Published in final edited form as:

Schizophr Res. 2017 June ; 184: 45–51. doi:10.1016/j.schres.2016.12.010.

The interplay of childhood behavior problems and IQ in the development of later schizophrenia and affective psychoses

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Abstract

Schizophrenia and affective psychoses are both associated with impaired social functioning, but the extent to which childhood behavioral impairments are present prior to onset of illness is less well studied. Moreover, the concurrent relationship of childhood behavior problems and premorbid IQ with subsequent psychotic disorder has not been established. We investigated whether

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Author contributions

All authors made substantial contributions to the conception and design or analysis and interpretation of the data, and to drafting the article or revising it critically for important intellectual content, as well as had final approval of the version to be published.

Role of the funders

The funders played no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

Conflicts of interest

The authors do not have any personal or financial conflicts of interest to disclose.

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childhood behavior problems are associated with increased risk for adult schizophrenia or affective psychosis, independently and in combination with IQ. The study included individuals with schizophrenia (N=47), affective psychoses (N=45) and non-psychotic controls (N=1,521) from the New England Family Study. Behavior problems were prospectively assessed from standardized clinician observations at ages 4 and 7. IQ was assessed with the Stanford-Binet at age 4 and the Wechsler Intelligence Scale for Children at age 7. We found externalizing problems at age 4 and externalizing and internalizing problems at age 7 were associated with later schizophrenia, and both internalizing and externalizing problems at ages 4 and 7 were associated with later development of affective psychoses. Lower IQ at ages 4 and 7 was associated with schizophrenia, while lower IQ was associated with affective psychoses at age 7 only. Examined simultaneously, both lower IQ and behavior problems remained associated with risk of schizophrenia, while only behavior problems remained associated with affective psychoses. Behavior problems appear to be a general marker of risk of adult psychotic disorder, while lower childhood IQ is more specific to risk of schizophrenia. Future research should clarify the premorbid evolution of behavior and cognitive problems into adult psychosis.

Keywords

Schizophrenia; affective psychosis; childhood behavior problems; premorbid cognition; premorbid IQ

1.1 Introduction

The neurodevelopmental model of schizophrenia posits that the disorder originates in the prenatal, perinatal and early childhood periods (Murray and Lewis, 1987; Weinberger, 1987), with precursors evident prior to the prodromal period and onset of the full syndrome (Fish, 1977). While there is clear evidence for childhood motor and cognitive problems among individuals who later develop schizophrenia (Seidman, 1990; Olin and Mednick, 1996; Niemi, 2003; Keshavan et al., 2005; Liu, et al., 2015), relatively less is known about premorbid behavioral problems (Tarbox and Pogue-Geile, 2008). Suggestive evidence can be found in early life history descriptions of schizophrenia patients by Kraepelin (Kraepelin, 1919) and Bleuler (Bleuler, 1950), and studies that find affective problems may precede onset of psychosis for some individuals (Yung and McGorry, 1996; Weiser et al., 2002; Weiser et al., 2008).

Evidence of premorbid neurodevelopmental abnormalities in affective psychotic disorders is less clear than for schizophrenia, at least with respect to premorbid cognitive impairment, with some studies suggesting individuals who later develop affective psychoses exhibit better neurocognitive performance in childhood than those who develop schizophrenia (Seidman et al., 2013; Agnew-Blais et al., 2015). However, whether the finding of less premorbid impairment for affective psychoses compared with schizophrenia extends to childhood behavior problems is uncertain, nor is it clear whether the age of onset, severity and type of behavior problems differ between those who develop schizophrenia and affective psychoses. We have previously found that children of individuals with schizophrenia and affective psychoses showed elevated risk for behavior problems, including internalizing and

externalizing behaviors at age 7 (Donatelli et al., 2010); however we have not investigated behavior problems among children who later develop these disorders themselves in later life.

Moreover, little research has been done regarding the relationship between cognition and behavior in the early premorbid period among individuals who later develop psychotic disorder. It may be that behavioral and cognitive problems tend to co-occur in childhood among individuals who later develop psychosis, or alternatively, that premorbid impairments in these domains are largely independent, suggesting more distinct pathways in relation to later psychosis risk.

Schizophrenia and affective psychosis have overlapping symptomatology and genetic susceptibility (Murray et al., 2004; Lichtenstein et al., 2009; Smoller, 2013), and a better, comparative understanding of the premorbid course of childhood development in these two disorders could shed light on differences in their neurodevelopmental trajectories and susceptibility profiles. This issue takes on increasing importance as the field moves to develop early intervention strategies (Liu et al., 2015; Seidman and Nordentoft, 2015). Given that these disorders share common symptoms of psychosis, a direct comparison of premorbid behavior problems and cognition among the psychoses provides a strong test of similarities and differences between them. Our aim was to investigate whether childhood behavior problems were associated with increased risk for adult schizophrenia or affective psychosis, independently and in combination with IQ. We hypothesized that: (a) premorbid behavior problems at ages 4 and 7 would be more strongly related to schizophrenia than affective psychoses, and (b) both lower IQ and behavior problems would be independently associated with increased risk of later schizophrenia. As we did not have a strong *a priori* hypothesis regarding whether internalizing versus externalizing problems would be differentially related to later risk, we examined these problems separately to identify potential specificity associated with type of behavior problem.

2 Methods

2.1 Study population

The Collaborative Perinatal Project (CCP) was established over half a century ago to study the pre- and perinatal origins of neurologic disease. The CPP followed pregnant women during prenatal visits and then their offspring at ages 4, 8 and 12 months and 4 and 7 years during visits that included physical, neurological and psychological evaluations (Broman, 1984). The New England Family Study (NEFS) includes the Boston, Massachusetts (MA) and Providence, Rhode Island (RI) sites of the CPP, and is composed of approximately 17,000 births. 60.6% (N=10,853) of study subjects participated in behavioral examinations at age 4, and 66.8% (N=11,968) participated in behavioral examinations at age 7.

2.2 Ascertainment and assessment of cases and controls

As described in previous reports (Donatelli et al., 2010; Seidman et al., 2013; Agnew-Blais et al., 2015), cohort members with a history of psychiatric hospitalization and/or possible psychotic illness were identified from: 1) nested follow-up and case-control studies, including interviews with approximately 20% of the cohort; 2) record linkages with public

hospitals, mental health clinics, and the MA and RI Departments of Mental Health; and 3) reports from participants in follow-up studies of a family member with a history of psychotic symptoms or diagnosis. Participants who consented to a follow-up interview were given the Structured Clinical Interview for DSM-IV (First et al., 1996). Trained diagnosticians completed best-estimate consensus diagnoses according to DSM-IV criteria (Goldstein et al., 2010; Goldstein et al., 2014). Diagnostic interviews were completed for 173 subjects; medical charts alone were available for 76 subjects. In total 114 subjects were determined to have a psychotic disorder; of those with available data, nine cases were determined to have psychosis from medical charts alone (Seidman, et al. 2013). Participants were identified as having schizophrenia psychoses [total N=52; schizophrenia (N=48) and schizoaffective disorder depressed-type (N=4)] or affective psychoses [total N=51; schizoaffective bipolar-type (N=16), bipolar disorder with psychotic features (N=25), major depressive disorder with psychosis (N=10)], or other non-affective psychotic disorders (total N=11). Because of small sample sizes and the variety of disorders included in the other non-affective disorder group, this latter subgroup was not examined in current analyses. Among participants who developed adult psychoses, complete cognitive testing data was available for 79 and 99 participants at ages 4 and 7, respectively, and complete behavioral data was available for 82 and 99 participants at age 4 and 7, respectively. Human subjects approval was granted by institutional review boards at Harvard University, Brown University, and local psychiatric facilities; written consent was obtained from all interviewed participants, and subjects were compensated for their participation.

2.3 Ascertainment and assessment of controls

Controls in primary analyses include all study subjects with data on IQ and behavior who were not identified as psychosis cases through the follow-up procedures described previously (Goldstein et al., 2010), and who received a brief screener for psychotic symptoms in adulthood. Screening questions for psychosis asked whether the participant had ever: (1) heard voices or seen visions others couldn't see or hear, or (2) believed someone was plotting against them, as well as follow-up questions that clarified whether hallucinations or delusions were due to alcohol or drugs, or common religious experiences. Only individuals who answered negatively to these questions were included as non-psychotic controls (N=1,492).

2.4 Demographics

Socioeconomic status (SES) in the CPP is an index based upon education-level of the head of household, occupation of head of household, and total family income (Myrianthopoulos and French, 1968). Other demographic variables measured prior to the child's birth included mother's education and ethnicity. Additionally, covariates were included for whether the subject was seen at age 8 month and 1 year follow-up appointments, as continued involvement in the study may be related to probability of being identified as a case.

2.5 Behavior measures at ages 4 and 7 years

Childhood behavior was assessed by clinicians during neurological and cognitive tests and a period of free play at study visits as described in Donatelli et al. (2010), who used the same behavior measures. At age 4 behaviors assessed included emotional reactivity, irritability,

dependency, duration of attention span, degree of cooperation, goal orientation, response to directions, level of activity, nature of activity, nature of communication, fearfulness and level of frustration tolerance. At age 7 behaviors included emotional reactivity, degree of dependency, duration of attention span, degree of cooperation, goal orientation, level of activity, nature of activity, nature of communication, reaction to separation from mother, fearfulness, rapport with examiner, self-confidence, level of frustration tolerance, assertiveness and hostility. Each behavior was rated on a Likert scale ranging from 1 to 5, with the midpoint reflecting adaptive functioning and poles reflecting qualitatively different behaviors (Bearden et al., 2000). For example, for emotional reactivity, one endpoint reflected “flat affect” and the other “unstable emotional response.” Therefore, to define problem behaviors we created two variables from each original item, each with a three-point scale (0=not true; 1=somewhat true; 2=very true); for example, from the original item of emotional reactivity we created two new variables: “flat affect” and “unstable emotional response.” An individual who was rated as “extremely flat” (score=1) on the original emotional reactivity item was scored as “very true” (score=2) on the new “flat affect” item and “none” (score=0) on the new “unstable emotional response” item. In our previous study focusing on children at genetic risk for psychosis, externalizing and internalizing behavior factors were derived from these same variables (Donatelli et al., 2010). In that paper, these items were entered into principal components analyses (PCA) (separately at age 4 and age 7) with varimax rotation. These analyses produced three scales at age 4, two externalizing behavior scales (hyperactive and oppositional behavior) and one internalizing behavior scale. At age 7, PCA yielded two scales, one externalizing and one internalizing. In the current study, the two age 4 externalizing scales were combined into one externalizing scale to compare the same types of behavior problems at the two ages (Donatelli et al., 2010). Items included on each scale are listed in Supplemental Table 1. Items within each scale were summed; due to the highly skewed distribution of these scales, each scale was dichotomized with individuals in the top 10% of the behavior scale (based on the distribution among the entire study population) considered to meet criteria for a ‘behavior problem.’ Individuals missing two or more of the original behavior items at age 4 or age 7 were excluded from analyses at that age point.

2.6 Neurocognitive measures at ages 4 and 7 years

At age 4, the assessment battery for general intellectual ability included the Stanford Binet Intelligence Scales (Terman and Merrill, 1960; Thorndike, 1973). At age 7, seven subtests from the Wechsler Intelligence Scale for Children (WISC, Wechsler, 1949) were used to derive an IQ estimate. The test-retest correlations of IQ from the Stanford-Binet ($r=0.83$) and WISC ($r=0.85$) in the CPP were high (Broman, 1984). The IQ data was previously presented (Seidman et al., 2013; Agnew et al., 2015).

2.7 Statistical analyses

Chi-square tests and t-tests were used to present comparisons of behavior and IQ in children who later were classified as non-psychotic controls, schizophrenia spectrum cases and affective psychoses cases on categorical and continuous predictors, respectively. To investigate our first hypothesis regarding childhood behavior problems and later schizophrenia and affective psychoses, we conducted logistic regression analyses to estimate

the odds of adult schizophrenia or affective psychosis associated with childhood externalizing or internalizing behavior problems relative to non-psychotic controls at ages 4 and 7 separately (Tables 2 and 3, models 1 and 2). We also conducted two interaction analyses to formally test whether the effect of behavior problems differed in predicting later psychosis by: (a) age at assessment, (age 4 versus age 7), or (b) type of later psychotic disorder (schizophrenia versus affective psychoses). To assess our second hypothesis regarding how IQ and behavior problems jointly contribute to risk for schizophrenia and affective psychoses, we conducted logistic regression analyses simultaneously including IQ and externalizing or internalizing problems (Tables 2 and 3, models 4 and 5). To further investigate this joint relationship, we examined the association of IQ with later psychoses separately among individuals with and without behavior problems at age 4 and 7. Finally, in exploratory analyses we examined the effect of persistent behavior problems by assessing risk for schizophrenia and affective psychoses among individuals who did not have behavior problems at either age 4 or 7, had behavior problems at one age only (either age 4 or age 7), or had behavior problems at both age 4 and 7. All regression models were adjusted for SES at birth, maternal race (white or non-white), years of maternal education, and gender, as well as intrafamilial correlation to address the presence of siblings in the cohort.

3 Results

Behavior problems at both ages 4 and 7 were more common among children with later schizophrenia and affective psychoses than controls. Both internalizing and externalizing problems were significantly elevated for these groups, with the exception of internalizing problems at age 4 for schizophrenia. As we have found previously (Seidman et al., 2013; Agnew-Blais et al., 2015), mean IQ was significantly lower among later schizophrenia cases than controls at ages 4 ($p < 0.001$) and 7 ($p = 0.002$); IQ scores for later affective psychoses cases were significantly lower than controls at age 7 only ($p = 0.02$) (Table 1).

3.1 Age 4 behavior problems and cognition and later psychoses.

Regarding our first hypothesis, in multivariable models, behavior problems at age 4 were associated with both later schizophrenia and later affective psychoses (Table 2). More specifically, in models examining later schizophrenia, externalizing problems were associated with elevated risk but internalizing problems were not, while when examining affective psychoses both externalizing and internalizing problems were associated with elevated risk.

With regards to our second hypothesis and risk of later schizophrenia, in models that jointly adjusted for age 4 externalizing problems and IQ, both remained significantly associated with later risk. When jointly adjusting for internalizing problems and IQ, internalizing problems remained unassociated, but higher IQ associated with lower risk for schizophrenia. When separately assessing groups with and without age 4 behavior problems, higher IQ remained associated with lower risk of schizophrenia both among individuals without ($OR = 0.75$, 95% CI 0.58, 0.97) and with ($OR = 0.76$, 95% CI 0.60, 0.98) behavior problems at age 4.

Examining our second hypothesis and affective psychoses, we found that when jointly adjusting for age 4 externalizing problems and IQ, neither was associated with increased risk; while when jointly adjusting for age 4 internalizing problems and IQ, internalizing problems remained associated with affective psychoses. When separately examining groups of individuals with and without behavior problems, IQ was not significantly associated with affective psychoses in either group.

3.2 Age 7 behavior problems and cognition and later psychoses.

Regarding our first hypothesis, externalizing and internalizing problems were associated with increased risk of both schizophrenia and affective psychoses (Table 3).

Examining our second hypothesis and schizophrenia risk, both types of behaviors problems remained associated with later schizophrenia while also adjusting for IQ. Among groups with and without behavior problems, higher IQ remained significantly associated with lower risk of schizophrenia only among individuals with age 7 behavior problems (OR=0.65, 95% CI 0.45, 0.94), but not among individuals without behavior problems (OR=0.90, 95% CI 0.72, 1.12).

Regarding affective psychoses, when examining IQ and behavior problems simultaneously only behavior problems remained significantly associated with risk of affective psychoses. Consistent with multivariable models, IQ was not significantly associated with affective psychoses when separately examining groups of individuals with and without behavior problems.

3.3 Behavior problems, age of testing and type of psychotic disorder.

There were no significant interactions between behavior problems and type of psychotic disorder, suggesting that the magnitude of the effect of behavior problems did not differ statistically when directly comparing their associations with later schizophrenia and affective psychoses. Similarly overall there was no significant interaction between behavior problems and age (age 4 versus age 7) and later schizophrenia or affective psychoses—only the interaction between age and internalizing problems in predicting schizophrenia was significant: the OR for age 4 internalizing problems was 0.76, while the OR for age 7 was 3.27. However this interaction should be interpreted with caution as there were only three individuals with internalizing problems at age 4 who developed schizophrenia. Additionally, we found that more persistent behavior problems (problems at both ages 4 and 7) were associated with excess risk of schizophrenia and affective psychoses compared to problems at one point only (Figure 1).

4 Discussion

Internalizing and externalizing behavior problems were associated with risk of schizophrenia and affective psychoses in this general population birth cohort. Cognition in childhood tended to be less impaired among individuals who later developed affective psychoses compared to schizophrenia. In this report, we show for the first time that both behavior problems and lower IQ remained significantly associated with schizophrenia when examined

simultaneously, while only behavior problems remained significantly associated with affective psychoses.

4.1 Specificity of behavior problems to schizophrenia or affective psychoses

While we initially hypothesized premorbid behavior problems would be more strongly related to schizophrenia, we found that the affective psychoses group also exhibited significant impairment in behavioral development as early as age 4, of a similar pattern and severity compared to those who later developed schizophrenia. The literature directly comparing premorbid behavior problems in schizophrenia and affective psychoses is sparse, but overall finds more behavior problems in later schizophrenia than affective psychoses: an investigation in the British National Child Development Study found individuals who later developed schizophrenia exhibited significantly more social maladjustment at ages 7 and 11 than individuals who later developed affective psychosis (Done et al., 1994). We found no significant interactions between behavior problems and type of psychotic disorder, suggesting behavior problems were not specific to later schizophrenia versus affective psychoses.

4.2 Age specificity of behavior problems

Disturbances in mood and affect are often apparent in the period directly prior to the onset of psychotic disorder (Addington et al., 2015). Here we find evidence for elevated behavior problems much earlier than the prodromal stage of psychotic illness. A study in the Philadelphia cohort of the CPP found premorbid behavior problems at age 7, but not age 4, were associated with schizophrenia (Bearden et al., 2000); however the absence of an age 4 effect could be due the combining of internalizing and externalizing problems, which may obscure an externalizing-specific association. Findings of premorbid behavior problems at such young ages suggest that it is not the onset of nascent psychotic symptoms in the later prodromal phase that is driving problems with behavior (see also Woodberry, et al. in press). Indeed, we did not find a significant interaction effect for age of behavior problem and later psychosis, suggesting the magnitude of the effect of behavior problems on later risk did not differ by whether the behavior problem occurred at age 4 or age 7.

We also found that behavior problems present at both age 4 and age 7, compared to one age only, were associated with a higher risk of schizophrenia and affective psychosis (Figure 1), suggesting that more persistent behavior problems were markers of an even greater risk of later psychotic disorder. However, these findings were exploratory and based on a small number of individuals with behavior problems at both ages so require future replication.

4.3 Joint effects of IQ and behavior problems

When jointly including IQ and behavior problems in regression models, both lower IQ and behavior problems remained significantly predictive of later schizophrenia, while only behavior problems remained associated with later affective psychoses. When restricting analyses to individuals free of or with behavior problems, at age 4 lower IQ was associated with later risk of schizophrenia among both those with and without a behavior problem while at age 7, the effect of lower IQ on later risk was found only among individuals with a behavior problem. This could suggest that as individuals who will later develop

schizophrenia progress through childhood, problems with behavior and cognition begin to converge in their contribution to later psychosis risk. IQ remained unassociated with later affective psychoses when separately examining groups with and without behavior problems, suggesting that the presence or absence of behavior problems did not change the effect of IQ on risk of later affective psychoses.

4.4 Specificity of externalizing and internalizing problems

Examining externalizing and internalizing problems separately, we found that both were related to elevated risk of schizophrenia and affective psychoses (although only externalizing problems at age 4 were associated with schizophrenia). However, overall we do not find a specific association between type of behavior problem and schizophrenia versus affective psychoses. This finding is consistent with a study by Kim-Cohen et al. that found that both schizophreniform disorder and mania were preceded by juvenile disorders characterized as externalizing, such as oppositional defiant disorder, as well internalizing, such as depression (Kim-Cohen et al., 2003).

4.5 Limitations

The main limitation is the scope and type of behavioral assessments, which included only childhood behavior assessed during research study visits, rather than in more naturalistic settings such as in the home or at school. Additionally, as we had a more limited sample size of participants with behavioral assessments at both ages 4 and 7, we could not perform a more in-depth investigation of the intraindividual trajectory of behavior problems across development. Finally, this subcohort of the NEFS birth cohort was not assessed for non-psychotic affective disorders; therefore we cannot investigate how IQ and behavior problems in childhood compare between those who later develop psychotic versus non-psychotic affective disorders in adulthood.

4.6 Conclusions and implications

Our findings suggest that childhood behavior problems are a general indicator of future risk for adult psychosis. This finding is especially relevant in light of recent interest in the ways in which schizophrenia and affective psychoses may represent overlapping disorders, given their shared genetic background and similarities in clinical presentation. We find that, just as disturbances in mood and affect are core features of both schizophrenia and affective psychoses, childhood behavior problems elevate risk for both disorders.

Behavior problems could represent precursor symptoms of adult psychotic disorder, as well as place individuals at higher risk for negative life events or exposures that could increase risk of adult disorder (Amminger et al., 1999). Future research could clarify the mechanisms that link childhood behavior problems and adult psychotic disorder. Moreover, more refined measures of cognition and behavior, in combination with other predictors, may improve our capacity to identify those at high risk for later disorder and provide opportunities for early intervention. While one aim of intervention may eventually be to attempt the ambitious goal of preventing later psychosis (Sommer et al., 2016), childhood interventions can also be reasonably designed to improve the functional capacity of children with clear behavioral or

cognitive impairments (Seidman and Nordentoft, 2015), such as family-oriented cognitive behavioral interventions for those with behavior problems (Uher et al., 2014).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

J Agnew-Blais was supported during work on this manuscript by NIMH T32MH017119. Larry J. Seidman is supported by the Commonwealth of Massachusetts (SCDMH82101008006) and NIMH R21 MH091461. The funders played no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

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Figure 1.

Behavior problems at one age (either age 4 or 7) or both ages 4 and 7 and odds of schizophrenia and affective psychosis

$p < 0.05$; ** $p < 0.01$, *** $p < 0.001$

Adjusted models include childhood SES, sex, maternal education, maternal race, and whether seen at 8 month and 1 year exams and gender. Schizophrenia psychoses include schizophrenia and schizoaffective disorder depressed-type; affective psychoses include schizoaffective bipolar-type, bipolar disorder with psychotic features, and major depressive disorder with psychosis.

TABLE 1

Demographic characteristics, behavior problems and IQ at ages 4 and 7 among non-psychotic controls, adult schizophrenia psychoses cases, and adult affective psychoses cases

	Non-psychotic controls	Schizophrenia psychoses	Affective psychoses
Demographics	N=1492	N=47	N=45
Male, N (%)	628 (42.0)	36 (76.6) ***	20 (44.4)
Non-white maternal race, N (%)	190 (12.7)	11 (23.4) *	8 (17.8)
SES at birth, Mean (SD)	5.0 (1.9)	5.3 (2.1)	5.8 (1.8)
Mother's education, Mean (SD)	11.2 (2.3)	10.55 (2.1)	10.8 (2.1)
Cognition	N=1341/1469 [§]	N=39/45 [§]	N=40/44 [§]
IQ age 4, Mean (SD)	107.0 (15.3)	95.7 (15.4) ***	102.9 (15.5)
IQ age 7, Mean (SD)	103.1 (12.8)	95.8 (15.3) ***	98.5 (13.3) *
Behavioral problems			
<i>Age 4</i>	N=1347	N=40	N=42
Any behavioral problems, N (%)	183 (13.6)	12 (30.0) **	14 (33.3) ***
Externalizing problems, N (%)	83 (6.2)	10 (25.0) ***	6 (14.3) *
Internalizing problems, N (%)	110 (8.2)	3 (7.5)	9 (21.4) **
<i>Age 7</i>	N=1465	N=45	N=44
Any behavioral problem, N (%)	205 (14.0)	16 (35.6) ***	16 (36.4) ***
Externalizing, N (%)	106 (7.3)	10 (22.2) ***	10 (22.7) ***
Internalizing, N (%)	112 (7.7)	9 (20.0) **	9 (20.5) **
<i>Ages 4 and 7</i>	N=1314	N=38	N=42
Never behavior problem, N (%)	984 (74.9)	20 (52.6) **	19 (46.3) ***
Any behavior problem at one age, N (%)	307 (23.4)	14 (36.8)	16 (39.0) *
Any behavior problem at both ages, N (%)	30 (2.3)	4 (10.5) **	7 (17.1) ***

* p<0.05

** p<0.01

*** p<0.001; statistical comparisons are with the non-psychotic control group.

[§] Denotes the number of study participants with available data at age 4 and at age 7, respectively

Table 2.

Age 4 externalizing and internalizing behavior problems, IQ and odds of schizophrenia psychoses and affective psychoses in multivariable-adjusted logistic regression models

	Model 1 Externalizing problems	Model 2 Internalizing problems	Model 3 IQ	Model 4 Externalizing problems and IQ	Model 5 Internalizing problems and IQ
OR (95% CI)					
Schizophrenia psychoses					
Age 4 externalizing problems	4.54 *** (2.08, 9.90)			2.69 * (1.12, 6.48)	
Age 4 internalizing problems		0.76 (0.22, 2.63)			0.42 (0.09, 1.95)
Age 4 IQ θ			0.73 *** (0.61, 0.88)	0.78 *** (0.65, 0.94)	0.72 *** (0.60, 0.87)
Affective psychoses					
Age 4 externalizing problems	2.56 * (1.05, 6.23)			1.37 (0.47, 3.95)	
Age 4 internalizing problems		2.92 ** (1.31, 6.52)			2.52 * (1.07, 5.951)
Age 4 IQ θ			0.86 (0.71, 1.04)	0.87 (0.72, 1.05)	0.88 (0.73, 1.06)

*
p<0.05

**
p<0.01

p<0.001

Regression models also include childhood SES, sex, maternal education, maternal race, and whether seen at 8 months and 1 year exams and gender. Schizophrenia psychoses include schizophrenia and schizoaffective disorder depressed-type; affective psychoses include schizoaffective bipolar-type, bipolar disorder with psychotic features, and major depressive disorder with psychosis.

θ ORs for FSIQ scaled to a half standard deviation (7.5 IQ points)

Table 3.

Age 7 externalizing and internalizing behavior problems, IQ and odds of schizophrenia psychoses and affective psychoses in multivariable-adjusted logistic regression models

	Model 1 Externalizing problems	Model 2 Internalizing problems	Model 3 IQ	Model 4 Externalizing problems and IQ	Model 5 Internalizing problems and IQ
OR (95% CI)					
Schizophrenia psychoses					
Age 7 externalizing problems	3.01 ** (1.38, 6.57)			2.55 * (1.21, 5.38)	
Age 7 internalizing problems		3.27 ** (1.47, 7.28)			2.63 * (1.17, 5.931)
Age 7 IQ ^θ			0.75 ** (0.61, 0.92)	0.78 * (0.64, 0.95)	0.78 * (0.63, 0.96)
Affective psychoses					
Age 7 externalizing problems	3.80 *** (1.80, 8.03)			3.43 ** (1.62, 7.28)	
Age 7 internalizing problems		3.24 ** (1.49, 7.04)			2.71 ** (1.29, 5.69)
Age 7 IQ ^θ			0.79 * (0.63, 1.00)	0.82 (0.66, 1.03)	0.83 (0.67, 1.04)

* p<0.05

** p<0.01

*** p<0.001

Regression models also include childhood SES, sex, maternal education, maternal race, and whether seen at 8 months and 1 year exams and gender. Schizophrenia psychoses include schizophrenia and schizoaffective disorder depressed-type; affective psychoses include schizoaffective bipolar-type, bipolar disorder with psychotic features, and major depressive disorder with psychosis.

^θ ORs for FSIQ scaled to a half standard deviation (7.5 IQ points)