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Childhood trauma and clinical high risk for psychosis

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ABSTRACT

As a risk factor for psychosis, childhood trauma rates are elevated in the clinical-high-risk (CHR) syndrome compared to the general population. However, it is unknown whether trauma is typically experienced in childhood or adolescence/young adulthood, whether it occurred prior to CHR syndrome onset, and how severe trauma relates to presenting symptoms. In this study, we examined the relationship of trauma history to symptoms and functioning in individuals diagnosed with the CHR syndrome on the Structured Interview for Psychosis-Risk Syndromes (N = 103). Trauma, defined as meeting the DSM-IV A1 criterion of actual or threatened death or injury, was assessed by semi-structured interview. A large proportion of CHR participants (61%) reported trauma exposure, including interpersonal trauma, trauma prior to CHR onset, and childhood trauma prior to age 12. Those with a trauma history (versus those without trauma) were rated as having more severe perceptual disturbances, general/affective symptoms and more impairment on the Global Assessment of Functioning Scale. The number of traumatic events correlated with more severe ratings in those three domains. Additionally, the number of interpersonal traumas was correlated with ratings of suspiciousness. Trauma was unrelated to specific measures of social and role functioning. A small proportion of CHR participants were diagnosed with formal PTSD (14%), which was unrelated to symptom severity or functioning. Thus, we demonstrate that trauma exposure is often early in life (before age 12), occurs prior to the onset of the CHR syndrome, and is related to both positive and affective symptoms.

1. Introduction

1.1. Childhood trauma and psychosis risk

Childhood trauma (CT) exposure is a risk factor for psychosis. A recent meta-analysis demonstrated this effect (OR = 2.78) across cross-sectional, case-control and prospective cohort studies, calculating that people with schizophrenia are 2.72 times as likely to have experienced adverse childhood events than healthy individuals (Varese et al., 2012). However, the majority of clinical cohort studies rely on retrospective self-report obtained after the onset of psychotic disorder. By assessing trauma history prior to the development of full psychosis, reporting biases can be minimized and possible mechanisms linking CT and psychosis onset can be explored. Thus, the clinical-high-risk syndrome (CHR) population, which has a 16–35% risk for developing full psychosis over the following 2.5 years after initial diagnosis (Fusar-Poli et al., 2012), is a natural choice for assessing CT prior to psychosis onset.

To date, twelve published studies have reported CT rates across nine CHR samples. All case-control studies reported higher CT rates in CHR samples compared to healthy controls, which were also similar to rates in first episode psychosis (Kline et al., 2016; O'Connor et al., 2017; Russo et al., 2014; Sahin et al., 2013; Stowkowy et al., 2016). A recent meta-analysis of six CHR studies calculated a mean CT prevalence

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rate of 87% in CHR samples, which was significantly higher than rates in controls, ranging from 42 to 60% (Kraan et al., 2015). Within CHR samples, CT has been associated with more severe positive symptoms (Falukozi and Addington, 2012; Kline et al., 2016; Kraan et al., 2015; Sahin et al., 2013; Thompson et al., 2009; Velthorst et al., 2013), affective symptoms (Kraan et al., 2015; Thompson et al., 2016), and worse neuropsychological performance, particularly attention, working memory, and cognitive flexibility (Üçok et al., 2015). In some cases, specific types of trauma were related to specific symptoms. For example, physical and sexual abuse were associated with positive symptom severity among ethnic minority participants (Thompson et al., 2009), although these associations were not found consistently across studies.

1.2. Age of trauma exposure

Stress-vulnerability models of psychosis risk have long posited that genetic vulnerability interacts with environmental stressors to cause psychotic disorders (Walker and Diforio, 1997; Zubin and Spring, 1977). Basic research has produced a wealth of evidence that the timing of stress has different effects on neurodevelopment, with early ("childhood" in humans) stress having a more severe and specific effect, creating a sensitization to later stressors in adolescence and adulthood (Lupien et al., 2009). Consistent with this model, epidemiological studies have found that psychotic-like experiences were already more common by age 12 in children previously exposed to CT (Arseneault et al., 2011).

Although evidence strongly suggests that overall trauma rates are higher in the CHR population as compared to healthy individuals, only one study so far has addressed the age of trauma exposure, by limiting results to trauma that occurred prior to age 16 (Stowkowy et al., 2016). CHR studies include individuals from approximately 12 to 30 years old, and trauma exposure may be cumulative, including measurement of adolescent or even adult trauma, in some cases. Previous work has also failed to differentiate between trauma experienced prior to the onset of the CHR syndrome with trauma experienced afterwards, despite the evidence that there is increased risk for trauma exposure (e.g. bullying) in vulnerable CHR youth (Stowkowy et al., 2016).

1.3. Trauma measurement

Most CHR studies used the Childhood Trauma Questionnaire (CTQ), a self-report survey focused on experiences of abuse and neglect (Bernstein et al., 2003). A few used other measures, including one study that utilized a semi-structured interview covering abuse, neglect and bullying that occurred prior to age 16 (Stowkowy et al., 2016). None, however, recorded the ages at which the adverse experiences occurred, and all assessed a range of experiences of varying severity, often excluding forms of trauma outside of abuse and neglect, or including less severe stressors. One alternative to these varying definitions of the trauma construct is to use the definition provided by the Diagnostic and Statistical Manual–IV or 5 of traumatic events that confer eligibility for Post-Traumatic Stress Disorder (PTSD; (American Psychiatric Association, 2000; American Psychiatry Association, 2013).

In the current study, we extend previous research by focusing on narrowly defined traumatic events and ages of events in order to assess the impact of trauma timing and severity on the symptoms and impairment associated with the CHR syndrome. We assessed trauma exposure in a sample of adolescents and young adults diagnosed with the CHR syndrome. Our primary a priori hypothesis was that trauma history would be related to more severe symptom severity and worse functioning. Our exploratory hypothesis was that participants diagnosed with PTSD would have worse symptoms and functioning than those without PTSD. We also expected that a significant proportion of the trauma would have occurred prior to age 12 and prior to CHR syndrome onset.

2. Methods

2.1. Participants

Study participants were 103 individuals diagnosed with the CHR syndrome aged 12–30 who were assessed as part of a longitudinal cohort study at the Prodrome Assessment, Research and Treatment Program, an early psychosis research clinic in the University of California San Francisco (UCSF) Department of Psychiatry. Participants were referred by community providers, school counselors, family members or self-referred from seeing information about the program on the Internet. Exclusionary criteria included: the presence of a neurological disorder, IQ < 70, current substance dependence, or the lifetime presence of a DSM-IV psychotic disorder (First et al., 2002).

2.2. Measures

2.2.1. Clinical diagnosis and symptoms

CHR participants were diagnosed as having at least one of three psychosis risk syndromes as assessed by the Structured Interview for Prodromal Syndromes (SIPS) (Miller et al., 2003): (1) Attenuated Positive Symptom Prodromal Syndrome (APS): attenuated positive psychotic symptoms present at least once per week, started or worsened in the past year (unusual thought content/delusional ideas, suspiciousness/persecutory ideas, grandiosity, perceptual abnormalities/distortions, and conceptual disorganization); (2) Brief Intermittent Psychosis Prodromal Syndrome (BIPS): brief and intermittent fully psychotic symptoms that have started recently; (3) Genetic Risk and Deterioration Prodromal Syndrome (GRDS): decline of at least 30% in the past 12 months on the Global Assessment of Function (GAF) scale PLUS either a family history of a psychotic disorder in any first-degree relative or meets criteria for schizotypal personality disorder. Individual positive, negative, disorganized and general/affective symptoms rated on the Scale for Assessment of Psychosis Risk Symptoms (SOPS) (Miller et al., 2003). Presence of a threshold psychosis syndrome (POPS) was also assessed (eligibility exclusion).

The presence of DSM-IV Axis I disorders, including Post-Traumatic Stress Disorder (PTSD), was assessed by semi-structured clinical interview using the Structured Clinical Interview for DSM-IV-TR (First et al., 2002) for participants age 16 or older, while the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) (Puig-Antich and Ryan, 1986) was administered to participants and parents for those aged 12–15. Wherever possible, collateral data on clinical measures were gathered from family members or treating clinicians. All semi-structured interviews were completed by master and doctoral level clinicians who received extensive training and supervision according to a standardized protocol, with diagnosis determined in regular consensus reliability rounds. Inter-rater reliability was calculated from staff ratings of training tapes, with an average intraclass correlation of 0.83 for symptom ratings and an average kappa value of 0.95 for diagnostic agreement.

2.2.2. Trauma assessment

Trauma history was assessed via the Traumatic Events Screening Inventory for Children (TESI-C) (Ford and Rogers, 1997), a semi-structured interview that assesses past exposure to a variety of traumatic events. Although the TESI-C was developed for use in child samples ages 8–18, the wording of the measure is clearly appropriate for older adolescents and adults, and allowed us to use a consistent measure across the full age span of the study. Events assessed by the interview include accidents and natural disasters, verbal, physical and sexual abuse, and domestic and community violence. All events were required to meet the DSM-IV Criterion A1: The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others (DSM-IV) (American Psychiatric Association, 2000). Two

specific trauma types were also calculated: sexual trauma, and interpersonal trauma, which was defined as any trauma involving a relationship to another person (e.g. abuse, neglect, assault, parental absence, death of a loved one), excluding events such as natural disasters and accidents.

2.2.3. Functioning

Functioning was assessed with the Global Functioning: Role and Social Scales, each containing a single clinician-rated item ranging from 1 to 10 developed for the late adolescent/young adult early psychosis population (Cornblatt et al., 2007). Global Assessment of Functioning (GAF) scores combining symptoms and functioning were made as part of the SIPS assessment.

2.3. Procedure

Participants or their parents completed a brief phone screen prior to attending the intake interview to assess study eligibility. At intake, all participants provided written consent, or assent and parental consent for minors. Participants completed clinical and trauma measures over two additional visits. Subjects were paid for their participation and all study procedures were approved by the UCSF committee on human research (institutional review board).

2.4. Statistical analyses

All symptom and functioning variables were normally distributed, with the exception of Grandiosity on the SOPS. CHR participants with and without a trauma history were compared on baseline SOPS symptoms and functioning with independent samples *t*-tests and a Mann-Whitney *U* test was used for Grandiosity. Spearman r correlations tested the association between number of traumatic events, which were non-normally distributed, and concurrent symptoms and functioning. Point-biserial correlations assessed the relationship between PTSD and symptoms and functioning due to the small number of participants with PTSD, with rank-biserial correlations for Grandiosity and number of traumatic events, which were non-normally distributed. A Bonferroni correction for multiple comparisons was applied to the exploratory analyses regarding PTSD diagnosis.

All analyses were completed in SPSS 24.

3. Results

3.1. Sample characteristics

Roughly half of the sample was female (52%), with a mean age of 18 years (SD = 4.2). The samples were racially and ethnically diverse, representing the population of the San Francisco Bay Area: 52% of participants identified as White/Caucasian, 18% Asian, 5% Black/African-American, 1% Native American/Other Pacific islander, 16% more than one race and 7% unknown or unreported. Twenty-four percent identified as Hispanic/Latinx. Socioeconomic status (SES) was determined using the two-factor Hollingshead Index, based on parental education and occupation (M = 37.7; SD = 16.9). Consistent with most CHR samples, the predominant diagnostic category met on the SIPS was APS with 98% of participants in that category (N = 101) and <1% BIPS (N = 1), plus 8.7% GRDS (N = 9), which could overlap with the other two diagnoses.

3.2. Trauma rates in CHR participants

Sixty-one percent of CHR participants (61%) reported lifetime exposure to traumatic events (see Table 1). Nearly all traumatic events were experienced prior to the onset of the CHR syndrome (58% of all CHR participants), with the exception of 3 participants who experienced the trauma after CHR onset but prior to study entry. Despite the high prevalence of trauma, only 22% ($n = 14$) of CHR participants with trauma exposure met criteria for Post-Traumatic Stress Disorder, equivalent to 14% of all CHR participants. CHR participants with a trauma history were more likely to be female ($\chi^2 = 8.1$; p = .004), but there were no other statistically significant differences on demographic variables, including family history of psychosis.

Table 1
Trauma rates for CHR participants (N = 103).

	N (%)
Any trauma	63 (61%)
Trauma < age 12	48 (47%)
Interpersonal trauma	38 (38%)
Interpersonal trauma < age 12	22 (21%)
Sexual trauma	18 (17%)
Sexual trauma < age 12	11 (11%)
Trauma < CHR syndrome onset	60 (58%)

3.3. Relationships between trauma and symptoms/functioning

CHR individuals with a trauma history had significantly more severe perceptual disturbances and general/affective symptoms on the SOPS, as well as lower GAF ratings than CHRs without trauma (Table 2). Similarly, the number of traumatic events was significantly correlated with more severe perceptual disturbances, general/affective symptoms and lower GAF ratings (Table 3). The number of interpersonal traumatic events was significantly correlated with more severe suspiciousness, perceptual abnormalities, general/affective symptoms and lower GAF scores. Given the small number of CHR participants reporting more than one sexual trauma event ($n = 5$), we did not conduct correlations with the sexual trauma score. None of the other symptom domains nor global social and role functioning scales showed significant differences between groups, nor correlations with events. Having a formal diagnosis of PTSD was moderately correlated with the number of traumatic events ($r = 0.44$ p < .001, one-tailed). PTSD diagnosis was also significantly correlated with worse SOPS General symptoms ($r = 0.19$ p = .029, one-tailed), although this did not survive a Bonferroni correction for multiple comparisons.

4. Discussion

4.1. Childhood trauma rates

In the current study, trauma exposure in a CHR sample (61%) was consistent with other studies of the CHR population and studies of individuals with schizophrenia or other psychotic disorders (Kraan et al., 2015; Varese et al., 2012), although our prevalence rates are slightly lower than those identified in a recent meta-analysis with a mean rate of 87%(Kraan et al., 2015), likely due to our severity criteria for

Table 2
CHR participants with and without trauma compared on symptoms and functioning.

	Trauma (N = 63)	No trauma (N = 40)	t or U	p
	M (SD)	M (SD)		
Unusual thinking	3.0 (1.7)	3.1 (1.4)	−0.27	.40
Suspiciousness	2.4 (1.7)	2.0 (1.3)	1.44	.08
Grandiosity[a]	0.7 (1.2)	1.2 (1.5)	1036	.08
Perceptual disturbances	2.7 (1.5)	1.9 (1.7)	2.38	.009*
Disorganized communication	1.2 (1.4)	1.4 (1.5)	−0.62	.27
Negative symptoms	11.9 (5.2)	12.4 (6.8)	−0.40	.35
Disorganized symptoms	6.0 (3.4)	5.7 (3.9)	0.33	.37
General/affective symptoms	9.5 (4.1)	7.3 (3.9)	2.67	.005*
Global Functioning: Social	6.1 (2.1)	5.9 (2.2)	0.46	.32
Global Functioning: Role	6.0 (1.4)	6.0 (1.5)	−0.03	.49
GAF	44 (11)	49 (9)	−2.19	.016*

[a] Mann-Whitney *U* test, two-tailed due to effect in opposite direction of hypothesis.
* p < .05, one-tailed.

Table 3
Correlations between number of traumatic events and symptoms and functioning.

	Total trauma		Interpersonal trauma	
	r	p	r	p
Unusual thinking	−0.02	.42	−0.01	.46
Suspiciousness	0.15	.06	0.28	.002*
Grandiosity	−0.08	.22	−0.05	.32
Perceptual disturbances	0.29	.002*	0.23	.009*
Disorganized communication	0.04	.34	0.11	.15
Negative symptoms	0.02	.44	0.02	.41
Disorganized symptoms	0.05	.32	−0.02	.43
General/affective symptoms	0.36	<.001*	0.28	.003*
Global Functioning: Social	−0.05	.32	0.04	.36
Global Functioning: Role	−0.01	.45	−0.09	.18
GAF	−0.33	<.001*	−0.29	.002*

* $p < .05$, one-tailed.

traumatic events. Given the lack of differences in rates of stressful life events in CHR samples compared to healthy controls in that meta-analysis but significant increase in traumatic events, we would argue that it is important to differentiate between truly potential "traumatic" events and less severe stressful life events.

To our knowledge, this is the first study to assess *childhood* trauma prior to age 12 and prior to onset of the CHR syndrome, suggesting that the impact of trauma on development of psychotic-like experiences may begin quite early in life, neither just as a triggering event at onset of psychosis, nor as a result of CHR risk status. Consistent with our results, Arseneault et al. (2011) found that 12 year old children with psychotic symptoms were more likely to have experienced maltreatment by an adult (relative risk 3.16), bullying by peers (relative risk 2.47), or have been in an accident (relative risk 1.47).

4.2. Trauma types and correlates

Also consistent with other CHR studies, trauma history and number of traumatic events were significantly associated with positive and general/affective symptoms, pointing to a broad impact of trauma on multiple symptom domains. This may reflect a nonspecific effect of CT on a variety of psychopathological outcomes, including mood and anxiety disorders (Kessler et al., 1997), or may reflect an affective pathway to psychosis (Myin-Germeys and van Os, 2007). Specifically, we replicated the findings of O'Connor et al. (2017) who reported that trauma and bullying both increased the odds of experiencing perceptual abnormalities in individuals with the CHR syndrome. CT has been associated with hallucinations in adults both with and without primary psychotic disorders (Daalman et al., 2012). Interpersonal stressors have been associated with the emergence of psychopathology, most notably depression (Vrshek-Schallhorn et al., 2015). To our knowledge, this is the first study to extend these findings to the psychosis prodrome by assessing interpersonal trauma in those diagnoses with the CHR syndrome. Consistent with cognitive models of psychosis linking interpersonal trauma with "personalizing" appraisals and paranoia in first-episode psychosis (Lovatt et al., 2010), we found that the number of interpersonal trauma events (versus non-interpersonal trauma) was uniquely correlated with suspiciousness. Importantly, elevated CT rates were not associated with family history of psychosis or lower socioeconomic status, thus pointing to a specific relationship to the CHR syndrome. The lack of association with social and role functioning measures suggests that the lower GAF scores in CHR individuals with CT found in prior research may reflect more severe symptoms, rather than impaired functioning, which is combined in the GAF scale.

Interestingly, although a formal PTSD diagnosis was associated with the number of traumatic events, it was not significantly associated with symptoms or functioning. PTSD diagnosis was associated with SOPS general symptoms before a conservative correction for multiple comparisons, but that score likely also reflects severity of PTSD symptoms, which are captured by the single SOPS item that assesses both mood and anxiety, as well as sleep symptoms assessed under that domain. This suggests the effects of trauma on positive symptoms are not restricted to those individuals with a formal PTSD diagnosis.

4.3. Strengths, limitations and future directions

Strengths of this study include the detailed trauma measurement via interview that assessed age and types of trauma with a clear trauma definition, as well as the diverse study sample. Limitations include the moderate sample size and lack of a control group. Future research could address this issue by including a psychiatric control group. Importantly, future research should aim to identify which mechanisms underlie the relationship of trauma to symptoms, including those that may be specific to positive symptoms and those that more generally contribute to an array of psychopathology (van Nierop et al., 2015). Multiple cognitive and biological models have been proposed to explain the relationship of CT to psychosis, including behavioral sensitization (Lardinois et al., 2011), cognitive appraisal (Lovatt et al., 2010) attachment style (Pilton et al., 2016), and effects of increased stress hormones on dopamine and glutamate (Howes et al., 2017; van Winkel et al., 2013). Additionally, these results highlight the importance of focusing on the specific mechanistic pathways of interpersonal trauma on CHR symptomatology. Finally, a critical avenue of investigation is whether CT raises the risk for transition to psychosis and other poor outcomes within the CHR population, which has not yet been unequivocally established (Bechdolf et al., 2010; Cannon et al., 2016; Stowkowy et al., 2016; Yung et al., 2015).

4.4. Clinical implications

The high prevalence of trauma in the CHR population and relationship to psychiatric symptoms implies that all individuals with CHR diagnoses should be adequately screened for a trauma history, in line with our own past recommendations, other investigators and good clinical practice in early psychosis (Hardy and Mueser, 2017; Mayo et al., 2017; Stowkowy et al., 2016). Given the lack of relationship between formal PTSD diagnosis and symptoms, it may not be sufficient to inquire about or address trauma only in those individuals who clearly meet full criteria for PTSD. Our results here also specifically highlight the need to screen for all forms of trauma, not only abuse and neglect. Unfortunately, there are a lack of evidence-based interventions for trauma in the CHR syndrome with only recent attention to PTSD treatment in schizophrenia, and many clinicians express discomfort with addressing trauma in psychotic-spectrum conditions (Cragin et al., 2017; Gairns et al., 2015). Thus, our current treatment recommendations are limited to individual adaptations of trauma-informed and trauma-focused treatments (Swan et al., 2017), pointing to a substantial clinical need and direction for future research.

Conflict of interest

Rachel Loewy has received honoraria from the Lundbeck International Neuroscience Foundation. Sophia Vinogradov is a site investigator on an SBIR grant to PositScience, Inc., a company with a commercial interest in cognitive training software. She is also on the Advisory Board of MindStrong Inc. and Alkermes. Dan Mathalon has served as a consultant for Boehringer Ingelheim, Takeda, Upsher-Smith, Alkermes, Roche, Bristol-Myers Squibb, and AstraZeneca. Sawsan Dabit is a Senior Clinical Research Associate at PositScience, Inc. Danielle Schlosser has a financial interest in and is an employee of Verily Life Sciences.

Contributors

Rachel Loewy designed and managed the study; she and Sarah Corey conducted statistical analyses and wrote the first draft of the manuscript. Daniel Mathalon, Rahel Pearson, Danielle Schlosser, Barbara Stuart and Sophia Vinogradov contributed to study design. Felix Amirfathi, Sawsan Dabit, Daniel Fulford and Jessica Hua managed study data and conducted study procedures. All authors contributed to and have approved the final manuscript.

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