Gender and Schizophrenia Outcome: A Clinical Trial of an Inpatient Family Intervention

by Gretchen L. Haas, Ira D. Glick, John F. Clarkin, James H. Spencer, and Alfred B. Lewis

Abstract

Several studies document sex differences in premorbid and intermorbid role functioning, showing less functional deficit among females. The specific nature of sex differences in role functioning is still poorly understood. The purpose of the present study was to investigate sex differences in symptomatology and role functioning in a sample of 92 inpatients hospitalized for an episode of DSM-III-diagnosed schizophrenic disorder. Patients were randomized at hospital admission to either of two treatment conditions: (1) multimodal hospital treatment with the addition of an inpatient family intervention (IFI) or (2) multimodal hospital treatment without IFI. Results indicated (1) sex differences in levels of substance abuse and antisocial behavior (worse for males both at admission and followup)—dimensions of psychopathology unrelated to the core features of schizophrenia; (2) superior family and occupational functioning in females at followup; and (3) superior clinical response of females to IFI. Data on family response to IFI suggest some ameliorative effects of IFI on critical family attitudes toward female patients as well as greater family compliance with IFI treatment among the families of females. Sex differences in intermorbid family and occupational functioning and response to a family-based psychosocial intervention are discussed in light of data on rejecting family attitudes toward the patient and sex differences in symptomatology. The possible influence of sex-differentiated social role demands on response to IFI is also discussed.

Gender differences in age of onset (Sartorius et al. 1978; Lewine 1981; Loranger 1984; Haas et al. 1987) and life course (Lewine 1985; Goldstein et al. 1989; Westermeyer et al. 1989) of schizophrenia suggest a more benign form of illness in females—typified by better premorbid adjustment (Farina et al. 1963; Schooler 1963; Forrest and Hay 1972; Eaton 1975; Zigler and Levine 1981; Salokangas 1983; Westermeyer and Harrow 1984), shorter hospital stays, and fewer relapses (Hogarty et al. 1978, 1986; Huber et al. 1975). Whether sex differences in the clinical character of schizophrenia (Haas et al. 1987; Goldstein et al. 1989) represent essential differences in underlying pathophysiology or differences in the phenotypic expression of a singular disorder is not known. Several studies indicate that schizophrenic females have higher mean levels of premorbid social and occupational adjustment (e.g., education, marital status, occupation, and employment history) (Sartorius et al. 1978; Loranger 1984). In fact, the bulk of the empirical findings on sex differences in schizophrenia focus on sex differences in premorbid or intermorbid functioning rather than clinical features of the disorder.

Results from quantitative assessment of sex differences in the clinical symptomatology of schizophrenia have been reported in only a few studies to date (World Health...
Findings suggest a tendency for more florid positive symptoms in females (World Health Organization 1979; Goldstein and Link 1988; Haas et al. 1989) and more negative symptoms in males (World Health Organization 1979; Lewine 1981; Goldstein and Link 1988; Haas et al. 1989), as well as a higher prevalence of affective symptoms in females (Lewine et al. 1984; Walker et al. 1985; Goldstein and Link 1988). Link 1988; Haas et al. 1989). The significance of such differences for understanding the etiology and pathophysiology of the disorder is an important area for further inquiry. Little is known about the temporal stability and course of sex-differentiated symptom patterns or how such sex differences in symptomatology may be related to intermorbid functioning. Existing studies have relied almost exclusively on data gathered during the acute phase of illness (e.g., at time of hospital admission). Whether the identified sex differences in symptomatology are limited to the acute phase of illness or generalized to the full course of illness has not been determined. Moreover, the relationship between putative sex-related variance in symptomatology and the sex differential in intermorbid functioning is a question not fully examined. For example, do males with more negative symptoms show a more impaired level of social functioning during the intermorbid phase? To our knowledge, sex differences in the course of specific dimensions of symptomatology have not been systematically examined.

The present study reports on data from a prospective, random assignment, clinical trial of an inpatient family treatment. The aims of this study were to examine sex differences in (1) severity of symptomatology during both the acute and stabilized phases of illness; (2) course of illness, including severity of symptoms and level of psychosocial adjustment during the intermorbid phase of illness; and (3) short- and long-term treatment response to a clinical trial of an inpatient family intervention.

**Methods**

**Setting.** Patients were recruited from all inpatient units of the Payne Whitney Clinic (The New York Hospital)—a 108-bed facility that admits voluntary patients who range in age from adolescent through elderly and represent all diagnostic categories. All patients are admitted from a central evaluation service or the emergency room (at night and on weekends).

**Subjects.**

**Selection criteria.** The sample included 92 (49 male and 43 female) consecutively admitted patients with DSM-III schizophrenic disorders (American Psychiatric Association 1980) (ages 18 to 45) hospitalized for an episode or exacerbation of illness, in regular contact with family members, and for whom a trial of an inpatient family intervention (IFI) was not contraindicated.

**Assignment to treatment.** Patients were assessed on a measure of prehospital role functioning—the Role Activity Performance Scale (Good-Ellis et al. 1987) and stratified into subgroups with good versus poor prehospital functioning on the basis of a cutting score of 3.5, which represented the midpoint of the scale. Patients in the two role-functioning groups were independently randomized to the two treatment conditions (IFI + multimodal hospital treatment vs. multimodal hospital treatment alone).

**Research diagnosis.** The initial diagnostic determination was made by two senior psychiatrists (I.D.G. and A.L.) on the basis of information available to the hospital treatment team at the time of hospital admission. Each case was reviewed at the 6- and 18-month followup assessments, and final research diagnoses were based on all available information. Separate analyses of outcome data using the research diagnoses and the initial admission diagnoses revealed no fundamental differences in the pattern of results for any of the groups. The data presented in this report are based on the final (18-month) research diagnosis.

**Treatment.**

**Multimodal hospital treatment.** The general components of the multimodal hospital treatment program included a partially fixed drug regimen (Glick and Hargreaves 1979) to ensure adequate clinical dosages to all patients. The mean neuroleptic dose per day over the course of hospitalization was 1,334 mg of chlorpromazine equivalent (range 150–2,920 mg/day). Other components of the treatment program included therapeutic activities (approximately 2 hours/day), individual psychotherapy (1–5 sessions/week), group therapy (two sessions/week), and milieu therapy focused on environmental structure, support, limit setting, social skills, and problem solving. A more detailed description of both treatments was presented in an earlier report (Haas et al. 1988).

**Family intervention.** IFI is a brief (mean number of sessions = 8.6, mode = 6.0) family treatment with a central psychoeducational compo-
nent that focuses on the nature of schizophrenia, adjusting expectations for patient functioning to an appropriate level, identifying past and potential future stressors, and educating both patient and family to the need for the patient's continued treatment after hospital discharge. The treatment draws on the family intervention models of Anderson and Hogarty from the University of Pittsburgh (Anderson et al. 1980) and of Goldstein and colleagues at UCLA (Goldstein and Kopeikin 1981).

IFI was integrated into the standard multimodal hospital treatment program for patients assigned to the IFI condition. Patients in the comparison condition were given the standard multimodal hospital treatment regimen with additional individual therapy sessions that roughly equalized the time of contact with therapist across the two treatment conditions. There was no difference between groups in the total numbers of treatment contacts, but more patient hours with therapist in the IFI (2.3 hours/week) versus the comparison treatment (1.7 hours/week) (t = 3.13, df = 95, p < 0.002) were found.

Assessment Procedures. Patients and families were assessed at four times—hospital admission, hospital discharge, and at 6- and 18-month followup—on a broad battery of clinical symptomatology and role-functioning measures.

Measures. Patient measures included the Global Assessment Scale (GAS; Endicott et al. 1976), a global measure of overall functioning and symptomatology; the Psychiatric Evaluation Form (PEF; Endicott and Spitzer 1972), which provides ratings of 19 symptoms and four dimensions of role function; the Role Activities Performance Scale (RAPS; Good-Ellis et al. 1987), which assesses role functioning in four key domains (work, social, family, and leisure activities) on a month-by-month longitudinal basis; and the Treatment and Medication Compliance Data Sheet (TMCD; Glick and Chen 1981), which accompanied a semistructured interview with patient and family for assessment of compliance with medication and psychosocial treatments before and after hospitalization.

Family measures were based on a composite interview instrument, The Family Attitude Inventory (FAI), a 53-item self-report rating inventory developed for this study (Haas et al. 1986). It includes Kreisman's (1987) Patient Rejection Scale (PRS) and selected items from the Family Evaluation Form (Spitzer et al. 1971), which taps family burden and attitude toward illness. A principal component analysis (Haas et al. 1986) on a larger sample of subjects (n = 169) yielded five major factors, measuring four facets of the family's experience with the patient and the hospital: (1) Patient Rejection, reflecting the family member's critical attitudes toward the patient—a dimension that may be similar, although not equivalent, to the critical comments dimension of Expressive Emotion (Brown et al. 1972; Brown 1984); (2) a subset of items from the PRS which reflect more extreme negative and rejecting attitudes toward the patient; (3) Family Attitude Toward Treatment, a factor that taps family attitudes toward hospital treatment and mental health professionals; and (4) Openness to Social Support, a factor that includes items that tap the family's willingness to acknowledge need for help and to communicate with family and friends about the patient's illness.

Patient composite measures. The treatment outcome study design called for inclusion of several outcome measures. To restrict Type I error, we reduced the dependent variables to composite outcome measures, as described in an earlier report (Spencer et al. 1988). A principal component analysis of the residualized (adjusted for baseline) patient measures for the larger study sample (n = 169) yielded two factors that accounted for 44 percent and 11 percent of the variance in outcome at 18 months, respectively. The first factor, identified as a dimension of Global Functioning/Symptomatology (what is referred to as "PCOMP-1") included the clinical status measures: the GAS, the "Overall Severity" item from the PEF (PEF-OS), and all PEF symptom scale measures with the exception of the Antisocial and Alcoholism scales (i.e., including the Disorganization, Subjective Distress, and Withdrawal scales). The second factor, identified as a Role-Functioning factor ("PCOMP-2"), included all the RAPS role-functioning subscales (i.e., work, social, family, and leisure activities). Each of the two composite patient measures was constructed by adding the residualized z score values (nonweighted) for the measures that loaded on each factor.

Statistical Analysis Procedures. Demographic characteristics/clinical features at baseline. Male and female patients were compared on key demographic variables and clinical symptomatology measures at baseline, using t tests (for continuous data) and contingency table analyses with chi-squared tests (for non-parametric data).
Symptomatology. Comparisons of males and females on dimensions of symptomatology (as measured on the PEF) at admission, discharge, and followup were based on multivariate analyses of each of the four symptom factors/subscales from the PEF (Spitzer et al. 1971), using (1) Hotelling's $T^2$ analyses of each of the five symptom clusters, and, when appropriate, (2) accompanying univariate analysis of variance (ANOVA) procedures for tests of significance on the individual constituent scale items.

Role Functioning. Hotelling's $T^2$ analyses were also conducted to compare males and females on the four role-functioning measures from the RAPS. These tests were performed using the same two-step procedure outlined above.

Treatment outcome. The effects of treatment assignment (IFI vs. the comparison treatment) on short-term (discharge) and longer-term (6- and 18-month followup) outcome were assessed using two-way (Treatment Assignment x Gender) ANOVA and (where appropriate) analyses of covariance (ANCOVA), wherein baseline values of the composite measure served as the covariate. To reduce the risk of Type I error in the multidimensional assessment of outcome, all analyses of treatment outcome were restricted to tests on the two composite patient measures—PCOMP-1 (global symptomatology/functioning) and PCOMP-2 (role functioning) using ANOVA and ANCOVA covariance (where appropriate). Given that these composite measures consisted of residual scores (adjusted for baseline values), the use of these composite measures provided an additional source of control of the potential influence of pretreatment variance in symptomatology and role functioning (i.e., within-subjects variance in baseline scores), including analyses wherein the criteria for ANCOVA procedures were not met.

Results

Demographic Characteristics. A higher percentage of females were married (18.6%) or previously married (14.0%) as contrasted with males (6.1% married and 4.1% previously married; $\chi^2 = 6.99, df = 2, p < 0.03$). There were no differences on any of the other demographic variables, including age, race, religion, and socioeconomic status (table 1).

Treatment History.

Previous hospitalizations. There was a trend for males to have a greater mean number of prior hospitalizations (mean = 2.43, SD = 3.10), as compared with the females (mean = 1.51, SD = 2.11; $t = 1.67, df = 90, p < 0.10$). A higher proportion of males had a history of previous hospitalization (32 out of 49, or 65.3%), as compared with females (22 out of 43, or 51.2%).
However, this difference was not statistically significant.

Clinical Characteristics at Admission. Males and females showed no differences on measures of global status at admission, including the global symptomatology/functioning composite measure (PCOMP-1) and the GAS. Clinical differences in the severity of symptoms were restricted to substance abuse and character disorder symptoms, as revealed in a multivariate (Hotelling’s T2) analysis of the antisocial scale (composed of the antisocial behavior and use of narcotics items from the PEF) with IFI showed a significant reduction of the patient (f = 1.71, df = 1.14, p < 0.054), with males showing greater use of narcotics and street drugs (p < 0.03), a trend for more severe antisocial attitudes and behavior (p < 0.09), and a near trend for greater alcohol abuse (p < 0.106), as measured on the Alcoholism factor of the PEF (table 2). Post hoc exploratory analyses revealed a trend for males to show more severe somatic concerns, as indicated by a significant difference at 18 months (F = 2.05; p < 0.04) and 18-month (F = 2.05; p < 0.04) followup in rejecting attitudes toward the patient, whereas families of males showed no such treatment effect, as indicated by a significant Treatment × Gender interaction effect (F = 5.58; df = 1.74; p < 0.02) in an ANCOVA (using the baseline score as the covariate). Families of males treated with IFI showed greater rejection of their patient than did families of females treated with IFI (F = 5.97; df = 1.87; p < 0.02).

Clinical Characteristics of Patients at Discharge. Length of hospital stay (in days) was essentially equivalent for males (mean = 51.3, SD = 32.2) and females (mean = 59.5, SD = 30.1). Males and females showed no significant differences on symptom dimensions at discharge, although post hoc exploratory analyses revealed trends for females to report greater anxiety (p < 0.09) and to show greater belligerence/negativism (p < 0.09) than males at discharge (table 2).

Clinical Characteristics of Patients at Followup. On the composite measure of global functioning/symptomatology (PCOMP-1), males showed (relative to females) worse outcome at 18 months (F = 4.45; df = 1.88; p < 0.04). Examination of mean scores on composite measures at both discharge and 6- and 18-month followup indicated that there was a progressive worsening for males (relative to females) from a near trend (p < 0.11) at 6 months to a significant difference at 18 months (figures 1a and 1b). With regard to positive symptoms, males consistently earned higher ratings on the PEF grandiosity factor at both 6-month (F = 2.67; df = 4.82; p < 0.04) and 18-month (F = 2.05;
Figure 1. Treatment outcome for IFI (open circle, triangle) vs. Comp (closed circle, triangle) treatment assignment groups on 2 composite variable measures, global symptomatology/functioning and role functioning for males (1a, 1b) and females (1c, 1d) as measured at 4 assessment points: admission, discharge (for symptomatology/functioning only), 6 months, and 18 months.

Patient Global Symptoms/Function for Males

Patient Global Symptoms/Function for Females

Patient’s Level of Role Functioning for Males

Patient’s Level of Role Functioning for Females


Univariate analyses revealed significant differences on the grandiosity item at both 6-month ($F = 7.23$, $df = 85$, $p < 0.009$) and 18-month ($F = 8.34$, $df = 1,83$, $p < 0.005$) followups. Male patients also showed more severe levels of disorganized behavior as assessed on the disorganization factor of the PEF at both 6-month ($F = 1.91$, $df = 5,77$, $p < 0.10$) and 18-month ($F = 1.56$, $df = 5,74$, $p < 0.10$) followup assessments. Univariate analyses of the constituent items revealed that males earned more severe ratings of inappropriate behavior at the 6-month ($F = 7.13$, $df = 1,81$, $p < 0.005$) and 18-month ($F = 5.91$, $df = 1,83$, $p < 0.05$) followups.
Table 2. Symptomatology ratings at time of admission and discharge, by gender

<table>
<thead>
<tr>
<th>Domain/dimension</th>
<th>Males (n = 49)</th>
<th>Females (n = 43)</th>
<th>Males (n = 49)</th>
<th>Females (n = 43)</th>
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<td>1.71</td>
<td>1.82</td>
<td>0.70</td>
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<td>Inappropriate affect, appearance, behavior</td>
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<td>1.73</td>
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<tr>
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<td>1.50</td>
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<td>0.97</td>
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Table 2. Symptomatology ratings at time of admission and discharge, by gender—Continued

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<td>Overall score</td>
<td>Mean</td>
<td>4.63</td>
<td>4.70</td>
<td>3.15</td>
<td>3.37</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>0.64</td>
<td>0.60</td>
<td>0.94</td>
<td>0.98</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.10.  
*p < 0.05.

and the 18-month (F = 4.74; df = 1.78; p < 0.04) followup assessments.

Consistent with the admission data, we found more severe alcohol abuse among males at 6 months, as measured on the alcohol abuse factor (F = 4.26; df = 1.89; p < 0.05), and more narcotics/drug abuse among males, as measured on the antisocial/drug abuse factor at 18 months (F = 6.15; df = 2.84; p < 0.003). Univariate analyses revealed that males showed more severe levels of narcotics/drug abuse (F = 12.13; df = 1.85; p < 0.001).

There were no significant differences on other symptom factors (including subjective distress and social withdrawal) factors, but post hoc analyses revealed greater disability among males in maintaining a daily routine (e.g., attending to schedule, personal health care, grooming, and hygiene) at 18 months (F = 7.31; df = 1.83; p < 0.03).

Role functioning. At 6 months, males and females showed no significant differences on any of the four key domains of role functioning (work, social, family, and leisure activities) tapped by the RAPS. At 18 months, males showed a trend for lower levels of overall role functioning (t = 1.75, df = 90, p < 0.09), and occupational functioning (t = 2.01, df = 90, p < 0.05) at 18 months.

Treatment Assignment as a Predictor of Outcome.

Clinical status. A three-way (Treatment Assignment × Prehospital Level of Functioning × Gender) analysis of variance on the symptomatology/global functioning composite outcome measure (PCOMP-1) indicated that treatment effects were modified by gender, and strengthened with time—as reflected by a trend for a Treatment × Gender interaction effect at 6 months (F = 3.03; df = 1.84;
Figure 2. Outcome on hypothesized mediating variables (posthospital medication compliance and patient rejection) for IFI (open circles, triangles) vs. Comp (closed circles, triangles) treatment groups for males (2a, 2b) and females (2c, 2d) as measured at 4 assessment points: admission, discharge (for patient rejection only), and 6- and 18-month followup.

Patient Medication Compliance for Males

Patient Medication Compliance for Females

Critical Family Attitudes (Patient Rejection Scale) for Males

Critical Family Attitudes (Patient Rejection Scale) for Females


$p < 0.09$ and a significant Treatment Assignment $\times$ Gender interaction effect at 18 months ($F = 5.54; df = 1.84; p < 0.02$) (figures 1a and 1c). Results indicated superior clinical outcome for females in association with assignment to the IFI treatment condition (table 3). Males showed slightly worse clinical symptom outcome with the addition of IFI to hospital treatment.

Role functioning. A three-way (Treatment Assignment $\times$ Prehospital Level of Functioning $\times$ Gender) ANCOVA was performed on the role functioning composite outcome measure (PCOMP-2). Results (table 3) revealed a trend for a Treatment Assignment $\times$ Prehospital Level of Functioning interaction effect at 6 months.
Table 3. Results of 3-way analyses of variance (ANOVA) and covariance (ANCOVA)\(^1\) on composite outcome measures (PCOMP-1 and PCOMP-2)

<table>
<thead>
<tr>
<th>3-way ANCOVA</th>
<th>6 months</th>
<th>18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCOMP-1</td>
<td>PCOMP-1</td>
</tr>
<tr>
<td></td>
<td>Global symptomatology</td>
<td>Role function</td>
</tr>
<tr>
<td></td>
<td>df</td>
<td>F</td>
</tr>
<tr>
<td>TA</td>
<td>1</td>
<td>0.84</td>
</tr>
<tr>
<td>Sex</td>
<td>1</td>
<td>1.47</td>
</tr>
<tr>
<td>LOF</td>
<td>1</td>
<td>2.17</td>
</tr>
<tr>
<td>TA x Sex</td>
<td>1</td>
<td>3.03</td>
</tr>
<tr>
<td>TA x LOF</td>
<td>1</td>
<td>0.00</td>
</tr>
<tr>
<td>Sex x LOF</td>
<td>1</td>
<td>0.00</td>
</tr>
<tr>
<td>TA x Sex x LOF</td>
<td>1</td>
<td>0.03</td>
</tr>
<tr>
<td>Covariate</td>
<td>1</td>
<td>7.55</td>
</tr>
<tr>
<td>Error</td>
<td>84</td>
<td>83</td>
</tr>
</tbody>
</table>

Note.—TA = treatment assignment, LOF = level of function.

\(^1\)Analyses of covariance (ANCOVA) were performed only on PCOMP-2, for which measures at baseline correlated with measures at followup and criteria for ANCOVA were met. In analyses of PCOMP-1, analyses of variance (ANOVA) were used, due to failure to meet criteria for ANCOVA.

(F = 3.72; df = 1.83; p < 0.06), indicating better outcome with IFI, for the poor prehospital functioning patients and a reversal of this effect (i.e., better outcome with the comparison treatment) among the good prehospital functioning patients. This interaction effect was attenuated at 18 months, at which time a trend for a Treatment x Gender interaction (F = 3.05; df = 1.83; p < 0.08) revealed that females assigned to IFI had superior role functioning (figures 1b and 1c).

Rehospitalization. Forty-three percent of the males and 28.6 percent of the females were rehospitalized at least once over the 18-month postadmission followup period—a non-significant difference between the sexes. Similarly, we found no sex differences in time to rehospitalization or in the mean number of rehospitalizations at either 6 or 18 months following the target hospitalization. Males showed a trend for a greater mean number of days of hospital stay (mean = 130, SD = 33.7) as compared with females (mean = 2.8, SD = 8.1) at the 6-month followup (t = 1.92, df = 90, p < 0.06); there was no sex differences in the number of days hospitalized over the 6- to 18-month followup period.

Mediating Variables Associated With Treatment Effects on Outcome. To assess the effects of the hypothesized mediating variables (patient rejection and posthospital medication compliance) on both composite outcome measures (PCOMP-1 and PCOMP-2), we conducted two sets of two-way (Treatment Assignment x Gender) ANCOVAs (in which baseline values were entered as covariates) to test the effects of treatment assignment on each of the mediating variables. Results revealed a significant Treatment x Gender interaction effect on patient rejection at time of hospital discharge (F = 5.79; df = 1.86; p < 0.02), indicating more positive attitudes among families of females treated with IFI (see figures 2a and 2b for graphing of mean scores). Results of two-way (Treatment Assignment x Gender) ANCOVAs on the posthospital medication compliance measure (from the TMCDS) indicated neither a significant main effects of treatment assignment nor an interaction of treatment assignment with...
gender to influence posthospital medication compliance at either 6- or 18-month followup assessment. We did, however, find a main effect of gender ($F = 6.85; df = 1.87; p < 0.01$) on medication compliance at 6 months, with better compliance being found for females (see figures 2a and 2c).

Finally, to test the relative contribution of treatment assignment and the hypothesized mediating variables (patient rejection and posthospital medication compliance) to the prediction of outcome at 18 months, we conducted two sets of multiple regression analyses in which five variables—(1) treatment assignment, (2) patient rejection (at 18 months), (3) medication compliance (over the 6- to 18-month period), (4) the interaction of treatment assignment with patient rejection, and (5) the interaction of treatment assignment with posthospital medication compliance—were entered simultaneously into the regression equations. Because we had found significant Treatment Assignment × Gender interaction effects on outcome for both the global symptomatology/functioning (PCOMP-1) composite and the role functioning (PCOMP-2) composite measures (above), independent regression analyses were performed for males and females.

Global symptomatology/functioning. Results of the multiple regression analyses for females were as follows: the five-factor model showed a strong trend (multiple $R^2 = 0.50$; $F = 2.43; df = 5.37; p < 0.053$), accounting for approximately 15 percent (adjusted $R^2 = 0.145$) of the variance in global symptomatology/functioning (PCOMP-1) at 18 months (table 4), and that treatment assignment, patient rejection, and the interaction of treatment assignment and patient rejection independently contributed to outcome. For males, the comparable five-factor model did not predict global symptomatology/functioning outcome ($F = 1.017; df = 5.43; NS$).

Role functioning. An equivalent set of multiple regression analyses were performed in which the role-functioning composite (PCOMP-2) was entered as the dependent variable. Results of these analyses for females indicated the following: the five-factor model showed a near trend (multiple $R = 0.45$; $F = 1.90; df = 5.37; p < 0.11$), accounting for approximately 10 percent (adjusted $R^2 = 0.097$) of the variance in role functioning (PCOMP-2) at 18 months (table 5), and treatment assignment, patient rejection, and the interaction of treatment assignment and patient rejection independently contributed to outcome. Again, we found that for males, the comparable five-factor model did not predict global symptomatology/functioning outcome ($F = 1.017; df = 5.43; NS$).

Discussion

This study examined sex differences in the prehospital adjustment, clinical history, and acute symptom patterns of schizophrenia, family attitudes toward the patient, rates of rehospitalization, and long-term posthospital outcome with an inpatient family intervention. Results of this study revealed a higher level of premorbid functioning among first admission schizophrenic females and more severe substance abuse and antisocial behavior among males at time of admission and followup. No significant sex differences were found for the core clinical features of schizophrenia. Results indicated no significant sex differences in the number of hospitalizations or level of prehospital functioning. Examination of critical and rejecting attitudes of the family toward the patient showed that: (1) the families of females were less critical than the families of males, and (2) treatment with IFI was associated with less critical attitudes at followup among families of the female patients. In contrast, among the families of males, less critical attitudes were associated with the comparison treatment.

Although the number of rehospitalizations and severity of symptomatology at 6- and 18-month followup did not differ significantly for the two sexes, we found that females showed superior occupational and family role functioning at 18 months. Moreover, analyses of the effects of treatment assignment on outcome revealed significant Treatment × Gender interactions which indicated that, for females, the addition of a family intervention was associated with superior clinical outcome (in both symptomatology and functioning), whereas males appeared worse off with the addition of this form of psychosocial treatment.

Results of this study raise several important questions about the clinical course of schizophrenia. In light of current data indicating a more benign course of illness for females, the findings of minimal differences in clinical symptomatology of schizophrenia were unexpected. Reasons for this negative finding are not clear, but possible explanations include the influence of sample selection characteristics (e.g., an inpatient sample may show a more...
Table 4. Results of multiple regression analysis on global symptomatology/functioning composite (PCOMP-1) at 18 months, for females

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>( \beta )</th>
<th>t</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment assignment (TA)</td>
<td>2.573</td>
<td>1.059</td>
<td>1.603</td>
<td>2.430</td>
<td>0.0201</td>
</tr>
<tr>
<td>Medication compliance (MC)</td>
<td>0.0304</td>
<td>0.2242</td>
<td>0.063</td>
<td>0.136</td>
<td>0.8928</td>
</tr>
<tr>
<td>Patient rejection (PR)</td>
<td>1.807</td>
<td>0.7088</td>
<td>1.594</td>
<td>2.549</td>
<td>0.0151</td>
</tr>
<tr>
<td>TA x MC</td>
<td>-0.004</td>
<td>0.1395</td>
<td>-0.016</td>
<td>-0.026</td>
<td>0.9794</td>
</tr>
<tr>
<td>TA x PR</td>
<td>-0.947</td>
<td>0.3942</td>
<td>-2.260</td>
<td>2.404</td>
<td>0.0214</td>
</tr>
<tr>
<td>Constant</td>
<td>-6.1460</td>
<td>1.8268</td>
<td></td>
<td>-3.364</td>
<td>0.0018</td>
</tr>
</tbody>
</table>

Note.—B = raw regression coefficient; SE B = standard error of the raw regression coefficient.

Table 5. Results of multiple regression analysis on role functioning composite (PCOMP-2) at 18 months, for females

<table>
<thead>
<tr>
<th>Variable</th>
<th>B</th>
<th>SE B</th>
<th>( \beta )</th>
<th>t</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment assignment (TA)</td>
<td>1.772</td>
<td>0.9205</td>
<td>1.3057</td>
<td>1.925</td>
<td>0.062</td>
</tr>
<tr>
<td>Medication compliance (MC)</td>
<td>0.007</td>
<td>0.1984</td>
<td></td>
<td>0.018</td>
<td>0.9698</td>
</tr>
<tr>
<td>Patient rejection (PR)</td>
<td>1.575</td>
<td>0.6160</td>
<td>1.644</td>
<td>2.556</td>
<td>0.015</td>
</tr>
<tr>
<td>TA x MC</td>
<td>-0.008</td>
<td>0.1213</td>
<td>-0.0398</td>
<td>-0.064</td>
<td>0.949</td>
</tr>
<tr>
<td>TA x PR</td>
<td>-0.741</td>
<td>0.3426</td>
<td>-2.0914</td>
<td>-2.164</td>
<td>0.037</td>
</tr>
<tr>
<td>Constant</td>
<td>-3.557</td>
<td>1.5877</td>
<td></td>
<td>-2.240</td>
<td>0.031</td>
</tr>
</tbody>
</table>

Note.—B = raw regression coefficient; SE B = standard error of the raw regression coefficient.

severe level of symptomatology than found in a sample of schizophrenic patients in the community, thus "selecting" for the most severe cases and/or cases which show severe manifestations of illness during periods of exacerbation. This sampling strategy may bias against the manifestation of sex differences that are likely to be more obvious during the outpatient phase and to appear in a nonhospitalized population. Several studies suggest that sex differences in clinical symptomatology and role functioning are less likely to be observed in a "narrow-band" (core deficit syndrome) type of schizophrenia. Cases selected from an inpatient population (as in this study) may be biased toward inclusion of the sicker (likely to be rehospitalized) patients and exclusion of patients whose symptoms remain in remission. A comparable, larger sample followup study of first admission patients is needed to determine whether, in fact, the failure to find significant sex differences in core schizophrenic symptoms may be attributable to such a sampling bias.

Also, sex differences seem to be most prominent during the outpatient (intermorbid) phase of illness, when aspects of adjustment to the community weigh heavily in determination of clinical status. With regard to the latter point, it is, of course, important to note that the study’s 18-month followup design afforded an opportunity to assess sex differences during the posthospital phase when the developmental course of illness factors (e.g., length of illness, adjustment to community, and influence of environmental stress) would likely contribute to deterioration of functioning. Assessment during this followup phase revealed significant sex differences in global functioning and specific dimensions of role functioning rather than in clinical symptoms of schizophrenia.

The patients included in this study necessarily had family available and willing to participate in their treatment—a factor that may have selected for relatively less ill and/or less problematic patients from the general population of patients with schizophrenia. However, it is important to note that over 40 percent of the cases were "first admission" patients—primarily young people who had shown relatively minimal manifestations of illness before admission. For these patients, it is possible that rejection of the patient played a less prominent role in the family’s willingness to participate than might be the case...
for more chronic cases. If so, the inclusion would tend to lessen the magnitude of such a potential sampling bias.

In contrast to the observed lack of significant sex differences in the psychopathology of schizophrenia, we found interesting treatment-related differences in long-term clinical outcome. Specifically, our data suggest that there may be a differential treatment response to the addition of a psychosocial treatment involving the family during the inpatient phase of treatment. As reported earlier by our group (Spencer et al. 1988; Glick et al., in press), this outcome may be due, in part, to enhanced patient compliance with outpatient psychosocial treatments. It is also possible that the effects of IFI on family attitudes (specifically, a reduction in patient rejection by time of hospital discharge) contributed to a superior outcome with IFI—among females. Results of multiple regression analyses tend to support this interpretation, indicating that it was treatment assignment and patient rejection, not medication compliance, that correlated most strongly with patient outcome among females at 18 months. Medication compliance, although correlated with outcome, could not account for differences in outcome associated with the two treatments.

Thus, it appears that the enhanced outcome with IFI, specific to females, could have been due, in part, to the direct impact of a family psychoeducational intervention on family attitude toward the patient and/or the indirect influence of IFI leading to enhanced psychosocial treatment compliance during the posthospital phase. Noteworthy in regard to the latter are the findings that the families of the females were highly reliable in attending family therapy sessions in the hospital and thus offered role models of good compliance with psychosocial treatment, whereas, on average, the families of the male patients showed a pattern of more missed sessions and late arrivals to sessions.

Our findings of superior response to inpatient-based psychosocial (in this case, family-based) intervention among females, and what may be a negative response to such intervention among males, are consistent with earlier reports of similar sex-related differential outcomes with psychosocial interventions (Evans et al. 1973; Hogarty et al. 1974). Our group has speculated on possible reasons for such sex differences in family treatment response (Haas et al. 1988); briefly, we suggest the following three factors may be operating to contribute to the sex-differential in treatment response: 1. Social and occupational role demands may be greater for males, leading to higher and, in many cases, less realistic expectations for male patient’s readjustment to living in the community. Given that in this study, families of males treated with IFI showed less support for the patient’s compliance with posthospital treatment (as compared with families of females treated with IFI) and no reduction in critical attitudes (patient rejection) toward the patient, it may be that the families of males were less successful in appropriately adjusting their expectations for the patient’s readjustment during the posthospital phase. In contrast, families of females treated with IFI showed a significant reduction of critical attitudes toward the patient by the time of discharge—an outcome that (we speculate) may be more readily attained in the context of more moderate social and occupational role demands on the patient. Measures of family member role demands and expectations would, of course, be important to test this explanatory hypothesis.

2. Due to traditional sex-role socialization practices that encourage greater dependency on family in females, female patients may more readily accept and respond to a psychosocial treatment in which family members play an integral role. In contrast, for males, family involvement in a psychosocial treatment runs counter to socialization practices that discourage dependency and verbal disclosure of feelings among males.

3. A third factor that may contribute to sex-differentiated treatment response is the premorbid and intermorbid social functioning of the patient. Results of a recent study by Mueser et al. (in press) showed superior social skills among schizophrenic females than among schizophrenic males, and provided concurrent support for our findings of superior posthospital family and occupational role functioning in females with schizophrenia. Given evidence of sex differences in social skills and role functioning that consistently favor females, it may be that the relatively more intact social skills of females enable them to interact more effectively with family members and, hence, to benefit more from the process of treatment with an inpatient family intervention. An argument against this interpretation would be that superior family role functioning among females was found only at the 18-month followup and thus would be more likely a consequence of, rather than an important antecedent to, the inpatient family intervention.

4. Finally, sex differences in symptomatology found at hospital admis-
sion and followup may have contributed to sex differences in IFI treatment response. That is, the fact that males presented higher levels of antisocial behavior, alcoholism, and substance abuse (on average) than their female counterparts may have contributed to both the males' poorer family and occupational functioning at 18-month followup and their poorer (in this case, negative) response to inclusion in an inpatient family intervention. Post hoc correlational analyses revealed significant correlations between these specific dimensions of symptomatology and role functioning for males only, suggesting that antisocial behavior and substance abuse may, in part, account for poorer family and occupational functioning among male patients. Likewise, antisocial behavior and substance abuse may in some fashion have prevented a therapeutic response to an inpatient family intervention among some males, over both the short- (inpatient) and longer-term (outpatient) phase of study.

In summary, results of this study reveal some important specific findings regarding the clinical psychopathology, treatment response, and course of illness in schizophrenia. The lack of sex differences in psychopathology is not altogether surprising since the current literature documents most differences in role functioning and rehospitalization rather than in the clinical symptomatology. The findings on treatment outcome are only preliminary and need replication, but they are suggestive of superior outcomes for females with the addition of a psychosocial and, specifically, a family-format treatment during hospitalization. Results of this study indicate a need for more systematic investigation of the clinical, biological, and psychosocial factors that may predispose females to respond positively to family interventions during episodes of illness exacerbation. Systematic research on sex differences in schizophrenia also offers a promising heuristic model for the study of the heterogeneity of the disorder.

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Announcement
The Sixth International Conference on Phenothiazines and Structurally Related Psychotropic Compounds will be held September 11-14, 1990, at the Pasadena Hilton, Pasadena, California.

For further information about the conference, please contact:

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