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Authors

Farris, Megan

Braun, Amy

Liu, Lu

et al.

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Longitudinal Impact of Trauma in the North American Prodrome Longitudinal Study (NAPLS-3)

Megan S. Farris[a], **Amy Braun**[a], **Lu Liu**[a], **Carrie E. Bearden**[b], **Kristin S. Cadenhead**[c], **Barbara A. Cornblatt**[d], **Matcheri Keshavan**[e], **Daniel H. Mathalon**[f], **Thomas H. McGlashan**[g], **Diana O. Perkins**[h], **William S. Stone**[e], **Ming T. Tsuang**[c,i], **Elaine F. Walker**[j], **Scott W. Woods**[g], **Tyrone D. Cannon**[k], **Jean Addington**[a]

[a]Department of Psychiatry, Hotchkiss Brain Institute, University of Calgary, Calgary, Alberta, Canada

[b]Departments of Psychiatry and Biobehavioral Sciences and Psychology, UCLA, Los Angeles, CA, United States of America

[c]Department of Psychiatry, UCSD, San Diego, CA, United States of America

[d]Department of Psychiatry, Zucker Hillside Hospital, Long Island, NY, United States of America

[e]Department of Psychiatry, Harvard Medical School at Beth Israel Deaconess Medical Center and Massachusetts General Hospital, Boston, MA, United States of America

[f]Department of Psychiatry, UCSF, and SFVA Medical Center, San Francisco, CA, United States of America

[g]Department of Psychiatry, Yale University, New Haven, CT, United States of America

[h]Department of Psychiatry, University of North Carolina, Chapel Hill, NC, United States of America

[i]Institute of Genomic Medicine, University of California, La Jolla, CA, United States of America

[j]Departments of Psychology and Psychiatry, Emory University, Atlanta, GA, United States of America

[k]Department of Psychology, Yale University, New Haven, CT, United States of America

Abstract

Aim: individuals at clinical high risk (CHR) for psychosis have been shown to experience more trauma than the general population. However, although the effects of trauma appear to impact some symptoms it does not seem to increase the risk of transition to psychosis. The aim of this

*Corresponding Author: Dr. Jean Addington (jmadding@ucalgary.ca), Mathison Centre for Research & Education. 3330 Hospital Drive NW, Calgary, Alberta T2N 4N1.

Conflicts of Interest

Authors declare they have no conflict of interest with respect to this study.

Data Sharing

The data that support the findings of this study are available on request from the corresponding author. The data are not currently publicly available.

paper was to examine the prevalence of trauma, and its association with longitudinal clinical and functional outcomes in a large sample of CHR individuals.

Methods: From the North American Prodrome Longitudinal Study-3 (NAPLS-3) 690 CHR individuals and 91 healthy controls from nine study sites between 2015–2018 were assessed. Historical trauma experiences were captured at baseline. Participants completed longitudinal assessments measuring clinical outcomes including positive and negative symptoms, depression, social and role functioning and assessing transition to psychosis.

Results: From the 690 CHR participants and 9 6 healthy controls, 343 (49.6%) and 15 (15.6%), respectively, reported a history of trauma ($p<0.001$). Emotional neglect (70.3%) was the most commonly reported type of trauma, followed by psychological abuse (57.4%). Among CHR participants, time to transition to psychosis was not associated with trauma. Baseline depression and suspiciousness/persecutory ideas were statistically significantly different between CHR individuals who did or did not experience trauma. However, when examining clinical and functional outcomes over 12-months of follow-up, there were no differences between those who experienced trauma and those who did not.

Conclusion: Overall, trauma is a significantly prevalent among CHR individuals. The effects of trauma on transition and longitudinal clinical and functional outcomes were not significant.

Keywords

trauma; clinical high risk; transition to psychosis; clinical outcomes; depression

Introduction

Childhood trauma including physical, sexual, and emotional abuse, and physical and emotional neglect, is experienced by many individuals globally with estimates of between 20%−50% of adults having been affected by childhood trauma (Stoltenborgh et al., 2015; Tink et al., 2017). Moreover, childhood trauma has been associated with a wide range of physical health problems and mental health disorders including depression, anxiety, bipolar disorder, eating disorders, and psychosis (Carr et al., 2020). In the general population, childhood trauma has been associated with psychotic symptoms (Bloomfield et al., 2021), the likelihood of which increases when individuals suffer a greater range of trauma subtypes and a higher frequency of trauma (Croft et al., 2019). Furthermore, higher rates of trauma have been reported among individuals with psychosis. For example, in one study, 89% of individuals experiencing a first episode of psychosis compared to 37% of healthy controls reported childhood trauma, with evidence of a dose-response relationship (Trauelsen et al., 2015).

This literature has led researchers to examine trauma in individuals who are at clinical high risk (CHR) for psychosis. In the most comprehensive to date review and meta-analysis of CHR and trauma, CHR individuals reported significantly more trauma than healthy controls, with prevalence rates ranging from 54%−90% (Peh et al., 2019). Although emotional and physical abuse were most often reported, there were no significant differences in the prevalence of trauma subtypes. Furthermore, these authors did not find any association between trauma overall and transition to psychosis. However, when examining different

types of trauma, the pooled estimate among five studies examining sexual abuse and transition to psychosis was statistically significant (Peh et al., 2019), but these results were mainly driven by one large study (Thompson et al., 2014). Another previously published review (Mayo et al., 2017) also found that sexual abuse was most commonly associated with transition to psychosis, relative to other types of trauma. The Peh meta-analysis (2019) further reported several studies finding a significant association between trauma and more severe attenuated psychotic symptoms, depression, and poorer social and role functioning. An additional study has supported the association of trauma with depression (de Vos et al., 2019).

The North American Prodrome Longitudinal Study (NAPLS) consortium examined trauma in their second CHR cohort, NAPLS-2, reporting significantly more trauma in CHR individuals than healthy controls at baseline, significant cross-sectional associations between trauma and subthreshold symptoms and depression, and no associations between trauma and transition to psychosis (Addington et al., 2013; Stowkowy et al., 2016). Even when trauma was considered in conjunction with several other potential predictors in the NAPLS risk calculator it was not significant in the model predicting transition to psychosis (Cannon et al., 2016).

In summary, childhood trauma is more common in CHR youth and is associated with a variety of symptoms. While there is evidence that trauma is related to psychosis development in the general population, there is little evidence to suggest that trauma is related to the later transition to psychosis in CHR youth. Therefore, different populations may have different risk factors/predictors for the development of psychosis. The aim of this study was to examine trauma in the new NAPLS-3 sample to confirm previous findings with respect to prevalence, transition, and baseline symptoms and social and role functioning and to also examine longitudinally the association of trauma with symptoms and functional outcomes.

METHODS

Participants

NAPLS-3 is a National Institute of Mental Health (NIMH) funded study conducted at nine sites: Emory University, Harvard University, University of Calgary, University of North Carolina Chapel Hill, Yale University, Zucker Hillside Hospital, and, the University of California Los Angeles (UCLA), San Diego (UCSD) and San Francisco (UCSF).

In total, 710 CHR individuals and 96 healthy controls were recruited between February 2015 to November 2018 and followed for up to two years. NAPLS-3 CHR participants were referred from health care providers, educators, or social service agencies or were self-referred in response to intensive community education efforts. Healthy controls were recruited by posting adverts in public and educational places as well as by word of mouth. Control recruitment lagged at least one month behind CHR recruitment in order to facilitate age and gender balance. Further information on recruitment can be found in Addington et al, (2020a). All participants were between the ages of 12 and 30 years. Participants were excluded from NAPLS-3 if they 1) met criteria for an Axis I psychosis disorder either

currently or during their lifetime, 2) had an IQ<70, 3) had a history of a central nervous system disorder, or 4) had diagnostic psychosis-risk symptoms that were clearly caused by an Axis I disorder. CHR participants met the Criteria of Psychosis-Risk Syndromes (COPS) (McGlashan et al., 2010) based on the Structured Interview for Psychosis-Risk Syndromes (SIPS) version 5.6. Healthy controls did not meet any criteria for a psychosis-risk syndrome; any current or lifetime psychotic disorder or Cluster A personality disorder diagnosis; had a first-degree family history of a psychotic disorder or any other disorder involving psychotic symptoms; or were currently using psychotropic medication.

Of the total NAPLS-3 sample, 690 CHR and 96 healthy controls had baseline trauma data and were the participants used to examine prevalence of trauma and baseline clinical symptom associations. Of this sample 69 (10%) CHR participants made the transition to psychosis during the follow-up and 334 (48.4%) remained in the study for two years.

Measures

Demographic characteristics were collected at baseline. The SIPS (McGlashan et al., 2010) was used to determine if participants met criteria for being CHR for psychosis, and the Scale of Psychosis-Risk Symptoms (SOPS) (McGlashan et al., 2010) was used to measure attenuated psychotic and negative symptoms. Social and role functioning were assessed with the GF:Social and GF:Role scales (Cornblatt et al., 2007). The GF:Social scale assesses peer relationships, peer conflict, age-appropriate intimate relationships, and family involvement. The GF:Role scale rates performance and amount of support needed in one's specific role (i.e., school, work). The Calgary Depression Scale for Schizophrenia (CDSS) assessed depression (Addington et al., 1993).

Trauma experiences before the age of 18 years were assessed at baseline using an adapted version of the Childhood Trauma and Abuse scale (Janssen et al., 2004). Information on childhood trauma was coded as "yes" trauma occurred through acknowledgement or information from a reliable source or "no" trauma was confirmed to not have occurred. Trauma was categorized into the following four domains: psychological abuse (being sworn at, receiving lesser treatment relative to siblings, unjustified punishment or blackmailing), physical abuse (being kicked, punched, or experiencing any other form of physical abuse), sexual abuse (touched sexually by anyone against ones will, forced to touch anyone or were pressured into sexual contact against one's will) and, emotional neglect (individuals at home did not listen to problems, problems were ignored, or not being able to find any attention or support). Participants were asked at what age period (0–6, 7–12, or 13–17 years) the trauma had occurred. Duration of trauma was categorized as having occurred for either <1 year or ≥1 year.

Procedures

All participants provided written informed consent (including parental consent for minors) to participate in the NAPLS-3 study. The NAPLS-3 study was approved by the Institutional Review Boards of all participating study sites.

Comprehensive details of study eligibility, symptom ratings and diagnoses were determined to construct a vignette for each CHR participant to achieve a consensus diagnosis

(Addington et al., 2020). Weekly consensus calls, chaired by J. Addington, were conducted between clinical raters from all nine sites to review each vignette and determine a diagnosis and study inclusion. Demographics, trauma, and clinical assessments were completed at baseline. Clinical assessments were completed every two months (i.e., 2-, 4-, 6-, and 8-months) for the first eight months of the follow-up, and additionally at the one-, and two-year follow-up visits.

Statistical Analysis

CHR and healthy control participants were compared on prevalence and duration of trauma using chi-squared and Fisher's exact analysis. Comparison of demographics between those who reported trauma and those who reported no trauma were conducted using the Student t-test for continuous variables and chi-square tests for categorical variables.

Baseline clinical symptoms were described and compared between CHR participants who experienced trauma versus not using Student t-tests. To accommodate missing data and account for intra-participant correlation over time, a generalized linear mixed model for repeated measures was used to determine changes over time (baseline, 2-, 4-, 6-, 8-, and 12-months) both between and within trauma groups.

Trauma as a potential predictor of the transition to psychosis was examined with Cox proportional hazards models, for the 334 CHR participants who completed the two-year assessment.

All statistical analyses were performed using IBM SPSS version 25 and SAS version 9.4.

RESULTS

Demographic characteristics for CHR participants are presented in Table 1. CHR participants who did not report trauma (n=347) were slightly younger, had less years of education, were more likely to live with their family, and were more likely to be unemployed, relative to CHR participants with a history of trauma (n=343).

Demographics for all CHR individuals and healthy controls are reported in Supplementary Table 1.

Trauma was reported in a statistically significantly higher proportion of CHR individuals (n=343; 49.6%) than healthy controls (n=15; 15.6%), (X^2=39.5; p<0.001). Of those who reported trauma, 286 (83.4%) CHR participants and 11 (73.3%) healthy controls experienced trauma for a duration of ≥1 year. Trauma was most often reported to have occurred between the ages of 13–17 years (n=282; 78.8%) followed closely by 7–12 years (n=276; 77.1%), and finally 0–6-years (n=180; 50.3%), respectively. For both CHR and healthy controls, emotional neglect was the most reported type of trauma, whereas sexual abuse was the least reported. See Table 2.

For CHR participants who completed the two-year assessment (n=334), there were no statistically significant associations between transition to psychosis and the overall measure of all types of trauma, nor any of the individual trauma domains. See Table 3.

At baseline, the only clinical differences were that those who experienced trauma had significantly higher scores on depression (7.41±4.62, versus 5.22±4.03; t=−6.61, p<0.001) and on the SOPS, P2 suspiciousness/persecutory ideas (3.20±1.29, versus 2.97±1.55; t=−2.17, p=0.030). These results are presented in Supplementary Table 2.

The two groups did not differ on any symptoms or functioning over 12 months. These results are presented in Supplementary Figures 1–6.

Dropouts were also captured at all follow-up timepoints but were not statistically significantly different between those who experienced trauma versus not (Supplementary Table 3).

DISCUSSION

We first examined prevalence of trauma in NAPLS-3 and observed that over half of the CHR participants had experienced trauma before the age of 18 years, with most experiencing trauma for more than one year. The most common type of trauma was emotional neglect, followed by psychological abuse. These results are consistent with previous literature. The Peh meta-analysis (2019) reported the prevalence rates of trauma to be over 50% and found that emotional abuse was the most often reported amongst CHR. As in NAPLS-2 (Stowkowy et al., 2016) and consistent with most previous literature (Peh et al., 2019), we found no association between any type of trauma and transition to psychosis. Although, the Mayo qualitative synthesis (2017) and the Peh meta-analysis (2019) did find that sexual abuse was associated with transition, but this was driven by one large study (Thompson et al., 2014).

As observed in previous studies (de Vos et al., 2019; Peh et al., 2019; Addington et al., 2013; Stowkowy et al., 2016), at baseline, those who had experienced trauma had higher ratings on depression and suspiciousness. There were no other baseline differences in symptoms between the two groups. In terms of longitudinal data, we examined whether the groups differed in symptoms or functioning over the course of 12 months. In this study, although the longitudinal data showed broadly similar patterns, in magnitude, relative to the baseline results, the differences did not reach statistical significance. Those who had experienced trauma continued to present with higher ratings on suspiciousness and depression over time, but these were not significant. However, these patterns should be interpreted with caution due to the high dropout rates across the follow-up assessments. Overall, results observed in the NAPLS-3 cohort generally support previous research.

Since trauma appears to have an impact on later mental health including psychosis, it is often expected that it may play a role in later transition to psychosis, although to date there is little support for that. First, it is possible that young people with a history of trauma are reluctant to seek treatment in either a clinic for “at-risk” youth or to volunteer for a study that is both long-term and has a heavy burden of assessments, such as NAPLS-3 (Addington et al., 2020) and therefore our sample of CHR with a history of trauma is limited. Secondly, , being at risk for psychosis due to a history of trauma in the general population is a different vulnerability from being at risk of developing psychosis once identified as being at CHR

for psychosis. For example, the key risk factors for the development of psychosis in the general population include trauma, cannabis use, urbanicity, and/or having family history of psychosis, while the risk factors for transition from CHR to psychosis include clinical factors such as: attenuated psychotic symptoms, poor cognition, poor social functioning, and a decline in social functioning; as well as the possibility of certain environmental factors such as: bullying, and cannabis use (Addington et al., 2020b). If trauma is a risk factor for psychosis, as has been observed in epidemiological general population studies it may already have had its impact by having an individual develop severe enough attenuated psychotic symptoms that they meet a CHR diagnosis, and therefore does not play a role in the later conversion to psychosis.

The strength of the NAPLS-3 study is that it is a large longitudinal sample of well-defined CHR participants from multiple sites across North America. However, there are limitations. First our measure of trauma was brief, requiring a yes/no response, whereas many studies use the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 2003), which inquires about specific traumatic experiences and has a range of continuous ratings between 28 and 140. However, Peh and colleagues (2019) found that a sensitivity analysis of only studies that used the CTQ demonstrated little impact on the overall effect size for severity of trauma suggesting that across study differences were not necessarily due to using different measures. Secondly, the risk of recall bias is always the concern with a retrospective assessment of trauma (Ramsaran et al., 2019). Thirdly, the frequency and intensity of trauma was not captured in this study, which may have provided additional insights into the impact of trauma. Finally, dropout rates were high across the two year of follow-up, which led to small sample sizes and potential bias. Although, the dropout rates did not differ between those who experienced trauma versus not.

In conclusion we have demonstrated that trauma is significantly prevalent among CHR individuals, however, within the CHR group trauma appears to have little impact on symptom presentation, functioning and transition to psychosis. Regardless, this does not negate the need to screen for childhood trauma amongst CHR youth as it may predispose to more symptoms or exacerbate current symptoms. Trauma should be an important target for intervention so that the best outcomes can be targeted for those within this vulnerable population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Demographic Characteristics for CHR Participants with and without Trauma

Characteristics	CHR with Trauma (n=343)	CHR with No Trauma (n=347)	Test Statistic	Effect Size
	Mean (SD)	Mean (SD)	t	d
Age (years)	19.08 (4.34)	17.28 (3.53)	−5.97***	0.46
Years of education	11.92 (3.04)	10.92 (3.03)	−4.35***	0.33
	n (%)	n (%)	χ^2	V
Male sex	175 (51.0)	200 (57.6)	3.04	0.07
Race				
Asian	37 (10.8)	35 (10.1)	4.69	0.08
Black	47 (13.7)	31 (9.0)		
Caucasian	211 (61.5)	221 (63.9)		
Other[a]	48 (14.0)	59 (17.1)		
Living with family	231 (67.3)	281 (81.2)	17.35***	0.16
Single marital status	331 (96.5)	333 (96.0)	0.14	0.01
Currently employed	128 (37.3)	85 (24.6)	12.94***	0.14
Currently enrolled as student	270 (78.7)	301 (86.7)	7.79	0.11

*p<0.01;

**p<0.005

***p<0.001

Abbreviations: CHR: clinical high risk; HC: healthy controls; SD: standard deviation.

[a]Other: First Nations, Hawaiian/Native Pacific Islander, Interracial.

Table 2.

Prevalence of Types of Trauma in CHR Individuals and Healthy Controls

Trauma Outcomes	CHR (n=343)	HC (n=15)	Significance
	n (%)	*n (%)*	*p-value*
Psychological abuse	197 (57.4)	5 (33.3)	0.11
Physical abuse	136 (39.7)	7 (46.7)	0.60
Sexual abuse	90 (26.2)	3 (20.0)	0.77
Emotional neglect	241 (70.3)	8 (53.3)	0.25

Abbreviations: CHR: clinical high risk; HC: healthy controls; SD: standard deviation.

Note: Types of trauma are not mutually exclusive; therefore, participants may have had multiple types of trauma and would be counted once for each type.

Table 3.

Trauma in CHR Individuals and Transition to Psychosis

Trauma Outcomes	Crude		Multivariable Adjusted	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Any trauma (yes/no)	0.70 (0.43–1.12)	0.135	0.67 (0.41–1.09)	0.103
Type of trauma				
Psychological abuse	1.00 (0.60–1.65)	0.986	0.90 (0.54–1.49)	0.673
Physical abuse	1.14 (0.66–1.97)	0.639	0.97 (0.58–1.62)	0.906
Sexual abuse	0.81 (0.39–1.69)	0.569	1.11 (0.63–1.95)	0.720
Emotional neglect	0.93 (0.56–1.52)	0.760	0.77 (0.36–1.64)	0.499

Abbreviations: CHR: clinical high risk; CI: confidence interval; HC: healthy controls; SD: standard deviation.

Note: Types of trauma are not mutually exclusive; therefore, participants may have had multiple types of trauma and would be counted once for each type.