated with clinically significant reductions in acute symptom severity and impairment compared with treatment as usual. ***Conclusion:*** The findings suggest that patients with psychotic depression can benefit from psychotherapy. Clinical and research recommendations in this area are presented.

There are several empirically supported biological and psychosocial treatment options currently available for individuals suffering from major depression. However, depression is a heterogeneous condition, and far less research has been conducted on the adaptation of treatments for specific diagnostic subtypes. Population studies estimate that psychotic features (i.e. hallucinations and/or delusions) are present in 14–19% of patients with major depression, giving it a lifetime population prevalence of over 2% [1, 2]. The rates tend to be particularly high in hospitalized depressed patients, with up to 25% meeting criteria for psychotic depression (PD) [3]. In this paper, we review the clinical features of PD and present the preliminary data to date on psychotherapy response in patients with PD. We then briefly discuss research and treatment implications based on current empirical knowledge.

Clinical Features and Course of PD

Patients with PD can be differentiated from those with nonpsychotic depression based on a number of neurobiological and neuropsychological abnormalities, including distinct patterns of structural brain anomalies, hypothalamic-pituitary-adrenocortical axis activity, dopamine and serotonin neurotransmission, and cognitive deficits [4–6]. Other clinical characteristics of PD include greater symptom severity, number of suicide attempts, psycho-

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motor disturbance, psychiatric comorbidity, axis II personality features and functional impairment [3, 7–9]. Compared with nonpsychotic depression, PD is characterized by a longer duration of illness, more frequent hospitalizations and relapses and a greater likelihood of recurrent psychotic symptoms [10–12]. Further, the poorer outcomes in PD have been shown to be independent of initial symptom severity, and patients continue to show poorer outcomes even after acute psychotic symptoms dissipate [12–14]. Research suggests that clinicians often fail to thoroughly assess for psychotic symptoms and patients tend to underreport symptoms due to paranoia or embarrassment [15]. The number of differences between psychotic and nonpsychotic subtypes has led some to argue that PD should be recognized as a unique diagnostic entity [14].

Current Somatic Treatments for PD

Patients with PD show a poorer response to antidepressant treatment with tricyclic or selective serotonin reuptake inhibitor medications alone compared with nonpsychotic depressed individuals [5, 6]. Many authors suggest that antidepressant plus antipsychotic treatment is superior to treatment with either medication alone, although the results have not always been consistent. In a recent Cochrane Systematic Review, Wijkstra et al. [16] concluded that currently there are insufficient data to support the superiority of combined antidepressant and antipsychotic treatment compared to antidepressant monotherapy. Additional evidence suggests that electroconvulsive therapy is an efficacious treatment for PD. Electroconvulsive therapy is at least as effective and in fact may be even more effective than combined antidepressant plus antipsychotic therapy based on results from meta-analyses [5, 17]. However, electroconvulsive therapy and neuroleptic medications have several disadvantages that can limit their effectiveness in clinical practice, including side effects, safety concerns and symptom persistence [5, 17, 18].

Psychotherapy Response in PD

Given the limitations of current somatic treatments for PD, a clear role exists for psychosocial interventions that can be used adjunctively to treat this disorder. In one of the only reports of its kind, Bishop et al. [19] described a case study detailing the successful treatment of a woman with PD who refused to take medications using cognitive therapy. However, we were unable to identify any full-scale clinical trials of psychotherapy specifically for PD. Cognitive behavior therapy (CBT) – a term we use to refer to the family of closely-related cognitive and behavioral interventions – has been found to be efficacious either alone or in combination with medications to treat severe forms of depression [20, 21]. Further, emerging evidence suggests that CBT produces medium effect size gains beyond treatment, as usual for patients with primary psychotic disorders [22, 23]. Although some past research has included small numbers of patients with PD [24], the vast majority of psychotherapy studies have excluded these patients from trials.

There also is a paucity of research investigating whether the poorer outcomes found in patients with psychotic versus nonpsychotic depression apply to treatments that include pharmacotherapy and psychotherapy. Gaudiano et al. [13] recently reported response to combined treatments in patients with PD. The data were pooled from clinical trials in which patients with psychotic and nonpsychotic major depression were provided with efficacious combined therapies (medication plus cognitive, behavioral or family therapies). Although similar in severity during acute hospitalization, patients with PD showed greater depression severity at postoutpatient treatment and at 6-month follow-up. Following treatment, patients with PD were over *4 times* as likely to exhibit severe levels of suicidal ideation and depression. The findings indicated that current state-of-the-art combined treatments may have poorer efficacy in depressed patients with psychotic symptoms, suggesting the need for adapted treatments better tailored to the needs of this population.

Pilot Findings Using an Acceptance-Based Psychotherapy for PD

Treatment Rationale and Description

Feasibility data for the psychosocial treatment of PD can be found in recent research using a brief form of Acceptance and Commitment Therapy (ACT) [25] to treat acutely ill patients with psychotic spectrum disorders. ACT is similar to other emerging behavioral approaches that incorporate acceptance and mindfulness elements, such as dialectical behavior therapy [26]. Preliminary evidence from over 10 preliminary randomized trials suggests the efficacy of ACT for treating a wide variety of problems, including anxiety and substance use disorders [27]. The results from 2 small trials comparing ACT to

traditional CBT in depressed outpatients found that both produced similar improvements in depression by post-treatment, but that ACT resulted in earlier changes in the believability of negative cognitions [27]. Whereas traditional cognitive therapy [28] focuses on directly modifying dysfunctional thought *content* through rational deliberation and guided discovery, ACT focuses on modifying the person's *relationship* to his/her thinking more broadly. The goals of ACT are to promote increased acceptance of unavoidable distress, to cultivate a mindful outlook (i.e. awareness of mental events as products of the mind rather than literal truths), to counteract excessive entanglement with cognitions and to work toward goals that are consistent with patients' personal values to motivate change [25]. To achieve these aims, ACT employs a variety of strategies, including the use of metaphors and stories to communicate treatment concepts and behavioral exercises to increase a person's willingness to contact the discomfort that often accompanies change efforts.

ACT theorizes that psychopathology is largely the result of *experiential avoidance*, which involves the overidentification with and excessive negative evaluation of internal events (e.g. thoughts, emotions, memories), a concomitant unwillingness to experience them, and the resulting efforts made to control or escape from them that can interfere with functioning and lead to behavior inflexibility [27, 29]. From a clinical perspective, patients high in experiential avoidance tend to engage in multiple maladaptive strategies in attempts to remove internal sources of distress, which often lead to increasing social isolation, obsessive rumination, suicidality and thought disturbance. Studies using clinical and nonclinical samples demonstrate that experiential avoidance is strongly correlated with various forms of psychopathology, including depression [29]. Research also suggests that chronic experiential avoidance may produce a paradoxical effect, in that attempts to escape or control unwanted private events may actually increase their frequency or intensity in the long run [30]. The negative effect of avoidance-based coping also has been implicated in psychosis. For example, Tait et al. [31] found that a 'sealing-over' recovery style after acute psychosis predicted several negative outcomes independent of insight into illness. 'Sealing over' is defined as a coping method in which the patients minimize the significance of their psychotic symptoms and are disinterested in exploring aspects of the experience in treatment, which has been shown to predict increased depression and impaired psychosocial functioning independent of the person's insight into illness.

Based on findings from an earlier trial [32], Gaudiano and Herbert [33] tested the efficacy of an ACT in a sample of hospitalized patients with psychotic symptoms, which included PD, schizophrenia, schizoaffective disorder and bipolar disorder. The patients were taught to increase their acceptance of unavoidable distress, to simply notice their psychotic symptoms without treating them as either true or false, and to identify and work toward personally valued goals despite their symptoms [34]. In this pilot trial, 40 patients were randomly assigned to enhanced treatment as usual (ETAU) or ETAU plus individual ACT sessions, the number of which varied based on a patient's length of stay (average 3 sessions). At hospital discharge, patients receiving ACT showed greater improvements in mood symptoms, hallucination-related distress and believability, illness disability and clinically significant change. The groups did not differ in the frequency of psychotic symptoms reported and both groups showed significant decreases from before to after treatment. Although the sample size was only modest, the ACT group had a 38% reduction in rehospitalization rate compared with ETAU alone by 4-month follow-up.

Treatment Response in Patients with PD

As a significant proportion of the sample in the ACT for psychosis study was diagnosed as having PD (ETAU + ACT: n = 9, ETAU only: n = 9): we conducted secondary analyses to investigate whether these patients also benefited from psychotherapy provided during hospitalization. The subsample of patients diagnosed as having PD based on admission diagnosis was 56% female and 78% unmarried. The average age was 40 years old (SD = 12). All participants were African-American (n = 17) or Hispanic (n = 1). In addition, 22% were homeless and 56% were receiving disability compensation. The average length of hospital stay was 9 days (SD = 8) and the patients received an average of 3 ACT sessions. Most graduated high school or had an equivalency diploma (61%).

Descriptive statistics for outcome measures are reported in table 1. Because of the small sample size, we limited our analyses to clinically meaningful outcomes using nonparametric tests. The results indicated that 44% of the PD patients in the ACT group showed clinically significant improvement by discharge ($\geq$2 SD change from before to after treatment) on Brief Psychiatric Rating Scale (BPRS) [35] total scores compared with 0% of the ETAU only group, $\chi^2 = 5.14$, $p < 0.05$. The rates of clinically significant change on BPRS mood symptoms subscale were 70% in the ACT group compared with 30% in the ETAU only group, $\chi^2 = 3.60$, $p = 0.058$. No signifi-

Table 1. Baseline and discharge scores for patients with PD treated in an inpatient hospital setting

	ETAU (n = 9)			ETAU + ACT (n = 9)		
	baseline	discharge	≥2 SD Δ	baseline	discharge	≥2 SD Δ
BPRS (18-item)						
Mood symptom subscale	25.1 ± 1.9	18.7 ± 4.9	3 (33)	27.0 ± 2.1	18.0 ± 4.2	7 (77)
Psychotic symptom subscale	10.0 ± 2.5	8.4 ± 2.3	0 (0)	9.9 ± 3.7	7.2 ± 2.3	1 (11)
Total	55.4 ± 5.0	43.3 ± 6.6	0 (0)	58.0 ± 7.3	42.6 ± 8.0	4 (44)
Self-ratings of hallucinations						
Frequency	5.1 ± 1.6	3.8 ± 1.8		6.0 ± 1.5	4.7 ± 1.9	
Distress	6.3 ± 2.9	7.3 ± 1.7		9.1 ± 1.7	6.7 ± 3.3	
Believability	8.3 ± 1.7	7.6 ± 2.5		8.6 ± 2.6	5.9 ± 4.2	

Values are means ± SD. Figures in parentheses represent the percentage. Clinically significant improvement defined as ≥2 SD change (Δ).

cant differences were found between the rates of clinically significant change on BPRS positive symptoms subscale (p = n.s.).

The patients were asked to rate the frequency (1 = none to 7 = almost constant), believability (0 = none to 10 = total belief) and distress (0 = none to 10 = very severe) associated with their hallucinations using single-item Likert ratings. Mann-Whitney U tests were computed on change scores of hallucination ratings. Pre- to posttreatment improvement in hallucination-related distress was significantly greater in the ACT group (mean = –2.4, SD = 3.3) compared with the ETAU group (mean = 1.0, SD = 2.2), which worsened slightly, $z = 1.97$, $p < 0.05$. Three patients from each condition were rehospitalized over 4-month follow-up.

It is important to note that the pilot trial was not without limitations. First, treatment was delivered in a brief format exclusively while patients were hospitalized. Patients with severe conditions such as PD are likely to benefit from continued treatment and follow-up after discharge. Second, although the results obtained from symptom measures were promising, assessors and hospital staff were not blind to treatment allocation. Third, the number of patients with PD in the sample was relatively small and diagnoses were not based on structured clinical interviews. Finally, although rehospitalization rates were assessed 4 months after discharge, the longer-term effects of the intervention on symptoms and functioning were not assessed. It will be important for future research to evaluate the efficacy of ACT in larger samples of patients with PD using more stringent methodology.

Considerations in the Psychological Treatment of PD

Given their documented and robust success in treating mood and psychotic disorders, CBT-based interventions appear promising for treating PD. However, we recommend caution in inferring that treatments that work well with nonpsychotic depression will be equally effective with PD. As noted, our data suggest that patients with PD respond less well to traditional psychotherapy than those with nonpsychotic depression and thus may require specific adaptations for optimal results [13]. Therefore, the following suggestions should be viewed as tentative and are subject to change based on much needed empirical verification. Although other forms of therapy may also prove efficacious (e.g. family therapy), we limit the current discussion to CBT approaches.

How Should Therapy Be Adapted?

Although a variety of common CBT techniques (e.g. cognitive restructuring, behavioral activation, problem solving, anxiety management techniques) may prove useful for treating PD, adaptations may be necessary. For example, the therapist should proceed cautiously and tentatively with the cognitive restructuring element of traditional cognitive therapy when treating psychotic in contrast to nonpsychotic depression. Pursuing disputation strategies too early or vigorously can alienate the patient and cause premature termination [36]. One potential advantage of acceptance-based models of CBT such as ACT is that they focus more on increasing acceptance of internal distress than altering putatively dysfunctional

thinking patterns to promote behavior change. The two pilot studies of ACT for psychotic inpatients suggest that acceptance techniques targeting psychotic symptoms can be used with the majority of patients in the first session [32, 33]. However, when employed during less acute periods of illness, traditional cognitive restructuring techniques may help the patient to develop skills in identifying and countering residual symptoms of psychosis to prevent more severe relapses [36]. In addition, it is important to consider potential cognitive deficits and limitations, which frequently are problems in PD [5]. The therapist can help mitigate this issue by focusing more on concrete behavioral goals and strategies when dealing with severely ill patients. The therapist can further tailor treatments for patients with cognitive limitations by explaining treatment concepts using simpler language (e.g. use of metaphors and stories in ACT), reviewing session information frequently and providing visual aids and patient handouts/workbooks.

Should Therapy Be Delivered Sequentially or Concurrently?

Some may argue that patients hospitalized with PD will be too severely ill to benefit from 'talk' therapy. However, available research indicates that acutely ill patients with severe mood and psychotic disorders can in fact benefit from adjunctive psychosocial interventions [21, 22]. During our research, we found it appropriate to begin therapy with most hospitalized patients when they were able to participate in other group therapy on the unit after initial psychiatric stabilization with medications. It is important to emphasize that psychiatric stabilization also is required for informed consent. Also, psychotherapy should be provided only after consultation with the patient's treating medical team. Regarding the treatment of outpatients, review of the literature suggests that concurrent pharmacotherapy and psychotherapy is appropriate for most patients [21], again assuming close consultation with the treating psychiatrist. Further, it is important for the therapist to provide a therapeutic rationale that does not undermine the other somatic treatments that the patient may be receiving. For patients with severe mental illnesses, a diathesis-stress model of illness can be used to acknowledge the role of genetic and neurobiological factors, yet account for environmental influences (e.g. stressors, learning history) and other psychological processes (e.g. experiential avoidance) affecting the patient's course of illness [36]. A sequential approach also could be considered [37]. After acute psychotic symptoms dissipate and antipsychotic medication is withdrawn, psychotherapy can be instated to help patients monitor residual symptoms and to learn to cope more effectively with stressors to prevent symptom reoccurrence. Moreover, sequential treatment with mindfulness-based CBT has been shown to reduce relapse rates in those at high risk (i.e. with multiple past depressive episodes) [38] and therefore may prove useful for those with PD, given the recurrent nature of the disorder.

What Level of Therapist Skill Is Necessary?

An additional consideration is the level of therapist skill necessary for treating patients with PD. Although many therapists may feel quite comfortable treating depression, they may lack experience treating severely ill populations, including those experiencing psychosis. Some researchers are beginning to address this issue. A recent study demonstrated that CBT for psychosis could be effectively provided by psychiatric nurses receiving minimal training [39]. Seminars and workshops on CBT for severely ill populations are frequently offered at professional conferences such as the annual meeting of the Association for Behavioral and Cognitive Therapies. We recommend that a therapist with experience treating patients using CBT for depression seek out additional training first and then obtain supervision from an experienced professional familiar with these issues for initial cases.

What Potential Problems Should Be Anticipated?

Patients with PD are 2–5 times more likely to have a history of suicide attempts [2]. Ongoing assessment and monitoring of suicidality constitutes an important component of treatment. Further, the therapist and patient should collaborate to develop a mutually agreed upon safety plan detailing actions to be taken in response to increased suicidal ideation. In addition, nonadherence to medication and other treatments is a frequent problem in PD [15]. The therapist should routinely monitor the patient's level of adherence to pharmacotherapy and psychotherapy. The therapist can help the patient problem solve issues surrounding medication management and promote closer consultation with the treating psychiatrist. Also, the involvement of a significant other to improve treatment adherence is a commonly used strategy in behavioral interventions. We have found it useful to hold 1 or 2 joint sessions with significant others (e.g. spouse, parent, sibling) to discuss ways in which the family can support the patient's treatment goals.

Are There Any Contraindications?

We found the ACT intervention to be generally well tolerated by patients and supported by hospital staff. However, we recommend caution when using formal, intensive meditation techniques with acutely ill psychotic patients, as some case reports suggest that intensive meditation may exacerbate psychosis [40]. ACT employs a number of nonmeditation-based exercises that foster mindfulness using alternative techniques [34]. Further, patients with PD may experience periods of acute illness that can make it difficult to proceed with the therapy. Therapy can be suspended until the patient is stabilized. During these periods, the therapist can collaborate with other providers to assess and monitor the patient to determine the need for hospitalization. Finally, we recommend tailoring therapy to patient severity so as not to overwhelm the individual with treatment goals and strategies. For example, the typical 1-hour session may be divided into 2 half-hour sessions during hospitalization or periods of acute illness.

Considerations for Future Research

As the previous review highlights, there is an urgent need to conduct systematic research on the psychosocial treatment of PD. We believe that CBT-based interventions, including newer acceptance-based approaches, are good candidates for further testing. As pharmacotherapy is considered the first-line treatment for PD, studies should first examine whether combined pharmacotherapy and psychotherapy result in better outcomes than pharmacotherapy alone. If this can be confirmed, further research should be conducted to examine the possible mechanisms of action of effective psychological treatments for PD. As PD is likely to be most prevalent in acutely ill samples, study designs that focus on the recruitment of patients initially hospitalized may aid in enrollment efforts. However, ethical issues become even more salient when dealing with hospitalized patients, and protocol safeguards are necessary to ensure informed consent. Structured clinical interviews administered by trained diagnosticians should be used to assess patients for study inclusion, as PD is often difficult to differentially diagnose. In addition, recent research suggests that the BPRS is a psychometrically sound instrument that has good sensitivity and specificity for assessing PD [41]. Finally, it will be important for studies to employ a range of outcome measures (e.g. symptom severity, psychosocial functioning, treatment adherence, long-term outcomes) that assess clinically (in addition to statistically) significant improvement in order to determine the potential benefits of psychotherapy for PD.

Conclusion

Adjunctive, psychosocial treatments for patients with PD are urgently needed due to the increased risk of morbidity and mortality associated with this population. Unfortunately, treatment development in this area currently is lacking, as patients with psychotic features have been excluded historically from psychotherapy trials of depression. Our pilot data suggest that patients with PD can benefit from modified CBT approaches. However, further research is needed to develop comprehensive adjunctive approaches for treating patients during all phases of illness.

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