Impaired Insight Into Delusions Predicts Treatment Outcome During a Randomized Controlled Trial for Psychotic Depression (STOP-PD Study)

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ABSTRACT

Background: Insight into delusional beliefs varies in patients with major depressive disorder (MDD) with psychotic features ("psychotic depression"). The relationship between impaired insight and illness severity and its impact on treatment outcomes has not been studied in psychotic depression. As such, the aim of this analysis was to explore the relationship among impaired insight, patient characteristics (ie, illness severity, cognition, suicidality, and social functioning), and treatment outcome (ie, remission) during acute treatment of psychotic depression.

Method: This secondary analysis is based on the data from the Study of Pharmacotherapy for Psychotic Depression (STOP-PD) in which 259 participants meeting *DSM-IV* criteria for MDD with psychotic features enrolled between December 2002 and June 2007 (including 142 aged ≥ 60 years) in a 4-center, 12- week, double-blind, randomized controlled trial funded by the US National Institutes of Health. Insight into delusions was assessed using the Delusion Assessment Scale (DAS). The primary outcomes were the predictive utility of insight into illness (ie, Hamilton Depression Rating Scale [HDRS] insight item) and insight into delusions (conviction factor derived from the DAS) on final treatment outcome at 12 weeks of treatment (ie, full remission, partial remission, and nonremission).

Results: At baseline, impaired insight into delusions was positively associated with illness severity (HDRS-16 which excluded the insight item, $r = 0.15$, $P = .016$) and negatively correlated with measures of cognition ($P < .05$). Improvement in insight was not associated with changes in cognition, suicidality, or social functioning after adjusting for covariates. Independent of the severity of depression or psychosis, impaired insight into delusions at baseline ($\chi^2 = 11.65$, $P = .020$) and after 3 ($\chi^2 = 9.62$, $P = .047$), 6 ($\chi^2 = 6.97$, $P = .031$), and 8 ($\chi^2 = 9.08$, $P = .011$) weeks of treatment predicted remission at the end of the trial.

Conclusions: Impaired insight into delusions appears to be an independent predictor of remission in MDD with psychotic features during acute treatment, suggesting that more attention should be paid to this symptom. Longitudinal studies are required to determine the impact of impaired insight into delusions on long-term outcomes, including relapse.

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Psychotic features are common (15%–20%) in major depressive disorder (MDD) and are associated with poorer short-term outcomes and greater mortality than nonpsychotic depression.[1–5] Patients with MDD with psychotic features ("psychotic depression") experience varying degrees of insight into their illness, symptoms, and need for treatment.[6–9] The study of insight has primarily focused on patients with schizophrenia in whom impaired insight contributes to poor outcomes, including treatment nonadherence, heightened risk of violence, poorer functioning, and possibly suicide.[10]

As a construct, insight has been understood as existing on a continuum and generally comprising several dimensions including illness awareness, symptom awareness, and awareness of the need for treatment.[11] Research on insight in mood disorders, and to an even greater degree in psychotic depression, is scant. Some consensus exists in the literature that insight is less impaired in patients with psychotic depression than in those with bipolar disorder or schizophrenia.[7–9] To our knowledge, the clinical impact of impaired insight in psychotic depression has not yet been studied.

In psychotic depression, impaired insight may simply represent greater symptom severity (ie, worse depression or psychosis) or a distinct phenomenon independent of illness severity. Impaired insight may also reflect cognitive deficits (eg, executive dysfunction).[12] Further, it may have an impact on key outcomes in addition to psychopathology, including cognition, suicidality, and social functioning. As such, we analyzed the database of a 12-week randomized controlled trial[13] in psychotic depression. We had 3 major aims: (1) to explore the relationships at baseline between impaired insight into being depressed or having delusions and participants' characteristics (ie, demographics, illness severity, cognition, suicidality, and social functioning); (2) to measure the degree to which changes in impaired insight into delusions are associated with changes in these characteristics during the 12 weeks of treatment; and (3) to assess whether impaired insight into being depressed or having delusions at baseline and during treatment predicts remission of psychotic depression after 12 weeks of treatment.

METHOD

This analysis is based on data from the Study of Pharmacotherapy for Psychotic Depression (STOP-PD), a relatively large (N = 259), 4-center, 12-week, double-blind, randomized controlled trial designed to compare remission rates of psychotic depression in those treated with a combination of atypical antipsychotic medication plus

a serotonin reuptake inhibitor versus those treated with antipsychotic monotherapy, the methodology of which is described in detail elsewhere.[13]

Participants

Patients were aged ≥ 18 years with moderately severe to severe depression (score ≥ 21 on the 17-item Hamilton Depression Rating Scale [HDRS-17][14]), admitted to the inpatient or ambulatory services of 4 academic sites between December 2002 and June 2007. Participants met *DSM-IV*[15] criteria for (nonbipolar) MDD with psychotic features as assessed with the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders.[16] Inclusion also required the presence of at least 1 delusional belief (a fixed idea that was held contrary to the laws of logic), a score of 2 or higher on 1 of the conviction items of the Delusion Assessment Scale (DAS),[17] and a score of 3 or higher on the delusion severity rating item of the Schedule for Affective Disorders and Schizophrenia (SADS).[18] A SADS delusion severity score of 3 is assigned when there is no more than a transient ability to consider the implausibility of an irrational belief.[13] All participants or their substitute decision-makers provided written informed consent prior to initiation of any study procedures.

Study Assessments

Baseline assessments were completed within 7 days of obtaining consent. Follow-up research assessments were conducted weekly for the first 6 weeks and then every other week until week 12 or termination. For this analysis, overall symptom severity was measured with the HDRS-16: HDRS-17 minus the insight item.[14] Severity of psychosis was measured with the 3-item Brief Psychiatric Rating Scale (BPRS) psychosis subscale (ie, unusual thought content, hallucinatory behavior, and suspiciousness).[19] Categorical treatment outcome (ie, full remission, partial remission, and nonremission) was defined as in the original report of STOP-PD (ie, remission requires resolution of both depressive and psychotic symptoms).[13] Global cognition was assessed with the Mini-Mental State Examination (MMSE),[20] and executive function was assessed with the raw scores from the Stroop Interference task[21] and the Dementia Rating Scale-2 (DRS) initiation/perseveration task.[22] Suicidality was assessed with the Scale for Suicide Ideation (SSI),[23] and social functioning was assessed with the 36-item Short-Form Health Survey (SF-36) Social Functioning scale.[24]

We assessed 2 dimensions of insight. First, insight into the presence of depression was assessed using the HDRS insight item, which is scored on a 3-point scale: 0 = any recognition of depressive symptoms; 1 = denies illness, but accepts possibility of being ill; 2 = complete denial of having any illness. Second, insight into delusions was assessed using the DAS.[17] For this analysis, our measure of delusional conviction (score range: 3–9) was based on a factor analysis of the DAS[17] that identified a "conviction factor" comprising 4 items: subjective feeling of certainty, temporal pressure during the interview, acting irrationally distrustful during the interview, and accommodation (ie, being unable to accommodate to the interviewer's confrontation with alternative explanations), with each item having a score of 1, 2, or 3. For instance, for the subjective feeling of certainty item, a score of 1 corresponds to being uncertain of one's thought content or recognizing it as delusional; 2 corresponds to being able to briefly consider that the belief may not be valid, but returning to full conviction; and 3 indicates being completely certain about the veracity of one's delusions. Given that the accommodation item was administered to only 206 of the 250 participants, and that the delusional conviction measures with and without the accommodation item are highly correlated ($r = 0.96$, n = 206, $P < .001$), for this analysis, the delusional conviction measure does not include the accommodation item and is based on the 3 other items of the conviction factor. Using this delusional conviction measure, we defined absent or minimal insight impairment as a score of 3–4, moderately impaired insight as a score of 5–6, and severely impaired insight as a score ≥ 7. As part of the STOP-PD protocol, if a participant's delusions were rated as having completely resolved, the DAS was not completed. Thus, in the absence of delusions, we assigned the lowest possible score (ie, 3) to the measure of delusional conviction.

Clinical Points

- Insight into delusions appears to be an independent predictor of treatment outcome in psychotic depression to which clinicians should pay more attention.
- Improvement of insight into delusions was significantly associated with improvement in the severity of depression and psychosis.
- By week 12 of treatment, 91% of participants had regained full insight into delusions or had minimal insight impairment.
- In psychotic depression, similar to schizophrenia, the association between measures of cognition (ie, global cognition and executive function) and insight into delusions are modest.

Statistical Analysis

Relationships at baseline between impaired insight into depression or delusions and participants' characteristics. Pearson correlations, χ^2 tests, and multinomial logistic regressions were used where appropriate to evaluate the baseline associations between impaired insight into depression (HDRS insight item) or insight into delusions (delusional conviction) and other measures, including illness severity, cognition, suicidality, and social impairment. Then, clinical and demographic variables were entered into a multiple linear regression to determine the best predictors of impaired insight into delusions at baseline as assessed by the delusional conviction measure. Variables were entered in the following order: HDRS-16, BPRS psychosis subscale, MMSE, DRS initiation/perseveration, Stroop interference task, duration of current depressive episode, age, gender, and race (see Table 3). The significance level for tests was established at $P \leq .05$.

Table 1. Baseline Relationship Between Impaired Insight Into Depression or Delusions and Participants' Characteristics

	All Patients (N = 259)	HDRS Insight Item		Delusional Conviction[a]	
		χ^2_2	*P* value	Statistic	*P* Value
Female:male	166:93[b]	0.27[c]	.875	$z = -1.29$[d]	.196
Age, mean (SD), y; % ≥ 60 y	58 (17.7); 54.8%	6.26	.044*	$r = 0.21$	.001**
Education, mean (SD), y	12.5 (3.4)	5.63	.060	$r = -0.05$	.470
Duration of current episode, mean (SD), mo	11.9 (25.4)	0.75	.688	$r = -0.04$	.504
Test score, mean (SD)					
HDRS insight item				$\chi^2_2 = 32.05$	< .001**
Delusional conviction[a]	5.5 (1.3)	32.05	< .001**		
HDRS-16	29.5 (5.2)	4.68	.097	$r = 0.15$	.016*
BPRS psychosis subscale[e]	13.0 (4.3)	3.37	.186	$r = 0.02$	.762
MMSE	26.9 (3.1)	10.39	.006**	$r = -0.14$	.026*
Stroop interference task[f]	24.9 (19.9)	4.19	.123	$r = -0.20$	.002**
DRS initiation/perseveration[f]	32.0 (5.3)	6.06	.048*	$r = -0.16$	.014*
Scale for Suicide Ideation	6.2 (8.9)	1.07	.585	$r = -0.05$	.445
SF-36–social impairment	41.7 (31.2)	8.46	.015*	$r = -0.05$	.928

[a]Score of the following 3 items of the Delusion Assessment Scale: subjective feeling of certainty, temporal pressure during interview, and acting irrationally distrustful during the interview.
[b]Value represents ratio.
[c]For the female:male ratio, the statistic is Pearson χ^2; for all other variables, the statistics in this column are likelihood ratio χ^2.
[d]Mann-Whitney *U* test.
[e]Score of the following 3 items of the BPRS: unusual thought content, hallucinatory behavior, and suspiciousness.
[f]Raw scores.
*$P < .05$. **$P < .01$.
Abbreviations: BPRS = Brief Psychiatric Rating Scale, DRS = Dementia Rating Scale-2, HDRS = Hamilton Depression Rating Scale, HDRS-16 = Hamilton Depression Rating Scale-17 item scale excluding the insight item, MMSE = Mini-Mental State Examination, SF-36 = 36-item Short-Form Health Survey.

Table 2. Baseline Comparison Between Participants With Good Versus Impaired Insight Into Depression

	Total Sample (N = 259)	HDRS Good Insight[a] (n = 199)	HDRS Impaired Insight[b] (n = 60)	*t* Value	*P* Value
Female:male[c]	166:93	126:73	40:20	0.23[c]	.635
Age, mean (SD), y; % ≥ 60 y	58 (17.7), 54.8%	56.5 (17.2), 50.8%	62.6 (18.6), 68.3%	−2.35	.020*
Education, mean (SD), y	12.5 (3.4)	12.8 (3.4)	11.6 (3.4)	2.39	.017*
Duration of current episode, mean (SD), mo	11.9 (25.4)	11.1 (23.9)	14.4 (29.7)	−0.88	.380
Test score, mean (SD)					
Delusional conviction[d]	5.5 (1.3)	5.3 (1.2)	6.2 (1.3)	−5.24	< .001**
HDRS-16	29.5 (5.2)	29.7 (5.4)	29.9 (4.8)	−0.21	.837
BPRS psychosis subscale[e]	13.0 (4.3)	13.0 (4.5)	13.2 (3.6)	−0.31	.758
MMSE	26.9 (3.1)	27.3 (2.8)	25.7 (3.5)	3.44	.001**
Stroop interference task[f]	24.9 (19.9)	25.7 (11.5)	22.0 (11.4)	2.01	.046*
DRS initiation/perseveration[f]	32.0 (5.3)	32.3 (5.1)	30.9 (5.8)	1.68	.094
Scale for Suicide Ideation	6.2 (8.9)	6.3 (8.9)	6.1 (9.0)	0.12	.902
SF-36–social impairment	41.7 (31.2)	28.1 (22.2)	39.5 (29.4)	−3.00	.003**

[a]HDRS item 17 score = 0.
[b]HDRS item 17 score = 1 or 2.
[c]Values represent ratio, not mean (SD), and statistic represents chi-square (χ^2).
[d]Score of the following 3 items of the Delusion Assessment Scale: subjective feeling of certainty, temporal pressure during interview, and acting irrationally distrustful during the interview.
[e]Score of the following 3 items of the BPRS: unusual thought content, hallucinatory behavior, and suspiciousness.
[f]Raw scores.
*$P < .05$. **$P < .004$ after Bonferonni correction for multiple testing (.05/12).
Abbreviations: BPRS = Brief Psychiatric Rating Scale, DRS = Dementia Rating Scale-2, HDRS = Hamilton Depression Rating Scale, HDRS-16 = Hamilton Depression Rating Scale-17 item excluding the insight item, MMSE = Mini-Mental State Examination, SF-36 = 36-item Short-Form Health Survey.

Relationship between change in insight into delusions and other clinical characteristics over 12 weeks of treatment. First, an analysis of variance (ANOVA) was performed to determine any effect of treatment group (ie, olanzapine + sertraline versus olanzapine + placebo) on changes in the delusional conviction scores over time. Since no effect was detected, treatment group was not considered in other analyses. To assess how insight into delusions changes in relation to various clinical characteristics, the generalized estimating equations (GEE) method[25] was used to assess the relationship between delusional conviction and outcome measures at different time points (weeks 1–6, 8, 10, and 12). The GEE generates a β-coefficient that represents the amount of change in the outcome variable (eg, HDRS-16 or SSI) for every 1 unit change in the predictor variable (ie, delusional conviction score). The same analysis was performed adjusting for the covariates age, gender, race, education, and duration of current episode, and also the

Table 3. Regression Analysis to Identify the Predictors of Impaired Insight Into Delusions at Baseline

Predictors of Delusional Conviction[a]	β	*P* Value	Semipartial Correlation	R^2	R^2 Change	*F*	*P* Value
HDRS-16	0.083	.237	0.08	0.012	0.012	2.58	.110
BPRS psychosis subscale[b]	0.020	.794	0.02	0.012	0.000	0.02	.887
MMSE	−0.027	.720	−0.02	0.026	0.014	3.09	.080
Stroop interference task[c]	−0.109	.221	−0.08	0.066	0.018	3.99	.047*
DRS initiation/perseveration[c]	−0.096	.230	−0.08	0.048	0.023	5.10	.025*
Duration (mo) of current episode	−0.055	.420	−0.05	0.070	0.003	0.80	.373
Age	0.093	.295	0.07	0.072	0.003	0.59	.443
Gender	−0.093	.175	−0.09	0.079	0.007	1.56	.213
Race	0.076	.275	0.07	0.084	0.005	1.20	.275

[a]Score of the following 3 items of the Delusion Assessment Scale: subjective feeling of certainty, temporal pressure during interview, and acting irrationally distrustful during interview.
[b]Score of the following 3 items of the BPRS: unusual thought content, hallucinatory behavior, and suspiciousness.
[c]Raw scores.
*$P \leq .05$.
Abbreviations: BPRS = Brief Psychiatric Rating Scale, DRS = Dementia Rating Scale-2, HDRS-16 = Hamilton Depression Rating Scale-17 item excluding the insight item, MMSE = Mini-Mental State Examination.

HDRS-16 and BPRS psychosis subscale, if these were not the outcome variables of interest.

Predictive value of impaired insight at baseline and during treatment on remission at 12 weeks. Multinomial logistic regression analyses were performed at baseline and each week of treatment to determine the predictive value of insight into depression (HDRS insight item) and delusions (delusional conviction) on final treatment outcome (ie, full remission, partial remission, and nonremission). The same analysis was performed adjusting for measures of illness severity (ie, HDRS-16 and BPRS psychosis subscale). The significance level for tests was established at $P \leq .05$.

RESULTS

Relationships at Baseline Between Impaired Insight Into Depression or Delusions and Participants' Characteristics

Tables 1 and 2 present participants' demographic and clinical characteristics and the relationship between these characteristics and impaired insight into depression (HDRS insight item) or delusions (delusional conviction) at baseline. Both impaired insight into depression and delusions were positively associated with age and negatively associated with measures of cognition in univariate analyses. In the regression analysis (Table 3), only the DRS initiation/perseveration score and the Stroop interference task explained a significant proportion of the variance of baseline insight into delusions, even after controlling for illness severity. These cognitive variables, however, were not independent of other variables entered in the model.

Relationship Between Change in Insight Into Delusions and Other Clinical Characteristics

There was no effect of treatment group on improvement in insight into delusions, as assessed with the delusional conviction measure (olanzapine + placebo versus olanzapine + sertraline, $F = 1.52$, $P = .139$) even after adjusting for severity of depression, as measured with the HDRS-16 ($F = 1.23$, $P = .273$), or psychosis, as measured with the BPRS psychosis subscale ($F = 1.45$, $P = .160$).

Figure 1 presents the distribution of participants' insight into depression and insight into delusions during the 12 weeks of treatment. Most participants (77%) demonstrated good insight into their depression at the beginning of treatment, and nearly all participants (99%) had good insight into depression by week 12 of treatment (Figure 1A). By contrast, at baseline, 25% of participants had absent or minimal insight impairment into their delusions (Figure 1B). By week 12, most participants had regained insight into their delusional beliefs: 91% had absent or minimal insight impairment (Figure 1B).

The GEE analysis showed that improvement of insight into delusions was significantly associated with improvement in HDRS-16 total score and BPRS psychosis subscale score (Table 4). However, changes in insight into delusions were not significantly associated with changes in cognition, suicide, or social functioning after adjusting for covariates.

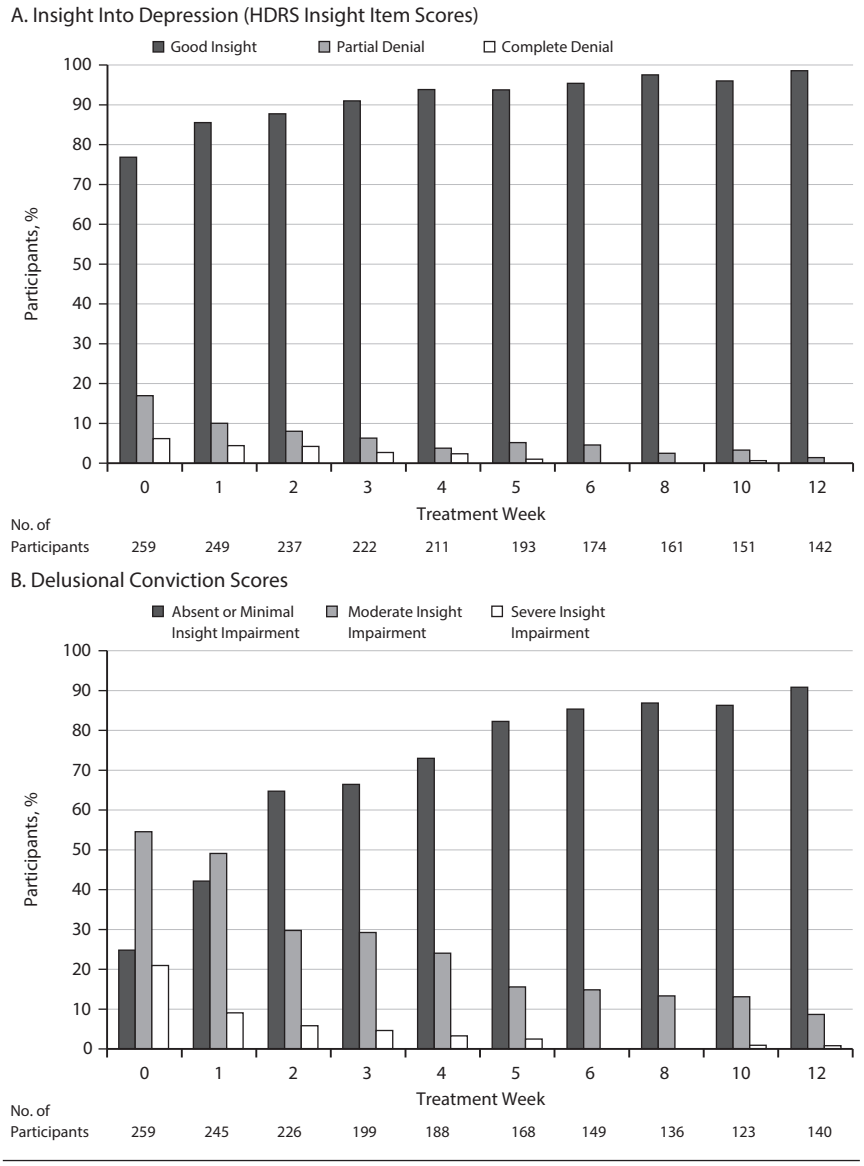
Predictive Value of Impaired Insight at Baseline and During Treatment on Remission at 12 Weeks

Insight into depression (HDRS insight item) at any week did not predict final remission status (Table 5). Insight into delusions at baseline and at each week of treatment (with the exception of week 1) predicted final remission status. After controlling for illness severity (HDRS-16 and BPRS psychosis subscale), insight into delusions at baseline and weeks 3, 6, and 8 still predicted final remission status.

DISCUSSION

Insight has been studied mostly in patients with schizophrenia. To our knowledge, this is the first study to explore the relationships over time among impaired insight, clinical characteristics, and treatment outcome in MDD with psychotic features ("psychotic depression"). Most participants had good insight into the fact they were depressed (Figure 1A), but at baseline lacked insight into their delusions (Figure 1B). The recognition by patients with psychotic depression

Figure 1. Distribution Scores During 12 Weeks of Treatment



of the presence of a mental illness (ie, their depression) distinguishes them from those with schizophrenia who tend to deny the presence of any illness during the acute phase.[8] Patients who had impaired insight into having depression were older, had fewer years of education, greater global cognitive dysfunction, and greater social impairment (Table 2).

All STOP-PD participants were treated with olanzapine. While the addition of sertraline was associated with improvement in depressive symptoms beyond what was observed with placebo,[13] insight into delusions improved similarly in patients taking sertraline or placebo. Our finding that insight into delusions improves during treatment as both depression and psychosis improve is consistent with similar analyses in patients with schizophrenia. For example, in the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), insight and illness severity were strongly associated during an 18-month follow-up period.[26]

In cross-sectional studies of schizophrenia, impaired insight is also typically associated with executive dysfunction (eg, performance on the Wisconsin Card Sorting Test [WCST]) and perseverative errors.[27–29] Similarly, in our study, impaired insight into delusions was associated with measures of executive function at baseline even after controlling for severity of depression and psychosis. The modest size of the relationship we observed appears to be similar to the size of this relationship in schizophrenia. In a recent meta-analysis,[30] insight into psychosis was correlated with global cognition ($r = 0.16$) and executive function ($r = 0.14$). By comparison, in our sample, insight into delusions was associated with global cognition (MMSE, $r = 0.14$) and measures of executive function (Stroop interference task, $r = 0.20$; DRS initiation/perseveration score, $r = 0.16$).

There is considerable debate in the schizophrenia literature regarding the relationship between insight and depressive symptoms, and the influence of insight on

Table 4. Relationship[a] Between Change in Insight Into Delusions and Other Clinical Characteristics Over 12 Weeks of Treatment

	Delusional Conviction[b]		After Adj for Covariates[c]	
Test Score	β	*P* Value	β	*P* Value
HDRS-16	0.06	<.0001[d]	0.06	<.0001[e]
BPRS psychosis subscale[f]	0.12	<.0001[d]	0.10	<.0001[e]
MMSE	−0.05	.007[d]	−0.01	.628
Stroop interference task[g]	−0.01	.011	−0.00	.523
DRS initiation/perseveration[g]	−0.03	.009[d]	−0.02	.227
Scale for Suicide Ideation	0.02	<.0001[d]	−0.01	.282
SF-36–social impairment	−0.00	.103	−0.00	.999

[a]β Coefficient representing the amount of change in the outcome variable (eg, HDRS-16 score) for every 1 unit change in the predictor variable (ie, delusional conviction score) over time.
[b]Score of the following 3 items of the Delusion Assessment Scale: subjective feeling of certainty, temporal pressure during interview, and acting irrationally distrustful during interview.
[c]Age, gender, race, education, duration of current episode, HDRS-16 (excluding the insight item), and BPRS psychotic subscale.
[d]β Coefficient significant.
[e]β Coefficient remained significant after adjusting for covariates.
[f]Score of the following 3 items of the BPRS: unusual thought content, hallucinatory behavior, and suspiciousness.
[g]Raw scores.
Abbreviations: BPRS = Brief Psychiatric Rating Scale, DRS = Dementia Rating Scale-2, HDRS-16 = Hamilton Depression Rating Scale-17 item excluding the insight item, MMSE = Mini-Mental State Examination, SF-36 = 36-item Short-Form Health Survey.

Table 5. Predictive Value of Impaired Insight at Baseline and During Treatment on Remission at 12 Weeks

Predictor	χ^2	*P* Value	χ^2 After Adjusting for Illness Severity[a]	*P* Value
HDRS insight item				
Baseline	1.50	.826	2.49	.647
Week 1	4.54	.337	3.66	.454
Week 2	8.87	.065	8.32	.080
Week 3	2.97	.564	4.59	.332
Week 4	4.70	.320	3.89	.422
Week 5	6.88	.143	3.85	.427
Week 6	2.17	.338	0.82	.664
Week 8	1.12	.570	0.60	.742
Week 10	2.90	.575	3.91	.418
Week 12	2.27	.322	0.03	.984
Delusional conviction[b]				
Baseline	11.92	.018*	11.65	.020*
Week 1	8.06	.089	2.25	.691
Week 2	19.81	.001*	4.31	.365
Week 3	29.72	<.001*	9.62	.047*
Week 4	25.28	<.001*	4.46	.348
Week 5	18.26	.001*	2.66	.617
Week 6	29.72	.001*	6.97	.031*
Week 8	31.03	<.001*	9.08	.011*
Week 10	25.79	<.001*	6.50	.165
Week 12	29.31	<.001*	10.62	.031*

[a]HDRS-16 and BPRS psychosis subscale.
[b]Score of the following 3 items of the Delusion Assessment Scale: subjective feeling of certainty, temporal pressure during interview, and acting irrationally distrustful during interview.
*$P \leq .05$.
Abbreviations: BPRS = Brief Psychiatric Rating Scale, HDRS = Hamilton Depression Rating Scale.

suicidal behavior.[31] Some have found no association between insight and suicide,[32] while others have suggested that poor insight may be associated with increased suicide risk.[10] Finally, others have found that improved insight leads to depression and an increased risk for suicide, particularly in younger patients.[33,34] In STOP-PD, we found a clear positive relationship between improvement in depression, psychosis, and insight into delusions with no association between insight into depression or delusions and suicide, either at baseline or during the acute phase of treatment for psychotic depression.

In psychotic disorders, such as schizophrenia, impaired insight is associated with medication nonadherence and poor treatment outcomes.[10] However, the literature has emphasized that impaired insight is less prevalent and possibly less impactful in patients with major depression than in those with other major mental illnesses, such as schizophrenia or bipolar disorder.[6–9] In this context, we believe our main finding is that impaired insight into delusions both at baseline and during the course of acute treatment predicted remission of psychotic depression after 12 weeks of treatment. This suggests that clinicians should pay more attention to this symptom.

To our knowledge, this is the first analysis of insight in psychotic depression. Thus, it is a hypothesis-generating paper rather than a paper confirming a priori hypotheses, and our results require confirmation. Our study had several other limitations. While our measure of insight into delusions is based in part on a factor analysis and has face validity, it has not been validated previously. However, when we repeated our analysis using only the subjective feelings of certainty item from the DAS, our results were qualitatively similar (data not shown). Also, our analysis examined only the short-term impact of impaired insight. A long-term study is needed to determine the degree to which impaired insight into delusions predicts future relapse or recurrence after remission of psychotic depression or contributes to other long-term clinical outcomes (eg, cognition, suicide, or social functioning). This is particularly important given that the long-term risk-benefit of antipsychotic treatment has not been established in psychotic depression and that there is no expert consensus on the optimal duration of antipsychotic use.[35,36]

Drug names: olanzapine (Zyprexa), sertraline (Zoloft and others).
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