Additional information is presented in detail below to further characterize study participants with regard to treatment history, drug use history, and co-morbid disorders in first-degree relatives as well as the relationship between class of pharmacological treatment, dose, and clinical ratings with cognition. In the smaller schizoaffective groups, power was reduced for select analyses (i.e,, multivariate profile analysis, estimating familiality) and were thus presented here as exploratory analyses. Similarly, sample sizes were insufficient to separately evaluate relatives of depressive and manic schizoaffective probands with and without Cluster A or B personality traits. Relatives of depressive and manic schizoaffective probands were combined below for exploratory analyses. Finally, a repeated measures MANOVA was conducted to determine whether there were unique profiles of neuropsychological performance across BACS subtests among unaffected relatives of schizophrenia and bipolar disorder probands.

Medication history and comorbid disorders in relatives

The degree to which treatment history and clinical symptoms were related to BACS composite scores were examined in both probands and relatives. As shown in Supplemental Table 1, BACS correlations with treatment history, clinical ratings, antipsychotic dose, and chlorpromazine equivalents were minimal for schizophrenia and bipolar probands and their relatives. Table 2 presents BACS composite correlations with the class of prior illicit drug use in probands and relatives. The relationship between both pharmacological treatment status and history of illicit drug use was modest for both proband and relative groups.

A sub-sample of relatives met diagnostic criteria for Axis I psychotic disorders including 4% schizophrenia, 1.6% schizoaffective, 1.3% psychotic bipolar, and 1.2% other psychotic disorders. Additionally, some relatives met diagnostic criteria for a mood disorder including

2.2% bipolar disorder without psychosis, 3.4% major depressive disorder, 1.7% dysthymia, and 1.9% other mood disorders.

Profile comparisons with schizoaffective disorders.

Few studies have examined neuropsychological profiles in schizoaffective probands and the degree to which these profiles may diverge from the patterns seen in schizophrenia and bipolar disorder. Repeated measures MANOVA testing for profile differences among all probands indicated a significant group by subtest interaction [$F(20,3151.74) = 5.91$, $p<.001$]. However, when the controls were excluded and the analyses included schizophrenia, bipolar, and schizoaffective probands only, the group by subtest interaction was not significant $F(15,1827.89) = 1.25$, $p=0.23$]. Schizoaffective probands showed a variable pattern across BACS subtests when compared to controls, but their profiles were similar in shape to schizophrenia and bipolar probands (Figure 2 of main manuscript).

Familiality in schizoaffective pedigrees

Estimated familiality for composite scores from the Brief Assessment of Cognition in Schizophrenia and the Wide Range Achievement Test – IV Reading were significant for schizoaffective pedigrees. These estimates were somewhat lower for the composite cognitive score (0.67; 90% Confidence Interval 0.52-0.72) than word reading (0.86; 90% Confidence Interval 0.70-1.02), but were largely consistent with familiality estimates for psychotic bipolar and schizophrenia pedigrees.

Personality traits in relatives of schizoaffective probands.

Relatives of schizoaffective probands with no history of psychosis or elevated Cluster A/ Cluster B traits did not differ from healthy controls [$F(1,418)=1.31$, $p=0.25$]. Those with elevated Cluster A and B traits showed significant impairments on Brief Assessment of

Cognition in Schizophrenia composite scores compared to controls [F(1,334)=10.04, p=0.002]. Although mean differences were not significant for unaffected relatives of schizoaffective probands with elevated Cluster A traits compared to those with elevated Cluster B traits [F(1,40)=2.74, p=0.11], these findings were based on very small samples (Elevated Cluster B: n = 11) and larger samples are needed for this comparison. Further research is needed to clarify the nature of cognitive abilities among unaffected relatives of schizoaffective and bipolar disorder probands with no elevated Cluster A traits. With regard to elevated Cluster A traits, the present findings indicate similar levels of cognitive dysfunction for relatives, regardless of proband diagnosis.

Correlational Analyses for Personality Traits

Evaluating personality traits continuously may reduce the bias associated with classifying participants with both elevated Cluster A and Cluster B traits as Cluster A. Thus, the number of criteria met in each cluster was correlated both across cluster and with cognitive performance. As presented in Table 3, unaffected bipolar relatives showed a significant correlation in which cognitive performance decreased as the number of either Cluster A or Cluster B traits increased. This was consistent with the significant interaction in which cognitive deficits were observed in bipolar relatives with elevated personality traits, but not in those without prominent personality traits. This is consistent with the notion that elevated Cluster A or B personality traits may indicate increased risk for cognitive impairment in families with a bipolar disorder proband.

Profile comparisons for unaffected relatives of schizophrenia and bipolar disorder probands.

Repeated measures MANOVA testing for profile differences indicated a significant group by subtest interaction [$F(10,1350) = 3.14$, $p<.001$]. In line with profile consistency across probands groups, this interaction was rendered non-significant $F(5,387) =2.14$, $p=0.06$], when

the controls were excluded from this analysis. Thus, there was no evidence of different patterns of neuropsychological performance in relatives of schizophrenia and bipolar disorder probands. This was consistent with findings in proband groups.

Supplemental Table 1: Relationship of BACS composite with the presence or absence of prior pharmacological treatment

	Probands				Relatives			
	Schizophrenia (SZ)		Bipolar w/ Psychosis (BP)		Schizophrenia (R-SZ)		Bipolar w/ Psychosis (R-BP)	
	n=293		n=227		n=314		n=255	
Drug Class	r	#	r	#	r	#	r	#
FGA	-0.14	56	-0.12	18	-0.19	5	-0.19	1
SGA	0.02	240	-0.17	151	-0.29	28	-0.20	17
Anti-Depressant	0.04	115	0.09	102	-0.05	49	0.01	58
Mood Stabilizer*	-0.15	44	-0.06	119	-0.19	13	-0.13	24
Lithium	0.12	16	-0.06	64	-0.10	3	-0.07	9
Stimulant	0.05	10	0.07	23	0.02	1	-0.02	13
Sedative/Hypnotic	0.00	56	-0.01	66	-0.07	25	-0.06	5
Anticholinergic	-0.21	52	-0.12	20	-0.26	7	-0.09	1
Correlation with Current Dose	r	n	r	n	r	n	r	n
CPZ[1] dose	-0.04	196	-0.23	134	-0.09	21	0.12	12
Benztropine Dose	-0.20	36	0.06	16	-0.41	5	--	--
Clinical Variables	r	n	r	n	r	n	r	n
PANSS Total	-0.17	288	-0.15	223	-0.06	41	-0.52	35
PANSS Pos	-0.13	288	-0.14	223	-0.10	41	-0.49	35
PANSS Neg	-0.19	288	-0.15	223	-0.08	41	-0.46	35
YMRS	-0.03	281	-0.09	222	-0.10	77	-0.15	50
MADRS	-0.05	271	-0.01	214	-0.12	77	-0.18	50

[1] {665}
r: Correlation for BACS composite and drug class
#: Number in group prescribed this drug class
FGA: First Generation Antipsychotic
SGA: Second Generation Antipsychotic
CPZ: Chlorpromazine equivalent
* Anticonvulsants

Supplemental Table 2: Relationship of Brief Assessment of Cognition in Schizophrenia composite scores with presence or absence of substance abuse history

	Probands				Relatives			
	Schizophrenia		Bipolar w/ Psychosis		Schizophrenia		Bipolar w/ Psychosis	
	n=293		n=227		n=314		n=255	
Drug Class	r	#	r	#	r	#	r	#
ETOH	0.14	29	0.06	34	0.04	33	0.11	20
Sedative/Hypnotic/ Anxiolytic	--	--	--	--	--	--	--	--
Cannabis	0.18	37	0.08	14	-0.08	14	0.02	14
Stimulants	--	--	--	--	--	--	--	--
Opioids	--	--	--	--	--	--	--	--
Cocaine	-0.01	5	--	--	--	--	0.00	4
Hallucinogenics	-0.09	5	-0.02	3	--	--	--	--
Other Illicit Substance	--	--	--	--	--	--	--	--
Any class of substance abuse	0.18	49	0.10	52	0.01	48	0.08	32

r: Binary correlation for BACS composite and illicit drug class
#: Number in group endorsing substance abuse history in this class
--: Insufficient data for correlation

Supplemental Table 3: Spearman Rank Order Correlations for Number of Personality Traits and composite on the Brief Assessment of Cognition in Schizophrenia

	Relatives of Schizophrenia Probands		Relatives of Bipolar Probands	
	BACS	Cluster A Count	BACS	Cluster A Count
Cluster A Count	− 0.17†	−−	− 0.30§	−−
Cluster B Count	− 0.07^{ns}	− 0.40†	− 0.18†	− 0.39§

† $p \leq .01$, § $p \leq .001$