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Cross-sectional and Longitudinal Relationships Between Insight and Attitudes Toward Medication and Clinical Outcomes in Chronic Schizophrenia

Somaia Mohamed[1–3], Robert Rosenheck[2,3], Joseph McEvoy[4], Marvin Swartz[4], Scott Stroup[5], and Jeffrey A. Lieberman[6]

[2]Venterans Integrated Service Network 1 Mental Illness, Research, Education and Clinical Center, West Haven, CT; [3]Yale Medical School, New Haven, CT; [4]Duke University, Durham, NC; [5]University of North Carolina Chapel Hill; [6]Columbia College of Physicians and Surgeons, New York, NY

Background: **We evaluated the cross-sectional and longitudinal association of measures of both insight and attitudes toward medication to outcomes that included psychopathology and community functioning.** ***Methods:*** **Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) was a large 18-month follow-up study pharmacotherapy of people with schizophrenia. Insight was measured using the Insight and Treatment Attitudes Questionnaire and attitudes toward medication by the Drug Attitude Inventory. Widely known scales were used to assess symptoms of schizophrenia and depression and community functioning. Medication adherence was globally assessed by the treating psychiatrist using several sources of information. Bivariate correlations and mixed model regression analyses were used to test the relationship of insight and medication attitudes to outcomes at baseline and during the follow-up period. Regression models were used to evaluate the relationship between change in insight and medication attitudes and changes outcomes.** ***Results:*** **There was a significant relationship at baseline between insight and drug attitudes and symptoms of schizophrenia and depression, as well as with community functioning. Higher levels of insight at baseline were significantly associated with lower levels of schizophrenia symptoms at follow-up while more positive medication attitudes were significantly associated with both lower symptom levels and better community functioning. Change in insight scores over time was associated with declining schizophrenia symptoms but increasing levels of depression. Change toward more positive medication attitudes was associated, independently of changes in insight, with significant decreases in psychopathology, improvement in community functioning, and greater medication compliance.** ***Conclusion:*** **Greater patient understanding of their illness and more positive attitudes toward medication may improve outcomes. Educational interventions that affect these attitudes may be an important part of psychosocial rehabilitation and/or recovery-oriented services.**

Key words: schizophrenia/insight/medication attitude/social functioning/quality of life

Introduction

Poor insight and denial of illness are prevalent features of schizophrenia[1,2] that are widely believed to have adverse clinical effects.[3] When individuals with schizophrenia do not perceive themselves as ill, they are less inclined to enter or remain in treatment, underappreciate the benefits of medication, and put themselves at higher risk of discontinuing treatments, with concomitant increase in the risk of relapse.[4] Poor insight into illness and negative attitudes toward medications may thus be important determinants of clinical outcome and may offer useful avenues for intervention.

Psychopharmacological and psychological treatments have both been found to significantly decrease symptoms in schizophrenia and improve functional capacity.[5,6] The long-term course of the illness is nevertheless often characterized by impaired social and occupational functioning and quality of life (QOL)[7–9] in part because in the absence of insight and positive attitudes toward available treatments the chances of realizing their benefits are limited.

In recent years, increasing emphasis has been put on the importance for people with schizophrenia of having a "recovery orientation" toward their lives, ie, an orientation characterized by realistic hopefulness and feeling of empowerment to achieve personal goals in spite of adversity.[10–15] Although the recovery orientation among people with serious mental illness is often contrasted with a medical model orientation, insight into illness may represent an important link between the 2 perspectives because people who understand their illness and recognize the value of available treatments are likely to feel

[1]To whom correspondence should be addressed; VA Connecticut Health Care System, 950 Campbell Avenue/182, West Haven, CT 06516; tel: 203-937-3850, fax: 203-937-3433, e-mail: Somaia.Mohamed@yale.edu.

more empowered and to be more successful at using treatment to achieve their personal goals. Acknowledgement of illness has been recognized as improving the capacity to make informed decisions about the future to free oneself from blame for difficulties linked with illness and to form sustaining bonds with others.[16]

Although it is impossible to randomly assign patients to different attitudinal states, observational methods can be used to evaluate the relationship between insight and attitudes toward medication and key outcomes such as schizophrenia symptoms, depression, social functioning, as well as medication compliance. Particular attention must be given in such studies to alternative explanations for the associations of insight and medication attitudes such as reverse causality and bidirectionality, and statistical adjustments should be used to reduce potential biases. By linking consumer attitudes and knowledge to use of treatment, and desirable outcomes, this line of research may provide an integrative link between the recovery and medical models.

Although researchers agree that there are multiple components of insight, there is empirical evidence suggesting that these dimensions actually represent components of a single construct. McEvoy et al[17] administered a standardized interview that assessed awareness of illness, need for treatment, and understanding the consequences of the disorder. A principal components analysis of these data resulted in a single-factor solution. A similar study involving a self-report measure that assessed awareness of illness, need for treatment, and recognition of the relationship of symptoms to the disorder[18] also obtained a single-factor solution in a principal components analysis. Most recently, Cuesta et al[19] administered 3 separate insight instruments to a group of psychotic patients and found a 2-factor solution ("general awareness" and "attitudes to treatment"). However, the first factor accounted for a much larger percentage of variance than the second (76.9% vs 9.4%), and the 2 dimensions were highly correlated, further suggesting that these dimensions are best viewed as multiple, correlated indices of a single construct.

Relationship of Insight to Psychopathology

Cross-sectional studies have found small but significant relationships[20] showing that greater insight is associated with lower levels of global psychopathology and of both positive and negative symptoms, including one study that examined these cross-sectional associations at 2 different time points.[21,22] Investigations that examined whether changes in insight are associated with changes in symptoms have reported less consistent results.[17,20,21,23–25] To our knowledge, no study has simultaneously investigated the predictive relationship of both insight and medication attitudes to outcomes by analyzing the relationship between these variables at baseline to outcomes at subsequent time points, nor has any study addressed the full range of pertinent outcomes including symptom severity, depression, QOL, and medication adherence, while controlling for potential baseline confounders.

Insight and Medication Adherence

Cross-sectional studies of the relationship between insight and adherence to treatment have reported that increased insight was associated with greater treatment adherence.[26–33] However, studies that examined the predictive power of insight and future treatment adherence have yielded mixed results with some studies finding no association[27,33,34] while one smaller study reported only a positive trend.[35] We are not aware of any studies that investigated the association between change in insight and change in medication adherence over time.

Insight and Functional Outcome

Some cross-sectional studies have reported significant associations between insight and functional outcomes,[24,31,36,37] while others have not.[38–42] Most longitudinal studies, in contrast, have reported significant predictive associations between insight and functioning.[43–47] However, most of these studies did not control for symptom severity at baseline and did not examine the association between change in insight and change in functioning.

In view of these complex and inconsistent findings, we sought to examine the strength of association of measures of both insight and attitudes toward medication to a broad array of outcome measures including schizophrenia and depressive symptoms, community functioning, and treatment adherence. We hypothesized that insight and medication attitudes would (a) be significantly associated with reduced psychopathology and better functional capacity in a cross-sectional analysis using baseline data and (b) predict net of baseline level of insight and medication attitude and other potentially confounding baseline factors (depression, age, QOL, psychopathology, and neurocognition), less future psychopathology, and better social/occupational functioning and treatment adherence at follow-up. (c) We further hypothesized that change in insight and medication attitudes from baseline to follow-up would also be significantly related to change in clinical measures, after controlling for potentially confounding factors.

Methods

Study Design

This study used data from the Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) schizophrenia study, a large, 18-month, National Institute of Mental Health–funded, randomized controlled trial designed

to compare outcomes of 1 conventional antipsychotic medication (perphenazine) and 4 second-generation antipsychotics (olanzapine, ripseridone, quetiapine, and ziprasidone).[48] CATIE was conducted between January 2001 and December 2004 at 57 US sites. The CATIE study was designed to compare the effectiveness and cost-effectiveness of currently available atypical and conventional antipsychotic medications through a randomized clinical trial involving a large sample of patients treated for schizophrenia at 57 sites, including both academic and community providers. Data were included from all the phases of CATIE.[49] Patients were 18–65 years of age who had received a diagnosis of schizophrenia, as determined with the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition)* Axis I Disorders (SCID),[50] and who were able to take oral antipsychotic medication as determined by the study doctor. Patients were excluded if they had a diagnosis of schizoaffective disorder, mental retardation, or other cognitive disorders; had a history of serious adverse reactions to the proposed treatments; had had only one schizophrenic episode; had a history of treatment resistance; were pregnant or were breast-feeding; or had a serious and unstable medical condition. A wide spectrum of patients with schizophrenia enrolled in the study, ranging from partially remitted outpatients who remain symptomatic (because of lack of efficacy or inability to tolerate an efficacious dose) or who suffer significant side effects to exacerbated inpatients. Patients who are seemingly doing well on their current medication but who wish to consider a change for reasons of greater improvement or better tolerability were also welcome to enroll.

Participants gave written informed consent to participate in protocols approved by local institutional review boards. Details of the study design and entry criteria have been presented elsewhere.[49] The diagnosis of schizophrenia was confirmed by the SCID. This study relies on baseline data and follow-up assessments at time points at which data on symptoms, insight, medication attitude, and social/vocational functioning were all available (1, 3, 6, 9, 12, 15 and 18 months).

In addition to medications, all participants were offered an individually tailored educational plan adapted from the successfully implemented Texas Medication Algorithm Project. The plan was conducted in several phases and invited family participation if desired by the patient. Contents of the various phases included education on diagnosis, medications, symptom self-monitoring, side effects, and change in symptoms.

Measures

Insight and Drug Attitudes. Insight was assessed by the Insight and Treatment Attitudes Questionnaire (ITAQ).[17] The ITAQ was designed to measure awareness of illness and insight into need for treatment in patients with schizophrenia. It is a single scale consisting of 11 items that are phrased as questions to elicit responses on Likert-type scales. Attitudes toward medication were assessed by the Drug Attitude Inventory (DAI).[51] The DAI is widely used, brief, and frequently self-administered but in the CATIE trial was read to the patient and true and false responses obtained. The instrument focuses on unpleasant and negative subjective responses that are common adverse effects of antipsychotic medications. A higher score reflects more negative attitudes toward medications. In this study, the scale was reverse scored to reflect positive attitudes toward medications so as to maintain the same directionality as the insight scale.

Schizophrenia and Depressive Psychopathology. Symptoms of schizophrenia were assessed by the Positive and Negative Syndrome Scale (PANSS)[52] that yields a total average symptom score, based on 30 items rated from 1–7 (with higher scores indicating more severe symptoms), as well as subscales reflecting positive, negative, and general psychiatric symptoms. In order to avoid statistical redundancy between the PANSS measure of general psychiatric symptoms and the ITAQ, the PANSS general and total subscales were modified to exclude an item that assesses insight. Co-occurring depressive symptomatology was assessed using the Calgary Depression Rating Scale (CDRS).[53,54] CDRS is a 9-item scale designed to assess severity of depressive symptoms in patients with schizophrenia. The CDRS has been shown to be a reliable and valid measure of depression in this population.[53]

Quality of Life. Psychosocial functioning and QOL were assessed using the Heinrichs-Carpenter Quality of Life (HQOL)[8] Scale and a single item from the Lehman Quality of Life Interview (LQOLI)[83]. The HQOL is a rater-administered scale that assesses overall QOL and functioning on 21 items rated from 0 to 6 (with higher scores reflecting better QOL) and yields measures on 4 subscales that address (a) interpersonal relations, (b) instrumental role functioning, (c) use of common objects and participation in activities, and (d) intrapsychic foundation (ie, sense of purpose, motivation, curiosity, and ability to experience pleasure). This scale has showed high sensitivity to both change and treatment effect, and moderate-high correlations with other measures of QOL.[55] The LQOLI is a structured self-report interview designed to generate ratings by a trained nonclinical interviewer. The single item from the LQOLI asks the patient to rate his well-being overall on a scale from terrible = 1 to delighted = 7.

Medication Adherence. Medication adherence was evaluated using monthly pill counts. Additionally, information from patients on structured questions about medication

adherence were asked at each appointment, along with information from clinicians and family documenting whether there had been prescription medications or shots for mental or emotional health problems that the patient was supposed to take but either did not take at all or took only some of the time were also obtained. A global judgment on a 1–4 scale with higher scores representing poorer adherence (representing 75%–100% compliance to 0%–25% compliance) was made by the treating psychiatrist based on synthesizing all available information including pill count data.[56] While each method of measuring medication adherence is imperfect, multiple methods improve estimates of adherence considerably.[84] For the analyses reported here, we reverse coded this scale to represent increased medication adherence.

Side Effects. The Barnes Akasthisia Scale (BAS)[57] was used to evaluate akasthisia. BAS contains 4 items, including objective akasthisia, subjective awareness of restlessness, subjective distress related to restlessness, and a global clinical assessment of akasthisia. We assessed the Abnormal Involuntary Movement Scale (AIMS) (Guy 1976) to rate symptoms of tardive dyskinesia. The AIMS has 12 items that rate severity of dyskinetic movements in various body parts and an overall severity item, on a scale ranging from 0 to 4. Extrapyramidal symptoms were assessed using the Simpson-Angus Extrapyramidal Side Effect Scale,[59] a scale that contains 10 items rated on a scale of 0–4.

Neurocognitive Functioning. Neurocognitive functioning was measured by separate test scores, described in previous publications,[60] that were converted to *z* scores and combined to construct 5 scales: Processing Speed, Verbal Memory, Vigilance, Reasoning, and Working Memory. The Neurocognitive Composite Score was the average of standardized scores (*z* scores) of these 5 subscale summary scores.

Analyses

First, Pearson product-moment correlations were used to evaluate the baseline bivariate associations between insight and medication attitudes, sociodemographic variables (age, education, and marital status), neurocognition, symptoms severity, depressive symptoms, functional status, and side effects. These correlations identified the baseline association of attitudinal measures and outcome measures as well as other variables that were significantly associated with insight and drug attitudes and that could thus potentially confound observed relationships between insight and attitudes and outcomes in longitudinal mixed models.

The purpose of the primary analyses was to evaluate the independent associations of insight and medication attitudes at baseline with subsequent outcome. Primary analyses were a series of mixed model regressions analyses of outcomes at all time points on the PANSS total score and subscales, the HQOL total score and subscales, CDRS, and medication adherence measures. Because these analyses include multiple observations from the same patients at different time points, random effects were modeled to adjust the SEs for the correlation of observations within individual patients along with fixed effects representing the time of each assessment (range 1–18 months). In these models, insight and attitudes toward medication at baseline were the independent variables of primary interest. The baseline value of each dependent variable as well as age, the baseline values of the LQOLI measure, neurocognition, depression, and the HQOL total scores were also included as covariates because they were significantly associated with the baseline measures of either insight or attitudes toward medication along with the month of the follow-up assessment.

Because insight was significantly related to some outcomes while medication attitude, when included in the same model, was not and reciprocally medication attitude was significantly related to other outcomes while insight was not, these analyses were repeated to include baseline insight or medication attitude each by itself, in separate models. These analyses were designed to identify cases in which the significant relationship of one of these variables to outcomes was not independent of the other measure.

Finally, to examine the longitudinal association between change in both insight and medication attitude and the change in symptomatology and HQOL (the association between change and change), we constructed an additional set of measures in which the baseline score on each measure for each subject was subtracted from each of their follow-up scores on the outcomes of interest as well as on the ITAQ and the DAI. The final set of regression models was used to test the associations between these measures of change, again using mixed models because multiple observations were included from each patient and controlling for potentially confounding baseline measures as described above including the baseline values of measures of insight and medication attitudes.

Because previous publications have demonstrated that there were few significant differences between treatments in CATIE on the QOLS,[61] neurocognitive functioning,[62] and symptoms,[63] we evaluated whether there were differences between treatments at follow-up on insight and medication attitudes. Because we found no significant differences in outcomes on these measures, treatment group was not included in any subsequent analysis.

Results

Sample Characteristics

Subjects were 1432 individuals with a *Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition)* diagnosis of schizophrenia validated by the SCID treated

Table 1. Sample Characteristics

	N (%)	Mean ± SD	Range
Demographic			
Age (y)		40.52 ± 11.09	18.00–67.00
Male (%)	1099 (74.0)		
Race/ethnicity (%)			
White	863 (60.3)		
African American	504 (34.9)		
Ethnicity			
Hispanic	169 (11.69)		
Marital status (%)			
Married	167 (11.53)		
Widowed	34 (2.36)		
Separated	298 (20.63)		
Divorced	87 (6.04)		
Never married	860 (59.44)		
Education (years)		12.10 ± 2.25	1–21
Clinical			
Positive and Negative Syndrome Scale (PANSS)			
Positive syndrome scale		18.47 ± 5.64	7–49
Negative syndrome scale		20.15 ± 6.40	7–40
General PANSS subscale[a] (no insight)		34.14 ± 8.82	16–112
Total[a] (no insight)		72.76 ± 16.97	30–210
Calgary Depression Rating Scale		1.57 ± 0.56	0–3
Medication Adherence at follow-up		1.19 ± 0.57	1–4
Side effects			
Akathisia (Barnes Akathisia Scale)		0.35 ± 0.55	0–5
Tardive dyskinesia (Simpson Angus Scale)		0.22 ± 0.32	0–4
Extrapyramidal symptoms (Abnormal Involuntary Movement Scale)		0.26 ± 0.46	0–4
Insight			
Insight and Treatment Attitudes Questionnaire		−0.04 ± 0.81	0–2
Drug Attitude Inventory		0.07 ± 0.50	0–10
SF 12 Survey Physical health		48.20 ± 10.18	0–100
SF 12 Survey Mental health		40.95 ± 11.63	1–100
Neurocognitive Composite Score		−0.02 ± 0.62	−2.7–1.7
Functional outcome			
Lehman Quality of Life		4.33 ± 1.40	0–6
Heinrichs-Carpenter Quality of Life Scale			
Interpersonal relations and social		2.53 ± 1.30	0–6
Instrumental role functioning		2.00 ± 1.65	0–6
Intrapsychic foundations		2.98 ± 1.15	0–6
Common Objects and Activities		3.23 ± 1.35	0–6
Total		2.74 ± 1.06	0–6

Note: SF, 12-Item Short-Form Health Survey.
[a]PANSS General and Total subscales were modified to exclude an item that assesses insight.

at 57 US sites (table 1). Patients were middle aged on average (mean age = 40.5 ± 11.1 years), mostly Caucasian (60.3%), chronic patients with a mean duration of illness of 16.5 + 11 years (table 1). As shown previously, the CATIE sample was similar in sociodemographic and clinical characteristics to participants in other major trials of atypical antipsychotics.[63]

Bivariate Analyses

Bivariate correlation analyses showed that the ITAQ and DAI were significantly positively correlated ($r = 0.32$, $P < .0001$). Correlations between these measures and other baseline measures showed significant relationships between both measures and age, lower PANSS scores, and higher HQOL scores. The relationship of insight and medication attitudes and depressive symptoms, neurocognitive performance, and the QOLLQOL ran in opposite directions such that more insight was correlated with better performance on cognitive measures, more depressive symptoms, and lower QOLLQOL scores, while more positive medication attitudes was associated with associations in the opposite directions on these measures. A significant relationship was observed between insight

Table 2. Correlations of Attitude Measures and Baseline Characteristics

	Age (y)	Education	Currently Married	Never Married	LQOLLQOL	HQOL Total	PANSS Total (no insight)	NC	Depression	AIMS	BAS	SAEPS ES
ITAQ	0.07**	0.04	0.084**	−0.084**	−0.07**	0.20***	−0.18***	0.06*	0.12***	0.01	0.01	−0.02
DAI	0.17***	−0.03	0.011	−0.047	0.15***	0.19***	−0.21***	−0.07*	−0.12***	0.04	0.05	−0.05

Note: LQOLI, Lehman Quality of Life Interview; HQOL, Heinrichs-Carpenter Quality of Life; PANSS, Positive and Negative Syndrome Scale; AIMS, Abnormal Involuntary Movement Scale; BAS, Barnes Akathisia Rating Scale; SAEPS, Simpson-Angus Extrapyramidal Side Effect Scale; ITAQ, Insight and Treatment Attitudes Questionnaire; DAI, Drug Attitude Inventory.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

and being currently or formerly married, but no such relationships were found with medication attitudes (table 2).

Longitudinal Analysis of Outcomes

All outcome measures showed significant improvement over the 18 months of the study (all P's $< .0001$). Higher levels of insight at baseline were significantly and independently associated with lower levels of schizophrenia symptoms at follow-up (including the PANSS total score as well as the positive and negative subscales) (table 3) after adjusting for potentially confounding baseline measures and for the time of each follow-up assessment. Insight was also associated with higher scores on the HQOL intrapsychic foundation score but not on the total or other subscales or with medication compliance (table 3).

A more positive attitude toward medication was also associated, independently of the insight measure, with significantly lower levels of symptoms on the total PANSS score as well as with lower levels of positive symptoms, general psychopathology, and depression (table 3). Positive attitudes toward medication were associated with higher scores on HQOL intrapsychic foundation subscale score and the measure of medication compliance.

Three outcome measures were significantly associated with baseline insight, only when drug attitudes were not included in the model: the HQOL total score ($B = 0.069$, $t = 2.32$, $df = 1, 1325$, $P < .05$), the HQOL social relations score ($B = 0.081$, $t = 2.28$, $df = 1, 1092$, $P < .05$), and medication adherence ($B = .043$, $t = 2.48$, $df = 1, 1325$, $P < .05$). Although these outcome measures were significantly associated with baseline insight, the relationships were not independent of positive attitudes toward medications.

Association Between Change in Insight, Medication Attitude, and Change in Outcome Measures

The final set of analyses showed that change in insight scores from baseline to follow-up was associated with decreased PANSS total scores, as well as positive, negative, and general symptoms scores; improvement in the HQOL total and all 4 subscales; and increased medication compliance, as well as with *increased* levels of depression (table 3). These analyses all adjusted for the baseline value of the dependent variable as well as for the potential confounding baseline measures previously identified and the time of each follow-up interview.

Change toward more positive medication attitudes, in these analyses, was associated, independently of changes in insight, with significant decreases in the PANSS total score, as well as in the positive, negative, and general symptom scores, and with *decreased* levels of depression. Change toward more positive attitudes toward medication was also associated with greater improvement in the HQOL total score, all 4 HQOL subscale scores, as well as improved medication compliance.

Discussion

This study used a large, longitudinal dataset to examine the relationship of both awareness of illness and attitudes toward medication with severity of schizophrenia and depressive symptoms, social functioning, and medication adherence (N = 1432). We found consistent relationships between both insight and attitudes toward medication and clinical outcomes, QOL, and medication adherence, albeit of varying strength and independence across analyses.

At baseline, greater insight and more positive attitudes toward medication were clearly associated with lower levels of schizophrenia symptoms, and higher HQOL scores, findings similar to those reported in other studies.[21,22] Greater insight was correlated not only with better performance on cognitive measures, as reported previously,[64] but also with more severe depressive symptoms.[65,66] Previous cross-sectional investigations have also reported weak but positive associations between insight and depressive symptoms (ie, depressive symptoms and insight increased in parallel)[22,47] as well as with increased suicidal ideation or behaviors.[45,67] Poor insight into illness has been viewed, traditionally, as serving a defensive function that preserves self-esteem and allows maintenance of an optimistic outlook in face of the discrepancy between one's and others' functioning or between current and desired functioning. Insight has in fact been considered by some to be responsible for postpsychotic depression.[68]

Table 3. Relationship of Baseline Insight and Medication Attitude to Psychopathology and Quality of Life at Subsequent Time Points

	PANSS Total	PANSS Positive	PANSS Negative	PANSS General	HQOL Total	HCSOC	HCINPSYC	HCINST	HCOBACT	QOLLQOL	Medication Compliance	Depression[a]
ITAQ	−0.95*	−0.202***	−0.404**	−0.07	0.045	0.062	0.076*	0.006	−0.007	−0.098**	0.014	0.018
DAI	−2.264***	−0.967***	−0.265	−1.165***	0.057	0.021	0.110*	0.029	0.057	0.283***	0.154***	−0.042*

Note: Abbreviations are explained in the first footnote to table 2. HCSOC, Heinrichs-Carpenter Interpersonal Relations and Social Networks; HCINPSYC, Heinrichs-Carpenter Intrapsychic Foundations; HCINST, Heinrichs-Carpenter Instrumental Role Functioning; HCOBACT, Heinrichs-Carpenter Common Objects and Activities. Days worked is dichotomous (0 = no, 1 = yes). The PANSS negative syndrome scale in this analysis omits 3 items directly reflecting neurocognition and community functioning: "difficulty in abstract thinking," "passive/apathetic withdrawal," and "emotional withdrawal." (1) These analyses adjust for baseline value of the dependent variable as well as of ITQ, DAI, age, QOLLQOL, neurocognition, depression and HQOL and time of follow-up.
* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
[a]Calgary Depression Rating scale score.

But the causal direction of these cross-sectional baseline associations, however, is ambiguous, and this relationship could also, as consistent with cognitive models, reflect depressive realism (ie, a higher levels of depression reflecting more accurate self-evaluations of current functioning, commonly found in depression, resulting in a higher levels of insight into the presence and the impact of a mental disorder.[69]

In the longitudinal analyses, we found consistent relationships between both insight and medication attitudes at baseline and lower symptoms and higher intrapsychic functioning at follow-up. Independent relationships with medication adherence and overall QOL (as well as with greater depressive symptoms) were only found with baseline medication attitudes and not with insight. However, when insight was examined without medication attitudes in the models, significant relationships were also observed between insight and both medication adherence and overall QOL, suggesting substantial shared variation between the 2 independent variables, perhaps explaining the findings of studies that failed to find a significant relationship between insight and future treatment adherence.[27,33,34] In contrast to insight, more positive attitudes toward medication was associated with lower levels of depressive symptoms, perhaps mediated by the more consistent use of effective drugs, primarily antipsychotics that have been found to be associated with reduced depressive symptoms[70,71] and concomitant medications such as antidepressants.

These longitudinal findings are consistent with and more suggestive of a causal relationship than cross-sectional analyses and suggest a potential value for interventions that improve patients' awareness of both the nature of their illness and the potential benefits of medications.

To examine the mediating effect of medication adherence on the relationship between both insight and medication attitudes and symptoms, we repeated the mixed regression models adding the measure of medication adherence as a covariate. While the strength of association between both insight and medication attitudes and symptoms (as measured by the size of the regression coefficients) decreased slightly, they all remained significant. Thus, greater mediation adherence only partially accounted for the observed association of insight and medication attitudes with lower symptoms. Analyses of the associations between "change and change" were highly consistent showing significant and independent relationships between change in both insight and medication attitudes and change in measures of, symptoms, QOL, and with medication adherence. The significant relationships with symptom change are strongly consistent with findings of several earlier symptom studies.[20,23,24,72] However, this is the first study to demonstrate significant associations between change in insight and change in community functioning, as well

Table 4. Relationship Between Change in Insight and Medication Attitude to Change in Psychopathology and Quality of Life

	PANSS Total	PANSS Positive	PANSS Negative	PANSS General	HQOL Total	HSOC	HINPSYC	HINST	HOBACT[a]	QOLLQOL	Medication compliance	Depression[b]
ITAQ	−1.7***	−0.642***	−0.734***	−1.254***	0.117***	0.140***	0.1118***	0.084*	NA	−0.04	0.078***	0.047***
DAI	−3.322***	−1.620***	−0.867***	−1.8***	0.195***	0.159***	0.238***	−0.199***	NA	0.311***	0.235***	−0.108***

Note: Abbreviations are explained in the first footnote to table 3. Days worked is dichotomous (0 = no, 1 = yes). The PANSS negative syndrome scale in this analysis omits 3 items directly reflecting neurocognition and community functioning: "difficulty in abstract thinking," "passive/apathetic withdrawal," and "emotional withdrawal." (1) These analyses adjust for baseline value of the dependent variable as well as of ITQ, DAI, age, LQOLLQOL, neurocognition, depression and HQOL and time of follow-up.

[a]This model did not converge on a stable solution so coefficients and *P* values could not be calculated.

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

[b]Calgary Depression Rating Scale Score.

as with greater medication adherence. The association between increased insight and decreased symptoms of schizophrenia and improved community functioning, in this large well-characterized sample, while not conclusive, adds further support for the possibility of a causal relationship between insight and outcomes.

Taken together, the results suggest that increasing patient insight into their illness and fostering positive attitudes toward medication may result in improved symptom and QOL outcomes. They suggest possible benefits of exploring negative attitudes toward medication in a client-centered manner. Such an approach should be based on the development of a supportive therapeutic alliance and a strong positive practitioner-consumer relationship. The nature of this relationship has undergone major developments in recent years shifting from a hierarchical medical model to a recovery-oriented model that requires new ways of understanding and approaching the issue of medication choice. Deegan and Drake[73] suggested that not taking medication as prescribed is more likely to occur when the medication is perceived to interfere with highly valued social or occupational activities. From this perspective, addressing patients rationale for not adhering to their medication regimen and personal problems perceived to be related to medication may improve adherence and outcomes. However, more research is needed to better understand how decisions to take medication are made and how such decisions can be influenced. For example, one approach to improving medication adherence involves the use of techniques designed to instill motivation by exploring the relevance of taking medication to achieving personal goals.[74,75] Pharmacologically, clozapine is the only medication reported in the literature to have a specific beneficial effect on patients' insight in addition to symptoms; thus far,[76] however other drugs have not been the focus of such studies. Greater insight in schizophrenia has been found by a few studies to be related to strong social support network,[77] and interventions such as vocational rehabilitation[40] and cognitive behavioral therapy[78] have shown some promise in increasing insight. Further intervention research related to insight and attitudes is needed.

Limitations

Several methodological limitations require comment. First, although we used a large longitudinal dataset, the findings remain associational in nature. The most persuasive set of analyses are the baseline-to-follow-up predictive models and the change-and-change models, but in the absence of an experimental design, we cannot conclude that insight and positive medication attitudes cause the benefits in symptoms and QOL. As noted earlier, alternative explanations for these associations such as reverse causality and bidirectionality are also plausible. That is, not only insight and positive medication attitudes

may lead to reduced symptoms and improved QOL but also reduction in symptoms attributable to medication effects may contribute to improved insight and more positive medication attitudes.

As noted previously, because we cannot randomly assign patients to varying levels of insight or attitudes toward medication, we must rely on associational data that are invariably less conclusive.

A second limitation of this study is that at many CAT-IE sites, the rater who administered the ITAQ and the DAI also completed the PANSS and the HQOL thus introducing a potential rater's bias. The results, nevertheless, point to the importance of exploring patients' attitudes toward their illness and prescribed medication as important factors that play an important role in the recovery process of schizophrenia. The association between increased insight and decreased in symptoms and better functioning on one hand and increased depression on the other fits with the consumer-oriented approach to recovery, which emphasizes a nonlinear process of recovery in which the consumer adapts to and moves beyond the illness on a journey with "bumps along the way."[79] Similarly, Hogan[80] in a report on the New Freedom Commission described recovery "as a process of positive adaptation to illness and disability, linked strongly to self-awareness and a sense of empowerment." While increase in depression may reflect the emergence of a discrepancy between an individual's current functioning and their desired functioning, the emergence of dysphoria due to awareness of this discrepancy could also serve to motivate individuals to reduce this discrepancy. This conceptualization follows the motivational interviewing paradigm[81] that emphasizes setting and pursuing personal goals, which could in the long run lower depression while preserving insight.

Finally, it should be noted that our measure of medication compliance was a global assessment by the treating psychiatrist and was not based on more objective measures of adherence such as blood level monitoring or microelectronic monitoring systems that record the specific time and date whenever the pill bottle is opened.[82]

Conclusion

This study found that greater patient insight into their illness and more positive attitudes toward medication were associated with improved symptom and QOL outcomes and with greater medication adherence. Interventions developed to improve these attitudes may form an important part of psychosocial rehabilitation and/or recovery-oriented service delivery.

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