# Impact of childhood adversities on the short-term course of illness in psychotic spectrum disorders

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## ABSTRACT

Accumulating evidence indicates an impact of childhood adversities on the severity and course of mental disorders, whereas this impact on psychotic disorders remains to be specified. Effects of childhood adversities on comorbidity, on symptom severity of the Positive and Negative Syndrome Scale and global functioning across four months (upon admission, 1 and 4 months after initial assessment), as well as the course of illness (measured by the remission rate, number of re-hospitalizations and dropout rate) were evaluated in 62 inpatients with psychotic spectrum disorders. Adverse experiences (of at least 1 type) were reported by 73% of patients. Patients with higher overall level of childhood adversities ($n=33$) exhibited more co-morbid disorders, especially alcohol/substance abuse and dependency, and higher dropout rates than patients with a lower levels of adverse experiences ($n=29$), together with higher levels of positive symptoms and symptoms of excitement and disorganization. Emotional and physical neglect were particularly related to symptom severity. Results suggest that psychological stress in childhood affects the symptom severity and, additionally, a more unfavorable course of disorder in patients diagnosed with psychoses. This impact calls for its consideration in diagnostic assessment and psychiatric care.

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## 1. Introduction

In the complex gene-environment interaction determining mental disorders (Rutter et al., 2006), environmental stress early in life (including psychological stress and adversities in childhood) is considered a factor that modifies the development of psychopathology (Morgan and Fisher, 2007; Read et al., 2008; van Os et al., 2010; Teicher and Samson, 2013; Schmitt et al., 2014). Supporting evidence has related psychological stress and childhood adversities to a higher risk for mental disorders, to more severe psychopathology and to a poorer course of illness (meta-analysis and reviews: Zanarini et al., 2006; Daruy-Filho et al., 2011; Nanni et al., 2012; Maniglio, 2013). For instance, patients with major depression and higher levels of childhood abuse and maltreatment exhibit an earlier onset of illness (Bernet and Stein, 1999; Widom et al., 2007), more complex and severe psychopathology including psychotic features (Gaudiano and Zimmerman, 2010), lower remission rates (Enns and Cox, 2005) or longer time to remission (Miniati et al., 2010). For patients diagnosed with bipolar disorder, a relationship between exposure to childhood sexual abuse with more comorbid alcohol and substance abuse/dependency (e.g., Brown et al., 2005; Teicher and Samson, 2013), a younger age at the onset of disease (Leverich et al., 2002), higher rates of rapid cycling and suicide attempts (e.g., Garno et al., 2005; Tunnard et al., 2014), more severe psychotic symptoms (Hammersley et al., 2003) and lower rates of remission (Neria et al., 2005) have been reported.

For psychotic disorders, evidence validates the genetic and neurobiological contributions to psychopathology (e.g. Schizophrenia Psychiatric GWAS Consortium, 2011; Svrakic et al., 2013; Graux et al., 2014), while the modulating role of childhood adversities seems less clear. Early-life stress is thought to influence neuronal development (Andersen et al., 2008; Murgatroyd et al., 2009) and neuroendocrine response (Heim et al., 2000) as well as epigenetic imprinting (Peedicayil 2011; Shonkoff et al., 2012; Svrakic et al., 2013), thereby interacting in a complex manner with genetic and epigenetic factors.

A diagnosis of schizophrenia spectrum disorder is related to a heterogeneous and dynamic symptom profile, and is often associated with chronic courses. Evidence of the impact of childhood adversities on the severity and course of psychotic disorder, as aimed for in the present study, should help to understand the impact of environmental factors in the complex gene-environment interaction, and should inform prognoses and the adjustment of therapeutic

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strategies to prevent unfavorable, chronic courses. In patients with psychotic disorders, evidence has linked childhood adversities to more severe psychopathology: psychotic patients exhibit more complex symptoms, including suicidality (see also Roy, 2005; Álvarez et al., 2011), self-mutilation, higher symptom severity and more comorbid disorders – in particular, alcohol/substance abuse (Compton et al., 2009; Conus et al., 2010). Childhood adversities affect the course of illness, as evident in a younger age of onset (Goff et al., 1991; Aas et al., 2011; Álvarez et al., 2011). Malla et al. (1990) showed that relapses were associated with proximal life events in schizophrenia. In first-episode patients, lower treatment compliance was associated with childhood trauma (Lysaker et al., 2005, for compliance in vocational training, Lecomte et al., 2008; Conus et al., 2010). Lysaker et al. (2011) reported an impact of childhood sexual abuse on metacognitive capacity. A history of adversities has been shown to vary with poorer social functioning and social withdrawal (Schenkel et al., 2005; Steinert et al., 2006), insecure attachment style (Gumley et al., 2014), with more severe cognitive impairments and functional disability (Compton et al., 2009).

Many of these studies focused on the number of childhood adversities or on traumatic experiences (such as sexual or physical abuse) in particular. Indeed, the overall stress load and the exposure to multiple types of maltreatment affect the severity of various mental disorders following a dose-response function in patients with posttraumatic stress disorder, depression and borderline personality disorder (Neuner et al., 2004; Weber et al., 2008; Pietrek et al., 2013). With the assessment of different types of childhood adversities and their effects on measures of severity and course of the disorder in a sample of patients diagnosed with psychotic spectrum disorders, the present study sought to clarify the impact of childhood adversities on the course of psychotic psychopathology. The profile of ten distinct adversities experienced in childhood and adolescence (up to age 18) was described in order to examine the importance of dose effect versus specific effects, and the explained variance by distinct types of experience. Severity of illness and course were quantified by the number of current comorbid psychiatric diagnoses, symptomatic remission, re-hospitalization and dropout rate as well as the short-term course across a four-month observation period of symptom severities and global level of functioning.

## 2. Methods

### 2.1. Participants, setting and procedure

Sixty-two patients ($n = 19$ female, age $M = 32.2$ S.D. $= 10.3$ years) with a primary diagnosis of psychotic spectrum disorder (International Classification of Mental and Behavioral Disorders Tenth Version (ICD-10): F20- F29, World Health Organization, 1992) were recruited from the inpatient pool at the local Center for Psychiatry (see Table 1 for demographic data). Patients met criteria of a diagnosis of schizophrenia F20 (77.4%), 16.1% a diagnosis of schizoaffective disorder, and 4.8% of acute polymorphic psychotic disorder. Forty-one percent of the sample was admitted for diagnosis and treatment of psychoses for the first time, 59% was chronically ill. Symptom severity and global level of functioning were assessed across a four-month period starting at admission. Patients received routine care including maintenance neuroleptic medication, group therapy, physical exercise and adjunct cognitive behavioral psychotherapy if needed. Data assessment (see below) took place in the post-acute phase. Prior to assessment, each participant was informed about the aim and procedure of the study and provided written informed consent. The responsible psychologist or the psychiatrists in charge verified that the patient sufficiently improved to provide informed consent and participate in data assessment. The study was reviewed and approved by the Institutional Review Board (Ethics Committee) of the University of Konstanz.

### 2.2. Measures and instruments

Childhood adversities were screened by the Maltreatment and Abuse Chronology of Exposure (MACE) scale administered as an interview (Isele et al., 2014; Teicher and Parigger, 2011). The MACE scale captures the exposure to ten types of adversity during childhood, up to age 18: parental physical and verbal abuse, parental non-verbal emotional abuse, familial and non-familial sexual abuse, witnessed physical violence towards parents, witnessing violence towards siblings, peer emotional and peer physical violence, emotional and physical neglect). Good psychometric properties of the MACE scale are documented by test-retest reliability, $r = 0.91$, $n = 75$ at 10 weeks, and correlation coefficients of $r = 0.75$ with the Childhood Trauma Questionnaire (Wingenfeld et al., 2010) in a German validation sample (Isele et al., 2014). The MACE MULTI score indicates the number of different types of childhood adversities that reached the defined severity, ranging from 0 to 10. The MACE SUM score indicates the overall severity of exposure to childhood adversities, ranging from 0 ("no childhood adversities at all") to 100 ("reporting maximal exposure to all types of childhood adversities"). Using a median split of the MACE MULTI score ($Mdn = 2$), patients of the present sample were assigned to a group with lower level of childhood adversities (0 or 1 types) or higher level of childhood adversities (2 or more types).

Symptom severity was evaluated three times – upon admission as well as one and four months after the initial assessment – using the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). The 30-item expert rating assesses

**Table 1**
Demographic data, childhood adversities, comorbidity and course of illness for the group with low and high childhood adversities.

| | Low childhood adversities ($n = 29$) | | High childhood adversities ($n = 33$) | | Statistics for group difference | |
|---|---|---|---|---|---|---|
| | $M/n$ | S.D./% | $M/n$ | S.D./% | | |
| **Demographic data** | | | | | | |
| Female sex ($n$, %) | 12 | 41% | 7 | 21% | $\chi^2(1, 62) = 2.95$ | $p = 0.104$ |
| Number of first admission ($n$, %) | 9 | 31% | 17 | 52% | $\chi^2(1, 62) = 2.66$ | $p = 0.127$ |
| Age (Years, M, S.D.) | 32.9 | 10.1 | 31.6 | 10.7 | $t(60) = 0.5$ | $p = 0.621$ |
| Total number of hospitalizations (M, S.D.) | 3.3 | 2.9 | 4.6 | 7.5 | $t(58) = -0.85$ | $p = 0.396$ |
| Duration of hospitalization (in days, M, S.D.) | 123 | 73 | 124 | 73 | $t(54) = -0.04$ | $p = 0.968$ |
| **Adverse childhood experiences** | | | | | | |
| Number of different types of childhood adversities (MACE Multi, M, S.D.) | 0.4 | 0.5 | 3.8 | 1.6 | $t(39.19) = -11.64$ | $p < 0.001$ |
| Severity of adverse childhood experiences (MACE sum score, M, S.D.) | 13.3 | 6.6 | 36.5 | 12.2 | $t(50.40) = -9.48$ | $p < 0.001$ |
| **Comorbidity** | | | | | | |
| Number of individuals with axis I comorbidities ($n$, %) | 1 | 3% | 16 | 49% | $\chi^2(1, 62) = 15.73$ | $p < 0.001$ |
| Number of Individuals with abuse or addiction diagnosis (ICD-10: F10- F19; ($n$, %) | 1 | 3% | 12 | 36% | $\chi^2(1, 62) = 10.09$ | $p = 0.002$ |
| **Course of illness** | | | | | | |
| Patients with remission ($n$, %) | 11 | 39%[a] | 6 | 26%[a] | $\chi^2(1, 51) = 0.99$ | $p = 0.381$ |
| Number of rehospitalisation within the period of observation ($n$, %) | 4 | 14% | 10 | 30% | $\chi^2(1, 62) = 2.41$ | $p = 0.141$ |
| Number of dropouts ($n$, %) | 1 | 3% | 10 | 30% | $\chi^2(1, 62) = 7.63$ | $p = 0.007$ |

*Note.* Mean (M), Standard Deviation (S.D.), absolute number of respondents ($n$), $t$-tests were used for continuous variables and $\chi^2$ tests were applied for nominal/binary variables; international classification of mental and behavioral disorders tenth version (ICD-10) chapter F.

[a] The total number and percentage include study completers ($n = 28$ patients of the low childhood adversity group and $n = 23$ of the high childhood adversity group).