Journal of Affective Disorders 370 (2025) 118–123

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Further evidence for the association between childhood trauma and suicidal ideation in young individuals: A twin based study

Nerea Moreno-Gamazo [a], Lotta-Katrin Pries [d], Laia Marqués-Feixa [a,b,c], Sergi Papiol [c,e], Soledad Romero [c,f,g], Claudia Menne-Lothmann [d], Jeroen Decoster [d,h,i], Ruud van Winkel [d,h], Dina Collip [d], Philippe Delespaul [d], Marc De Hert [h], Catherine Derom [j,k], Evert Thiery [l], Nele Jacobs [d,m], Marieke Wichers [d,n], Jim van Os [d,o,p], Bart P.F. Rutten [d], Lourdes Fañanás [a,b,c,*,1], Sinan Guloksuz [d,q,**,1]

[a] Department of Evolutionary Biology, Ecology and Environmental Sciences, Faculty of Biology, University of Barcelona, 08028 Barcelona, Spain
[b] Biomedicine Institute of the University of Barcelona (IBUB), 08028 Barcelona, Spain
[c] Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Instituto de Salud Carlos III, 28029 Madrid, Spain
[d] Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience, Maastricht University, Fac. Health, Medicine and Life Sciences, 6200MD Maastricht, the Netherlands
[e] Dept. Falkai, Max Planck Institute of Psychiatry, 80804 Munich, Germany
[f] Department of Child and Adolescent Pychiatry and Psychology, Institut Clínic de Neurociències, Hospital Clínic Universitari, Barcelona, Spain
[g] Institut d'Investigacions Biomediques August Pi I Sunyer (IDIBAPS), Barcelona, Spain
[h] Department of Neurosciences, University Psychiatric Centre KU Leuven, 3000 Leuven, Belgium
[i] Brothers of Charity, University Psychiatric Centre Sint-Kamillus Bierbeek, 3360 Bierbeek, Belgium
[j] Centre of Human Genetics, University Hospitals Leuven, KU Leuven, 3000 Leuven, Belgium
[k] Department of Obstetrics and Gynecology, Ghent University Hospitals, Ghent University, 9000 Ghent, Belgium
[l] Department of Neurology, Ghent University Hospital, Ghent University, 9000 Ghent, Belgium
[m] Faculty of Psychology and Educational Sciences, Open University of the Netherlands, 6419 AT Heerlen, the Netherlands
[n] Department of Psychiatry, Interdisciplinary Center Psychopathology and Emotion Regulation (ICPE), University of Groningen, University Medical Center Groningen, 9700 AD Groningen, the Netherlands
[o] Department of Psychiatry, Brain Centre Rudolf Magnus, University Medical Centre Utrecht, 3584, CX, Utrecht, the Netherlands
[p] Department of Psychosis Studies, Institute of Psychiatry, King's Health Partners, King's College London, London SE5 8AF, UK
[q] Department of Psychiatry, Yale School of Medicine, New Haven, CT 06511, USA

ARTICLE INFO

Keywords:
Childhood trauma
Suicidal ideation
Within twin-pair differences
Monozygotic
Dizygotic
Twin study

ABSTRACT

Background: Suicide is a major cause of death among youth. Childhood trauma (CT) has emerged as a leading environmental risk factor for suicidal ideation (SI). The present study intends to understand the association between CT and SI in a sample of twins, highlighting the relevance of CT *per se*, regardless of genetic vulnerability.

Methods: Data were derived from a general population young twin study, the TwinssCan project ($N = 796$; mean age = 17.4). Different types of CT (physical, emotional and sexual) were explored with CTQ and SI through SCL-90-R. The discordance within twin-pairs was used to dissect the genetic and CT effects in SI.

Results: Total CT and all subdomains were associated with an increased risk for SI. The within-pair differences analysis in monozygotic and dizygotic twins suggested that part of this association is not attributable to genetic predisposition, which points out the relevance of CT itself upon the increase of SI. This result converged with CT subdomain analyses of physical abuse and neglect.

* Correspondence to: L. Fañanás, Department of Evolutionary Biology, Ecology and Environmental Sciences, Faculty of Biology, University of Barcelona, Av. Diagonal, 643, 08028 Barcelona, Spain.
** Correspondence to: S. Guloksuz, Department of Psychiatry and Neuropsychology, School for Mental Health and Neuroscience, Maastricht University Medical Center, P.O. Box 616, 6200 MD Maastricht, the Netherlands.
E-mail addresses: lfananas@ub.edu (L. Fañanás), sinan.guloksuz@maastrichtuniversity.nl (S. Guloksuz).
[1] These authors contributed as joint last authors.

https://doi.org/10.1016/j.jad.2024.10.125
Received 28 June 2024; Received in revised form 25 October 2024; Accepted 28 October 2024
Available online 31 October 2024

Limitations: While within-pair twin analyses control for genetic risk, additional environmental shared and individual characteristics should be controlled for (such as poverty or protective factors). More detailed information on SI would be of great interest to better capture the complexity of this construct.
Conclusion: CT appears to be an important environmental risk factor for SI and at least partly independent of Gene-Environment correlation (rGE). This study highlights the importance of including the history of CT in psychiatric evaluations of patients. The burden of the psychosocial environment on SI could be disentangled by further research on environmental risk and protective factors.

1. Introduction

Throughout the human lifespan, several periods are at considerable risk for the critical phenomenon that is suicide. Although there is a great risk of suicidal behavior in late adulthood, great concern relies on the youth, as suicide is the second leading cause of death among 15–29-year-olds in Europe, and the fourth worldwide (eurostat, 2021; World Health Organization, 2021). Adolescence (10–19 years of age) is a critical stage in which the youth acquire social-emotional skills to cope with vital challenges, and confront psychopathological conditions, which may trigger suicidal behaviors.

More than 700,000 people die by suicide every year, according to the World Health Organization WHO (2021). But even so, about two-thirds of people with suicidal ideation (SI) never make a suicide attempt, and even fewer die by suicide. By directing attention to SI, we can reach a larger number of people at risk of suicidal behavior and other mental health issues, thereby preventing further instances of such behavior. Actually, SI could be considered a nuclear symptom of Major Depressive Disorder (MDD) and other affective disorders (Chen et al., 2023; Lundberg et al., 2023). Moreover, it seems that SI could have a genetic predisposition that overlaps with the genetic factors contributing to mental disorders such as MDD. This shared genetic basis has been studied in genome-wide association studies (GWAS) as well as twin studies, highlighting a common vulnerability underlying both conditions (Hernández-Díaz et al., 2019; Mullins et al., 2022; Zalsman, 2012).

Besides, the SI usually stems from stressful or traumatic life events. Specifically, childhood trauma (CT) has emerged as one of its most important associated environmental risk factors (Angelakis et al., 2019). CT is associated with disruption in early brain development and potentially leads to a whole spectrum of psychiatric conditions (Nelson et al., 2020; Oral et al., 2015). Furthermore, all distinct subtypes of CT (abuse, neglect, physical, psychological and sexual) are themselves associated with SI (Angelakis et al., 2019) and other suicide behaviors (Yao et al., 2023). However, it is noteworthy that there is limited research aimed at isolating and accounting for the genetic component from this association.

CT is a potent environmental risk factor for multiple adverse outcomes, including SI, with potential genetic components exacerbating susceptibility. Research suggests a complex interplay between genetic predisposition and environmental factors in influencing the risk of suicidality, through the gene-environment interactions (GxE). GxE refers to how both genetic factors and environmental influences interact to shape individual characteristics or outcomes. Some studies have indicated that the development of SI may occur in individuals with a specific genetic predisposition and exposure to CT (González-Castro et al., 2023; Warrier and Baron-Cohen, 2021), yet others do not inherently imply this GxE (Richmond-Rakerd et al., 2018).

On the other hand, some studies show that genetic factors contribute to differential exposure to CT (Sanabrais-Jiménez et al., 2019; Segura et al., 2019). These findings suggest gene-environment correlation (rGE), meaning that genetic factors could influence the degree of exposure to a given environmental factor. For instance, individuals with specific polymorphisms, such us the serotonin transporter gene (5-HTTLPR) may exhibit heightened sensitivity to stressful life events. The genetic vulnerability in this neurotransmitter, which is crucial in regulating serotonin levels in the brain, can lead to an increased likelihood of experiencing adverse environments—such as familial instability or social isolation—subsequently exacerbating feelings of hopelessness and suicidal ideation. For this, twin studies provide a great advantage in the investigation of common and differential genetic factors involved in complex phenotypes, such as SI.

Monozygotic (MZ) twins are genetically identical, although they may differ in smaller changes in mitochondrial DNA and epigenetics. Thus, phenotypic discordance between twin-pairs can give us an estimate of how genetic that trait may be. Therefore, the within twin-pair discordance for a trait could be analyzed in MZ twins, and this would partial out the effect of genetic predisposition of an outcome (Lecei et al., 2019). It is also interesting to compare this approach with dizygotic (DZ) twins, who share approximately only 50 % of their genetic material. By comparing the degree of similarity between MZ and DZ twins, it is plausible to extract the relative contributions of genetic and environmental factors to a particular trait or disease (Castillo-Fernandez et al., 2014; Hannon et al., 2018).

In this study, we aimed to investigate the association between CT and SI without the confounding effect of rGE by using the twin-pair discordance design to leave out the shared heritable components of both CT and SI. The existence of literature elucidating the putative relationship between different domains of CT separately and SI risk is scarce; but it suggests a similar effect to combined (Angelakis et al., 2019). Therefore, we also aim to understand the individual effects of the CT subdomains upon SI.

2. Methods

2.1. Participants and procedure

Data were derived from the first wave of the TwinssCan project, a longitudinal general population cohort, which recruited participants from the East Flanders Prospective Twin Survey in Belgium (EFPTS; Derom et al., 2019). The sample includes 796 subjects (292 MZ twins, 486 DZ twins, and 18 twins part of a triplet), 43 non-twin siblings, and 363 parents. Baseline data was assessed from April 2010 to April 2014 (Pries et al., 2017). Twin participants were 15–35 years old and the mean age was 17.4 (SD = 3.6) years (MZ: 18.0 [SD = 4.2]; DZ: 16.9 [SD = 2.8]). From all participants, 60 % were female (MZ: 63 %; DZ: 57 %; triplets: 61 %; siblings: 70 %) (TwinssCan; Pries et al., 2019b). Baseline assessment included an extensive battery of validated self-report, structured interview, and experimental test measures; placenta, blood, and saliva samples; and DNA isolations. In this study, 720 subjects (262 MZ and 458 DZ twins) with complete data on CT and SI were used (excluding the missing rate of 7 %).

Participants were included if they could understand and communicate for the study procedures, and when they agreed to participate voluntarily by means of written informed consent. Signed parental consent was also required when participants were under 18 years. Participants were not eligible if caregivers' records indicated the presence of a pervasive mental disorder, such as autism or schizophrenia. However, subjects with other types of mental illnesses were included in the sample (see Pries et al. (2019b) for more detail). Participants were excluded if, upon assessment by the instructor, study coordinator, or neuropsychological tester, it was determined that they exhibited an inability to successfully complete the tests or interviews (deemed invalid

or unreliable).

2.2. Measures

Childhood trauma was assessed with the Dutch translation of the short version of the Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003), which comprises 28 items about 5 subdomains of CT: physical abuse (PA), emotional abuse (EA), sexual abuse (SA), physical neglect (PN), and emotional neglect (EN). Participants were asked to rate the 28 items on a 5-point scale from 1 "never" to 5 "always". Mean scores of the CTQ total scale and each CT subdomains were constructed.

To assess suicidal ideation, the Symptom Checklist-90-Revised (SCL-90-R; Derogatis and Unger, 2010) was used. SCL-90-R is a validated instrument to assess multiple recent symptoms. Specifically, SI mean score was captured by taking the mean of two items from this self-report: "thoughts of ending life" and "thoughts of death and dying", rated on a 5-point scale ranging from 0="not at all" to 4 = "very much".

2.3. Data analysis

The sample data were analyzed with Stata/SE 16.1. Associations between CT exposure and SI were investigated using multilevel regression analysis, which included the identification codes of each twin-pair as a random variable. The CT total or subdomain scores were used as independent variables and the SI scores as the dependent variable. To ensure data quality, we assessed multicollinearity and normality, finding no issues. We excluded cases with missing data for the three key variables.

To partial out the effect of genetic predisposition, association analyses based on within-pair difference values of the SI, CT total, and CT subdomain scores were performed separately (Carlin et al., 2005). Briefly, within-pair differences were calculated for each twin-pair and transformed into absolute values. For the regression model, the within-pair difference scores of one of the twins in the pair were used. This approach allowed a twin-pair discordance of a dependent variable to be regressed on that of the independent variables with the intercept constrained to zero.

Analyses were performed separately for MZ and DZ twins since the within-pair differences of these two types of twins cannot be compared due to their different genetic resemblance. All analyses were adjusted for age and biological sex.

3. Results

3.1. Descriptive statistics

A total of 720 subjects (MZ: n = 262 and DZ: n = 458) without missing data were analyzed. As reported in Table 1, 59.7 % of the sample was female, and the mean age was 17.2 (SD = 3.3).

Table 1
Demographic variables and frequency of the CT experiences in the final MZ and DZ twins.

	Total	MZ twins	DZ twins
Age (mean ± SD)	17.23 ± 3.35 [15–34]	18.03 ± 4.19 [15–34]	16.85 ± 2.82 [15–30]
Biological sex			
Male	290 (40.28 %)	92 (35.11 %)	198 (43.23 %)
Female	430 (59.72 %)	170 (64.89 %)	260 (56.77 %)
Childhood trauma			
Emotional abuse	226 (31.39 %)	78 (29.77 %)	148 (32.31 %)
Physical abuse	29 (4.03 %)	9 (3.44 %)	20 (4.37 %)
Sexual abuse	48 (6.67 %)	23 (8.78 %)	25 (5.46 %)
Emotional neglect	311 (43.19 %)	115 (43.89 %)	196 (42.79 %)
Physical neglect	118 (16.39 %)	41 (15.65 %)	77 (16.81 %)

The distribution of the CT subdomains in the MZ and the DZ twins is similar in proportion. Emotional neglect (43 %) and abuse (31 %) had the highest and second highest prevalence within the total sample. Furthermore, sexual abuse was more prevalent than physical abuse in the current sample.

3.2. Mixed effects multi-linear regression models

3.2.1. Childhood trauma and suicidal ideation

Table 2 reports the association of CT (total and each subdomain) with SI. Total CT was associated with an increased risk of SI in the total sample (B = 0.46, 95%CI = 0.35–0.56, p < .001). Analyses of the CT subdomains showed similar results and were all associated with an increased risk of SI. These results remained similar and significant in the models adjusted for age and sex.

3.2.2. Childhood trauma and suicidal ideation within-pair differences

Table 3 reports the association between CT and SI in the within-pair differences models. The analysis of within-pair differences showed a significant association between CT and SI in the MZ twins (B = 0.49, 95%CI = 0.14–0.84, p = .006). Subdomain analyses converged with this result for the following CT subdomains: physical abuse (B = 0.08, 95% CI = 0.01–0.15, p = .023), emotional abuse (B = 0.06, 95%CI = 0.03–0.09, p < .001) and physical neglect (B = 0.10, 95%CI = 0.03–0.16, p = .003). However, emotional and sexual abuse were not statistically significantly associated with SI in the within-pair differences model.

The significant correlations between CT and SI discordances in DZ twins converged with the results in MZ twins for the total CT (B = 0.53, 95%CI = 0.23–0.84, p = .001) and the subdomains of physical abuse (B = 0.06, 95%CI = 0.00–0.12, p = .039) and physical neglect (B = 0.05, 95%CI = 0.01–0.08, p = .019). However, emotional abuse was statistically significantly associated with SI (B = 0.05, 95%CI = 0.02–0.08, p = .001), whereas emotional neglect was not significantly associated with SI (B = -0.00, 95%CI = −0.03–0.03, p = .915). Sexual abuse, as in the MZ-twins analysis, also does not show significant association.

4. Discussion

In consistency with previous studies, we emphasize that childhood trauma and suicidal ideation were significantly associated (Park et al., 2021; Wang et al., 2022). Besides, our findings also provide converging evidence for the association of SI with all CT subdomains (Angelakis et al., 2019). Consequently, we must bear in mind that the increased risk for SI in youths is evident regardless of the type of trauma.

The novel contribution of the present study was the use of the discordance between twins to discern the effect of genetic background and their experiences of CT on SI. Our primary finding indicated a significant association between CT and SI discordances in MZ twins, in accordance with studies in similar outcomes (Lecei et al., 2019; Silberg et al., 2016). Therefore, shared genetics is most certainly excluded from

Table 2
Association between SI and total CT and specific subdomain scores.

	Unadjusted effects		Adjusted effects[a]	
	B	95 % CI	B	95 % CI
Childhood trauma	0.46	0.35–0.56***	0.45	0.35–0.56***
Emotional abuse	0.04	0.03–0.05***	0.04	0.03–0.05***
Physical abuse	0.09	0.06–0.11***	0.09	0.06–0.11***
Sexual abuse	0.05	0.03–0.08***	0.05	0.03–0.08***
Emotional neglect	0.03	0.02–0.04***	0.03	0.02–0.04***
Physical neglect	0.06	0.04–0.08***	0.06	0.04–0.09***

B - regression coefficient, CI - confidence interval.
[a] Adjusted for age and sex.
*** p < .001.

Table 3
Association of the within-pair differences of SI with the total CT and CT subdomain scores.

	MZ twins		Adj. R^2	DZ twins		Adj. R^2
	B	95 % CI		B	95 % CI	
Childhood trauma	0.49	0.14–0.84**	0.04	0.53	0.23–0.84**	0.06
Emotional abuse	0.00	−0.03–0.04	−0.02	0.05	0.02–0.08**	0.05
Physical abuse	0.08	0.01–0.15*	0.02	0.06	0.00–0.12*	0.02
Sexual abuse	0.03	−0.01–0.08	0.00	0.04	−0.02–0.1	0.01
Emotional neglect	0.06	0.03–0.09***	0.09	−0.00	−0.03–0.03	0.00
Physical neglect	0.10	0.03–0.16**	0.05	0.05	0.01–0.08*	0.03

B - regression coefficient, CI - confidence interval, Adj. R^2 – adjusted R square.
* $p < .05$.
** $p < .01$.
*** $p < .001$.

these associations, as well as other shared environmental factors. This finding would highlight the importance of individual experiences in the development of SI, beyond, for example, family psychiatric history or stressful situations in their shared context. This finding converges for DZ twins, considering that they only share part of the genetic background. These results demonstrate the harmful effect of traumatic experiences *per se* during childhood and their relevance for understanding SI in later adolescence. However, our results do not rule out the GxE underlying the link between CT and SI. In fact, heritable components have been described for SI under the influence of trauma-like circumstances (Ludwig et al., 2018; Richmond-Rakerd et al., 2018).

For instance, some subdomains of CT may interact more with specific genetic predisposition in some individuals in the development of SI. Specifically, the strongest evidence is limited to physical abuse and neglect. These associations confirm that trauma related to physical events (abuse or neglect), significantly contributes to SI development. These findings would be consistent with previous findings that physical maltreatment may have the greatest impact on mental health (Xiao et al., 2023). However, we know that traumatic events typically converge in the same environment, and physical maltreatment tends to coexist with emotional abuse and neglect (Marques-Feixa et al., 2023), which are usually in the background when physical maltreatment is detected. It may therefore be an indicator of greater aggregation or severity of complex trauma rather than an indicator of the nature of abuse itself (Hughes et al., 2017).

Secondly, emotional neglect discordances exhibit a clear association with SI discordances in our MZ twins, excluding the genetic input to the association. However, we did not observe this in DZ twins. This could suggest other shared environmental factors involved in this association or that we cannot entirely dismiss genetic vulnerability. These results are in line with previous research suggesting GxE (Brodsky, 2016), and still support emotional neglect as an underlying subdomain of the other types of trauma (Marques-Feixa et al., 2023).

Intriguing results emerge from the subdomains of emotional and sexual abuse. The absence of association between emotional abuse and SI within-pair differences in MZ twins suggests that, while there would be discordances for EA, this type of trauma alone would not exert significant influence on SI. In light of these findings in MZ twins, it is important to note that the potential influence of other shared environmental factors should also be excluded. In this regard, some authors propose that the relationship between these two variables may be mediated by intermediate factors such as resilience (Yao et al., 2023) or problems in emotional regulation (Laghaei et al., 2023). Therefore, the significant association between emotional abuse and SI discordances in DZ twins raises the possibility of the unshared genetic influence on this development of SI as previous studies already suggested (Lengvenyte et al., 2022; Segura et al., 2019). This could be attributed to the presence of unshared environmental factors that may be jointly associated with CT and/or SI.

A similar discussion holds for sexual abuse, as unexpectedly no significant association was found in MZ nor DZ twins. Sexual abuse may represent a particular event in the history of CT (Hom et al., 2017), and while it is associated with SI itself, the shared environment of the twin-pair may exert more influence on the outcome than the isolated event. While some studies have reported significant associations between childhood SA and self-harm, as a form of emotional self-regulation rather than death ideation (David Klonsky and Moyer, 2018; Roley-Roberts et al., 2023).

The study provides evidence for the complex interplay between genetic and environmental factors in determining the impact of maltreatment on suicidal ideation. Emotional maltreatment appears to be more susceptible to genetic influences, suggesting that individuals with certain genetic predispositions may be more vulnerable to the negative consequences of this type of abuse. Physical abuse, on the other hand, seems to be more strongly influenced by shared environmental factors, such as the overall family dynamic or the severity of the abuse. Sexual abuse may have a more indirect effect on SI, potentially through its association with other mental health conditions like PTSD or anxiety.

The overall picture of different suicidal behaviors is nuanced. In fact, recent research suggests that the relationship between CT and SI may be influenced also by genetic factors (González-Castro et al., 2023; Segura et al., 2019; Warrier and Baron-Cohen, 2021). For instance, variations in genes related to neurotransmitter systems like serotonin transporter gene, have been implicated in MDD when combined with stressful life events (Agis-Balboa et al., 2023). Similarly, the interaction between the HTR2A gene variant and negative life events has been associated with an increased risk of suicide attempts among patients with MDD (Pang et al., 2024).

While the present study suggests an independent association between CT and SI, future research should investigate more nuanced interactions of CT subdomains with other shared environmental factors, such as the socioeconomic status (SES), a protective family environment, personality traits, or even family psychiatric and health records. (Lodebo et al., 2017; Yang et al., 2021). In fact, recent studies highlight the importance of the exposome approach, that is, everything in the environment an individual is exposed to throughout life, when exploring the non-genetic risk factors of SI (Barzilay et al., 2021; Pries et al., 2019a).

4.1. Strengths and limitations

It is important to consider the results' strengths and weaknesses while interpreting them. We were able to adjust for genetic factors by employing a MZ twin differences strategy, and the results suggest that at least some of the link between CT and SI is real. Although the sample of twins is very broad, there is an age range that includes adolescents and young adults, which could influence in the nature of SI, and be affected by proximity to CT experiences. Reports of trauma exposure were in self-report and retrospective, which according to earlier research, may be trustworthy (Fisher et al., 2011), and they are more likely to underestimate prevalence than to overestimate it (Hardt and Rutter, 2004). We understand the limitation of not being able to assess the complexity of SI using a broader scale. In addition, SI was assessed over the past week, which may have resulted in an underestimation of the condition. However, the model employed allows us to capture to some extent the degree of severity and modes of approximation of SI. A multilevel model using available suicide questionnaires could be further explored to complement the results and understand the effects of the different subtypes. Furthermore, while the MZ twin differences method properly controls for genetic risk, additional environmental characteristics shared by MZ twins may still play a role between CT and SI.

4.2. Clinical implications

CT is likely to be a sufficiently relevant risk factor to increase SI. Therefore, we can see that inquiring about the history of maltreatment in the clinical contexts and distinguishing their nature can provide us with a more accurate assessment of potential mental health risk, and specifically, suicidal behavior. Although, there is a possibility that genetic susceptibility may interact with environmental factors, especially for emotional and sexual abuse subtypes. Assessing SI is essential because it allows reduced stigma, a better understanding of public health issues, and informed clinical practice to improve prevention and early intervention to reduce the overall burden of suicide on society.

5. Conclusion and future directions

Twin studies confirm that childhood trauma appears to be an important environmental risk factor for suicidal ideation in youth, at least partly independent of rGE, and especially for physical abuse and neglect. Future research should further address the nature of this relationship and the causal effect of emotional neglect and abuse, as well as the impact of the co-occurrence, severity, and chronicity of these CT experiences. These studies could leverage the longitudinal cohort studies spanning the entire life course and genetically informed causal inference methods. They should also bear in mind other multiple environmental risk and protective factors that influence the onset of SI, beyond the risk due to genetic or psychiatric family history. The role of GxE-oriented research using polygenic risk scores could help gain insight toward the link between CT and SI.

CRediT authorship contribution statement

Nerea Moreno-Gamazo: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Conceptualization. **Lotta-Katrin Pries:** Writing – review & editing, Validation, Supervision, Software, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Laia Marqués-Feixa:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision. **Sergi Papiol:** Writing – review & editing, Validation, Supervision. **Soledad Romero:** Writing – review & editing, Supervision. **Claudia Menne-Lothmann:** Validation, Project administration. **Jeroen Decoster:** Validation, Project administration. **Ruud van Winkel:** Validation, Project administration. **Dina Collip:** Validation, Project administration. **Philippe Delespaul:** Validation, Project administration. **Marc De Hert:** Validation, Project administration. **Catherine Derom:** Validation, Project administration. **Evert Thiery:** Validation, Project administration. **Nele Jacobs:** Validation, Project administration. **Marieke Wichers:** Validation, Project administration. **Jim van Os:** Validation, Project administration, Investigation, Funding acquisition. **Bart P.F. Rutten:** Validation, Project administration, Investigation, Funding acquisition. **Lourdes Fañanás:** Writing – review & editing, Validation, Supervision, Funding acquisition, Conceptualization. **Sinan Guloksuz:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare no conflicts of interest.

Acknowledgements

The authors thank Jill Ielegems, Katrien Lyssens, Davinia Verhoeven, and Debora op't Eijnde for data-collection. Further, the authors would like to acknowledge that the East Flanders Prospective Twin Survey (EFPTS) is partly supported by the Association for Scientific Research in Multiple Births and that the TwinssCan project is part of the European Community's Seventh Framework Program under grant agreement No. HEALTH-F2-2009-241909 (Project EU-GEI). Dr. Pries is supported by the Kootstra Talent Fellowship of Maastricht University. Drs van Os and Guloksuz are supported by the Ophelia research project, ZonMw grant 636340001. Dr Rutten was funded by a Vidi award (91718336) from the Netherlands Scientific Organisation. Dr. van Os, Dr. Guloksuz, and Dr. Rutten are supported by the YOUTH-GEMs project, funded by the European Union's Horizon Europe program under the grant agreement number: 101057182. This study was also supported by a grant from the Spanish Ministry of Economy and Competitiveness, Instituto de Salud Carlos III through the University of Barcelona multicenter project (PI22/01245)-PI L. Fananas and by the Comissionat per a Universitats i Recerca del DIUE, of the Generalitat de Catalunya regional authorities (2021SGR00706). This study was facilitated by the 2nd Georgina Barbosa Grant (Fundació Barbosa i Petit), and Pre-doctoral Health Research Training Contracts (PFIS), grant number FI23/00144 (Instituto de Salud Carlos III), to Nerea Moreno Gamazo.

References

Agis-Balboa, C., Lopez-Fernandez, H., & Peedicayil, J. (2023). Genome–environment interactions and psychiatric disorders. Biomedicines 2023, Vol. 11, page 1209, 11 (4), 1209. doi:https://doi.org/10.3390/BIOMEDICINES11041209.

Angelakis, I., Gillespie, E.L., Panagioti, M., 2019. Childhood maltreatment and adult suicidality: a comprehensive systematic review with meta-analysis. Psychol. Med. 49 (7), 1057–1078. https://doi.org/10.1017/S0033291718003823.

eurostat, 2021. Statistics Explained: Young people - health. In: Eurostat (ISSN 2443-8219). Retrieved February 6, 2024, from. https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Young_people_-_health&oldid=635498Q6.

Barzilay, R., Moore, T.M., Calkins, M.E., Maliackel, L., Jones, J.D., Boyd, R.C., Warrier, V., Benton, T.D., Oquendo, M.A., Gur, R.C., Gur, R.E., 2021. Deconstructing the role of the exposome in youth suicidal ideation: trauma, neighborhood environment, developmental and gender effects. Neurobiol. Stress 14. https://doi.org/10.1016/J.YNSTR.2021.100314.

Bernstein, D.P., Stein, J.A., Newcomb, M.D., Walker, E., Pogge, D., Ahluvalia, T., Stokes, J., Handelsman, L., Medrano, M., Desmond, D., Zule, W., 2003. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl. 27 (2), 169–190. https://doi.org/10.1016/S0145-2134(02)00541-0.

Brodsky, B.S., 2016. Early childhood environment and genetic interactions: the diathesis for suicidal behavior. Curr. Psychiatry Rep. 18 (9). https://doi.org/10.1007/S11920-016-0716-Z.

Carlin, J.B., Gurrin, L.C., Sterne, J.A.C., Morley, R., Dwyer, T., 2005. Regression models for twin studies: a critical review. Int. J. Epidemiol. 34 (5), 1089–1099. https://doi.org/10.1093/IJE/DYI153.

Castillo-Fernandez, J.E., Spector, T.D., Bell, J.T., 2014. Epigenetics of discordant monozygotic twins: implications for disease. Genome Med. 6 (7). https://doi.org/10.1186/S13073-014-0060-Z.

Chen, P., Feng, Y., Li, X.H., Li, J.X., Wang, Y.Y., Zheng, W.Y., Su, Z., Cheung, T., Ungvari, G.S., Ng, C.H., Sha, S., Xiang, Y.T., 2023. Systematic reviews and meta-analyses on major depressive disorder: a bibliometric perspective. Front. Psychol. 14, 1136125. https://doi.org/10.3389/FPSYT.2023.1136125/BIBTEX.

World Health Organization [WHO], 2021. One in 100 deaths is by suicide: WHO guidance to help the world reach the target of reducing suicide rate by 1/3 by 2030. In: World Health Organization. Retrieved June 27, 2023, from. https://www.who.int/news/item/17-06-2021-one-in-100-deaths-is-by-suicide.

David Klonsky, E., & Moyer, A. (2018). Childhood Sexual Abuse and Non-suicidal Self-injury: Meta-analysis. doi:https://doi.org/10.1192/bjp.bp.106.030650.

Derogatis, L. R., & Unger, R. (2010). Symptom Checklist-90-Revised. The Corsini Encyclopedia of Psychology, 1–2. doi:https://doi.org/10.1002/9780470479216.CORPSY0970.

Derom, C., Thiery, E., Rutten, B.P.F., Peeters, H., Gielen, M., Bijnens, E., Vlietinck, R., Weyers, S., 2019. The East Flanders prospective twin survey (EFPTS): 55 years later. Twin Res. Hum. Genet. 22 (6), 454–459. https://doi.org/10.1017/THG.2019.64.

Fisher, H.L., Craig, T.K., Fearon, P., Morgan, K., Dazzan, P., Lappin, J., Hutchinson, G., Doody, G.A., Jones, P.B., McGuffin, P., Murray, R.M., Leff, J., Morgan, C., 2011. Reliability and comparability of psychosis Patients' retrospective reports of childhood abuse. Schizophr. Bull. 37 (3), 546–553. https://doi.org/10.1093/SCHBUL/SBP103.

González-Castro, T.B., Juárez-Rojop, I.E., Tovilla-Zárate, C.A., Ovando-Ricárdez, J.A., Hernández-Díaz, Y., López-Narváez, M.L., Genis-Mendoza, A.D., Rodríguez-Pérez, C., 2023. Gene-environment interaction between HPA-axis genes and trauma exposure in the suicide behavior: a systematic review. J. Psychiatr. Res. 164, 162–170. https://doi.org/10.1016/J.JPSYCHIRES.2023.06.011.

Hannon, E., Knox, O., Sugden, K., Burrage, J., Wong, C. C. Y., Belsky, D. W., Corcoran, D. L., Arseneault, L., Moffitt, T. E., Caspi, A., & Mill, J. (2018). Characterizing Genetic and Environmental Influences on Variable DNA Methylation Using Monozygotic and Dizygotic Twins. doi:https://doi.org/10.1371/journal.pgen.1007544.

Hardt, J., Rutter, M., 2004. Validity of adult retrospective reports of adverse childhood experiences: review of the evidence. J. Child Psychol. Psychiatry 45 (2), 260–273. https://doi.org/10.1111/J.1469-7610.2004.00218.X.

Hernández-Díaz, Y., González-Castro, T.B., Tovilla-Zárate, C.A., Juárez-Rojop, I.E., López-Narváez, M.L., Pérez-Hernández, N., Rodríguez-Pérez, J.M., Genis-Mendoza, A.D., 2019. Association between FKBP5 polymorphisms and depressive disorders or suicidal behavior: a systematic review and meta-analysis study. Psychiatry Res. 271, 658–668. https://doi.org/10.1016/J.PSYCHRES.2018.12.066.

Hom, M.A., Matheny, N.L., Stanley, I.H., Rogers, M.L., Cougle, J.R., Joiner, T.E., 2017. Examining physical and sexual abuse histories as correlates of suicide risk among firefighters. J. Trauma. Stress. 30 (6), 672–681. https://doi.org/10.1002/JTS.22230.

Hughes, K., Bellis, M.A., Hardcastle, K.A., Sethi, D., Butchart, A., Mikton, C., Jones, L., Dunne, M.P., 2017. The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. Lancet Public Health 2 (8), e356–e366. https://doi.org/10.1016/S2468-2667(17)30118-4.

Laghaei, M., Mehrabizadeh Honarmand, M., Jobson, L., Abdollahpour Ranjbar, H., Habibi Asgarabad, M., 2023. Pathways from childhood trauma to suicidal ideation: mediating through difficulties in emotion regulation and depressive symptoms. BMC Psychiatry 23 (1), 1–13. https://doi.org/10.1186/S12888-023-04699-8/TABLES/4.

Lecei, A., Decoster, J., De Hert, M., Derom, C., Jacobs, N., Menne-Lothmann, C., van Os, J., Thiery, E., Rutten, B.P.F., Wichers, M., van Winkel, R., 2019. Evidence that the association of childhood trauma with psychosis and related psychopathology is not explained by gene-environment correlation: a monozygotic twin differences approach. Schizophr. Res. 205, 58–62. https://doi.org/10.1016/J.SCHRES.2018.05.025.

Lengvenyte, A., Sundaresh, A., Strumila, R., Boukouaci, W., Wu, C.L., Sugunasabesan, S., Guillaume, S., Sénèque, M., Leboyer, M., Olié, E., Tamouza, R., Courtet, P., 2022. Combined effects of nitric oxide synthase 3 genetic variant and childhood emotional abuse on earlier onset of suicidal behaviours. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 119. https://doi.org/10.1016/J.PNPBP.2022.110617.

Lodebo, B.T., Möller, J., Larsson, J.-O., Engström, K., 2017. Socioeconomic position and self-harm among adolescents: a population-based cohort study in Stockholm, Sweden. Child Adolesc. Psychiatry Ment. Health 11, 46. https://doi.org/10.1186/s13034-017-0184-1.

Ludwig, B., Kienesberger, K., Carlberg, L., Swoboda, P., Bernegger, A., Koller, R., Wang, Q., Inaner, M., Zotter, M., Kapusta, N.D., Haslacher, H., Aigner, M., Kasper, S., Schosser, A., 2018. Influence of CRHR1 polymorphisms and childhood abuse on suicide attempts in affective disorders: a GxE approach. Front. Psychiatry 9 (APR), 304445. https://doi.org/10.3389/FPSYT.2018.00165/BIBTEX.

Lundberg, J., Cars, T., Lampa, E., Katarina, Selling, E., Leval, A., Gannedahl, A., Själin, M., Björkholm, C., Hellner, C., 2023. Determinants and outcomes of suicidal behavior among patients with major depressive disorder supplemental content. JAMA Psychiatry 80 (12), 1218–1225. https://doi.org/10.1001/jamapsychiatry.2023.2833.

Marques-Feixa, L., Palma-Gudiel, H., Romero, S., Moya-Higueras, J., Rapado-Castro, M., Castro-Quintas, Á., Zorrilla, I., José Muñoz, M., Ramírez, M., Mayoral, M., Mas, A., José Lobato, M., Blasco-Fontecilla, H., Fañanás, L., 2023. Childhood maltreatment disrupts HPA-axis activity under basal and stress conditions in a dose-response relationship in children and adolescents. Psychol. Med. 53 (3), 1060–1073. https://doi.org/10.1017/S003329172100249X.

Mullins, N., Kang, J.E., Campos, A.I., Coleman, J.R.I., Edwards, A.C., Galfalvy, H., Levey, D.F., Lori, A., Shabalin, A., Starnawska, A., Su, M.H., Watson, H.J., Adams, M., Awasthi, S., Gandal, M., Hafferty, J.D., Hishimoto, A., Kim, M., Okazaki, S., et al., 2022. Dissecting the shared genetic architecture of suicide attempt, psychiatric disorders, and known risk factors. Biol. Psychiatry 91 (3), 313–327. https://doi.org/10.1016/J.BIOPSYCH.2021.05.029.

Nelson, C.A., Scott, R.D., Bhutta, Z.A., Harris, N.B., Danese, A., Samara, M., 2020. Adversity in childhood is linked to mental and physical health throughout life. BMJ (Clin. Res. Ed.) 371. https://doi.org/10.1136/BMJ.M3048.

Oral, R., Ramirez, M., Coohey, C., Nakada, S., Walz, A., Kuntz, A., Benoit, J., Peek-Asa, C., 2015. Adverse childhood experiences and trauma informed care: the future of health care. Pediatr. Res. 2016 79:1 79 (1), 227–233. https://doi.org/10.1038/pr.2015.197.

Pang, J.Y., Wang, Y.P., Teng, H.M., He, J., Luo, R., Feng, S.M., Yue, W.H., Li, H.F., 2024. Interaction between HTR2A rs3125 and negative life events in suicide attempts among patients with major depressive disorder: a cross-sectional study. BMC Psychiatry 24 (1). https://doi.org/10.1186/S12888-024-05713-3.

Park, C., Park, I.-H., Yoo, T., Kim, H., Ryu, S., Lee, J.-Y., Kim, J.-M., Kim, S.-W., 2021. Association between childhood trauma and suicidal behavior in the general population. Chonnam Med. J. 57 (2), 126. https://doi.org/10.4068/CMJ.2021.57.2.126.

Pries, L.K., Lage-Castellanos, A., Delespaul, P., Kenis, G., Luykx, J.J., Lin, B.D., Richards, A.L., Akdede, B., Binbay, T., Altinyazar, V., Yalinçetin, B., Gümüş-Akay, G., Cihan, B., Soygür, H., Ulaş, H., Cankurtaran, E.Ş., Kaymak, S.U., Mihaljevic, M.M., Petrovic, S.A., et al., 2019a. Estimating exposome score for schizophrenia using predictive modeling approach in two independent samples: the results from the EUGEI study. Schizophr. Bull. 45 (5), 960–965. https://doi.org/10.1093/SCHBUL/SBZ054.

Pries, L.K., Snijders, C., Menne-Lothmann, C., Decoster, J., Van Winkel, R., Collip, D., Delespaul, P., De Hert, M., Derom, C., Thiery, E., Jacobs, N., Wichers, M., Guloksuz, S., Van Os, J., Rutten, B.P.F., 2019b. TwinssCan - gene-environment interaction in psychotic and depressive intermediate phenotypes: risk and protective factors in a general population twin sample. Twin Res. Hum. Genet. 22 (6), 460–466. https://doi.org/10.1017/THG.2019.96.

Pries, L.-K., Guloksuz, S., Menne-Lothmann, C., Decoster, J., Van Winkel, R., Collip, D., Delespaul, P., De Hert, M., Derom, C., Thiery, E., Jacobs, N., Wichers, M., Simons, C. J. P., Rutten, B. P. F., & Van Os, J. (2017). White Noise Speech Illusion and Psychosis Expression: An Experimental Investigation of Psychosis Liability. doi:https://doi.org/10.1371/journal.pone.0183695.

Richmond-Rakerd, L.S., Trull, T.J., Gizer, I.R., McLaughlin, K., Scheiderer, E.M., Nelson, E.C., Agrawal, A., Lynskey, M.T., Madden, P.A.F., Heath, A.C., Statham, D.J., Martin, N.G., 2018. Common genetic contributions to high-risk trauma exposure and self-injurious thoughts and behaviors. Psychol. Med. 49 (3), 421–430. https://doi.org/10.1017/S0033291718001034.

Roley-Roberts, M.E., Charak, R., Jeffs, A.J., Hovey, J.D., 2023. The unique relationship between childhood sexual abuse, self-injury and suicide ideation: the mediating role of emotion dysregulation. Child Abuse Rev. 32 (2), e2787. https://doi.org/10.1002/CAR.2787.

Sanabrais-Jiménez, M. A., Sotelo-Ramirez, C. E., Ordoñez-Martinez, B., Jiménez-Pavón, J., Ahumada-Curiel, G., Piana-Diaz, S., Flores-Flores, G., Flores-Ramos, M., Jiménez-Anguiano, A., & Camarena, B. (2019). Effect of CRHR1 and CRHR2 gene polymorphisms and childhood trauma in suicide attempt. J. Neural Transm. (Vienna), 126(5). doi:https://doi.org/10.1007/S00702-019-01991-4.

Segura, A.G., Mitjans, M., Jiménez, E., Fatjó-Vilas, M., Ruiz, V., Saiz, P.A., García-Portilla, M.P., González-Blanco, L., Bobes, J., Vieta, E., Benabarre, A., Arias, B., 2019. Association of childhood trauma and genetic variability of CRH-BP and FKBP5 genes with suicidal behavior in bipolar patients. J. Affect. Disord. 255, 15–22. https://doi.org/10.1016/J.JAD.2019.05.014.

Silberg, J.L., Copeland, W., Linker, J., Moore, A.A., Roberson-Nay, R., York, T.P., 2016. Psychiatric outcomes of bullying victimization: a study of discordant monozygotic twins. Psychol. Med. 46 (9), 1875–1883. https://doi.org/10.1017/S0033291716000362.

Wang, Y., Warmenhoven, H., Feng, Y., Wilson, A., Guo, D., Chen, R., 2022. The relationship between childhood trauma and suicidal ideation, the mediating role of identification of all humanity, indifference and loneliness. J. Affect. Disord. 299, 658–665. https://doi.org/10.1016/J.JAD.2021.12.052.

Warrier, V., Baron-Cohen, Simon, 2021. Childhood trauma, life-time self-harm, and suicidal behaviour and ideation are associated with polygenic scores for autism. Mol. Psychiatry 26, 1670–1684. https://doi.org/10.1038/s41380-019-0550-x.

Xiao, Z., Murat Baldwin, M., Wong, S.C., Obsuth, I., Meinck, F., Murray, A.L., 2023. The impact of childhood psychological maltreatment on mental health outcomes in adulthood: a systematic review and meta-analysis. Trauma Violence Abuse 24 (5), 3049–3064. https://doi.org/10.1177/15248380221122816/ASSET/IMAGES/LARGE/10.1177_15248380221122816-FIG 7.JPEG.

Yang, C., Chen, P., Xie, J., He, Y., Wang, Y., Yang, X., 2021. Childhood socioeconomic status and depressive symptoms of young adults: mediating role of childhood trauma. Front. Psychol. 12, 706559. https://doi.org/10.3389/FPSYT.2021.706559.

Yao, K., Chen, P., Zhou, H., Ruan, J., Chen, D., Yang, X., Zhou, Y., 2023. The effect of childhood trauma on suicide risk: the chain mediating effects of resilience and mental distress. BMC Psychiatry 23 (1), 1–10. https://doi.org/10.1186/S12888-023-05348-W/TABLES/3.

Zalsman, G., 2012. Genetics of Suicidal Behavior in Children and Adolescents. In: Dwivedi, Y. (Ed.), The Neurobiological Basis of Suicide. CRC Press/Taylor & Francis. Chapter 14. https://www.ncbi.nlm.nih.gov/books/NBK107198/.