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Family history of psychosis negatively impacts age at onset, negative symptoms, and duration of untreated illness and psychosis in first-episode psychosis patients

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Abstract

Family history (FH) of psychosis has been a focus of investigations attempting to explain the heterogeneity in schizophrenia. Previous studies have demonstrated that FH is associated with earlier age at onset, severity of positive and negative symptoms, and the duration of untreated illness (DUI). The current study examined the impact of FH on the clinical presentation and help-seeking behaviors of a well-characterized, first-episode sample. The present study utilized the Symptom Onset in Schizophrenia (SOS) Inventory, the Positive and Negative Syndrome Scale (PANSS), and structured interviews on FH to examine these relationships in a large (n = 152) sample of predominantly African American patients. Results showed that patients with a first-degree FH of psychosis had a younger age at onset of both the prodrome and psychosis, but did not differ in duration of prodromal period. Furthermore, FH and sex interacted to influence severity of negative, but not positive symptoms. Finally, FH interacted with sex to influence both the DUI and DUP in that only males with FH had longer DUI and DUP. The findings have implications for understanding the impact of specific family-related mechanisms on both clinical and help-seeking factors, as well as for informing future family-based intervention efforts.

Keywords

Age at Onset; Duration of Untreated Psychosis (DUP); Family History; First-Episode Psychosis; Schizophrenia

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Declaration of Interest
None

1. Introduction

Schizophrenia is a heterogeneous psychiatric disorder that is often chronic and associated with substantial disability, and there have been numerous research endeavors aimed at understanding the heterogeneity of the disorder as a way to identify possible targets for prevention and intervention efforts. Some of these endeavors have focused on static predictors, such as sex. For example, although schizophrenia typically has an age at onset during late adolescence or early adulthood, one of the most stable and reliable findings in the literature is that sex influences age at onset of psychotic symptoms, with males showing an earlier age at onset relative to females (Angermeyer and Kühn, 1988). Other researchers have focused on the influence of a family history (FH) of psychotic illness as a possible predictor of the heterogeneity in such variables as age at onset of psychosis, positive and negative symptoms, and the durations of untreated illness (DUI) and psychosis (DUP).

The impact of FH has been a widely-studied phenomenon, and is an area of research that has yielded highly variable findings. To date, the FH-related association that is best supported is age at onset: probands with schizophrenia who have a FH of psychosis have been shown to have a younger age at onset relative to probands without a FH of psychosis (Albus et al., 1994; Gorwood et al., 1995; Alda et al., 1996; Jablensky and Cole, 1996; Malaspina et al., 1996; Suvisaari et al., 1998; Ritsner et al., 2005; 2007). The impact of FH on age at onset has also been examined within the context of sex; the well-established sex difference in age at onset mentioned above is not supported in patients with a FH of psychosis (Pulver et al., 1990; Leboyer et al., 1992; Albus & Maier, 1995; Gorwood et al., 1995; Naqvi et al., 2005).

There is less support for an influence of FH on heterogeneity in the severity of positive and negative symptoms. The impact of FH on severity of positive symptoms is especially minimal (Baron et al., 1992; Sautter and McDermott, 1994), with most research demonstrating that having a FH of psychosis is associated with more severe negative symptoms (Vasquez-Barquero et al., 1996; Van Os et al., 1997; Malaspina et al., 2000; Martin-Reyes et al., 2004; Ritsner et al., 2005; Arajärvi et al., 2006). Relatedly, others have suggested that probands with a FH of psychotic illness have a more severe longitudinal course of symptoms (Sautter and McDermott, 1994; Verdoux et al., 1996; Deshpande et al., 2004), longer duration of hospitalization (Suvisaari et al., 1998), and poorer treatment response (Malaspina et al., 2000; Joober et al., 2005; Tabatabaee et al., 2008).

Findings of the influence of FH on the DUI (i.e., the length of time between onset of the prodrome and the initiation of psychiatric treatment) and DUP (i.e., the length of time between the onset of psychotic symptoms and the initiation of psychiatric treatment) are even more discrepant. For example, Norman and colleagues (2007) found that probands with a FH of psychosis had a longer DUI when compared to probands without a FH of psychosis. This finding points to the possibility of differences in length of prodromal period, a suggestion that is supported in Morley et al. (2008), who found that males with a FH of psychotic illness had a longer duration of prodrome relative to patients with no FH of psychiatric illness. Others have found that FH of psychosis is associated with a shorter DUP (Chen et al., 2005), while others have found no relationship between FH of psychosis and DUP (Verdoux et al., 1998; de Haan et al., 2002). Thus, we currently lack an understanding of the true impact of FH on DUI and DUP.

A recent meta-analysis from our research group examined the literature on the impact of FH to date (Esterberg et al., 2010), and found that probands with a FH of psychotic illness have a younger age at onset of psychosis as well as more severe negative symptoms, suggesting that FH may serve as a marker for discrete etiologic subtypes that vary according to clinical characteristics. Further study of the true impact of a FH of psychosis on clinical presentation

is warranted, and could guide intervention efforts. For example, future intervention efforts could focus on the identification of potentially negative prognostic factors such as FH, and target the intensity of pharmacological and psychotherapy efforts accordingly. Further, as Lewis and colleagues (1987) highlight, the identification of more homogeneous subgroups has the potential to further guide etiological research in schizophrenia.

However, our current understanding of the impact of FH is limited in part by the study of heterogeneous patient samples. For example, the majority of studies include a mix of patients with first-episode psychosis (FEP) and chronic psychotic disorders, and there is a dearth of pure FEP research studies (Jablensky and Cole, 1997; Castle et al., 1998; Konnecke et al., 2000; Norman et al., 2007; Chen et al., 2007; Tabatabaee et al., 2008). Studying the impact of FH on FEP patients may be particularly beneficial in that clinical characteristics are not further complicated by chronicity or medication effects, thus potentially obscuring the true impact of FH. Therefore, the current study aimed to study the impact of FH on age at onset, DUI/DUP, and severity of positive and negative symptoms in a relatively large sample of FEP patients.

2. Method

2.1 Participants

Patients included in these analyses—all of whom were hospitalized in a psychiatric unit of a large, university-affiliated, public-sector hospital or a suburban county psychiatric crisis stabilization unit—were enrolled in two consecutive studies investigating potential determinants of DUP (Compton et al., 2008; Compton et al., 2009a; Compton et al., 2009b; Compton et al., 2010) and the impact of premorbid cannabis use on early-course features (Compton and Ramsay, 2009; Compton et al., 2009c). Both settings care for patients who are predominantly low-income, urban, and African American. Patients completed an interview-based clinical research assessment during hospitalization, after acute psychosis was stabilized sufficiently to allow for informed consent and research participation. This study was approved by all relevant institutional review boards.

2.2 Procedure

The study included participants with first-episode non-affective psychosis recruited between July 2004 and June 2008. As reported previously (Compton et al., 2011), patients who were eligible but not enrolled (e.g., due to declining to participate or being discharged before an assessment could be conducted), did not differ from the participating patients in terms of age, gender, or race/ethnicity (the only variables available for comparison).

Inclusion criteria required that patients were aged 18–40 years, were able to speak English, had a Mini-Mental State Examination (MMSE; Cockrell and Folstein, 1988) score of ≥23, and were able to give informed consent after a full explanation of procedures and possible benefits and risks. Exclusion criteria included the presence of a significant medical condition that could compromise ability to participate in the evaluation, known mental retardation (as determined by the patient's, family's, or treating clinician's report of a prior diagnosis), prior outpatient antipsychotic treatment of >3 months duration, and previous hospitalization for psychosis prior to 3 months before index hospitalization.

2.3 Measures

Basic sociodemographic data were obtained via an interviewer-administered questionnaire. Diagnoses of psychotic disorders and substance use disorders were determined with the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First et al., 1988) using all available sources of data, including the patient assessment, a thorough chart review, and

an informant/family member interview when possible. Basic clinical data such as history of treatment-seeking were collected via an interviewer-administered questionnaire that inquired about all previous attempts to initiate treatment as well as the outcomes of these attempts. Hospital length of stay was computed based on admission date and discharge date obtained from a chart review. Symptoms were rated with the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) using data gathered from a chart review and an in-depth semi-structured interview focused on the patient's recent (past-month) symptoms.

The presence of a FH was assessed using a semi-structured interview of patients, and when available, family members, one or two informant family members were available for 45 patients (29.6%). The interview was developed by our research team and used a family-tree approach to inquire about all first-degree relatives and their mental health status. Open-ended questions probed the exact nature of symptoms and course, as well as medications and hospitalizations, among any first-degree relatives who appeared to be affected by a psychiatric disorder. Particular attention was given to questions about the possible presence of a psychotic disorder in general, and non-affective psychosis specifically. A consensus-based, best-estimate approach—using all available data from both the patient and the informant family members—was used to classify patients into two categories: (1) those with a first-degree relative with a non-affective psychotic disorder, and (2) those patients who did not have a first-degree family member with a non-affective psychotic disorder.

To address the complexities involved in pinpointing exact dates for the onset of prodromal and psychotic symptoms, conventions were employed as described previously (Compton et al., 2010), such as extensive cross-referencing with milestones and memorable anchoring events (e.g., birthdays, holidays). Consensus-based best estimates of the dates of onset of prodrome and psychosis were derived using both patient and informant/family member data (when available) from the Symptom Onset in Schizophrenia (SOS) inventory (Perkins et al., 2000). Onset of the prodrome was operationalized as the date of first prodromal symptom(s), from among 14 provided in the SOS, contiguous (without clearly discernible periods of wellness intervening; Keshavan et al., 2003) with subsequent onset of psychosis. Duration of prodrome was defined as the number of weeks from onset of prodromal symptoms to onset of psychosis. Regarding the latter time point, onset of psychosis was operationalized as the date at which hallucinations or delusions were estimated to have crossed the SOS threshold for either or both of those items. The DUI was defined as the time period between the onset of the prodrome and initiation of adequate treatment (which, in this study, was operationalized as psychiatric hospitalization), and DUP was defined as the time period between the onset of psychosis and hospitalization.

2.4 Statistical Analyses

Basic sociodemographic and clinical data were assessed using descriptive analyses. Presence of a first-degree FH of psychosis was the independent variable of interest, and patients were dichotomized into two groups (FH versus no FH). Univariate factorial analysis of variance (ANOVA) and multivariate factorial analysis of variance (MANOVA) were used in age-at-onset and symptom analyses. Transformation procedures were unsuccessful in imparting normality on the DUI/DUP variables; thus, non-parametric procedures (i.e., Mann-Whitney U test for two independent samples) were used for DUI/DUP analyses. The non-parametric analyses were conducted on the entire sample to examine the overall impact of FH on DUI/DUP, as well as conducted separately by both sex and FH status to examine potential interactions between sex and FH.

3. Results

3.1 Clinical Characteristics

Table 1 presents sociodemographic characteristics of the FEP sample, while Table 2 presents clinical information on the sample. The sample (n = 152) was predominantly African American (89.5%) and male (75.0%), and most were involuntarily hospitalized (81.6%). The sample was primarily recruited from the psychiatric inpatient unit of a large, urban hospital (86.8%), and over half were diagnosed with schizophrenia (57.9%). Over half of the sample was unemployed (63.6%), and most patients lived with family members (73.6%). Twenty-three (15.1%) participants were determined to have at least one first-degree family member with schizophrenia or another psychotic disorder.

Regarding sex differences, males and females did not differ in the proportion with a FH of psychosis, nor did they differ in severity of PANSS positive or negative symptoms. Of most interest was the lack of significant sex differences in age at onset of prodrome and age at onset of psychosis that have been well-established in previous research, though differences were in the expected direction numerically. There were also no sex differences in DUI/DUP. Finally, the two FH groups (FH versus no FH) did not differ with respect to current mean age, race/ethnicity, or distribution of type of psychotic disorder.

3.2 Ages at Onset of the Prodrome and Psychosis and Durations of Untreated Illness and Psychosis

Univariate factorial ANOVA was used to examine the influence of FH on the ages at onset of both the prodrome (Table 3) and psychosis (Table 4), as well as to examine possible interactions between positive FH and sex. Given the high correlation between the two dependent variables (>0.80), separate analyses were conducted. Results supported a significant main effect of FH on age at onset of the prodrome (F=6.25, p<0.05), with a small effect size (partial η^2=0.04). Patients with a FH (n=23) had an age at onset of the prodrome of 16.13 ± 5.29 years, compared to an age at onset of 19.24 ± 4.78 years for patients without a FH (n=126). There was no significant interaction between FH and sex, and as expected given earlier analyses, there was no significant main effect for sex.

There was also a significant main effect of FH on age at onset of psychosis (F=9.13, p<0.01), with a medium effect size (partial η^2=0.06). Patients with a FH had an age at onset of psychosis of 18.26 ± 4.63 years, compared to an age at onset of 21.59 ± 4.42 years for patients without a FH. Again, there was no significant interaction between FH and sex for age at onset of psychosis, nor was there a significant main effect of sex. Finally, potential differences in the duration of the prodrome were examined. Results showed that patients with a FH and those without a FH did not differ on duration of the prodromal period (Mann-Whitney U=1443.50, p=ns).

Results showed a significant difference in DUP, but not DUI, between patients with a FH and patients without a FH of psychosis (Mann-Whitney U=1783.00, p<0.05); patients with a FH had a longer DUP compared to patients without a FH. To examine potential interactions between FH and sex, the same non-parametric tests were run separately for males and females as well as separately for FH and no FH patients. Among males, those with a FH had a significantly longer DUI (Mann-Whitney U=969.00, p<0.05) and DUP (Mann-Whitney U=1083.00, p<0.001) compared to those without a FH. Interestingly, among females, those with a FH had a shorter DUI relative to those without FH, although this difference was not statistically significant. Among patients with a FH, males had a significantly longer DUI (Mann-Whitney U=97.00, p<0.05) and DUP (Mann-Whitney U=108.5, p<0.01) relative to females. There were no sex differences in either DUI or DUP among patients without a FH.

3.3 Positive and Negative Symptom Severity

Multivariate analysis of variance (MANOVA) was used to examine the impact of FH on severity of positive and negative symptoms, as well as potential interactions between FH and sex (Table 5). Results showed a significant main effect of sex ($F=4.83$, $df=2, 147$, $p<0.01$) as well as a significant interaction between FH and sex ($F=4.39$, $df=2, 147$, $p<0.05$). Univariate results then revealed a significant main effect of sex on negative symptoms only ($F=9.67$, $p<0.01$), with males showing slightly more severe symptoms (21.74 ± 6.27) relative to females (19.97 ± 6.22). The interaction between FH and sex was also significant for negative symptoms ($F=8.79$, $p<0.01$). Among patients with a FH, males (25.50 ± 3.50) had significantly more severe negative symptoms relative to females (16.67 ± 6.04; $t=3.98$, $p<0.01$). Stated differently, males with a FH had significantly more severe negative symptoms (25.50 ± 3.50) relative to males without a FH (21.21 ± 6.39; $t=3.78$, $p<0.01$). There was no significant main effect of FH on severity of either positive or negative symptoms.

4. Discussion

Previous studies have suggested that, in various possible ways, FH of psychosis negatively influences certain clinical characteristics in patients with a psychotic disorder. The present study sought to replicate and extend the findings of these previous studies by utilizing a relatively large FEP sample to examine the impact of a FH of psychosis on ages at onset of the prodrome and psychosis, length of the DUI and DUP, and severity of symptoms. Among the findings were that FEP patients with a FH of psychosis had a younger age at onset of the prodrome as well as a younger age at onset of psychosis. Regarding age at onset of psychosis, these findings are in line with much of the previous literature (Albus et al., 1994; Gorwood et al., 1995; Jablensky & Cole, 1996; Malaspina et al., 1996; Alda et al., 1996; Ritsner et al., 2005; 2007) and complement findings from a recent meta-analysis from our group (Esterberg et al., 2010), which found that patients with a FH of psychosis have a significantly younger age at onset relative to patients with no FH.

Regarding age at onset of the prodrome, the current study is one of the first to examine the impact of a FH on age at onset of the prodrome in a purely FEP sample. Our results suggest that FH acts similarly on the onset of the subtler, subthreshold psychotic symptoms that define the prodrome as it does on the onset of frank psychotic symptoms, such that early illness indicators appear at a younger age in patients with a FH of psychosis. However, we found that because patients who have a FH of psychosis also have a younger age at onset of psychosis, they do not appear to differ in the duration of their prodromal period.

This latter result is in contrast to a recent epidemiological study finding that FEP males with a FH of psychosis had a longer prodromal period relative to FEP males with no FH of psychiatric illness (Morley et al., 2008). Differences in operationalization of FH might provide some explanation regarding the difference in findings from the Morley et al. (2008) study and our own. Nonetheless, our results suggest that the presence of a FH is associated with a nearly four-year age difference in age at onset of both the prodrome and psychosis, which, from clinical and public health perspectives, is quite significant.

Regarding DUI and DUP, previous research has suggested that FH may also influence help-seeking and treatment delay, with research pointing to several potential mechanisms. Hambrecht (1995) suggested that multiplex families are *less* adept at recognizing the onset of non-specific “prodromal” symptoms in a newly prodromal family member, which likely results in a longer time between onset of prodromal symptoms and onset of psychotic symptoms. However, Hambrecht (1995) also hypothesized that multiply-affected families are *more* adept at recognizing the onset of positive symptoms, thereby reducing the time

between onset of psychotic symptoms and initiation of treatment for a newly psychotic family member. In line with the former hypothesis, Norman et al. (2007) discovered that the presence of a FH of psychosis is associated with a longer DUI (but not shorter DUP). In line with the latter hypothesis that FH is associated with a shorter DUP, Chen et al. (2005) found that FH of psychiatric illness was a significant predictor of a shorter DUP.

The present findings do not replicate the results of either of these two previous studies, in that we found that a FH of psychosis is associated with a *longer* DUP, but that it is not related to the DUI. We also found that this relationship is not explained by differences in the length of the prodromal period; rather, it seems that FEP patients with a FH of psychosis spend a longer period of time with untreated psychosis relative to FEP patients without a FH, but statistically do not have an overall longer DUI. Furthermore, the current findings are the first to show that sex of the patient should be taken into account when examining the relationships between FH and DUI/DUP in that males with a FH of psychosis had a significantly longer DUI and DUP relative to males with no FH of psychosis.

There are several possible explanations for these discrepancies. While the current study is similar to the previous studies in several ways (e.g., FEP patient samples, large sample sizes, and similar operationalizations of DUI/DUP), there are several important methodological differences. First, our study utilized a strict definition of FH that was defined as the presence of a non-affective psychotic disorder in a first-degree relative of the patient, whereas both Chen et al. (2005) and Norman et al. (2007) included both first- and second-degree relatives. Second, the current study focused only on the presence of psychosis in family members, whereas Chen et al. (2005) included any psychiatric illness. Third, the previous studies did not examine the impact of FH on DUI/DUP separately for males and females, thus potentially obscuring interesting sex differences with respect to the influence of FH. Given that males in general have been found to have a longer DUP (Chang et al., 2011), sex is a potentially important variable to take into account.

Finally, our study utilized a very unique sample that consisted primarily of African American individuals in a large, urban setting. It is possible that particular cultural factors may be responsible for explaining the discrepancies between the current study's findings and those findings of previous studies, especially with respect to culturally-specific treatment seeking behaviors that may delay onset of treatment. For example, research has demonstrated differences between African Americans and other ethnicities in type of care utilized (Hu et al., 1991), attitudes toward mental health care (Marwaha and Livingston, 2002), and beliefs about the etiology of mental illness (Schnittker et al., 2000). This, in combination with the notion that having a FH of psychosis may differentially impact an African American family, provides a culturally-sensitive explanation for differences in research findings.

The final aim of our study was to examine the impact of a FH on severity of positive and negative symptoms. Most of the previous studies in this area have utilized small and heterogeneous patient samples, and have shown inconsistent findings. With respect to positive symptoms, the majority of findings have provided little to no support for an impact of FH (Feldmann et al., 2001; Malaspina et al., 2004; Martin Reyes et al., 2004; Chen et al., 2005; Norman et al., 2007). There is more evidence for a moderate relationship between FH and negative symptoms; however, here again the findings have been somewhat mixed (Sautter et al., 1994; Norman and Malla, 2001; Tabarés-Seisdedos et al., 2003; Ritsner et al., 2005;Arajärvi et al., 2006; Norman et al., 2007). Our findings show that FH alone does not exert an effect on severity of symptoms. However, it does interact with sex to influence negative symptom presentation, such that males with a FH show the most severe negative symptom severity.

Discrepancies between current findings and past research might be explained by the focus herein on only FEP patients as well as the inclusion of sex as a potential moderator in the relationship between FH and symptoms. Research has suggested that males have a more severe course of illness, with female patients experiencing fewer relapses and hospitalizations, briefer hospitalizations, more rapid symptom remission, and better response to traditional antipsychotic medications than their male counterparts (Bardenstein and McGlashan, 1990; Salem and Kring, 1998; Leung and Chue, 2000; Räsänen et al., 2000; Taylor and Langdon, 2006; Thorup et al., 2007). The findings suggest that the presence of FH might act as a "double-hit" to further increase the severity of illness in males.

These findings should be interpreted in light of several methodological limitations. First, while standardized methods were used to gather the most reliable data possible, retrospective assessment of age at onset is fraught with difficulty. Second, assessing the presence of FH can also be quite difficult, and data collected from patients alone (without family member informants) may be less reliable. However, we made every effort to interview one or two family members in addition to the patient when possible to ensure that the most accurate data on FH were obtained. Third, the non-epidemiological and homogeneous nature of our sample may limit the generalizability of our findings. However, the dearth of knowledge of the impact of FH on minority populations suggests that the current findings fill an important gap. Finally, the current study is limited by the inclusion of relatively few females, which may have influenced our ability to detect important differences between females with a FH of psychosis and those without such FH.

The present study adds to an existing body of research suggesting that FH of psychosis is associated with a younger age at onset of psychosis, and is one of the first to demonstrate that FH acts similarly on age at onset of the prodrome. This is especially important given that earlier age at onset has adverse prognostic implications for illness course and outcome. Furthermore, findings suggest that FH interacts with sex to influence negative symptom severity as well as the DUI and DUP. These findings, in combination with other research demonstrating that FH influences treatment response and longitudinal course of symptoms, have implications for understanding the specific effects of potentially important etiologic mechanisms. Future research should focus on attempting to understand potential mediators and moderators of FH and its influence on the clinical presentation in schizophrenia. For example, untangling the relationships between FH of psychosis, age at onset of illness/psychosis, delays in treatment, and course and severity of symptoms has the potential to greatly inform future prevention and early intervention efforts that aim to target help-seeking behaviors among multiply-affected families that may be at greater risk for more severe outcomes.

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Table 1

Sociodemographic Characteristics

Variable		Entire Sample	FH	No FH
		***n*=152**	***n*=23**	***n*=129**
Mean Age (years)		22.9 ± 4.5	24.0 ± 2.9	23.1 ± 4.7
Sex (male)		114 (75.0%)	14 (60.9%)	100 (77.5%)
Race	*African American/Black*	136 (89.5%)	23 (100.0%)	113 (87.6%)
	Caucasian/White	8 (5.3%)	0 (0.0%)	8 (6.2%)
	Asian	2 (1.3%)	0 (0.0%)	2 (1.6%)
	Other	5 (3.3%)	0 (0.0%)	6 (4.7%)
Employed (yes)		53 (34.9%)	6 (26.1%)	47 (36.4%)
Involuntary hospitalization		124 (81.6%)	18 (78.3%)	106 (82.2%)
Referral Source	*Family Member*	50 (32.9%)	9 (39.1%)	41 (31.8%)
	Police	43 (28.3%)	5 (21.7%)	38 (29.5%)
	EMS or Ambulance	22 (14.5%)	4 (17.4%)	18 (14.0%)
	Self	12 (7.9%)	1 (4.3%)	11 (8.5%)
	Mobile Crisis Unit	8 (5.3%)	3 (13.0%)	5 (3.9%)
	Other	17 (11.1%)	1 (4.3%)	16 (11.0%)
Education	*Did Not Graduate High School*	68 (44.7%)	10 (43.5%)	58 (45.0%)
	High School Graduate or GED	34 (22.3%)	4 (17.4%)	30 (23.3%)
	Some College or Technical School	40 (26.3%)	9 (39.1%)	31 (24.0%)
	College Graduate	10 (6.6%)	0 (0.0%)	10 (7.8%)

FH=family history, GED=general equivalency diploma, EMS=emergency medical services

Table 2

Clinical Characteristics

Variable		Entire Sample	FH	No FH
		***n*=152**	***n*=23**	***n*=129**
Diagnosis	*Schizophrenia*	88 (57.9%)	11 (47.8%)	77 (59.7%)
	Schizophreniform Disorder	27 (17.8%)	4 (17.4%)	23 (17.8%)
	Psychosis NOS	11 (11.2%)	4 (17.4%)	13 (10.1%)
	Schizoaffective Disorder	14 (9.2%)	4 (17.4%)	10 (7.8%)
	Brief Psychotic Disorder	4 (2.6%)	0 (0.0%)	4 (3.1%)
	Delusional Disorder	2 (1.3%)	0 (0.0%)	2 (1.6%)
Substances	*Alcohol Use Disorder*	32 (21.1%)	6 (26.1%)	24 (19.2%)
	Cannabis Use Disorder	77(51.0%)	12 (44.4%)	65 (52.4%)
	Cocaine Use Disorder	9 (5.9%)	2 (8.7%)	6 (4.8%)
Mean Age at Onset of Prodrome (in years)	*Entire Sample*	18.8 ± 4.9	16.1 ± 5.3	19.2 ± 4.8
	Males	18.7 ± 5.2	15.3 ± 5.9	19.2 ± 4.9
	Females	18.9 ± 4.2	17.4 ± 4.0	19.4 ± 4.2
Mean Age at Onset of Psychosis (in years)	*Entire Sample*	21.1 ± 4.6	18.3 ± 4.6	21.6 ± 4.4
	Males	20.9 ± 4.6	17.5 ± 5.1	21.5 ± 4.4
	Females	21.3 ± 4.6	19.4 ± 3.7	21.9 ± 4.7
Mean PANSS Positive Symptoms	*Entire Sample*	24.1 ± 4.9	23.5 ± 5.7	24.2 ± 4.9
	Males	24.3 ± 4.7	23.9 ± 5.1	24.4 ± 4.7
	Females	23.6 ± 5.7	22.9 ± 6.8	23.8 ± 5.4
Mean PANSS Negative Symptoms	*Entire Sample*	21.3 ± 6.3	22.0 ± 6.3	21.2 ± 6.3
	Males	21.7 ± 6.3	25.5 ± 3.5	21.2 ± 6.4
	Females	19.9 ± 6.2	16.7 ± 6.0	21.0 ± 6.0
Median DUI (in weeks)	*Entire Sample*	131.0	211.0	116.5
	Males	141.5	298.5	116.5
	Females	102.0	53.0	126.0
Median DUP (in weeks)	*Entire Sample*	23.5	57.0	21.0
	Males	21.5	173.5	17.0
	Females	33.5	5.0	44.0
Median Length of Prodrome (in weeks)	*Entire Sample*	48.5	87.0	39.0
	Males	52.0	95.5	40.0
	Females	39.0	49.0	37.0

FH=family history, NOS=not otherwise specified, PANSS=Positive and Negative Syndrome Scale, DUI=duration of untreated illness, DUP=duration of untreated psychosis

Table 3

Family History x Sex Factorial Analysis of Variance for Age at Onset of Prodrome

Source	*df*	*F*	*partial* η^2	*p*
Family history	1	6.25	0.04	0.01
Sex	1	0.99	0.01	0.32
FH x sex (interaction)	1	0.71	0.01	0.40
Error (within groups)	143			

FH=family history

Table 4

Family History x Sex Factorial Analysis of Variance for Age at Onset of Psychosis

Source	*df*	*F*	*partial* η^2	*p*
Family history	1	9.13	0.06	< 0.01
Sex	1	1.26	0.01	0.26
FH x sex (interaction)	1	0.47	0.00	0.49
Error (within groups)	142			

FH=family history

Table 5

Family History x Sex Multivariate Analysis of Variance for Positive and Negative Symptoms [a]

Source		*df*	*F*	*partial* η^2	*p*
Family history	*Positive symptoms*	1	0.31	0.00	0.58
	Negative symptoms	1	0.00	0.00	0.99
Sex	*Positive symptoms*	1	0.45	0.00	0.50
	Negative symptoms	1	9.67	0.06	< 0.01
FH x sex (interaction)	*Positive symptoms*	1	0.04	0.00	0.84
	Negative symptoms	1	8.79	0.06	< 0.01
Error (within groups)	*Positive symptoms*	148			
	Negative symptoms	148			

[a]MANOVA omnibus F non-significant for positive symptoms

FH=family history