Insight: Demographic Differences and Associations with One-Year Outcome in Schizophrenia and Schizoaffective Disorder

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Abstract

Background: Insight is increasingly seen as an important variable for study in psychotic illness, particularly in relation to treatment adherence. This study aims to quantify the association of insight with outcome, sociodemographic variables and diagnosis in a large stable patient sample. **Method:** Data are from a one-year, open-label, international, multicenter trial (n=670) of long-acting risperidone in adult symptomatically stable patients with schizophrenia or schizoaffective disorder. Psychopathology and insight were quantified using the Positive and Negative Syndrome Scale (PANSS). Patients were assessed at four time points over the year of the study. **Results:** 31.2% of the sample showed clinically significant deficits in insight at baseline. There were no differences based on sex, but significant differences in age and diagnosis, with oldest patients and schizophrenia patients (cf., schizoaffective disorder) showing more deficits. Baseline insight impairment was correlated with change in PANSS score at one year ($r=-0.243$, $p<0.001$). Recursive partitioning showed that, of those whose symptoms improved, those whose insight also improved were more likely to complete the trial. **Conclusions:** Insight is important above and beyond the effects of symptoms for predicting continuation in drug trials. This may have implications for the design and analysis of such trials, as well as suggesting the importance of targeting insight in treatment to increase likelihood of adherence to treatment. There also appear to be small but significant differences in insight based on age and diagnosis within the schizophrenia spectrum.

Key Words: Insight, Awareness, Compliance, Clinical Trial, Demographic, Outcome

Introduction

The concept of insight in psychotic illness has been rejuvenated as a topic of study over the last twenty years (1). Whilst once considered a unitary concept, more recent work has proposed insight to be graded and multifaceted (2). Although difficult to define, insight is conceptualized as encompassing an awareness of having an illness, the ability to recognize aberrant experiences as symptoms of illness, and understanding a need for treatment. It is thought that between 50 and 80% of schizophrenic patients do not believe themselves to be ill (3-5), though the WHO International Pilot Study of Schizophrenia (6) reported an even higher rate of deficit in insight at 81%. It has been shown to have important implications for outcome, with particular consequences for treatment nonadherence (7). Someone who denies having anything wrong with them will be less likely to accept treatment than someone who accepts that they are ill. As such, research on insight is relevant in developing effective treatment strategies.

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Clinical Implications

We found differences in completion rate of the study based on insight amongst those people who showed improved symptoms. This suggests that while treatment that improves symptoms is useful, the effects of improving insight alongside this should not be underestimated. This has some significant clinical implications for the effectiveness of therapies for schizophrenia. Some psychological interventions for schizophrenia and other psychoses have emphasized the importance of insight, and can aim to improve it, directly or indirectly, through cognitive behavioral therapy for schizophrenia (46, 47), metacognitive (cognitions about cognitions) training (48) or through compliance therapy (28, 49). Our results suggest that these interventions may have important implications for treatment adherence and, in turn, improved prognosis. Further research is needed into the effects of different psychological therapies on insight and its effect on outcome. Furthermore, the differences in insight based on demographic factors and diagnosis allow clinicians to predict which patients are more likely to show limited insight and, as such, to be aware that compliance may be more of a problem and should be closely monitored.

A number of factors have emerged as being reliably associated with insight: neurocognitive deficits clearly appear to contribute to lack of insight (8-11). More severe psychopathology tends to correlate positively with poorer insight (e.g., David et al. [12]), while depressed mood shows the opposite trend so that lower mood is related to better insight (e.g., Moore et al. [13]; see Mintz et al. [14] for meta-analysis). Whether there are any sex or age differences in insight in psychotic disorders has been investigated in some studies, but without consistent results. McEvoy et al. (15) assessed insight in 251 patients experiencing their first episode of psychosis, who had been ill for less than five years, and found that older age and female gender were associated with better insight. However, the oldest patient studied was only 40-years old, and the mean age was less than 24. Another large (n=1,432) study showed a small but significant correlation between insight and age (16). Rossell et al. (17) found no difference in insight on the basis of age in 78 male schizophrenia patients. Other studies have failed to find any insight difference between sex and age (12, 18-20). Regarding diagnosis within psychoses, some authors (15, 18) have contrasted schizophrenia versus schizoaffective disorder, but found no insight differences. Others have found differences (5, 21), with schizophrenia patients having the greater deficit.

Most studies that investigate changes in insight over time show an overall mean improvement in insight over time (22, 23). The current literature is inconsistent as to how well initial insight can predict outcome measures, such as symptom improvement or remission of illness (24). Drake et al. (25) report that those with the most insight had a rate of relapse that was 39% of those with poor insight. Rosen and Garety (26) showed insight to be the best predictor retrospectively of whether someone experiencing their first psychotic episode would go on to experience any further episodes. Another study (27) showed that the "insight into treatment" component of insight predicted less hospitalization and better social adjustment. Furthermore, several studies have shown positive predictive power of insight on compliance (28-32), while others have not (33, 34).

However, a review of longitudinal studies on insight by Lincoln et al. (35) highlights that correlations between insight and better long-term functioning may be explained by its association with symptoms. The discrepancies between all these results may be related to the type of patient studied (first episode vs. chronic), status (acute vs. in remission), numbers of patients (i.e., low statistical power), different assessment tools and time of investigations (admission, discharge or follow-up).

The purpose of this study was to determine whether key variables such as age, gender and diagnosis are indeed related to levels of insight in a large cohort of stable patients with schizophrenia and related disorders taking part in an open-label, one-year clinical trial that evaluated the long-term safety and efficacy of long-acting risperidone. Finally, we sought to examine whether baseline insight or changes in insight over time might predict remaining in the study, which might shed light on dropping out of treatment and nonadherence in naturalistic settings. The study made use of a large sample size to add significantly to the existing literature on the relationship between insight, demographic factors, symptoms and outcome, often reliant on smaller samples. The longitudinal design was anticipated to help clarify the role of insight on outcome, particularly in the context of continuation in the trial, which is likely to be relevant to cooperation with treatment and medication compliance.

Method

A one-year, open-label, international, multicenter trial was conducted to evaluate the long-term outcome of treatment with long-acting risperidone given as an intramuscular injection every two weeks. A more detailed description of the study methodology is provided elsewhere (36).

Patients

Eligible patients were at least eighteen-years old and had a *DSM-IV* diagnosis of schizophrenia or schizoaffective

disorder. Both diagnoses were included firstly in order to investigate differences in insight between them, and secondly because they are treated similarly and, as such, the relationship between insight and outcome is important for both. Patients were required to be symptomatically stable, as judged by the treating physician, be receiving a stable dose of an antipsychotic drug for at least four weeks before the trial and be in good general physical health. The main exclusion criteria were substance dependence, history of tardive dyskinesia, neuroleptic malignant syndrome or clinically significant physical abnormalities. Patients who had been treated with clozapine within two months of entry into the trial or with a conventional depot antipsychotic drug within one treatment cycle were also ineligible.

Study Medication

After a two-week run-in period, during which time antipsychotics other than risperidone were discontinued, patients were started on oral risperidone at a daily dose between 1 mg and 6 mg based on the judgment of the treating physician. The oral dose given was used as a guide to the starting dose of long-acting injectable risperidone of 25, 50 or 75 mg. Supplementation with oral risperidone was given for 2 to 3 weeks following the first injection of long-acting risperidone to provide antipsychotic coverage during the 3-week latency period after the first injection (37). Some concomitant medications could be initiated or continued at the discretion of the investigator.

Measures

Diagnoses based on *DSM-IV* were performed by trained clinicians. The Positive and Negative Syndrome Scale (PANSS) was the primary measure of treatment efficacy (38, 39). It was repeated at 3-month intervals through the study period by clinicians trained in the use of the Structured Clinical Interview for PANSS (38). All raters underwent thorough training in administration and scoring of the PANSS, and achieved good levels of agreement in rating patient videos.

Insight was assessed using item 12 on the general psychopathology subscale of the PANSS (G12): "lack of insight and judgment." Although insight has been proposed as a multidimensional component (2), previous research shows that single-item measures of insight provide a good estimate of insight as they are strongly correlated with more extensive schedules (22, 40). Despite the fact that the PANSS scale takes into account both insight and judgment, it still shows a correlation coefficient of 0.895 with the Schedule of Assessment of Insight (SAI-E) and 0.845 with the Insight and Treatment Attitudes Questionnaire (ITAQ), two of the most generally accepted scales of assessing insight.

Sample

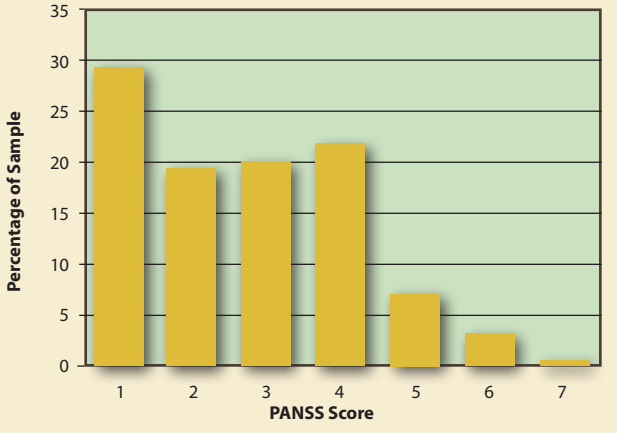
A total of 670 patients with schizophrenia (n=564) or schizoaffective disorder (n=106) were included (males=437; females=233). 95% of them were white and the mean age was 42 years (standard deviation [SD]=14.00, range=18–84). The mean (SE) PANSS total score at baseline was 66.3 (SD=18.46). Seventy percent of the total cohort completed the one-year trial period.

Statistical Analysis

An analysis of covariance (ANCOVA) was used to examine association of patient characteristics with deficits in insight at baseline; with symptoms as measured by the total score (minus insight item) on the PANSS as covariate.

A classification tree (CHAID recursive partitioning, SPSS 16.02) assessed the predictors of termination of study participation (based on variables of PANSS change, age, sex, diagnostic group, baseline insight and insight change). CHAID is a recursive partitioning method that creates a decision tree to predict a given outcome, in this case dropout, by finding the optimal ways to split the data. Splitting criteria are determined by the optimal statistical analysis. Thus, for example, if age is the most salient predictor, variable optimal age groupings to predict outcome would be identified, followed by further data splits on salient predictor variables.

Figure 1 Distribution of PANSS G12 Scores



The most common score was 1 (no impairment), and 68.8% showed only minor impairment in insight and judgment (PANSS score 1-3).

Results

A total of 670 patients took part in the study, of whom 71% (n=474) completed the PANSS at all time points across the study period. The main reasons for patient noncompletion included the length of the assessment battery, problems with the medication, becoming untraceable to the research team and severe deterioration of condition requiring a change in medication. There was no significant difference in

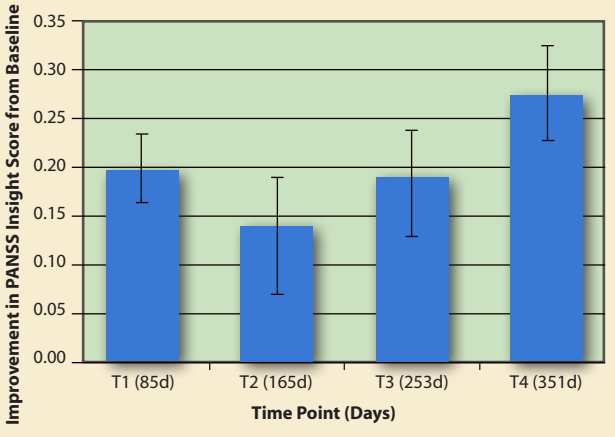
Table 1 Results of ANCOVAs Comparing Insight Score with Age, Sex and Diagnosis

Variable		N=	Mean Insight (95% C.I.)	F Value	P=
Age	18–28	121	2.630 (2.411; 2.848)	8.257	<0.0001
	28–42	237	2.364 (2.197; 2.530)		
	42–56	196	2.518 (2.344; 2.691)		
	56+	113	2.991 (2.772; 3.209)		
Sex	Female	235	2.610 (2.450; 2.770)	0.11	0.74
	Male	435	2.641 (2.641; 2.782)		
Diagnosis	Schizophrenia	561	2.788 (2.686; 2.890)	7.4	0.007
	Schizoaffective	106	2.463 (2.249; 2.676)		

insight at baseline between those who completed and those who dropped out.

At baseline, 29.3% of participants showed no impairment in insight (1 on PANSS item G12; see Figure 1). However, if the cutoff point is made between scores of 3 and 4 on the PANSS item (a standard cutoff point for impairment [22, 41]), then only 31.2% of participants here show clinically significant impairments in insight, broadly similar to some studies, such as Mintz et al. (22), where 35.6% showed clinically significant impairments. These compare to 54.7% in a similarly large study of first-episode psychosis patients (4).

Figure 2 Improvement in Insight (i.e., a reduction in score on PANSS G12)



Insight improves in the first time point, before worsening at T2, and then continuing to steadily improve until T4.

An analysis of covariance (ANCOVA), controlling for overall baseline severity of illness (as measured by PANSS total score minus insight item), was carried out to investigate differences in baseline insight on the basis of age, sex and diagnosis. The results are shown in Table 1. Significant differences were found between age groups ($F=8.257$, $p<0.0001$), with the oldest group showing greatest impairment, followed by the youngest group, with the two other groups falling between. Groups were split based by starting with the mean and split based on each standard deviation from there. There were no significant differences in insight between males and females ($F=0.11$, $p=0.74$). People with a diagnosis of *DSM-IV* schizophrenia had significantly greater deficit in insight than those with schizoaffective disorder ($F=7.4$, $p=0.007$).

There was a significant positive correlation between baseline insight score and PANSS total score ($r=.61$, $p<.001$). Mean PANSS total score was higher with each point scored on the insight item; however, only 2 subjects scored the highest level of insight impairment. There was also a significant correlation between baseline insight impairment and change in PANSS total score one year later ($r=-0.243$, $p<0.001$). This is likely due to those with high insight scores having greater room for improvement over the assessment period. Average improvement in insight over the trial is shown in Figure 2. Mean change is calculated on the basis of all subjects remaining in the trial at each time point (T1-4).

A classification tree (recursive partitioning) of termination status of the study was conducted, with variables including PANSS change to endpoint, age, sex, diagnostic group, baseline insight, and change in insight. This showed that, of those people whose symptoms improved during the study, those whose insight also improved were more likely to complete the study than those whose symptoms improved but insight did not ($p<0.001$). Insight here has a significant effect on compliance within the study, on top of the effect of severity of symptoms.

Weak but statistically significant correlations (r ranges between 0.08 at baseline and 0.18 at T4; all $p<0.05$) were found at all time points between depression and G12, calculating depression based on a subscale of PANSS incorporating depression, anxiety, guilt feelings and tension (items 2, 3, 4 and 6) from the general psychopathology subscale.

Discussion

This study followed a large sample of patients with schizophrenia and schizoaffective disorder for one year as part of a clinical trial, with assessments at three-month intervals to investigate improvement in insight and psychopathology. The association of key patient characteristics (age, sex and diagnostic group) and insight were also examined.

The results show a relatively high level of insight in this sample compared to other studies of schizophrenia patients. This is to be expected given the requirement of symptomatic stability ruling out some of the more severe (and more likely to be severely impaired in insight) patients. For a medica-

tion trial, it is more likely that patients will be generally more compliant and have some interest in their medication, plus a desire to find medication that is more beneficial. However, the sample is not atypical, and the 71% showing some deficit is in line with the most often cited results on the proportion of patients with impaired insight (6).

Statistically significant differences in insight based on age were found in this sample. Contrary to the findings of a large study of first-episode psychotics by McEvoy et al. (15), the oldest patients demonstrated the worst insight here. They were followed by the youngest group, with the two intermediate groups showing significantly better insight than the others. As the McEvoy et al. study looked just at first-episode psychotic patients, with none over the age of 40 (while our oldest group contained 113 people over age 56, with the oldest 84-years old), the results may not be directly comparable. If no patients older than 40 had been included in the present study, the results may well have paralleled those of McEvoy et al. (15). Furthermore, Thompson et al. (42) show that there are differences in overall awareness between first-episode and multiple-episode patients, which they attributed to "socialization" into the sick role, so caution must be taken when comparing results.

It is possible that patients of older age have greater impairment in insight due to longer duration of illness. Though this information was not recorded, it is likely that these patients had been ill for many years (given the young age associated with onset of illness). They are, therefore, patients who showed a greater severity of illness, whereas those with less severe illness are more likely to have recovered and, therefore, not be represented in the study. In the younger groups, some less severe patients may stand a greater chance of recovery as they get older, therefore bringing down the average severity of the group. Additionally, over time, older patients' views on their illness are likely to have become entrenched, whereas it is possible that younger patients are more labile in their illness perceptions. With time, their perceptions may crystallize such that they lose what partial awareness they may have had at a younger age. It should also be noted that, although statistically significant, the mean differences between the groups were small.

There were no significant differences in insight on the basis of sex found in this study. Whilst this, again, contradicts McEvoy et al. (15), who found greater insight in female first-episode psychotic patients (they did not control for level of symptom severity), our results are in general agreement with several other previous studies (18, 19, 43) finding no difference. The large sample here (n=670) suggests that if genuine sex differences were present in insight they would have probably been demonstrated.

Furthermore, a small but significant difference was observed between patients with schizophrenia and schizoaffective disorder, with schizophrenia patients demonstrating worse insight. These findings concur with those of Amador et al. (21) based on a large sample recruited as part of the *DSM-IV* field trials. It could be speculated that this difference lies in the mood component of schizoaffective disorder leading to an increased ability to accurately make judgments about one's condition. A review of insight in mood disorders (44) suggests that people with bipolar disorder or depressive disorder (both psychotic and nonpsychotic) show better insight than those with schizophrenia (though bipolar disorder is closer to schizophrenia, and perhaps shows greater insight impairment than schizoaffective disorder [21]). This may support a model based on depressive realism (45), suggesting that people with depressive tendencies will be more accurate in their self-perception, as would be demonstrated by better insight. A mood component in psychotic illness may, thus, modulate the degree of insight into the condition.

Like the majority of other studies, our patients showed an improvement in insight over time, though this was not the case at each three-month time point. The greatest improvement in insight was in the first three months, but this was followed by a small deterioration in insight in the second time period, before steadily improving at the remaining points. The change in the first three months is likely to be, in part, due to the improvements of symptoms related to the start of a new medication. These may be psychological as well as medical. The attention and contact time involved in taking part in such a trial, as well as a potential placebo effect of new medication, may contribute toward the positive treatment effects observed, at least initially. Insight continues to improve for the remainder of the study.

We found differences in completion rate of the study based on insight amongst those people who showed improved symptoms. This suggests that while treatment that improves symptoms is useful, the effects of improving insight alongside this should not be underestimated. This has some significant clinical implications for the effectiveness of therapies for schizophrenia. Some psychological interventions for schizophrenia and other psychoses have emphasized the importance of insight, and can aim to improve it, directly or indirectly, through cognitive behavioral therapy for schizophrenia (46, 47), metacognitive (cognitions about cognitions) training (48) or through compliance therapy (28, 49). Our results suggest that these interventions may have important implications for treatment adherence and, in turn, improved prognosis. Further research is needed into the effects of different psychological therapies on insight and its effect on outcome. Furthermore, the differences in insight based on demographic factors and diagnosis allow clinicians to predict which patients are more likely to show limited insight and, as such, to be aware that compliance may be more of a problem and should be closely monitored.

The strengths of this study lie in its size and, hence, statistical power, the homogeneity of the assessments which were prospective, and the one-year duration of follow-up allowing some predictive effects of insight to be tested. The weaknesses concern the likelihood of some selection bias in the sample as noted above, given that patients were enrolled to a clinical trial—albeit open label and, hence, not too demanding. As well as affect entry criteria, the fact of the trial and its evaluation of a novel formulation for maintenance treatment may have had somewhat unpredictable effects in shaping attitudes to treatment, which are a component of insight. In any event, caution should be exercised in extrapolating to more acutely ill patients with comorbidities and a more negative attitude to treatment. Also, the attrition rate means that firmer conclusions on outcome and change in insight are harder to draw, as some of the sample is not followed consistently. It is possible that those who withdrew from the study are those whose condition worsened, and as such would have affected the results.

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