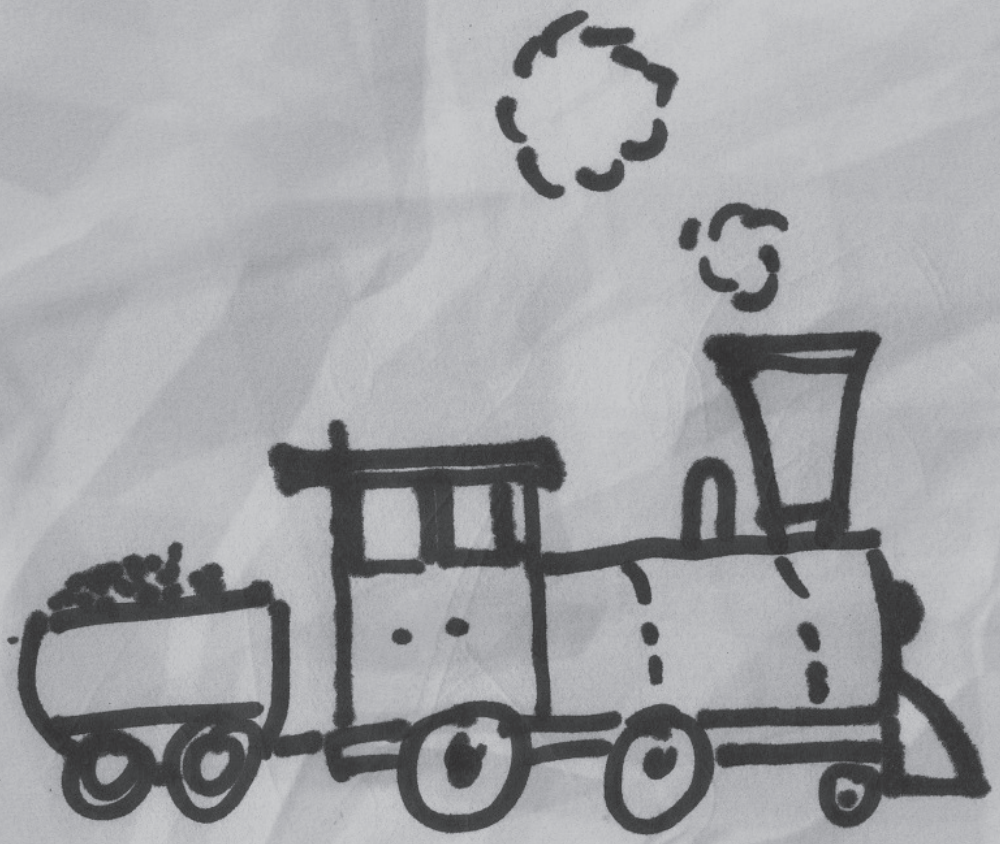
Childhood psychopathology and development of adult schizotypal symptoms

Fagel, S.S.A.A.

Chapter 3



Development of schizotypal symptoms following psychiatric disorders in childhood or adolescence

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Abstract

It was examined how juvenile psychiatric disorders and adult schizotypal symptoms are associated. 731 patients of the Department of Child and Adolescent Psychiatry of the University Medical Centre Utrecht, the Netherlands, with mean age of 12.1 years (*SD*=4.0) were reassessed at the mean age of 27.9 years (*SD*=5.7) for adult schizotypal symptoms using the Schizotypal Personality Questionnaire-Revised (SPQ-R; Vollema & Hoijtink, 2000). Differences between thirteen juvenile DSM categories and normal controls (*n*=80) on adult schizotypal total and factor scores were analyzed, using (M)ANCOVA. Pervasive developmental disorders (PDD), attention deficit hyperactivity disorders (ADHD), deferred diagnosis, sexual and gender identity disorders and depressive disorders had higher SPQ total scores when compared to normal controls ($p<0.001$). Higher levels of disorganized schizotypal symptoms were found for PDD, ADHD, and deferred diagnosis ($p<0.001$). The same diagnostic groups showed higher level of negative schizotypal.

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 & Spitznagel, 2001). These conditions have different gradient 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), and are considered to be persistent and lifelong and are supposed to present themselves differently at different ages. Consequently, developmental origins of schizophrenia spectrum pathology have been intensively studied throughout the years.

Longitudinal studies have demonstrated that the majority of adults with schizophrenia or psychosis could have been identified as clinically at high risk long before the onset of these disorders. For example, the results of the birth cohort study of Kim-Cohen et al. (2003) showed that 75 % of adults who were diagnosed with schizophrenia did receive a psychiatric diagnosis in childhood or adolescence before the age of eighteen, representing a broad array of juvenile disorders, such as juvenile anxiety, depression, attention deficit hyperactivity disorder (ADHD), and conduct and/or oppositional defiant disorder (ODD). The finding of a broad spectrum of disorders in childhood or adolescence preceding the development of schizophrenia and psychosis in adulthood has been confirmed by other studies that have reported diagnostic shifts towards schizophrenia and psychosis in childhood psychiatric disorders such as attention deficit disorders, disruptive disorders (De la Serna et al., 2010; Keshavan, Sujata, Mehra, Montrose, & Sweeney, 2002; Menkes, Rowe, & Menkes, 1967; Rubino et al., 2009), anxiety and depressive disorders (Kim-Cohen et al., 2003; Ambelas, 1992; Meyer et al., 2005), and pervasive developmental disorders (PDD; Rubino et al., 2009; Larsen & Mouridsen, 1997; Mouridsen, Rich, & Isager, 2008; Stahlberg, Soderstrom, Rastam, & Gillberg, 2004; Van Engeland & Van der Gaag, 1994).

These studies provide important information on how disorders of childhood and adolescence are associated with the development of psychopathology at the extreme end of the schizophrenia spectrum, i.e., meeting the Diagnostic Statistical Manual (DSM) criteria of schizophrenia or psychosis. However, since the majority of at-risk individuals do not meet these criteria at follow-up, but rather tend to manifest subclinical schizophrenia-like abnormalities (Chapman, Chapman, Kwapil, Eckblad, & Zinser, 1994; Raine, 1991; Tsuang, Stone, Tarbox, & Faraone, 2002), i.e., schizotypal symptoms, these individuals are absent

in these studies' samples. As a result, literature so far precludes deciding how disorders in childhood or adolescence may develop into these milder symptoms of schizophrenia spectrum pathology in adulthood. This makes the investigation of disorders in childhood or adolescence and its association with adult schizotypal symptoms a valid and noteworthy, yet relatively understudied, area of exploration with strong implications for clinical practice and research.

The present follow-up study therefore aims to investigate the development of adult-specific schizotypal symptoms in relation to psychopathology in childhood and adolescence. In line with the results of earlier studies focusing on disorders within the schizophrenia spectrum (Kim-Cohen et al., 2003; De la Serna et al., 2010; Keshavan et al., 2002; Rubino et al., 2009; Meyer et al., 2005; Larsen and Mouridsen, 1997; Mouridsen, Rich, & Isager, 2008), it is hypothesized that psychiatric disorders in childhood and adolescence such as PDD, ADHD, ODD, anxiety disorders, and depressive disorders are 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 whether juvenile psychopathology is specifically associated with one or more of the three main schizotypal symptom domains.

Methods

Procedure and participants

This study is part of a longitudinally prospective study designed to evaluate both global and clinical outcomes in adulthood of patients, referred during 1984–2004 (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 a follow-up study during 2006–2010 (T2): (1) a diagnosis based on DSM criteria of the American Psychiatric Association (1980; 1987; 1994) at T1, (2) aged 18 years or younger at T1, (3) no axis II DSM diagnosis of mental retardation (IQ<70) at T1, (4) no axis I DSM diagnosis before or at T1 with child psychotic disorder, schizophrenia or any other psychotic disorder, bipolar disorder or dissociative disorder, and (5) aged 18 years or older at T2. The 2083 patients who were eligible for follow-up were sent a letter with information about the aims of the study, asking them to participate. Whenever possible, the patients were contacted by phone to encourage participation. A total of 1315 patients declined participation, leaving 768 patients in the study. Because there were too few (<20)

Table 1. The number of participants by juvenile DSM diagnostic category.

Juvenile DSM diagnostic categories of the participants	***n***
Eating disorders	153
Pervasive Developmental Disorders	100
Disruptive disorders	89
Depressive disorders	82
Attention Hyperactivity Disorders	78
Other conditions that may be a focus of clinical attention	44
Anxiety disorders	43
Somatoform disorders	28
Deferred diagnosis	27
Other disorders of infancy, childhood, or adolescence	26
Adjustment disorders	21
Tic-disorders	20
Sexual and Gender Identity disorders	20

cases of learning disorders (*n*=6), communication disorders (*n*=9), elimination disorders (*n*=11), sleep disorders *(n*=1), impulse-control disorders not elsewhere classified (*n*=2), unspecified mental disorder (non-psychotic) (*n*=6), delirium, dementia, amnestic and other cognitive disorders (*n*=1), and substance-related disorders (*n*=1) to provide adequate power to test group differences, these subjects (*n*=37) were not evaluated. The final sample consisted of 731 (327 males and 404 females; 35.1%) patients, distributed across thirteen DSM diagnostic categories, with mean age of 12.1 years (*SD*=4.0) at T1, and reassessed at the mean age of 27.9 years (*SD*=5.7) at T2. The intelligence of the patient group was within the normal range with a total IQ of 103.3 (*SD*=14.7), a performance IQ of 103.8 (*SD*=15.7), and a verbal IQ of 103.1 (*SD*=14.5).

Eighty male normal controls were recruited from the general population using recruitment advertisements. Mean age of this group was 29.9 years (*SD*=7.2). None of the controls met the criteria for an axis I psychiatric disorder in adulthood, as shown by screening with the mini-international neuropsychiatric interview plus (MINI-plus; Sheehan et al., 1998). All subjects voluntarily agreed to participate in this study and signed informed consent. 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 the representativeness of the sample, age and gender distributions as well as the distribution of the juvenile DSM classifications of participants and non-participants were compared. Proportionally more participants appeared to be female (55.3% female participants vs. 37.8% female non-responders; $F(1,2083)=58.796$, $p<0.001$). The participants were slightly older at time of childhood assessment (M=12.1 year; *SD*=4.0) than the non-responders (M=11.3 year; *SD*=4.0) at T1, ($F(1,2057)=21.403$, $p<0.001$, $\eta_p^2=0.01$), although this was a very small effect. Participants had a slightly higher intelligence than non-responders, i.e., total IQ (M=103.3; *SD*=14.7 vs. M=99.7; *SD*=14.2), ($F(1,858)=12.259$, $p<0.001$, $\eta_p^2=0.014$), verbal IQ (M=103.1; *SD*=14.5 vs. M=98.8; *SD*=14.4), ($F(1,811)=16.400$, $p<0.001$, $\eta_p^2=0.020$). No differences were found in performance IQ ($p=0.074$). The participants did not differ from the nonparticipants on age at T2 ($p=0.758$). Although the distribution of juvenile DSM classifications within the non-participants and participants was similar for most diagnostic categories, an relative overrepresentation of participants was found in eating disorders (20.9 vs. 9.9%), and a relative underrepresentation of participants was found in ADHD (10.7 vs. 16.4%), ($F(21,2083)=143.763$, $p<0.001$).

Measures

Psychiatric disorders in childhood

Psychiatric diagnosis at time of referral resulted from consensus between at least two board certified psychiatrists on the basis of a complete child psychiatric examination, consisting of a semi-structured clinical diagnostic interview focused on the presence of DSM criteria, the subjects' developmental history, a review of medical records and observation of the child. All diagnoses were converted to DSM-IV-TR (APA, 2000) classifications based on DSM-IV-TR conversion guidelines. DSM-IV-TR preference rules were handled: PDD diagnosis was preferred above comorbid ADHD diagnosis. The juvenile psychiatric records of thirteen subjects in which axis II was used to indicate prominent maladaptive personality features, indicating a personality disorder in development, were reexamined by a senior psychiatrist. This resulted in all of these thirteen subjects being assigned to the category of 'deferred diagnosis'. Juvenile disorders were grouped into the following thirteen broad diagnostic categories: (1) PDD (299.0; 299.80), (2) Tic disorders (307.23; 307.22; 307.21; 307.20), (3) anxiety disorders (300.0; 300.01; 300.02; 300.21; 300.23; 300.29; 300.3; 309.81), (4) somatoform disorders (300.11; 300.7; 300.82; 307.80), (5) sexual and gender identity disorders (302.2;302.3; 302.6; 302.81; 306.85; 302.89; 302.9), (6) Eating disorders (307.1; 307.51; 307.50), (7) adjustment disorders (309.0; 309.24; 309.28; 309.3; 309.4; 309.9), (8) other conditions that may be a focus of clinical attention (V61.10; V61.20; V61.80; V61.90; V62.3; V62.81; V62.82; V62.89; 313,82; V15.81; V61.21), (9) ADHD (314.00; 314.01; 314.9), (10) disruptive disorders (312.9; 313.81; 312.89), (11) depressive disorders (296.2; 296.3;300.4; 311.0), (12) deferred diagnosis (301.0; 301.2; 301.22; 301.4;301.81; 301.9; 301.83; 301.7; 301.5; 799.9), and (13) other disorders of infancy, childhood, or adolescence (307.3; 313.23; 313.89; 313.9; 309.21).

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 traits, modeled on the diagnostic and statistical manual of mental disorders (American Psychiatric Association, 1994) conceptualization of schizotypy (Raine, 2006). Factor analytical studies have revealed three dimensions of schizotypy, i.e., positive, negative, and disorganized schizotypy (Vollema & Hoijtink,

2000; Raine et al., 1994). This factor structure has been found to be invariant to gender, ethnicity, religion, and social background (Reynolds et al., 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 (Vollema et al., 2002). Higher scores on the SPQ-R indicate higher levels of schizotypal symptoms.

Statistical analysis

Statistical analyses were performed using the statistical package for the social sciences 18.0 (SPSS Inc, Chicago, Il, USA). All variables were screened for normality and outliers, defined as more than 2.5 standard deviations away from the mean of each group. Outlier scores were replaced with scores 2.5 standard deviations away from the group mean accordingly. Sixty-nine scores were replaced: fifteen high total SPQ scores, twenty-six high positive SPQ scores, fifteen high negative SPQ scores, and thirteen high disorganized SPQ scores. We examined age at T2 and gender as potential confounding variables. As only age at T2 was associated with adult schizotypal symptoms, this variable was included in our statistical model as covariate. After square root transformation, univariate and multivariate analyses of covariances ((M)ANCOVA) were performed, using simple contrasts with the normal controls as reference category, with SPQ-R total score and its three-factor scores as dependent variables, respectively, contrasting each DSM category with the normal controls. When the MANCOVA resulted in a significant multivariate effect, the univariate group effects on specific subscales were examined. Partial eta squared (η_p^2) was calculated to estimate effect sizes, with η_p^2~0.03 representing a weak, η_p^2~0.06 a moderate effect and $\eta_p^2 \geq 0.14$ a large effect (Stevens, 2002). Conservative $p<0.01$ by two-tailed test was considered as statistically significant.

Results

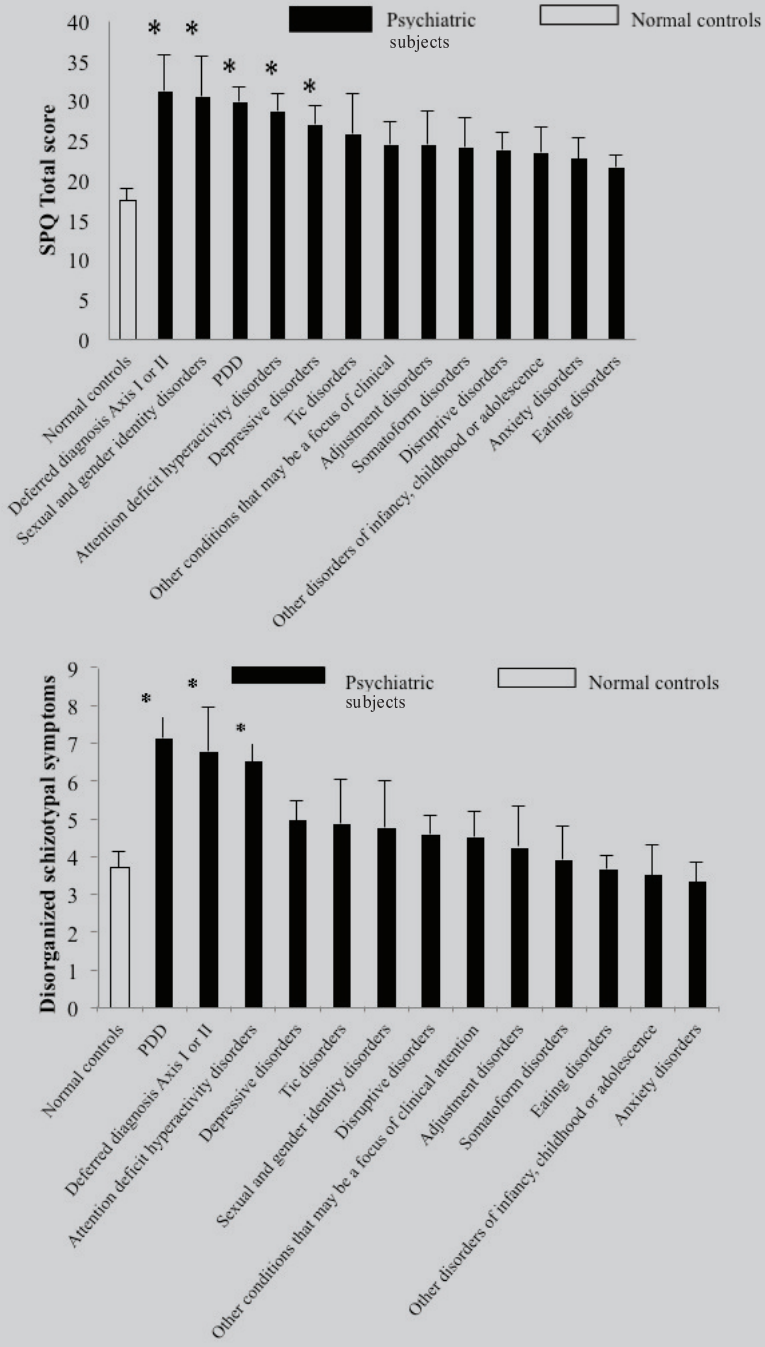
Psychiatric disorders in childhood and adolescence and adult schizotypal symptoms

The ANCOVA of the SPQ-R total score revealed a significant weak effect for group (F(13,796)=2.629, p=0.001, η_p^2=0.041), with no effect of age at T2 (p=0.239). Although all adults with a juvenile psychiatric diagnosis had higher SPQ total scores in comparison with normal controls, the simple contrast with normal controls revealed that differences were significant for five diagnostic groups, i.e., deferred diagnosis, sexual and gender identity disorders, PDD, ADHD, and depressive disorders (0.001<p<0.007), and not for the other categories (0.05<p<0.222). (See Fig. 1).

Psychiatric diagnoses during childhood and adolescence and adult-specific schizotypal symptoms

The MANCOVA of the three schizotypal factors revealed a significant weak multivariate effect of group (F(39,2388)=2.631, p<0.001, η_p^2=0.041), but not of age at T2 (p=0.308). The univariate simple contrast analysis, with normal controls as reference, revealed a significant weak effect of group on negative schizotypal symptoms (F(13,796)=4.631, p=0.001, η_p^2=0.042) for seven juvenile diagnostic groups, i.e., PDD, ADHD, deferred diagnosis, sexual and gender identity disorders, depressive disorders, disruptive disorders, and other conditions that may be a focus of clinical attention (0.001<p<0.01). A significant moderate effect was found for group on disorganized schizotypal symptoms (F(13,796)=3.510, p<0.001, η_p^2=0.063) for three juvenile diagnostic groups, i.e., PDD, ADHD, and deferred diagnosis (0.001<p<0.009; see Figs. 2 and 3). No significant differences between normal controls and juvenile DSM diagnostic groups were found for positive schizotypal symptoms (p=0.110).

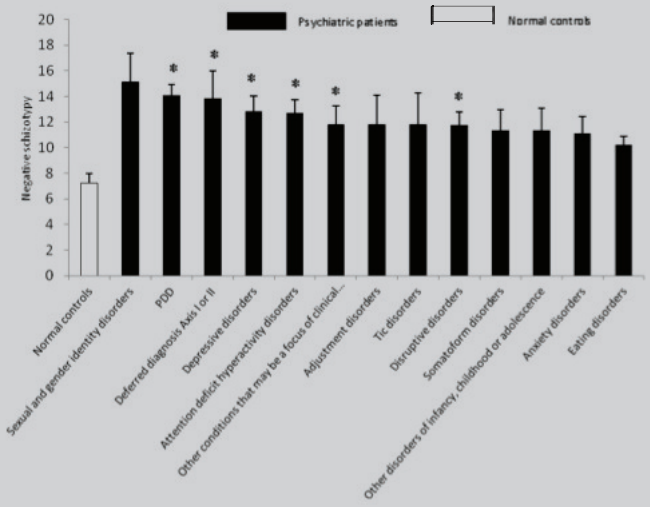
Figure 1. Adult schizotypal symptoms in juvenile psychiatric subjects and normal controls



Values are means, with standard error of the mean represented by vertical bars. * = $p<.01$.

Figure 3.

Level of adult negative schizotypal symptoms in juvenile psychiatric subjects and normal controls



Values are means, with standard error of the mean represented by vertical bars. * = $p<.01$.

Discussion

The present follow-up study explored how and to what extent children and adolescents with a broad range of psychiatric disorders presented with general as well as specific schizotypal symptoms in adulthood. All psychiatric diagnostic categories scored higher on general schizotypal symptoms when they were adults in comparison with normal controls. This suggests a certain generality for the psychopathological domains. A caveat is in place, however. It was found that only children and adolescents diagnosed with PDD, ADHD, deferred diagnosis, sexual and gender identity disorders or depressive disorders scored significantly higher on general schizotypal symptoms than normal controls when they were adults. Also, for three psychiatric disorders, i.e., PDD, ADHD, and Deferred diagnosis, the levels of both disorganized and negative symptoms in adulthood were higher. Four other groups of children with psychiatric disorders showed higher scores on negative schizotypal symptoms in adulthood, i.e., sexual and gender identity disorders, depressive disorders, disruptive disorders, and 'other conditions that may be a focus of clinical attention'. No significant higher levels were found for positive schizotypal symptoms in adulthood. It is concluded that childhood diagnoses are differentially associated with future development of general and specific schizotypal symptoms. This underscores in our view that, apart from a general association between childhood pathology and future symptomatology, certain childhood pathologies are more liable than others to future unfavorable psychopathological development.

The elevated levels of general schizotypal symptoms in the respective DSM categories add to the outcome of previous studies on the association between a variety of juvenile psychiatric disorders and the development of adult disorders within the extreme end of the schizophrenia spectrum. This is further remarkably in line with the legacy of both Kraepelin and Kahlbaum (Hoenig, 1995). Kahlbaum noted that 'snapshot' observations of patients' symptoms could be misleading because how an illness manifests itself may vary over time. Kraepelin noted that symptoms change with time and patients should therefore be observed throughout their life. However, from a historical context of clinical specialization, the focus of clinicians devoting their practice and research to disorders of childhood was separated from clinicians with focus on disorders of adulthood (Frances, First, & Pincus, 1995). This has led to an arbitrary bifurcation in conceptualization and classification of mental disorders across developmental stages (Pine et al., 2002). The current result thus stresses the importance for clinicians to acknowledge the developmental and heterogenetic course of juvenile psychiatric disorders.

The higher levels of schizotypal symptomatology reported for the five DSM

diagnostic categories might be suggestive for the idea that psychiatric disorders in childhood or adolescence are a more general expression of a liability to schizophrenia spectrum pathology in future life. This finding is in line with the neurodevelopmental hypothesis of schizophrenia spectrum pathology (Weinberger, 1987; Murray & Lewis, 1987). This hypothesis states that, in at least a subgroup of subjects, schizotypal symptomatology might be due to pathological processes originating from either a genetic predisposition or a spontaneous genetic mutation in early life, which by interplay with environmental factors during prenatal, perinatal or postnatal life, will affect plastic neural systems during development (Weinberger, 1987; Murray & Lewis, 1987).

PDD and ADHD were the two neurodevelopmental disorders that were significantly associated with the development of higher levels of adult disorganized as well as negative schizotypal symptoms. The existing literature has so far mainly reported about ADHD (De la Serna et al., 2010; Keshavan et al., 2002; Menkes et al., 1967; Rubino et al., 2009) and PDD (Rubino et al., 2009; Van Engeland and Van der Gaag, 1994) being associated with the risk for development of psychopathology at the extreme end of the schizophrenia spectrum, i.e. schizophrenia and psychosis. The current results suggest that a disorder within the ADHD and PDD spectrum might be associated with higher risk for development of schizotypal symptomatology, especially with respect to negative symptoms and disorganized behavior. Previous studies did not focus on disorganized and negative symptoms in adulthood in subjects who were diagnosed with ADHD at childhood or adolescence.

The current finding of higher levels of negative symptoms and disorganized behavior in adults who were diagnosed with PDD in childhood is in line with the outcome of studies that reported illogical thinking and loose associations in children with PDD (Solomon, Ozonoff, Carter, & Caplan, 2008; Van der Gaag, Caplan, Van Engeland, Loman, & Buitelaar, 2005), and about the presence of disorganized (Dykens, Volkmar, & Glick, 1991; Konstantareas & Hewitt, 2001) and negative symptoms (Konstantareas & Hewitt, 2001; Rumsey, Andreasen, & Rapoport, 1986) in adolescents and adults with PDD.

Surprisingly, there is no evidence for any of the evaluated diagnostic groups of an increased level of positive schizotypal symptoms. Since insight is more or less inversely proportional to the level of positive symptoms (Trevisi et al., 2012), one might argue that the use of a self-report questionnaire might have consequently led to an underestimation of the reported positive symptoms. This certainly being probable, one may also wonder whether this issue poses a threat to the validity of the Schizotypal Personality Questionnaire to assess schizotypal positive symptoms. The SPQ, however, has good convergent validity and evidence exists that the SPQ constitutes a valid way to

assess positive schizotypal symptoms. For example, Raine (1991) showed high correlations with the two SPQ subscales that together cover the positive symptoms (r=0.58 with odd beliefs/magical thinking and r=0.65 with odd speech) with dimensional scores for schizotypal personality disorder from SCID Interview.

Children with a 'non-descriptive' diagnosis, i.e., 'deferred diagnosis on axis I or II' represent a diagnostic group showing the highest level of overall schizotypal symptomatology, the second highest level of disorganized schizotypal symptoms, and the third highest level of negative schizotypal symptoms in adult life. This subgroup of children with atypical behavior that does not fit any DSM category has not been associated with the development of schizophrenia spectrum pathology in the literature before. This juvenile behavior that is best described as 'odd' or 'incongruent' (Ambelas, 1992; Hollis, 1995; Zeitlin, 1986) is probably labeled by clinicians as 'deferred diagnosis' to stress the severity of these developmental problems, but yet find no category that fits their behavior in childhood or adolescence. It might be speculated that the nature of these associations possibly relates to a disruption of communication processes, where the problem of communication lies in the appropriate expression and understanding of meaning in a social context. Hollis (1995) proposed that as a result of this failure to utilize socially agreed rules of communication, social isolation might follow. This might explain the present association of this juvenile diagnosis being associated with higher levels of negative schizotypal symptoms in adulthood. The association with higher levels of adult disorganized behavior might be the result of a developmental progression from a long-standing communication disorder to the onset of thought disorder and disorganized behavior (Hollis, 1995). Future research should clarify these issues.

Four juvenile psychiatric groups, i.e., sexual and gender identity disorders, depressive disorders, disruptive disorders, and 'other conditions that may be a focus of clinical attention', showed higher levels on negative schizotypal symptoms, in comparison with normal controls. With regard to earlier studies that reported an association between depressive and disruptive disorders with future schizophrenia spectrum pathology in general (Kim-Cohen et al., 2003; Rubino et al., 2009; Ambelas, 1992; Meyer et al., 2005), the current finding further specifies that these disorders are only associated with negative schizotypal symptoms in adult life in the present study.

Of note is the finding that children and adolescents with sexual and gender identity disorders and 'other conditions that may be a focus of clinical attention' demonstrate high levels of negative schizotypal symptoms in adulthood. The association between sexual and gender identity disorders and the development of subclinical symptoms within the schizophrenia spectrum has only sparsely been addressed (De Cuypere, 1993; Finney, Brandsma, Tondow, & Lemaistre, 1975), which is probably due to the extremely low prevalence of the disorder for both males (1 of 12,000) and females (1 of 30,000; Bakker, Van Kesteren, Gooren, & Bezemer, 1993). Replication of this finding is important to evaluate its stability. As of yet, no studies report about the risk for schizophrenia symp-

tomatology in adulthood of the childhood condition 'other conditions that may be a focus of clinical attention'. This category is used when the problem identified is either unrelated to a separate mental disorder, or is significant enough to require attention separate from the mental disorder, and is taken to constitute a 'milder' type of psychiatric problem, but the current report of high levels of negative schizotypal symptomatology suggests otherwise. More specifically, the present group of 44 children consists in majority of subjects diagnosed with relational problems (*n*=27) and with a phase of life problem (*n*=14) at juvenile age, suggesting the existence of interaction and social problems. The association between social impairment and the risk for development of schizophrenia spectrum pathology has been extensively addressed by retrospective studies (Foerster, Lawis, Owen, & Murray, 1991; Rossi, Pollice, Daneluzzo, Marinangeli, & Stratta, 2000; Watt & Lubensky, 1976; Zigler et al. 1977) and birth cohort studies (Bearden et al., 2000; Crowe, Done, & Sacker, 1995; Davidson et al., 1999; Malmberg et al., 1998).

Although anxiety disorder in childhood or adolescence has been associated with the development of psychopathology at the extreme end of the schizophrenia spectrum, i.e., schizophrenia and psychosis, in earlier studies (Kim-Cohen et al., 2003; Ambelas, 1992; Meyer et al., 2005), the present study did not find any association between this disorder and specific future schizotypal symptoms. Since this is the first study to report on specific schizotypal symptoms, this issue needs further investigation.

Obviously, the nature of the associations between psychiatric disorders in childhood and adolescence and adult disorganized and/or negative schizotypal symptoms needs further investigation. With regard to disorganized schizotypal symptoms, the results of some studies suggest that impaired thinking appears to reflect poorer communication skills (Van der Gaag, Caplan, Van Engeland, Loman, & Buitelaar, 2005), while others suggest that impaired thinking originates from deficits in executive functioning (Barneveld, De Sonneville, Van Rijn, Van Engeland, & Swaab, 2013; Kerns, 2007). In addition, in light of Bleuler's distinction between fundamental symptoms (i.e., basic or primary symptoms that are direct manifestations of the morbid condition) and accessory symptoms (i.e. secondary symptoms which represent an adaptation to the primary disturbance; Bleuler, 1961; Raskin, 1975), it needs to be clarified whether negative schizotypal symptoms might (partly) be the consequence of a variety of other factors, such as neuroleptic side effects, living with a chronic disorder, environmental understimulation (Flaum & Andreasen, 1995), or the effect of environmental stressors that these children with psychopathology might experience, which, when combined with a relevant genetic risk for neuropsychiatric disorders, might result in adult-onset neuropsychiatric disorders, such as psychotic depression (Niwa et al., 2013).

To rule out any effect of age, we covaried for age in the analyses of risk for the development of schizophrenia spectrum pathology. Hence, the association between psychiatric disorders of childhood and adolescence and adult schizotypal traits was independent of age.

Strengths and limitations of the study

Inherent to a long follow-up period (15.3 years), the present study suffered from attrition, being able to followup on 35% of the original sample. Nevertheless, the number of 731 subjects in the final sample is considered to be substantial and representative. The background variables of the participants were quite similar to that of the non-participants, with slightly more female and older participants at follow-up and a slightly higher intelligence in comparison to the non-responders. 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. Moreover, since the mean age of participants was 27.9 (*SD*=5.7) years, not all subjects may have passed the (full) period of risk for schizophrenia spectrum psychopathology, the level of schizotypal symptomatology might therefore be underestimated. Because we did not assess schizotypal symptoms in childhood, it was therefore not possible to determine whether these symptoms have increased in severity at follow-up. In addition, the screening by self-report does carry some limitations, as compared with interviews or observations. 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). In future studies, direct observation of these specific symptoms might be a way to address these additional questions. Besides these limitations, the current follow-up study suited the purpose to illustrate the complex dynamics of psychopathology in childhood or adolescence and the development of symptoms within the schizophrenia spectrum. We feel confident to state that it seems important for clinicians to be aware of the higher risk for schizotypal symptomatology in adulthood following childhood psychiatric disorders and that specific patterns of adult schizotypal symptomatology are associated with different types of juvenile psychiatric disorder. Thus, future research is necessary to address the mechanisms underlying this risk.

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