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Environmental adversities and psychotic symptoms: The impact of timing of trauma, abuse, and neglect

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ABSTRACT

Background: Trauma and adverse childhood experiences (ACE) occur more often in mental illness, including psychosis, than in the general population. Individuals with psychosis (cases) report a higher number and severity (dose) of adversities than healthy controls. While a dose-dependent increase of adversities has been related to more severe psychopathology, the role of type and timing is still insufficiently understood on the exacerbation of positive and negative psychotic symptoms. Moreover, dissociative symptoms were examined as potential mediator between adversities and severity of psychotic symptoms.

Methods: Exposure to adversities were assessed by interviews in $n = 180$ cases and $n = 70$ controls. In cases, symptom severities were obtained for psychotic symptoms and dissociation. Conditioned random forest regression determined the importance of type and timing of ACE for positive and negative symptom severity, and mediator analyses evaluated the role of dissociative symptoms in the relationship between adversities and psychotic symptoms.

Results: Cases experienced substantially more abuse and neglect than controls. Adversities were related in a dose-dependent manner to psychotic disorder. An array of adversities was associated with more severe positive symptoms, while the conditioned random forest regression depicted neglect at age 10 as the most important predictor. Dissociative symptoms mediated the small relation of trauma load in childhood and positive symptoms.

Conclusion: The role of trauma and ACE on psychotic symptoms can be specified by neglect during frontocortical development in the exacerbation of positive symptoms. The mediating role of dissociation is restricted to the relation of childhood trauma and positive symptoms.

1. Introduction

Traumatic and adverse childhood experiences (ACE) are commonly found in mental illness, including psychosis (Beards et al., 2013; Morgan et al., 2014; van Nierop et al., 2014; Varese et al., 2012b). Several studies described a dose-dependent relation between the level of exposure to adversities and the risk of psychosis (e.g., Heins et al., 2011; Trauelsen et al., 2015). Yet, understanding the role of adverse and traumatic experiences in the generation of psychopathology remains insufficient without understanding how specific adversities experienced during defined developmental periods affect the severity of symptoms and course within psychosis. Exposure to specific adversities interacts with genetic susceptibility thus increasing psychopathology (Teicher and Samson, 2013). Indeed, studies confirmed more severe psychopathology in individuals with psychotic disorder (cases) and a history of adversities (Bentall et al., 2014) and, more precisely, elevated levels of positive symptoms (delusions and hallucinations) in relation to past traumatic experiences (Goff et al., 1991), physical and sexual abuse (Kilcommons and Morrison, 2005), and neglect in childhood (Vogel et al., 2009). In contrast to positive symptoms, a relation between negative symptoms and adversities was inconsistently reported (Ruby et al., 2015; Vogel et al., 2011). Still, evidence remains inconclusive in respect to the specificity of the type and timing of ACE that sensitize for symptom exacerbation. Diversity of methods to assess ACE limited the comparability across studies. While some studies focused on cumulative measures to account for the co-occurrences of various types of ACE (e.g., Heins et al., 2011), others emphasized a major type of ACE (e.g., sexual abuse in Lysaker et al., 2001). Yet, recent evidence indicates that trajectories of

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brain development follow a pattern of sensitivity to type and timing of exposure (Teicher et al., 2016), thereby advocating the consideration of types together with the time of experience during development. As recently shown this consideration significantly contributed to the understanding of cognitive deficits in psychosis (Schalinski et al., 2017). Thus, the developmental perspective may further the understanding of how environmental adversities increase heterogeneity within psychosis.

Dissociative symptoms result from exposure to adversities (Schalinski et al., 2015b), and contribute to positive and negative symptoms in psychosis (Kilcommons and Morrison, 2005; Read and Ross, 2003; Ross and Keyes, 2004; Vogel et al., 2013). Dissociative symptoms following traumatic stress have been explained within the defense cascade model of Schauer and Elbert (2010) as shutting down of perceptual, emotional, cognitive and behavioral processes at a certain stage of proximity to threat and helplessness. Ongoing shutdown dissociation may explain the relationship between adversities and psychotic symptoms. Dissociation enhances positive symptoms due to the loss of contact to the internal and external reality and negative symptoms due to the loss of emotional connection, and disruptive cognitive process. Psychotic individuals with a history of adversities show elevated levels of dissociative symptoms (Holowka et al., 2003; Şar et al., 2010; Schäfer et al., 2012; Vogel et al., 2009). Furthermore, dissociation enhances illness severity and moderates or mediates the relationship of adversities on psychotic symptoms (Muenzenmaier et al., 2015; Perona-Garcelán et al., 2012; Varese et al., 2012a), and on psychotic-like symptoms in students (Moskowitz et al., 2005).

The present study compared exposure to adversities of cases and controls. The relationship among the exposure to abuse, neglect, their timing and psychotic symptoms was delineated within cases, and dissociative symptoms as mediating factor in the relationship between adversities and psychotic symptoms was evaluated.

2. Methods

2.1. Participants

In total, $n = 180$ cases ($n = 57$, 31.7% females, mean age of $M = 28.6$, $SD = 8.8$) were recruited for the assessment. Cases met criteria of schizophrenia (75%), acute polymorph psychotic disorder (13.3%), schizoaffective disorder (11.1%), and delusional disorder (0.6%). Most cases ($n = 172$) were currently treated with neuroleptics (chlorpromazine equivalent dosage of $M = 518$, $SD = 390$). The average symptom severity per score on the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) was $M = 66.5$, $SD = 13.2$ (see Table 2 for means of positive and negative symptoms). For comparison, $n = 70$ individuals (40% females, mean age $M = 25.8$, $SD = 7.1$) without past and present mental illness as evaluated with the Mini International Neuropsychiatric Interview (Ackenheil et al., 1999) were recruited from the community. The present sample overlapped with a subsample of $n = 62$ cases for whom the symptoms over the course of illness were reported in Schalinski et al. (2015a), a subsample of $n = 75$, for whom the relation of ACE and dissociation was reported in Schalinski and Teicher (2015), and a subsample of $n = 168$, for whom the impact of ACE on cognitive deficits were reported in Schalinski et al. (2017).

Institutional Review Board of the University of Konstanz approved the study. The psychologist/psychiatrists in charge verified that cases were in a sufficiently improved state to provide written informed consent.

2.2. Instruments

2.2.1. Measures of adversities

The Life Events Checklist (LEC) was applied in interviews to assess the exposure to 17 different types of traumatic experiences (Gray et al., 2004). Only those types were considered that involved a serious injury, a life threat or sexual assault for the individual him or herself or the witnessing of such an event. Furthermore, each type of event was categorized according to the time of occurrence (first 18 years of life = childhood, and >18 years to the date of the assessment = adulthood). Independent of the frequency for each type, we calculated the trauma load (number of different types of traumatic experiences) in childhood and adulthood.

The Maltreatment and Abuse Chronology of Exposure scale (MACE; Teicher and Parigger, 2015; German version KERF by Isele et al., 2014) provided a developmental framework to capture retrospectively the exposure to ten forms of ACE up to age 18, assigned to 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 neglect (emotional and physical neglect). For each of the 75 items that were coded with yes-responses, the age of occurrence was specified in the same binary format for each single year up to age 18. Items were assigned to 10 subscales (8 forms of abuse, 2 forms of neglect) and linearly interpolated in respect to the total number of item per subscale to obtain severity scores for each subscale that range from 0 to 10. The sum of all subscale determined the overall severity (ranging from 0 to 100). Similarly to the MACE, the cut-off scores for KERF were based on the raw values of positively endorsed items per subscale that exceeds a certain threshold. An index of the number of different forms (multiplicity) presents the number of subscales that exceeded the cut-off (Isele et al., 2014). All scores can be evaluated for each year (timing), for each type (abuse or neglect) and for cumulative measures (severity and multiplicity). A duration index measured the years of multiplicity score ≥ 1 (ranging from 0 to 18). The scales demonstrated high-quality psychometric properties (Isele et al., 2014; Teicher and Parigger, 2015).

2.2.2. Measures of psychopathology

Psychotic symptoms were evaluated at treatment admission with the PANSS (Kay et al., 1987). Trained psychiatrist/psychologists rated 30 items based on information reported by the patient and direct observations made by health care staff or family members, on a 7 point-rating scale (1 = absent, 2 = minimal, 3 = mild, 4 = moderate, 5 = moderate to severe, 6 = severe, 7 = extreme). The positive and negative subscales were used to determine the severity of the respective subscale (Kay et al., 1987).

Dissociative symptoms were measured with the Shutdown Dissociation Scale which assesses frequency of the following signs: fainting, blurred vision, dizziness and transitory blindness, alteration in hearing or hearing loss, changed visual perception, numbness, transitory paralysis, analgesia, tonic immobility, physical weakness, feeling of nausea, out-of-body perception, inability to speak and weakness (Schalinski et al., 2015b). The frequency was recorded for the past 6 months (0 = not at all, 1 = once a months or less, 2 = several times a month, 3 = several times a week), and ratings were summed up to a score ranging from 0 to 39. This scale has demonstrated excellent psychometric properties (Schalinski et al., 2015b).

2.3. Analysis strategy

Analyses were conducted using R (version 3.0.2.). The level of exposure to adversities was divided into quartile based on the distribution in controls and then contrasted to the proportion of cases. Linear-by-linear associations were used to test for dose-dependent relation between exposure to adversities and psychotic disorder.

Within cases, Spearman's partial correlations were calculated for associations between measures of adversities and symptoms controlling for age and gender (R package 'ppcor'; Kim, 2015). Furthermore, two approaches were combined to identify the most important predictor for symptom severity as dependent variable using the R packages 'glmnet', 'party', and 'caret': conditioned random forest and least absolute shrinkage and selection operator (LASSO)-penalized regression. Both techniques are robust to small samples and collinear predictors (Strobl et al., 2007; Tibshirani, 1996). Conditioned random forest

regression constitutes a machine learning strategy that detects important predictors from a large set of predictors: 18 neglect and 18 abuse variables for each year from age 1 to 18 were chosen from the MACE. The duration, severity and multiplicity of ACE, the trauma load in childhood and adulthood, as well as gender and age were used as additional predictors. The variant of Breiman's approach with conditional trees has no particular assumptions on distribution or descriptive characteristics, and it is superior to other approaches in the analysis of complex data structures (Breiman, 2001; Strobl et al., 2009). The conditional grid is based on discretizing of the means of partition of the feature space of each individual tree, thereby compensating for collinearity and avoiding that correlated predictors appear to be artificially more important. The algorithm has a built-in validation through splitting the data into a training (75%) and holdout sample (25%). This protects against overfitting and estimate the permutation based importance (Strobl et al., 2009). Furthermore, distribution-free empirical probability scores were extracted based on 5000 permutations of each randomly reassigned predictor to estimate the likelihood of each predictor having occurred by chance. Furthermore, findings were converged with the results of leave-group-out cross-validation of the LASSO-penalty regression (Tibshirani, 1996).

The mediating role of dissociation in the relationship between adversities and psychotic symptoms was tested with bootstrap-based methods using the R package 'mediation' (Imai et al., 2010), and semi-parametric generalized additive models. Average estimates of total and direct effect (of adversity on psychotic symptom), the mediation effect (of dissociation), are based on non-parametric methods (Imai et al., 2010), and non-parametric bootstrapped based confidence intervals were retrieved (using the percentile method with 10,000 resamples).

3. Results

3.1. Prevalence of adversities

The majority of cases were exposed to at least one form of abuse (76.7%) or neglect (69.8%) compared to 47.1% of abuse and 11.1% of neglect in controls, respectively. The ratios between cases and controls increased proportionally for trauma load in childhood ($\chi^2_{(df=1)} = 4.95$, $p = 0.026$), and adulthood ($\chi^2_{(df=1)} = 8.72$, $p = 0.003$), and for duration ($\chi^2_{(df=1)} = 21.34$, $p < 0.001$), multiplicity ($\chi^2_{(df=1)} = 31.57$, $p < 0.001$), and overall severity of ACE ($\chi^2_{(df=1)} = 39.33$, $p < 0.001$),

Table 1
Differences of prevalence of exposure to adversities expressed by number of different traumatic experiences in childhood and adulthood, MACE global measure, and severity of abuse, and neglect in cases ($n = 180$) versus controls ($n = 70$).

Measure of adversities	Category[a]	Controls		Cases		Odd ratios	Statistics
		n	%	n	%		
Trauma load							
In childhood	0	16	22.9%	35	19.4%	1[b]	
	1	19	27.1%	33	18.3%	0.8	
	2	16	22.9%	24	13.3%	0.7	
	≥ 3	19	27.1%	88	48.9%	2.1	
						Linear by linear association	$\chi^2_{(df=1)} = 4.95$, $p = 0.026$
In adulthood	0	19	27.1%	27	15.0%	1[b]	
	1	19	27.1%	52	28.9%	1.9	
	2	20	28.6%	26	14.4%	0.9	
	≥ 3	12	17.1%	75	41.7%	4.4	
						Linear by linear association	$\chi^2_{(df=1)} = 8.72$, $p = 0.003$
MACE global measures							
Duration[c]	0 (0)	36	51.4%	42	23.3%	1[b]	
	1 (range: 1–3)	17	24.3%	44	24.4%	2.2	
	2 (range 4–18)	17	24.3%	94	52.2%	4.7	
						Linear by linear association	$\chi^2_{(df=1)} = 21.34$, $p < 0.001$
Multiplicity[d]	0	34	48.6%	33	18.3%	1[b]	
	1	18	25.7%	42	23.3%	2.4	
	2	11	15.7%	28	15.6%	2.6	
	≥ 3	7	10%	77	42.8%	11.3	
						Linear by linear association	$\chi^2_{(df=1)} = 31.57$, $p < 0.001$
Overall[e] severity	1 (range 0–6)	18	25.7%	5	2.8%	1[b]	
	2 (range > 6–13.1)	17	24.3%	27	15.0%	5.7	
	3 (range > 13.1–23.7)	18	25.7%	43	23.9%	8.6	
	4 (range > 23.7–70.4)	17	24.3%	105	58.3%	22.2	
						Linear by linear association	$\chi^2_{(df=1)} = 39.33$, $p < 0.001$
MACE severity of types							
Abuse	1 (range: 0–5)	18	25.7%	8	4.4%	1[b]	
	2 (range: >5–11.2)	17	24.3%	29	16.1%	3.9	
	3 (range: >11.2–19.5)	18	25.7%	42	23.3%	5.4	
	4 (range: >19.5–58.4)	17	24.3%	101	56.1%	13.6	
						Linear by linear association	$\chi^2_{(df=1)} = 32.09$, $p < 0.001$
Neglect	1 (0)	24	34.3%	18	10.0%	1[b]	
	2 (1)	13	18.6%	22	12.2%	2.3	
	3 (range: 2–3)	18	25.7%	47	26.1%	3.5	
	4 (range: 4–19)	15	21.4%	93	51.7%	8.3	
						Linear by linear association	$\chi^2_{(df=1)} = 29.31$, $p < 0.001$

Note. MACE = Maltreatment and Abuse Chronology of Exposure.
[a] Categories are based on the distribution in the control group.
[b] The ratio in the category with lowest exposure serves as the denominator (reference category).
[c] Years with a multiplicity score ≥ 1 (ranging from 0 to 18).
[d] Number of different forms (ranging from 0 to 10).
[e] Severity of childhood adversities (ranging form 0 to 100).

Table 2
Descriptive statistics and associations (Spearman's partial correlation corrected for age and gender) between measures of adversities, and severity of psychotic psychopathology (PANSS positive, and negative symptoms) and shutdown dissociation.

Measure of adversities	M (SD)	PANSS positive symptoms	PANSS negative symptoms	Shutdown dissociation
M (SD)		14.7 (4.3)	17.1 (5.9)	4.8 (5.2)
Trauma load				
In childhood	3.0 (2.8)	0.22*, $p = 0.002$	−0.04, $p = 0.562$	0.37*, $p < 0.001$
In adulthood	2.5 (2.2)	0.12, $p = 0.120$	−0.10, $p = 0.186$	0.23*, $p = 0.002$
MACE global measures				
Duration[a]	6.5 (6.4)	0.28*, $p < 0.001$	0.08, $p = 0.309$	0.34*, $p < 0.001$
Multiplicity[b]	2.6 (2.2)	0.26*, $p < 0.001$	−0.05, $p = 0.480$	0.39*, $p < 0.001$
Overall severity[c]	28.7 (15.2)	0.29*, $p < 0.001$	−0.05, $p = 0.467$	0.44*, $p < 0.001$
MACE severity of types				
Neglect	5.7 (4.5)	0.27*, $p < 0.001$	0.04, $p = 0.586$	0.33*, $p < 0.001$
Abuse	23.0 (12.8)	0.25*, $p < 0.001$	−0.09, $p = 0.223$	0.40*, $p < 0.001$

[a] Years with a multiplicity score ≥ 1 (ranging from 0 to 18).
[b] Number of different forms (ranging from 0 to 10).
[c] Severity of childhood adversities (ranging form 0 to 100). MACE = Maltreatment and Abuse Chronology of Exposure. PANSS = Positive and Negative Syndrome Scale.
* Statistically significant at the adjusted alpha level using the Benjamini-Hochberg correction: $p = 0.031$.

exposure to abuse ($\chi^2_{(df=1)} = 32.09, p < 0.001$) and neglect ($\chi^2_{(df=1)} = 29.31, p < 0.001$, Table 1).

3.2. Associations between the exposure to adversities and pathology within psychosis

A higher trauma load childhood, duration, severity and multiplicity of ACE were associated with increased levels of positive symptoms (Table 2). Moreover, positive symptoms were related to the severity of neglect and abuse. None of the measures of adversities showed significant associations with negative symptoms. In contrast, traumatic experiences in childhood and adulthood as well as all measures of the ACE were positively correlated with shutdown dissociation (Table 2).

3.3. Type and timing of childhood adversities for psychotic symptoms

Considering the complex structure of collinearity of ACE, the two analytic methods converged in defining exposure to neglect at age 10 as significant predictor for the severity of positive symptoms (Table 3; Fig. 1A). In contrast, negative symptoms were predicted by abuse at age 12 as a trend, while gender and age significantly contributed to negative symptoms. Fig. 1C–F illustrates the timing of exposure to abuse and neglect for cases with symptom levels below and above the median.

Table 3
Results for those predictors that were selected by LASSO-penalized regression analysis, and those that showed significance in conditioned random forest regression. Predictors that are highlighted in bold were selected by the LASSO-penalized regression analysis and showed significance based on permutation in the conditioned random forest regression.

	Potential predictors	Variable importance M (SD)	Permutation based *p*-value	B_{minMSE}[a]
PANSS positive symptoms	Abuse at age 3	0.001 (0.02)	$p = 0.423$	0.09
	Abuse at age 17	1.11 (0.16)	$p = 0.069$	0.06
	Abuse at age 18	1.16 (0.10)	$p = 0.057$	0.05
	Neglect at age 10	2.05 (0.17)	$p = 0.002$	0.32
	Neglect at age 11	1.24 (0.11)	$p = 0.008$	–
	Adulthood trauma load	0.38 (0.07)	$p = 0.161$	0.11
	Age	0.51 (0.06)	$p = 0.122$	0.02
PANSS negative symptoms	Abuse at age 12	1.30 (0.21)	$p = 0.081$	0.14
	Gender (1 = male, 0 = female)	3.11 (0.27)	$p = 0.003$	2.6
	Age	3.91 (0.42)	$p < 0.001$	0.13

[a] B_{minMSE} = beta estimates based on the optimal lambda to find the minimum mean squared error in LASSO-(least absolute shrinkage and selection operator) penalized regression analysis. PANSS = Positive and Negative Syndrome Scale.

3.4. Mediating role of dissociative symptoms

Dissociative symptoms were significantly related to positive symptoms (Spearman's partial $r = 0.18$, $p = 0.013$, controlled for age and gender). Dissociation mediated the relation of trauma load in childhood trauma on positive symptoms with an average mediation effect of 0.07, $p = 0.032$, 95% CI[0.01, 0.16], accounting for 25.9% of the total effect. The direct effect was no longer significant (0.20, $p = 0.060$, 95% CI[−0.01, 0.42]), when considering dissociative symptoms. A mediation/moderation effect was not found when abuse, neglect, or neglect at age 10 was considered (Table 4).

4. Discussion

Present results confirmed case-control differences in exposure to adversities, and the 'dose-dependent' increase for psychotic disorder (Varese et al., 2012b). Furthermore, the study specified an impact of types and timings of ACE on psychotic symptoms within cases beyond the dose-effect: the severity of neglect at the age of 10 was a critical determinant for more severe positive psychotic symptoms. This extends previous results on adversity-symptom relationship that either focused on a limited number of adversities or used cumulative measures (e.g., Heins et al., 2011; Lysaker et al., 2001).

The results stipulates research questions of biological mechanisms and gene-environment-interactions that contribute to increased levels of positive symptoms in the following ways: Primarily adversity-related and transdiagnostic factors may be abnormalities of brain structures and functioning of the frontal lobe, amygdala, hippocampus, stress-regulatory systems, or immune system (Hoy et al., 2012; Pruessner et al., 2017; Read et al., 2014; Teicher et al., 2016). Following this line of argument, periods around the age of 10 are important for the frontocortical development (Giedd, 2004), and adversities in this period varied with altered volumes of the right amygdala (Pechtel et al., 2014). Furthermore, the adversity-related transdiagnostic perspective receives support from association of exposure to adversities and psychotic-like symptoms in first-degree relatives, non-clinical samples, and individuals with other diagnoses of mental illness (Heins et al., 2011; Moskowitz et al., 2017). In contrast to the transdiagnotic perspective on the adversity-relation, the results may be specific to psychosis, as differential effects of adversities have been established in schizophrenia compared to other clinical samples (Quidé et al., 2017; Vogel et al., 2013). Furthermore, psychotic individuals report on average lower levels of adversities compared to borderline personality disorder (Pietrek et al., 2013), but show higher levels of positive symptoms (Kingdon et al., 2010). To what extent the effect of neglect and the timing is restricted to psychotic disorder needs further evaluation e.g., in other clinical samples to estimate the transdiagnostic nature of the present result.

Negative symptoms were neither correlated with adversities nor with dissociative symptoms. More severe negative symptoms were observed in male and elderly cases, probably confounded with duration of illness. Gender differences in negative symptoms are a common finding and the origin is unclear: multiple contributing factors are discussed (Mendrek and Mancini-Marïe, 2016).

Dissociative symptoms mediated the relationship between trauma load in childhood and positive psychotic symptoms, aligning with previous findings (Muenzenmaier et al., 2015; Perona-Garcelán et al., 2012; Varese et al., 2012a). Dissociative symptoms did not account for the relationship between neglect and positive symptoms, despite significant correlation, and highest importance of neglect for dissociation (Schalinski and Teicher, 2015; Schalinski et al., 2016). The present

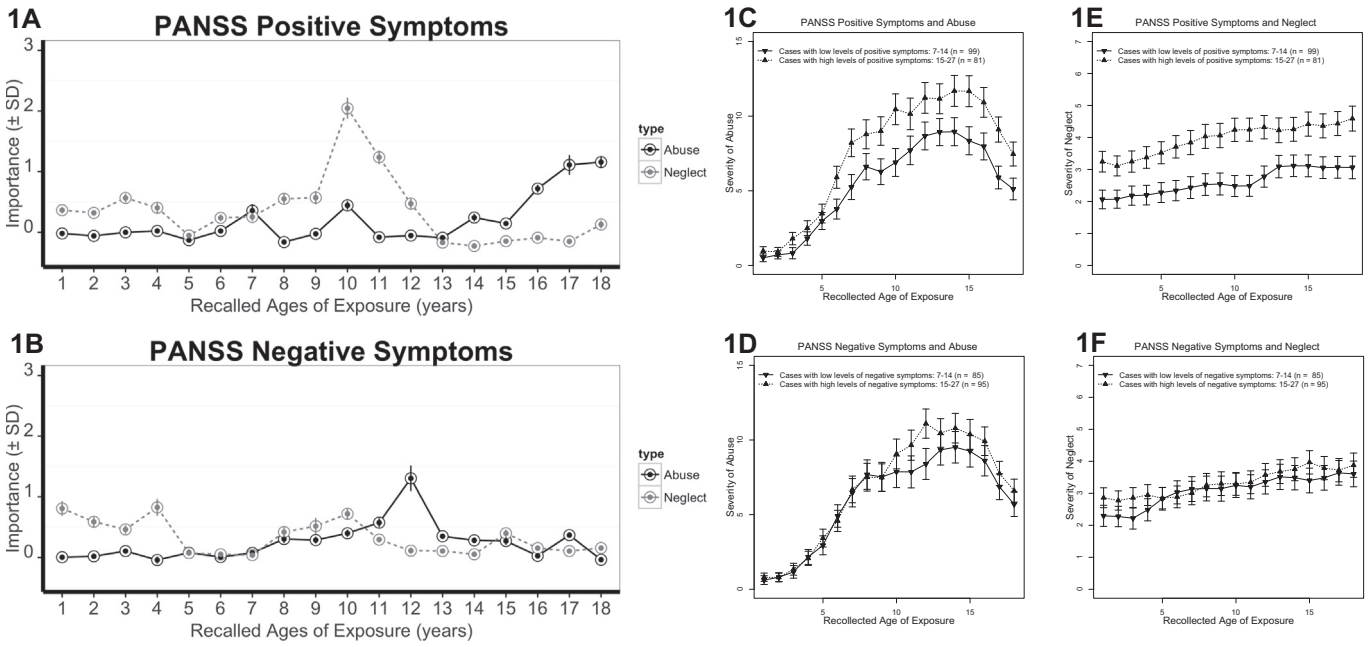

Fig. 1. Variable importance of abuse and neglect for (1A) PANSS positive, and (1B) PANSS negative symptoms. The abscissa presents the years between 1 and 18 and the error bars the standard deviation. The time course of exposure to abuse (1C, 1D) and neglect (1E, 1F) is presented as a function of cases with low and high psychopathology (for PANSS positive (1C, 1E) and negative symptoms (1D, 1F)). Data is adjusted for age and gender. The error bars in 1C-1F present the standard error. Importance, reflecting the relative strength of abuse and neglect in the prediction of psychotic symptoms. Positive values that clearly vary above the range of negative values are important for the outcome and are considered important. PANSS = Positive and Negative Syndrome Scale.

analysis suggests distinct pathways for childhood trauma and neglect to positive symptoms via trauma-related dissociation and via other consequences of neglect that might fuel positive psychotic symptoms and dissociation. However, more specific inference is limited as the mediation analysis was based mainly on small associations and the cross-sectional nature of the study design. A final limitation is the still ongoing evaluation of the power of conditioned random forest regression to predict outcomes from real exposure data.

Taken together, scrutinizing type specific periods in the development in cases with co-occurrences of other forms of adversities, is critically important to understand 'what' amplifies pathology, and further informs research questions on 'how' experience contribute to psychosis. The assessment of adversities by type and timing not only fosters the stepwise delineation of the complex gene-environment-interaction in the exacerbation of psychotic psychopathology, but might also foster understanding of individual variability of symptoms.

Contribution

IS, MHT & BR designed the study concept. Data collection was performed by VH, SB, MO & IS. MT provided the scripts for conditioned random forest regression, and IS accomplished the data analysis. IS and BR drafted the manuscript, all authors provided critical review. All authors approved the final version of the paper prior to submission.

Conflict of interest

All authors declare that they have no conflicts of interest.

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Table 4
Estimates, and non-parametric bootstrapped based confidence intervals, for the mediation effect (of dissociative symptoms), the direct effect, and the total effect of measures of adversities on PANSS positive symptoms.

Measures of adversities	Mediation effect	Direct effect	Total effect	Proportion of total effect that is mediated
Trauma load in childhood	0.07, $p = 0.032^*$, 95%CI[0.01, 0.16]	0.20, $p = 0.060$, 95%CI[−0.01, 0.42]	0.27 $p = 0.011^*$, 95%CI[0.06, 0.49]	0.26
Abuse	0.02, $p = 0.082$, 95%CI[−0.002, 0.04]	0.05, $p = 0.030^*$, 95%CI[0.01, 0.10]	0.07, $p = 0.003^*$, 95%CI[0.02, 0.12]	0.23
Neglect	0.03, $p = 0.102$, 95%CI[−0.01, 0.08]	0.24, $p = 0.002^*$, 95%CI[0.09, 0.37]	0.27, $p < 0.001^*$, 95%CI[0.13, 0.40]	0.12
Neglect at age 10	0.04, $p = 0.123$, 95%CI[−0.01, 0.10]	0.40, $p < 0.001^*$, 95%CI[0.18, 0.59]	0.44, $p < 0.001^*$, 95%CI[0.24, 0.61]	0.08

PANSS = Positive and Negative Syndrome Scale.
* $p \leq 0.050$.

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