Childhood Trauma and Psychosis in a Prospective Cohort Study: Cause, Effect, and Directionality

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Objective: Using longitudinal and prospective measures, the authors assessed the relationship between childhood trauma and psychotic experiences, addressing the following questions: 1) Does exposure to trauma predict incident psychotic experiences? 2) Does cessation of trauma predict cessation of psychotic experiences? 3) What is the direction of the relationship between childhood trauma and psychotic experiences?

Method: This was a nationally representative prospective cohort study of 1,112 school-based adolescents 13–16 years of age, assessed at baseline and at 3-month and 12-month follow-ups for childhood trauma (physical assault and bullying) and psychotic experiences.

Results: A bidirectional relationship was observed between childhood trauma and psychosis, with trauma predicting psychotic experiences over time and vice versa. However, even after accounting for this bidirectional relationship with a number of strict adjustments (only newly incident psychotic experiences occurring over the course of the study following exposure to traumatic experiences were examined), trauma was strongly predictive of psychotic experiences. A dose-response relationship was observed between severity of bullying and risk for psychotic experiences. Moreover, cessation of trauma predicted cessation of psychotic experiences, with the incidence of psychotic experiences decreasing significantly in individuals whose exposure to trauma ceased over the course of the study.

Conclusions: After a series of conservative adjustments, the authors found that exposure to childhood trauma predicted newly incident psychotic experiences. The study also provides the first direct evidence that cessation of traumatic experiences leads to a reduced incidence of psychotic experiences.

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A relationship between childhood trauma, psychotic experiences, and psychosis is well established (1–13). There is still much debate, however, as to whether the relationship is causal (14, 15). A number of prospective cohort studies have addressed this issue (16–23), but key epidemiological questions remain unanswered. One issue is related to temporality. While several longitudinal studies have shown that childhood trauma assessed at one time point predicted psychotic experiences assessed at a later time point, most have not accounted for the possibility that the psychotic experiences were present prior to the first assessment (19–22). Two notable studies have attempted to control for psychotic experiences occurring prior to childhood trauma (17, 18), but to our knowledge, no research to date has demonstrated that in a cohort of individuals with repeated assessments over time, traumatic experiences predicted newly incident psychotic experiences—that is, in a sample of individuals free of psychotic experiences at baseline, exposure to trauma predicted subsequent psychotic experiences. A further key epidemiological issue in determining causal relationships that has not, to our knowledge, been addressed to date is that of cessation of cause leading to cessation of effect. That is, does reduction in the incidence of trauma in the population lead to reduction in the incidence of psychotic experiences? Beyond causal debates, this is also the most significant question from a clinical or intervention perspective, since it informs us as to whether interventions to reduce or prevent childhood trauma might have an effect on the incidence of psychotic experiences in the population, an issue epidemiologists have been criticized for neglecting (24).

Another issue that has been largely overlooked in the literature is that of causal direction. Research to date has focused on the hypothesis that childhood trauma increases the risk for psychosis. An important criterion in establishing causality, however, is consideration of alternative explanations for a relationship (25). It cannot be ruled out that psychotic experiences may in fact increase risk of exposure to trauma rather than vice versa. It is also possible that the relationship is bidirectional, with childhood trauma being both a cause and an effect of psychotic experiences. To our knowledge, only one study has addressed this issue to date, with conflicting results. In a longitudinal study of an adolescent population sample, De Loore et al. (17) reported that psychotic experiences at baseline did not predict trauma (sexual abuse or bullying) over time. They did find, however, that psychotic experiences at baseline predicted a greater number of life events that participants rated as

"unpleasant" at follow-up. Further research on the directionality of the relationship between childhood trauma and psychotic experiences is needed.

In this study of a population-based, nationally representative cohort of Irish adolescents, we used prospective measures of trauma (physical assault and bullying) and psychotic experiences at multiple time points to address the following questions:

1. Does exposure to trauma predict incident psychotic experiences?

2. Does cessation of trauma predict cessation of psychotic experiences?

3. What is the direction of the relationship between childhood trauma and psychotic experiences?

Method

The data we analyzed came from the Irish center of the Saving and Empowering Young Lives in Europe (SEYLE) study (26, 27). The study is a randomized controlled trial to assess prevention strategies for suicidal behavior across 11 countries (28). For each study site, a nationally representative catchment area was identified and a list of eligible schools was generated. Eligible schools were categorized by size as either small (less than or equal to the median number of pupils in all schools in the study catchment area) or large (greater than the median number of pupils in all schools in the study catchment area). In each school selected at the Irish site, we surveyed every class (regardless of size) in which at least 50% of the pupils were at least 14 years of age. Psychotic experiences were assessed at the study's Irish site only. A total of 17 randomly selected schools in counties Cork and Kerry took part in the study. In total, 1,602 consent forms were distributed, and 1,112 adolescents (69%) took part in the first wave of the study. The measures were repeated at 3-month and 12-month follow-ups. Ninety percent of baseline participants completed the 3-month follow-up and 88% completed the 12-month follow-up. The demographic characteristics of the participants are summarized in Table 1.

TABLE 1. Demographic Characteristics of Participants in a Study of Trauma and Psychosis (N=1,112)

Characteristic	N	%
Age (years)		
13	409	37
14	598	54
15	55	5
16	29	3
Female	496	45
Country of birth		
Born in Ireland	907	82
Mother born in Ireland	857	79
Father born in Ireland	874	81
Living with		
Both parents	914	83
Mother only	142	13
Father only	23	2
Other	17	2

Exposure and Outcome Measures

Participants completed a self-report survey, administered in the classroom, in which they were asked about a number of childhood trauma exposures, including physical abuse and bullying. To assess physical abuse, participants were asked at baseline if they had been physically attacked in the past 12 months ("Have you, during the past 12 months, been physically attacked?" Answer: yes or no). They were then asked if the attack had been perpetrated by a parent, other relative, schoolmate, other acquaintance, or an unknown individual. A series of yes-or-no questions were used to assess bullying at baseline ("In the past 12 months, have others often spread rumors about you? Teased you? Deliberately left you out of activities? Taken money, property, or food from you? Called you names? Made fun of how you look or talk?"). These questions were used to create a binomial variable of bullying, with an answer of yes to any of the six questions being categorized as bullying. These questions were also used to create a measure of bullying severity: a continuous variable scored 0 to 6, indicating the number of questions endorsed. These measures were repeated at the 3-month and 12-month follow-ups, with the wording adjusted to inquire about the time interval since the previous assessment.

Psychotic experiences were assessed using an item validated as part of the Adolescent Psychotic Symptom Screener (29). We previously showed that the question "Have you ever heard voices or sounds that no one else can hear?" demonstrates excellent positive and negative predictive value for phenomena that, on subsequent interview, are clinically verifiable as psychotic in nature (29). In a community survey of adolescents, this item not only detected young people with auditory hallucinations (compared with clinical-interview-verified auditory hallucinations; positive predictive value=71%, negative predictive value=90%), but psychotic symptoms in general (hallucinations and delusions) (positive predictive value=100%, negative predictive value=88%). Therefore, we used this validated question specifically to assess for psychotic experiences in our sample at baseline and at 3 and 12 months.

The study received ethical approval from the European Commission as a precondition of funding approval for the project. Ethical approval was also obtained in each participating country, including from the clinical research ethics committee of the Cork Teaching Hospitals in Ireland. An independent ethical adviser supervises the implementation of the ongoing project to ensure maximum protection of vulnerable individuals. Participants were informed that all answers were confidential (including a report of psychotic experiences) with the exception of some answers to questions relating to suicidal behavior. Specifically, a response of sometimes, often, very often, or always to the question "Have you ever reached the point where you seriously considered taking your life, or perhaps made plans how you would go about doing it?" or a response of yes to the question "Have you ever made an attempt to take your own life?" were considered emergency cases (27). Pupils identified as emergency cases were immediately referred for clinical evaluation to health care services.

Statistical Analysis

All analyses were performed using Stata, version 11.1 (StataCorp, College Station, Tex.). Analyses were controlled for sex.

Abuse as a predictor of psychotic experiences. First, we report the prevalence of psychotic experiences, physical assaults, and bullying in the sample across each of the three assessment points (baseline, 3 months, and 12 months). We tested whether physical assault reported at baseline predicted psychotic experiences at 3 months and at 12 months. Since psychotic experiences may have been present before physical assault, we adjusted analyses to exclude individuals who had psychotic experiences at baseline (that is, we included in the analyses only individuals without baseline psychotic experiences). Next, we tested whether bullying reported at baseline predicted psychotic experiences at 3 months and at 12 months, again adjusting for baseline psychotic

experiences. Since our hypothesis was that cessation of trauma would lead to cessation of psychotic experiences, and this could mask the effect of trauma on psychotic experiences (since physical assault and bullying ceased for many of the participants over the course of the study and thus might predict cessation of psychotic experiences in this subgroup), we created a variable to identify cases in which trauma ceased over the relevant time periods (3-month and 12-month follow-ups) and controlled for this in our analyses by including this variable in a multivariate regression model.

Cessation of abuse as a predictor of cessation of psychotic experiences. Next, we tested whether cessation of trauma predicted cessation of psychotic experiences. To do this, we first created a group comprising only individuals who reported physical assault at baseline. We then divided this group into individuals who experienced further physical assault between baseline and 3-month follow-up (abuse continued) and those who did not experience further physical assault during this period (abuse ceased). We used logistic regression to investigate whether psychotic experiences were less prevalent at 3 months among individuals who did not experience further physical abuse between baseline and 3-month follow-up compared with individuals who continued to experience physical abuse. We then created a group made up of individuals who reported physical assault between baseline and 3-month follow-up and divided this group into individuals who experienced further physical assault between the 3-month and the 12-month follow-up (abuse continued) and those who did not experience further physical assault during this period (abuse ceased). Again, we used logistic regression to investigate whether psychotic experiences were less prevalent at 12 months among individuals who did not experience further physical abuse between the 3-month and 12-month follow-ups compared with individuals who continued to experience physical abuse. We then repeated these analyses for bullying.

Psychotic experiences as a predictor of trauma. We used logistic regression to test whether psychotic experiences reported at baseline predicted physical assault or bullying at 3 months and at 12 months. Since physical assault or bullying may have been present at baseline, in which case it would not precede a baseline report of psychotic experiences, we adjusted analyses to exclude individuals who reported physical assault or bullying at baseline. Since cessation of psychotic experiences over time may have led to a reduced incidence of physical assault or bullying (if the relationship is causal), which could mask the effect of psychotic experiences on trauma (since psychotic experiences ceased for many of the participants over the course of the study and thus might predict cessation of physical assault or bullying in this subgroup), we created a variable to identify cases in which psychotic experiences ceased over the relevant time periods (3-month and 12-month follow-ups) and controlled for this in our analyses by including this variable in a multivariate model.

Results

Prevalence of Psychotic Experiences, Physical Assault, and Bullying

Psychotic experiences. Seven percent of the sample (N=77) reported psychotic experiences at baseline, 5.5% (N=54) reported psychotic experiences at the 3-month follow-up, and 4.5% (N=42) reported psychotic experiences at the 12-month follow-up. Among those who reported psychotic experiences, the experiences persisted from baseline to 3-month follow-up in 41% and from 3-month to 12-month follow-up in 40%.

Physical assault. At baseline, 10% of the sample (N=111) reported being physically attacked in the past 12 months: 45% by a schoolmate, 16% by a relative, 14% by another known acquaintance, and 37% by an unknown individual (some participants reported more than one attacker, so the percentages total more than 100%). Eight percent (N=78) reported having been physically attacked between baseline and the 3-month follow-up: 54% by a schoolmate, 21% by a relative, 17% by another known acquaintance, and 21% by an unknown individual. Eight percent (N=78) reported being physically attacked between the 3-month and 12-month follow-ups: 45% by a schoolmate, 12% by a relative, 19% by another known acquaintance, and 32% by an unknown individual.

Bullying. Overall, 39% (N=409) reported being bullied at baseline, 30% (N=281) reported being bullied at the 3-month follow-up, and 33% (N=322) reported being bullied at the 12-month follow-up.

Childhood Trauma and Incident Psychotic Experiences

Next, we looked at traumatic experiences reported at baseline and psychotic experiences reported at 3 months and at 12 months. Physical assault reported at baseline predicted psychotic experiences at 3 and 12 months, even after adjusting for psychotic experiences at baseline (Table 2). Similarly, bullying reported at baseline predicted psychotic experiences at 3 and 12 months, even after adjusting for psychotic experiences at baseline. The odds of reporting psychotic experiences increased in a dose-response fashion with increasing severity of bullying, as assessed by the number of bullying questions endorsed at each of the three assessments (Table 3).

Cessation of Childhood Trauma and Cessation of Psychotic Experiences

A total of 111 individuals reported a 12-month history of physical assault at baseline (odds ratio for psychotic experiences, 4.02, 95% CI=2.30–7.05, $p<0.001$). Of these individuals, 37% also reported at least one physical assault between baseline and the 3-month follow-up. Individuals whose experience of physical assault did not reoccur between baseline and the 3-month follow-up had a lower risk of psychotic symptoms at 3 months compared with those whose experience of physical assault continued (odds ratio=0.17, 95% CI=0.04–0.71, p=0.015) (Figure 1). Similarly, individuals whose experience of physical assault did not reoccur between the 3-month and 12-month follow-ups had a lower risk of psychotic symptoms at 12 months compared with those whose experience of physical assault continued (odds ratio=0.16, 95% CI=0.05–0.53, $p<0.003$).

Next, we looked at whether cessation of bullying predicted cessation of psychotic experiences. A total of 409 individuals reported a 12-month history of bullying at baseline (odds ratio for psychotic experiences, 3.05, 95% CI=1.85–5.02, $p<0.001$). Of these individuals, 56% also reported bullying

TABLE 2. Bullying or Physical Assault Reported at Baseline and Odds of Psychotic Experiences at 3-Month and 12-Month Follow-Ups

	Psychotic Experiences at 3 Months				Psychotic Experiences at 12 Months			
Subgroup	N	%	Odds Ratio	95% CI	N	%	Odds Ratio	95% CI
Victim of bullying (N=369)	35	9.5	4.35	1.80–10.53	24	6.9	3.40	1.35–8.55
Victim of physical assault (N=111)	12	13.3	4.80	1.33–17.39	11	12.9	6.19	1.64–23.30

TABLE 3. Number of Bullying Items (Out of Six) Endorsed and Odds of Psychotic Experiences at Baseline and at 3-Month and 12-Month Follow-Ups

	Baseline			3-Month Follow-Up			12-Month Follow-Up		
Number of Items	N	Odds Ratio[a]	95% CI	N	Odds Ratio[b]	95% CI	N	Odds Ratio[c]	95% CI
One only	200	3.51	1.48–8.28	106	1.51	0.75–3.05	100	3.80	1.76–8.18
Two only	132	4.09	1.39–11.99	68	4.55	2.37–8.73	73	4.14	1.65–10.40
Three or more	159	9.48	4.28–21.00	66	5.01	2.60–9.67	96	7.94	3.68–17.14

[a] Test for linear trend, Z=5.30, p<0.001.
[b] Test for linear trend, Z=5.97, p<0.001.
[c] Test for linear trend, Z=5.80, p<0.001.

between baseline and the 3-month follow-up. Individuals whose experience of bullying did not reoccur between baseline and the 3-month follow-up had a lower risk of psychotic experiences at 3 months compared with those whose experience of bullying continued (odds ratio=0.28, 95% CI=0.12–0.65, p=0.003). Similarly, individuals whose experience of bullying did not reoccur between the 3-month and 12-month follow-ups had a significantly lower risk of psychotic experiences at 12 months compared with individuals whose experience of bullying continued (odds ratio=0.35, 95% CI=0.15–0.84, p=0.019).

Psychotic Experiences and Exposure to Childhood Trauma

Psychotic experiences reported at baseline predicted physical assault at 3 months and at 12 months, even after adjusting for baseline reports of physical assault (3-month odds ratio=7.21, 95% CI=2.30–22.58, p=0.001; 12-month odds ratio=12.56, 95% CI=3.26–48.44, p<0.001). Similarly, psychotic experiences reported at baseline predicted bullying at 3 months, even after adjusting for baseline reports of bullying (3-month odds ratio=5.32, 95% CI=1.16–24.40, p=0.032). There was a nonsignificant trend for psychotic experiences reported at baseline to predict bullying at 12 months after adjusting for baseline reports of bullying (odds ratio=3.22, 95% CI=0.53–19.60, p=0.20).

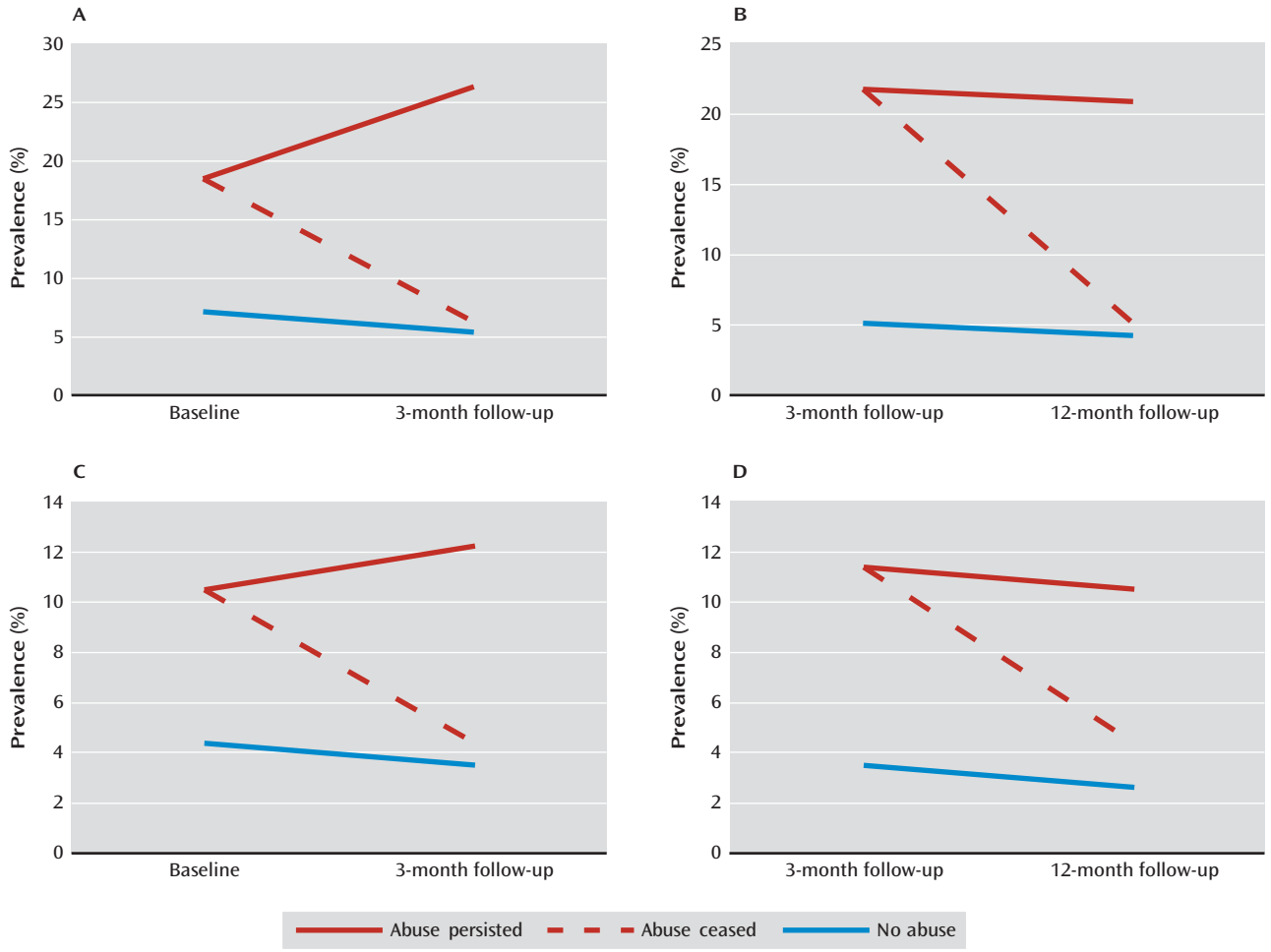
Discussion

Does Childhood Trauma Cause Psychotic Experiences?

A number of criteria have been put forward, based on the U.S. Surgeon General's seminal report on smoking and health, to judge whether an epidemiological association is causal (25). A necessary, though insufficient, criterion to establish a causal relationship is temporality; that is, exposure to the supposed cause must precede the effect. Other criteria that support a causal relationship include 1) strength of association—the stronger the association, the more likely that it is causal; 2) dose-response relationship—as the dose of exposure increases, so should the odds of the outcome increase; 3) cessation of exposure—if exposure ceases or decreases, then the odds of the outcome should cease or decrease; 4) consideration of alternative explanations; and 5) biological plausibility.

This study demonstrated a clear temporal relationship between exposure to childhood trauma and the onset of psychotic experiences, looking only at the effect of trauma exposure on individuals who were free of psychotic symptoms at baseline. The strength of this relationship, in terms of odds ratios, was large. We demonstrated a dose-response relationship between childhood trauma and psychotic experiences, with the odds of psychotic experiences increasing in line with increasing levels of bullying (see Table 3). Beyond this, we demonstrated that cessation of childhood trauma was associated with cessation of psychotic experiences: in individuals who had been exposed to childhood trauma, cessation of traumatic experiences predicted a significantly reduced incidence of psychotic experiences compared with individuals for whom the traumatic experiences continued. We also assessed the important alternative explanation that psychotic experiences may lead to exposure to childhood trauma rather than vice versa. There was evidence that this was the case and that there is in fact a bidirectional relationship between childhood trauma and psychotic experiences. There are a number of possible explanations for this. One is that psychotic experiences may lead to behavior that attracts hostile or bullying responses. Another is that children with psychotic experiences may live in social circumstances where traumatic experiences are more likely to happen, in which case psychotic experiences may predict traumatic experiences but not necessarily cause them. A third is that children with

FIGURE 1. Point Prevalence of Psychotic Experiences in Individuals for Whom Abuse Ceased or Persisted Across Two Time Points, Compared With Individuals Who Did Not Report Abuse at Either Time Point[a]



[a] Panel A shows the point prevalence of psychotic experiences in individuals whose physical abuse ceased from baseline to 3-month follow-up compared with individuals whose physical abuse persisted. Panel B shows the point prevalence of psychotic experiences in individuals whose physical abuse ceased from 3-month to 12-month follow-up compared with individuals whose physical abuse persisted. Panel C shows the point prevalence of psychotic experiences in individuals whose bullying ceased from baseline to 3-month follow-up compared with individuals whose bullying persisted. Panel D shows the point prevalence of psychotic experiences in individuals whose bullying ceased from 3-month to 12-month follow-up compared with individuals whose bullying persisted.

psychotic experiences may interpret negative interactions with others in a more paranoid way and may be more likely than children without psychotic experiences to label such experiences as bullying. There is less room for misinterpretation of intention, however, when it comes to physical assault. In any case, by removing all individuals with baseline psychotic experiences from our analysis, we removed the possibility that psychotic experiences were responsible for subsequent childhood trauma. Even after these strict adjustments, we found that traumatic experiences predicted new incidences of psychotic experiences.

In relation to biological plausibility, a growing body of research has demonstrated important biological sequelae of childhood trauma. In a recent genome-wide methylation study of victims of childhood trauma, for example, Labonté et al. (30) showed a host of differentially methylated promoter regions within the genome relative to comparison subjects. Genes involved in cellular/neuronal plasticity were most significantly affected, in line with findings of increased risk for psychiatric illness. Childhood trauma also appears to have negative effects on catecholamine regulation and hypothalamic-pituitary-adrenal axis function. Sensitization of the pituitary-adrenal and autonomic stress response has been demonstrated both in mouse models of childhood trauma (31) and in human victims of abuse (32). Catecholamine deregulation resulting from this may lead to an increased propensity for psychotic reactions to stressful events. Complementary psychological theories have also presented hypotheses on how psychotic experiences may result directly from repeated exposure to childhood trauma (15, 33, 34). Research suggests, for example, that exposure to childhood trauma can result in the development of negative schematic beliefs about the self and others and that these negative beliefs may result in a sense of

powerlessness, a lack of agency, a view of the self as vulnerable, and appraisals of normal events as threatening, ultimately manifesting in paranoia and misinterpretation of normal stimuli (15, 33–38). This work has been supported empirically by recent research suggesting that childhood trauma may have a direct impact on self-esteem, locus of control, and symptoms of depression and anxiety and that this may in turn lead to the onset of psychotic experiences (22).

Preventing Bullying and Physical Assault

An encouraging finding of the present study is that cessation of physical abuse and bullying was predictive of cessation of psychotic experiences. This suggests that intervention may lead to reduced psychotic experiences in the population. Since most bullying occurs in the school (39), one approach that we would advocate is an increased emphasis in teacher training on the role of the teacher in bullying prevention and intervention. Bullying is more severe in schools where teachers are lax about bullying intervention (40), and the degree of commitment of the teaching staff to bullying intervention is important to the success of such interventions (39). While the emphasis in teacher training is typically on knowledge and understanding of the curriculum, we would advocate a shift in emphasis so that the focus is on overall healthy child development from a much broader perspective than the acquisition of a certain set of educational skills. We would argue that training on the provision of a safe and positive environment that promotes optimal overall child development should form the core of teacher training programs. Formal training on evidence-based interventions to prevent and stop bullying (39) should form the backbone of such a program. This approach would also be beneficial in addressing physical assaults, since the single biggest group responsible for perpetrating physical assaults in the present study was schoolmates.

Strengths and Limitations

A notable strength of this study is its longitudinal nature, which allowed us to assess whether childhood trauma predicted psychotic experiences over time and vice versa. We used prospective measures of trauma collected repeatedly over 12 months, rather than retrospective assessments of trauma that occurred over the entire lifetime. Furthermore, our sample was population based and nationally representative, allowing us to generalize our findings to the community. A limitation is that it is not possible to know the degree to which the objectively adverse events (physical assault and bullying) were subjectively traumatic to the individuals: for some, a physical assault may have been extremely traumatic, while for others the event may not have had a severe subjective impact. Future research should attempt to assess the degree to which the objective event was subjectively traumatic, as this may have an impact on risk for psychotic experiences. Physical assault and bullying were self-reported in the study, without independent confirmation. However, research has shown that even individuals with severe mental illness, including psychotic disorders, tend to be as accurate in recalling abusive experiences as other individuals in the general population (41, 42). The types of traumatic experiences investigated in this study were limited to physical assault and bullying. A number of studies have reported an association between a wider range of traumatic experiences and psychosis, most notably sexual abuse (2, 42, 43). It will be beneficial to repeat our findings with expanded measures of trauma. Research incorporating data on potential mediating factors in the relationship between trauma and psychotic experiences will also be beneficial. Alemany et al. (44), for example, found that psychotic experiences were associated with an interaction between trauma and the brain-derived neurotrophic factor Val66Met polymorphism. Fisher et al. (22), meanwhile, found that the relationship between childhood trauma and psychotic experiences may be partially mediated by effects of trauma on self-esteem, locus of control, and symptoms of depression and anxiety. Further research incorporating data on potential biological and psychological mediators will be valuable. Our assessment of psychotic experiences was based on a validated item with established high positive and negative predictive value for psychotic symptoms in the general adolescent population (29). However, the face validity for this item is for hallucinations, and its high positive and negative predictive value for psychotic symptoms in adolescence may be related to the fact that hallucinations are more common than delusions in this age group (29). Further research looking specifically at older populations, in which delusional beliefs are more common, will be beneficial for determining the causal relationship between trauma and delusions specifically.

Conclusions

In a nationally representative prospective cohort study, we have demonstrated that, even when using a series of conservative adjustments, exposure to childhood trauma was strongly predictive of psychotic experiences. Furthermore, we showed that cessation of traumatic experiences was associated with a significant reduction in the incidence of psychotic experiences. Consideration of alternative causal directions provided support for the hypothesis that psychotic experiences may lead to increased exposure to childhood trauma as well as vice versa. However, we accounted for this bidirectional relationship in our analyses by looking specifically at whether traumatic experiences predicted newly incident psychotic experiences. These findings place new weight on calls for more comprehensive prevention and intervention strategies against childhood trauma in the community (24), from abuse at home to bullying at school. Our findings provide the first direct evidence that this may lead to a reduced incidence of psychotic experiences in the community and ultimately, we hope, a similar reduction in the incidence of psychotic disorders.

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