The New York High-Risk Project:

Prevalence and Comorbidity of Axis I Disorders in Offspring of Schizophrenic Parents at 25-Year Follow-up

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Abstract

Background—The New York High-Risk Project is a study of offspring of patients with schizophrenia (HRSz group) or affective illness (HRAff group) and psychiatrically normal parents (NC group) observed prospectively from childhood to adulthood. We herein present lifetime prevalence and comorbidity rates of Axis I disorders in subjects and their siblings from sample A of the project.

Methods—Schedule for Affective Disorders and Schizophrenia–Lifetime Version interviews conducted with the offspring in adulthood were used to obtain diagnoses of Axis I disorders.

Results—Schizophrenia and unspecified psychoses occurred only in the HRSz group. However, schizoaffective and psychotic affective disorders occurred equally in the HRSz and HRAff groups. Total rates of psychosis in these groups were significantly higher than in the NC group. All groups had similar rates of nonpsychotic affective and substance abuse disorders. The HRAff group, however, had significantly more total affective illness than the NC group and tended to have more anxiety disorders than the other groups. Comorbidity rates in the HRSz and HRAff groups were nearly twice those of the NC group.

Conclusions—The familial liabilities to schizophrenia and affective disorders show specificities and commonalities, differing markedly from each other in their expression of some disorders and sharing others. Patterns of comorbidity are generally, although not entirely, similar to these liabilities.

Family studies have demonstrated repeatedly that schizophrenia is greatly increased in relatives of schizophrenic probands compared with relatives of normal control subjects or the general population expectancy rate for this illness.^{1–7} Relatives of schizophrenic probands usually, ^{5,6,8,9} although not always, ¹⁰ have shown markedly higher risks for schizophrenia than relatives of probands with affective illness.

Several studies have compared risks for affective disorders in families of schizophrenic probands and families of normal controls or probands with affective illness.^{10–14} Others have attempted to clarify the familial relationship between schizophrenia and different forms of schizoaffective disorder.^{4,12,14,15} Less attention, however, has been paid to comparative risks for other Axis I disorders or comorbidity of psychiatric diagnoses in relatives of schizophrenics. However, family studies may identify variable forms of expression of the genetic liability underlying a particular disorder^{16–18} by comparing relatives of different types of probands with respect to differential patterns of risks and comorbidities across a range of disorders. Our goal herein is to examine differences in risk rates and comorbidity patterns in adult offspring of patients with schizophrenia (HRSz group) or affective illness (HRAff group) and normal controls (NC group).

In a previous report,¹⁹ the lifetime prevalence rates of adulthood psychotic disorders and *DSM-III-R*²⁰ cluster A personality disorders after 23 years of prospective follow-up of this offspring sample in the New York High-Risk Project (NYHRP) were presented. As expected, the HRSz group had highly elevated rates of schizophrenia and unspecified psychoses compared with the NC and HRAff groups. Schizoaffective disorder, subclassified as mainly schizophrenic (SAS), however, was most common in the HRAff group. Prevalence rates of psychotic affective disorders (PAD) did not differ among the 3 groups. Axis II cluster A personality disorders occurred equally often in both risk groups but at a higher frequency than in the N group.

We herein present lifetime prevalence rates of all major Axis I disorders of adulthood and patterns of comorbidity of these disorders in the same sample of subjects—who have been studied extensively from midchildhood to midadulthood. In addition, we include data on their adult siblings, whom we have been able to assess clinically in recent years, thereby enhancing the sample size by approximately 50%.

SUBJECTS AND METHODS

SUBJECT SELECTION AND DIAGNOSTIC ASSESSMENTS

The NYHRP subjects and the collection of Axis I diagnostic information on the offspring in adulthood have been described previously.¹⁹ The previous and present reports concern only the first cohort (sample A) of the NYHRP.

Mentally ill parents, identified from consecutive admissions to state psychiatric facilities in lower New York State in 1971, were interviewed on average 5.5 years later using the Schedule for Affective Disorders and Schizophrenia–Lifetime Version (SADS-L).²¹ Diagnoses according to the Research Diagnostic Criteria²² were assigned based on the interview and information from the index and subsequent hospitalization records without reference to hospital diagnoses; details of the reclassification of parental diagnoses from

those made in 1971 to those based on the Research Diagnostic Criteria were reported earlier.¹⁹ Parents of potential NC group children underwent screening and were determined to be free of any major mental disorder or psychiatric treatment history before inclusion of the family in the study. All parents were white and English speaking, with at least 1 child aged 7 to 12 years, and still married to the other biological parent of the child(ren) at entry into the study.

Children in each group, besides being within the target age range, had to have an IQ of at least 70, show no overt signs of a major psychiatric disturbance, and have received no treatment for emotional problems. These children are the target subjects of the NYHRP. Sample A target subjects have been examined in 6 evaluation rounds (A-1 through A-6), at mean±SD ages of 9.5±1.7, 11.5±2.0, 15.0±1.9, 20.0±1.9, 23.5±2.0, and 27.8±2.0. Telephone interviews were conducted annually throughout the project to assess current psychiatric status and life circumstances of all family members.

Siblings of the target subjects (ie, siblings outside the 7- to 12-year-old age range at the family's entry into the study) were not tested or interviewed individually in childhood. At the A-5 evaluation, however, full siblings aged 18 years or older were given diagnostic interviews; at the A-6 evaluation, they received a complete assessment battery, including laboratory testing and diagnostic interviews.

As previously described,¹⁹ we administered the full SADS-L interview to the target subjects aged 18 years or older at the A-4 and A-6 evaluations and an abbreviated version covering only the major Axis I disorders at the A-5 evaluation. Based on all available interviews, hospital records, and updated assessments of subjects with new onsets since the A-6 evaluation, one of us (U.H.A.) assigned lifetime Axis I diagnoses and estimates of age at onset. Lifetime diagnoses for the siblings, based on the A-5 and A-6 SADS-L interviews and other available clinical materials, were assigned by Robert Simon, MA (an expert diagnostician from the team of Dr Endicott, Department of Research Assessment and Training, New York State Psychiatric Institute, New York) and T. Jeff Adamo, MA (a long-time interviewer and rater for the NYHRP). Interrater reliability (κ) between Mr Simon and the author (U.H.A.) was 1.00; between Mr Simon and Mr Adamo, 0.90. Agreement between the author (U.H.A.) and Mr Adamo was not specifically tested.

Lifetime Axis I diagnoses were available for 188 target subjects and 99 siblings (Table 1) with a cutoff date of August 31, 1995.

Axis I disorders considered herein are (1) psychosis, separated into schizophrenia-related psychoses (schizophrenia, unspecified psychosis, and SAS), PAD (bipolar I or II disorder, unipolar disorder, and mainly affective schizoaffective disorder [SAA]), and drug-induced psychosis; (2) nonpsychotic affective disorders (NPAD), separated into bipolar I and II and unipolar disorders and other affective disorders (hypomania and intermittent depression); (3) anxiety disorders (generalized anxiety disorder, panic disorders, and phobias); and (4) substance abuse disorders (alcohol and other drug abuse).

Although no subject had more than 1 psychotic disorder, some had a psychotic and nonpsychotic disorder or 2 or more nonpsychotic disorders. We counted comorbidity as

the lifetime occurrence in an individual of 2 or more disorders, whether or not they occurred simultaneously.

STATISTICAL METHODS

Although the observations of the target subjects and siblings were not entirely independent, we were unaware of appropriate corrections and, therefore, combined the data as is commonly done in analyses of family data. We computed prevalence rates (mean $\pm$ SE), not corrected for age, and age-corrected morbidity risks calculated by the Kaplan-Meier method of survival analyses.²³ Reliability of estimates of age at onset used for survival analyses was reported previously.¹⁹ We used 1-tailed tests (treating 2-tailed P .10 as significant) when we had a priori directional hypotheses. Hypotheses about prevalence rates were that the HRSz group would have the highest rate of schizophrenia and all schizophrenia-related psychoses taken together; the HRAff group would have the highest rates of PAD and NPAD combined, NPAD alone, and anxiety disorders; and the NC group would have the lowest overall rate of Axis I disorders. Hypotheses about comorbidity were that the NC group would have the lowest rate of comorbidity, and the HRAff group would have the highest rate of comorbidity of NPAD and anxiety disorders together. We used 2-tailed tests (treating P .05 as significant) for all other comparisons.

For comparisons of lifetime prevalences and questions about comorbidity among the 3 subject groups, we used logistic regression²⁴ to calculate odds ratios and their significance. Where appropriate, we also calculated χ^2 statistics, using the Fisher exact test when cell sizes were small. For comparison of the risks for development of a disorder over time in the 3 groups, we used the Mantel-Cox test of the Kaplan-Meier method.²³

We also examined onset histories of subjects who had a substance abuse disorder and psychotic disorder or NPAD to determine which disorder occurred earlier.

Review of the complete picture of Axis I diagnoses and comorbidity in relatives of schizophrenic patients vs relatives of affectively ill patients may help clarify further questions about the separation, or lack of it, between these disorders.

RESULTS

LIFETIME PREVALENCE OF AXIS I DISORDERS

As hypothesized, the NC group had significantly more subjects without any Axis I disorder, compared with the HRSz and HRAff groups, which did not differ from each other (Table 2).

Psychoses—Prevalence rates did not differ within group between target subjects and their siblings for the psychotic disorders. Thus, any changes in the significance of between-group differences in the present analyses, compared with the previous ones,¹⁹ result from increased statistical power contributed by the sibling data.

Psychosis as a whole was more prevalent in the HRSz and HRAff groups than in the NC group (Table 2), as had been seen previously for target subjects alone.¹⁹

Also as found previously, schizophrenia and unspecified psychosis continued to be seen only in the HRSz group, whereas SAS continued to be observed in all subject groups.¹⁹ The rate of all schizophrenia-related psychoses together was significantly lower in the NC group than in either risk group, but with the sibling data added, the difference between the HRSz and HRAff groups achieved significance ($P=.04$) as well.

As further indicated in Table 2, prevalence rates for PAD were significantly higher in each risk group than in the NC group, whereas, when the target subjects alone were examined,¹⁹ the sole difference was between the age-corrected risks of the HRAff and NC groups.

Two cases of completed suicide (not shown) occurred in this sample, in an HRSz target subject and an HRSz sibling (from 2 different families), both with diagnoses of schizophrenia.

All Affective and Other Disorders—Our hypothesis of increased prevalence of all affective illness (PAD and NPAD combined) in the HRAff group was confirmed (1-tailed test) only for the comparison with the NC group. The 3 subject groups did not differ significantly in rates of any main category of nonpsychotic diagnoses or most individual disorders (Table 2). The anxiety category, however, nearly attained significance (1-tailed test) for the HRAff group compared with the other groups. There were some notable group differences also in the pattern of substance abuse disorders. Compared with NC subjects, both risk groups had higher rates of abuse of drugs other than alcohol. Also (data not shown), abuse of other drugs without alcohol tended to be higher ($P=.09$), and abuse of alcohol without other drugs was significantly lower ($P=.01$) in the HRSz than the NC group.

Controlling for gender effects did not change any of the between-group comparisons shown in Table 2 for main diagnostic categories or individual disorders.

LIFETIME MORBIDITY RISKS

On the whole, age-corrected morbidity risks²³ (data not shown) were similar to the lifetime prevalence rates presented in Table 2, and in no case were the between-group comparisons different for the age-corrected and raw prevalence figures. (Age-specific cumulative hazard functions are available from L.E.-K. on request.)

COMORBIDITY

Under each major diagnostic category in Table 3, we differentiate subjects who had no other Axis I disorder or a disorder from the same or a specific other major diagnostic category. As hypothesized, the proportion of subjects with comorbidity as a whole, ie, any 2 or more disorders, was significantly lower in the NC group than in either risk group. Subjects in the NC group who had NPAD, anxiety, or substance abuse disorders tended to have these disorders without a comorbid disorder more often than those in the HRSz or HRAff groups. However, the difference achieved significance ($P=.04$) only in the NC and HRAff comparison for anxiety disorders.

We had also hypothesized that comorbidity between NPAD and anxiety disorders would be more prevalent in the HRAff group. This hypothesis was confirmed only for the comparison

with the NC group ($P .05$). (The same is true for comorbidity of anxiety disorders with all affective disorders—PAD and NPAD combined.)

Although the overall rate of substance abuse disorder was the same for the 3 groups (Table 2), visual inspection of the comorbidity data (Table 3) led us to perform 2 post hoc tests of significance between groups. The first showed that combined alcohol and other drug abuse (in the same individual) was significantly lower in the NC group than in either risk group ($P .05$ for each comparison). The second, comparing the rate of comorbidity between substance abuse and anxiety disorders in the 3 groups, revealed no significant differences.

ONSET OF SUBSTANCE ABUSE BEFORE OR AFTER PSYCHOSIS OR MAJOR AFFECTIVE DISORDER

We examined ages at onset in subjects who had a substance abuse disorder and psychotic disorder or NPAD to determine whether the substance abuse disorder more frequently preceded or followed onset of the other disorder. We omitted 5 subjects in whom the substance abuse and other disorders started within the same year. Among the remaining 51 subjects (all groups combined), 35 (69%) had onset of a substance abuse disorder at least 1 year before onset of the other disorder ($\chi^2=7.08$; $P .01$). The percentage of subjects with substance abuse occurring first was higher (81%) in the HRSz group than in the HRAff and NC groups (62% and 63%, respectively).

COMMENT

Family studies can help to delineate the range of clinical expressions associated with a given major mental disorder and, as such, are necessary for the success of the numerous molecular genetic studies attempting to resolve etiology through linkage findings. Here, we have used the opportunity provided by the NYHRP to compare differential rates and patterns of expression of specific Axis I disorders in relatives (adult offspring) of schizophrenic, affectively ill, and normal control probands. The family study literature and previous findings in the NYHRP with the target subjects alone¹⁹ suggested several hypotheses about specific between-group differences in the combined target subject and sibling data. Among others, we hypothesized and confirmed lower rates of Axis I disorders and comorbidity as a whole in the NC group, compared with the HRSz or HRAff group. The lower prevalence of disorders was attributed chiefly to a reduced rate of psychosis in the NC group, as expected.

PSYCHOSES

The NYHRP continued to support the specificity of schizophrenia and unspecified psychosis to relatives of schizophrenic probands—a finding frequently reported in the literature^{1–9} and described previously for our target subjects alone.¹⁹ Schizophrenia rates (both uncorrected and corrected for age) in the HRSz subjects were similar to those from other contemporary high-risk studies^{25,26} and accumulated family studies.²⁷

The familial relationship of schizoaffective disorder to schizophrenia and the affective illnesses was not clarified further by inclusion of the sibling data. Rates of SAS tended to be elevated in the HRAff group, whereas rates of SAA were similar in both risk groups. Classification by polarity (ie, unipolar vs bipolar)^{13,28–31} did not improve the differentiation

between the two risk groups. Thus, schizoaffective disorder remains a challenge in this and a number of other family studies of schizophrenia and affective illness.^{12,19,32–36}

Inclusion of the sibling data did change the former¹⁹ findings with respect to PAD, which had not differed between the HRSz and NC target subjects alone. Here, the prevalence rates (and age-corrected morbidity risks) of both risk groups significantly exceeded those of the NC group. Thus, the earlier conclusion¹⁹ that the NYHRP data do not support the inclusion of PAD in the familial liability to schizophrenia is seriously weakened in the present analysis. However, the specific composition of subjects with PAD differed considerably between the two risk groups, ie, 80% bipolar illness in the HRAff group vs 40% bipolar illness and 40% SAA in the HRSz group. We will be able to explore differences between these groups in their expression of PAD further through follow-up of our younger sample (sample B).

OTHER AXIS I DISORDERS AND COMORBIDITY

Our findings concur with those of the recent Roscommon Family Study³⁷ in showing no increase in rate of PAD and NPAD combined, NPAD alone, anxiety disorders, substance abuse disorders as a whole, and alcohol abuse in particular among relatives of schizophrenic probands compared with relatives of normal controls.

We had expected, however, that affective illness combined, NPAD alone, anxiety disorders, and comorbidity of NPAD and anxiety disorders would show the greatest aggregation in the HRAff group. Gender effects alone were expected to produce elevated rates of these disorders in the HRAff group, given that the group contained an excess of female subjects (Table 1) and that these disorders are usually more common in females than males. In fact, gender effects were relatively unimportant in the NYHRP, as controlling for gender did not change our unadjusted results.

Rates of total affective illness, but not NPAD, were higher in the HRAff than NC group. Thus, familial aggregation of NPAD in the HRAff group is not strongly supported here. As the parents, all of whom were identified through state hospitals and 46% of whom were psychotic, probably constituted a more severely ill sample¹⁹ than most epidemiologically identified samples, it is not unreasonable that the offspring showed familial aggregation of the more severe, psychotic forms of the illness. Possibly, the HRAff group was too young at follow-up (mean±SD age, 32.4±4.7 years) to have expressed their full potential for affective disorders. However, they had already passed their parents' mean±SD age at onset (26.3±9.2 years) by several years. In at least 1 study, rates of major depressive disorder were similar in relatives of affectively ill probands and controls, although the nature of the episodes differed qualitatively in terms of severity and duration.³⁸

Rates of all affective disorders and NPAD in the HRSz group did not differ from those in either other group. At least 1 other recent study⁵ reported no difference in rates of major depressive disorders between relatives of schizophrenic and affectively ill probands, although in that study, both groups differed from relatives of normal controls. Figures presented in another study³⁷ also appear not to differ between relatives of schizophrenic probands and relatives of affective probands. Thus, our results and those of others suggest

lower specificity for certain types of affective disorders to families of probands with affective illness than is sometimes assumed.⁵

Anxiety disorders, frequently reported to be associated with affective illness,¹⁸ tended to occur more often in the HRAff group and to have greater comorbidity with NPAD in that group than in the other groups. Although the HRAff group thus appears to present a similar pattern to that reported in some studies,^{18,39} it is too small to explore complex subgroupings that have been introduced into many recent studies of comorbidity.⁴⁰

Approximately one third of each subject group had a substance abuse disorder. The similarity of prevalence rates in the risk and NC groups suggests that substance abuse is largely independent of genetic liabilities for schizophrenia or affective illness. The fact that onset of substance abuse disorders preceded—often by several years—onset of psychosis or NPAD in the majority of subjects comorbid for such disorders further suggests that use of alcohol or other drugs usually was not a self-medicating attempt to reduce other psychiatric symptoms. On the other hand, with a mean delay of about 5 years between onset of a substance abuse disorder and psychosis or NPAD, substance abuse clearly did not trigger the onset of the other disorder, although sustained abuse probably served as a long-term risk factor in many cases.

Despite similarities in total rates of substance abuse in the 3 groups, specific patterns differed between the NC and risk groups. The NC group showed less comorbidity of substance abuse with other Axis I disorders and less comorbidity of alcohol and other drug abuse combined. Moreover, in the NC group, alcohol was more commonly abused than other drugs, whereas in the other groups—especially the HRSz group—the opposite was true.

LIMITATIONS

Comorbidity of psychiatric disorders is often considered as a possible pointer to shared etiological factors, eg, common genes, underlying the disorders in question.^{18,41}

Comorbidity has not been well studied in the relatives of schizophrenic probands or, to our knowledge, contrasted with relatives of probands with affective illness. The NYHRP offered an opportunity to begin comparisons of Axis I comorbidities in a well-characterized sample of relatives of these different kinds of probands. Because of the moderately small sizes of our 2 risk groups, however, the figures obtained for comorbidity must be regarded as estimates, and conclusions about etiological associations are limited. Our efforts to compare Axis I rates and comorbidity patterns will be assisted by future addition of data on sample B target subjects and siblings.

Comorbidity of psychiatric disorders may also be considered a gauge of severity of functional impairment. In this sense, we can check the usefulness of comorbidity estimates by considering the extent of agreement between the subjects' levels of comorbidity and functioning. Multiple independent assessments of the subjects' global levels of functioning have been performed (blinded to parent group or offspring diagnoses) in the NYHRP.^{42,43} Recent analyses (unpublished data from a study we are conducting) showed good agreement between these ratings of functioning and comorbidity status. Lower overall comorbidity in the NC group was in line with higher functional ratings assigned to this group, and in all

groups, subjects with more than 1 Axis I disorder had significantly poorer functional ratings than subjects with only 1 disorder.

Although great care has been taken to ensure the diagnostic accuracy for the parents and offspring, some questionable diagnoses remain, as in all studies.⁴⁴ These are, fortunately, few and probably do not affect the overall conclusions about comparisons among the subject groups of the NYHRP. Our confidence in the parent and offspring diagnoses is bolstered by recently completed analyses demonstrating high predictive accuracy and specificity of cognitive and neuromotor measures originally selected as childhood indicators of the liability to schizophrenia, for differentiating between the HRSz and HRAff groups and identifying HRSz subjects in whom schizophrenia-related psychoses later develop.⁴⁵

The combined data on the target subjects and siblings from the NYHRP sample A continue to support the specificity of the familial liability to schizophrenia. Prevalence rates of NPAD, anxiety, and substance abuse disorders are not increased in the HRSz group. The occurrence of PAD equally in the HRSz and HRAff groups, however, suggests that genes for psychosis may be shared by the liabilities to schizophrenia and affective illness.

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Characteristics of Target Subjects and Siblings at Follow-up

[†] Indicates percentage of all siblings in the group living and aged 18 years or older at the time of diagnostic assessments.

Table 2

Lifetime Prevalences of Axis I Disorders in Target Subjects and Siblings Combined*

Diagnosis	Subject Groups					P	
	Prevalence, % (±SE)					HRSz vs NC	HRAff vs NC
	HRSz (n=84)	HRAff (n=67)	NC (n=136)	HRSz vs HRAff	HRSz vs NC		
No Axis I disorders	29.8±5.0	29.9±5.6	41.9±4.3	.99	.07		.10
All psychoses	23.8±4.7	13.4±4.2	1.5±1.0	.11	.00		.00
Schizophrenia-related psychoses	17.9±4.2	6.0±2.9	0.7±0.7	.04	.00		.06
Schizophrenia	13.1±3.7	0±0	0±0	.00	.00		...
Schizoaffective, mainly schizophrenic	1.2±1.2	6.0±2.9	0.7±0.7	.14	.73		.06
Unspecified	3.6±2.0	0±0	0±0	.25	.05		...
Affective psychoses	6.0±2.6	7.5±3.2	0±0	.75	.01		.00
Bipolar I	2.4±1.7	4.5±2.6	0±0	.66	.14		.03
Bipolar II	0±0	1.5±1.5	0±0	.44	...		.33
Schizoaffective, mainly affective	2.4±1.7	1.5±1.5	0±0	1.00	.14		.33
Major depression	1.2±1.2	0±0	0±0	1.00	.38		...
Acute drug-induced psychosis	0±0	0±0	0.7±0.7	...	1.00		1.00
Psychotic and nonpsychotic affective disorders	42.9±5.4 [‡]	49.3±6.2	35.3±4.1	.43	.26		.06
Nonpsychotic affective disorders	38.1±5.3	41.8±6.1	35.3±4.1	.64	.67		.37
Bipolar I	1.2±1.2	0±0	0±0	1.00	.38		...
Bipolar II	4.8±2.3	9.0±3.5	4.4±1.8	.34	1.00		.22
Major depression	26.2±4.8	29.9±5.6	27.2±3.8	.62	.87		.69
Other affective [‡]	10.7±3.4	10.5±3.8	8.1±2.4	.96	.51		.58
Anxiety disorders	15.5±4.0	25.4±5.4	16.9±3.2	.13	.78		.15
General anxiety disorder	9.5±3.2	22.4±5.1	11.0±2.7	.03	.72		.04
Panic	4.8±2.3	3.0±2.1	2.2±1.3	.69	.43		.67
Phobic	6.0±2.6	7.5±3.2	5.9±2.0	.75	1.00		.76
Substance abuse disorders	34.5±5.2	38.8±6.0	31.6±4.0	.59	.66		.31
No alcohol abuse (other drug abuse only)	15.5±4.0	11.9±4.0	8.1±2.4	.53	.09		.38
Alcohol abuse only (no other drug abuse)	4.8±2.3	10.5±3.8	17.7±3.3	.19	.01		.18

* Explanation of the abbreviations is given in the first footnote to Table 1. Sexes were combined.

[‡]Indicates hypomania and intermittent depression.

[‡]One subject with psychotic and nonpsychotic affective disorders is counted once.

Table 3

Specific Combinations of Comorbidity in Target Subjects and Siblings Combined *

	Subject Groups, No. (%)		
	HRSz	HRAff	NC
Comorbid Axis I Disorders	(38/84 [45]) [†]	(33/67 [49]) [‡]	(38/136 [27.9])
Psychosis			
	(n=20)	(n=9)	(n=2)
No other disorder	5(25)	1 (11)	0(0)
Other disorder(s) of same category	0(0)	0(0)	0(0)
Nonpsychotic affective disorders	3(15)	0(0)	1(50)
Anxiety disorders	3(15)	2(22)	0(0)
Substance abuse disorders	10(50)	6(67)	2 (100)
Nonpsychotic Affective Disorders			
	(n=32)	(n=28)	(n=48)
No other disorder	12(37)	10(36)	22 (46)
Other disorder(s) of same category	5(16)	5(18)	6(12)
Psychosis	3(9)	0(0)	1 (2)
Anxiety disorders	8(25)	12(43)//	10(21)
Substance abuse disorders	11 (34)	12(43)	22 (46)
Anxiety Disorder			
	(n=13)	(n=17)	(n=23)
No other disorder	2(15)	2(12)//	10(43)
Other disorder(s) of same category	3(23)	3(18)	3(13)
Psychosis	3 (23) [§]	2(12)	0(0)
Nonpsychotic affective disorders	8(61)	12(71)	10(43)
Substance abuse disorders	3(23)	7(41)	9(39)
Substance Abuse Disorder⁰			
	(n=29)	(n=26)	(n=43)
No other disorder	8(28)	7(27)	17 (39)
Alcohol and drug abuse together	12(41) [§]	11(42)//	8(19)
Psychosis	10 (34) [†]	6 (23)//	2(5)
Nonpsychotic affective disorders	11 (38)	12(46)	22(51)
Anxiety disorders	3(10)	7(27)	9(21)

* Explanation of the abbreviations is given in the first footnote to Table 1. Statistical tests between groups are for odds ratios of comorbid disorders among subjects with the primary Axis I category shown.

[†] $P < .01$, HRSz vs NC groups.

[‡] $P < .01$, HRAff vs NC groups.

[§] $P < .05$, HRSz vs NC groups.

// $P < .05$, HRAff vs NC groups.