Type of Symptomatology as a Form of Volunteer Bias

Antonio Convit, MD; Stewart Levine, MD; Stefanie Berns, BS; and Chito Evangelista, MD

We sought to explore the relationship between type of psychopathology and consent bias. Using the Brief Psychiatric Rating Scale we assessed a group of 48 forensic psychiatric inpatients. These patients were later independently approached by a researcher who attempted to get their consent for a study on the validity of self-reported criminal behavior. Thirty agreed to participate and 18 did not. The consenting patients were significantly younger and had significantly more negative symptoms than the nonconsenters. The difference in negative symptoms remained significant after age and medication dose, in chlorpromazine equivalents, were covaried out. The authors discuss the implications of these findings for forensic research.

In clinical research one of the most crucial parameters used to assess the importance of a finding is how representative it is in describing the population of interest. Bias may be introduced by the selection of the study subjects: those who volunteer could be different from those who refuse to participate.[1] In psychiatric research volunteer bias is probably significant, but there is a lack of consensus in the literature on its type or extent.[2,3] Apart from the bias imparted from refusal to participate, there may be further patient selection once the study is under way. Edlund and Swann[4] have recently reported that those who remain in a study may be different from those who drop out.

The willingness of a patient to participate in psychiatric research may be related to particular symptom clusters or even to the very characteristics being studied (e.g., ability to respond to a specific psychotropic medication). To assess the importance and generalizability of research findings the psychiatric reader must rely on the details provided by the investigators. However, most psychiatric investigators do not provide information on the patients who were approached but who refused to participate. In a review of all the articles published in three prominent psychiatric journals during a two-year period, a group of investigators reported that only 9.5 percent of the nontreatment studies listed the number

Dr. Convit is affiliated with the Kirby Forensic Psychiatric Center in New York. Address reprint requests to Dr. Convit, Director of Research, Kirby Forensic Psychiatric Center, Ward's Island, New York 10035. Dr. Convit is also affiliated with the Nathan S. Kline Psychiatric Research Institute in New York. Dr. Levine is affiliated with the Beth Israel Medical Center Department of Psychiatry in New York. Ms. Berns is affiliated with Barnard College Department of Psychology in New York. Dr. Evangelista is affiliated with the Nathan S. Kline Psychiatric Research Institute in New York.

of participants and refusers and only 2.7 percent mentioned pertinent characteristics of the refusers.[5] Edlund *et al.*[5] go on to report that none of 84 treatment studies they reviewed gave the numbers or any characteristics of the refusers. The findings raise significant concerns about the ability of most researchers in psychiatry to recognize the importance of refusal bias on clinical studies.

There is a small and disparate literature on the possible bias imparted by subject selection. One study found differences in the level of psychopathology between consenting inpatients and outpatients: the inpatients who consented were more seriously ill than those who refused to participate. The pattern was reversed for outpatients: the consenting group was less disturbed than the refusing group.[2] Other investigators explored the biasing effects of nonparticipation directly. In an interview study Kokes *et al.*[3] compared 50 participating patients with 50 refusing patients and found that the two groups did not differ significantly on any demographic feature, type or severity of psychopathology, and type of treatment. They describe a nonsignificant trend among those who refused to participate to be hostile, suspicious, or socially withdrawn.[3] These findings are similar to those reported by Edlund *et al.*[5]

Some investigators, studying the impact of patient characteristics or the level of risk of the protocol on participation, give only information about the patients who signed up for these studies.[6,7] Ironically, both of these studies about subject participation fail to give the reader any information about the patients who refused to volunteer. In our view, this weakness does not allow their conclusions to shed any new light on the subject of how nonparticipation biases research.

In our experience recruiting patients for psychiatric studies, between 10 and 90 percent of patients decline to participate depending on the type of study. We felt that there would be differences in psychiatric symptoms and perhaps even in demographic variables between those who sign-up and those who refuse to participate. We decided to test this formally by contrasting, along demographic variables and psychiatric symptoms as measured by the Brief Psychiatric Rating Scale (BPRS),[8] patients who refused to participate in an interview study with those who did participate. The study for which we sought consent entailed contrasting the patients' self-reports of criminal behavior with the information obtained from RAP sheets and court records. The study also tested patients' memory.

Methods

In New York State Psychiatric facilities, research is highly regulated. Both a member of the research team and a clinician not affiliated with the research team are required to clinically evaluate a patient to ascertain if that patient is capable of understanding the information contained in the consent form, and therefore competent to agree to participate. This creates a window of opportunity to assess the impact of psychopathology on patients' participation in re-

search. Our approach was approved by the committee which protects human subjects.

One of two research psychiatrists (AC and SL) asked each of the identified potential study patients to speak to him. At the end of each clinical interview, the psychiatrist completed a BPRS and a Clinical Global Impression scale.[8] The two clinicians were reliable in the administration of the BPRS with a Pearson's correlation coefficient for total score of 0.86.

Either the same day or the next day, a research associate would independently approach the patient and explain the proposed validity and memory study to him. The research associate would then attempt to obtain informed consent. The prospective subject was told that the study offered no physical risk to him. He was also told that the study would entail talking to the research associate about his past medical, personal, and psychiatric history and to complete a simple memory test. The patient was assured that all the information was strictly confidential and that if he refused to participate, his treatment or the length of time he had to spend in the hospital would not be affected.

Subjects The study patients were all male patients, who were found not guilty by reasons of insanity (NGRI), present on December 1, 1988 at the Kirby Forensic Psychiatric Center, a high security hospital for mentally-ill offenders serving primarily Manhattan. These patients remain in a high security facility until they are deemed to be no longer dangerous, at which time they are transferred to a civil hospital, or are discharged to the community. As a rule, NGRI patients have a long length of hospitalization, which is not necessarily determined by their level of psychopathology, but by their perceived dangerousness.

There were 52 NGRI patients in the hospital on the first day of the study. All but four of the patients were interviewed by the study psychiatrists before they were approached by the research associate for consent. Demographic information, DSM-III-R chart diagnoses,[9] and current neuroleptic medication (in chlorpromazine equivalents), were obtained from the hospital record on all patients.

Analyses The consenting patients were contrasted with the nonconsenting patients along age, marital status, race, age of first psychiatric hospitalization, chronicity of illness, number of psychiatric hospitalizations, length of current hospitalization, diagnosis, medication dose in chlorpromazine equivalents, BPRS total score, BPRS factors (positive symptoms, negative symptoms, depression/anxiety, activation, hostility, and thought disorder),[10] Chi-squares were used for the dichotomous variables and *t*-tests for the continuous variables. All of the reported significance values are two-tailed.

Results

Of the 52 identified potential subjects two refused to talk to the research psychiatrists and two were discharged from the hospital before they could be interviewed. No BPRS was completed on them and they were hence not ap-

proached for consent in the interview study.

Patients ranged in age from 21 to 68 years with an average of 39.4 and a standard deviation of 10.6. Seventy-five percent of the patients were single, four percent were married, 15 percent were divorced, and 6 percent were widowed. The group was 54 percent African American, 25 percent Caucasian, 19 percent Hispanic, and 2 percent Oriental. Clinical diagnoses were established by the ward psychiatrists using DSM-III-R criteria. Seventy-nine percent were diagnosed as schizophrenics, 12 percent as personality disorders, and 8 percent as substance abuse disorders. The mean age at first psychiatric hospitalization was 22 with a range of 5 to 63 years and a standard deviation of 11. Of the 48 patients who were interviewed clinically by the study psychiatrists, 18 refused to participate in the study. See Table 1 for the breakdown of the demographic variables in the two groups.

There were no significant differences between consenters and refusers for race, diagnoses, or marital status (see Table 1). The consenting group was significantly younger and had been admitted to the hospital for the first time at a younger age than the nonconsenting group. However, the chronicity of illness (number of years since the first psychiatric hospitalization) was very similar between the consenters and nonconsenters (Table 1). The mean number of psychiatric hospitalizations for the 48 subjects was 6.8 with a standard deviation of 6.7 and a range between 1 and 40 hospitalizations. The consenting group had a smaller mean number of hospitalizations than the nonconsenters (5.6 versus 8.7), but the difference was not statistically significant. All the patients had a long index hospitalization ranging from 6 to 47 months in duration. The average length of hospitalization was 1,098 days with a standard deviation of 311 days. There were no significant differences between consenters and nonconsenters for length of hospitalization.

The consenting patients tended to have a higher total BPRS score than the nonconsenters (33.4 versus 28.1), however, this did not reach statistical significance (Table 2). Clear differences emerged between the consenters and nonconsenters for the negative symptom BPRS factor with the consenters having a significantly higher mean score ($t = 3.19$, $df = 46$, $p = 0.003$; see Table 2). The consenters tended to have a higher mean anxiety/depression BPRS factor, but because of the large standard deviation for this variable, these differences did not reach statistical significance. There were no differences between consenters and nonconsenters for positive symptoms, BPRS activation factor, hostility rating, or medication dose in chlorpromazine (CPZ) equivalents (Table 2). The overall clinical global impression was in the direction of the consenting patients being rated as more impaired, but it did not differ significantly between groups. Although there were no significant differences between the two groups on antipsychotic medication dose, we felt that the medication dose could potentially confound the results. The non-

Table 1
Comparison between Consenters and Nonconsenters: Demographic Variables

	Consent = yes (n = 30)	Consent = no (n = 18)
Age	37.2 *SD* = 9.6	43.4 *SD* = 10.4*
Age at first Psychiatric Hospitalization	20.3 *SD* = 7.9	26.9 *SD* = 14.4†
Number of Years since First Psychiatric Hospitalization	17.7 *SD* = 9.2	15.3 *SD* = 9.6
Race		
Black	44.4%	56.7%
White	16.7%	23.3%
Hispanic	38.9%	16.7%
Other	0%	3.3%
Marital		
Single	77.8%	70%
Married	5.6%	3.3%
Divorced	16.7%	16.7%
Widowed	0%	10%
Diagnoses		
Psychoses	83.3%	76.7%
Personality	5.6%	10%
Substance abuse	11.1%	13.3%

* $p < 0.01$.
† $0.01 < p < 0.1$.

Table 2
Comparison between Consenters and Nonconsenters: Symptomatology

	Consent = yes (n = 30)	Consent = no (n = 18)
Total BPRS Score	33.4 *SD* = 10.1	28.1 *SD* = 7.8†
Negative Symptoms BPRS Factor	8.0 *SD* = 2.1	6.2 *SD* = 1.6*
Anxiety/Depression BPRS Factor	6.8 *SD* = 2.5	5.4 *SD* = 2.4†
Thought Disorder BPRS Factor	8.4 *SD* = 5.1	6.2 *SD* = 3.5
Positive Symptom BPRS Factor	13.9 *SD* = 6.9	11.6 *SD* = 4.0
Activation BPRS Factor	4.8 *SD* = 1.7	4.6 *SD* = 1.4
Hostility	5.5 *SD* = 2.5	5.3 *SD* = 1.8
Clinically Global Impression	3.3 *SD* = 0.8	3.7 *SD* = 1.1
Medication Dose in CPZ Equivalents	555 *SD* = 678	963 *SD* = 1052

* $p < 0.01$.
† $0.01 < p < 0.1$.

consenters received a higher average dose than the consenters. To ensure that the relationship between negative symptoms and consent was independent of medication dose, we used medication dose in chlorpromazine equivalents as a covariate. The relationship between type of psychiatric symptoms and willingness to participate in research was unaffected when the medication, in CPZ equivalents, was taken into account (ANCOVA, $F = 7.55$, $df = 1$, and $p = 0.009$ for the main effect of negative symptoms). Because the consenters were

younger than the nonconsenters, we explored the importance of age on the relationship between negative symptoms and group membership. When age was used as a covariate the relationship between negative symptoms and willingness to participate remained significant (ANCOVA, $F = 8.75$, $df = 1$, $p = 0.005$).

Discussion

We found no differences between participating and nonparticipating patients for race, diagnoses, chronicity of illness (number of years since the first psychiatric hospitalization), number of psychiatric hospitalizations, length of the current psychiatric hospitalization, and neuroleptic dose. We could not explore the impact of gender on willingness to participate since all our subjects were male.

The consenting group was significantly younger than the nonconsenting group. However, age was not related to the level of psychopathology: age did not affect the relationship between consenting group and the BPRS negative symptom factor. Because the BPRS rating was done before and independently of the patient being approached for the study, the rating of hostility and uncooperativeness did not reflect the patients' refusal to participate in the study as may have been the case with other studies.[3,5] Our finding that participating patients tended to be more symptomatic (higher total BPRS score and CGI) than nonparticipating patients is in agreement with some reports[2] and in disagreement with others.[3] To our knowledge, there has been no report of a clear difference in negative symptoms, as measured by the BPRS negative symptom factor, between consenters and nonconsenters. Our findings are bolstered by the fact that the level of psychopathology was established prospectively using a reliable instrument and that the rating was in close time proximity to the patients being approached for the study.

We found clearly significant differences between participants and nonparticipants in the BPRS negative symptom factor. Because overmedication can give patients a more withdrawn/passive appearance, and this can in turn affect the BPRS items which make up the negative symptom factor, we accounted for the possible effect of medication dose. The differences between groups in the BPRS negative symptom factor remained significant after the medication, in chlorpromazine equivalents, was taken into account.

The differences between the consenters and the nonconsenters for the total BPRS score, the anxiety/depression factor, and the thought disorder factor, although not statistically significant, are in the same direction as the negative symptom factor findings: the consenters have a higher mean score than the nonconsenters. Their lack of statistical significance should not be interpreted as meaning, in general, that consenters will not differ from nonconsenters in those variables. It was only the within group variability which made them nonsignificant. Perhaps if we had studied a larger group of patients these variables would have also distinguished the consenters from the nonconsenters.

Our findings may not generalize to psychiatric inpatients in general since the study population, a group of mentally-ill offenders, may be different from civil psychiatric inpatients. Forensic cases may differ systematically from civil cases in their attitudes towards authority, trust placed on facility staff, and determinants of response to requests. The population studied, however, was very similar to that which would be found in a metropolitan civil State hospital as far as the proportions of diagnostic groups and symptom profiles is concerned.

Our findings indicate that in forensic populations the more passive/negative symptomed patients are more likely to participate in research. Patients with more predominant negative symptoms may be more likely to have neuropsychiatric deficits, which may affect the generalizability of the biological research being conducted in forensic populations. Furthermore, if our findings were to apply to a general psychiatric population, studies on the clinical effectiveness of psychoactive agents could be biased. Patients with more negative symptoms may be more refractory to treatment, and hence, there may be investigational therapeutic agents that are not considered effective based on the biased population on which they were studied. The potentially important impact of our findings warrants that this study be replicated using a population representative of acute civil patients from both public and private institutions.

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