# Childhood psychopathology and development of adult schizotypal symptoms

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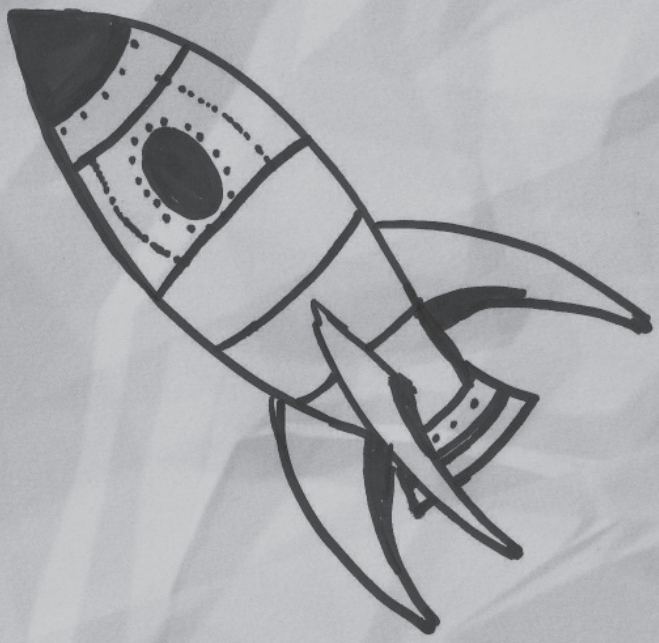
# Chapter 6



# General discussion

The majority of children and adolescents at risk for a schizophrenia spectrum disorder does not meet the criteria for a schizophrenia spectrum disorder in adulthood, but tends to manifest subclinical schizophrenia-like abnormalities (Chapman, Chapman, Kwapil, Eckblad, and Zinser, 1994; Raine, 1991; Tsuang, Stone, Tarbox, and Faraone, 2002), i.e., schizotypal symptoms. The investigation of how behavioral and intellectual (dys)functioning develops into adult schizotypal symptoms, and how these schizotypal symptoms affect a person's QoL therefore constitutes a valid and noteworthy, yet relatively understudied, area of exploration with strong implications for clinical practice and research. Moreover, with most studies only including typically developing controls for comparison and since psychiatric disorders such as depression (Ishak et al., 2011), ADHD (Danckaerts et al., 2010), and psychopathology in general (Lehman, 1983) have commonly been found to unfavorably affect OQoL and SQoL, and other psychiatric disorders in adulthood, such as ADHD (De la Serna et al., 2010; Keshavan et al., 1967; Rubino et al., 2009), anxiety and depressive disorders (Kim-Cohen et al., 2003; Meyer et al., 2005; Zammit et al., 2004; Koenen et al., 2009) have also been associated with juvenile behavioral and intellectual markers, it is presently unclear whether the identified abnormalities are specifically indicative for the development of symptoms within the schizophrenia spectrum or might be predictive of development of psychopathology in general. We therefore investigated juvenile behavioral and intellectual precurors of schizotypal symptoms and the patient's QoL, selecting a broad sample of patients who all sought psychiatric care during child age. Further, as the clinical presentation of symptoms of future disorders at the extreme of the schizophrenia spectrum are different in boys and girls (Done, Crow, Johnstone, and Sacker, 1994; Salem and Kring, 1998; Welham et al., 2009), the specificity of the reported behavioral and intellectual problems in relation to schizotypal symptoms in adulthood for both boys and girls is further explored.

In sum, the current series of studies aimed to identify to what extent behavioral

and emotional problems and its underlying mechanisms in juvenile psychopathology are associated with the development of adult schizotypal symptoms and what the impact of these symptoms is on a person's Quality of Life. In addition, it is studied whether the outcome is different for boys and girls.

In contrast to earlier studies that have mainly evaluated QoL comparing psychiatric patients with typically developing controls, the study that is reported in chapter two focused on the question whether and how the presence of adult schizotypal symptoms influences the level of objective and subjective QoL using a sample of patients covering a wide spectrum of psychiatric disorders. It was found that each schizotypal dimension, i.e., positive, negative and disorganized schizotypal symptoms, unfavorably affected each domain of objective QoL. However, impoverished subjective QoL, and in particular dissatisfaction with social contacts, was predominantly related to negative schizotypal symptoms. These findings show that the presence of schizotypal symptomatology in subjects alters QoL in an unfavorable way. Negative schizotypal symptoms most strongly affected OQoL and SQoL.

In chapter three we studied how and to what extent children and adolescents with a broad range of psychiatric disorders presented with schizotypal symptoms in adulthood. We therefore used the nosological approach embodied in the Diagnostic and Statistical Manual (DSM) of the American Psychiatric Association (APA, 1980; 1987; 1994) at the time of juvenile assessment. Albeit all children and adolescents with psychiatric diagnoses scored higher on general schizotypal symptoms than typically developing controls when they were adults, the differences were only significant for five psychiatric categories, namely Pervasive Developmental Disorders (PDD), Attention Deficit Hyperactivity Disorders (ADHD), Deferred diagnosis, Sexual and Gender Identity Disorders and Depressive disorders. 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. These groups were Sexual and Gender Identity disorders, Depressive disorders, Disruptive disorders, and 'Other conditions that may be a focus of clinical attention'. No significantly higher levels were found for positive schizotypal symptoms in adulthood. Therefore we concluded that individuals with juvenile psychiatric problems were more likely to develop negative and disorganized schizotypal symptoms in adulthood when compared to normal controls and that specific patterns of adult schizotypal symptomatology were associated with different types of juvenile psychiatric disorders.

Whereas in chapter three the nosological approach of the DSM was applied,

in chapter four we opted for a dimensional approach. In addition to the vast majority of studies using information from parents about a child's behavior, we studied how behavioral problems in childhood and adolescence as reported by their teachers precede distinctive schizotypal symptoms in adulthood. It was further examined whether the outcome was different for boys and girls. We found that five out of eight behavioral subscales as measured by the Teacher Report Form (TRF; Verhulst, Van der Ende, & Koot, 1997) were associated with disorganized schizotypal symptoms. Thought problems and rule breaking behavior in childhood were associated with positive schizotypal symptoms in adulthood. Remarkably, thought problems and positive and disorganized schizotypal symptoms were only associated in boys, while in girls externalizing problems were associated with disorganized symptoms. We therefore concluded that thought problems (observed by the teacher) were identified as strongest behavioral indicator of future schizotypal symptoms, especially in boys and that subjects burdened by a broad range of behavioral problems in childhood and adolescence are likely to be the ones that will show the most severe adult disorganized symptoms.

In chapter five it was studied whether level of intellectual (dys)functioning in juvenile psychopathology was associated with the development of adult distinctive schizotypal symptomatology, whether this relation was valid for specific intellectual subdomains, and whether this relation held for schizotypal symptoms in general or for specific schizotypal symptom domains. Again, the role of gender was explored. We found no evidence for general and specific domains of intelligence in juvenile psychopathology being related to the development of general or distinctive schizotypal symptomatology in adulthood. This was true for boys as well as for girls. 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 at 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). Studies have reported better premorbid functioning during childhood and adolescence among females (compared to males) who later develop schizophrenia (Goldberg et al., 1995; Walker, 1993; Walder, Mittal, Trotman, McMillan, & Walker, 2008). Because of the present findings are concerning a sample only consisting of patients who presented with juvenile psychopathology, the absence of associations might be interpreted as follows. First, the

present results are based on the study of individuals who all show juvenile psychopathology. However, juvenile intellectual markers have also been identified in relation to the development of other psychiatric disorders, such as ADHD (De la Serna et al. 2010; Menkes, Rowe, & Menkes, 1967), anxiety and depressive disorders (Zammit et al., 2004; Koenen et al., 2009). In addition, premorbid intelligence and the development of adult schizophrenia spectrum pathology has only been investigated among schizophrenic patients who were compared to typically developing controls. Therefore the present absence of associations might be interpreted as telling us that intellectual markers are related to psychopathology in general rather than being specific for the development of schizotypal symptoms. In addition, with the present study focusing on subclinical schizotypal symptoms instead of disorders at the extreme end of the schizophrenia spectrum, the current results suggest that intellectual markers are too subtle to detect developmental risk in milder forms of schizophrenia spectrum pathology, i.e., schizotypal symptomatology, and may only be found at the extremes of the spectrum, i.e., when looking at the development of schizophrenia or psychosis (Park et al., 2012).

So in conclusion, the results of the present studies show how schizotypal symptoms may develop following all kinds of childhood problems and how these symptoms unfavorably influence a person's quality of life. It is important for clinicians to be aware of the higher risk for schizotypal symptomatology in adulthood following juvenile psychopathology and juvenile behavioral problems and to be aware of the risk that psychopathology may manifests itself in changing symptom patterns over time.

## *Comparison with other follow-up studies*

In this section possible explanations for the present findings, as well as methodological limitations of the study, are discussed.

One of the main factors distinguishing the present study from the majority of other longitudinal studies is that these studies were primarily based on individuals with disorders at the extreme end of the schizophrenia spectrum, such as schizophrenia or psychosis. By applying a nosological approach, these studies start with the assumption that disorders either are present or absent, based on present-versus-absent judgments of each critical feature (Verhulst et al., 1995). However, this approach is often criticized for its inability to classify subthreshold traits and symptoms. Moreover, the majority of individuals at risk does not show a disorder at the extreme end of the schizophrenia spectrum,

but rather tends to manifest a host of subclinical schizophrenia-like abnormalities (Raine, 1991; Chapman et al., 1994; Tsuang et al., 2002), i.e., schizotypal symptoms, that also impair daily functioning. With the present studies investigating behavioral and intellectual (dys)functioning in childhood or adolescence and its association with adult schizotypal symptoms and how these affect QoL therefore constitutes a valid and noteworthy, yet relatively understudied, area of exploration with strong implications for clinical practice and research.

Second, schizophrenia spectrum pathology is a very heterogeneous condition, with a variety of diagnostic criteria and definitions (Kendell, 1987; Pfol & Andreasen, 1986). The variability within schizophrenia spectrum pathology is even more underscored by the fact that patients generally yield a greater score variance compared to normal controls (Shakow, 1963). One approach that might progress insight into the mechanisms that facilitate development of schizophrenia spectrum pathology is therefore the investigation of more homogeneous symptom clusters of schizophrenia spectrum pathology, i.e., positive (hallucinations and delusions), negative (emotional and behavioral disturbances), and disorganized symptoms (difficulty in pursuing a logical train of thought and understanding and utilizing information). Following this approach, the present results revealed more insight in that specific symptoms of schizophrenia spectrum pathology were associated with different types of juvenile psychiatric disorders and behavioral abnormalities, and that negative schizotypal symptomatology most strongly affected OQoL and SQoL. These findings underscore that the investigation of type of schizotypal symptomatology matters.

Another important factor relates to the type of sample of the present study that only consisted of individuals with juvenile psychopathology. This choice contrasts the majority of studies using typical developing controls for comparison and might explain the relatively small effects that we found across the different studies. However, the study of individuals with juvenile psychopathology is of marked importance, since similar juvenile behavioral and intellectual markers have been identified in relation to other psychiatric disorders, such as ADHD (De la Serna et al., 2010; Keshavan, Sujata, Mehra, Montrose, & Sweeney, 2002; Menkes et al., 1967; Rubino et al., 2009), anxiety and depressive disorders (Kim-Cohen et al., 2003; Meyer et al., 2005; Zammit et al., 2004; Koenen et al., 2009), and QoL is also lower in general psychopathology (Lehman, 1983). The present results show that even in a group of patients who all show psychiatric problems, several juvenile behavioral problems and psychiatric disorders in particular are more at risk for development of schizotypal symptomatology in adult life and that level of schizotypal symptoms, in particular negative symptoms most strongly affected OQoL and SQoL. No associations

were found between juvenile intelligence and the development of adult schizotypal symptoms within the present sample of subjects presenting with juvenile psychopathology.

A third issue relates to the decision to explore outcome in relation to gender. The majority of studies focused on general populations of subjects with men being grossly overrepresented, and this may have biased literature from a male perspective. The sample sizes of the present studies enabled to delineate meaningful associations between behavioral and intellectual (dys)functioning and future schizotypal symptomatology in relation to gender. This distinction has led to important insight into gender specific results. For example, with regard to behavioral abnormalities in childhood and adolescence as reported by the child's teachers, thought problems and positive and disorganized schizotypal symptoms were only associated in boys, while in girls externalizing problems were associated with disorganized symptoms. These findings show that it is important to examine gender specific indicators of schizophrenia spectrum pathology.

## Limitations

First, inherent to the long follow-up period of no less than eleven to fifteen years, the present study suffered from attrition. Dependent on the criteria that were applied in the study, this has led to different numbers of patients that were included for follow-up in each study. Nevertheless, the numbers of subjects in the samples were considered to be substantial and representative, with the background variables of the participants being quite similar to that of the nonparticipants.

Second, although we were able to control for several important background variables in the present study, we were not able to take aspects into account that are known to delay, if not prevent, the development of disorders at the extreme end of the schizophrenia spectrum (McGlashan et al., 2006; McGorry et al, 2002; Morrison et al., 2004), such as the application of pharmacotherapy, or psychological and psychosocial interventions. This might have influenced the present findings.

A third issue relates to the mean age of the participants in adulthood. Since the participants were in their mid twenties, not all subjects may have passed the (full) period of risk for schizophrenia spectrum psychopathology. Therefore, the level of schizotypal symptomatology might have been underestimated. Future studies using a longer follow-up period might reveal insight into this issue.

A fourth issue concerns the screening by self-report that 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 and schizotypal individuals seem to have no significant loss of insight, in that it would affect their self-perceptions and thus invalidate the results on subscales of schizotypal signs (Raine, 1991).

A fifth issue relates to the level of intelligence in the present sample. While the majority of studies using psychiatric samples are characterized by a relatively low level of intelligence, the level of intelligence of the current sample was relatively high and fits perfectly within the normal range. With regard to the study of how intellectual functio-ning in childhood and adolescence is associated with adult schizotypal symptoms, this might have restricted the number and magnitude of the significant correlations.

Finally, the present study concerns a clinically referred sample. The findings might therefore pertain to those subjects who presented with considerable juvenile behavioral impairments and not to those subjects who were relatively inconspicuous as a child.

Besides these limitations, the present study suited the purpose to illustrate the complex dynamics of psychopathology and intellectual functioning in childhood and adolescence and the development of symptoms within the schizophrenia spectrum and how this affects a subjects' quality of life. In the next section clinical implications of the present study will therefore be addressed.

## Clinical and research implications

For intervention and prevention purposes it is of importance to know which and to what extent behavioral abnormalities and intellectual domains are especially important as predictor for later development of schizotypal symptomatology. In addition, it is important to know how these symptoms affect a person's life. Although we have strategically focused on more homogeneous symptoms within the heterogenetic course of schizophrenia spectrum pathology, we should note that although we did find some clues to the development of schizotypal symptomatology, the effects of these findings were relatively small. Clinicians should therefore interpret the reported findings as being a small step

forward in the unraveling of the developmental course of what Bleuler characterized as the ´Group of Schizophrenias` (Bleuler, 1911).

On the other hand, the present findings did show that even across the long follow-up period of eleven to fifteen years, the investigation of more homogeneous symptoms within the spectrum has progressed insight in that some behavioral problems and aspects of intellectual (dys)functioning in juvenile psychopathology were indeed associated with the development of schizotypal symptomatology. This result has progressed insight into the mechanisms that facilitate schizophrenia spectrum pathology and provides several important implications for clinical and research purposes.

First, these results stress the importance to acknowledge the developmental and heterogenetic course of behavioral problems in childhood and adolescence and the importance to follow patients across the lifespan. This is an important message for clinical practice, that from a historical context of clinical specialization has devoted their practice and research to disorders of childhood or adulthood (Frances, First, & Pincus, 1995) which has led to an arbitrary bifurcation in conceptualization and classification of mental disorders across developmental stages (Pine et al., 2002). In addition, our results stress the challenge that has been articulated in the recent article of Van Os (2013). Van Os proposes that the challenge in the years to come is to understand how the earliest expressions of psychopathology form part of a dynamic circuit of symptoms that affect and reinforce each other, gradually differentiating across stages of psychopathology into more specific, but still largely overlapping, clinical syndromes.

Second, the finding that subjects with juvenile psychopathology were more likely to develop severe adult schizotypal symptomatology as compared to typically developing subjects stresses the importance to acknowledge the developmental and heterogenetic course of psychiatric disorders in childhood and adolescence and the importance of intervention strategies for the prevention of continuity of psychopathology into adulthood.

Third, the present findings revealed that it seems important for clinicians to be aware of the higher risk for schizotypal symptomatology in adulthood following some psychiatric disorders of childhood and adolescence in particular. This is especially important to target future intervention strategies.

Fourth, it was demonstrated that teachers can be considered valuable informants on the behavior of children. Although the use of multiple informants (and therefore teacher reports) in assessing psychopathology has already become general practice in child and adolescent psychiatry, this finding stresses the importance of incorporating teacher reports in clinical research on the development of adult psychopathology.

Fifth, the finding that both Subjective as well as Objective QoL within a group of subjects with juvenile psychopathology is diminished in accordance to the level of schizotypal symptomatology stresses the severity of schizotypal symptomatology in relation to psychopathology in general.

Sixth, that especially negative schizotypal symptomatology was found to unfavorably affect a person's Subjective QoL is an important finding, which might bring us closer to an effective intervention for the impairments of schizophrenia spectrum pathology.

Seventh, because the present findings show that gender matters in relation to the development of schizotypal symptomatology, the investigation of the development of psychopathology as well as clinical practice ought to take account of the possible differences that exist in the development of schizotypal symptomatology between boys and girls.

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