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Childhood psychopathology and development of adult schizotypal symptoms

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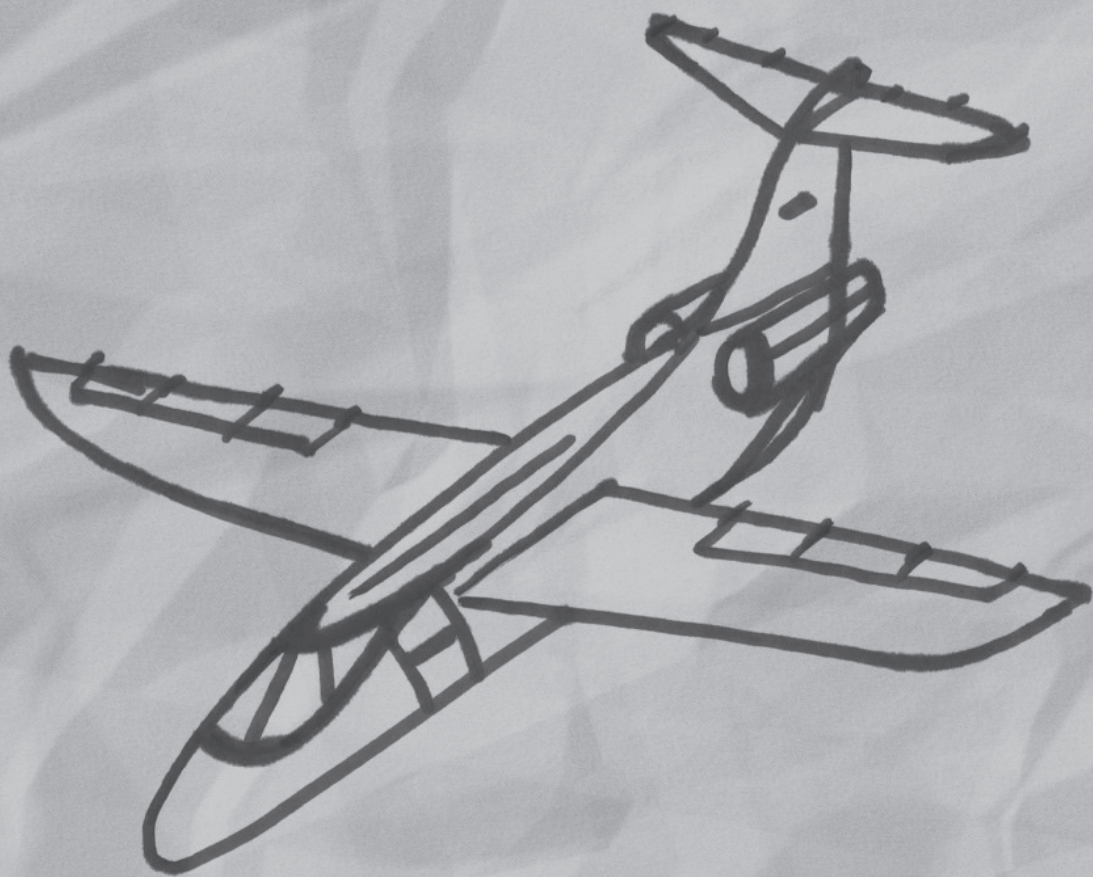
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Chapter 5



Adult schizotypal symptoms following juvenile psychopathology: no relation with juvenile intellectual functioning

Fagel, S.S.A.A., De Sonnevile, L.M.J., Van Engeland, H., & Swaab, H. Adult schizotypal symptoms following juvenile psychopathology: no relation with juvenile intellectual functioning. *Under review.*

Abstract

Because of the frequent finding that the developmental course of patients with disorders such as schizophrenia or psychosis is often marked by a significantly lower level of premorbid intelligence in comparison with healthy controls, the association between intellectual functioning in juvenile psychopathology and adult schizotypal symptoms, including the role of sex, was examined. 317 patients of the Department of Child and Adolescent Psychiatry of the University Medical Centre Utrecht, the Netherlands, were reassessed after 13.2 ($SD=5.2$) years for adult schizotypal symptoms by using the Schizotypal Personality Questionnaire-Revised (SPQ-R; Vollema & Hoijtink, 2002; Raine, 1991). The relation between intellectual functioning in juvenile psychopathology and adult schizotypal symptoms was examined by Spearman's bivariate correlations. No evidence was found for general or specific domains of intelligence in juvenile psychopathology being related to general and specific adult schizotypal symptomatology. This result also held when boys and girls were studied separately. The absence of associations between juvenile intelligence and adult schizotypal symptomatology in a sample of subjects presenting with juvenile psychopathology might be interpreted as juvenile intellectual markers not being suitable to predict development of milder symptoms within the schizophrenia spectrum.

Introduction

Schizophrenia spectrum pathology is composed of multiple conditions that are characterized by distortions of cognitive and perceptual reality, collectively known as positive symptoms, interpersonal withdrawal (negative symptoms), and disorganized speech and behavior (disorganized symptoms) (Liddle, 1987; Suhr, 2001). These conditions have different gradients of dysfunction, ranging from a milder, non-clinical form of schizotypy to conditions at the extreme end of the spectrum, such as schizophrenia and psychosis (Meehl, 1989). Because there is evidence for neurodevelopmental origins being part of its etiology in (at least) a subgroup of patients (Weinberger, 1987; Murray & Lewis, 1987), the association of cognitive impairments and especially intellectual impairments with development of schizophrenia or psychosis has been extensively studied throughout the years.

Longitudinal studies have well-established that intellectual functioning in childhood or adolescence is lower in patients that developed disorders within the schizophrenia spectrum in adulthood, such as schizophrenia (Woodberry, Giuliano, & Seidman, 2008; Cannon, Bearden, Hollister, Rosso, Sanchez, & Hadley, 2000; Mortensen, Sorensen, Jensen, Reinisch, & Mednick, 2005; Ott et al., 1998; Seidman, Buka, Goldstein, & Tsuang, 2006), and (non-affective) psychotic disorders (Mortensen et al., 2005; Urfer-Parnas, Mortensen, Saebye, & Parnas, 2010; Zammit et al., 2004). However, studies are less consistent when it comes to deciding whether specific domains of intellectual functioning may relate to this general impairment. While the results of the army cohort study of David and colleagues (1997), the birth cohort study of Seidman et al. (2006), the genetic high-risk study of Ott et al. (1998), and the meta-analysis of Aylward, Walker and Bettes (1984) found that pre-schizophrenic children were especially marked by deficits in verbal intelligence in comparison to typically developing controls, the results of the clinical follow-up study of Amminger et al. (2000), and the birth cohort study of Jones, Rodgers, Murray and Marmot (1994) have pinpointed deficits in nonverbal juvenile intelligence in pre-schizophrenic children in comparison to typically developing controls as precursors. Then again, the results of the genetic high-risk study of Sørensen, Mortensen, Parnas and Mednick (2006), the birth cohort study of Cannon and colleagues (2000), and the meta-analysis of Khandaker, Barnett, White and Jones (2011) are suggestive for verbal as well as non-verbal juvenile capacities being equally affected in patients with schizophrenia when compared to typically developing controls.

Similar inconsistency in results is found when looking at subdomains of intellectual functioning. Some studies have found that persons who developed disorders

within the schizophrenia spectrum had lower scores on subtests pertaining to juvenile verbal intelligence when compared with typically developing controls. For example, the prospective birth cohort study of Seidman and colleagues (2006) reported lower scores on Information and digit span at child age in persons who developed schizophrenia in adulthood. The prospective high-risk study of Sørensen and colleagues (2010) found lower scores on similarities in persons who developed disorders such as schizophrenia, schizotypal personality disorder, delusional disorder, paranoid personality disorder, schizotypal disorder, and paranoid psychosis when compared with typically developing controls. On the other hand, studies have also shown that this unfavorable development is associated with weaknesses in non-verbal components of intelligence in childhood or adolescence. For example, the prospective cohort study of Niendam, Bearden, Rosso, Sanchez and Hadley (2003) found pre-schizophrenic subjects having lower scores on Coding in comparison with their unaffected siblings. This deficit in coding on child age was also found in the cohort study of Sørensen and colleagues (2006) in persons who developed disorders such as schizophrenia, schizotypal personality disorder, and other disorders within the schizophrenia spectrum in comparison with typically developing controls. The prospective high-risk study of Sørensen and colleagues (2010) reported lower scores in the subtest mazes, and object assembly being associated with the development of schizophrenia in comparison with typically developing controls.

These studies have exclusively investigated disorders within the schizophrenia spectrum which might arguably account for the inconsistencies in results. Schizophrenia spectrum pathology is a very heterogeneous condition, with substantial variability within each diagnostic group of schizophrenia spectrum patients (Kendell, 1987; Pfol, 1986). For example, some of the patients with disorders within the schizophrenia spectrum respond poorly to all available treatments and have a poor outcome, while others respond well to treatment, and sometimes even have full remission of all symptoms and full recovery even to the premorbid level of functioning (McGrath, 2008). One approach that might advance insight into the mechanisms that facilitate the development of schizophrenia spectrum pathology is to focus on more homogeneous symptoms within the spectrum. Since it is found that the majority of individuals at risk to develop schizophrenia spectrum pathology will not show manifest illness (Meehl, 1990; Gottesman, 1982; Raine, 1991; Chapman, 1994; Tsuang, 2002), but will rather present with milder schizotypal symptoms, it would be relevant to examine precursors of milder features of schizophrenia spectrum pathology along its dimensions. In particular this strategy has recently been promoted as a way to provide important insights into the origins and mechanisms of schizophrenia (Raine, 2006).

Thus far, studies that have focused on intellectual functioning and distinctive symptoms of schizophrenia spectrum pathology have only cross-sectionally investigated this association in adult patients. These studies have reported inverse associations of general intellectual functioning with negative (Barrantes-Vidalatal, 2002) and positive schizotypal symptoms (Barrantes-Vidalatal, 2002; Matheson & Langdon, 2008). With regard to specific subdomains of intellectual functioning Noguchi and colleagues (2008) showed that lower verbal intelligence was associated with positive symptoms. To our knowledge, no study as yet has longitudinally investigated how intellectual functioning in children and adolescents with psychopathology is associated with the development of distinctive symptoms of schizophrenia spectrum pathology in adulthood.

It has been shown that lower premorbid intelligence is also linked to numerous other psychiatric disorders, such as depression (Koenen et al., 2009; Zammit et al., 2004), affective disorders (Koenen et al., 2009; Urfer-Parnas et al., 2010), adjustment disorders (Mortensen et al., 2005), personality disorders (Mortensen et al., 2005; Urfer-Parnas et al., 2010), alcohol and substance-use-related disorders (Mortensen et al., 2005), neurotic and stress disorders (Urfer-Parnas et al., 2010), and psychiatric illness in general (Koenen et al., 2009). Since the relationship between premorbid intelligence and the development of adult schizophrenia spectrum pathology is only investigated in patients by comparison to typically developing controls, a more promising approach may be to investigate how intelligence and schizotypal symptoms are related independent of general psychopathology, i.e., focusing on level of intellectual functioning and degree and type of schizotypal symptoms.

Finally, there is general agreement that women and men with schizophrenia differ in onset age (Sartorius et al., 1978; Lewine, 1981; Loranger, 1984), and life course (Lewine, 1985; Goldstein, Tsuang, & Faraone, 1989; Westermeyer, Harrow & Marengo, 1989). However, few studies have examined sex differences in intellectual functioning prior to the onset of disorders within the schizophrenia spectrum (Aylward, Walker, & Bettes, 1984; Weiser et al., 2000). The vast majority of studies indicate better premorbid functioning during childhood among females (compared to males) who later developed schizophrenia (Goldberg, Cold, Torrey, & Weinberger, 1995; Walker & Lewine, 1993; Walder et al., 2008). Noticeably absent from the literature are efforts to examine sex differences in intellectual functioning in predicting distinctive symptoms of schizophrenia spectrum pathology. The investigation of such differences is important for understanding the etiology of schizophrenia spectrum pathology.

The present follow-up study aims to investigate how intellectual (dys) functioning in childhood and adolescence is associated with the development of adult distinc-

tive schizotypal symptoms in a cohort of subjects presenting with juvenile psychopathology. In line with the result of the cross-sectional study of Noguchi and colleagues (2008) investigating intellectual functioning and its relation with distinctive schizotypal symptoms, it is hypothesized that lower levels of general intellectual functioning in childhood and adolescence, in particular verbal intelligence, will be most strongly linked to adult schizotypal symptoms and especially positive and negative symptoms. Whether this relation is valid for specific intellectual subdomains is further explored, as well as the role of sex.

Methods

Sample and procedure

This study is part of a longitudinally prospective study designed to evaluate both global and clinical outcomes in adulthood of patients, referred during 1984 to 2004 (T1), to the Department of Child and Adolescent Psychiatry at the University Medical Centre of Utrecht (UMCU), the Netherlands. Patients 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) presence of axis I diagnosis based on Diagnostic Statistical Manual (DSM) criteria of the American Psychiatric Association (APA, 1980, 1987, 1994), (4) no axis II DSM diagnosis (APA, 1980, 1987, 1994) of mental retardation ($IQ < 70$) at T1, (5) no axis I DSM diagnosis before or at T1 with child psychotic disorder, schizophrenia or another psychotic disorder, bipolar disorder or dissociative disorder, and (6) juvenile intellectual assessment at T1. There were 912 non-retarded patients who 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. 317 (153 male and 164 female) adult patients were traced and were willing to participate. Subjects were reassessed after a mean period of 13.2 years ($SD=5.2$), at the mean age of 25.7 years ($SD=4.7$) at T2, with subjects assessed at T1 at 3 to 12 years ($n=155$) being reassessed at the mean age of 25.0 years ($M=4.5$) and subjects assessed at T1 at 13 to 18 years ($n=162$) being reassessed at the mean age of 26.2 years ($SD=5.0$). With a Full Scale IQ (FSIQ) score of the total group of 103.1 ($SD=14.7$) the subjects perfectly fit in the normal intelligence range. 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

Table 1. Number of participants per juvenile DSM diagnostic category (n=317)

Juvenile DSM diagnostic categories of the participants	<i>n</i>
Eating disorders	55
Pervasive Developmental Disorders	50
Depressive disorders	35
Attention Hyperactivity Disorders	34
Disruptive disorders	27
Anxiety disorders	24
Other conditions that may be a focus of clinical attention	20
Sexual and Gender Identity disorders	13
Deferred diagnosis	12
Other disorders of infancy, childhood, or adolescence	12
Adjustment disorders	11
Somatoform disorders	7
Learning disorders	5
Elimination disorder	5
Tic-disorders	4
Communication disorder	1
Non-specific psychiatric disorder (non-psychotic)	1
Substance-related disorder	1

Table 2. Means and SD's for age at T1, T2, SPQ scores and IQ scores of the total study sample and sex specific subgroups.

	Total group (n=319)	Males (n=153)	Females (n=164)
	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>
Age at T1	12.4(3.3)	11.2(3.2)	13.6(2.9)
Age at T2	25.7(4.8)	26.0(5.0)	25.3(4.5)
SPQ total score	27.4(19.1)	27.3(17.5)	27.4(20.5)
SPQ positive factor	9.1(7.5)	8.6(6.3)	9.6(8.4)
SPQ negative factor	12.9(9.6)	13.0(9.4)	12.8(9.9)
SPQ disorganized factor	5.4(4.7)	5.7(5.0)	5.0(4.4)
Full scale IQ	103.1(14.7)	101.9(15.3)	104.2(14.1)
Verbal IQ	102.4(14.5)	101.1(13.8)	103.6(15.1)
Information	10.0(3.1)	10.4(3.2)	9.7(3.0)
Similarities	10.5(2.9)	10.1(3.0)	10.8(2.9)
Arithmetics	10.2(3.2)	10.1(3.2)	10.3(3.1)
Vocabulary	10.0(2.8)	10.2(2.9)	9.7(2.8)
Comprehension	10.0(2.8)	9.8(2.7)	10.3(2.9)
Digit span	9.3(3.0)	8.9(2.9)	9.7(3.2)
Performance IQ	103.3(16.1)	102.3(17.9)	104.2(14.3)
Picture completion	9.5(3.0)	9.9(2.9)	9.2(3.1)
Picture arrangement	10.5(3.1)	10.8(3.2)	10.4(2.9)
Block design	10.5(3.3)	10.7(3.6)	10.3(3.1)
Object assembly	10.2(3.4)	10.1(3.7)	10.3(3.2)
Digit symbol	9.9(3.3)	9.0(3.1)	10.8(3.2)

Medical Ethical Committee of the University Medical Centre of Utrecht (number 05-319/K). Table 1 represents the number of participants by juvenile DSM diagnostic category. Table 2 represents the background variables of participants.

Representativeness

To check representativeness of the sample, age, intelligence scores and sex distribution of participants and nonparticipants were compared. Chi-square analysis revealed that proportionally more participants appeared to be females (51.7% female participants versus 34.6% females in the nonparticipants group), ($\chi^2(1,912)=25.121, p<.001$). Multivariate analysis of variances (MANOVA) revealed that participants had a slightly higher Verbal IQ (VIQ) ($M=102.4; SD=14.5$ vs. $M=99.3; SD=14.0$), ($F(1,888)=9.802, p=.002, \eta_p^2=.011$) and Full Scale IQ ($M=103.1; SD=14.7$ vs. $M=100.5; SD=14.0$), ($F(1,888)=6.562, p=.011, \eta_p^2=.007$). No differences between participants and those lost to follow-up were found for age at T1 ($F(1,888)=.474, p=.491$), age at T2 ($F(1,888)=1.626, p=.203$) and Performance IQ (PIQ) ($F(1,888)=1.159, p=.282$).

Intellectual assessment in childhood and adolescence

Cognitive functioning was evaluated using standardized scores of Wechsler Intelligence Scales at time of juvenile assessment; i.e. WPPSI (Wechsler, 1967), WISC (Wechsler, 1949), WISC-R (Wechsler, 1974) or WISC-III (Wechsler, 1991) was administered to subjects aged younger than 16 years and WAIS (Wechsler, 1955) or WAIS-R (Wechsler, 1981) was administered to subjects aged 16 years and older. FSIQ, VIQ, and PIQ scores were computed. WISC and WAIS versions comprised an overlap in eleven Wechsler subscales; i.e., information, vocabulary, comprehension, similarities, arithmetic, digit span, picture completion, block design, coding, picture arrangement, and object assembly. Standardized scores were calculated for these eleven subscales, and five subtests were omitted because they were not included in both Wechsler versions (mazes, matrix reasoning, symbol search, geometrical figures, and letter-number sequencing).

Adult schizotypal symptoms

Adult schizotypal symptoms were measured using the Schizotypal Personality Questionnaire-Revised (SPQ-R; Raine, 1991; Vollema & Hoijtink, 2000). 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 sex, ethnicity, religion, and social background (Reynolds, Raine, Mellinger, 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 schizophrenic family members. 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, with a range of 0 to 100 for the SPQ total score, 0 to 38 for the SPQ positive factor, 0 to 43 for the SPQ negative factor, and 0 to 19 for the SPQ disorganized factor.

Statistical analysis

To control for possible confounding effects, the association of three background variables, i.e., age at T1, age at T2, and time interval between T1 and T2, with SPQ total and factor scores was explored. None of these variables appeared to be significantly associated with SPQ total or factor scores ($.130 < p < .970$). In addition, to analyze possible differences between boys and girls on background and SPQ and IQ variables, a MANOVA was performed with background (age at T1 and T2) and SPQ total, factor scores and IQ full scale and subscale scores as dependent variables. 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 $\eta_p^2 \geq 0.14$ representing a large effect (Cohen, 1992). Because the SPQ total and factor scores were all positively skewed, the strength of the relation with IQ full scale, and subscale 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 sex specific characteristics, these analyses were replicated for boys and girls separately. In order to adjust the type 1 error for multiple testing, Sidak adjustment for correlated outcomes was performed and alpha was lowered to .002, two-tailed for all analyses. $p < .01$ was adopted as trend-level significant. Statistical analyses were performed using the Statistical Package for the Social Sciences 20.0 (SPSS Inc, Chicago, IL, USA).

Results

Sample characteristics of the total study sample and sex specific subgroups

Table 2 shows means and *SDs* for the age at T1 and T2 and SPQ and IQ variables for the total study sample as well as sex specific subgroups. The MANOVA of sex with age at T1, age at T2, IQ scores and SPQ scores revealed a significant and large multivariate effect of Sex ($F(19,297)=7.105, p < .001, \eta_p^2 = .312$). The univariate analyses showed that males were younger than females at T1 ($F(1,315)=47.230, p < .001, \eta_p^2 = .130$), and had lower scores in comparison with females on Substitution ($F(1,315)=25.805, p < .001, \eta_p^2 = .076$).

Intelligence in childhood and adolescence and adult schizotypal symptoms of the total group

Performing Spearman's bivariate correlations for juvenile intelligence scores and SPQ Total and Factor scores, revealed significant correlations between lower scores on Arithmetics ($r_s = -.148, p = .008$), Vocabulary ($r_s = -.153, p = .006$), and FSIQ ($r_s = -.144, p = .010$) and higher levels of positive schizotypal symptoms. None of the other juvenile intelligence scores were associated with severity of SPQ total and factor scores ($.017 < p < .968$). (See Table 3).

Sex specific associations between juvenile intelligence and adult schizotypal symptoms

The Spearman's bivariate correlations for boys and girls separately revealed the following results. With regard to boys, only Comprehension was trend significantly correlated with positive schizotypal symptoms ($r_s = -.214, p = .008$). None of the other juvenile intelligence scores were associated with severity of SPQ total and factor scores ($.022 < p < .931$). With regard to girls, none of the juvenile intelligence scores were significantly associated with SPQ total and factor scores ($.016 < p < .883$). (See Table 3). However, none of the aforementioned intelligence scores remained significant after correction for multiple comparisons.

Discussion

The present follow-up study revealed no evidence for general and specific domains of intelligence in juvenile psychopathology being related to the development of general and distinctive schizotypal symptomatology in adulthood. These results also held when boys and girls were studied separately.

The absence of associations between intellectual functioning in children and adolescents with juvenile psychopathology and adult schizotypal symptomatology was surprising, since longitudinal studies have well-established that intellectual functioning in childhood or adolescence is lower in patients that develop disorders within the extreme end of the schizophrenia spectrum in adulthood, such as schizophrenia (Cannon, Bearden, Hollister, Rosso, Sanchez, & Hadley, 2000; Mortensen, Sorensen, Jensen, Reinisch, & Mednick, 2005; Ott et al., 1998; Seidman, Buka, Goldstein, & Tsuang, 2006), and (non-affective) psychotic disorders (Mortensen et al., 2005; Urfer-Parnas, Mortensen, Saebye, & Parnas, 2010; Zammit et al., 2004). Furthermore, studies have reported better premorbid functioning during childhood and adolescence among females (compared to males) who later develop schizophrenia (Goldberg et al, 1995; Walker & Lewine, 1993; Walder et al., 2008). However, several issues are important to consider when interpreting the present results in light of the existing literature.

First, the present outcome is the result of a correlational analysis in individuals who all show juvenile psychopathology. The present absence of associations between intelligence and extent of schizotypal symptoms might be interpreted as that intellectual markers, such as identified in comparison studies using normal controls, do not play a

Table 3. Spearman's rank order correlations between juvenile intelligence and SPQ Total and factor scores for total sample and gender specific subgroups

	Total schizotypal symptoms			Positive schizotypal symptoms		
	Total	Males	Females	Total	Males	Females
Full scale intelligence	-.096	-.019	-.169	-.144*	-.128	-.170
Verbal intelligence	-.086	-.019	-.147	-.134	-.114	-.166
Information	-.009	.071	-.080	-.034	.052	-.103
Similarities	.012	.078	-.043	-.010	.036	-.056
Arithmetics	-.094	-.090	-.095	-.148*	-.134	-.167
Vocabulary	-.135	-.085	-.185	-.153*	-.114	-.188
Comprehension	-.138	-.185	-.095	-.141	-.214*	-.188
Digit span	-.041	-.024	-.055	-.072	-.063	-.090
Performance intelligence	-.072	-.027	-.122	-.108	-.118	-.110
Picture completion	.021	.166	-.101	-.017	.077	-.084
Picture arrangement	-.050	-.044	-.047	-.055	-.080	-.021
Block design	-.040	-.031	-.050	-.098	-.110	-.081
Object assembly	-.059	-.061	-.051	-.045	-.054	-.035
Digit symbol	-.018	-.055	.008	-.024	-.101	.012

* Trend significant at $p \leq .01$

	Negative schizotypal symptoms			Disorganized schizotypal symptoms		
	Total	Males	Females	Total	Males	Females
	-.095	-.010	-.171	-.020	.068	-.106
	-.087	-.007	-.157	-.010	.051	-.063
	-.025	.039	-.087	.034	.077	-.014
	-.010	.052	-.059	.050	.127	-.012
	-.044	-.040	-.041	-.075	-.068	-.069
	-.140	-.100	-.180	-.068	.002	-.143
	-.136	-.162	-.115	-.090	-.115	-.053
	-.014	.010	-.028	-.042	-.039	-.035
	-.065	-.011	-.121	-.021	.041	-.092
	.026	.157	-.085	.053	.170	-.066
	-.055	-.051	-.049	-.022	.012	-.063
	-.014	-.006	-.024	-.004	.016	-.029
	-.062	-.071	-.047	-.046	-.034	-.045
	.002	.006	.009	-.065	-.073	-.051

substantial role in the development of schizotypal symptoms.

Second, with the present study focusing on dimensions of schizotypal symptoms instead of on disorders within the extreme end of the schizophrenia spectrum, the current results might be suggestive for intellectual markers being too subtle to detect vulnerability in milder forms of schizophrenia spectrum pathology, i.e., schizotypal symptomatology, and may only be found relevant for the extremes of the spectrum, i.e., when looking at the development of schizophrenia or psychosis (Park et al., 2012).

Third, while the majority of studies using psychiatric samples are characterized by a relatively low intelligence level, the level of intelligence of the present sample fitted perfectly within national norms, i.e., normal range, with Full scale IQ $M=103.1$ ($SD=14.7$). As a result, this might have restricted the number and magnitude of the significant correlations and might preclude generalizability of findings to more impaired populations.

Strengths and limitations of the study

The long follow-up period of 13.2 ($SD=5.2$) years of the current cohort was highly suitable to investigate long-term associations between level of intelligence in childhood or adolescent psychopathology and (development of) distinctive adult schizotypal symptoms. Inherent to this long follow-up period, this study suffers from attrition which resulted in follow-up data available for 35% of the subjects. However, analyses of the background variables at T1 revealed that the participants and non-participants were quite similar, with slightly higher Full scale and Verbal IQ of the participants in comparison with the non-participants and a slight overrepresentation of female subjects in the group of participants. It remains, however, unknown how the non-participants developed at T2. Since the mean age of participants at follow up was 25.7 ($SD=4.8$) years, not all subjects may have passed the complete period of risk for schizophrenia spectrum pathology, which may have led to an underestimation of level of schizotypal symptomatology. Because we did not assess schizotypal symptoms at T1, it was not possible to determine that these symptoms have increased in severity at follow-up. In addition, the screening by a self-reported questionnaire might 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, which might be due to some of the questions

assessing signs are worded so that the subject reports on external corroboration of these signs rather than relying solely on self-analyses. 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).

References

- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (3rd ed.)*. (1980). Washington, DC: American Psychiatric Association Press.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (3rd revised ed.)*. (1987). Washington, DC: American Psychiatric Association Press.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (4th ed.)*. (1994). Washington, DC: American Psychiatric Association Press.
- Amminger, G., Schölgelhofer, M., Lehner, T., Ott, S., Friedrich, M., & Aschauer, H. (2000). Premorbid performance IQ deficit in schizophrenia. *Acta Psychiatr Scand*, 102(6), 414–422.
- Aylward, E., Walker, E., & Bettes, B. (1984). Intelligence in schizophrenia: Meta-analysis of the research. *Schizophr Bull*, 10(3), 430-459.
- Barrantes-Vidal, N., Fananas, L., Rosa, A., Caparros, B., Riba, M.D., & Obiols, J.E. (2002). Neurocognitive, behavioural and neurodevelopmental correlates of schizotypy clusters in adolescents from the general population. *Schizophr Res*, 61, 293–302.
- Blakesley, R.E., Mazumdar, S., Dew, M.A., Houck, P.R., Tang, G., Reynolds, C.F., & Butters, M.A. (2009). Comparisons of methods for multiple hypothesis testing in neuropsychological research. *Neuropsychology*, 23(2), 255–264.
- Cannon, T.D., Bearden, C., Hollister, J.M., Rosso, I.M., Sanchez, L.E., & Hadley, T. (2000). Childhood cognitive functioning in schizophrenia patients and their unaffected siblings. *Schizophr Bull*, 26(2), 379–393.
- Chapman, L.J., Chapman, J.P., Kwapił, T.R., Eckblad, M., & Zinser, M.C. (1994). Putatively psychosis-prone subjects 10 years later. *J Abnormal Psychol*, 103(2), 171–183.
- Cohen, J. (1992). A power primer. *Psychol Bull*, 112(1), 155–15.
- David, A.S., Malmberg, A., Brandt, L., Allebeck, P., & Lewis, G. (1997). IQ and risk for schizophrenia: a population-based cohort study. *Psychol Med*, 27(6), 1311–1323.
- De la Serna, E., Baeza, I., Toro, J., Andrés, S., Puig, O., Sánchez-Guistau, V., Romero, S., Bernardo, M., & Castro-Fornieles, J. (2010). Relationship between clinical and neuropsychological characteristics in child and adolescent first degree relatives of subjects with schizophrenia. *Schizophr Res*, 116(2-3), 159-67.
- Goldberg, T., Cold, J., Torrey, F., & Weinherger, D. (1995). Sex differences and neurocognition in schizophrenia (abstract). *Schizophr Res*, 15, 118.
- Goldstein, J.M., Tsuang, M.T. & Faraone, S.V. (1989). Gender and schizophrenia: Implications for understanding the heterogeneity of the illness. *Psychiatry Res*, 28, 243-253.
- Gottesman, I.I., & Shields, J.A. (1982). *Schizophrenia, the epigenetic puzzle*. Cambridge: Cambridge University Press.
- Jones, P., Rodgers, B., Murray, R. & Marmot, M. (1994). Child developmental risk factors for adult schizophrenia in the British 1946 birth cohort. *Lancet*, 334(8934), 1393-1402.
- Kendell, R.E. (1987). *Schizophrenia: clinical features*. In: Michels, R., & Cavenar, J. (Eds.). *Psychiatry*, Vol 1. Philadelphia: JB Lippincott.
- Kendler, K.S. (1988). Familial aggregation of schizophrenia and schizophrenia spectrum disorders. Evaluation of conflicting results. *Arch Gen Psychiatry*, 45(4), 377-383.
- Kendler, K., McGuire, M., Gruenberg, A.M., O'Hare, A., Spellman, M., & Walsh, D. (1993). The Roscommon family study: I. methods, diagnosis of probands, and risk of schizophrenia in relatives. *Arch Gen Psychiatry*, 50(7), 527–540.
- Khandaker, G.M., Barnett, J.H., White, I.R., Jones, P.B. (2011). A quantitative meta-analysis of population-based studies of premorbid intelligence and schizophrenia. *Schizophr Res*, 132(2-3), 220-7.
- Koenen, K.C., Moffitt, T.E., Roberts, A.L., Martin, L.T., Kubzansky, L., Harrington, H., Poulton, R., & Caspi, A. (2009). Childhood IQ and adult mental disorders: a test of the cognitive reserve hypothesis. *Am J Psychiatry*, 166(1), 50–57.
- Lewine, R.R.J. (1981). Sex differences in schizophrenia: Timing or subtype? *Psychol Bull*, 90, 432-444.
- Lewine, R.R.J. (1985). Schizophrenia: An amotivational syndrome in men. *Can J Psychiatry*, 30, 316-318.
- Liddle, P.F. (1987). The symptoms of chronic schizophrenia. A reexamination of the positive and negative dichotomy. *Br J Psychiatry*, 151, 145.
- Loranger, A.W. (1984). Sex difference in age at onset of schizophrenia. *Arch Gen Psychiatry*, 41, 157-161.
- Matheson, S., & Langdon, R. (2008). Schizotypal traits impact upon executive working memory and aspects of IQ. *Psychiatry Res*, 159(1-2), 207-14.
- McGrath, J. (2008). Dissecting the heterogeneity of schizophrenia outcomes. *Schizophr Bull*, 34, 247-8.
- Meehl, P.E. (1989). Schizotaxia revisited. *Arch Gen Psychiatry*, 46(10), 935–944.
- Meehl, P.E. (1990). Toward an integrated theory of schizotaxia, schizotypy, and schizophrenia. *J Pers Disord*, 4, 1-99.
- Menkes, M.M., Rowe, J.S., & Menkes, J.H. (1967). A twenty-five year follow-up study on the hyperkinetic child with minimal brain dysfunction. *Pediatrics*, 39(3), 393-9.

- Mortensen, E.L., Sorensen, H.J., Jensen, H.H., Reinisch, J.M., & Mednick, S.A. (2005). IQ and mental disorder in young men. *Br J Psychiatry*, 187, 407–415.
- Murray, R.M., & Lewis, S.W. (1987). Is schizophrenia a neurodevelopmental disorder? *Br Med Journal*, 295, 681–82.
- Niendam, T.A., Bearden, C.E., Rosso, I.M., Sanchez, L.E., & Hadley, T. (2003). A prospective study of childhood neurocognitive functioning in schizophrenic patients and their siblings. *Am J Psychiatry*, 160 (11), 2060–2062.
- Noguchi, H., Hori, H., & Kunugi, H. (2008). Schizotypal traits and cognitive function in healthy adults. *Psychiatry Res*, 161(2), 162–169.
- Ott, S.L., Spinelli, S., Rock, D., Roberts, S., Amminger, G.P., & Erlenmeyer-Kimling, L. (1998). The New York High-Risk Project: social and general intelligence in children at risk for schizophrenia. *Schizophr Res*, 31(1), 1–11.
- Park, S., Hong, J.P., Lee, H.B., Samuels, J., Bienvenu, O.J., Chung, H.Y., Eaton, W.W., Costa, P.T. Jr., & Nestadt, G. (2012). Relationship between personality disorder dimensions and verbal memory functioning in a community population. *Psychiatry Res*, 196(1), 109–114.
- Pfohl, B., & Andreasen, N. (1986). *Schizophrenia: diagnosis and classification*. In: Hales, F.A. (Ed.): *Psychiatry update*, Vol. 5 (pp. 38–51). Washington DC: American Psychiatric Press.
- Raine, A. (1991). The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophr Bull*, 17(4), 555–564.
- Raine, A., Reynolds, C., Lencz, T., Scerbo, A., Triphon, N., & Kim, D. (1994). Cognitive- perceptual, interpersonal, and disorganized features of schizotypal personality. *Schizophr Bull*, 20(1), 191–201.
- Raine, A. (2006). Schizotypal personality: neurodevelopmental and psychosocial trajectories. *Annu Rev Clin Psychol*, 2, 291–326.
- Reynolds, C., Raine, A., Mellingen, K., Venables, P., & Mednick, S. (2000). Three-factor model of schizotypal personality: invariance across culture, gender, religious affiliation, family adversity, and psychopathology. *Schizophr Bull*, 26(3), 603–618.
- Sartorius, N., Jablensky, A., Stromgren, E., & Shapiro, R. (1978). Validity of diagnostic concepts across cultures. In: Wynne, L.C., Cromwell, R.L., & Matthysse, S. (Eds). *The Nature of Schizophrenia: New Approaches to Research and Treatment* (pp. 657–669). New York: John Wiley & Sons, Inc.
- Schuklenk, U. (2001). Helsinki declaration revisions. *Issues Med Ethics*, 9(1), 29.
- Seidman, L.J., Buka, S.L., Goldstein, J.M., & Tsuang, M.T. (2006). Intellectual decline in schizophrenia: Evidence from a prospective birth cohort 28 year follow-up study. *J Clin Exp Neuropsychol*, 28(2), 225–242.
- Sidak, Z. (1967). Rectangular confidence regions for the means of multivariate normal distributions. *J Am Stat Assoc*, 62, 626–633.
- Sorensen, H.J., Mortensen, E.L., Parnas, J., & Mednick, S.A. (2006). Premorbid neurocognitive functioning in schizophrenia spectrum disorder. *Schizophr Bull*, 32(3), 578–583.
- Sorensen, H.J., Mortensen, E.L., Schiffman, J., Ekström, M., Denenney, D., & Mednick, S.A. (2010). Premorbid IQ and adult schizophrenia spectrum disorder: Verbal performance subtests. *Psychiatry Res*, 178(1), 23–26.
- Suhr, J.A., & Spitznagel, M.B. (2001). Factor versus cluster models of schizotypal traits. I: a comparison of unselected and highly schizotypal samples. *Schizophr Res*, 52(3), 231–239.
- Tsuang, M., Stone, W., Tarbox, S., & Faraone, S. (2002). An integration of schizophrenia with schizotypy: identification of schizotaxia and implications for research on treatment and prevention. *Schizophr Res*, 54(1), 169–175.
- Urfer-Parnas, A., Mortensen, E.L., Saebye, D., & Parnas, J. (2010). Premorbid IQ in mental disorders: a Danish draft-board study of 7486 psychiatric patients. *Psychol Med*, 40(4), 547–556.
- Vollema, M., & Hoijtink, H. (2000). The multidimensionality of self-report schizotypy in a psychiatric population: an analysis using multidimensional rasch models. *Schizophr Bull*, 26(3), 565–575.
- Vollema, M., Sitskoorn, M., Appels, M., & Kahn, R. (2002). Does the schizotypal personality questionnaire reflect the biological-genetic vulnerability to schizophrenia? *Schizophr Res*, 54(1–2), 39–45.
- Walder, D.J., Mittal, V., Trotman, H.D., McMillan, A.L., & Walker, E.F. (2008). Neurocognition and conversion to psychosis in adolescents at high-risk. *Schizophr Res*, 101, 161–168.
- Walker, E., & Lewine, R. (1993). Sampling biases in studies of gender and schizophrenia. *Schizophr Bull*, 19, 1–7.
- Wechsler, D. (1949). *Wechsler Intelligence Scale for Children (WISC)*. San Antonio, TX: The Psychological Corporation.
- Wechsler, D. (1955). *Manual for the Wechsler Adult Intelligence Scale (WAIS)*. New York: Psychological Corporation.
- Wechsler, D. (1967). *Wechsler Preschool and Primary Scale of Intelligence (WPPSI)*. New York: The Psychological Corporation.
- Wechsler, D. (1974). *Manual for the Wechsler Intelligence Scale for Children—Revised (WISC-R)*. New York: Psychological Corporation.
- Wechsler, D. (1991). *Manual for the Wechsler Intelligence Scale for Children, Third Edition (WISC-III)*. San Antonio, TX: Psychological Corporation.
- Wechsler, D. (1981). *Manual for the Wechsler Adult Intelligence Scale-Revised (WAIS-R)*. New York: The Psychological Corporation.

Weinberger, D.R. (1987). Implications of normal brain development for the pathogenesis of schizophrenia. *Arch Gen Psychiatry*, 44(7), 660-669.

Weiser, M., Reichenberg, A., Rabinowitz, J., Kaplan, Z., Mark, M., Nahon, D., & Davidson, M. (2000). Gender differences in premorbid cognitive performance in a national cohort of schizophrenic patients. *Schizophr Res*, 45(3), 185-90.

Westermeyer, J.F., Harrow, M., & Marengo, J.T. (1989). Gender and outcome in schizophrenia and depression. *Presented at the Annual Meeting of the American Psychiatric Association*, San Francisco, CA.

Woodberry, K.A., Giuliano, A.J., & Seidman, L.J. (2008). Premorbid IQ in schizophrenia: a meta-analytic review. *Am J Psychiatry*, 165(5), 579-87.

Zammit, S., Allebeck, P., David, A.S., Dalman, C., Hemmingsson, T., Lundberg, I., & Lewis, G. (2004). A longitudinal study of premorbid IQ score and risk of developing schizophrenia, bipolar disorder, severe depression, and other nonaffective psychoses. *Arch Gen Psychiatry*, 61(4), 354-360.

