Decisional Capacity to Consent to Research Among Patients With Bipolar Disorder: Comparison With Schizophrenia Patients and Healthy Subjects

Barton W. Palmer, Ph.D.; Laura B. Dunn, M.D.; Colin A. Depp, Ph.D.; Lisa T. Eyler, Ph.D.; and Dilip V. Jeste, M.D.

Objective: Although clinical trials are needed to advance treatments for bipolar disorder, there has been little empirical research on the capacity of bipolar patients to consent to research. The aim of the present study was to evaluate levels of decisional capacity of bipolar patients compared with those of schizophrenia patients and healthy comparison subjects, as well as to examine whether symptom and neurocognitive deficits correlate with patients' decisional abilities.

Method: Participants were 31 outpatients with bipolar disorder, 31 outpatients with schizophrenia, and 28 healthy comparison subjects; each participant's decisional capacity was evaluated with the MacArthur Competence Assessment Tool for Clinical Research. Patient participants were also evaluated with standardized clinical rating scales and neurocognitive tests. Data were collected from April 2002 through November 2005.

Results: Bipolar patients had worse understanding than healthy comparison subjects, and their level of decisional capacity did not differ from that of schizophrenia patients. Within the combined patient sample, neurocognitive deficits and negative symptoms were significantly correlated ($p < .05$) with the level of decisional capacity (particularly, understanding of disclosed information). Repeating the missed information improved the level of understanding in all groups.

Conclusions: The presence of bipolar disorder appears to be a risk factor for impaired understanding of information disclosed under standard consent procedures but should not be equated with a lack of competence to consent. The observed improvement in understanding with redisclosure of information suggests that enhanced consent procedures may be useful during enrollment of bipolar patients in research.

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Drs. Palmer, Dunn, Depp, Eyler, and Jeste report no other financial affiliations relevant to the subject of this article.

Corresponding author and reprints: Barton W. Palmer, Ph.D., Division of Geriatric Psychiatry 116A-1, University of California, San Diego, Veterans Affairs San Diego Healthcare System, 3350 La Jolla Village Dr., San Diego, CA 92161 (e-mail: bpalmer@ucsd.edu).

Bipolar disorder is a common and serious mental illness that often affects cognition and insight.[1,2] Although pharmacologic treatments are the primary means of managing this condition, there remains an ongoing need for clinical research to identify more effective and safer pharmacologic and psychosocial interventions.[3] Advances will derive, in large part, from clinical trials enrolling patients volunteering as research participants. Yet, there are cogent reasons to suspect that some patients with bipolar disorder may not have adequate decisional capacity due to impaired insight and neurocognitive factors.[4] These issues may be particularly salient among middle-aged and older patients. The numbers of older patients with bipolar and other psychiatric disorders are increasing,[5] and there remains a particular need for clinical research focused on such patients.[6–8] Neurocognitive deficits among middle-aged and older patients with bipolar disorder are common and generalized, even among clinically stabilized outpatients.[2] Research with schizophrenia patients consistently indicates that decisional capacity is strongly related to neurocognitive functioning.[9–15] Given the normal age-related changes in neurocognitive functioning and evidence that aging in bipolar disorder (as a proxy for the number of lifetime affective

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episodes) may lead to further neurocognitive deterioration,[16] the issue of capacity to consent to research may be particularly germane among middle-aged and older bipolar patients.

There have been only 2 published studies of decisional capacity among bipolar patients of any age group.[17,18] Howe et al.[17] examined capacity to consent to treatment among 21 acutely hospitalized patients with bipolar disorder, as well as 110 with schizophrenia and 64 with schizoaffective disorder. They found no significant differences in capacity to consent to treatment among the 3 diagnostic groups. Cairns et al.[18] also studied capacity to consent to treatment in acutely hospitalized psychiatric inpatients with various diagnoses; 13 of 21 patients (62%) with diagnoses of bipolar disorder were judged incapable of consenting to treatment. To our knowledge, there have been no other published studies on capacity to consent to treatment among patients with bipolar disorder and no prior published studies on capacity to consent to research among patients with bipolar disorder.

The primary goal of the present study was to evaluate the levels of 4 dimensions of decisional capacity for research participation (understanding, appreciation, reasoning, and expression of a choice)[19] among outpatients with bipolar disorder over age 40 years, in comparison with outpatients with schizophrenia and healthy comparison subjects (HCs). Given that repetition of information has been shown to enhance understanding in patients with schizophrenia as well as in other populations,[14,20–22] we also evaluated the effects of reexplaining initially misunderstood components. We also examined the degree to which overall neurocognitive functioning, insight, and severity of psychopathology were associated with decisional capacity in the combined (bipolar and schizophrenia) patient sample.

Decisional capacity is inherently specific to the nature of the decision to be made[19]; in this study, we evaluated capacity to consent to an actual study of the long-term effects of U.S. Food and Drug Administration (FDA)–approved second-generation antipsychotics among patients aged greater than 40 years. (Hereafter referred to as the "parent study.") We hypothesized that bipolar patients would have lower decisional capacity than HCs, but higher capacity than patients with schizophrenia (whose neurocognitive deficits may be more severe than those of patients with bipolar disorder[2]). We also hypothesized that bipolar patients, as well as the participants in the other 2 groups, would show improved understanding with repeated disclosure of initially misunderstood information. We further postulated that, in the combined patient sample, decision-making capacity would correlate positively with neuropsychological test performance and level of insight and negatively with age and severity of psychiatric symptoms.

METHOD

Participants

This report is based on analysis of data collected (April 2002 through November 2005) from a larger study of capacity to consent to research among middle-aged and older psychiatric patients (without dementia) receiving antipsychotic medications. The present study sample included 28 HCs, 31 outpatients with bipolar disorder, and 31 outpatients with schizophrenia. Healthy comparison subjects were recruited through flyers posted in the community as well as via personal contacts and word of mouth. Recruitment of patients was coordinated through our National Institute of Mental Health (NIMH)–funded Advanced Center for Intervention and Services Research at the University of California, San Diego (UCSD); recruitment sources included board-and-care facilities, day treatment programs, and the UCSD and the Veterans Affairs San Diego Healthcare System (VASDHS) outpatient psychiatry services. (Nineteen [61%] of the bipolar patients and 22 [71%] of those with schizophrenia were residents at local board-and-care assisted living facilities.) Decisional capacity data from 16 of the 31 patients with schizophrenia were included in a prior report,[14] but none of the data from the HCs or bipolar patients have been previously published.

Inclusion criteria were (a) DSM-IV diagnosis of schizophrenia or bipolar disorder (with 1 or more current or past psychotic symptoms), as determined by patients' treating clinicians, or, for the HCs, absence of psychiatric illness as established with the Mini-International Neuropsychiatric Interview[23] administered by trained research assistants (under the supervision of B.W.P. and L.B.D.); (b) current age greater than or equal to 40 years; (c) fluency in English; (d) absence of a DSM-IV diagnosis of current substance use disorder, dementia, or other known conditions likely to influence neurocognition; and (e) (for patients only) current treatment with a second-generation (atypical) antipsychotic medication. To facilitate comparison of results to the bipolar sample, we selected a subset of participants with schizophrenia (for whom we had a larger sample), keeping blind to information about the clinical, neurocognitive, or decisional capacity variables. Exact one-to-one matching was not achieved, but in selecting the schizophrenia subset, we attended to the demographics of each person (age, education, ethnicity, and gender) in the bipolar group so that the 2 patient samples would be generally comparable in terms of size as well as demographic characteristics.

This study was approved by the Human Research Protections Program (HRPP) for UCSD and VASDHS; after complete description of the capacity study, a written informed consent was obtained from every participant. (This study meets the federal definition of a "minimal risk" protocol; so, per our HRPP guidelines, formal as-

sessment of capacity to consent to the capacity study was not required, although 1 potential participant was excluded due to a clear lack of understanding of the nature of the research.)

Description of Parent Study

The parent study was a longitudinal study of side effects, including tardive dyskinesia, of FDA–approved second-generation antipsychotic medications among middle-aged and older patients.[24] We selected the aforementioned study as the focus of this consent capacity study because it was a long-term project in our Research Center, enabling us to enroll a relatively large number of patients who were actually considering research participation. The HCs, who were not eligible for the parent study, were asked to imagine that they were considering enrollment in that study. Other than a minimum age of 40 years and the requirement that the participant's condition be appropriate for treatment with a second-generation antipsychotic, there were few exclusion criteria, permitting us to evaluate a diverse group of patients. The parent study procedures included clinical interviews, psychopathology ratings, brief cognitive testing, and evaluations for tardive dyskinesia and other side effects. It was a minimal risk protocol, as the evaluations and procedures were safe or at least consistent with the risks associated with standard clinical care, there was no placebo control, participants could stay on their current medication(s), and treatment was under the control of each patient's treating physician. The decisional capacity evaluation for subjects in the present study was conducted prior to the formal consent process and enrollment for those who expressed interest in the parent study.

Measures

We collected information on participants' age, education, gender, ethnicity, and age at onset of illness via interview and/or review of available records.

Decisional capacity. All participants were evaluated with the MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR),[25] which provides quantitative scores for 4 commonly recognized dimensions of decision-making capacity (understanding, appreciation, reasoning, and expression of a choice). We conducted semiannual checks to ensure adequate interrater reliability on this measure (intraclass correlation coefficient [ICC] ≥ 0.80). The research assistants also met regularly with 2 authors (B.W.P. and L.B.D.) to review and discuss administration or scoring issues.

As per standard MacCAT-CR procedures,[25] the item content was tailored to the parent study protocol, and information for questions on the understanding subscale was repeated when participants initially provided suboptimal answers. The standard procedures provide for 1 such redisclosure per understanding item if a participant's initial response suggests suboptimal comprehension, but to evaluate the effects of further repeated disclosure, we permitted up to 2 redisclosures (providing for scores referred to below as understanding trials 1, 2, and 3, respectively). In general, appropriate response to the MacCAT-CR questions requires not mere "parroting back" of the words said by the examiner, but rather a sufficient description by the respondent to suggest understanding. The examiner asked the participant follow-up questions when needed to clarify a response. For the first redisclosure (trial 2), the information was presented using the same predetermined wording as in the initial disclosure. When a second redisclosure was needed (trial 3), rather than repeating the predetermined wording, the research assistant adjusted the information, i.e., changing, repeating, or explaining words and concepts in a form that was appropriate to the individual participant's observed conversational skills. Thus, this second reexplanation was less standardized, but we chose to do so for these final reexplanations as we were interested in determining what a participant could understand under the best of circumstances. We eliminated 1 item from the understanding subscale and another from the reasoning subscale that were not applicable to the parent study, but to aid comparison to other studies, we prorated the understanding and reasoning subscale scores so that they were expressed in terms of the standard MacCAT-CR subscale score ranges.

There is no established criterion for categorizing people as "capable" versus "incapable," but we compared the proportion of people in each group who earned an understanding score greater than or equal to 16 (of 26 possible points) at trials 1, 2, and 3; this criterion was applied in the NIMH-sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia study to determine which patients could give independent consent to participate.[15]

Psychopathology ratings. Among patient participants, severity of psychopathology was evaluated with the Positive and Negative Syndrome Scale (PANSS)[26] positive, negative, and general symptom subscales and with a 4-item PANSS mania factor that has previously been shown to have high concordance with the Young Mania Rating Scale.[27] We also administered the 17-item Hamilton Rating Scale for Depression (HAM-D)[28] and the Birchwood Insight Questionnaire (BIQ).[29] Higher scores on the BIQ indicate better insight; the remainder of the psychopathology scores are scaled such that higher scores indicate worse psychopathology. Our research assistants undergo extensive training for these instruments and are required to demonstrate reliable scoring on the psychopathology rating scales (ICC > 0.80) relative to ratings from an experienced psychiatrist (D.V.J.).

Neurocognitive functioning. A majority of patient participants were also administered a neuropsychological test battery. This battery comprised tests representing a

range of neurocognitive abilities, including verbal crystallized knowledge (vocabulary, information, and similarities subtests from the Wechsler Adult Intelligence Scale-Third Edition [WAIS-III][30]), perceptual organization (WAIS-III picture completion, block design, and matrix reasoning subtests[30]), attention and working memory (WAIS-III digit span, letter number sequencing, and arithmetic subtests[30]), processing speed (Trail Making Test Part A,[31] WAIS-III digit symbol and symbol search subtests,[30] and Letter and Animal Fluency[32,33]), and executive functioning (Trail Making Test Part B,[31] Wisconsin Card Sorting Test-64 Card Version,[34] and Stroop Task[35]), as well as verbal and visual learning (Hopkins Verbal Learning Test-Revised,[36] Story Memory Test,[37] Brief Visual-Spatial Memory Test-Revised,[38] and the family pictures subtest from the Wechsler Memory Scale-Third Edition[39]). Each test score was coded such that higher scores indicated better performance; scores were transformed to a z score scale using the normalized rank function in SPSS version 12.01 (SPSS, Inc., Chicago, Ill.). As recent research from our group[12,14] and others[10,11] indicates little evidence that specific neurocognitive abilities differentially predict specific subcomponents of decisional capacity, we calculated a mean z score across the test battery as the neurocognitive variable for the analyses described below.

Procedures

The measures were individually administered to each participant by trained Bachelor's level–research assistants under the supervision of the first author (B.W.P.). The research assistant administering the MacCAT-CR was kept unaware of the participant's scores and responses on the psychopathology rating scales and neurocognitive tests and vice versa. The MacCAT-CR and symptom measures were generally completed on the same day: 82% of the patients completed the MacCAT-CR and psychopathology and insight measures on the same day, and 95% completed these measures within a week of MacCAT-CR administration. The research assistants were not blind to diagnosis, but they were not informed of our hypotheses regarding differences in level of decisional capacity among the groups.

Statistical Analyses

We examined the distribution of all variables in terms of skew and kurtosis to ensure that the assumptions for parametric analyses were met. Significant skew (skewness divided by the standard error of skewness ≥ 3.00) was found in 1 or more groups for current age, PANSS mania factor, and the BIQ, but each was successfully reduced within the accepted limits for parametric analyses using logarithmic functions. There was also significant skew observed in most of the MacCAT-CR variables, but we were unable to identify a transformation that sufficiently reduced the skew in all groups, so nonparametric tests were used for analyses involving MacCAT-CR scores. Age and education among the 3 groups were compared with 1-way analyses of variance and follow-up pairwise comparisons using Tukey's honestly significant difference procedure. Gender and ethnicity were compared with Pearson's χ^2. Psychopathology ratings, age at illness onset, and the neurocognitive composite score were compared between the 2 patient groups using independent t tests. Differences on the MacCAT-CR subscale scores were evaluated with the Kruskal-Wallis test, with follow-up comparisons via pairwise Mann-Whitney U tests for those variables with significant overall differences. Improvement in understanding over the 3 MacCAT-CR understanding trials was assessed within each group using Friedman's analysis of ranks. We also used Pearson's χ^2 to evaluate differences in the proportion of participants in each group with understanding subscale totals greater than or equal to 16 at trials 1, 2, and 3. Using the combined sample of participants from the 2 patient groups, bivariate associations between the MacCAT-CR understanding, reasoning, and appreciation subscale scores and psychopathology ratings and the neurocognitive composite score were evaluated using Spearman's rho. (Even among patients with schizophrenia, few have difficulty with the choice subscale.[40]) Significance for all analyses was defined as $p < .05$ (2-tailed).

RESULTS

Demographic Characteristics, Psychopathology Ratings, and Neurocognitive Functioning

There were no significant demographic differences among the 3 groups (Table 1). Among the 2 patient groups, there were no significant differences in age at illness onset, severity of psychopathology, or overall neurocognitive test performance.

Decisional Capacity

Significant overall group differences were observed on all 3 MacCAT-CR understanding trials, as well as on the appreciation subscale (all $\chi^2 \geq 7.14$, df = 2, $p < .05$) (Table 1). Specifically, HCs had better understanding scores than both patient groups and better appreciation scores than the schizophrenia group. Even the latter finding, however, belies the degree of within-group heterogeneity, e.g., 58% (N = 18) of the schizophrenia patients earned full credit on the appreciation subscale. There were no significant differences between the bipolar and schizophrenia patient groups on any of the MacCAT-CR subscales. Also, there were no significant differences among any of the 3 groups in terms of the MacCAT-CR expression of a choice subscale; full credit (2 points) on the expression of a choice score was earned by all 31 patients with bipolar disorder, 30 of the 31 schizophrenia patients, and 27 of the 28 HCs.

Table 1. Comparison of Demographic Characteristics, Psychopathology Ratings, Overall Neurocognitive Scores, and Decisional Capacity in the 3 Subject Groups[a]

Variable	Healthy Comparison Group (N = 28)	Bipolar Disorder Group (N = 31)	Schizophrenia Group (N = 31)	Test Result	df	p
Age, mean (SD), y	56.6 (11.1)	53.1 (8.0)	52.4 (7.0)	F = 1.44	2,87	.243
Education, mean (SD), y	13.9 (2.5)	13.6 (2.2)	13.0 (1.8)	F = 1.18	2,87	.312
Gender, % women	53.6	45.2	51.6	$\chi^2 = 0.47$	2	.792
Ethnic minorities, %	17.9	19.4	22.6	$\chi^2 = 5.66$	8	.686
Age at onset, mean (SD), y	NA	29.3 (14.5)	27.7 (10.4)	t = 0.467	53	.643
Positive and Negative Syndrome Scale score, mean (SD)						
Positive syndrome		15.2 (6.7)	16.6 (6.1)	t = 0.853	60	.397
Negative syndrome		13.9 (5.1)	13.8 (5.7)	t = 0.094	60	.925
Mania factor		6.8 (3.1)	6.5 (3.3)	t = 0.356	60	.723
General psychopathology		30.5 (9.2)	29.6 (6.7)	t = 0.444	60	.658
Hamilton Rating Scale for Depression score, mean (SD)		11.4 (5.3)	10.5 (6.0)	t = 0.631	59	.531
Birchwood Insight Scale score, mean (SD)		8.6 (2.4)	9.4 (2.4)	t = 1.646	58	.105
Neurocognitive z score, mean	NA	–0.03	–0.15	t = 1.00	50	.321
MacCAT-CR score, mean (SD)						
Understanding (range, 0–26)						
Trial 1	21.4 (3.8)	18.2 (5.4)	18.7 (5.1)	$\chi^2 = 7.14$	2	.028[b]
Trial 2	25.2 (1.6)	22.5 (5.2)	23.6 (3.6)	$\chi^2 = 11.20$	2	.004[b]
Trial 3	25.9 (0.4)	24.0 (5.0)	24.4 (3.3)	$\chi^2 = 8.65$	2	.013[b]
Appreciation (range, 0–6)	5.8 (0.8)	5.5 (0.9)	4.8 (1.6)	$\chi^2 = 7.82$	2	.020[c]
Reasoning (range, 0–8)	7.7 (0.6)	7.4 (1.5)	7.1 (1.7)	$\chi^2 = 2.91$	2	.233
Expression of a choice (range, 0–2)	2.0 (0.2)	2.0 (0.0)	1.9 (0.4)	$\chi^2 = 1.07$	2	.586

[a]Group differences on MacCAT-CR scores were evaluated with the Kruskal-Wallis test, with follow-up comparisons via pairwise Mann-Whitney U. All other continuous variables were evaluated with 1-way analyses of variance, with follow-up comparisons using Tukey's honestly significant difference procedure or (for comparisons involving only the 2 patient groups) independent t tests. Group comparisons of categorical variables were evaluated with Pearson's χ^2 tests.
[b]Healthy comparison group > bipolar group and schizophrenia group.
[c]Healthy comparison group > schizophrenia group.
Abbreviations: MacCAT-CR = MacArthur Competence Assessment Tool for Clinical Research, NA = not available.

Understanding improved significantly among the patients with bipolar disorder with repeated disclosure of initially misunderstood information, from overall means (SDs) of 18.2 (5.4) points at trial 1, 22.5 (5.2) points at trial 2, and 24.0 (5.0) points at trial 3 (Friedman's analysis of ranks $\chi^2 = 50.96$, df = 2, N = 31, $p < .001$). As shown in Figure 1, similar improvements were also observed among the HCs and patients with schizophrenia ($\chi^2 > 43$, $p < .001$ for both groups). In terms of the CATIE study criterion for "capable" status (understanding score ≥ 16),[15] there was a significant group effect on the proportion of capable subjects ($\chi^2 = 6.64$, df = 2, N = 90, p = .036) at trial 1; pairwise comparisons revealed this difference to be attributable to higher rates of "capable" status among HCs (96.4% [N = 27]) relative to the bipolar disorder patients (77.4% [N = 24]) and schizophrenia patients (71.0% [N = 22]). However, by trial 2, 90% or more of the participants in each group earned scores in the capable range. There were no significant differences between the 2 patient groups in the proportion of capable subjects on any of the 3 trials.

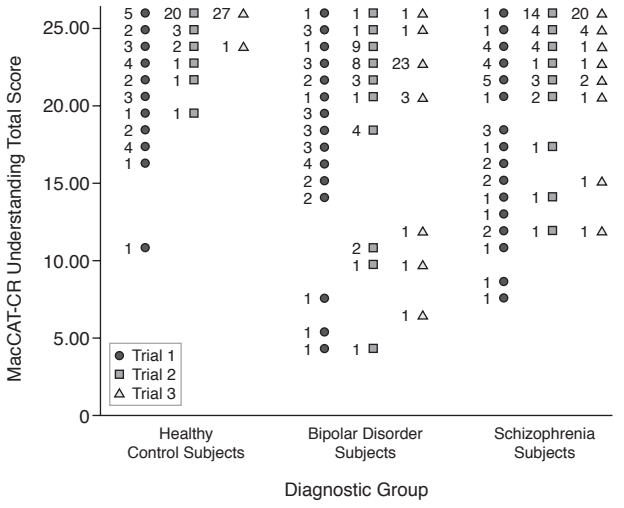
Correlates of Decisional Capacity in the Combined Patient Sample

Age was not a significant correlate of decisional capacity. Overall neurocognitive function was correlated with understanding scores at trials 1, 2, and 3 at r = 0.352 and p = .010, r = 0.352 and p = .011, and r = 0.473 and $p < .001$, respectively, and with appreciation scores at r = 0.424 and p = .002. The PANSS negative syndrome subscale scores were correlated with scores at all 3 trials of understanding (all rs were between –0.254 and –0.319, all $p < .05$), but not with any other MacCAT-CR subscale scores. The PANSS general psychopathology subscale score was modestly correlated with the second and third trials of understanding (r = –0.290 and p = .022 and r = –0.266 and p = .037, respectively), but not with any other MacCAT-CR scores. The only significant correlation between severity of positive symptoms and decisional capacity was that of the MacCAT-CR appreciation subscale score (r = –0.338, p = .007). The PANSS mania factor score was not significantly correlated with any of the MacCAT-CR scores (data not shown). Severity of depressive symptoms (HAM-D score) was significantly correlated only with understanding trial 2 (r = –0.265, p = .039) and reasoning scores (r = –0.350, p = .006).

DISCUSSION

The present study is, to our knowledge, the first empirical evaluation of capacity to consent to research among patients with bipolar disorder. Consistent with our hypotheses, bipolar patients had worse understanding than HCs. Contrary to our expectations, the level of decisional capacity among the bipolar patients did not differ significantly from that in patients with schizophrenia.

Figure 1. MacCAT-CR Understanding Total Scores for Trials 1, 2, and 3 by Diagnostic Group



Abbreviation: MacCAT-CR = MacArthur Competence Assessment Tool for Clinical Research.

These findings are noteworthy because the bipolar patients were generally minimally symptomatic outpatients, yet they still showed impaired understanding of disclosed information at a level comparable to that in the schizophrenia group. On the other hand, as hypothesized, repeated disclosure of initially misunderstood information did aid understanding in bipolar patients, as well as in the schizophrenia and HC groups. After a single redisclosure, greater than or equal to 90% of the participants (regardless of diagnostic group) earned a MacCAT-CR understanding total score in the range that was accepted as evidence of sufficient decisional capacity for enrollment in the NIMH–sponsored CATIE study, which was a recent large-scale multisite study of the effectiveness of atypical antipsychotic medications.[15] There was no effect of age on decisional capacity, but as postulated, neurocognitive deficits, along with negative symptoms, tended to be the strongest correlates of lower decision-making capacity (particularly understanding).

Consistent with prior published reports of schizophrenia patients,[40] none of the 3 groups manifested difficulty on the MacCAT-CR expression of a choice subscale. In regard to appreciation, the only significant difference among the 3 groups was that the schizophrenia group had a significantly lower mean appreciation score than HCs. However, even among the schizophrenia patients, a majority (58%) earned full credit on the appreciation subscale. There were no significant differences among the 3 groups in regard to MacCAT-CR reasoning.

We chose the MacCAT-CR for the present study because it remains the best validated scale of capacity to consent to research.[41,42] However, the understanding subscale is probably the strongest among the 4 MacCAT-CR subscales from a psychometric perspective and may therefore be more sensitive than the other subscales at detecting meaningful deficits in their respective constructs. (The potential range of scores on the MacCAT-CR understanding subscale is 0–26, whereas the range for appreciation is only 0–6, that for reasoning is 0–8, and that for expression of a choice is 0–2.) Further research incorporating more comprehensive measurements of appreciation and reasoning is warranted to fully delineate the presence or absence and predictors of any ethically relevant deficits among patients with bipolar disorder in these areas.

Data for the present study were drawn from a larger study of decisional capacity, and the aims of that study were not focused on specific aspects of bipolar disorder or diagnostic group comparisons. In general, the concurrent severity of depressive and manic symptoms was in the mild range in our sample, and in general, the severity of these symptoms did not correlate significantly with decisional capacity. But, while patients were generally recruited and evaluated as stabilized outpatients, we lacked information characterizing the participants in terms of illness phase at study entry (manic, depressed, mixed, or euthymic), bipolar I versus II subtype, and number of lifetime affective episodes. The lack of more detailed clinical data limits our ability to generalize these findings directly to the larger population of people with bipolar disorder. Greater impairment in decisional capacity and a stronger relationship with psychopathology would likely be found among patients in acute depressed, hypomanic, or manic episodes and in those with concurrent substance abuse disorders (which are common among patients with bipolar disorder,[43] but for which the presence of was an exclusion criterion in the present study). On the other hand, the types of clinical services from which patients were recruited (e.g., board-and-care homes) may have resulted in a lower functioning sample than may be modal within the wider population of people with this condition. Given the relatively small sample size within groups, it is also possible that the lack of significant difference between the schizophrenia and bipolar groups could reflect type II error. However, at least some of the mean MacCAT-CR understanding scores among the bipolar disorder group were equal to or slightly lower than the means for schizophrenia patients, so the observed lack of significant differences among these 2 patient groups does not appear likely attributable to lack of statistical power.

Two additional potential limitations of the present study are that the research assistants were not kept blind to diagnosis when administering the MacCAT-CR and the fact that diagnoses were established clinically rather than with a standardized diagnostic procedure. However, it seems likely that, if knowledge of diagnosis were to bias the research assistants' ratings, that bias would likely

be toward lower capacity ratings for schizophrenia patients. Also, regarding the clinically established diagnoses, it should be noted that these were not generally "first impression" clinical diagnoses (such as may be given when a clinician first assesses a patient during an acute hospitalization); rather, these diagnoses represented those maintained by treating clinicians in a longer-term outpatient context.

Despite the above limitations, the present findings are noteworthy for several reasons. In contrast to decisional capacity in schizophrenia, there has been no published research on capacity to consent to research among bipolar patients of any type or clinical state. The present findings, albeit from a limited segment of the wider spectrum of people with bipolar disorder, clearly illustrate that capacity to consent to research is an issue of relevance to investigators conducting clinical trials involving people with bipolar disorder. This is particularly true with regard to initial comprehension of disclosed information, thus pointing to the need for larger-scale prospective empirical investigations, as well as consideration of what a participant has in fact understood during the consent process.

The present data suggest that researchers should be particularly alert to potential impairments in understanding of disclosed information when enrolling patients with neurocognitive impairments and/or more substantive negative symptoms. There was considerable heterogeneity in the level of understanding after the initial disclosure of information (trial 1) among both patient groups. However, these deficits were at least partially improved through simple reexplanation of initially misunderstood information. For instance, significantly fewer participants in the 2 patient groups passed the CATIE study criterion ("capable" defined as MacCAT-CR understanding score ≥ 16) at trial 1, but after a reexplanation, greater than or equal to 90% of participants in each group passed this criterion. The CATIE criterion admittedly represents a relatively low threshold for capacity and is focused solely on the understanding dimension.[44] Nonetheless, consistent with a growing literature on enhanced consent,[20] the observed improvements illustrate that a participant's level of understanding may be most appropriately viewed as the outcome of, and affected by, the quality of the consent process and dialogue between the investigator and potential research participant.

There remains a clear and unmet public health need for many types of clinical research to improve the lives of people affected by bipolar disorder,[3] including older bipolar patients.[6] The present results point to a clear need for larger-scale prospective research regarding clinical factors underlying heterogeneity and/or changes in decisional capacity among bipolar patients to guide investigators and institutional review boards in the ethical enrollment of patients in clinical research related to bipolar disorder.

REFERENCES

1. Akiskal HS, Bourgeois ML, Angst J, et al. Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. J Affect Disord 2000;59(suppl 1):S5–S30
2. Krabbendam L, Arts B, van Os J, et al. Cognitive functioning in patients with schizophrenia and bipolar disorder: a quantitative review. Schizophr Res 2005;80:137–149
3. DePaulo JR Jr. Bipolar disorder treatment: an evidence-based reality check. Am J Psychiatry 2006;163:175–176
4. Misra S, Ganzini L. Capacity to consent to research among patients with bipolar disorder. J Affect Disord 2004;80:115–123
5. Jeste DV, Alexopoulos GS, Bartels SJ, et al. Consensus statement on the upcoming crisis in geriatric mental health: research agenda for the next 2 decades. Arch Gen Psychiatry 1999;56:848–853
6. Depp CA, Jeste DV. Bipolar disorder in older adults: a critical review. Bipolar Disord 2004;6:343–367
7. Depp CA, Lindamer LA, Folsom DP, et al. Differences in clinical features and mental health service use in bipolar disorder across the lifespan. Am J Geriatr Psychiatry 2005;13:290–298
8. Depp CA, Davis CE, Mittal D, et al. Health-related quality of life and functioning of middle-aged and elderly adults with bipolar disorder. J Clin Psychiatry 2006;67:215–221
9. Carpenter WT, Gold JM, Lahti AC, et al. Decisional capacity for informed consent in schizophrenia research. Arch Gen Psychiatry 2000; 57:533–538
10. Kovnick JA, Appelbaum PS, Hoge SK, et al. Competence to consent to research among long-stay inpatients with chronic schizophrenia. Psychiatr Serv 2003;54:1247–1252
11. Moser DJ, Schultz SK, Arndt S, et al. Capacity to provide informed consent for participation in schizophrenia and HIV research. Am J Psychiatry 2002;159:1201–1207
12. Palmer BW, Dunn LB, Appelbaum PS, et al. Correlates of treatment-related decision-making capacity among middle-aged and older patients with schizophrenia. Arch Gen Psychiatry 2004;61:230–236
13. Palmer BW, Dunn LB, Appelbaum PS, et al. Assessment of capacity to consent to research among older persons with schizophrenia, Alzheimer disease, or diabetes mellitus: comparison of a 3-item questionnaire with a comprehensive standardized capacity instrument. Arch Gen Psychiatry 2005;62:726–733
14. Palmer BW, Jeste DV. Relationship of individual cognitive abilities to specific components of decisional capacity among middle-aged and older patients with schizophrenia. Schizophr Bull 2006;32:98–106
15. Stroup S, Appelbaum P, Swartz M, et al. Decision-making capacity for research participation among individuals in the CATIE schizophrenia trial. Schizophr Res 2005;80:1–8
16. Denicoff KD, Ali SO, Mirsky AF. Relationship between prior course of illness and neuropsychological functioning in patients with bipolar disorder. J Affect Disord 1999;56:67–73
17. Howe V, Foister K, Jenkins K, et al. Competence to give informed consent in acute psychosis is associated with symptoms rather than diagnosis. Schizophr Res 2005;77:211–214
18. Cairns R, Maddock C, Buchanan A, et al. Prevalence and predictors of mental incapacity in psychiatric in-patients. Br J Psychiatry 2005;187: 379–385
19. Appelbaum PS, Roth LH. Competency to consent to research: a psychiatric overview. Arch Gen Psychiatry 1982;39:951–958
20. Dunn LB, Jeste DV. Enhancing informed consent for research and treatment. Neuropsychopharmacology 2001;24:595–607
21. Dunn LB, Lindamer LA, Palmer BW, et al. Improving understanding of research consent in middle-aged and elderly patients with psychotic disorders. Am J Geriatr Psychiatry 2002;10:142–150
22. Palmer BW, Nayak GV, Dunn LB, et al. Treatment-related decision-making capacity in middle-aged and older patients with psychosis: a preliminary study using the MacCAT-T and HCAT. Am J Geriatr Psychiatry 2002;10:207–211
23. Sheehan DV, Lecrubier Y, Sheehan KH. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59(suppl 20):22–33
24. Dolder CR, Jeste DV. Incidence of tardive dyskinesia with typical versus atypical antipsychotics in very high risk patients. Biol Psychiatry 2003; 53:1142–1145

25. Appelbaum PS, Grisso T. MacCAT-CR: MacArthur Competence Assessment Tool for Clinical Research. Sarasota, Fla: Professional Resource Press; 2001
26. Kay SR, Fiszbein A, Opler LA. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. Schizophr Bull 1987;13:261–276
27. Lindenmayer JP, Brown E, Baker RW, et al. An excitement subscale of the Positive and Negative Syndrome Scale. Schizophr Res 2004; 68:331–337
28. Hamilton M. Development of a rating scale for primary depressive illness. Br J Soc Clin Psychol 1967;6:278–296
29. Birchwood M, Smith J, Drury V, et al. A self-report insight scale for psychosis: reliability, validity and sensitivity to change. Acta Psychiatr Scand 1994;89:62–67
30. Wechsler D. Wechsler Adult Intelligence Scale-Third Edition (WAIS-III). San Antonio, Tex: The Psychological Corporation; 1997
31. Reitan RM, Wolfson D. The Halstead-Reitan Neuropsychological Test Battery: Theory and Clinical Interpretation. 2nd ed. Tucson, Ariz: Neuropsychology Press; 1993
32. Gladsjo JA, Schuman CC, Evans JD, et al. Norms for letter and category fluency: demographic corrections for age, education, and ethnicity. Assessment 1999;6:147–178
33. Lezak MD, Howieson DB, Loring DW, et al. Neuropsychological Assessment. 4th ed. Oxford, England: Oxford University Press; 2004
34. Kongs S, Thompson L, Iverson G, et al. Wisconsin Card Sorting Test-64 Card Version. Professional Manual. Odessa, Fla: Psychological Assessment Resources, Inc; 2000
35. Golden CJ, Freshwater SM. Stroop Color and Word Test: A Manual for Clinical and Experimental Uses. 2nd ed. Wood Dale, Ill: Stoelting Co; 2002
36. Benedict R, Schretlen D, Groninger L, et al. Hopkins Verbal Learning Test-Revised: normative data and analysis of inter-form and test-retest reliability. Clin Neuropsychol 1998;12:43–55
37. Heaton RK, Miller W, Taylor MJ, et al. Revised Comprehensive Norms for an Expanded Halstead-Reitan Battery: Demographically Adjusted Norms for African American and Caucasian Adults. Professional Manual. Lutz, Fla: Psychological Assessment Resources, Inc; 2004
38. Benedict R. Brief Visual-Spatial Memory Test-Revised. Professional Manual. Odessa, Fla: Psychological Assessment Resources, Inc; 1997
39. Wechsler D. Wechsler Memory Scale-Third Edition (WMS-III). San Antonio, Tex: The Psychological Corporation; 1997
40. Jeste DV, Depp CA, Palmer BW. Magnitude of impairment in decisional capacity in people with schizophrenia compared to normal subjects: an overview. Schizophr Bull 2006;32:121–128
41. Dunn LB, Nowrangi M, Palmer BW, et al. Assessing capacity to consent to treatment and research: a review of instruments. Am J Psychiatry 2006;163:1323–1334
42. Sturman ED. The capacity to consent to treatment and research: a review of standardized assessment tools. Clin Psychol Rev 2005;25:954–974
43. Levin FR, Hennessy G. Bipolar disorder and substance abuse. Biol Psychiatry 2004;56:738–748
44. Dunn LB, Palmer BW, Appelbaum PS, et al. Prevalence and correlates of adequate performance on a measure of abilities related to decisional capacity: differences among three standards for the MacCAT-CR in patients with schizophrenia. Schizophr Res 2007;89:110–118

