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Treatment History in the Psychosis Prodrome: Characteristics of the North American Prodrome Longitudinal Study Cohort

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Abstract

Aim—Early identification and better characterization of the prodromal phase of psychotic illness can lead to targeted treatment and perhaps prevention of many of the devastating effects of a first psychotic episode. The primary aim of this manuscript is to describe the treatment histories of a large cohort of individuals who entered into one of seven prodromal research programs in a North American Prodrome Longitudinal Study consortium.

Methods—Treatment histories from 372 clinical high risk subjects are described along with demographic, symptom, diagnostic and functional variables that may have contributed to treatment decisions for this group of individuals.

Results—Of all subjects included, 82.1% had received psychosocial and/or pharmacologic treatment prior to entry. Psychosocial interventions were more common in the attenuated psychotic syndrome prodromal sample, especially those with more negative, disorganized or general symptoms and more impaired functioning. Psychotropic medication had been administered to individuals with a history of Axis I disorders.

Conclusions—Given the many potential clinical presentations, treatments, and ethical issues connected with the psychosis-risk syndrome, it is not surprising that clinicians administered a broad range of interventions to study participants prior to their entry into the various research programs. Those individuals with milder and nonspecific symptoms were more likely to have received psychosocial treatments, while those with more severe symptoms received pharmacologic intervention. Clinical treatment research is needed that addresses the complexities

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of these psychosis-risk states and helps to specify appropriate treatment at different stages of the psychosis prodrome.

Keywords

Pharmacotherapy; Prodrome; Psychosis; Schizophrenia; Treatment

Introduction

Early identification of individuals at "clinical high risk" and potentially in the prodromal phase of a psychotic illness can lead to earlier treatment and perhaps prevention of many of the devastating effects of a first psychotic episode. International research efforts have demonstrated the success of community outreach and education regarding the schizophrenia prodrome and it is now possible to use empirically defined criteria to identify individuals at a substantially increased risk for a psychotic illness(Cannon, Cadenhead et al. 2008). Preliminary treatment studies have demonstrated initial success in reducing the severity of symptoms and improving functional outcome in clinical high-risk samples (Morrison, French et al. 2004; Marshall and Rathbone 2006; McGlashan, Zipursky et al. 2006; Cornblatt, Lencz et al. 2007).

The North American Prodrome Longitudinal Study (NAPLS) consortium includes a group of 7 North American Universities with independent grant funding to study the psychotic prodrome(Addington, Cadenhead et al. 2007). In an effort to increase the power of any one study alone in characterizing the prodrome, the consortium has merged data from 372 clinical high risk subjects. The NAPLS consortium has published manuscripts describing the methods of classifying and merging this large dataset (Addington, Cadenhead et al. 2007) and on the rate and predictors of psychotic conversion (35% over 2.5 years) in a subsample of 291 clinical high risk subjects defined using the Structured Interview for Prodromal Syndromes (SIPS)(Cannon, Cadenhead et al. 2008).

The clinical high-risk sample meets criteria for 1 of 3 prodromal syndromes defined by the SIPS based on subsyndromal psychotic symptoms and/or a family history of psychosis and deterioration in functioning. The sample is clinically heterogeneous, with 35% meeting criteria for a DSM-IV Axis I mood disorder and 30% meeting criteria for an anxiety disorder(Addington, Cadenhead et al. 2007). Twenty percent of the sample had abused drugs while 15% had abused alcohol. Individuals who were most likely to convert to psychosis had a family history of psychosis, symptoms of suspiciousness or delusional-like experiences, a decline in social functioning, and/or a history of drug abuse(Cannon, Cadenhead et al. 2008). A combination of any 3 of these criteria increased the positive predictive power to 80%, suggesting that it may be possible to develop staging criteria and an algorithm for treatment that will target specific stages with appropriate interventions.

The primary aim of this manuscript is to describe the treatments that the clinical high risk NAPLS sample actually received as a first approximation of treatment in this high risk group in order to contribute to the development of treatment guidelines for the psychotic prodrome.

Methods

The NAPLS sites include Emory University, Harvard University, University California Los Angeles, University of North Carolina, University of California San Diego, University of Toronto, Yale University, and Zucker Hillside Hospital. Institutional Review Board approval was obtained at each site to merge de-identified data into a federated database.

Similar recruitment methods were used across sites as well as common assessment measures including the Structured Interview for Prodromal Syndromes (SIPS, including the Scale of Prodromal Symptoms, SOPS) to verify the clinical high risk state (Addington, Cadenhead et al. 2007). All NAPLS sites received training in the SIPS from Yale University investigators (Kappa 0.90 across all sites) (Addington, Cadenhead et al. 2007). Axis I and II disorders as well as symptom ratings were evaluated using structured measures already in place at the individual sites (Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I), Positive and Negative Syndrome Scale (PANSS), The Diagnostic Interview for Genetic Studies (DIGS) and Kiddie-SADS-Present and Lifetime Version (K-SADS-PL).

Standard functional measures including the Global Assessment of Functioning (GAF) (Hall and Parks 1995) and Premorbid Adjustment Scale (van Mastrigt and Addington 2002) were rated for all patients while Social, Role and Psychological Functioning scales were developed specifically for the NAPLS consortium and scored retrospectively based on available clinical data (Addington, Cadenhead et al. 2007; Cornblatt, Auther et al. 2007).

A summary of treatment history was included in the assessment at all sites. Treatment status at initial assessment and lifetime psychosocial and medication treatment were documented for each subject. These data were then organized by category of psychosocial treatment (any therapy, psychotherapy, family therapy, group therapy, or school support) and medication (any psychotropic, antidepressant, antipsychotic, stimulant, mood stabilizer, or benzodiazepine).

Exploratory analyses were performed to assess the proportion of individuals who had received treatment prior to entering the study and to determine the association of treatment history and type of treatment received to demographic data, diagnosis and symptom ratings. Significant associations within the broad category of lifetime or baseline psychosocial or psychotropic treatment were followed up with type of therapy or medication by category.

Results

Sample Characteristics

The sample included a total of 372 clinically high-risk individuals (37.9% female and 62.1% male). The majority of the sample was non-Hispanic (84.8%), with Caucasians accounting for 77.7% of the sample, followed by African-American (9.1%), multi-racial (5.9%), Asian (4.3%), Pacific Islander (0.3%), or other (2.7%). The mean age of the sample was 18.24 years (4.71 SD) and mean education of the sample with education data (N=366) was 10.34 years (3.03 SD), with 35.5% having completed 12th grade or higher and 7.7% having completed a college degree or higher.

The majority (N=355) of clinical high risk subjects met SIPS criteria for the Attenuated Positive Symptom Group (APS), 14 subjects met criteria for the Brief Intermittent Psychosis (BIP) group while only 3 met criteria for the Genetic Risk and Deterioration Group (GRD) alone (36 of 355 APS and 1 of 14 BIP subjects also fit the GRD criteria for a total N=40).

Treatment History

Treatment History—82.1% of the clinical high-risk sample had a lifetime history of receiving psychotherapy and/or psychotropic medications (Table 1). Of those who received therapy, the majority had received psychotherapy or school support. Of those who had taken a psychotropic agent (60.1%), the majority had received an antidepressant, with lower proportions having received an antipsychotic, stimulant, mood stabilizer or benzodiazepine (Table 2).

Correlates of Treatment History

NAPLS Site—Lifetime history of psychosocial treatment differed by site (χ^2=27.62, df=5, *P*<0.001) (Table 3). Across all sites, the majority of subjects had received psychosocial treatment but Yale's subjects were most likely (95.1%) to have received psychosocial treatment and UNC's the least likely (66.7%). Site differences in psychosocial treatment history at baseline were similar.

The use of psychotropic medication at baseline or during lifetime also differed by site (Table 3). The sites had between 66.7% and 77.8% of subjects with a lifetime history of psychotropic use (χ^2=36.37, df=6, *P*=0.001). At entry into the study, Yale had the smallest sample of subjects currently on psychotropic medication—21.0% and UCLA had the highest —67.6% (χ^2=45.912, df=6, *P*=0.001).

Year of Entry—Lifetime medication use rates were lowest in 1998 and highest in 2002 (χ^2=15.88, df=7, *P*<0.05) (Table 3). In addition, those who entered in 1998 were not medicated at baseline because the earliest studies excluded individuals on medication, while those entering in 2003 had the highest rate of baseline medication use. Follow-up of the year of entry finding by type of medication showed that there were significant differences by year for both antidepressant and antipsychotic medication that accounted for the significant differences in overall medication history (Table 4). It cannot be determined from this data whether the differences by year and site reflect changes in community practice over time or site differences in inclusion criteria.

Demographics—Lifetime psychosocial treatment differed by age (t[311].=2.36, P<0.01) (Table 5), education (t[308]=2.86, P<0.005) and race (χ^2=12.24, df=4, *p*<0.05), with Caucasians being the most likely to have received psychosocial treatment (85.3%) and African-Americans the least likely (62.5%, followed by 66.7% of Asians).

Lifetime medication use also differed by education (those with more education were more likely to have received pharmacotherapy) but there were no differences in medication use by age, gender, race, ethnicity or family history of psychosis. Baseline medication use also differed by parental education (χ=18.41, df=7, *P*=0.01) Those whose parents had some high school education or a high school diploma only were least likely to be medicated at baseline. Participants who had a parent with a post-graduate degree were most likely to be on medication at entry into the study (80%).

Clinical Ratings (See Table 4)—Psychosocial treatment at baseline and lifetime was associated with high baseline SOPS scores, more negative symptoms (decreased ideational richness, deterioration in role functioning), disorganized symptoms (odd behavior/ appearance, bizarre thinking), general symptoms (dysphoria, motor disturbances, impaired stress tolerance) or meeting criteria for a diagnosis of schizotypal personality disorder. Psychotropic medication (primarily antidepressants) was more likely to have been administered to clinical high-risk subjects scoring high on the dysphoria scale from the SOPS.

Prodromal Subgroup (See Table 4)—Interestingly, psychosocial treatment history was associated with meeting the APS prodromal syndrome while a psychotropic medication history was more common in those individuals who did not meet the genetic risk and deterioration subgroup. The genetic risk and deterioration group, however, included only 3 out of 41 subjects who met GRD alone. The majority of the GRD group also met criteria for the APS group (N=37) while only one also met criteria for the brief intermittent psychosis group.

Axis I Disorders (See Table 4)—Psychotropic medication history was also associated with a history of an Axis I disorder including Major Depression, Social Phobia or Panic Disorder, Alcohol or Substance.

Functional Measures (See Table 4)—Psychosocial treatment history was associated with impaired global, premorbid, role or social functioning at baseline assessment while psychotropic medication (antipsychotics or stimulants) history was present in those with impairments in global psychological functioning at baseline

Discussion

Individuals who are referred to prodromal programs and meet the criteria for a prodromal syndrome are generally help seeking and clinically heterogeneous, with a history of mood, anxiety and attenuated psychotic symptoms(Addington, Cadenhead et al. 2007). The majority of the clinical high risk subjects in the NAPLS sample had subsyndromal psychotic symptoms that had either begun or worsened in the last year while a small subgroup also had a family history of psychosis plus a recent deterioration in functioning (Miller, McGlashan et al. 2003). Impaired social and role functioning at the time of entry into the study (Ballon, Kaur et al. 2007; Cornblatt, Auther et al. 2007) was also evident in this group of individuals. The majority of the sample had at one time been treated with a variety of psychosocial treatments and/or psychotropic medications in the community, suggesting that as a group they were in distress prior to entry into the various programs and that these community-based treatments had not been fully effective or entirely uniform. The most common treatment received was psychotherapy followed by medication treatment with antidepressant or antipsychotic agents. Although this is a cross sectional description of treatment received by this sample and it is unclear what effect the various treatments had on the clinical presentation, it is representative of what treatment might look like in the community in a group of individuals at high risk for psychosis.

The baseline characteristics of the NAPLS sample and the corresponding treatment they had already received were also related to the level of severity and specificity of symptoms. Psychosocial interventions history was more common in individuals in the APS prodromal group who also had high ratings on negative, disorganized or general symptoms or impairment in premorbid, global, role or social functioning. Given that many individuals who meet the prodromal criteria are also experiencing nonspecific symptoms that could be due to an array of factors related to adolescent development, drug abuse, affective or anxiety disorders, the community standard appears to be to offer psychosocial treatments more frequently than pharmacologic intervention.

Psychotropic medication was more likely to have been prescribed to those individuals with a history of an affective, anxiety, or alcohol/substance use disorders, or who appeared most symptomatic on a scale of psychological functioning. It is clear that the standard of care in the community is to initiate pharmacologic treatment when there is a diagnosable condition that requires a specific treatment modality. Additionally, it was Caucasian individuals and those from families with higher education who were more likely to have received pharmacologic treatment suggesting that cultural and sociodemographic factors may have played a role in access to such care.

Early identification and treatment in the early phase of psychosis has been an area of increased interest and ethical debate over the last decade(Falloon, Coverdale et al. 1998; Cornblatt, Lencz et al. 2001; McGlashan 2001; McGorry, Yung et al. 2003; Perkins 2004; Corcoran, Malaspina et al. 2005; Haroun, Dunn et al. 2006). Given the range of possible presentations of the psychotic prodrome and potential treatments, the prospect of developing

clinical staging criteria and treatment algorithms is daunting. Although the clinical high risk population is help seeking, they do not necessarily require a “one size fits all” treatment approach but are better suited to needs based treatment(Haroun, Dunn et al. 2006). Clinical, demographic, and vulnerability marker assessment tools are needed to better identify those who are at greatest risk for psychosis. Translational studies are essential to understand the mechanism by which psychosis evolves and inform preventive treatment.

The concept of clinical staging for psychotic disorders, similar to that which has been developed in the treatment of illnesses such as cancer or diabetes, has been suggested by McGorry et al (McGorry, Hickie et al. 2006). Those individuals with milder symptoms and/or fewer risk factors would be treated with psychosocial treatments while those who have more severe symptoms and risk factors would be treated with pharmacotherapy in addition to psychosocial treatment.

Preliminary treatment algorithms (Haroun, Dunn et al. 2006; McGorry, Hickie et al. 2006; Yung, Yuen et al. 2007) have been proposed that describe a graded treatment approach in the prodrome that begins with a thorough clinical assessment, differential diagnosis, psychoeducation and observation. Psychosocial treatments such as CBT, crisis intervention or supportive psychotherapy, substance abuse reduction and family psychoeducation are recommended for all stages. Neuroprotective strategies such as Omega 3 Fatty Acids, atypical antipsychotics and/or antidepressants and mood stabilizers would be initiated when the individual has more severe prodromal symptoms or Axis I pathology. However, the development of definitive treatment algorithms for those who may be at clinical high risk for psychosis is clearly hindered by the lack of published treatment studies that are rigorously controlled.

Conclusions

Individuals who meet the prodromal syndrome criteria are clinically heterogeneous but help-seeking and have often received a range of different treatments prior to entry into prodromal research programs. Less than 40% of those who meet the SIPS criteria are likely to become psychotic but those with additional risk factors such as a family history of psychosis, more severe ratings on delusional-like symptoms, social functioning deficits or substance abuse are even more likely to develop schizophrenia or an affective disorder. Translational studies are needed to better understand the neuropathological changes in the early stages of psychosis and to assess neuroprotective strategies that might be beneficial in the prodormal period. Finally, clinical trials of both psychosocial and pharmacologic interventions are needed to better inform treatment decisions. For now the best recommendation for clinicians encountering clinical high risk patients is to monitor symptoms carefully in all patients and judiciously to offer treatment using a needs based approach, recognizing that the prodromal syndrome may either be transient or evolve into a more serious condition with a range of diagnostic and functional outcomes.

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Table 1

Psychosocial Treatment History in Clinical High Risk Subjects(N=372)+

Baseline Psychosocial Treatment	
Any Therapy	55.0%
Psychotherapy	46.3%
Family Therapy	4.2%
Group Therapy	1.9%
School Support	8.3%
Lifetime Psychosocial Treatment	
Any Therapy	82.1%
Psychotherapy	73.7%
Family Therapy	8.1%
Group Therapy	5.5%
School Support	15.9%

+N=59–65(15.9–17.5%) had missing data in the individual categories

Table 2

Psychotropic Medication Use in Clinical High Risk Subjects(N=372)+

Baseline psychotropic medication	
Any psychotropic	41.1%
Antidepressant	31.4%
Antipsychotic	12.3%
Stimulant	4.0%
Mood Stabilizer	4.6%
Benzodiazepine	4.9%
Lifetime psychotropic medication	
Any psychotropic	60.1%
Antidepressant	49.4%
Antipsychotic	23.7%
Stimulant	13.7%
Mood Stabilizer	11.2%
Benzodiazepine	9.8%

+N=14–24 subjects(3.8–6.5%) had missing data in the individual categories

Table 3

Treatment History by Site and Year of Entry into the Study

	Baseline		Lifetime	
	Psychotropic Medication (N=350)	**Psychosocial Treatment (N=313)**	**Psychotropic Medication (N=358)**	**Psychosocial Treatment (N=313)**
Site				
UNC	(N=51) 54.9%**	(N=48) 39.6%**	(N=51) 74.5%**	(N=48) 66.7%**
Emory	(N=9) 66.7%	(N=8) 50.0%	(N=9) 66.7%	(N=8) 87.5%
LIJ	(N=44) 43.2%	(N=44) 36.4%	(N=44) 72.7%	(N=44) 81.8%
Toronto	(N=34) 26.5%	(N=35) 48.6%	(N=39) 46.2%	(N=36) 72.2%
UCLA	(N=34) 67.6%	-	(N=36) 77.8%	-
UCSD	(N=59) 57.6%	(N=57) 38.6%	(N=59) 72.9%	(N=55) 72.7%
Yale	(N=119) 21.0%	(N=121) 77.7%	(N=120) 41.7%	(N=122) 95.1%
Year				
1998	(N=17) 0%**	(N=17) 64.7%	(N=18) 33.3%*	(N=17) 94.1%
1999	(N=25) 16.0%	(N=26) 57.7%	(N=25) 36.0%	(N=26) 88.5%
2000	(N=41) 24.4%	(N=45) 62.2%	(N=47) 55.3%	(N=45) 80.0%
2001	(N=43) 46.5%	(N=39) 46.2%	(N=43) 65.1%	(N=38) 73.7%
2002	(N=52) 51.9%	(N=40) 55.0%	(N=52) 69.2%	(N=41) 78.0%
2003	(N=59) 52.5%	(N=49) 57.1%	(N=59) 64.4%	(N=49) 87.8%
2004	(N=91) 46.2%	(N=78) 49.5%	(N=92) 65.2%	(N=78) 79.5%
2005	(N=22) 31.8%	(N=19) 31.8%	(N=22) 73.7%	(N=19) 89.5%

** $p<0.01$

* $p<0.05$

Table 4

Treatment History by Year and Type of Medication

Year	Baseline Antipsychotic	Baseline Antidepressant
1998	0%	0%
1999	0%	12.0%
2000	2.5%	17.1%
2001	16.3%	34.9%
2002	30.8%	34.6%
2003	13.6%	42.4%
2004	8.9%	39.6%
2005	13.6%	27.3%

Table 5

Lifetime and Baseline Treatment History in Clinical High Risk Subjects

	Baseline						Lifetime					
	Psychotropic Medication		p	Psychosocial Treatment		p	Psychotropic Medication		p	Psychosocial Treatment		p
Mean(SD)	Yes N=144	No N=206		Yes N=172	No N=141		Yes N=215	No N=143		Yes N=257	No N=56	
Demographics												
Age	18.11(4.47)	18.38(4.96)	NS	17.42(4.70)	19.54(4.81)	<.0.01	18.63(4.49)	17.79(5.05)	NS	17.98(4.79)	19.83(4.72)	<0.01
Gender (% male)	58.3%	61.7%	NS	63.4%	57.4%	NS	62.3%	58.7%	NS	61.5%	55.2%	NS
Ethnicity (% Hispanic)	12.7%	12.8%	NS	15.7%	12.8%	NS	12.7%	16.9%	NS	14.8%	12.5%	NS
Education	10.39(3.04)	10.4(3.11)	NS	9.78(3.10)	11.18(2.90)	<0.01	10.76(3.04)	9.80(2.99)	<0.01	10.15(3.09)	11.47(3.10)	<0.01
Fam Hx Psychosis	41.0%	46.9%	NS	49.6%	38.1%	NS	42.0%	49.0%	NS	46.5%	36.0%	NS
Structured Interview for Prodromal Syndromes												
Unusual Thought Content	3.04(1.53)	3.13(1.60)	NS	3.09(1.54)	3.04(1.58)	NS	3.13(1.55)	3.08(1.59)	NS	3.03(1.55)	3.25(1.60)	NS
Suspiciousness	2.86(1.57)	2.83(1.46)	NS	2.89(1.41)	2.85(1.59)	NS	2.91(1.55)	2.78(1.42)	NS	2.86(1.46)	2.95(1.63)	NS
Grandiosity	1.12(1.34)	1.11(1.38)	NS	1.12(1.36)	1.01(1.30)	NS	1.15(1.40)	1.06(1.28)	NS	1.06(1.27)	1.16(1.59)	NS
Hallucinations	2.92(1.72)	2.96(1.75)	NS	3.09(1.70)	2.75(1.82)	NS	3.05(1.68)	2.83(1.78)	NS	2.98(1.73)	2.73(1.89)	NS
Disorganized Communication	1.65(1.32)	1.95(1.50)	NS	1.95(1.48)	1.63(1.48)	NS	1.77(1.39)	2.01(1.51)	NS	1.82(1.52)	1.70(1.28)	NS
Positive Total	11.60(3.69)	11.97(4.25)	NS	12.14(3.79)	11.29(4.33	NS	12.02(3.96)	11.76(4.20)	NS	11.76(3.94)	11.79(4.53)	NS
Social Anhedonia	2.42(1.82)	2.46(1.99)	NS	2.62(1.97)	2.27(1.90)	NS	2.48(1.84)	2.46(2.06)	NS	2.51(1.94)	2.20(1.86)	NS
Avolition	2.42(1.66)	2.25(1.76)	NS	2.36(1.71)	2.12(1.69)	NS	2.47(1.67)	2.16(1.79)	NS	2.29(1.71)	2.20(1.61)	NS
Expression of Emotion	1.50(1.56)	1.40(1.60)	NS	1.52(1.64)	1.39(1.63)	NS	1.48(1.53)	1.48(1.70)	NS	1.48(1.62)	1.38(1.71)	NS
Experience of Emotion/Self	1.54(1.79)	1.41(1.63)	NS	1.33(1.62)	1.43(1.72)	NS	1.64(1.81)	1.29(1.52)	NS	1.42(1.69)	1.25(1.63)	NS
Ideation Richness	1.21(1.42)	1.22(1.50)	NS	1.43(1.53)	0.88(1.35)	<0.01	1.27(1.46)	1.25(1.53)	NS	1.21(1.49)	1.00(1.36)	NS
Occupation Functioning	2.85(1.82)	3.21(1.89)	NS	3.25(1.74)	2.73(2.02)	<0.05	3.05(1.86)	3.12(1.88)	NS	3.14(1.82)	2.50(2.19)	<0.05
Negative Total	11.80(6.43)	11.94(7.02)	NS	12.33(6.46)	10.81(7.05)	NS	12.28(6.54)	11.78(7.35)	NS	11.91(6.59)	10.52(7.38)	NS
Odd Behavior/Appearance	1.35(1.36)	1.41(1.52)	NS	1.71(1.45)	1.05(1.38)	<0.01	1.35(1.37)	1.49(1.58)	NS	1.53(1.46)	0.84(1.28)	<0.01
Bizarre Thinking	1.57(1.45)	1.78(1.56)	NS	1.96(1.58)	1.42(1.47)	<0.01	1.64(1.44)	1.82(1.64)	NS	1.86(1.56)	1.09(1.35)	<0.01
Trouble w/Focus and Attention	2.46(1.27)	2.48(1.46)	NS	2.52(1.42)	2.45(1.40)	NS	2.46(1.39)	2.51(1.38)	NS	2.50(1.44)	2.45(1.32)	NS

	Baseline						Lifetime					
	Psychotropic Medication		p	Psychosocial Treatment		p	Psychotropic Medication		p	Psychosocial Treatment		p
Mean(SD)	**Yes N=144**	**No N=206**		**Yes N=172**	**No N=141**		**Yes N=215**	**No N=143**		**Yes N=257**	**No N=56**	
Personal Hygiene	0.90(1.28)	0.79(1.22)	NS	0.90(1.25)	0.76(1.27)	NS	0.91(1.32)	0.77(1.15)	NS	0.90(1.27)	0.61(1.20)	NS
Disorganized Total	6.29(3.69)	6.44(3.89)	NS	7.08(3.83)	5.68(3.91)	<0.01	6.36(3.72)	6.59(4.02)	NS	6.78(3.86)	4.98)3.83)	<0.01
Sleep Disturbance	2.03(1.63)	1.98(1.75)	NS	2.13(1.70)	1.83(1.75)	NS	2.06(1.69)	1.97(1.73)	NS	2.09(1.72)	1.66(1.68)	NS
Dysphoric Mood	3.36(1.59)	2.84(1.82)	<0.01	3.06(1.68)	2.92(1.83)	NS	3.26(1.64)	2.76(1.83)	<0.01	3.12(1.69)	2.52(1.89)	<0.05
Motor Disturbance	0.75(1.12)	0.68(1.23)	NS	0.65(1.14)	0.74(1.18)	NS	0.73(1.12)	0.71(1.29)	NS	0.65(1.12)	0.91(1.33)	NS
Impaired Tolerance to Normal Stress	2.26(1.77)	2.11(1.74)	NS	2.26(1.75)	2.11(1.83)	NS	2.23(1.79)	2.14(1.72)	NS	2.31(1.77)	1.68(1.75)	<0.05
General Total	8.40(4.19)	7.59(4.54)	NS	8.08(4.27)	7.60(4.64)	NS	8.27(4.28)	7.57(4.58)	NS	8.16(4.36)	6.77(4.62)	<0.05
SIPS Total	37.89(14.74)	38.11(14.74)	NS	39.57(13.50)	35.33(15.04)	<.0.05	38.77(13.24)	37.96(15.62)	NS	38.52(13.88)	34.05(15.62)	<0.05
Prodromal Syndrome												
Attenuated Positive Symptoms	95.1%	96.6%	NS	96.5%	95.7%	NS	96.3%	95.8%	NS	97.3%	91.1%	<0.05
Brief Intermittent Psychotic Symptoms	4.2%	3.9%	NS	2.9%	5.0%	NS	4.2%	3.5%	NS	2.7%	8.9%	<0.05
Genetic Risk & Deterioration	8.2%	13.4%	NS	13.3%	10.3%	NS	9.0%	16.3%	<.0.05	13.2%	7.8%	NS
Functioning												
Premorbid functioning	0.30(0.15)	0.33(0.17)	NS	0.26(0.17)	0.33(0.16)	NS	0.32(0.16)	0.32(0.16)	NS	0.33(0.16)	0.30(0.17)	<0.01
GAF	47.23(12.72)	45.92(11.76)	NS	43.85(10.15)	50.07(12.99)	<0.01	46.53(11.78)	46.35(12.79)	NS	44.94(11.12)	53.61(12.73)	<0.01
Social Function	6.31(1.42)	6.13(1.54)	NS	6.04(1.35)	6.47(1.58)	<0.01	6.21(1.37)	6.13(1.66)	NS	6.15(1.41)	6.66(1.71)	<0.05
Role Function	6.12(1.84)	6.06(1.61)	NS	5.99(1.52)	6.49(1.67)	<0.01	5.99(1.78)	6.20(1.58)	NS	6.12(1.54)	6.59(1.84)	<0.05
Psychological Function	5.58(1.07)	5.76(0.85)	NS	5.73(0.77)	5.89(0.95)	NS	5.6(1.06)*	5.84(0.85)	<0.05	5.78(0.83)	5.95(0.98)	NS
Comorbid Conditions												
Schizotypal Personality Disorder	20.0%	28.6%	NS	36.1%	19.4%	<0.01	23.9%	29.1%	NS	32.4%	9.1%	<0.01
Alcohol Use	49.3%	43.6%	NS	41.7%	52.2%	0.10	51.5%	36.4%	<0.01	44.5%	52.8%	NS
Substance Use	41.0%	39.9%	NS	35.0%	44.8%	0.10	44.8%	32.6%	<0.05	38.1%	42.6%	NS
Depression	38.0%	24.2%	<.0.01	27.0%	23.2%	NS	37.2%	17.9%	<0.01	26.5%	20.0%	NS
Panic Disorder	10.9%	4.8%	<0.05	4.5%	8.1%	NS	10.5%	2.2%	<0.05	7.0%	4.0%	NS
Social Phobia	15.5%	10.3%	NS	11.6%	10.5%	NS	16.0%	6.5%	<0.05	11.4%	10.0%	NS