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Childhood trauma predicts multiple, high lethality suicide attempts in patients with schizophrenia

Sauliha Alli[a], Samia Tasmim[a], Christopher Adanty[a], Ariel Graff[a], John Strauss[a,b], Clement Zai[a,b], Philip Gerretsen[a,b], Carol Borlido[a], Vincenzo De Luca[a,b,*]

[a] Centre for Addiction and Mental Health, Toronto, ON, Canada
[b] Department of Psychiatry, University of Toronto, Toronto, ON, Canada

ABSTRACT

Childhood trauma has been shown to increase the risk of suicide attempts in individuals with schizophrenia. However, previous literature has been limited by considerable heterogeneity within the category of suicide attempters. Here we tested the predictive effect of childhood maltreatment on lifetime suicide attempt in a homogeneous sample of 650 patients with schizophrenia spectrum disorders. Childhood trauma was assessed using the Childhood Trauma Questionnaire-Short Form and suicide history was measured using subjective and objective validated scales as well as medical chart reviews. We refined our sample into two homogenous groups: 1) suicide attempters: patients who had attempted suicide multiple times, with highly lethal results (medical hospitalization required) (n = 24); and 2) non-ideators: patients who had no personal history of suicide attempt or ideation, or family history of attempt (n = 25). Binary logistic regression models revealed that total childhood trauma (β = 0.002; OR: 1.07; 95% CI: 1.00–1.14) and emotional abuse (β = 0.04; OR: 1.38; 95% CI: 1.08–1.77), but not other trauma subtypes, significantly predicted lifetime multiple, high lethality suicide attempts after adjusting for demographic and clinical covariates. Thus, childhood trauma is a weak, independent risk factor for extreme suicide attempts in patients with schizophrenia spectrum disorders.

1. Introduction

Schizophrenia (SCZ) and other psychotic spectrum disorders are associated with an alarmingly high mortality rate. In fact, the greatest difference in mortality ratio between patients with SCZ and the general population is attributable to suicide (Ko et al., 2018). 25–50% of patients with SCZ will attempt suicide at least once in their lifetime (Meltzer, 1999) and 4.9% will be successful (Palmer et al., 2005). Given this high prevalence and mortality rate, the ability to accurately predict and prevent suicidal behavior in patients with SCZ and other psychotic spectrum disorders is of utmost interest.

1.1. Risk factors for suicide in SCZ

1.1.1. Demographic and clinical factors

Several demographic and clinical risk factors for suicide attempt (SA) have been established in the SCZ literature. Younger age, male gender and higher levels of education are the most consistently reported predictors (Hor and Taylor, 2010; Kasckow et al., 2011). Clinical presentation is also predictive of SA, with greater positive symptoms (Martin-Fumadó and Hurtado-Ruíz, 2012; Kasckow et al., 2011; Cassidy et al., 2017; Hor and Taylor, 2010), fewer negative symptoms (McGirr et al., 2006; Hor and Taylor, 2010), greater levels of insight (Bourgeois et al., 2004; Crumlish et al., 2005), and comorbid substance abuse disorders (Gut-Fayand et al., 2001) increasing the likelihood of attempting. Finally, patients with longer durations of illness are more inclined to make SAs (Tarrier et al., 2004). Thus, demographic and clinical features of patients with SCZ spectrum disorders may influence proclivity to attempt suicide.

1.1.2. Suicide history

Several studies have demonstrated that a history of SA increases the risk for further SAs (Roy, 1992; Hor and Taylor, 2010; Kasckow et al., 2011; Popovic et al., 2014; Cheng et al., 1990). The use of more lethal methods in previous attempts has also been shown to increase re-attempt likelihood (Kasckow et al., 2011). In addition to prior attempts, current suicidal ideation also increases the short-term risk of SA (Clapham et al., 2019; Young et al., 1998). Finally, a family history of SA has been shown to augment the risk of making multiple, high lethality attempts by a factor of 3.2 (Trémeau et al., 2005). Thus, there is considerable evidence for the relationship between personal or family suicide history and the risk of future attempts in SCZ spectrum populations.

1.1.3. Childhood trauma

There is strong evidence for a correlation between childhood trauma

* Corresponding author at: Center for Addiction and Mental Health, 250 College St., Room 340, Toronto, ON M5T 1R8, Canada.
E-mail address: Vincenzo.Deluca@camh.ca (V. De Luca).

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and SA (Conus et al., 2009; Roy, 2005; Üçok and Bıkmaz, 2007; Hassan et al., 2016). One case-control study (Roy, 2005) compared 50 suicide attempters with 50 non-attempters and found that the former had significantly higher physical abuse and neglect, emotional abuse and neglect, sexual abuse and total trauma, as measured using the Childhood Trauma Questionnaire. These findings for sexual abuse, but not other forms of trauma were replicated in a sample of patients with first episode psychosis (Üçok and Bıkmaz, 2007). Another study in first-episode SCZ demonstrated a correlation between attempted suicide and past physical or sexual abuse using medical chart reviews (Conus et al., 2009), and one found no association between Childhood Trauma Questionnaire-Short Form (CTQ-SF) scores and SA (Togay et al., 2015). The majority of these studies, however, are limited by a lack of adjustment for confounding predictors of SA.

Most recently, an observational study of 361 SCZ patients with and without childhood trauma history matched for demographic and hereditary variables was conducted (Hassan et al., 2016). Total childhood trauma and subtypes predicted SA in a dose–response relationship after controlling for demographic and clinical covariates. One weakness of this study, common to previous studies in the field, is the considerable sample heterogeneity in the definition of a suicide attempter. Suicide attempters have differed in the number, methods, and lethality of their SAs among other factors, and consequently, individuals who vary on these dimensions also vary in their suicide risk.

1.2. The present study

The present study sought to investigate whether childhood trauma increased the risk for SAs in a homogenous subgroup of ultra-high-risk patients with SCZ spectrum disorders who had multiple, high lethality SAs (hereby referred to as extreme attempters), and an ultra-low-risk control group who had no personal or family history of SA, and had never experienced suicidal ideation (hereby referred to as non-ideators). We hypothesized that extreme attempters would have greater childhood trauma of all subtypes (including emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse) compared with non-ideators, after adjusting for demographic and clinical covariates.

2. Methods

2.1. Population sample

We recruited 650 patients with SCZ spectrum and other psychotic disorders from the Center for Addiction and Mental Health (CAMH) in Toronto, Ontario, Canada. Inclusion criteria for the study were a) a diagnosis of schizophrenia, schizoaffective disorder, or other psychotic disorder according to DSM-IV, b) provision of consent c) age between 18–75, and d) capacity to communicate in English. We excluded patients who had a) organic causes of mental illness (psychosis secondary to head trauma, neurological disorder, or substance abuse) or b) intellectual disability according to DSM-IV.

2.2. Variables

2.2.1. Demographic and clinical variables

Diagnosis of SCZ spectrum or other psychotic disorder was ascertained using the Mini International Neuropsychiatric Interview Plus 6.0 (MINI) for DSM-IV (Sheehan et al., 1998), and confirmed by chart reviews in the CAMH electronic medical record system. Age, gender, level of education and duration of illness were collected during the interview based on patient self-reports. Additionally, lifetime drug abuse (ascertained using the MINI), and level of insight (assessed using the Schedule for Assessment of Insight (David, 1990)) were assessed. Negative symptoms were measured using the negative symptoms factor score of the Brief Psychiatric Rating Scale - Anchored (BPRS) (Woerner et al., 1988), and the reality distortion factor score was used as a proxy for positive symptoms. The latter approximation is consistent with a recent study of factor structure for BPRS scale, which demonstrated considerable overlap between items in the reality distortion score and a positive symptoms factor (Lachar et al., 2001).

2.2.2. Suicidality

Suicide history, including ideation, attempts, and lethality of attempt was assessed using the Columbia Suicide Severity Rating Scale (C-SSRS), an interview questionnaire that has been shown to have high sensitivity and specificity (Posner et al., 2011). The C-SSRS defines a suicide attempt as “a potentially self-injurious act committed with at least some wish to die, as a result of act” (Posner et al., 2011). This differs from non-suicidal self-injurious behavior or self-harm, where intent to die is absent. Lethality of attempt was defined as the medical damage that resulted from the SA, which can range from having surface scratches, to the need for medical hospitalization, to death. Suicidal ideation reported on the C-SSRS interview questionnaire was corroborated with the Beck Scale for Suicide Ideation (BSS) (Beck and Steer, 1991), a self-report measure of suicidal thoughts and behavior. SA and ideation were confirmed by medical chart reviews, with the exception of 12 patients due to lack of consent to review medical records ($n = 8$), or unavailability of data in the electronic medical record system ($n = 4$). In these cases, eligibility for extreme attempter or non-ideator group membership was based solely on interview data.

2.2.3. Childhood trauma

The Childhood Trauma Questionnaire – Short Form (CTQ-SF) is a 28-item self-report screening measure that was used to assess five types of subjective childhood trauma (sexual abuse, emotional abuse, physical abuse, physical neglect, and emotional neglect), as well as total trauma, which is a composite of all subscores (Bernstein et al., 2003). The scale has been shown to have high internal consistency (Cronbach's $\alpha = 0.89$ for overall scale, and $\alpha = 0.58$–0.88 for subscales) and convergent validity (Sullivan et al., 2006).

2.3. Refinement of groups

Fig. 1 illustrates the procedure used to refine the original sample ($N = 650$) into groups of extreme phenotype attempters and non-ideators. The extreme phenotype attempter group was created by first refining our sample into patients who had multiple suicide attempts according to the C-SSRS. This group was further refined to those patients who had moderately severe or worse medical damage according to the C-SSRS (actual lethality score was greater than three, indicating that medical hospitalization and likely intensive care was required as a result of the attempt) for at least one of the attempts. Finally, this group was refined to those patients whose medical chart reports of suicide attempt were consistent with their interview, and whose diagnosis met study inclusion criteria ($n = 24$).

The non-ideator group was created by first selecting all patients who had no history of SA according to the C-SSRS. This group was further refined to those patients who reported never having experienced suicidal ideation according to the C-SSRS, and further, according to the BSS, and who additionally reported having no family history of suicidal attempt according to the Family Interview for Genetic Studies (FIGS) (Maxwell, 1992). Finally, those patients whose suicide history according to the medical chart were inconsistent with their interview C-SSRS, or who did not have a SCZ spectrum diagnosis according to medical records were excluded from the sample, for a final non-ideator group size of $n = 25$.

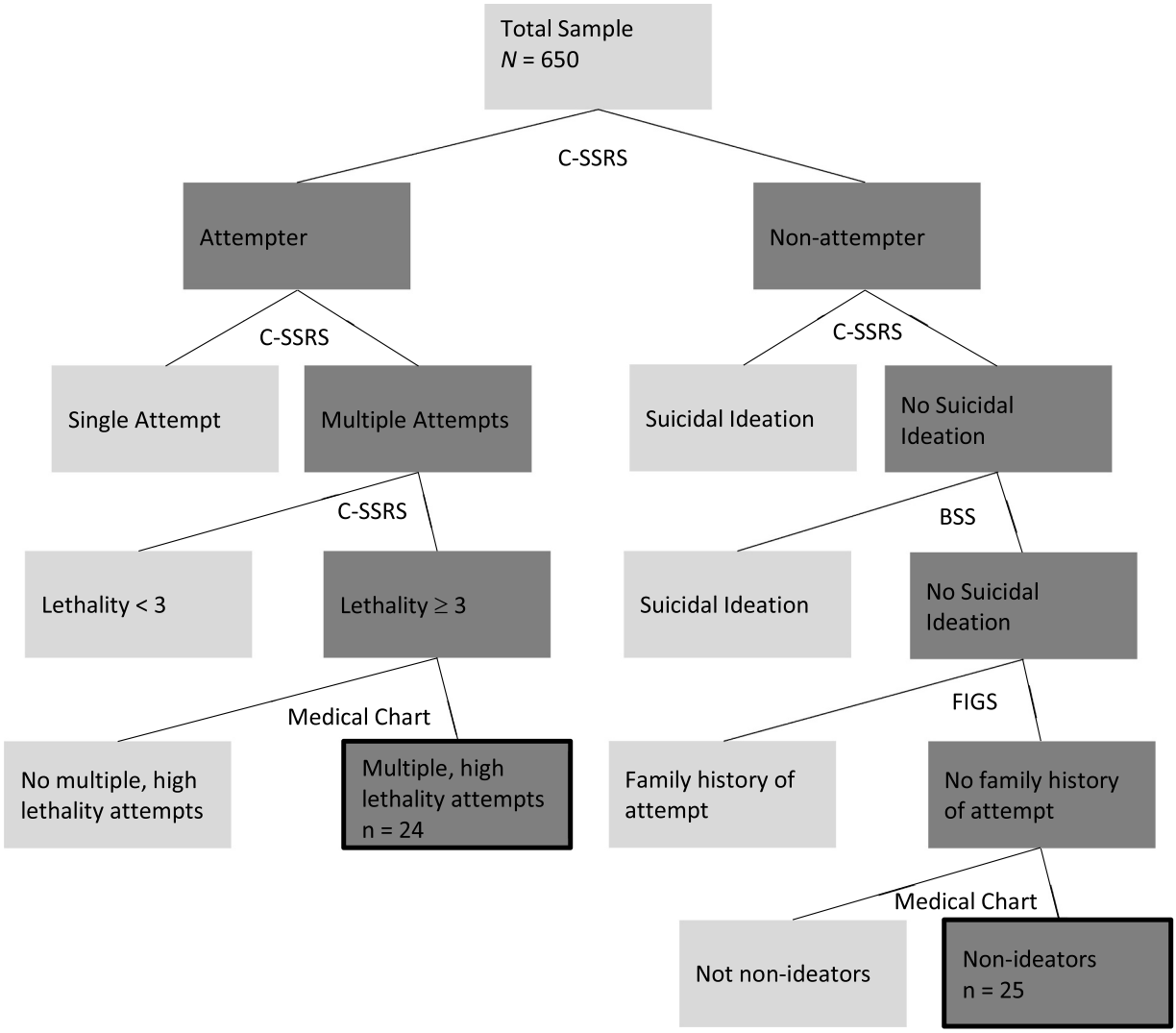

Fig. 1. Flow diagram of selection of extreme attempter and non-ideator samples from $N = 650$ patients with schizophrenia spectrum disorders. Final groups used for analysis are outlined with a box border.

3. Results

3.1. Demographic and clinical characteristics of attempters and non-ideators

Overall, our sample ($N = 49$) consisted primarily of patients with SCZ (current or lifetime diagnosis) ($n = 27$, 55.1%), followed by schizoaffective disorder (current or lifetime diagnosis) ($n = 18$, 36.7%), and other psychotic spectrum disorders ($n = 4$, 8.2%). Suicide attempters and non-ideators were compared on demographic as well as clinical characteristics using two-tailed, independent samples *t*-tests for continuous variables, and chi-squared tests of independence for categorical variables (see Table 1). All statistical analyses were conducted using SPSS for Windows, Version 24. Level of significance was set to $\alpha = 0.05$. Attempters ($M = 51.3$, SD = 8.66) were significantly older than non-ideators ($M = 42.2$, SD = 12.8), $t(42.39) = -2.93$, $p = .005$, and had longer durations of illness ($t(45) = -3.26$, $p = .002$). There were no significant differences between groups in terms of gender, level of education, lifetime drug abuse, positive symptoms, negative symptoms, and insight.

3.2. Univariate regressions

To identify which demographic, clinical, and childhood trauma-related factors significantly predicted extreme attempters, we conducted univariate binary logistic regressions using multiple, high lethality attempts as the outcome variable. To avoid overfitting, we planned to include only those demographic and clinical variables that significantly predicted multiple, high lethality attempts at $\alpha = 0.1$ in the final model. Odds ratio (OR) was used to describe effect size with 95% confidence intervals (CI). As shown in Table 2, significant predictors of extreme attempts were age ($\beta = 0.002$; OR: 1.08; 95% CI: 1.02–1.15; $p = .01$), insight ($\beta = 0.02$; OR: 1.22; 95% CI: 0.97–1.53; $p = .09$), illness duration ($\beta = 0.003$; OR: 1.09; 95% CI: 1.03–1.16; $p = .006$), and emotional abuse ($\beta = 0.01$; OR: 1.13; 95% CI: 1.01–1.27; $p = .03$) all of which increased the risk of multiple, high lethality attempts.

3.3. Multivariate regressions

Hierarchical, binary logistic regression models were constructed using each of the childhood trauma subscores and total score as predictors, with the presence of multiple, high lethality attempts as the primary outcome. Additionally, significant demographic and clinical predictors of multiple, high lethality attempts (age, insight, and illness duration) from the univariate analyses were controlled for. These covariates were entered simultaneously in Step 1, and the CTQ-SF total or subscore (emotional abuse, physical abuse, sexual abuse, emotional neglect, or physical neglect) was entered in Step 2. Thus, a total of six

Table 1
Demographic and clinical characteristics of extreme suicide attempters and non-ideators with schizophrenia spectrum disorders.

Demographic or Clinical variable	Non-ideators (n = 25)	Attempters (n = 24)	p
Age (M ± SD)	42.2 ± 12.8	51.3 ± 8.7	0.005***
Sex (M: F)	19:6	14:10	0.19
Education (n)			0.24
(1) Grade 6 or less	0	0	–
(2) Grade 7–12, not completing high school	4	6	–
(3) Graduated high school or equivalent	1	4	–
(4) Some college	10	4	–
(5) Graduated 2-year college/ university	4	5	–
(6) Graduated 4-year college/ university	4	4	–
(7) Completed post-undergraduate studies	2	0	–
Lifetime drug abuse (Y:N)	5:20	7:17	0.46
Positive symptoms[a] (M ± SD)	6.13 ± 4.28	7.45 ± 4.91	0.33
Negative symptoms[a] (M ± SD)	5.25 ± 2.80	4.14 ± 2.46	0.16
Insight[b] (M ± SD)	9.75 ± 3.81	15.3 ± 15.3	0.13
Illness duration (M ± SD)	17.6 ± 12.9	28.4 ± 9.24	0.002***

[a] Measured using the Brief Psychiatric Rating Scale (BPRS).
[b] Measured using the Schedule for the Assessment of Insight (SAI).
*** $p < .01$.

Table 2
Univariate regressions of demographic, clinical, and childhood trauma-related predictors of extreme suicide attempts in patients with schizophrenia spectrum disorders.

Variable	β	p	OR (95% CI)
Age	0.002	0.01**	1.08 (1.02–1.15)
Sex[a]	−0.51	0.19	0.44 (0.13–1.51)
Education	N/A	0.49	N/A
Lifetime drug abuse	−0.34	0.46	0.61 (0.16–2.27)
Positive symptoms	0.005	0.33	1.07 (0.93–1.22)
Negative symptoms	−0.02	0.17	0.84 (0.66–1.08)
Insight	0.02	0.09*	1.22 (0.97–1.53)
Illness duration	0.003	0.006***	1.09 (1.03–1.16)
Emotional abuse	0.01	0.03**	1.13 (1.01–1.27)
Physical abuse	0.01	0.08*	1.14 (0.98–1.32)
Sexual abuse	0.01	0.07*	1.14 (0.98–1.32)
Emotional neglect	0.003	0.37	1.05 (0.94–1.17)
Physical neglect	0.005	0.43	1.06 (0.91–1.24)
Total childhood trauma	0.001	0.05*	1.04 (1.00–1.07)

[a] Males were coded 0, Females, 1.
* $p < .10$.
** $p < .05$.
*** $p < .01$.

Table 3
Hierarchical regression of childhood emotional abuse on extreme suicide attempts, controlling for age, insight, and illness duration in patients with schizophrenia spectrum disorders.

Trauma predictor	Multiple, high lethality (Extreme) attempts		
	β	p	OR (95% CI)
Emotional abuse	0.04	0.01**	1.38 (1.08–1.77)
Physical abuse	0.05	0.08	1.34 (0.97–1.84)
Sexual abuse	0.06	0.07	1.41 (0.97–2.04)
Emotional neglect	0.01	0.45	1.07 (0.90–1.27)
Physical neglect	0.0003	0.99	1.00 (0.78–1.29)
Total childhood trauma	0.002	0.04**	1.07 (1.00–1.14)

** $p < .05$.

multivariate logistic regression models were constructed. The assumption of linear relationship between continuous independent variables and the logit transformation of the dependent variable was verified by adding the squares of the childhood trauma predictors to the models. These squared predictors were not significantly related to the extreme suicide attempt outcome, providing evidence for linearity. The results are summarized in Table 3. Both the emotional abuse subscores (β = 0.04; OR: 1.38; 95% CI: 1.08 – 1.77; p = .01) and CTQ-SF total score (β = 0.002; OR: 1.07; 95% CI: 1.00 – 1.14; p = .04) significantly predicted extreme attempts. We did not observe any significant predictive effect between the other forms of childhood trauma and extreme attempts.

4. Discussion

To the best of our knowledge, this is the first study to test the predictive effect of multiple forms of childhood maltreatment on SA in a sample of extreme phenotype suicide attempters and non-ideators with psychotic spectrum disorders. We conducted these analyses using a highly defined group of extreme attempters and non-ideators, and a strong methodological design that controlled for demographic and clinical covariates of SA. The use of these homogenized groups reduced the risk of overlap between the groups in terms of demographic and clinical features, improving the accuracy of our results. The findings support our hypothesis that total childhood trauma and childhood emotional abuse increases the risk for future, multiple, high lethality SA. Contrary to our hypothesis and some of the extant literature (Hassan et al., 2016; Roy, 2005), however, we did not observe a significantly increased history of physical abuse, sexual abuse, physical neglect, and emotional neglect trauma subtypes among extreme suicide attempters. There are several possible explanations for these findings.

The observation that multiple, high lethality suicide attempters had significantly higher total childhood trauma scores than non-ideators, but not higher physical abuse, sexual abuse, physical neglect and emotional neglect subscores is unexpected. Childhood trauma may operate in an additive manner to increase suicide risk, such that the child who experiences one form of abuse may be at lesser suicide risk than the child who experiences multiple forms of abuse. Indeed, this pattern has been observed in adult male patients with depression, where having multiple forms of childhood trauma increased the risk for PTSD symptoms (Agorastos et al., 2014).

Our finding that childhood emotional abuse independently increased the risk for extreme SAs is not explained by this additive effect, however. Rather, this result may be explained by the fact that studies tend to find an especially large effect size for the relationship between emotional abuse and SA (Liu et al., 2017), and our study may have only had adequate statistical power to detect an effect of this size. Alternatively, these diverging findings might suggest that extreme phenotype attempters differ significantly from attempters as a whole in terms of type of childhood trauma experienced. Studies in larger samples are needed to confirm the findings of the present study.

4.1. Gene-childhood trauma interactions

The homogeneous, extreme attempter group defined in this study could be an interesting population for genetic and neuroimaging studies. Sensitivity to genetic and neuroanatomical biomarkers of SA may be elevated among these individuals. Diatheses such as genetic predisposition and childhood trauma can interact with environmental stressors to increase suicidal behavior through epigenetic changes that are translated into structural or functional brain abnormalities (Kim and Lee, 2016). These neuroanatomical changes may then disrupt cognition (Lee and Hoaken, 2007) and emotional regulation (Lincoln et al., 2017), leading to treatment refraction and suicidal psychopathology (Kim and Lee, 2016). Investigation of the genetic and neuroanatomical profiles of extreme attempters is suggested to test for the presence of potential biomarkers.

4.2. Limitations

One limitation of this study is that the refinement of our sample into well-characterized, homogenized groups came inevitably with reduced sample size and statistical power. Furthermore, our study did not control for comorbid psychiatric disorders such as depression which may influence SA propensity. Replication in larger sample sizes would permit statistical control of more covariates, improving the robustness of the results.

Another limitation is that clinical data (positive symptoms, negative symptoms, and insight) reflected symptom presentation during the assessment instead of at the time of an attempt. These symptoms are expected to fluctuate in response to life stressors and may be more elevated prior to a SA. In our study, we assumed that clinical symptoms at the interview could be used as a proxy for symptoms at the time of SAs. Indeed, after patients become stable, negative symptoms do tend to remain close to those at psychosis onset when SAs are most common (Hoff et al., 1999). The decrease in positive symptoms after stabilization is much greater, however, and may not reflect severity at the time of attempt (Hoff et al., 1999). Similarly, we used age at the interview date instead of at the time of SA. Current age may, however, be an appropriate proxy for age at the most recent SA, given that age reflects duration of illness, which is related to a history of attempted suicide (Modestin et al., 1992).

Finally, our sample consisted of adults aged 18–75, who were assessed for childhood trauma using the CTQ-SF. As this scale is based on retrospective self-reports, participant recall accuracy could have limited the accuracy of the trauma data collected.

4.3. Strengths of the present study

Despite these limitations, our study provides some evidence for a causal link between childhood trauma and later SA. Except in rare cases of childhood psychosis, childhood trauma would occur prior to the first attempt, suggesting that our predictor variable was temporally precedent to our outcome. The use of statistical methods to control for confounding factors helps to rule out alternative explanations for our findings. While the inherent complexity of the population studied limits our ability to adequately adjust for all confounding variables, several key demographic and clinical predictors were accounted for. Thus, our study supports the possibility of a causal link between childhood maltreatment and multiple, high lethality SAs.

The major strength of our analysis is our characterization of a homogenous phenotype of extreme attempters and non-ideators. Indeed, we propose that future research take into account this heterogeneity in order to better understand, and prevent, suicide risk. Further studies on this sample of patients is recommended in order to better characterize the risk factors for multiple, high lethality attempts, and differentiate this phenotype from that of other attempters with SCZ spectrum disorders. A next step of this research is to further stratify the extreme attempter group to include patients with a history of violent attempts, which may increase SA propensity. Extreme attempters with multiple, high lethality, violent attempts may be a specialized subtype that differs significantly from other attempters, and thorough characterization of the phenotype may allow for appropriate differential diagnosis and treatment.

Declaration of Competing Interest

There are no actual or potential conflicts of interests between the authors and this work.

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