Attitudes of Schizophrenia Outpatients Toward Psychiatric Medications: Relationship to Clinical Variables and Insight

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Background: Attitude toward medications is important for medication adherence. A patient's drug attitude probably reflects a weighing of benefits against experienced or anticipated side effects or risks associated with the medication. We predicted (1) that drug attitudes would be more positive among schizophrenia patients taking second-generation compared to first-generation antipsychotics because of their greater tolerability and efficacy; and (2) that greater insight into illness, fewer extrapyramidal symptoms, and better social functioning would be associated with better attitudes toward psychiatric medication.

Method: In a cross-sectional study of 81 DSM-IV–diagnosed schizophrenia outpatients, we used multivariate analysis to determine clinical and demographic predictors of drug attitude. Drug attitude was assessed with the 10-item Drug Attitude Inventory (DAI). The relationship between the DAI and psychopathology, insight, extrapyramidal symptoms, level of functioning, and type of antipsychotic (first-generation versus second-generation versus clozapine) was examined.

Results: Less awareness of current symptoms, presence of deficit symptoms, and employment predicted a negative attitude toward psychiatric medications. Extrapyramidal symptoms did not predict drug attitude. Drug attitudes were no different between patients taking first- or second-generation antipsychotics or clozapine.

Conclusion: Patients may not favor second-generation over first-generation antipsychotics, and extrapyramidal symptoms may not be a primary factor determining attitudes. While attitudes may be more positive in patients who recognize therapeutic drug effects, patients who work may view medications particularly negatively, possibly due to a sense of stigma. Because drug attitudes may reflect compliance and are difficult to predict, clinicians should inquire directly.

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One key determinant of outcome in schizophrenia is adherence to antipsychotic medication.[1] Rather than being "idiosyncratic" and unpredictable, the decision to take medication could be viewed as the result of weighing perceived benefits against adverse effects.[2,3] Under this model, the patient's perception of benefit would follow from awareness of illness and medication benefits as gauged by the experience of residual symptoms (awareness of symptoms) and level of functioning (quality of life and employment). Disadvantages of medications include side effects such as extrapyramidal symptoms (EPS), cost, and the stigma and inconvenience associated with having to take psychiatric medications.[4] The drug attitude construct could be regarded as a convenient proxy measure of this risk-benefit decision process: the more perceived benefit, the better the attitude toward medication and vice versa, possibly even predicting medication adherence.

One validated scale with good internal consistency and high-retest reliability to measure drug attitude of psychiatric patients is available: the Drug Attitude Inventory (DAI).[5] It was originally constructed with 30 self-report items measuring a wide range of attitudes and beliefs about taking psychotropic medications. In addition, the scale has been shown to have predictive value for noncompliance. Discriminative analysis in a sample of 150 patients with schizophrenia identified 10 items that best predicted compliance over a 1-year period. Based on this analysis, 89% of the sample were correctly assigned to compliant and noncompliant groups. The predictive value of the DAI is supported by a preliminary report of a sig-

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Table 1. Demographic and Clinical Characteristics of 81 Schizophrenia Outpatients

Variable	N	%	Mean	SD	Range
Demographic characteristics					
Age, y			43.22	9.43	21 to 69
Gender					
Male	60	74.1			
Female	21	25.9			
Ethnicity					
White, non-Hispanic	57	70.4			
Hispanic	1	1.2			
Black	22	27.2			
Asian	1	1.2			
Education, y			11.75	2.33	4 to 18
≤ Eighth grade	7	8.6			
9–12 y	53	65.4			
13–16 y	20	24.7			
≥ College (17+ y)	1	1.2			
Marital status					
Never married	64	79.0			
Ever married	17	21.0			
Duration of illness, y			19.10	9.12	1 to 43
Employment status					
Unemployed	60	74.1			
Employed	21	25.9			
Clinical characteristics					
Rating scale	81				
DAI score			4.5	4.29	–10 to 10
SUMD (items 4–20)			74.19	8.58	44 to 85
SUMD (item 1)			1.73	1.16	0 to 5
SUMD (item 2)			1.72	1.20	0 to 5
SUMD (item 3)			1.75	1.50	0 to 5
QLS total score			59.65	14.49	33 to 101
QLS subscale 1			21.80	7.57	2 to 42
QLS subscale 2			7.09	4.70	0 to 20
QLS subscale 3			24.17	4.87	11 to 36
QLS subscale 4			6.59	1.82	3 to 10
PANSS total score			61.78	13.35	38 to 99
PANSS positive subscale			14.41	5.47	7 to 29
PANSS negative subscale			17.92	4.27	9 to 35
PANSS general subscale			29.46	7.30	18 to 52
SANS total			41.17	14.77	13 to 82
HAM-D total			11.26	4.53	2 to 26
BAS total			1.73	2.26	0 to 9
AIMS total			1.94	2.23	0 to 11
SAS total			3.89	3.87	0 to 16
Total number psychotropics	81		2.25	1.20	1 to 6
Antipsychotic monotherapy	56	69.1			
Typical	19	23.5			
Atypical[a]	24	29.6			
Clozapine	13	16.0			

[a]Does not include clozapine.
Abbreviations: AIMS = Abnormal Involuntary Movement Scale, BAS = Barnes Akathisia Scale, DAI = Drug Attitude Inventory, HAM-D = Hamilton Rating Scale for Depression, PANSS = Positive and Negative Syndrome Scale, QLS = Heinrichs-Carpenter Quality of Life Scale, SANS = Scale for the Assessment of Negative Symptoms, SAS = Simpson-Angus Extrapyramidal Side Effects Scale, SUMD = Scale to Assess Unawareness of Mental Disorder.

nificant positive relationship between patients' attitudes, as assessed by the DAI, and compliance.[6]

Side effect burden, including but not limited to EPS and akathisia, is often viewed as an important reason for noncompliance.[7] Given that atypical antipsychotics produce fewer EPS, tend to be better tolerated, and are associated with modestly better compliance,[8,9] the risk-benefit model of drug attitude would predict that the second-generation antipsychotics would be viewed more positively than older antipsychotics. Such a finding would be consistent with studies linking EPS with dysphoria.[10] However, Hofer and colleagues[11] found no difference in drug attitudes as assessed by the 30-item version of the DAI between patients receiving older versus newer antipsychotics; sedation but not EPS predicted less enthusiasm for medication.

We tested this risk-benefit model of drug attitude in a cross-sectional study of 81 outpatients with schizophrenia. If the model is valid, drug attitude should reflect the benefits and adverse effects of treatment: greater insight into illness, fewer residual symptoms, and better social functioning should correlate with more positive drug attitudes, whereas more extrapyramidal side effects should be associated with more negative drug attitudes. We expected to find patients receiving newer antipsychotics to indicate more positive drug attitudes due to the perception that these medications are more effective and less noxious.

METHOD

Subjects

Our sample consisted of an outpatient cohort of 81 patients with schizophrenia. As participants in a genetic study, this cohort was well characterized with regard to diagnosis (DSM-IV diagnosis of schizophrenia confirmed by SCID interview), clinical status (rating scales for many aspects of psychopathology in addition to a quality of life measure), and demographic variables. Ratings of drug attitude, extrapyramidal side effects, and insight were added to test our hypotheses. Demographic characteristics of the sample are summarized in Table 1.

All study participants provided written, informed consent, and the study was approved by the responsible institutional review boards.

Drug Attitude Measure

Drug attitude was assessed with the 10-item DAI,[5] which is a self-report instrument of true-false statements about the nature of the patient's experience with taking psychotropic medications. Items in the DAI reflect how the patient feels about medication and his or her attitudes and beliefs about medication. Some statements are worded in a positive direction (e.g., "My thoughts are clearer on medication"), and some are worded negatively (e.g., "Medications make me feel tired and sluggish"). Scores range from –10 to +10, with higher scores indicating a more positive attitude toward and a more positive experience with medication.

Insight Measures

Current insight was measured with the Scale to Assess Unawareness of Mental Disorder (SUMD).[12] The SUMD utilizes a semistructured interview to rate awareness on 20

items based on a 5-point Likert scale. Higher scores indicate poorer insight. We used the 3 global insight items—current awareness of mental disorder (item 1), current awareness of achieved medication effects (item 2), and current awareness of social consequences of medications (item 3)—and the subscale, current awareness of symptoms (items 4 to 20), to assess current insight.

Clinical Variables

Psychopathology was measured using the Positive and Negative Syndrome Scale (PANSS),[13] the Scale for the Assessment of Negative Symptoms (SANS),[14] and the Hamilton Rating Scale for Depression (HAM-D).[15] Quality of life was assessed by the Heinrichs-Carpenter Quality of Life Scale (QLS).[16] The QLS is a 21-item semistructured interview comprised of the following 4 subscales: interpersonal relationships, instrumental role activities, "intrapsychic foundations" (i.e., deficit syndrome characteristics), and common objects and activities. Extrapyramidal medication side effects were rated with the Barnes Akathisia Scale (BAS),[17] the Abnormal Involuntary Movement Scale (AIMS),[18] and the Simpson-Angus Extrapyramidal Side Effects Scale (SAS).[19]

Data Analysis

Exploratory factor analysis was used to determine the factor structure of the DAI. Factors were extracted by principal components analysis. Item loadings of .40 were used as the cutoff for item inclusion within factors. Maximum likelihood squared multiple correlations were used as initial communality estimates, and the final solution was rotated using an oblique rotation, as factors were theorized to be correlated with one another. The optimal number of factors to extract was determined by analysis of the scree plot (as per Gorsuch[20]). Multivariate analysis was used to examine predictors of drug attitude. In the multivariate analysis, 3 separate hierarchical regressions were used to predict variability in total DAI and the factors of the DAI generated by exploratory factor analysis. Predictors entered into the model were age, gender, duration of illness, marital status, employment status (0 = employed, 1 = not employed); SUMD items 4–20 (symptom score), SUMD item 1 (awareness of mental disorder), SUMD item 2 (awareness of the achieved effects of medication), SUMD item 3 (awareness of the social consequences of mental disorder); PANSS total score, PANSS general psychopathology subscale, PANSS positive and negative subscales, SANS score, HAM-D score; BAS score, AIMS total score, SAS total score; subscales of the QLS; and total number of medications.

Level of significance was set at .05 for all analyses. Statistical analyses were done with SPSS 11.0 (SPSS Inc., Chicago, Ill.).

Table 2. Factor Loadings for Drug Attitude Inventory (DAI) Items

Item No.[a]	Item Wording	Factor 1	Factor 2
1	For me, the good things about my medications outweigh the bad.	.69	
4	Medications make me feel more relaxed.	.59	
7	I feel more normal on my medications.	.79	
9	My thoughts are clearer on medications.	.58	
10	By staying on medications, I can prevent getting sick.	.84	
2	I feel weird, like a "zombie" on my medications.		.50
5	Medications make me feel tired and sluggish.		.76
6	I take medications only when I am sick.		.73
8	It is unnatural for my mind and body to be controlled by medications.		.43

[a]Item no. 3, "I take medications of my own free choice," did not load on either Factor 1 or 2.

RESULTS

A 2-factor solution was extracted as most parsimonious, accounting for 43.1% of the variability in DAI total score. Items assessing positive attitudes about and expectations of medication comprised Factor 1 (statements 1, 4, 7, 9, 10), and items assessing negative attitudes about and expectations of medication comprised Factor 2 (statements 2, 5, 6, 8). Only item 3, "I take medications of my own free choice," did not load on either Factor 1 or 2 (loadings < .4) (Table 2). The negative and positive attitudes factors were not correlated ($r = 0.19$, $p = .10$).

Results from clinical ratings are summarized in Table 1. The DAI scores ranged from –10 to +10, with a median of 6.0, a mean of 4.5, and standard deviation of 4.29. Scores were thus negatively skewed, reflecting an overrepresentation of more positive attitudes toward psychiatric medication. On average, subjects received 2.25 medications, ranging from 1 to 6. Of the total 81 subjects in our sample, 56 (69.1%) were receiving antipsychotic monotherapy: 19 (23.5%) received a first-generation antipsychotic, 24 (29.6%) received a second-generation antipsychotic (except clozapine), and 13 (16.0%) received clozapine. No differences were found in drug attitude between the 3 groups. Of the participants prescribed antipsychotic monotherapy, those receiving first-generation antipsychotics had a mean DAI score of 5.79 (SD = 3.52), those receiving second-generation antipsychotics (except clozapine) had a mean DAI score of 3.92 (SD = 4.11), and those receiving clozapine had a mean DAI score of 6.0 (SD = 3.16), $F = 1.91$, $df = 2,53$; $p = .16$.

Bivariate correlations showed several significant correlates of the DAI. Not surprisingly, items of the SUMD whose content overlaps with the DAI were correlated with the DAI. Better attitudes toward medication reported by patients on the DAI were associated with greater awareness of mental disorder ($r = –0.32$, $p < .01$), endorsement of the belief that medication lessens symptoms ($r = –0.38$, $p < .001$), and greater awareness of the social consequences of mental disorder ($r = –0.27$, $p < .05$).

More negative attitudes on the DAI were expressed by individuals rated as having more severe psychopathology across several symptom domains, including more prominent deficit symptoms ($r = 0.27$, $p < .05$), more negative symptoms ($r = –0.25$, $p < .05$), more depressive symptoms ($r = –0.25$, $p < .05$), more positive symptoms ($r = –0.25$, $p < .05$), and more severe general psychopathology ($r = –0.25$, $p < .05$). Thus, participants with more positive symptoms (PANSS), general psychopathology (PANSS general and total scores), negative symptoms (SANS), deficit syndrome symptoms (QLS), and depression (HAM-D) reported more negative attitudes toward medication on the DAI. Other variables such as demographics, SUMD symptom score, and EPS were not significantly correlated with the DAI.

The multivariate analysis identified insight and socio-occupational functioning as independent predictors of the DAI score. Total variance explained by the regression model was 41.8%. Employment predicted more negative attitudes toward medication as reflected by total DAI score ($\beta = 3.79$, $SE = 1.75$, $p < .05$). Greater awareness of symptoms of illness, as reflected by the SUMD symptom score, was negatively correlated with total DAI score, indicating that awareness of symptoms was associated with a more favorable attitude toward medication ($\beta = –.183$, $SE = .09$, $p < .05$).

Like the DAI total score, Factor 1 of the DAI was predicted by the awareness of symptoms item on the SUMD. SUMD total score was an independent predictor of DAI Factor 1 ($\beta = –047$, $SE = .02$), indicating that participants with better symptom awareness were more willing to view medications positively ($p < .05$). Total variability in Factor 1 of the DAI explained by the regression model was 43.9%.

Factor 2 of the DAI was predicted by employment status, instrumental role functioning (QLS), and deficit symptom subscale of the QLS. Individuals who were employed reported more negative attitudes toward medication as assessed by Factor 2 ($\beta = 1.28$, $SE = .41$, $p < .01$). Similarly, those rated on the QLS as having better role functioning reported more negative views of medication ($\beta = .086$, $SE = .41$, $p < .05$). Individuals who were rated on the QLS as having fewer deficit syndrome characteristics reported less negative views of medication ($\beta = .09$, $SE = .04$, $p < .05$). Total variability in Factor 2 of the DAI explained by the model was 42.5%.

DISCUSSION

Our hypothesis that newer, second-generation antipsychotics lead to a more positive drug attitude was not supported. This confirms the finding by Hofer and colleagues,[11] who did not find a difference in attitude between patients treated with typical versus atypical antipsychotics either. This is clinically relevant as one should not assume (drug advertising aside) that a patient is more accepting of medication simply because a newer antipsychotic is prescribed. However, since treatment was not randomized, patients with a worse drug attitude could have been preferentially treated with newer agents.

Contrary to our predictions, we did not find greater extrapyramidal side effects to be predictive of negative drug attitude or better global functioning to be predictive of better drug attitude. Our results rather suggest that better occupational and role functioning might serve as clinical "red flags" for a negative attitude toward psychiatric medications. Maybe patients who work are frustrated about having no choice but to take medications with side effects to function. This replicates the finding of Hofer and colleagues[11] that employed patients had less positive regard for medication than patients who were unemployed. Their sample was Austrian, which suggests that this finding is not the result of cultural factors unique to our Boston sample. As opposed to the findings of Hofer and colleagues, severity of positive symptoms did not predict drug attitude in multivariate analyses. Instead, negative symptoms as assessed by the deficit subscale of the QLS (lack of a sense of purpose, amotivation, low curiosity, anhedonia, and spending a lot of time alone in passive activity) predicted a negative attitude, suggesting that poor social functioning might be associated with more negative drug attitudes.

We found one aspect of insight, awareness of current symptoms, to predict drug attitude: those patients who were aware of their symptoms had more favorable views of medication. One can imagine that those patients correctly identify medication benefit in terms of symptom reduction. This possibility finds support in one study in which patients who experienced symptom relief from medication were more likely to comply with medications.[21] Similarly, patients' perceived lack of efficacy was given as one reason for noncompliance in another study.[22] Drug attitude in our cohort was generally good, comparable with the aforementioned cohort of patients with schizophrenia in Austria and with other cohorts.[23,24] The factor analysis of the DAI identified 2 uncorrelated factors, one of which tapped into conceptualization of medication as helpful, the other, the perception that medication had negative effects and was only necessary when someone felt sick. This suggests that drug attitude is not on a continuum from negative to positive, but rather that there are 2 separate dimensions of drug attitude—positive and negative attitude dimensions.

Our findings cannot be generalized beyond this sample of stable voluntary patients who attend an outpatient clinic. Most patients received psychotropics in addition to antipsychotics, which confounds comparisons made between patients grouped according to antipsychotic treatment. Our sample size was small, and not all analyses (such as the comparison between the 3 antipsychotic

groups) were based on the full sample of 81 patients. Any inferences are limited by the cross-sectional design of the study and nonrandom assignment to treatment. Associations between predictors of drug attitude and measured drug attitude in particular have to be interpreted with caution. They may be confounded by the initial treatment assigned, if the (nonrandom) treatment assignment was influenced by the very factors that we found as predictors. Prior treatment experience might have determined the current choice of antipsychotic as well; we did not collect past treatment history. We did not assess medication side effects comprehensively or antipsychotic side effects specifically (e.g., by using the Systematic Assessment for Treatment Emergent Events [SAFTEE][25] or the Approaches to Schizophrenia Communication [ASC],[26] respectively), limiting our ability to detect the perceived risks of atypical antipsychotics.

While the 10-item DAI is easy to administer, the scale is older and has only been validated before the advent of newer antipsychotics. The scale nevertheless has face validity for evaluating classes of medications that were not available when the scale was developed. The DAI focuses on rather global aspects of medication benefits, not medication-specific effects or side effects. Other scales like the Rating of Medication Influences (ROMI)[27] yield additional information that can be more pertinent in predicting medication compliance in certain patients; an example would be a noncompliant patient who scores high on the DAI but simply cannot afford to buy medication. Since compliance is difficult to measure in clinical practice, it would be valuable to know if the DAI can "flag" potential noncompliance, particularly in settings where drug noncompliance is a strong possibility but medication is not outright rejected (e.g., in involuntarily committed patients who apparently comply with treatment only to go to great lengths to "cheek" medication[28]). In a preliminary retrospective analysis, the DAI predicted compliance.[5] Future studies need to prospectively investigate if drug attitude "matters," that is, if drug attitude predicts the ultimate variable of interest, compliance.

Our results do not invalidate the risk-benefit model. They rather suggest that perception of side effects in particular varies according to the eye of the beholder and that medication effectiveness can be perceived as negative by patients if it enhances stigma (e.g., working and having to take psychiatric medication). In at least 2 other studies contrasting compliant and noncompliant patients, the *compliant* group experienced *more* akathisia[29] or was not different in experiencing drug side effects.[6] Thus, there is no substitute for inquiring directly about a patient's drug attitude since it can only be partially predicted from demographic and clinical variables.

Drug name: clozapine (Clozaril, Fazaclo, and others).

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