Adverse Childhood Experiences and Psychotic-like Experiences Are Associated Above and Beyond Shared Correlates: Findings from the Adolescent Brain Cognitive Development Study

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Abstract

Adverse childhood experiences (ACEs) are associated with increased risk for psychotic-like experiences (PLEs). However, ACEs and PLEs are also both associated with several shared factors (e.g., internalizing symptoms, suicidality). Few studies have explicitly examined whether the association between ACEs and PLEs remains over and above shared correlates. To address this question, using 10,800 9-11-year-olds, we examined whether ACEs and school-aged PLEs were associated when accounting for shared correlates, and whether there was evidence of mediation in associations between PLEs, ACEs, and these shared factors. Greater number of ACEs were associated with greater PLEs, including several specific ACEs (e.g., bullying). Importantly, ACEs and PLEs were related even when accounting for shared correlates. Further, PLEs partially mediated the relationships between ACEs and both internalizing symptoms and suicidality, including suicidal behavior. The current study helps clarify the nature of the associations between PLEs and ACE and has important clinical implications for addressing PLEs.

Keywords

adverse childhood experiences; psychotic-like experiences; suicidality; internalizing symptoms; trauma

1. Introduction

Adverse childhood experiences (ACEs) are a common experience worldwide, with the results of the original ACEs study finding that almost two-thirds of participants reported at least one ACEs before adulthood (CDC and Permanente, 2016). Definitions of ACEs vary, and can encompass a range of experiences, including sexual abuse, physical abuse, emotional/psychological abuse, and peer victimization (e.g., bullying) (Afifi et al., 2020). Research indicates that ACEs may result in neural alterations affecting the hypothalamus-pituitary-adrenal (HPA) axis, thereby leading to a host of functional impairments (Isvoranu

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et al., 2017). For example, ACEs are associated with greater risk for a range of health problems, including increased risk of anxiety disorders, depression, and psychotic disorders (Croft et al., 2019; Loewy et al., 2019). However, research is limited regarding the extent of these associations in school-age children, particularly in relation to psychotic spectrum symptoms. Therefore, the current study examined the associations between ACEs and psychotic-like experiences (PLEs) in a large sample in middle childhood.

PLEs, or nonclinical schizophrenia spectrum symptoms (e.g., unusual beliefs, perceptual abnormalities) in childhood are associated with greater odds of developing psychiatric disorders, including psychotic disorders, during adulthood (Poulton et al., 2000). Importantly, research generally indicates that exposure to childhood ACEs is associated with increased risk of psychotic disorders (Croft et al., 2019; Loewy et al., 2019). A recent meta-analysis found that approximately 87% of individuals at ultra-high risk for psychosis endorse an ACE (Kraan et al., 2015). Some research indicates that specific types of traumatic experiences with intention to harm (Moriyama et al., 2018), such as the experience of bullying (Strauss et al., 2018) or sexual abuse (McGrath et al., 2017), may be most strongly associated with PLEs. However, more work is needed to determine if one or more of these types of ACEs are specifically associated with PLEs, or if there is a more general relationship between ACEs and PLEs.

Critically, ACEs and PLEs are both associated with a number of shared correlates (Figure 1a) (Isvoranu et al., 2017), including everyday stress (Cristobal-Narvaez et al., 2016), impairments in cognition (e.g., fluid cognition) (Mansueto et al., 2019), depression and generalized anxiety (Barzilay et al., 2019), and suicidality (Grivel et al., 2018), including both suicidal ideation and suicidal behavior (e.g., attempts) (Gaweda et al., 2020; Merrick et al., 2017; Yates et al., 2019). In addition, family history of mental illness (e.g., family history of psychosis) is a risk factor for both PLEs and ACEs (Felitti et al., 1998; Polanczyk et al., 2010). However, few studies have examined evidence that the association between ACEs and PLEs remains over and above these shared correlates (Arseneault et al., 2011; Barzilay et al., 2019). For example, ACEs and PLEs might appear to be related because they are both associated with stress, internalizing symptoms, and impaired cognitive function, but may no longer demonstrate an independent relationship to each other once accounting for these shared correlates.

There is a need for more research on the interrelationships of PLEs, ACEs and their shared correlates, specifically to begin to understand the nature of these associations, including whether PLEs are the mechanism underlying the association between ACEs and other negative psychopathological correlates (i.e., greater anxiety/depression and suicidality). Research has focused on internalizing symptoms and cognitive impairments as potential mediators of the association ACEs and PLEs (Figure 1b) (Gaweda et al., 2019; Mansueto et al., 2019; Williams et al., 2018). There is evidence that depression and anxiety partially mediate the association between trauma and PLEs (Fisher et al., 2013). However, conceptually, previous research also supports the possibility that PLEs lead to increased anxiety and depressive symptoms and suicidal outcomes following a trauma (Conus et al., 2010; Gaweda et al., 2020), suggesting the possibility that PLEs might mediate at least some aspects of the relationships between ACEs and other mental health outcomes (Figure 1c).

Along these lines, there is support for PLEs mediating the association between ACEs and suicidality (Gaweda et al., 2020). Thus, while evidence indicates that PLEs mediate the association between ACEs and suicidality, the direction of mediation is less clear for other correlates, such as internalizing symptoms (i.e., whether PLEs mediate the association between ACEs and internalizing symptoms, or whether internalizing symptoms mediate the association between ACEs and PLEs). Clarifying these interrelationships has important clinical implications, including understanding the mechanisms contributing to the development of PLEs and other negative psychopathological correlates.

The current study examined the associations between ACEs and PLEs using data from 9-11-year-olds in the Adolescent Brain Cognitive Development (ABCD) study. First, we examined whether, as expected, greater endorsement of ACEs is associated with greater report of PLEs. We also examined whether PLEs were associated with specific types of ACEs, such as sexual abuse, physical abuse, and bullying. Also, given evidence for shared correlates between ACEs and PLEs, we examined whether the association between ACEs and PLEs remained when accounting for stress, cognitive deficits, internalizing symptoms, family history of psychosis, and suicidality. Lastly, we examined whether there was evidence of PLEs mediating the associated between ACEs and stress, fluid cognition, internalizing symptoms, suicidality or vice versus.

2. Materials and methods

2.1 Participants

A sample of 11,874 individuals was obtained from the ABCD study, a large-scale study tracking 9–11-years-olds recruited from 21 research sites across the United States. Study exclusion criteria are listed in Supplement. All procedures comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All parents provided written informed consent and all children provided assent.

ABCD data were accessed from the National Institutes of Mental Health Data Archive (Acknowledgments). Participants were removed from analyses due to missing data (n=1,074; Supplemental Table 1). The final sample size was 10,800 individuals (47.9% female; 52.8% White, 20.0% Hispanic, 14.5% African American, 2.2% Asian, and 10.6% Other).

2.2 Measures

2.2.1 Symptom Measures—Child participants completed the Prodromal Questionnaire-Brief Child Version (PQ-BC), a 21-item self-report questionnaire that has been previously validated for use with school-age children using the ABCD sample (Karcher et al., 2018). Consistent with previous research (Karcher et al., 2018; Loewy et al., 2011), distress scores were calculated, which are the total number of endorsed questions weighted by level of distress [i.e., 0=no, 1=yes (but no distress), 2–6=yes (1+score on distress scale)]. PQ-BC distress scores were also divided into two separate scores, one for questions

pertaining to unusual beliefs and another for perceptual abnormalities in follow-up analyses (Supplemental Table 2) (Karcher et al., 2019).

The parent and child versions of the validated and computerized Kiddie-Structured Assessment for Affective Disorders and Schizophrenia (K-SADS) for DSM-5 (Kobak et al., 2013, April) were used as measures of other psychopathology (Barch et al., 2018). The computerized self-administered parent and child versions of the K-SADS show good to excellent concordance with the clinician-administered computerized K-SADS (Townsend et al., 2020). The ACEs variable was defined as summations of parent-rated child experience of traumatic experiences from the K-SADS, a parent-rated question from the K-SADs about whether the child was bullied at school or in the neighborhood, and seven parent-rated questions of financial adversity from a demographic questionnaire (e.g., "Were evicted from your home for not paying the rent or mortgage?"; see Supplement for all financial adversity questions, results using an alternative definition of ACEs; Supplemental Table 3 for frequencies of endorsement of each ACE). Therefore, our definition of ACEs included a number of traumatic life experiences and chronic financial stress. Information regarding the timing of ACE and onset of PLEs is not available in the ABCD sample, precluding the ability to examine causal associations.

In addition, internalizing symptoms were examined using summations of current child-rated depression and generalized anxiety disorder (GAD) symptoms from the K-SADS (see Supplement for analyses with externalizing symptoms). Suicidality was examined using summations of endorsements of current child-rated suicidal ideation (i.e., thinking of a method for a suicide attempt, suicidal thinking with intent to act, thinking of a specific suicidal plan) and suicidal behavior (i.e., self-injury with intent to die, self-injury and thinking you could die from behavior, made preparation for a suicide attempt, aborted or interrupted suicide attempts, the method of an actual suicide attempt, or a suicide attempt in which they thought they could die) from the K-SADS. Stress was measured using the stress subscale from the parent-rated Child Behavior Checklist (Achenbach, 2009).

2.2.2   Other Measures—Participants completed all National Institutes of Health Toolbox Cognitive Battery (NIHTB-CB) tests (Weintraub et al., 2014). The current study utilized uncorrected NIHTB-CB fluid composite scores, but all analyses include age and sex as covariates (see Supplement and (Weintraub et al., 2013)) for descriptions of individual NIHTB-CB tests and for analyses for total composite scores). The family history of psychotic disorder in first-degree relatives was assessed using the parent-rated Family History Assessment Module Screener (Rice et al., 1995), with each scored as either present or absent.

2.3   Statistical Analyses

The analyses used hierarchical linear models (HLMs), with all multiple comparisons False Discovery Rate corrected (FDR-corrected). Analyses were conducted in R lme4 package (Bates et al., 2015) (multcomp package for multiple comparison analyses (Hothorn et al., 2008)), with family unit and research site modeled as random intercepts, and age, sex (see Supplement for additional analyses of sex differences), and race/ethnicity included as

covariates. Results are expressed as standardized estimates (βs) with 95% bootstrapped (5000 iterations) confidence intervals (CIs). Due to significant skew and zero inflation of PQ-BC scores, we also examined log-transformed scores, with consistent results. Differences between significant correlations with each type of ACE were examined using Meng's z-test procedures (Meng et al., 1992). HLMs examined the association between PLEs and a) number of ACEs, and b) individual ACEs (and ACE composites of accidents, disaster, physical abuse, emotional abuse, and sexual abuse; Table 1). Associations between ACEs and individual PLE items were analyzed using ordered logistic regressions (R package ordinal (Christensen, 2015)). We also examined whether associations between PLEs and number of ACEs remained when accounting for shared correlates, including family history of psychosis, stress, fluid cognition, internalizing symptoms, and suicidality. We performed model-based mediation analyses using the lavaan package in R (Rosseel, 2012) to better understand whether PLEs mediated the association between ACEs and stress, fluid cognition, internalizing symptoms, and/or suicidality.

3. Results

3.1 Associations between PLEs and ACEs

Greater number of ACEs were associated with greater PLEs (β=.102, p<.001, full model R^2=.320, partial R^2=.033; Table 1). In terms of covariates, being African American (β=0.306, FDR-corrected p<.001), Hispanic (β=0.225, FDR-corrected p<.001), male (β=−0.053, FDR-corrected p=.004), and younger (β=−0.052, FDR-corrected p<.001) were all significantly associated with greater PLEs.

3.1.1 Associations between PLEs and individual ACEs.—In a model including all of the individual ACEs simultaneously, greater PLEs were associated with several specific ACEs, including witnessing domestic violence (β=0.100, FDR-corrected p=.04; partial R^2=.025), traumatic grief (β=0.066, FDR-corrected p=.025; partial R^2=.025), bullying (β=0.304, FDR-corrected p<.001; partial R^2=.037), and financial adversity (β=0.046, FDR-corrected p<.001; partial R^2=.028). Note, these results did not change when removing low frequency ACE items (i.e., <1% reported frequency), or when using ACE composite scores (Table 1). Bullying was significantly more strongly related to PLEs than witnessing domestic violence (Z=16.354, p<.001), traumatic grief (Z=18.593, p<.001), or financial adversity (Z=20.664, p<.001). Furthermore, witnessing domestic violence was significantly more strongly related to PLEs than either traumatic grief (Z=2.866, p=.002) or financial adversity (Z=5.086, p<.001).

3.1.2 Associations between individual PLEs and ACEs.—We also examined whether specific types of PLEs were associated with ACEs. First, both unusual beliefs (delusion-like experiences; β=0.047, FDR-corrected p<.001) and perceptual abnormalities (hallucination-like experiences; β=0.036, FDR-corrected p=.001) were associated with ACE composite score. Examining each of the PQ-BC items individually, ACEs were significantly associated with every single item (Zs>2.91, FDR-corrected ps<.01). However, in a model that included each of the 21 PLE items simultaneously predicting ACEs, the only items that were independently significantly associated with greater ACEs were grandiosity (question 4;

β=0.056, FDR-corrected p=.003; Supplemental Table 2 for individual items), suspiciousness (question 8; β=0.024, FDR-corrected p=.003), perceptual abnormalities (question 10: β=0.026, FDR-corrected p=.01; question 17: β=0.036, FDR-corrected p=.01), and disorganized speech (question 21; β=−0.026, FDR-corrected p=.04).

3.2 Associations between PLEs, ACEs, and Shared Correlates

Each of the shared correlates were significantly associated with PLEs (Table 2; FDR-corrected ps<.001). Furthermore, almost all of these factors were also associated with ACEs (Table 2; FDR-corrected ps<.05). Importantly, the association between ACEs and PLEs remained significant when accounting for these shared correlates (βs>0.069, FDR-corrected ps<.001; note the associations of PLEs with the shared correlates remained significant when the ACE composite score were in the model; Table 2).

3.3 Evidence of PLEs Mediating Associations between ACEs and Shared Correlates

Given the evidence for associations between these shared correlates and both ACEs and PLEs, we next examined whether there was evidence of PLEs mediating the associations between ACEs and these shared correlates. There was evidence that PLEs partially mediated the relationship between ACEs and internalizing symptoms (Supplemental Figure 1; indirect effect [path ab] bias-corrected 95%CI:0.028-0.048; proportion mediated=41.30%). In contrast, we found that evidence that internalizing symptoms mediated only 1.55% of the association between ACEs and PLEs.

There was also evidence that PLEs partially mediated the relationship between ACEs and suicidality (Figure 2; indirect effect [path ab] bias-corrected 95%CI:0.017-0.032; proportion mediated=46.30%). In contrast, we found evidence that suicidality only mediated 2.02% of the association between ACEs and PLEs. We found evidence that PLEs mediated 37.50% of the association between ACEs and suicidal ideation and 58.49% of the association between ACEs and suicidal behavior. In terms of other shared correlates (i.e., fluid cognition, and stress, there was evidence that PLEs mediated less than 7.59% of these associations. However, there was evidence that family history of psychosis mediated 28.57% of the association between ACE and PLEs, fluid cognition mediated 8.33% of the association between ACE and PLEs, and stress mediated 20.0% of the association between PLEs and ACEs.

4. Discussion

Using data from the ABCD study, a prospective longitudinal study assessing children aged 9-11-years-old, we found that exposure to adverse experiences during childhood was associated with psychotic-like experiences. Critically, this association was not explained by a range of other predictors of psychotic-like experiences, including genetic risk for psychotic disorders, general stress, cognitive impairment, internalizing symptoms, and suicidality, indicating a relationship between ACEs and PLEs that exists above and beyond these shared correlates. Exposure to adverse experiences in general was associated with psychotic experiences, but several types of adverse experiences were individually associated with PLEs, including bullying, financial adversity, domestic violence exposure, and traumatic

grief. The current study also found evidence consistent with PLEs mediating the association between adverse experiences and both internalizing symptoms and suicidality (especially suicidal behavior).

Our findings of an association between adverse experiences and PLEs replicates several lines of previous research connecting trauma and psychotic experiences (Bailey et al., 2018; Cristobal-Narvaez et al., 2016; Croft et al., 2019; Fisher et al., 2013; Loewy et al., 2019; Strauss et al., 2018; Varese et al., 2012). However, some research has failed to find associations between trauma and psychosis (for reviews of studies, including studies that failed to find a significant effect, see (Bailey et al., 2018)), lending credence towards the possibility that childhood and adolescence is a particularly sensitive time for the association between ACEs and PLEs (Croft et al., 2019). It has been hypothesized that the etiological underpinning of the association between ACEs and PLEs may be attributable to trauma leading to impairment in HPA axis functioning, which in turn leads to PLEs (Aas et al., 2019). According to this model, prolonged elevated cortisol levels resulting from ACEs leads to dysfunction in the HPA axis, which in turn can cause long-term increases in glucocorticoids, which may increase dopamine release (consistent with the dopamine hypothesis of schizophrenia (Howes and Kapur, 2009)). Such a consistent increase in glucocorticoids and dopamine could result in the cognitive impairments and symptoms associated with schizophrenia spectrum disorders (Ruby et al., 2014).

These results are also consistent with the idea that PLEs are associated with several specific types of trauma, notably bullying, financial adversity, witnessing domestic violence, and traumatic grief. Associations with bullying are consistent with several previous studies, possibly due to bullying leading to distorted cognitions (i.e., mild delusional ideation or unusual beliefs) and increased suspiciousness (Jack and Egan, 2018). Other possibilities include that social deficits associated with PLEs make children more susceptible to bullying (Strauss et al., 2018) or perhaps that suspiciousness may lead to interpreting other children's behavior as bullying. The association with financial adversity supports several lines of research implicating a relationship between financial stress and lower socioeconomic status with PLEs (Mansueto and Faravelli, 2017), perhaps as a result of chronic stress (Burns et al., 2014). The current results also support at least one previous study finding an association between PLEs and bereavement (Mansueto and Faravelli, 2017). Furthermore, the association with witnessing domestic violence is consistent with the hypothesis that being the indirect target of abuse can also be associated with PLEs. A key question is how this more indirect type of stress relates to PLEs. One speculative hypothesis is that this more indirect form of ACE lends itself to the development of PLEs at least in part as due to general elevations in stress and/or appraisals that the child might make even when they are not direct target of the abuse. For example, the child might develop increased suspiciousness as a result of feeling increased anxiety in the home or may view the home as unsafe as a result of witnessing domestic violence (Kelleher et al., 2015).

There was also some evidence that particular types of PLEs were specifically associated with ACEs. Consistent with previous research (Kline et al., 2016), an item relating to suspiciousness was associated with ACEs even when using all PQ-BC items as predictors, congruent with the idea that exposure to ACEs may lead to greater mistrust for others and

suspiciousness (Fisher et al., 2013). This relationship is also consistent with the possibility that elevated levels of suspiciousness following exposure to ACEs may reflect hypervigilance or wariness on the part of the victim. In contrast, it is also possible that the experience of hypervigilance may have in part lead to the development of PLEs. Furthermore, the current study also replicated an association between ACEs and grandiosity (Kline et al., 2016), consistent with the speculative hypothesis that experiences of trauma may result in children developing distorted cognitions regarding 'special abilities' as a coping mechanism. Lastly, the results also indicate, consistent with previous work, that perceptual abnormalities are associated with ACEs (Bailey et al., 2018). It should be noted that the aforementioned possibilities all rely on the premise that the experience of ACEs leads to the formation of PLEs, as the field is increasingly finding evidence for a causal association between the two constructs (Bendall et al., 2008). However, it is also possible that either: a) the two share an underlying common set of mechanisms, or b) the experience of PLEs leads to greater experience of ACEs, although there is notably less support for the latter idea.

Mediation analyses found evidence for PLEs mediating the association between ACEs and both internalizing symptoms and suicidality. One possible explanation for these interrelationships is that the experience of trauma leads to the development of distorted cognitive appraisals, which manifest as PLEs (Appiah-Kusi et al., 2017; Gaweda et al., 2019), and that these distorted appraisals in turn lead to other mental health consequences, including increased anxiety, depression, and suicidality. Few studies have examined the interrelationships between PLEs, ACEs, and shared correlates such as internalizing symptoms and suicidality (Gaweda et al., 2020; Williams et al., 2018). Recent work indicates that PLEs, as well as cognitive biases and depression, partially mediate the relationship between ACEs and suicidality in young adults (Gaweda et al., 2020). In school-age children, the current study found that PLEs mediated the relationship between ACEs and suicidal behavior. We also found evidence for PLEs partially mediating the association between ACEs and internalizing symptoms. Evidence that over 58% of the association between ACEs and suicidal behavior was mediated by PLEs indicates that reducing distressing PLEs may be a critical target in efforts to reduce suicidality already evident in this childhood population (current suicidality endorsed by 4.4% of this sample). Finally, we found evidence consistent with shared correlates (i.e., family history of psychosis, fluid cognition, and stress) mediating associations between ACEs and PLEs, consistent with previous work (Gibson et al., 2019; Williams et al., 2018).

The current study has a number of limitations. First, we do not have information regarding the timing of ACES and onset of PLEs to disentangle causal associations between these two constructs. Additionally, we assessed early PLEs in middle childhood; although a limited subset of participants endorsing PLEs will later develop schizophrenia spectrum diagnoses (Poulton et al., 2000), for a larger subset, PLEs will be a transient phenomena. Thus, future research should examine the degree to which more clinically relevant PLEs (e.g., sustained PLEs) are more strongly associated with ACE than transient PLEs. Longitudinal analyses will be required to examine these relationships. Another limitation is our measure of ACEs is based on parent report of the child's experience of events, which is inherently limited by the parent's knowledge of the event and willingness to report (Chan, 2012). This lack of

knowledge or willingness to report may have contributed to low prevalence rates for several of the ACEs (e.g., 0.8% reporting their child has been beaten by a parent). The low prevalence rates of several of the ACEs, combined with evidence that PLEs were specifically associated with the most frequently endorsed ACE items, indicates that future research will need to assess the generalizability of the associations between PLEs and specific ACEs. In addition, we could not exactly replicate the traditional definition of ACEs (CDC and Permanente, 2016) due to lack of information about parental incarceration. Instead of using the traditional definition, we chose to focus on trauma as opposed to household challenges, such as divorce or parental incarceration. Future waves of ABCD data can examine the traditional definition of ACEs, as information regarding parental incarceration will become available when full year 1 data is released (see Supplement for results using a modified version of the traditional definition of ACEs, with results generally replicating). Furthermore, there is some conceptual overlap between questions of the PQ-BC inquiring about depersonalization experiences and severe dissociation associated with trauma, which may inflate the association between PLE and ACEs. However, the PQ-BC questions most strongly associated with ACEs did not assess depersonalization or derealization. In addition, a limitation of the current study is that self-report of PLEs in the ABCD study is not followed up with a clinical interview. Lastly, associations with other self-reports were in the small-moderate range (βs .15; although note for the association between bullying and PLE, β=.304), although findings are consistent with the existing literature (Croft et al., 2019; Fisher et al., 2013; Gaweda et al., 2020) and are generally expected in a non-help seeking childhood population without schizophrenia spectrum disorder diagnoses.

The current research makes an important contribution finding an association between ACEs and PLEs, demonstrating that this relationship exists above and beyond associations with shared correlates, consistent with previous work (Barzilay et al., 2019). Furthermore, this work points to some specificity in this relationship both on the part of ACEs and PLEs, with certain ACEs more strongly associated with PLEs, including bullying, financial adversity, witnessing domestic violence, and traumatic grief. Furthermore, in terms of PLEs, suspiciousness, grandiosity, and perceptual abnormalities may be more strongly associated with ACEs. Lastly, this work found evidence consistent with PLEs mediating associations between trauma and both internalizing symptoms and suicidality. This work has important implications regarding mechanisms underlying the development of negative psychological outcomes and implications for treatment pathways following trauma. The results of the current study suggest that subsequent to a client's disclosure of trauma, clinicians should assess PLEs. Additionally, following client endorsement of PLEs, clinicians should consider using evidence-based assessments to determine the presence of trauma and, if found, trauma-focused interventions that address PLEs (Folk et al., 2019) as a tool for potentially reducing associated internalizing symptoms and suicidality following trauma.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

Aas M, Pizzagalli DA, Laskemoen JF, Reponen EJ, Ueland T, Melle I, Agartz I, Steen NE, Andreassen OA, 2019 Elevated hair cortisol is associated with childhood maltreatment and cognitive impairment in schizophrenia and in bipolar disorders. Schizophr Res 213, 65–71. 10.1016/j.schres.2019.01.011 [PubMed: 30660575]

Achenbach TM, 2009 The Achenbach System of Emprically Based Assessment (ASEBA): Development, Findings, Theory and Applications. University of Vermont Research Center for Children, Youth, and Families, Burlington, VT.

Afifi TO, Salmon S, Garces I, Struck S, Fortier J, Taillieu T, Stewart-Tufescu A, Asmundson GJG, Sareen J, MacMillan HL, 2020 Confirmatory factor analysis of adverse childhood experiences (ACEs) among a community-based sample of parents and adolescents. BMC Pediatr 20(1), 178 10.1186/s12887-020-02063-3 [PubMed: 32316954]

Appiah-Kusi E, Fisher HL, Petros N, Wilson R, Mondelli V, Garety PA, McGuire P, Bhattacharyya S, 2017 Do cognitive schema mediate the association between childhood trauma and being at ultra-high risk for psychosis? Journal of psychiatric research 88, 89–96. 10.1016/j.jpsychires.2017.01.003 [PubMed: 28103519]

Arseneault L, Cannon M, Fisher HL, Polanczyk G, Moffitt TE, Caspi A, 2011 Childhood trauma and children's emerging psychotic symptoms: A genetically sensitive longitudinal cohort study. Am J Psychiatry 168(1), 65–72. 10.1176/appi.ajp.2010.10040567 [PubMed: 20952460]

Bailey T, Alvarez-Jimenez M, Garcia-Sanchez AM, Hulbert C, Barlow E, Bendall S, 2018 Childhood Trauma Is Associated With Severity of Hallucinations and Delusions in Psychotic Disorders: A Systematic Review and Meta-Analysis. Schizophr Bull 44(5), 1111–1122. 10.1093/schbul/sbx161 [PubMed: 29301025]

Barch DM, Albaugh MD, Avenevoli S, Chang L, Clark DB, Glantz MD, Hudziak JJ, Jernigan TL, Tapert SF, Yurgelun-Todd D, Alia-Klein N, Potter AS, Paulus MP, Prouty D, Zucker RA, Sher KJ, 2018 Demographic, physical and mental health assessments in the adolescent brain and cognitive development study: Rationale and description. Dev Cogn Neurosci 32, 55–66. 10.1016/j.dcn.2017.10.010 [PubMed: 29113758]

Barzilay R, Calkins ME, Moore TM, Wolf DH, Satterthwaite TD, Cobb Scott J, Jones JD, Benton TD, Gur RC, Gur RE, 2019 Association between traumatic stress load, psychopathology, and cognition in the Philadelphia Neurodevelopmental Cohort. Psychol Med 49(2), 325–334. 10.1017/s0033291718000880 [PubMed: 29655375]

Bates D, Mächler M, Bolker B, Walker S, 2015 Fitting Linear Mixed-Effects Models Using lme4. J Stat Softw 67, 1–48. 10.18637/jss.v067.i01

Bendall S, Jackson HJ, Hulbert CA, McGorry PD, 2008 Childhood trauma and psychotic disorders: a systematic, critical review of the evidence. Schizophr Bull 34(3), 568–579. 10.1093/schbul/sbm121 [PubMed: 18003630]

Burns JK, Tomita A, Kapadia AS, 2014 Income inequality and schizophrenia: increased schizophrenia incidence in countries with high levels of income inequality. The International journal of social psychiatry 60(2), 185–196. 10.1177/0020764013481426 [PubMed: 23594564]

CDC, Permanente K, 2016 The ACE study survey data [unpublished data]. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, GA.

Chan KL, 2012 Comparison of Parent and Child Reports on Child Maltreatment in a Representative Household Sample in Hong Kong. Journal of family violence 27(1), 11–21. 10.1007/s10896-011-9405-1 [PubMed: 22389552]

Christensen RHB, 2015 ordinal---Regression Models for Ordinal Data. R package version 2015.6-28. https://doi.org/http://www.cran.r-project.org/package=ordinal/

Conus P, Cotton S, Schimmelmann BG, McGorry PD, Lambert M, 2010 Pretreatment and outcome correlates of sexual and physical trauma in an epidemiological cohort of first-episode psychosis patients. Schizophr Bull 36(6), 1105–1114. 10.1093/schbul/sbp009 [PubMed: 19386579]

Cristobal-Narvaez P, Sheinbaum T, Ballespi S, Mitjavila M, Myin-Germeys I, Kwapil TR, Barrantes-Vidal N, 2016 Impact of Adverse Childhood Experiences on Psychotic-Like Symptoms and Stress

Reactivity in Daily Life in Nonclinical Young Adults. PLoS One 11(4), e0153557 10.1371/journal.pone.0153557 [PubMed: 27082442]

Croft J, Heron J, Teufel C, Cannon M, Wolke D, Thompson A, Houtepen L, Zammit S, 2019 Association of Trauma Type, Age of Exposure, and Frequency in Childhood and Adolescence With Psychotic Experiences in Early Adulthood. JAMA Psychiatry 76(1), 79–86. 10.1001/jamapsychiatry.2018.3155 [PubMed: 30477014]

Felitti VJ, Anda RF, Nordenberg D, Williamson DF, Spitz AM, Edwards V, Koss MP, Marks JS, 1998 Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. American journal of preventive medicine 14(4), 245–258. [PubMed: 9635069]

Fisher HL, Schreier A, Zammit S, Maughan B, Munafo MR, Lewis G, Wolke D, 2013 Pathways between childhood victimization and psychosis-like symptoms in the ALSPAC birth cohort. Schizophr Bull 39(5), 1045–1055. 10.1093/schbul/sbs088 [PubMed: 22941743]

Folk JB, Tully LM, Blacker DM, Liles BD, Bolden KA, Tryon V, Botello R, Niendam TA, 2019 Uncharted Waters: Treating Trauma Symptoms in the Context of Early Psychosis. J Clin Med 8(9), 1456 10.3390/jcm8091456

Gaweda L, Goritz AS, Moritz S, 2019 Mediating role of aberrant salience and self-disturbances for the relationship between childhood trauma and psychotic-like experiences in the general population. Schizophr Res 206, 149–156. 10.1016/j.schres.2018.11.034 [PubMed: 30545759]

Gaweda L, Pionke R, Krezolek M, Frydecka D, Nelson B, Cechnicki A, 2020 The interplay between childhood trauma, cognitive biases, psychotic-like experiences and depression and their additive impact on predicting lifetime suicidal behavior in young adults. Psychol Med 50(1), 116–124. 10.1017/s0033291718004026 [PubMed: 30626466]

Gibson LE, Reeves LE, Cooper S, Olino TM, Ellman LM, 2019 Traumatic life event exposure and psychotic-like experiences: A multiple mediation model of cognitive-based mechanisms. Schizophr Res 205, 15–22. 10.1016/j.schres.2018.02.005 [PubMed: 29463456]

Grivel MM, Leong W, Masucci MD, Altschuler RA, Arndt LY, Redman SL, Yang LH, Brucato G, Girgis RR, 2018 Impact of lifetime traumatic experiences on suicidality and likelihood of conversion in a cohort of individuals at clinical high-risk for psychosis. Schizophr Res 195, 549–553. 10.1016/j.schres.2017.09.006 [PubMed: 28935167]

Hothorn T, Bretz F, Westfall P, 2008 Simultaneous inference in general parametric models. Biometrical journal 50(3), 346–363. 10.1002/bimj.200810425 [PubMed: 18481363]

Howes OD, Kapur S, 2009 The dopamine hypothesis of schizophrenia: version III--the final common pathway. Schizophr Bull 35(3), 549–562. 10.1093/schbul/sbp006 [PubMed: 19325164]

Isvoranu AM, van Borkulo CD, Boyette LL, Wigman JT, Vinkers CH, Borsboom D, 2017 A Network Approach to Psychosis: Pathways Between Childhood Trauma and Psychotic Symptoms. Schizophr Bull 43(1), 187–196. 10.1093/schbul/sbw055 [PubMed: 27165690]

Jack AH, Egan V, 2018 Childhood Bullying, Paranoid Thinking and the Misappraisal of Social Threat: Trouble at School. School mental health 10(1), 26–34. 10.1007/s12310-017-9238-z [PubMed: 29503671]

Karcher NR, Barch DM, Avenevoli S, Savill M, Huber RS, Simon TJ, Leckliter IN, Sher KJ, Loewy RL, 2018 Assessment of the Prodromal Questionnaire-Brief Child Version for Measurement of Self-reported Psychoticlike Experiences in Childhood. JAMA Psychiatry 75(8), 853–861. 10.1001/jamapsychiatry.2018.1334 [PubMed: 29874361]

Karcher NR, O'Brien KJ, Kandala S, Barch DM, 2019 Resting-State Functional Connectivity and Psychotic-like Experiences in Childhood: Results From the Adolescent Brain Cognitive Development Study. Biol Psychiatry 86(1), 7–15. 10.1016/j.biopsych.2019.01.013 [PubMed: 30850130]

Kelleher I, Wigman JT, Harley M, O'Hanlon E, Coughlan H, Rawdon C, Murphy J, Power E, Higgins NM, Cannon M, 2015 Psychotic experiences in the population: Association with functioning and mental distress. Schizophr Res 165(1), 9–14. 10.1016/j.schres.2015.03.020 [PubMed: 25868930]

Kline E, Millman ZB, Denenny D, Wilson C, Thompson E, Demro C, Connors K, Bussell K, Reeves G, Schiffman J, 2016 Trauma and psychosis symptoms in a sample of help-seeking youth. Schizophr Res 175(1-3), 174–179. 10.1016/j.schres.2016.04.006 [PubMed: 27107632]

Kobak KA, Kratochvil CJ, Stanger C, Kaufman J, 2013, 4 Computerized screening of comorbidity in adolescents with substance or psychiatric disorders, Paper presented at the Anxiety Disorders and Depression Conference, La Jolaa, CA.

Kraan T, Velthorst E, Smit F, de Haan L, van der Gaag M, 2015 Trauma and recent life events in individuals at ultra high risk for psychosis: review and meta-analysis. Schizophr Res 161(2-3), 143–149. 10.1016/j.schres.2014.11.026 [PubMed: 25499046]

Loewy RL, Corey S, Amirfathi F, Dabit S, Fulford D, Pearson R, Hua JPY, Schlosser D, Stuart BK, Mathalon DH, Vinogradov S, 2019 Childhood trauma and clinical high risk for psychosis. Schizophr Res 205, 10–14. 10.1016/j.schres.2018.05.003 [PubMed: 29779964]

Loewy RL, Pearson R, Vinogradov S, Bearden CE, Cannon TD, 2011 Psychosis risk screening with the Prodromal Questionnaire--brief version (PQ-B). Schizophr Res 129(1), 42–46. 10.1016/j.schres.2011.03.029 [PubMed: 21511440]

Mansueto G, Faravelli C, 2017 Recent life events and psychosis: The role of childhood adversities. Psychiatry research 256, 111–117. 10.1016/j.psychres.2017.06.042 [PubMed: 28628791]

Mansueto G, Schruers K, Cosci F, van Os J, 2019 Childhood adversities and psychotic symptoms: The potential mediating or moderating role of neurocognition and social cognition. Schizophr Res 206, 183–193. 10.1016/j.schres.2018.11.028 [PubMed: 30527930]

McGrath JJ, McLaughlin KA, Saha S, Aguilar-Gaxiola S, Al-Hamzawi A, Alonso J, Bruffaerts R, de Girolamo G, de Jonge P, Esan O, Florescu S, Gureje O, Haro JM, Hu C, Karam EG, Kovess-Masfety V, Lee S, Lepine JP, Lim CC, Medina-Mora ME, Mneimneh Z, Pennell BE, Piazza M, Posada-Villa J, Sampson N, Viana MC, Xavier M, Bromet EJ, Kendler KS, Kessler RC, 2017 The association between childhood adversities and subsequent first onset of psychotic experiences: a cross-national analysis of 23 998 respondents from 17 countries. Psychol Med 47(7), 1230–1245. 10.1017/s0033291716003263 [PubMed: 28065209]

Meng X-L, Rosenthal R, Rubin DB, 1992 Comparing correlated correlation coefficients. Psychological bulletin 111(1), 172.

Merrick MT, Ports KA, Ford DC, Afifi TO, Gershoff ET, Grogan-Kaylor A, 2017 Unpacking the impact of adverse childhood experiences on adult mental health. Child abuse & neglect 69, 10–19. 10.1016/j.chiabu.2017.03.016 [PubMed: 28419887]

Moriyama TS, Drukker M, Gadelha A, Pan PM, Salum GA, Manfro GG, Mari JJ, Miguel EC, Rohde LA, Polanczyk GV, van Os J, Bressan RA, 2018 The association between psychotic experiences and traumatic life events: the role of the intention to harm. Psychol Med 48(13), 2235–2246. 10.1017/s0033291717003762 [PubMed: 29331167]

Polanczyk G, Moffitt TE, Arseneault L, Cannon M, Ambler A, Keefe RS, Houts R, Odgers CL, Caspi A, 2010 Etiological and clinical features of childhood psychotic symptoms: results from a birth cohort. Arch Gen Psychiatry 67(4), 328–338. 10.1001/archgenpsychiatry.2010.14 [PubMed: 20368509]

Poulton R, Caspi A, Moffitt TE, Cannon M, Murray R, Harrington H, 2000 Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. Arch Gen Psychiatry 57(11), 1053–1058. [PubMed: 11074871]

Rice JP, Reich T, Bucholz KK, Neuman RJ, Fishman R, Rochberg N, Hesselbrock VM, Nurnberger JI Jr., Schuckit MA, Begleiter H, 1995 Comparison of direct interview and family history diagnoses of alcohol dependence. Alcoholism, clinical and experimental research 19(4), 1018–1023.

Rosseel Y, 2012 Lavaan: An R package for structural equation modeling and more. Version 0.5–12 (BETA). J Stat Softw 48(2), 1–36.

Ruby E, Polito S, McMahon K, Gorovitz M, Corcoran C, Malaspina D, 2014 Pathways Associating Childhood Trauma to the Neurobiology of Schizophrenia. Frontiers in psychological and behavioral science 3(1), 1–17. [PubMed: 25419548]

Strauss GP, Raugh IM, Mittal VA, Gibb BE, Coles ME, 2018 Bullying victimization and perpetration in a community sample of youth with psychotic like experiences. Schizophr Res 195, 534–536. 10.1016/j.schres.2017.08.056 [PubMed: 28888357]

Townsend L, Kobak K, Kearney C, Milham M, Andreotti C, Escalera J, Alexander L, Gill MK, Birmaher B, Sylvester R, Rice D, Deep A, Kaufman J, 2020 Development of Three Web-Based Computerized Versions of the Kiddie Schedule for Affective Disorders and Schizophrenia Child

Psychiatric Diagnostic Interview: Preliminary Validity Data. Journal of the American Academy of Child & Adolescent Psychiatry 59(2), 309–325. [PubMed: 31108163]

Varese F, Smeets F, Drukker M, Lieverse R, Lataster T, Viechtbauer W, Read J, van Os J, Bentall RP, 2012 Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. Schizophr Bull 38(4), 661–671. 10.1093/schbul/sbs050 [PubMed: 22461484]

Weintraub S, Dikmen SS, Heaton RK, Tulsky DS, Zelazo PD, Bauer PJ, Carlozzi NE, Slotkin J, Blitz D, Wallner-Allen K, Fox NA, Beaumont JL, Mungas D, Nowinski CJ, Richler J, Deocampo JA, Anderson JE, Manly JJ, Borosh B, Havlik R, Conway K, Edwards E, Freund L, King JW, Moy C, Witt E, Gershon RC, 2013 Cognition assessment using the NIH Toolbox. Neurology 80 (11 Suppl 3), S54–64. 10.1212/WNL.0b013e3182872ded [PubMed: 23479546]

Weintraub S, Dikmen SS, Heaton RK, Tulsky DS, Zelazo PD, Slotkin J, Carlozzi NE, Bauer PJ, Wallner-Allen K, Fox N, Havlik R, Beaumont JL, Mungas D, Manly JJ, Moy C, Conway K, Edwards E, Nowinski CJ, Gershon R, 2014 The cognition battery of the NIH toolbox for assessment of neurological and behavioral function: validation in an adult sample. J Int Neuropsychol Soc 20(6), 567–578. 10.1017/S1355617714000320 [PubMed: 24959840]

Williams J, Bucci S, Berry K, Varese F, 2018 Psychological mediators of the association between childhood adversities and psychosis: A systematic review. Clinical psychology review 65, 175–196. 10.1016/j.cpr.2018.05.009 [PubMed: 30243100]

Yates K, Lang U, Cederlof M, Boland F, Taylor P, Cannon M, McNicholas F, DeVylder J, Kelleher I, 2019 Association of Psychotic Experiences With Subsequent Risk of Suicidal Ideation, Suicide Attempts, and Suicide Deaths: A Systematic Review and Meta-analysis of Longitudinal Population Studies. JAMA Psychiatry 76(2), 180–189. 10.1001/jamapsychiatry.2018.3514 [PubMed: 30484818]

Figure 1.
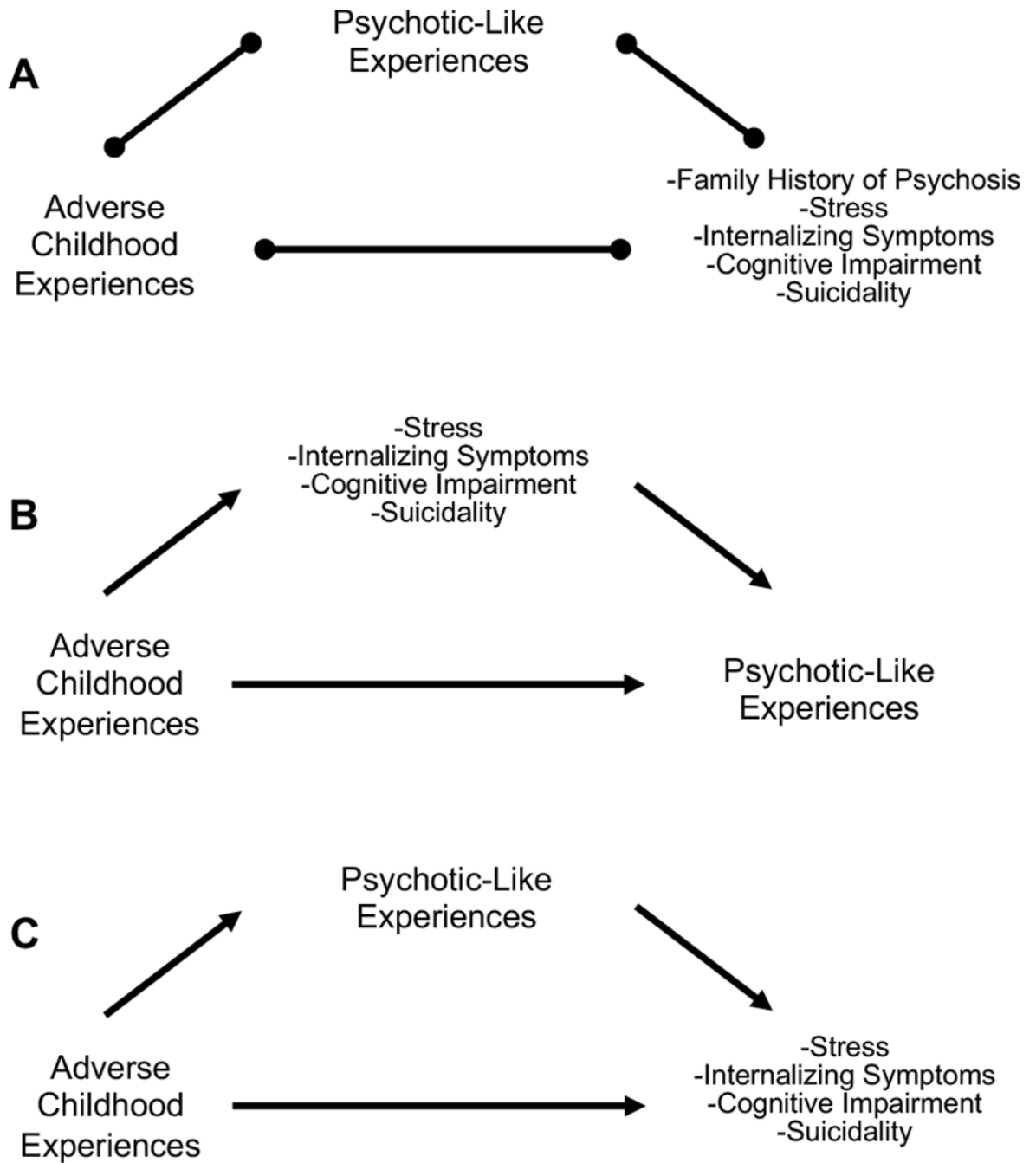Illustration of the potential relationships among ACES, PLEs and shared correlates. **A**: Representation of evidence that ACEs, PLEs, and a number of factors are all intercorrelated based on prior research; **B**: A model whereby the shared correlates of ACEs and PLEs mediate the relationship between ACEs and PLEs; **C:** A model whereby PLEs mediate the relationship between ACEs and these shared correlates.
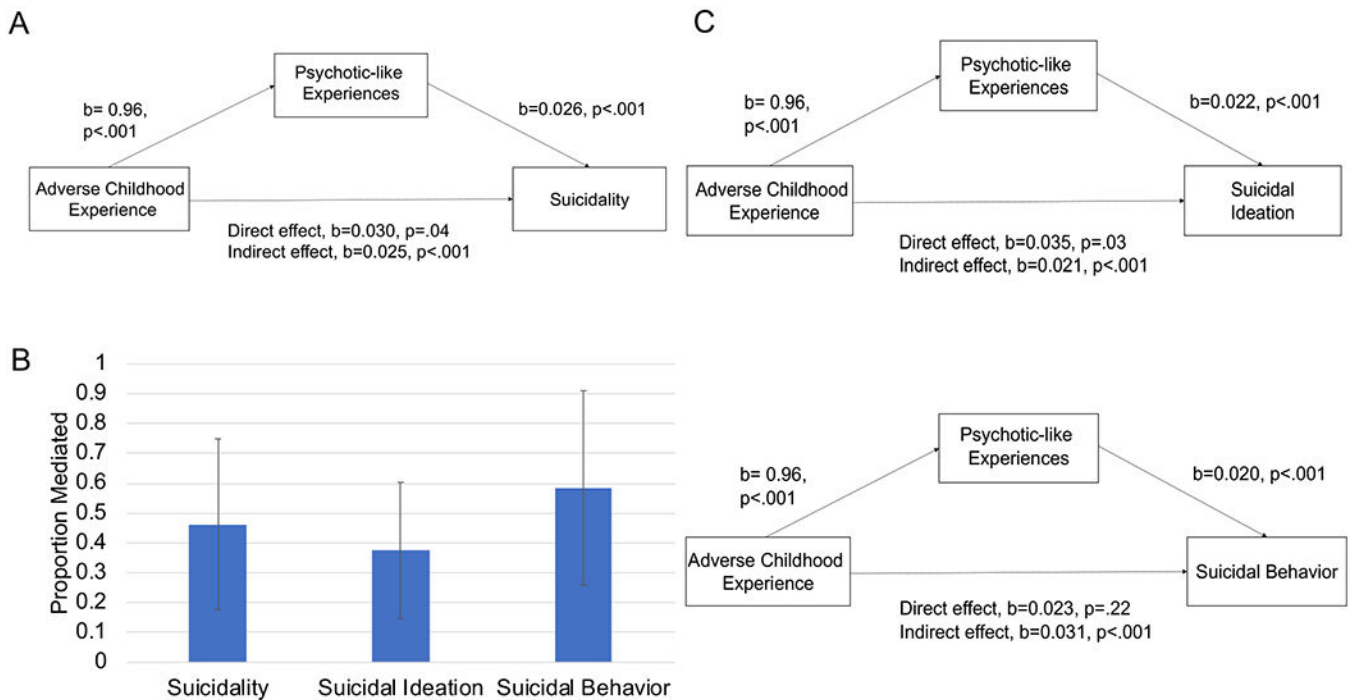
Figure 2.
Evidence of psychotic-like experiences (PLEs) mediating the associations between adverse childhood experiences (ACEs) and suicidality. **A:** The mediation model, including unstandardized regression coefficients, depicting the association between ACEs, PLEs, and suicidality. The mediation analysis partitioned the total variance (total effect) explained by ACEs into the portion that is independent of PLEs (direct effect) and the portion that is accounted for by PLE (indirect effect). **B**: The proportion of the association between ACEs and each of the suicidality indices that was mediated by PLEs. **C**: The mediation model depicting the association between ACEs, PLEs, and suicidal ideation. **D:** The mediation model depicting the association between ACEs, PLEs, and suicidal behavior.

Table 1.

Model Estimates for Associations between ACEs and PLEs

	β	lower CI	upper CI	t[a]	p	FDR p
Number of ACEs Endorsed	0.102	0.083	0.120	10.430	<.001	<.001
Types of ACEs						
Accident	0.052	−0.010	0.113	1.646	.10	.25
Car Accident	0.048	−0.051	0.147	0.944	.35	.50
Other Significant Accident	0.007	−0.083	0.097	0.145	.89	.89
Disaster	0.010	−0.069	0.090	0.242	.81	.81
Fire	−0.032	−0.167	0.101	−0.480	.63	.71
Natural Disaster	−0.033	−0.156	0.090	−0.521	.60	.71
Terrorism	0.063	−0.394	0.522	0.273	.79	.83
War Zone	0.181	−0.172	0.535	0.989	.32	.50
Community Violence	0.177	−0.048	0.403	1.528	.13	.35
Physical Abuse	0.020	−0.084	0.124	0.375	.71	.81
Shot or Brutally Beaten by Non-family Member	−0.422	−0.907	0.058	−1.713	.09	.28
Shot or Brutally Beaten by Family Member	−0.141	−0.632	0.344	−0.563	.57	.71
Beaten by Family Member	0.083	−0.168	0.335	0.642	.52	.71
Emotional Abuse	0.098	−0.039	0.237	1.402	.16	.27
Threatened by Non-Family Member	0.169	−0.088	0.424	1.304	.19	.41
Threatened by Family Member	−0.156	−0.454	0.142	−1.028	.30	.50
Witnessed Domestic Violence	0.100	0.027	0.174	2.658	.01	.04
Sexual Abuse	0.093	0.002	0.182	2.006	.045	.23
Sexual Abuse by Family Member	−0.327	−0.666	0.021	−1.854	.06	.24
Sexual Abuse by Non-Family Member	0.197	−0.080	0.476	1.391	.16	.39
Sexual Abuse by Peers	0.108	−0.065	0.283	1.219	.22	.42
Traumatic Grief	0.066	0.022	0.110	2.892	.004	.03
Bullying	0.304	0.252	0.356	11.461	<.001	<.001
Financial Adversity	0.046	0.026	0.066	4.563	<.001	<.001

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Abbreviations: ACEs=Adverse Childhood Experiences; PLEs=Psychotic-like Experiences; β=standardized regression coefficient; CI=95% Confidence Interval; t=t-test test statistic; p=p-value; FDR=False Discovery Rate-corrected for multiple comparisons.

[a] two-tailed.

Schizophr Res. Author manuscript; available in PMC 2021 August 01.

Table 2.

Model Estimates for Associations between PLEs and Shared Correlates, between PLEs and Shared Correlates including ACEs in the Model, and between ACEs and Shared Correlates.

	β	lower CI	upper CI	t^a	p	FDR p
Models Predicting PLEs						
Family History of Psychosis	0.037	0.018	0.055	3.875	<.001	<.001
Stress	0.109	0.090	0.129	10.613	<.001	<.001
Fluid Cognition	−0.068	−0.087	−0.049	−7.021	<.001	<.001
Internalizing Symptoms	0.370	0.354	0.387	42.962	<.001	<.001
Depression	0.337	0.320	0.354	38.566	<.001	<.001
Generalized Anxiety	0.236	0.218	0.253	26.248	<.001	<.001
Suicidality	0.234	0.216	0.251	26.039	<.001	<.001
Suicidal Ideation	0.203	0.185	0.221	22.490	<.001	<.001
Suicidal Behavior	0.123	0.112	0.135	20.633	<.001	<.001
Models Predicting PLEs that also include ACEs as a Predictor						
Family History of Psychosis	0.028	0.009	0.046	2.884	.004	.004
Stress	0.093	0.073	0.114	8.950	<.001	<.001
Fluid Cognition	−0.064	−0.082	−0.045	−6.602	<.001	<.001
Internalizing Symptoms	0.365	0.348	0.382	42.274	<.001	<.001
Depression	0.332	0.314	0.349	37.897	<.001	<.001
Generalized Anxiety	0.232	0.215	0.249	25.893	<.001	<.001
Suicidality	0.230	0.212	0.247	25.649	<.001	<.001
Suicidal Ideation	0.199	0.181	0.216	22.067	<.001	<.001
Suicidal Behavior	0.121	0.110	0.133	20.408	<.001	<.001
Models Predicting ACEs						
Family History of Psychosis	0.085	0.068	0.104	9.198	<.001	<.001
Stress	0.169	0.150	0.188	17.403	<.001	<.001
Fluid Cognition	−0.027	−0.043	−0.011	−3.276	.001	.001
Internalizing Symptoms	0.061	0.046	0.076	7.797	<.001	<.001
Depression	0.061	0.046	0.076	7.791	<.001	<.001

	β	lower CI	upper CI	t^a	p	FDR p
Generalized Anxiety	0.030	0.014	0.045	3.781	<.001	<.001
Suicidality	0.025	0.010	0.041	3.179	.001	.001
Suicidal Ideation	0.026	0.011	0.042	3.346	.001	.001
Suicidal Behavior	0.010	0.000	0.021	1.965	.049	.049

Abbreviations: ACEs=Adverse Childhood Experiences; PLEs=Psychotic-like Experiences; β=standardized regression coefficient; CI=95% Confidence Interval; t=t-test test statistic; p=p-value; FDR=False Discovery Rate-corrected for multiple comparisons.