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Childhood psychopathology and development of adult schizotypal symptoms

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Chapter 4



School-associated problem behavior in childhood and adolescence and development of adult schizotypal symptoms: a follow-up of a clinical cohort

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Abstract

How school-associated behavioral problems in childhood and adolescence precede distinctive adult schizotypal symptoms was examined. Gender specific findings were explored. 159 patients of the Department of Child and Adolescent Psychiatry of the University Medical Centre Utrecht, the Netherlands, were reassessed after 11.6 ($SD=3.1$) years for adult schizotypal symptoms. Severity of behavioral symptoms in childhood and adolescence using Teacher Report Form (TRF; Verhulst et al., 1997) and adult schizotypal symptoms using Schizotypal Personality Questionnaire-Revised (Raine, 1991) were examined by Spearman's bivariate correlations. Multiple regression analyses were performed to determine the combined predictive value of significant TRF subscales for schizotypal symptomatology. Moderation was tested by adding the interactions of gender with TRF subscales to the models. Disregarding gender, correlational analyses revealed that TRF total problems, in specific thought problems, social problems, and attentional problems were associated with disorganized schizotypal symptoms in adult life. TRF thought problems was also associated with future positive schizotypal symptoms. When gender was taken into account, for boys only thought problems was associated with adult positive schizotypal symptoms, whereas for girls externalizing problems, specifically attentional and aggressive problems, were associated with the higher levels of adult disorganized schizotypal symptoms. Moderated regression analyses provided

trend significant evidence confirming that in girls externalizing problems were positively associated with general and disorganized schizotypal symptoms. When using teachers as informants, it was found that juvenile behavioral abnormalities were differentially associated with type of adult schizotypal symptoms, with these associations being further modified by gender.

Introduction

Schizophrenia spectrum pathology is considered a persistent and lifelong condition with varying expression across the lifespan. Consequently, childhood behavioral indicators that are associated with the development of psychopathology at the extreme end of the schizophrenia spectrum, i.e., schizophrenia and psychosis, have been intensively studied throughout the years. As a result, literature provides evidence for a wide range of childhood behaviors being associated with the risk for future development of schizophrenia. However, the majority of subjects at risk based on childhood behaviors do not meet the criteria for a schizophrenia spectrum disorder in adulthood, but tend to manifest subclinical schizophrenia-like abnormalities (Chapman, Chapman, Kwapil, Eckblad, & Zinser, 1994; Raine, 1991; Tsuang, Stone, Tarbox, & Faraone, 2002), i.e., schizotypal symptoms. Although these schizotypal symptoms are a milder manifestation on the continuum of schizophrenia spectrum pathology, these symptoms may have a very profound effect on a subject's quality of life, as, apart from the risk of development of schizophrenia (Vollema, Sitskoorn, Appels, & Kahn, 2002), severe functional impairments across a broad range of domains can be found, such as academic, social, and occupational dysfunctioning (Chapman et al., 1994; Gooding, Tallent, & Matts, 2005; Kwapil, 1998). The investigation of childhood behavior and its association with adult schizotypal symptoms therefore constitutes a valid and noteworthy, yet relatively understudied, area of exploration with strong implications for clinical practice and research.

Longitudinal studies so far have resulted in the identification of a very broad spectrum of childhood behaviors that are associated with the development of schizophrenia spectrum disorders. Retrospective studies for example, found social impairments to be especially present in subjects who later developed disorders within the schizophrenia spectrum (Foerster, Lawis, Owen, & Murray, 1991; Rossi, Pollice, Dane-luzzo, Marinangeli, & Stratta 2000; Watt & Lubensky, 1976; Zigler, Levine, & Zigler, 1977). Genetic high-risk (HR) studies reported that high risk babies already showed lower communicative competence (Goodman, 1987) and appeared to be more quiet (Fish, 1987). HR

adolescents showed more anxious and hostile behavior (Goodman, 1987), more disruptive behavior, and aggression at school (Mednick & Schulsinger, 1968; Weintraub, Prinz, & Neale, 1978), poor peer relations (Ayalon & Merom, 1985), poor affective control (Fish, 1987; Nagler & Glueck, 1985), more situational anxiety, more nervous tension and more depression (Cunningham, Miller, Lawrie, & Johnstone, 2005), compared to children and adolescents without genetic risk for schizophrenia spectrum pathology. In addition, birth cohort studies have found evidence for developmental precursors of schizophrenia spectrum disorders in four behavioral domains: delay in neuromotor development (Fish, Marcus, Hans, Auerbach, & Perdue, 1992; Jones, Rodgers, Murray, & Marmot, 1994; Crow, Done, & Sacker, 1995; Cannon et al., 1999; Walker, Lewis, Loewy, & Palyo, 1999; Rosso et al., 2000), delays in aspects of language development (DeLisi et al., 1991; Jones et al., 1994; Bearden et al., 2000), problems in the area of social functioning (Crow et al., 1995; Malmberg, Lewis, David, & Allebeck, 1998; Davidson et al., 1999; Bearden et al., 2000), and high levels of aggressive behavior (Miller et al., 2002).

So far, to our knowledge, only two longitudinal studies have studied adult outcome of childhood behavioral indicators for schizophrenia spectrum pathology using comparison groups of patients diagnosed with affective disorders (Dworkin, Lewis, Cornblatt, & Erlenmeyer-Kimling, 1994), and anorexia (Muratori, Salvadori, D'Arcangelo, Viglione, & Picchi, 2005), respectively. This approach led to the affirmation of the finding that social problems precede schizophrenia spectrum disorders in adulthood (Dworkin et al., 1994; Muratori et al., 2005), and to the identification of specific childhood problems in more restricted behavioral domains: the regulation of thought (Muratori et al., 2005), and regulation of attention (Muratori et al., 2005).

In addition, behavioral problems in childhood and adolescence of future patients with schizophrenia spectrum pathology have been found to differ between boys and girls. For example, studies have reported that boys exhibit more aggression (Welham et al., 2009), social problems (Salokangas, 1983; Welham et al., 2009), and thought problems (Welham et al., 2009), whereas girls prior to their schizophrenia diagnosis were more likely to be rated as withdrawn, unforthcoming, and depressed (Done, Crow, Johnstone, & Sacker, 1994). Hence, it is possible that the gender of the child may moderate associations between behavioral problems and adult schizotypal symptomatology; however, additional research is needed to fill this gap in the literature.

All of the cited studies have used intra-familial sources, i.e., in majority parent report. Studies using an extra-familial source, i.e., teacher's reports, in assessing behavioral problems in children are scarce. Although parents form an important source (Van der Valk, Van den Oord, Verhulst, & Boomsma, 2001; Arseneault et al., 2003; Bartels et al., 2003),

situational variation in children's behaviors at home and at school makes teachers an important source of information (Polderman, Posthuma, De Sonneville, Verhulst, & Boomsma, 2006). For example, teachers may have a unique view on problems that are specific to the classroom or other school situations, such as problems in the social interactions with other children, or task-oriented situations (Polderman et al., 2006). Teachers also have an advantage over parents in their wide exposure to children of the same age, which makes them able to compare the child's behavior with that of many same-aged peers (Verhulst et al., 1997). Thus far, only one study has used data from teachers to examine how juvenile school-associated problem behavior is associated with the development of adult schizophrenia spectrum pathology (Olin et al., 1997). They found that children who later developed schizotypal personality disorder were hypersensitive to criticism in comparison with HR children who were not mentally ill in adulthood.

The present study is a follow-up study of a clinical cohort and investigates the development of adult schizotypal symptoms in relation to school-associated behavioral problems in childhood and adolescence. In line with the results of other studies (Amminger et al., 1999; Miller et al., 2002; Johnstone, Ebmeier, Miller, Owens, & Lawrie, 2005; Muratori et al., 2005; Scott et al., 2009), it is hypothesized that severity of school-associated behavioral problems is associated with higher levels of adult schizotypal symptoms. The cited comparative studies further suggest that childhood problems in the social domain (Dworkin et al., 1994; Muratori et al., 2005), in both regulation of thought (Muratori et al., 2005), and in attention regulation (Muratori et al., 2005) are particularly associated with adult schizotypal symptoms. Therefore, it is hypothesized that severity of school-associated behavioral problems in these behavioral domains in childhood and adolescence is associated with higher levels of adult schizotypal symptoms. Using a three-factor model of schizotypal symptoms, discriminating between positive, negative, and disorganized symptoms (Vollema & Hoijtink, 2000), it is further explored how different domains of school-associated behavioral problems are related to the three schizotypal symptom domains. Finally, as symptoms of future schizophrenia spectrum pathology are highly variable in their clinical presentation between boys and girls (Done et al., 1994; Salem & Kring, 1998; Welham et al., 2009), this study examined whether the association between juvenile school-associated behavioral problems and adult schizotypal symptoms was moderated by gender.

Methods

Sample and procedure

This study is part of a longitudinally prospective study designed to evaluate both global and clinical outcomes in adulthood of children and adolescents with psychopathology, referred during 1984 to 2004 (T1), to the Department of Child and Adolescent Psychiatry at the University Medical Centre of Utrecht (UMCU), the Netherlands. Children and adolescents meeting the following criteria were approached for participation in this follow-up study during 2006 to 2010 (T2): (1) aged 18 years or younger at T1, (2) aged 18 years or older at T2, (3) no axis I DSM diagnosis before or at T1 of child psychotic disorder (schizophrenia or any other psychotic disorder), bipolar disorder or dissociative disorder, (4) no DSM diagnosis of mental retardation ($IQ < 70$) at T1, (5) presence of a Teacher Report Form (TRF; Verhulst et al., 1997) at T1. In total, 451 patients were eligible for follow-up. They were sent a letter informing them about the aims of the study and checking their willingness to participate in the study. The patients who did not respond were contacted by phone when they could be traced in the public phone registry to explain the aim of the study and to encourage participation. A total of 292 patients declined participation, resulting in a final sample of 159 (75 male and 84 female) adult patients. These patients were distributed across six broad DSM diagnostic categories at T1, i.e., Affective disorders (20.1%), Attention-deficit and disruptive behavior disorders (16.4%), Pervasive Developmental Disorders (16.4%), Eating disorders (18.2%), No diagnosis (3.1%), and a category consisting of low prevalence disorders such as Communication disorders, Tic-disorders, Other disorders of infancy, childhood and adolescence and Deferred diagnoses (25.8%). Using standardized scores of Wechsler Intelligence Scales at time of juvenile assessment (T1); i.e., WPPSI (Wechsler, 1967), WISC (Wechsler, 1949), WISC-R (Wechsler, 1974), WISC-III (Wechsler, 1991), WAIS (Wechsler, 1955) or WAIS-R (Wechsler, 1981), the intelligence level of the group was within the normal range with a total IQ of 104.2 ($SD=15.6$), a performance IQ of 103.5 ($SD=15.8$), and a verbal IQ of 103.8 ($SD=15.4$). Subjects were reassessed after a mean period of 11.6 years ($SD=3.1$), at a mean age of 24.4 years ($SD=4.1$) at T2. All subjects voluntarily agreed to participate in this study and signed an informed consent form. The ethical principles of the Helsinki Declaration (Schuklenk, 2001) were followed and approval was obtained from the Medical Ethical Committee of the University Medical Centre of Utrecht (number 05-319/K).

Representativeness

To check whether the participants assessed at this follow-up were representative of the subjects eligible for follow-up, age and gender distributions as well as the distribution of TRF scores were compared between participants and nonparticipants. Chi-square analyses revealed that proportionally more participants appeared to be female (52.8% female participants versus 30.5% female nonparticipants), ($F(1,451)=21.750, p<.001$). Differences between participants and nonparticipants on other background variables were evaluated by univariate analyses of variances (ANOVA). This revealed that participants were somewhat older at T1 ($M=12.3; SD=3.5$ vs. $M=11.2; SD=3.3$), ($F(1,436)=11.307, p<.001, \eta_p^2=.025$) and at T2 ($M=24.4; SD=4.1$ vs. $M=22.2; SD=3.5$), ($F(1,449)=34.419, p<.001, \eta_p^2=.071$). Participants had a higher Total IQ score at T1 ($M=104.2; SD=15.6$ versus $M=99.6; SD=13.6$), ($F(1,231)=5.507, p=.020, \eta_p^2=.023$) and a higher Performance IQ ($M=103.5; SD=15.8$ versus $M=99.4; SD=14.2$), ($F(1,227)=4.080, p=.045, \eta_p^2=.018$). No difference was found on Verbal IQ ($M=103.8; SD=15.4$ versus $M=100.3; SD=14.7$), ($p=.096$). Differences were found on two TRF subscales; those lost to follow-up had a higher score on rule breaking behavior ($M=57.2; SD=8.2$ versus $M=59.7; SD=8.8$), ($F(1,364)=7.058, p=.008, \eta_p^2=.019$), and aggressive behavior ($M=59.1; SD=9.5$ versus $M=62.2; SD=10.9$), ($F(1,364)=11.538, p<.001, \eta_p^2=.031$).

School-associated behavioral problems in childhood and adolescence

School-associated behavioral symptoms at time of referral were evaluated using the Dutch translation of the Teacher Report Form (TRF) at T1 for which good reliability and validity have been obtained (Verhulst et al., 1997). The TRF is an extensively used questionnaire to assess a broad range of emotional and behavioral problems in children and adolescents from the age of five to eighteen years. The TRF consists of 120 items that are scored on a three point scale ranging from zero (not true) to two (very true) by teachers who have known a pupil in a school setting for at least two months. The TRF provides standardized composite T-scaled scores for behavioral problems on eight specific problem scales, i.e., withdrawn behavior, anxious and depressed behavior, somatic complaints, social problems, aggressive behavior, rule breaking behavior, attention

problems, and thought problems. The first three problem scales are summed to compute the internalizing problems score, and the aggressive and rule-breaking behavior scores are summed to obtain the externalizing problems score. Total behavior problems include scales for social, thought, and attention problems that are neither internalizing nor externalizing problems. Higher scores are indicative for higher levels of problems.

Adult schizotypal symptoms

Adult schizotypal symptoms were assessed using the Schizotypal Personality Questionnaire-Revised (SPQ-R; Vollema & Hoijtink, 2000; Raine, 1991). The SPQ-R is a self-report measure of schizotypal symptoms, modeled on the Diagnostic and Statistical Manual of Mental Disorders (APA, 1987) criteria for schizotypal personality disorder (Raine, 1991). In the study of Raine (1991) a chi-square analysis indicated a significant association between 'group membership' based on scores on the SPQ (high/low) and clinical diagnosis (yes/no) of schizotypal personality disorder ($\chi^2=7.3, p=.007$). The point-biserial correlation between diagnosis of schizotypal personality disorders and SPQ scores was also significant ($r=.60, p=0.001$; Raine, 1991). These analyses demonstrate that high scores on the SPQ are indicative of a diagnosis of schizotypal personality disorder. Factor analytical studies have revealed three schizotypal dimensions, i.e., positive, negative, and disorganized symptoms (Raine et al, 1994; Vollema & Hoijtink, 2000). This factor structure has been found to be invariant to gender, ethnicity, religion, and social background (Reynolds, Raine, Mellingen, Venables, & Mednick, 2000), and it parallels the factor structure obtained in schizophrenia patients (Raine, 2006). Vollema, Sitskoorn, Appels, and Kahn, (2002) suggested that the SPQ may be regarded as an indicator of the (genetic) vulnerability for schizophrenia, because it is sensitive to gradient levels of schizophrenia, proportional to the risk for schizophrenia associated with the degree of kinship with family members diagnosed with schizophrenia. The SPQ has high internal reliability (0.91), test-retest reliability (0.82), convergent validity (0.59 to 0.81), discriminant validity (0.63), and criterion validity, 0.68) (Raine, 1991). Higher scores on the SPQ-R indicate higher levels of schizotypal symptoms.

Statistical analysis

To control for possible confounding effects, the association of three background varia-

bles, i.e., IQ at T1, age at T1 and age at T2, with SPQ total and factor scores was explored. None of these variables appeared to be significantly associated with SPQ total or factor scores ($.077 < p < .901$). In addition, possible differences between boys and girls on age at T1 and T2, SPQ total and factor scores, and TRF total, internalizing, externalizing, and eight subscales scores were analyzed using MANOVA. Partial eta squared (η_p^2) was used to estimate effect sizes, with $\eta_p^2 \sim 0.03$ representing a weak effect, $\eta_p^2 \sim 0.06$ representing a moderate effect and $\eta_p^2 \geq 0.14$ significantly a large effect (Cohen, 1992). Because the SPQ total and factor scores were all positively skewed, the strength of the relation with TRF subscales, internalizing, externalizing and total scores were examined by computing bivariate Spearman's correlation analysis (small effect size: $r_s = 0.1-0.23$; medium: $r_s = 0.24-0.36$; large: $r_s \geq 0.37$; Cohen, 1992). To explore gender specific characteristics, these analyses were replicated for boys and girls separately. The TRF subscales, internalizing, externalizing or total scores that showed significant correlations were entered in multiple regression analyses using the Enter method, to determine their combined predictive value for the development of adult schizotypal symptoms in general and each of its three factor scores. To test whether gender modified the associations between the TRF (subscales internalizing, externalizing and total score) and the SPQ (factors and total score), moderated multiple regression analyses were performed by adding the interaction term(s) (gender * TRF total/TRF factor/TRF subscale scores) to the model. To construct robust models for testing interactions and reducing multicollinearity all continuous predictor variables were centered (Cronbach, 1987). In order to adjust the type 1 error, i.e. alpha, for multiple testing, alpha was set to .005, two-tailed, for all analyses. Statistical analyses were performed using the Statistical Package for the Social Sciences 18.0 (SPSS Inc, Chicago, IL, USA).

Results

Sample characteristics of the total study sample and gender specific subgroups

Table 1 shows means and *SDs* for the age at T1 and T2 and behavioral data for the total study sample as well as gender specific subgroups. The MANOVA of gender with age at T1, age at T2, TRF scores and SPQ scores revealed a significant medium effect of Group, ($F(16,142)=4.206, p < .001, \eta_p^2 = .322$) on age at T1, T2, and TRF attention, aggressive, and externalizing problem scores. This effect was due to boys being younger than

Table 1. Age at T1 and T2, and behavioral variables at T2 of the total study sample and gender specific subgroups.

		Total sample (n=159)	Male sample (n=75)	Female sample (n=84)
		<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>
Age	at T1	12.5 (3.6)	10.8 (3.4)	13.9 (3.2)
	at T2	24.4 (4.1)	23.4 (3.8)	25.3 (4.3)
SPQ^a	Total score	26.9 (19.3)	25.4 (18.2)	28.3 (20.2)
	Positive factor	8.8 (7.1)	8.2 (6.3)	9.4 (7.7)
	Negative factor	12.8 (10.0)	11.9 (9.6)	13.6 (10.4)
	Disorganized factor	5.3 (4.6)	5.3 (4.9)	5.4 (4.4)
TRF^b	Total problems	61.3 (10.0)	63.1 (9.5)	59.8 (10.2)
	Internalizing problems	61.1 (10.5)	59.8 (9.3)	62.3 (11.4)
	Externalizing problems	57.2 (10.7)	59.6 (11.4)	55.1 (9.5)
	Withdrawn behavior	61.5 (10.4)	61.3 (10.6)	61.7 (10.2)
	Anxious/depressed behavior	60.9 (9.7)	59.0 (8.4)	62.6 (10.4)
	Social problems	61.6 (9.3)	62.7 (9.5)	60.6 (9.0)
	Attentional problems	59.7 (9.2)	62.6 (9.4)	57.2 (8.1)
	Thought problems	63.2 (11.6)	64.3 (11.9)	62.3 (11.4)
	Somatic complaints	56.0 (8.5)	55.2 (8.1)	56.7 (8.9)
	Aggressive behavior	59.1 (9.5)	61.8 (10.7)	56.8 (7.6)
	Rule breaking behavior	57.2 (8.2)	58.6 (7.8)	55.8 (8.3)

^aSPQ= Schizotypal Personality Questionnaire; ^bTRF= Teacher Report Form.

Table 2. Spearman's rank order correlations between TRF Total, broad band and subscale scores (left column) and SPQ Total and factor scores (rows) for the total study sample and gender specific groups.

	Total schizotypal symptoms			Positive schizotypal symptoms		
	Total <i>n</i> =159	Males <i>n</i> =75	Females <i>n</i> =84	Total <i>n</i> =159	Males <i>n</i> =75	Females <i>n</i> =84
Internalizing problems	.159	.197	.098	.146	.186	.090
Externalizing problems	.139	.006	.309*	.168	.098	.267
Withdrawn behavior	.102	.180	.034	.047	.123	-.006
Somatic complaints	.115	.006	.203	.164	.089	.213
Anxious and depressive behavior	.130	.158	.081	.131	.159	.084
Social problems	.183	.249	.131	.170	.234	.120
Thought problems	.242*	.303	.178	.230*	.332*	.132
Attention problems	.133	.042	.249	.093	.014	.184
Rule breaking behavior	.187	.126	.261	.217	.207	.239
Aggressive behavior	.117	-.012	.300	.147	.078	.262
Total problems	.190	.151	.260	.186	.197	.207

* significant at $p \leq .005$.

	Negative schizotypal symptoms			Disorganized schizotypal symptoms		
	Total n=159	Males n=75	Females n=84	Total n=159	Males n=75	Females n=84
	.117	.215	-.001	.226*	.230	.220
	.045	-.062	.211	.223*	.075	.411*
	.097	.224	-.017	.169	.193	.145
	.092	.013	.157	.067	-.081	.203
	.073	.151	-.023	.211	.233	.201
	.125	.233	.030	.272*	.282	.257
	.181	.279	.091	.291*	.296	.280
	.076	.026	.179	.244*	.129	.372*
	.102	.077	.162	.218	.148	.298
	.030	-.078	.209	.200	.054	.402*
	.112	.126	.155	.290*	.204	.393*

Figure 1. Moderation effect of gender with TRF externalizing problems for SPQ total en disorganized symptoms

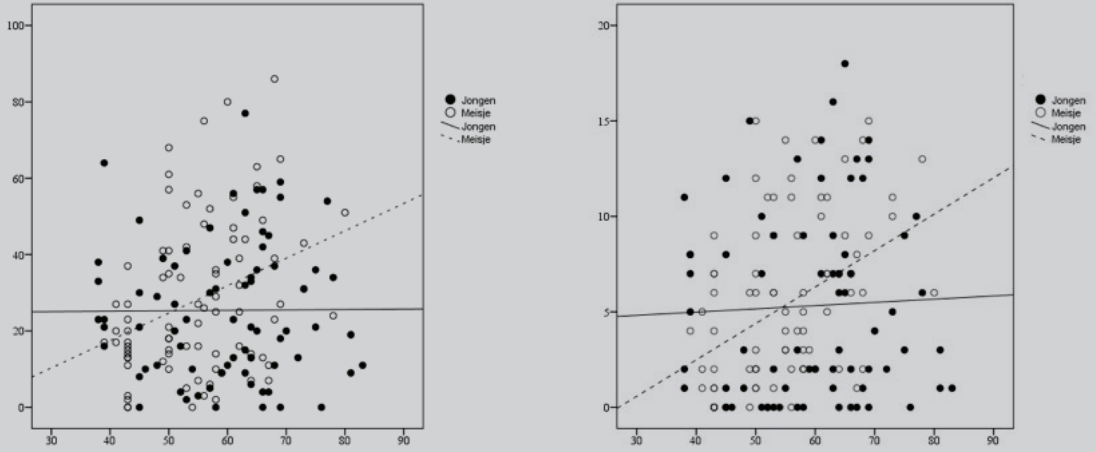


Table 3 Regression analyses for testing the moderation models (n=159)

Criterion variable	Predictor variable	F	R ²	β	p
SPQ total score	TRF externalizing problems	3.984	.072	.006	.953
	Gender			.117	.143
	TRF externalizing problems * gender			.256	.015*
SPQ positive factor	TRF thought problems	4.070	.073	.295	.008**
	Gender			-.057	.607
	TRF thought problems * gender			.106	.174
SPQ disorganized factor	TRF attention problems	2.683	.081	-.092	.459
	TRF aggressive problems			-.037	.741
	Gender			.078	.342
	TRF attention problems * gender			.106	.449
	TRF aggressive problems * gender			.163	.219
	TRF externalizing problems	4.622	.082	.039	.710
	Gender			.053	.501
	TRF externalizing problems * gender			.263	.012*
	TRF total problems	5.080	.090	.214	.070
	Gender			.051	.514
TRF total problems * gender			.107	.358	

* p<.05, **p<.01

girls at T1 ($F(1,158)=34.027, p<.001, \eta_p^2=.178$), and T2 ($F(1,158)=9.113, p=.003, \eta_p^2=.055$). In addition, boys had higher scores in comparison with girls on TRF attention problems ($F(1,158)=15.041, p<.001, \eta_p^2=.087$), and TRF aggressive behavior ($F(1,158)=11.836, p=.001, \eta_p^2=.070$). The difference in TRF externalizing problems between boys and girls did not reach significance ($p=.007$).

School-associated behavior problems during childhood and adolescence and adult schizotypal symptoms

TRF total problems ($r_s=.290, p<.001$), internalizing problems ($r_s=.226, p=.004$), externalizing problems ($r_s=.223, p=.005$), thought problems ($r_s=.291, p<.001$), social problems ($r_s=.272, p<.001$), and attention problems ($r_s=.244, p=.002$) correlated significantly with severity of adult disorganized schizotypal symptoms. Also significant correlations were found for TRF thought problems with adult schizotypal symptoms in general ($r_s=.242, p=.002$) and positive schizotypal symptoms ($r_s=.230, p=.004$) with adult disorganized schizotypal symptomatology. None of the TRF scales were correlated with negative schizotypal symptoms in adulthood ($.023<p<.709$). (See Table 2).

Within the total group, the multiple regression analysis (Enter method) of the constituting TRF subscales, i.e. social problems, thought problems, and attention problems produced a significant model ($R^2=.094, F(3,155)=5.349, p=.002$), but none of the three TRF subscales were significant as predictors ($.113<p<.296$).

Gender specific associations between school-associated behavior problems during childhood and adolescence and adult schizotypal symptoms

Testing for an interaction between gender and juvenile school-associated behavioral problems was done to examine the possible moderating effects of gender on development of schizotypal symptoms in adulthood. First, correlational analyses were conducted. Spearman's bivariate correlations for boys and girls separately showed different patterns. With regard to boys, only TRF thought problems was significantly associated with positive schizotypal symptoms ($r_s=.332, p=.004$). None of the TRF scales were significantly associated with severity of adult negative ($.015<p<.91$) or disorganized schizotypal symptoms ($.01<p<.644$). (See Table 2). With regard to girls, TRF total problems was significantly associated with adult disorganized schizotypal symptoms ($r_s=.393, p<.001$),

which was specifically due to externalizing problems ($r_s = .411, p < .001$), and on subscale level to attention problems ($r_s = .372, p < .001$), and aggressive behavior ($r_s = .402, p < .001$). A significant correlation was found for TRF externalizing problems ($r_s = .309, p = .004$) with severity of total schizotypal symptoms. None of the TRF scales were associated with positive or negative schizotypal symptoms in adulthood ($.014 < p < .956$). (See Table 2).

The moderated regression analyses revealed a trend significant interaction between TRF externalizing problems and gender for the SPQ total and disorganized scores (See Table 3), such that the positive association of externalizing problems with general and disorganized schizotypal symptoms were evident for girls, but not for boys (See Figure 1). Thought problems was the only school-associated behavioral problem that was significantly related to the SPQ positive factor and was therefore selected for inclusion in regression analysis. The moderation model was found to approach significance, ($F(3,155) = 4.070, p = .008, \eta_p^2 = .073$), with a trend significant main effect for TRF thought problems, but neither for gender nor for the interaction term (See Table 3). With regard to TRF, aggressive problems and attention problems, and development of SPQ disorganized symptoms, the moderation model was found to approach significance ($F(5,153) = 2.683, p = .024, \eta_p^2 = .081$). However, none of the main effects and the interaction term were significant. (See Table 3).

Discussion

This study adds to the literature by using an extra-familial source to assess school-associated behavioral problems in children (TRF; Verhulst et al., 1997), and its association with adult schizotypal symptomatology in a population presenting with psychopathology at childhood or adolescence. It was found that juvenile behavioral abnormalities that are tied to a school's environment and its specific demands were differentially associated with type of adult schizotypal symptoms. These associations were further modified by gender. Disregarding gender, teacher-reported thought problems in childhood was identified as the strongest indicator of future schizotypal symptoms, since it was significantly associated with disorganized and positive schizotypal symptoms. In addition, school-associated social problems and attention problems in childhood and adolescence were also identified as indicators of future disorganized schizotypal symptoms. However, when gender is taken into account, for girls school-associated externalizing problems, specifically attention and aggressive problems, were associated with the development of higher levels of adult disorganized schizotypal symptoms.

Severity of school-associated childhood and adolescent problems and adult schizotypal symptoms

Data suggest that subjects who are burdened by a broad range of behavioral problems in childhood and adolescence as reported by their teacher are at higher risk for disorganized schizotypal symptoms during adult life. This finding adds to earlier studies (Miller et al., 2002; Amminger et al., 1999; Muratori et al., 2005; Johnstone et al., 2005; Scott et al., 2009) that so far have mainly focused on intra-familial sources and have revealed that early problem behavior was associated with elevated risk for future schizophrenia spectrum pathology in general, without evaluating the specific association to distinctive domains of schizotypal symptoms.

Childhood thought problems and schizotypal symptoms

Within the total sample, higher levels of disordered thinking as assessed by the TRF in childhood were found to be associated with higher levels of future schizotypal symptoms within the domain of positive symptoms as well as within the domain of disorganized symptoms. If schizotypal symptoms are considered to represent a genetically related, milder variant of schizophrenia, lying on a continuum of schizophrenia spectrum pathology, this finding suggests that thought problems in childhood and adolescence as reported by their teachers is indicative for the development of specific behavior within the schizophrenia spectrum. This tentative conclusion adds to the well-known notion of Krapelin (1919) and Bleuler (1961), who attributed, already a century ago, a central role in the development of schizophrenia spectrum disorders to 'impaired thinking'. Meehl (1962, 1990) further posited that associative loosening or what he called 'cognitive slippage' was the primary manifestation of a schizophrenia diathesis. The current results extend the insight into the outcome of cross-sectional (Johnston & Holzman, 1979; Arboleda & Holzman, 1985; Tompson, Asarnow, Goldstein, & Milkowitz, 1990) and more recent longitudinal studies (Muratori et al., 2005; Velthorst et al., 2009), revealing that children who will later develop schizophrenia spectrum pathology exhibit more severe school-associated thought problems, than high risk children who do not develop adult schizophrenia disorders later on, or children who do not eventually develop other non-psychotic psychiatric pathology. In addition to the results of these studies that have only used intra-familial sources to describe juvenile behavioral problems, in the present study it is found that out of a broad range of juvenile problem behaviors and within a

school's context, teacher reported levels of thought problems stand out as the factor being strongest associated with future disorganized and positive schizotypal symptoms. Consequently, interventions that can affect these school-associated thought problems may have crucial implications for long-term outcome in children and adolescents at high risk for the development of schizophrenia spectrum pathology.

The cognitive mechanisms that mediate the association between school-associated thought problems and distinctive schizophrenia spectrum symptomatology, however, need further investigation. Since especially disorganized behavior is associated with poor executive functioning (Cohen, Barch, Carter, & Servan-Schreiber, 1999; Moritz, Andresen, Naber, Krausz, & Probsthein, 1999; Kerns & Berenbaum, 2002; Kerns, 2006), impairments in executive functioning might be among other candidate markers of future adult symptoms of disorganization. With respect to positive schizotypal symptoms, such as delusions and hallucinations, these might be specifically associated with deficits in attention and information processing during development (Blackwood, Howard, Bentall, & Murray, 2001). For example, hallucinations were found to be associated with impairments in attentional processes and perceptions that lead to the intrusion of unintended information into conscious awareness (Bentall & Slade, 1985; Bentall, Kaney, & Dewey, 1991; Bentall, Baker, & Havers, 1991; Ventura, Thames, Wood, Guzik, & Hellemann, 2010). Additional research is warranted to determine whether these cognitive deficits mediate the association between positive and disorganized schizotypal symptoms in general and different facets of impaired thinking (Caplan, Guthrie, Tang, Komo, & Asarnow, 2000).

School-associated social and attentional problems in childhood and adolescence and adult schizotypal symptoms

Severity of social and attention problems in childhood and adolescence within a school's environment was associated with disorganized schizotypal symptoms in adulthood in the total sample. This adds to earlier findings of studies that, based on the use of intra-familial sources, have reported about the presence of childhood social problems in relation to the development of future schizophrenia spectrum pathology in comparison to typically developing controls (Jones et al., 1994; Tarbox & Pogue-Geile, 2008; Welham et al., 2009) as well as in comparison with subjects with affective disorder (Dworkin et al., 1994), and anorexia (Muratori et al., 2005). Muratori and colleagues (2005) also identified specific childhood problems in regulation of attention. However, these studies did not differentiate between specific schizotypal symptoms. Our study suggests a specific con-

nection between early social and attention problems that are tied to demands on school and disorganized behavior later in life.

School-associated behavioral indicators of future schizotypal symptoms in boys and girls

As the majority of studies focuses on general populations of high risk subjects with men being grossly overrepresented, the literature may have been biased from a male perspective. Because of the present follow-up study consisting of a sample of 75 boys and 84 girls who all sought psychiatric help during childhood or adolescence, it was therefore possible to delineate meaningful gender specific behavioral pathways of future schizotypal symptoms.

Surprisingly, in girls school-associated externalizing problems and not internalizing problems were associated with higher levels of exclusively disorganized schizotypal symptoms. These gender specific findings contrast earlier findings of externalizing problems being particularly associated with the development of future schizophrenia spectrum disorders in men (McGlashan & Bardenstein, 1990), and internalizing problems being related with future schizophrenia spectrum disorders in women (Goldstein & Link, 1988; Jones et al., 1994; Addington, Addington, & Patten, 1996; McGlashan et al., 1990; Yung, Phillips, Yuen, & McGorry, 2004; Johnstone et al., 2005). However, the use of an extra-familiar instead of an intra-familiar source to assess behavioral problems might explain present results. Agreement among informants can differ according to type of psychopathology (Achenbach, McConaughy, & Howell, 1987; Smith, 2007), with greater levels of correspondence for informants' ratings of externalizing problems when compared with informants' ratings of internalizing problems (Achenbach, McConaughy, & Howell, 1987; Duhig, Renk, Epstein, & Phares, 2000). This difference is often interpreted as suggesting that informant agreement is better for problems that are presumably less observable and depend more on interpretation by informants (internalizing problems) than problems that are more observable (externalizing problems) such as fighting or teasing. In addition, parents have been found to report higher levels of problem behavior than teachers and judge problem behavior of boys and girls differently from teachers (Van der Ende & Verhulst, 2005). For example, teachers report lower levels of externalizing behavior in boys as opposed to parents (Van der Ende & Verhulst, 2005). Further investigation of gender specific behavioral problems using different informants is therefore warranted.

It was found that certain types of school-associated juvenile behavior appeared

to be associated with the development of specific symptoms of schizophrenia spectrum pathology.

The regression analysis demonstrated that the combination of the three subscales improved the predictive power (R^2) relative to the separate correlations (r^2). However, the improvement was modest (9.4% vs. 8.4% for thought problems that showed the highest correlation).

Strengths and limitations

The long follow-up period of 11.6 ($SD=3.1$) years of the current cohort was highly suitable to investigate how school-associated behavioral problems in childhood and adolescence were related with distinctive adult schizotypal symptoms. In addition, the present sample showed clearly elevated levels of SPQ total score as compared to the typically developing controls reported by Fagel and colleagues (2013) ($M=26.9$; $SD=19.3$ vs. $M=17.3$; $SD=12.6$). This underscores severity of schizotypal symptomatology of the present sample. Inherent to this long follow-up period, this study suffered from attrition which resulted in follow-up data available for 159 (35%) of the subjects. However, analyses of the background variables at T1 revealed that participants and non-participants were quite similar, with slightly higher Full scale IQ and Performance IQ and less severe rule breaking and aggressive behavior of the participants in comparison with the non-participants. It remains unknown, however, how the non-participants developed at T2. Further, since the present study concerns a clinically referred sample, the current findings might pertain to those subjects who presented with considerable and progressive juvenile neurobehavioral impairments and not to those subjects who were relatively inconspicuous as a child. Then, the mean age of participants at follow up was 24.4 ($SD=5.1$) years. As a result not all subjects may have passed the complete period of risk for schizophrenia spectrum pathology. In addition, the screening by self-report does carry some limitations, as compared with interviews. For example, self-report questionnaires might not ensure sufficient sensitivity and specificity for specific schizotypal signs such as an odd or guarded appearance, an expression of aloofness, or poor eye contact, and restricted affect (Kendler, 1988) and people may not be accurate in their self-judgments of appearance and speech (Raine, 1991). However, the SPQ has high reliability and validity. This may be because some of the questions assessing signs were worded so that the subject reports on external corroboration of these signs (e.g., "People sometimes comment on my unusual mannerisms and habits" or "People sometimes find it hard to understand

what I am saying”) rather than relying solely on self-analysis. Schizotypal individuals therefore seem to have no significant loss of insight that would affect their self-perceptions and thus invalidate the results on subscales of schizotypal signs (Raine, 1991). Although the TRF is not intended to replace the full assessment of a child’s functioning including clinical interviews, it should be noted that in addition to information from parents about a child’s behavior, teacher information is a valuable additional source of information (Van der Ende & Verhulst, 2005). Within a school’s structured setting, teachers are in a unique situation to compare the behavior of one child with the behavior of many other same-aged, older or younger children, and to judge whether the behavior of the child is appropriate for his or her age. However, as parents may have a possible rater bias by lacking internal standards to determine ‘normal’ levels of behavior, teachers may too have their own kinds of ‘bias’ (Polderman et al., 2006). Besides these limitations, the current follow-up study suited the purpose to illustrate the complex dynamics of school-associated behavioral problems in childhood and adolescence and the development of distinctive adult schizotypal symptoms.

From a clinical point of view, clinicians should be aware of the higher risk for schizotypal symptomatology in adulthood following school-associated juvenile behavioral problems, and that specific patterns of adult schizotypal symptomatology are associated with different types of juvenile behavioral problems.

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