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Defining the impact of childhood adversities on cognitive deficits in psychosis: An exploratory analysis

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ABSTRACT

Background: Exposure to adverse childhood experiences (ACE) and cognitive deficits are both prevalent in psychosis. While it has been repeatedly demonstrated that ACE contribute to cognitive dysfunctions, the specific nature of this contribution remains elusive. Recent evidence suggests that types of adversities during critical periods have deleterious effects on brain structures that are important for cognitive functioning. The present study sought to clarify which types of adversities experienced at which time during development aggravate cognitive deficits in psychosis.
Methods: Exposure to abuse and neglect during childhood and adolescence were retrospectively assessed in $N = 168$ adult individuals with psychotic disorder. Conditioned random forest regression was used to define the importance of type and timing of ACE for predicting domains of the MATRICS Consensus Cognitive Battery (MCCB).
Results: Significant importance of ACE was determined for 5 out of 7 MCCB domains. Particularly abuse at age 3 contributed to dysfunctional cognitive domains attention, learning, and working memory. Social cognition was related to neglect experienced at 11–12 years, and to cumulative ACE.
Conclusion: Abuse and neglect at periods when children spend substantial time in their families affect cognitive functioning, and hence aggravate dysfunction in psychosis. Results support the neurodevelopmental perspective on psychosis and the diagnostic value of type and timing of ACE.

1. Introduction

Exposure to adverse childhood experiences (ACE) and cognitive deficits are both prevalent in psychosis. With an attributional risk of 33%, ACE are reliably related to psychosis (Varese et al., 2012) and have been integrated in etiological models (Read et al., 2014). In psychosis, cognitive deficits display a major source of disability (Nuechterlein et al., 2014), and individuals perform poorly on cognitive tasks with levels more than one standard deviation below those of controls (Carolus et al., 2014; Heinrichs, 2004).

Several studies report inverse associations of ACE and various cognitive tasks (Lysaker et al., 2001; Schenkel et al., 2005; Shannon et al., 2011), also at early stages of psychosis (Aas et al., 2011; Campbell et al., 2013). Yet, inverse relationships between ACE and cognition were not confirmed in all studies (McCabe et al., 2012; Sideli et al., 2014), or were even found to be positive (Ruby et al., 2015).

Neurodevelopmental models offer the theoretical framework for understanding the link of ACE and cognitive functioning in general (Bick and Nelson, 2016) and in psychosis (Catts et al., 2013; Feinberg, 1983; Keshavan et al., 2014). Brain systems enabling cognitive functions, in particular hippocampus and frontal cortex, follow different developmental trajectories from infancy to early adolescence, and these periods are sensitive for environmental factors including ACE (Bick and Nelson, 2016; Pechtel and Pizzagalli, 2011; Teicher et al., 2016). Accordingly, cognitive dysfunction may be associated with ACE-modified development of these structures (Aas et al., 2013; Hoy et al., 2012; Catts et al., 2013; Ruby et al., 2014). Theoretical models based on normative brain development (Bick and Nelson, 2016) and on sensitive developmental periods (Teicher et al., 2016) suggest the hypothesis that within-group variance in cognition can be partially explained by types and timings of ACE.

So far, studies focused on cumulative ACE (Shevlin et al., 2008), major abuse, particularly sexual abuse (Lysaker et al., 2001), or distinct age windows (e.g., ACE at 0–6 years of age in Hoy et al., 2012).

The present study evaluated more precisely which types and timings during development were important for cognitive domains that are typically impaired in schizophrenia according to the Measurement and Treatment Research in Schizophrenia (MATRICS). Together with the MATRICS Consensus Cognitive Battery (MCCB; Nuechterlein and Green, 2006), we used the Maltreatment and Abuse Chronology of

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Exposure (MACE) Scale (Teicher and Parigger, 2015) to retrieve retrospectively forms of abuse and neglect during childhood and adolescence. The detailed information of exposure poses a statistical challenge of high collinearity in adjacent years as well as the large number of potential predictors. Data mining offers an adequate technique to overcome these obstacles and to identify important predictors (Breiman, 2001). Relationships of ACE and cognitive domains were expected along the maltreatment-related alternations of brain circuits that are sensitive to type and timing of ACE and important for cognitions.

2. Methods

2.1. Participants

A total $N = 168$ individuals with main diagnoses of psychotic spectrum disorder (World Health Organization, 1992) were recruited at the local center of psychiatry. Cognitive and ACE data of a subsample ($n = 62$, 36.9%) were reported in a thematically different context (Carolus et al., 2014; Schalinski et al., 2015). Expert psychiatrists/psychotherapist made diagnosis upon admission: participants met criteria of a diagnosis of schizophrenia 76.2%, schizoaffective disorder 10.7%, and acute polymorphic psychotic disorder 13.1%. Ninety-five individuals with psychosis were admitted for the first time (Table 1). We characterized the severity of psychopathology with the Positive and Negative Syndrome Scale (Kay et al., 1987). The majority of individuals with psychosis ($n = 160$) was treated with neuroleptics for at least 2 weeks without change in dosage and type with a chlorpromazine equivalent dose of $M = 534.5$ ($SD = 413.6$), which is close to the commonly recommended maintenance dosage. For comparison purposes, $n = 50$ non-psychotic individuals with similar age and education were recruited from the community.

The study was reviewed and approved by the Institutional Review Board of the University of Konstanz. For all participants assessment took place in the post-acute phase. The responsible psychologist/psychiatrists verified that the individual was in a sufficiently improved state to provide written informed consent and understand test and interview questions.

2.2. Materials

The MACE scale was developed to retrospectively capture the exposure to ten forms of ACE between infancy and age 18, covering abuse (physical, verbal, non-verbal emotional abuse, witnessing interparental abuse and abuse of siblings, peer-related verbal abuse and physical bullying, and intra-, extra-familial or peer-related sexual abuse) and emotional and physical neglect (Teicher and Parigger, 2015; Isele et al., 2014). For each of the 75 items (assigned to 10 subscales) experience was coded as yes-no. For 'yes' responses the age of occurrence was evaluated in the same binary format for each year of life up to age 18. For each subscale, positively endorsed items were linearly interpolated to obtain severity scores that range from 0 to 10. The overall severity of ACE was calculated using the sum of all 10 subscale-severities (ranging from 0 to 100). The number of different forms (multiplicity) was operationalized as the number of those subscales that exceeded the defined cut-off severity for clinically relevant exposure levels according to Isele et al. (2014). Similarly to the American version, the cut-off scores are based on the raw values of positively endorsed items per subscale (Teicher and Parigger, 2015). The scores can be evaluated for each year (timing) and for each subscale (forms) and for cumulative measures (severity and multiplicity). ACE duration score summarizes the years of experience with a multiplicity score ≥ 1 (ranging from 0 to 18). Forms of ACE were assigned to two types: abuse and neglect. The MACE scales demonstrate high-quality psychometric properties: good convergent validity and an excellent retest-reliability (Isele et al., 2014; Teicher and Parigger, 2015).

Cognitive performance was assessed with the MCCB ((Nuechterlein and Green, 2006), which covers the seven cognitive domains speed of processing, attention, working memory, verbal learning, visual learning, reasoning, and social cognition) with ten tests (Trail Making Test: Part A, Brief Assessment of cognition in Schizophrenia: Symbol Coding, Hopkins Verbal Learning Test- Revised, Wechsler Memory Scale- 3rd Ed.: Spatial Span, Letter Number Span, Neuropsychological Assessment Battery: Mazes, Brief Visual Memory Test- Revised, Category Fluency: Animal Naming, Mayer-Salovey-Caruso-Emotional-Intelligence Test: Managing Emotions, Continuous Performance Test-Identical Pairs). For evaluation of performance the raw scores are converted into age-and gender-corrected T-scores based on data of the representative US

Table 1
Demographic and clinical data and adversity-related characteristics of individuals with psychosis ($N = 168$) and controls ($N = 50$).

	Individuals with psychosis	Controls	Group comparison
Demographic and clinical data			
Age (in years) *M* (*SD*)	27.9 (8.4)	26.8 (7.9)	$t(216) = -0.83$, $p = 0.407$
Female sex *n* (%)	56 (33.3%)	22 (44%)	$\chi^2_{(1)} = 1.91$, $p = 0.181$
First admission *n* (%)	95 (56.5%)		
Years of education *M* (*SD*)	11.7 (1.7)	11.4 (1.37)	$t(216) = -1.04$, $p = 0.298$
PANSS sum score *M* (*SD*)	66 (13.3)		
Childhood adversities			
Duration[a] *M* (*SD*)	6.8 (6.3)	1.7 (2.8)	$t(183.26) = -8.03$, $p < 0.001$, $d = 1.04$
Multiplicity[b] *M* (*SD*)	2.7 (2.2)	0.7 (0.9)	$t(192.54) = -9.17$, $p < 0.001$, $d = 1.19$
Severity[c] *M* (*SD*)	29.1 (15.4)	13.7 (8.6)	$t(147.18) = -9.06$, $p < 0.001$, $d = 1.23$
Participants with multiplicity > 0 *n* (%)	140 (83.3%)	22 (44%)	$\chi^2_{(1)} = 31.23$, $p < 0.001$, $\phi = 0.38$
MCCB			
Overall composite score	37.00 (10.17)	49.32 (8.41)	$t(216) = 7.81$, $p < 0.001$, $d = 1.32$
Processing speed	39.93 (10.69)	52.1 (8.88)	$t(216) = 7.32$, $p < 0.001$, $d = 1.24$
Attention	36.34 (9.44)	43.66 (9.37)	$t(216) = 4.82$, $p < 0.001$, $d = 0.78$
Working memory	44.22 (10.19)	51.34 (8.38)	$t(216) = 4.51$, $p < 0.001$, $d = 0.76$
Verbal learning	46.45 (9.94)	52.36 (10.63)	$t(216) = 3.63$, $p < 0.001$, $d = 0.57$
Visual learning	39.62 (11.96)	47.08 (9.65)	$t(216) = 4.03$, $p < 0.001$, $d = 0.69$
Reasoning and problem solving	45.15 (9.57)	53.96 (6.00)	$t(129.51) = 7.83$, $p < 0.001$, $d = 1.10$
Social cognition	42.26 (10.83)	47.34 (8.46)	$t(216) = 3.05$, $p = 0.003$, $d = 0.52$

Note. PANSS = Positive and Negative Syndrome Scale. MCCB = MCCB = MATRICS Consensus Cognitive Battery. *d* = Cohen's *d*.
[a] Years with a multiplicity score ≥ 1 (ranging from 0 to 18).
[b] Number of different types (ranging from 0 to 10).
[c] Severity of childhood adversities (ranging from 0 to 100).

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