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Childhood trauma and its impact on depressive and anxiety symptomatology in adulthood: A 6-year longitudinal study

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ABSTRACT

Background: Childhood trauma (CT) is a risk factor for depressive and anxiety disorders. However, whether CT is more strongly linked to specific clinical features of these disorders remains inconclusive. The current study comprehensively examined cross-sectional and longitudinal associations between CT and depressive/anxiety symptomatology in a large adult sample with current and remitted depressive and/or anxiety disorders.
Methods: Baseline ($n = 1803$), 2-year ($n = 1735$), 4-year ($n = 1585$), and 6-year follow-up ($n = 1475$) data from the Netherlands Study of Depression and Anxiety were used. CT (emotional neglect, emotional/physical/sexual abuse) was assessed at baseline, while depressive/anxiety symptomatology with relevant dimensions (e.g., mood/cognitive, melancholic, general distress, and somatic depression) was assessed at each wave using self-reported questionnaires. Linear regressions and linear mixed models determined cross-sectional and longitudinal associations.
Results: Individuals with CT, especially, severe CT, compared to those without CT, had significantly higher scores in overall depressive symptomatology (Cohen's $d = 0.674$), mood/cognitive depression ($d = 0.691$), melancholic depression ($d = 0.587$), general distress ($d = 0.561$), and somatic depression severity ($d = 0.549$). Differences were lower, but still highly significant for anxiety ($d = 0.418$), worry ($d = 0.362$), and fear/phobic symptomatology ($d = 0.359$). Effects were consistent across CT types and maintained over six years.
Limitations: Retrospectively-reported CT.
Conclusions: CT is a risk factor for depressive and anxiety symptomatology across all dimensions and enduring over multiple years. Screening for CT is essential to identify individuals at risk for more severe and chronic manifestations of affective disorders.

1. Introduction

Childhood trauma (CT), conceptualized as emotional, physical, and sexual abuse, or emotional and physical neglect before the age of 18, has been well-established to contribute to the development and the poorer course of mental disorders in adulthood (Agnew-Blais and Danese, 2016; Hovens et al., 2010; Kessler et al., 2010; Mandelli et al., 2015; Nanni et al., 2012; Spinhoven et al., 2010). Increasing evidence further suggests that CT-related depressive and anxiety disorders may constitute a clinically distinct subtype of psychopathology, characterized by earlier emergence, more chronic course of symptoms, a higher risk for comorbid disorders, and worse treatment outcomes, be it psychotherapy or pharmacotherapy (Hovens et al., 2012; Lippard and Nemeroff, 2020; Miniati et al., 2010; Nanni et al., 2012; Nelson et al., 2017; Teicher and Samson, 2013). However, specific pathways through which CT exerts its adverse effects on mental health outcomes are complex and heterogenous, likely affecting multiple layers of the brain, mind, and body (Danese and Baldwin, 2017; Danese and McEwen, 2012; Jaffee, 2017; Kuzminskaite et al., 2021).

In the context of depression and anxiety, two highly comorbid

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conditions (Kessler et al., 2003; Lamers et al., 2011), understanding CT's pathophysiology is even more difficult. Although highly comorbid, both depressive and anxiety disorders are also largely heterogeneous, often presenting significant between-patient differences in symptomatology (Fried and Nesse, 2015; Unick et al., 2009). Yet, most of the previous research has been focused on diagnoses rather than symptoms, limiting the understanding of these disorders' heterogeneity and etiology. As a result, it is challenging to identify who is more vulnerable to developing specific depressive and anxiety symptoms and who would ultimately benefit from a personalized cross-disorder treatment approach.

CT, a common underlying risk factor for depression and anxiety, may shed more light on these disorders' existing heterogeneity and etiology. Previous findings have suggested stronger associations between CT and adult depressive than anxiety disorders, with the strongest associations in the comorbid group (Hovens et al., 2010). On a depressive symptom level, compared to depressed adults without CT, those with CT have been more likely characterized by higher severity of individual anhedonic, panic/phobic, and cognitive symptoms (Cohen's $d = 0.24–0.32$) (Medeiros et al., 2020), with the latter being particularly heightened in the presence of emotional maltreatment (Klein et al., 2009; Vares et al., 2015). Earlier studies have also linked various CT types with more severe atypical depression features in adulthood, including reversed neurovegetative features such as oversleeping or overeating (Levitan et al., 1998; Matza et al., 2003; Medeiros et al., 2020; Miniati et al., 2010; Withers et al., 2013). However, conflicting findings and significant associations with melancholic depression have also been reported (Harkness and Monroe, 2002; Klein et al., 2009; Lamers et al., 2010; Medeiros et al., 2020). Significantly higher levels of suicidality and psychotic features in adult depression have been associated with CT as well, which seemed to be particularly true in the case of sexual and physical abuse (Gaudiano and Zimmerman, 2010; Harkness and Monroe, 2002; Kim et al., 2013; Klein et al., 2009; Medeiros et al., 2020). Although understudied, evidence on CT and the clinical features of anxiety has suggested that CT, especially emotional maltreatment, is related to more severe social anxiety symptoms in adulthood (Bruce et al., 2012; Simon et al., 2009).

Despite growing evidence, there is considerable methodological heterogeneity among the individual studies and a lack of large-scale longitudinal comprehensive projects focusing on multiple CT types (together, but also individually) and various depressive/anxiety symptomatology in a single sample, making drawing firm conclusions difficult. Consequently, it is currently unclear whether CT is more strongly linked to broader depressive and anxiety symptoms or more specific clinical features of these disorders, whether the course of these symptoms is more chronic (consistently elevated over time) in individuals with CT, and whether these associations vary as a function of CT severity and its type. A deeper understanding of how CT and its types are related to specific psychiatric symptoms in the context of affective disorders is likely to provide a better picture of the pathophysiology of CT, necessary to develop personalized (preventative) interventions and treatment planning.

The current study aimed to: (1) examine which depressive and anxiety symptoms differentiate individuals with retrospectively-reported CT and those without CT (including the differentiation among the CT severity and its types), as well as (2) investigate the impact of CT on the 6-year course of symptoms in a large cohort of adults with current and/or remitted depressive and anxiety disorders: The Netherlands Study of Depression and Anxiety (NESDA) (Penninx et al., 2008). Previous NESDA studies suggested robust cross-sectional associations for emotional neglect with anhedonic depression and sexual abuse with anxious arousal, controlling for different CT types (van Veen et al., 2013). All CT types, especially emotional abuse/neglect, were also associated with psychological distress, including depression, anxiety, and fear/phobic symptom severity, which remained significant and stable over time (Spinhoven et al., 2016). However, no studies to date comprehensively examined how multiple depressive/anxiety symptoms, including not only total scale scores, but also symptom dimensions, are related to CT presence, severity, and types or whether such associations remain consistently present over the long-term follow-up.

2. Methods

2.1. Sample

Data came from an ongoing longitudinal cohort (NESDA; $n = 2981$) (Penninx et al., 2008). Participants were Dutch-fluent adults (18–65 years) with or without depressive and/or anxiety disorder (current or remitted; Composite International Diagnostic Interview, CIDI) (Robins et al., 1988) recruited for the baseline assessment between September 2004 and February 2007 from three different settings: community, primary health care, and specialized mental health care. Patients with a primary diagnosis of other than depressive or anxiety disorder (e.g., post-traumatic stress disorder, bipolar disorder, psychotic disorder, obsessive-compulsive disorder) were excluded. Follow-up assessments used in the current study were conducted at 2, 4, and 6 years after baseline. During each wave, participants were assessed on various sociodemographic, lifestyle, (mental) health, and biological factors. The current study focuses on the data of 1803 participants with current (past 6-month) and/or remitted (lifetime, but not past 6-month) depressive (major depressive disorder, dysthymia) and/or anxiety disorder (social anxiety disorder, agoraphobia, generalized anxiety disorder, panic disorder with or without agoraphobia) at baseline, who had an available measure of CT, all valid outcome data of depressive/anxiety symptoms at baseline (total scale scores and symptom dimensions), and at least one of the outcomes available at follow-up. The response rates for the 2-, 4-, and 6-year waves were 96.23 % ($n = 1735$), 87.91 % ($n = 1585$), and 81.81 % ($n = 1475$), respectively. Overall, 1803 unique participants contributed to the analyses, with >6000 observations for longitudinal analyses. NESDA's protocol was approved by the ethical review board of each participating research center in Amsterdam, Leiden, and Groningen. All participants provided written informed consent. More information regarding NESDA can be found in Penninx et al. (2008).

2.2. Measures

2.2.1. Childhood trauma

CT was assessed retrospectively at the baseline by trained research staff using the *Childhood Trauma Interview* (CTI) (de Graaf et al., 2004). The CTI is a structured interview assessing four CT types before the age of 16 years: emotional neglect, emotional abuse, physical abuse, and sexual abuse. Each CT type is answered as “no” or “yes” with a further frequency indication as (0) - “never”, (1) - “once or sometimes”, and (2) - “regularly, often, or very often” (range 0–2). A continuous cumulative CT severity score (range 0–8) is calculated as a sum of the number of types and frequency of CT with a higher score indicating more severe CT (Hovens et al., 2010; Wiersma et al., 2009). In the current study, CT was coded and analyzed dichotomously: present (experienced once, sometimes, regularly, often, or very often) vs. absent (no experience of CT); severe CT (CTI score 4–8) vs. no CT (CTI score 0); mild CT (CTI score 1–3) vs. no CT; and separate four CT types (emotional neglect, emotional abuse, physical abuse, and sexual abuse experienced once, sometimes, regularly, often, or very often) referenced to no experience of CT. The CTI has previously been shown to have good psychometric properties (Fink et al., 1995; Hovens et al., 2012; Spinhoven et al., 2014).

2.2.2. Depressive/anxiety symptoms and their dimensions

The severity of depressive and anxiety symptomatology was assessed at the baseline, 2-, 4-, and 6-year follow-up using five well-validated self-reported scales: 30-item *Inventory of Depressive Symptomatology* (IDS) (Rush et al., 1996), 30-item *Mood and Anxiety Symptom Questionnaire* (MASQ-30) (Clark and Watson, 1991; Wardenaar et al., 2010a), 21-item *Beck Anxiety Inventory* (BAI) (Beck et al., 1988), 15-item *Fear*

Questionnaire (FQ) (Marks and Mathews, 1979), and 11-item *Penn State Worry Questionnaire* (PSWQ) (Meyer et al., 1990). The IDS assessed total depression severity (score range 0–84) with five depression dimensions: mood/cognitive (range 0–33), somatic (range 0–24), sleep (range 0–12), melancholic (range 0–24), and atypical/energy-related (range 0–15) (Khan et al., 2006; Lamers et al., 2020; Wardenaar et al., 2010b). The BAI assessed total anxiety severity (range 0–63) with two specific anxiety dimensions: subjective (range 0–21) and somatic (range 0–42). The MASQ-30 assessed the tripartite model of depression and anxiety: general distress (negative affect; range 10–50), anhedonic depression (lack of positive affect; range 10–50), and anxious arousal (range 10–50). The FQ assessed total fear/phobic severity (range 0–120) with three specific phobia dimensions: agoraphobia (range 0–40), blood injury phobia (range 0–40), and social phobia (range 0–40). Last, the PSWQ assessed worry engagement severity with the total score ranging from 11 to 55. Higher scale scores indicated higher presence of depressive/anxiety symptoms. For the list of individual symptoms for each dimension, please see the supplement.

2.2.3. Covariates

Sociodemographic covariates for all analyses included age in years, sex, and years of education at the baseline. Baseline antidepressant medication use (*tricyclic antidepressants (TCAs)*, anatomical therapeutic chemical (ATC) code N06AA; *selective serotonin reuptake inhibitors (SSRIs)*, ATC code N06AB; *other types*, ATC code: N06AX, N06AG, N06AF, not N06AA, not N06AB; no/yes frequent use) was additionally included to check if main findings could be confounded by antidepressant use.

2.3. Data-analyses

Sample characteristics were explored descriptively and presented as means with standard deviations (SD), medians with interquartile ranges (for non-normally distributed variables), or numbers with percentages at each wave. Spearman correlation (ρ) was used to determine intercorrelations between total scale scores and dimensions of depressive and anxiety symptoms at the baseline. Study dropouts between the baseline and 6-year wave were compared to study completers on baseline age, gender, education, CT, and current depressive and/or anxiety disorder status. For further analyses, skewed outcome variables (assessed by values of skewness and kurtosis as well as QQ plots) were naturally $\log_e$-transformed ($\ln(x + 1)$ for scales including zero).

To cross-sectionally examine which psychiatric symptoms differentiate individuals with CT and those without CT at the baseline, we performed multiple linear regression analyses with CT as a predictor and severity of symptoms as outcome variables. Any CT was first examined as a dichotomous variable (yes vs. no), followed by dichotomized division as based on the severity of CT (mild vs. no; severe vs. no), as well as the dichotomized division as based on the four types of CT. All CT types were examined in separate models with no CT as a reference group. Psychiatric symptoms were examined as standardized (z-scores) continuous total scale scores (for IDS, BAI, FQ, PSWQ), followed by dimensional scores (additionally for MASQ-30). If robust associations were seen with specific dimension, we further zoomed into individual psychiatric symptoms. Separate analyses were conducted for different symptoms (as applicable: total scores, dimensions, or individual symptoms). All analyses were adjusted for baseline sociodemographic factors. To check if the main findings between CT and symptoms could be confounded by antidepressant medication use, we additionally adjusted for antidepressant use. Similarly, to check if main associations could be moderated by sex, we additionally included CT × sex interaction term.

To further examine whether individuals with CT showed a more chronic course of symptoms (consistently elevated over the 6-year follow-up), we ran linear mixed regression models. CT, time (coded categorically, representing baseline, 2-, 4-, and 6-year follow-up), CT × time interaction, and baseline covariates (age, sex, education) were included as fixed independent variables with a random effect for patient ID, using an unstructured covariance type. Depressive and anxiety symptom scores were included as time-varying standardized outcomes at baseline, 2-, 4-, and 6-year. Because mixed regression takes nested data structure into account and deals with missing data, missing values were not imputed. Longitudinal analyses were conducted only for total CT, mild CT, and severe CT (referenced to no CT) groups, as well as for total IDS, BAI, FQ, and PSWQ scores. To check if main associations could be moderated by sex, we additionally included CT × sex×time, CT × sex, and sex×time interaction terms.

Cohen's *d* was calculated as a measure of between-group effect size (based on unstandardized regression coefficients for baseline analyses and mixed model estimated means for longitudinal analyses). For all analyses, the statistical significance was based on a p-value $< .05$. Benjamini-Hochberg False Discovery Rate (FDR p-value $<.05$) corrected for multiple analyses (17 tests for cross-sectional and 4 tests for longitudinal analyses) (Benjamini and Hochberg, 1995). Analyses were conducted using IBM SPSS 25, while FDR adjustment and effect size calculation was conducted using R Studio 1.3.959 software (IBM Corp, 2017; R Core Team, 2020).

3. Results

3.1. Sample characteristics

Sample characteristics across the four waves are presented in Table 1. At baseline, the mean age of the sample ($n = 1803$) was 42.76 (SD = 12.56), and the majority was female (68.8 %). Of 1803 participants at baseline, 70.4 % had a current (past 6-month) depressive and/or anxiety disorder diagnosis, with 17.2 % having only depression, 23.9 % only anxiety, and 29.3 % comorbid depression and anxiety disorder. Around half of the sample had an experience of at least one type of CT (53.9 %: mild, 29.1 %; severe, 24.8 %), with emotional neglect and emotional abuse being the most prevalent types (44.0 % and 28.5 %, respectively). All depressive and anxiety symptoms and their dimensions were significantly correlated within and between the scales (total scores, $\rho = 0.430$ to 0.737; IDS dimensions, $\rho = 0.334$ to 0.813; BAI dimensions, $\rho = 0.683$; MASQ dimensions, $\rho = 0.451$ to 0.655; FQ dimensions, $\rho = 0.376$ to 0.569, all p values $<.001$; Table S1). Study dropouts between the baseline and 6-year wave ($n = 328$) did not differ from study completers ($n = 1475$) in terms of age and gender. Compared to completers, study dropouts were significantly less educated, had a higher prevalence of CT, and a current depressive and/or anxiety disorder diagnosis.

3.2. Baseline associations between CT and depressive/anxiety symptoms

CT was significantly associated with all total scale scores and dimensions of depressive and anxiety symptoms ($B = 0.182$ to 0.467, $p < .001$; Table 2) with the strongest association for total depressive symptoms ($B = 0.434$, $p < .001$), and, especially, the mood/cognitive depression dimension ($B = 0.467$, $p < .001$). Results were substantially unchanged after additional adjustment for antidepressant use; no significant CT × sex interactions were observed, suggesting that associations between CT and symptoms were consistent across the sexes. After categorizing CT severity, participants with mild and severe CT had significantly higher scores in multiple depressive and anxiety symptoms ($B = 0.110$ to 0.312, $p < .05$ and $B = 0.249$ to 0.656, $p < .001$, for mild and severe CT, respectively). Almost all associations remained significant after multiple comparison adjustment (17 tests).

Standardized between-group effect sizes (Cohen's *d*; Fig. 1) ranged from small to medium (from $d = 0.183$ for agoraphobia to $d = 0.480$ for mood/cognitive depression) with the strongest effects for severe CT (from $d = 0.251$ for blood injury phobia to $d = 0.691$ for mood/cognitive depression). Individuals with severe CT scored somewhat higher on total depressive symptoms ($d = 0.674$, 95 % CI = 0.556 to 0.792) than anxiety (d = 0.418, 95 % CI 0.302 to 0.534), worry (d = 0.362, 95 % CI 0.246 to

Table 1
Sample characteristics across the waves.

Characteristics	Baseline, $n = 1803$	2-Year FU, $n = 1735$[a]	4-Year FU, $n = 1585$[b]	6-Year FU, $n = 1475$[c]
Demographics				
Age in years, mean (±SD)	42.76 (±12.56)	44.91 (±12.58)	46.88 (±12.54)	48.76 (±12.55)
Sex, female, n (%)	1241 (68.80)	1195 (68.90)	1095 (69.10)	1017 (68.90)
Education, years, mean (±SD)	12.22 (±3.25)	12.42 (±3.31)	12.67 (±3.33)	12.80 (±3.30)
Clinical characteristics				
Depressive symptoms (IDS), mean (±SD)	24.08 (±13.13)	18.28 (±12.02)	18.01 (±12.10)	17.62 (±11.81)
Mood/cognitive (IDS), median (IQR)	9.00 (10.00)	6.00 (9.00)	5.00 (8.00)	5.00 (8.00)
Somatic (IDS), mean (±SD)	7.26 (±4.15)	5.56 (±3.84)	5.50 (±3.91)	5.38 (±3.89)
Sleep (IDS), mean (±SD)	3.44 (±2.24)	2.98 (±2.07)	3.06 (±2.09)	3.06 (±2.05)
Melancholic (IDS), median (IQR)	5.00 (6.00)	3.00 (5.00)	3.00 (4.00)	2.00 (5.00)
Atypical/energy-related (IDS), median (IQR)	3.00 (3.00)	2.00 (3.00)	2.00 (3.00)	2.00 (3.00)
Anxiety symptoms (BAI), median (IQR)	11.00 (13.00)	8.00 (12.00)	7.00 (11.00)	8.00 (11.00)
Subjective (BAI), median (IQR)	5.00 (6.00)	3.00 (5.00)	2.00 (4.00)	2.00 (4.00)
Somatic (BAI), median (IQR)	7.00 (9.00)	4.00 (7.00)	4.00 (7.00)	5.00 (7.00)
Mood and anxiety symptoms (MASQ)				
General distress (MASQ), median (IQR)	20.00 (13.00)	17.00 (11.00)	16.00 (11.00)	16.00 (11.00)
Anhedonic depression (MASQ), mean (±SD)	35.38 (±9.23)	33.33 (±9.44)	34.00 (±9.32)	34.02 (±9.54)
Anxious arousal (MASQ), median (IQR)	15.00 (8.00)	14.00 (7.00)	14.00 (7.00)	14.00 (6.00)
Fear/phobic symptoms (FQ), median (IQR)	24.00 (27.00)	18.00 (27.00)	16.00 (25.00)	16.00 (24.00)
Agorophobia (FQ), median (IQR)	4.00 (12.00)	2.00 (9.00)	2.00 (9.00)	2.00 (8.00)
Blood injury phobia (FQ), median (IQR)	5.00 (9.00)	4.00 (9.00)	3.50 (8.00)	3.00 (8.00)
Social phobia (FQ), mean (±SD)	12.85 (±8.87)	10.59 (±8.41)	10.11 (±8.57)	9.66 (±8.27)
Worry engagement symptoms (PSWQ), mean (±SD)	33.65 (±11.05)	30.76 (±11.16)	28.33 (±10.97)	28.65 (±11.36)
Current depression or anxiety, n (%)	1269 (70.40)	797 (45.90)	630 (39.70)	526 (35.70)
Current depression only, n (%)	310 (17.20)	209 (12.00)	172 (10.90)	158 (10.70)
Current anxiety only, n (%)	431 (23.90)	290 (16.70)	254 (16.00)	197 (13.40)
Current comorbid depression and anxiety, n (%)	528 (29.30)	298 (17.20)	204 (12.90)	171 (11.60)
Remitted depression or anxiety, n (%)	534 (29.60)	938 (54.10)	955 (60.30)	949 (64.30)
Antidepressant use, yes, n (%)	559 (31.00)	484 (27.90)	409 (25.80)	372 (25.20)
Childhood trauma (CT)				
Any CT, n (%)	972 (53.90)	926 (53.40)	852 (53.80)	775 (52.50)
Mild CT (score 1–3), n (%)	524 (29.10)	498 (28.70)	462 (29.10)	431 (29.20)
Severe CT (score 4–8), n (%)	448 (24.80)	428 (24.70)	390 (24.60)	344 (23.30)
Emotional neglect, n (%)	794 (44.00)	757 (43.60)	698 (44.00)	631 (42.80)
Emotional abuse, n (%)	514 (28.50)	490 (28.20)	445 (28.10)	396 (26.80)
Physical abuse, n (%)	278 (15.40)	263 (15.20)	242 (15.30)	212 (14.40)
Sexual abuse, n (%)	355 (19.70)	336 (19.40)	314 (19.80)	274 (18.60)

Note. FU, follow-up; SD, standard deviation, IQR, interquartile range; IDS, Inventory of Depressive Symptomatology, BAI, Beck Anxiety Inventory; MASQ, Mood and Anxiety Symptom Questionnaire; FQ, Fear Questionnaire; PSWQ, Penn State Worry Questionnaire.

[a] Missing data for 5 (IDS total), 6 (IDS mood/cognitive, IDS sleep, IDS atypical/energy-related), 9 (IDS somatic), 13 (IDS melancholic), 4 (BAI), 97 (MASQ), 8 (FQ), 98 (PSWQ) participants.

[b] Missing data for 1 (IDS sleep), 8 (IDS melancholic), 1 (BAI total), 2 (BAI subjective, BAI somatic), 2 (MASQ), 1 (FQ), 2 (PSWQ) participants.

[c] Missing data for 3 (IDS total), 4 (IDS mood/cognitive), 1 (IDS somatic, IDS sleep), 8 (IDS melancholic), 2 (IDS atypical-energy-related), 3 (BAI total), 5 (BAI subjective), 4 (BAI somatic), 3 (MASQ general distress, MASQ anxious arousal), 4 (MASQ anhedonic depression), 20 (FQ total), 18 (FQ agorophobia, FQ blood injury phobia), 13 (FQ social phobia), 5 (PSWQ) participants.

0.478), or fear/phobic symptoms (d = 0.359, 95 % CI 0.243 to 0.475). In terms of dimensions, the largest effect sizes ($d > 0.50$) for severe CT were seen for mood/cognitive depression ($d = 0.691$, 95 % CI = 0.573 to 0.808), melancholic depression ($d = 0.587$, 95 % CI = 0.469 to 0.704), general distress ($d = 0.561$, 95 % CI = 0.444 to 0.678), and somatic depression ($d = 0.549$, 95 % CI = 0.432 to 0.666). Compared to mild CT, individuals with severe CT scored significantly higher on almost all depressive and anxiety symptoms, especially on mood/cognitive depression dimension (between-group $d = 0.375$, 95 % CI 0.246 to 0.503). Further exploration of individual symptoms of this dimension (Table S2; Fig. S1) suggested that associations were mostly driven ($d > 0.50$) by individuals with severe CT scoring significantly higher on interpersonal sensitivity ($d = 0.597$, 95 % CI 0.479 to 0.712) and diminished quality of mood ($d = 0.522$, 95 % CI 0.405 to 0.639).

Considering CT types (Table S3; Fig. 1), individuals reporting emotional and physical abuse were characterized by having somewhat higher severity of depressive and anxiety symptoms and their symptom dimensions. However, no apparent differences between the CT types were observed (with 95 % CI around *d* largely overlapping).

3.3. 6-year longitudinal associations between CT and depressive/anxiety symptoms

Individuals with CT, especially those with severe CT, had consistently higher severity of total depressive ($B = 0.642$, $p < .001$, $d = 0.577$, 0.518, and 0.529), anxiety ($B = 0.365$, $p < .001$, d = 0.401, 0.384, and 0.354), worry engagement ($B = 0.340$, $p < .001$, d = 0.372, 0.361, and 0.358), and fear/phobic symptoms ($B = 0.294$, $p < .001$, d = 0.363, 0.359, and 0.442) at 2-, 4-, and 6-year follow-ups compared to individuals without CT history (Table 3; Fig. 2).

Overall, CT × time interaction effects in models predicting depressive, anxiety, and worry engagement symptoms were not statistically significant, suggesting that the differences in these symptoms across the groups remained consistent over time. In the model predicting fear/phobic symptoms a statistically significant CT × time interaction (6-year follow-up) was found, indicating a steeper decline in symptoms from baseline to 6-year follow-up in individuals without CT compared to those with CT ($B = 0.129$, $SE = 0.040$, $p = .001$), especially with severe CT ($B = 0.160$, $SE = 0.050$, $p = .001$). All associations remained significant after multiple comparison adjustment (4 tests). Additional adjustment for baseline antidepressant use did not impact the association estimates; no significant CT × sex×time or CT × sex interactions were observed.

4. Discussion

The state of knowledge on CT and clinical features of depression and anxiety was scarce and heavily relied on methodologically heterogeneous cross-sectional studies, focusing on a limited range of depressive/anxiety symptoms, with largely understudied anxiety. Thus, understanding whether individuals with CT could be more vulnerable to developing specific symptoms of affective disorders was inconclusive.

Table 2
Multiple regression results on standardized depressive/anxiety symptoms associated with CT ($n = 1803$).

Depressive/anxiety symptoms	CT[a]				Mild CT[a]				Severe CT[a]			
	Beta[b]	SE	p	FDR[c]	Beta[b]	SE	p	FDR[c]	Beta[b]	SE	p	FDR[c]
Total scale scores												
Depressive symptoms (IDS)	0.434	0.046	**<0.001**	**<0.001**	0.263	0.053	**<0.001**	**<0.001**	0.642	0.057	**<0.001**	**<0.001**
Anxiety symptoms (BAI)[d]	0.261	0.047	**<0.001**	**<0.001**	0.139	0.054	**0.011**	**0.014**	0.410	0.058	**<0.001**	**<0.001**
Worry engagement symptoms (PSWQ)	0.271	0.047	**<0.001**	**<0.001**	0.200	0.055	**<0.001**	**<0.001**	0.357	0.059	**<0.001**	**<0.001**
Fear/phobic symptoms (FQ)[d]	0.264	0.047	**<0.001**	**<0.001**	0.191	0.055	**0.001**	**0.002**	0.354	0.058	**<0.001**	**<0.001**
Dimensions												
Mood/cognitive depression (IDS)	0.467	0.046	**<0.001**	**<0.001**	0.312	0.053	**<0.001**	**<0.001**	0.656	0.057	**<0.001**	**<0.001**
Melancholic depression (IDS)	0.401	0.046	**<0.001**	**<0.001**	0.267	0.054	**<0.001**	**<0.001**	0.565	0.057	**<0.001**	**<0.001**
General distress (MASQ)	0.367	0.047	**<0.001**	**<0.001**	0.224	0.055	**<0.001**	**<0.001**	0.542	0.058	**<0.001**	**<0.001**
Somatic depression (IDS)	0.325	0.046	**<0.001**	**<0.001**	0.155	0.054	**0.004**	**0.006**	0.531	0.057	**<0.001**	**<0.001**
Atypical/energy-related depression (IDS)[d]	0.291	0.047	**<0.001**	**<0.001**	0.165	0.054	**0.002**	**0.003**	0.443	0.058	**<0.001**	**<0.001**
Social phobia (FQ)[d]	0.340	0.047	**<0.001**	**<0.001**	0.266	0.055	**<0.001**	**<0.001**	0.431	0.058	**<0.001**	**<0.001**
Anhedonic depression (MASQ)	0.304	0.047	**<0.001**	**<0.001**	0.212	0.054	**<0.001**	**<0.001**	0.417	0.058	**<0.001**	**<0.001**
Somatic anxiety (BAI)[d]	0.234	0.047	**<0.001**	**<0.001**	0.095	0.054	0.079	0.084	0.403	0.058	**<0.001**	**<0.001**
Subjective anxiety (BAI)[d]	0.266	0.047	**<0.001**	**<0.001**	0.188	0.055	**0.001**	**0.002**	0.361	0.059	**<0.001**	**<0.001**
Anxious arousal (MASQ)[d]	0.187	0.047	**<0.001**	**<0.001**	0.063	0.055	0.250	0.250	0.338	0.058	**<0.001**	**<0.001**
Sleep (IDS)	0.188	0.047	**<0.001**	**<0.001**	0.097	0.055	0.077	0.084	0.298	0.059	**<0.001**	**<0.001**
Agoraphobia (FQ)[d]	0.182	0.047	**<0.001**	**<0.001**	0.110	0.055	**0.044**	0.053	0.270	0.058	**<0.001**	**<0.001**
Blood injury phobia (FQ)[d]	0.194	0.048	**<0.001**	**<0.001**	0.148	0.056	**0.008**	**0.011**	0.249	0.059	**<0.001**	**<0.001**

Note. Analyses adjusted for age, sex, education. CT ($n = 972$), mild CT ($n = 524$), severe CT ($n = 448$), no CT ($n = 831$).
Boldface indicates statistical significance ($p < .05$). CT, childhood trauma; SE, standard error; IDS, Inventory of Depressive Symptomatology, BAI, Beck Anxiety Inventory; MASQ, Mood and Anxiety Symptom Questionnaire; FQ, Fear Questionnaire; PSWQ, Penn State Worry Questionnaire.

[a] Reference group: no CT.
[b] Unstandardized beta.
[c] FDR adjustment for 17 tests.
[d] Log-transformed (ln).

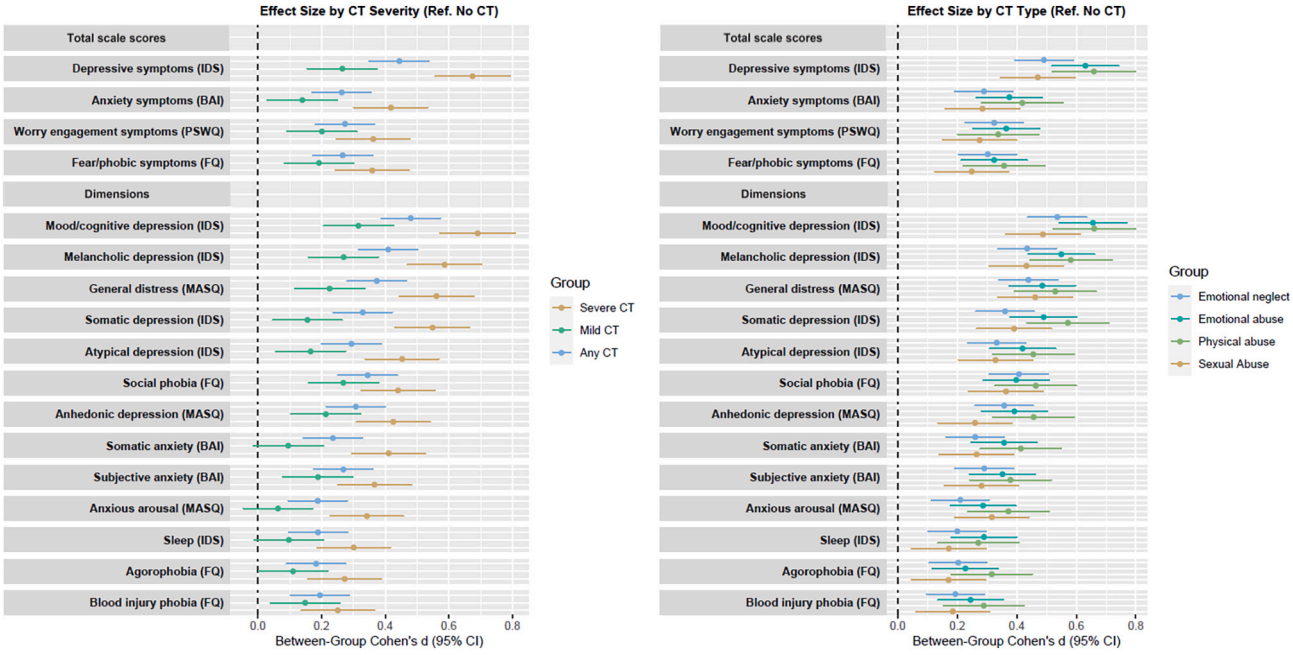

Fig. 1. Forest plot of between group effect sizes with corresponding 95 % confidence intervals (based on unstandardized regression coefficients) of standardized depressive and anxiety symptoms by CT severity and CT type.
Note. Adjusted for age, sex, education. CT types analyzed in separate models with no CT as reference group.
CT ($n = 972$), mild CT ($n = 524$), severe CT ($n = 448$), no CT ($n = 831$); Emotional neglect ($n = 794$), emotional abuse ($n = 514$), physical abuse ($n = 278$), sexual abuse ($n = 355$).
CT, childhood trauma; IDS, Inventory of Depressive Symptomatology, BAI, Beck Anxiety Inventory; MASQ, Mood and Anxiety Symptom Questionnaire; FQ, Fear Questionnaire; PSWQ, Penn State Worry Questionnaire.

Table 3
Longitudinal mixed model results on standardized depressive/anxiety symptoms based on CT severity (n = 1803).

Depressive/anxiety symptoms	CT[a]				Mild CT[a]				Severe CT[a]			
	Beta[b]	SE	p	FDR[c]	Beta[b]	SE	p	FDR[c]	Beta[b]	SE	p	FDR[c]
Depressive symptoms (IDS)	0.433	0.045	**<0.001**	**<0.001**	0.261	0.052	**<0.001**	**<0.001**	0.642	0.056	**<0.001**	**<0.001**
Anxiety symptoms (BAI)[d]	0.230	0.046	**<0.001**	**<0.001**	0.121	0.054	**0.025**	**0.025**	0.365	0.057	**<0.001**	**<0.001**
Worry engagement symptoms (PSWQ)	0.259	0.046	**<0.001**	**<0.001**	0.192	0.054	**<0.001**	**0.001**	0.340	0.057	**<0.001**	**<0.001**
Fear/phobic symptoms (FQ)[d]	0.220	0.046	**<0.001**	**<0.001**	0.159	0.054	**0.003**	**0.004**	0.294	0.057	**<0.001**	**<0.001**

Note. Main effects from model without interaction. Analyses adjusted for baseline age, sex, education.
CT (*n* max = 972), mild CT (*n* max = 524), severe CT (*n* max = 448), no CT (*n* max = 831).
SE, standard error; IDS, Inventory of Depressive Symptomatology, BAI, Beck Anxiety Inventory; FQ, Fear Questionnaire; PSWQ, Penn State Worry Questionnaire.
[a] Reference group: no CT.
[b] Unstandardized beta.
[c] FDR adjustment for 4 tests.
[d] Log-transformed (ln). Boldface indicates statistical significance ($p < .05$).

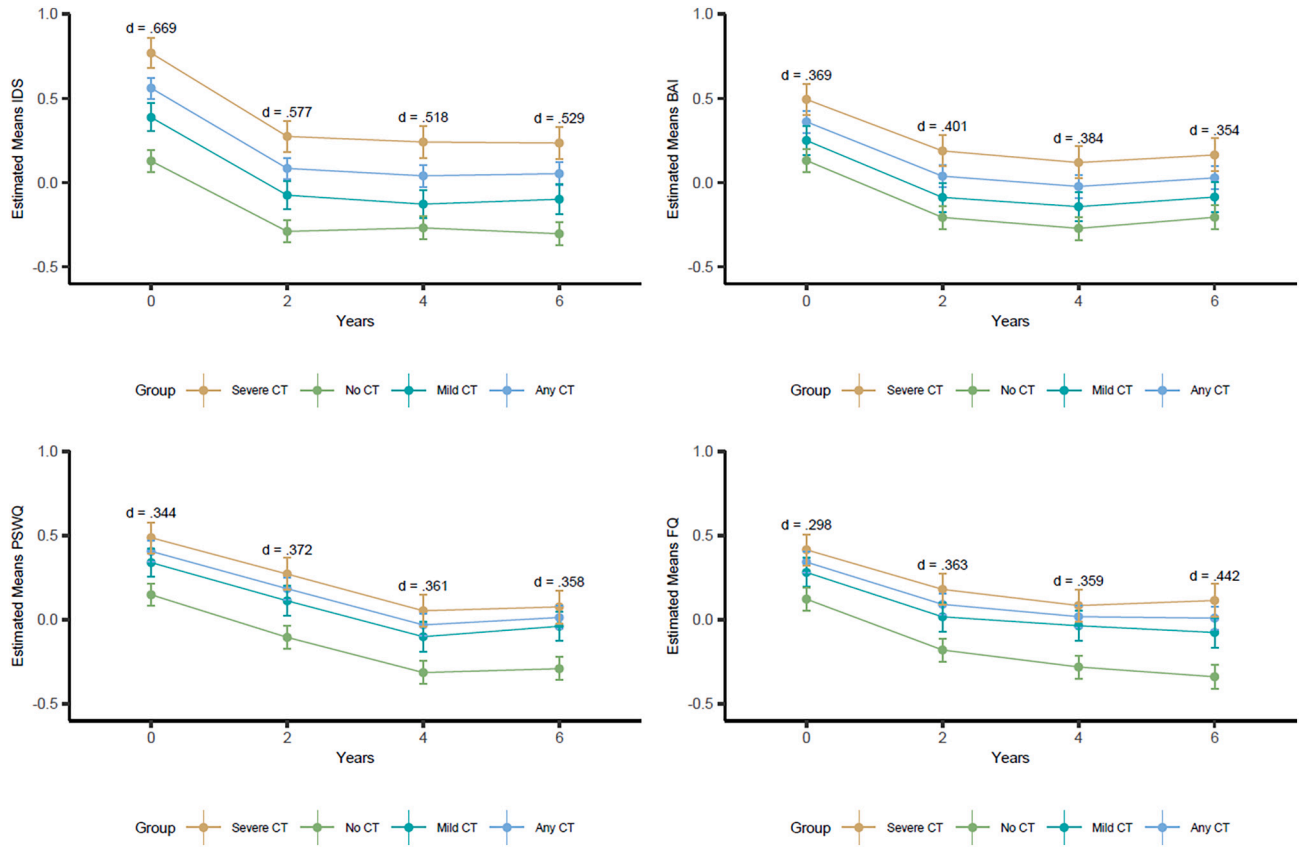

Fig. 2. Estimated 6-year course of standardized depressive and anxiety symptoms by CT severity.
Note. Adjusted for baseline age, sex, education. d - between-group Cohen's d for severe CT compared to no CT. CT (*n* = 972), mild CT (*n* = 524), severe CT (*n* = 448), no CT (*n* = 831). CT, childhood trauma; IDS, Inventory of Depressive Symptomatology, BAI, Beck Anxiety Inventory; FQ, Fear Questionnaire; PSWQ, Penn State Worry Questionnaire.

Our study added novel insights by comprehensively examining cross-sectional and longitudinal associations between CT, its severity and types, and depressive/anxiety symptomatology in a large adult sample with current and remitted depressive and/or anxiety disorders. Results showed that individuals with CT, compared to those without CT, were characterized by higher severity of all symptoms (from total depressive, anxiety, and worry to fear/phobic), suggesting that the impact of CT is broad and aspecific across multiple expressions of psychopathology. The strongest associations were with mood/cognitive depression, melancholic depression, general distress, and somatic depression dimensions. All CT types showed detrimental effects with no significant differences observed. Symptoms were consistently higher over the 6-year follow-up, indicating more chronicity in those with CT, especially severe CT. Findings were not explained by antidepressant use and were consistent in males and females.

Somewhat stronger associations of CT with depressive rather than anxiety symptomatology are in line with previous NESDA research on CT showing a higher risk of developing depressive than anxiety disorders in adulthood (Hovens et al., 2010). Effect sizes were primarily small, consistent with earlier depressive symptomatology findings (Medeiros et al., 2020), but reached medium for severe CT cases, suggesting particularly increased (d > 0.50) severity of mood/cognitive, melancholic, general distress, and somatic depression symptoms out of all depressive/anxiety symptom dimensions. This is a new addition to the literature also supporting previous depression studies, showing one of the strongest associations between CT and cognitive features of

depression, such as impaired concentration/decision making or self-criticism (Klein et al., 2009; Medeiros et al., 2020; Vares et al., 2015). Out of mood/cognitive symptoms, the most prominent effect was seen for interpersonal sensitivity, which was previously found to be a significant risk factor for the development and poorer course of depressive episodes (Boyce et al., 1992; Sakado et al., 2000). We found CT associations with both melancholic and atypical/energy-related depression dimensions, with the former showing more extensive effects. Previous research on melancholic versus atypical depression in CT is mainly inconsistent, with some studies showing links with melancholic, some with atypical, and some with both depression dimensions (Harkness and Monroe, 2002; Medeiros et al., 2020; Withers et al., 2013). These inconsistencies are likely explained by methodological heterogeneity in samples and assessment tools among the studies. Out of different anxiety symptoms, the most prominent effect was seen on the social phobia dimension. This expands scarce evidence of the role of CT in specific anxiety symptomatology and is also consistent with previous findings on CT being related to more severe social anxiety symptoms in adulthood (Bruce et al., 2012; Simon et al., 2009). Although emotional and physical abuse showed somewhat larger effects, no considerable differences between the CT types were observed. Therefore, the impact of CT is likely stemming from the "context of abuse", including frequent recurrence of CT, especially emotional maltreatment, and co-occurrence of CT types (Rosenman and Rodgers, 2004). Our findings support this hypothesis and are in line with the previous study, showing the worst clinical presentation in individuals with severe CT, who experienced multiple types of traumas (Medeiros et al., 2020).

The long-lasting effect of CT on more severe and chronic manifestations of depressive/anxiety symptomatology could be explained by stress-induced alterations in the brain, mind, and body (Kuzminskaite et al., 2021). For instance, exposure to CT may alter basic cognitive assumptions about the self and others, which over time may become a part of an individual's personality. Indeed, individuals with a history of CT are more often characterized by negative cognitive schemas and negative self-associations, which could explain the specific development of more severe mood/cognitive depression symptoms (Gibb, 2002; Gibb et al., 2001; van Harmelen et al., 2010). CT, especially severe CT, can also irreversibly dysregulate the functioning of the major bodily stress systems, in particular, the hypothalamic-pituitary-adrenal (HPA)-axis and the immune-inflammatory system by chronically stimulating the release of cortisol and the secretion of pro-inflammatory cytokines (Baumeister et al., 2016; Danese and Baldwin, 2017; Koss and Gunnar, 2018; Kuzminskaite et al., 2020). These dysregulations can lead to more severe manifestations of depressive/anxiety symptomatology and, especially, melancholic and somatic depression symptoms (Duivis et al., 2013; Vinkers et al., 2021). Increased engagement in health-harming behaviors such as smoking or heavy alcohol/drug use in individuals with CT is also noteworthy (Hughes et al., 2017), as poorer lifestyle has been consistently observed as a risk factor for worse mental health outcomes in adulthood (Berk et al., 2013; Cuijpers et al., 2007; Gemes et al., 2019; Sarris et al., 2014). Sustained activation of the stress systems is also hypothesized to alter brain development in individuals with CT (Danese and Baldwin, 2017). As a result, various structural and functional brain alterations, such as reductions in connectivity patterns of networks related to emotion regulation, decision making, and self-reflecting processing, are observed, likely relating to more negative cognitive schemas and worse symptomatology (van der Werff et al., 2013). Together, these psychological, behavioral, and biological changes could serve as potentially modifiable targets of interest for early prevention and intervention of more severe and chronic symptom manifestations in individuals with CT.

4.1. Strengths and limitations

Unlike previous studies, the current study utilized a large sample of individuals with remitted or current depressive and/or anxiety disorders followed up to six years, focusing on multiple CT types and exploring various depressive/anxiety symptomatology. To our knowledge, this is the most comprehensive study to date, allowing direct effect comparisons across multiple expressions of affective symptomatology. However, some limitations have to be acknowledged. First, CT was assessed retrospectively, which may have been affected by recall bias, especially in the sample of individuals with psychopathology. Nevertheless, it has been shown that the reporting of CT does not seem to be considerably affected by a person's psychiatric status (Fergusson et al., 2011; Spinhoven et al., 2014). Previous studies have also suggested that the agreement between prospective and retrospective CT reports is low, identifying distinct groups of individuals with potentially different mechanisms through which CT affects mental health outcomes (Baldwin et al., 2019; Danese and Widom, 2020). Therefore, the generalizability of our findings is limited to retrospective CT reports, which are also more applicable to clinical practice. Second, although depressive/anxiety symptomatology was assessed with multiple questionnaires, they were all relatively short and self-reported. It may well be that current questionnaires did not tap into all depressive/anxiety features comprehensively, requiring more extensive assessment tools. Reliance on self-reported data may be prone to bias; however, as depressive/anxiety symptoms are inevitably viewed through an individual lens, the best person to ask is the individual themselves. Finally, due to methodological design limitations, causal inferences between CT and depressive/anxiety symptomatology should be made with caution.

4.2. Conclusion and future research

In the current study, CT was identified as a prominent risk factor for depressive and anxiety symptomatology across all dimensions and enduring over multiple years. All CT types showed comparable adverse effects. The worst clinical presentation was observed in individuals with severe CT, highlighting the importance of frequency and comorbidity of CT types. Future large-scale longitudinal projects are required to understand better the underlying CT mechanisms that bridge early trauma and future mental health outcomes. Comprehensive screening for CT in clinical practice is essential to identify individuals at risk for a more severe and chronic course of affective disorders. These individuals may benefit from the development of personalized treatment planning (e.g., additional lifestyle-based intervention or intervention targeting stress-system dysregulation).

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Data availability statement

According to European law (GDPR) data containing potentially identifying or sensitive patient information are restricted; our data involving clinical participants are not freely available in a public repository. However, data are – under some specifications – available upon request via the NESDA Data Access Committee (nesda@ggzingeest.nl). See also our website: www.nesda.nl

CRediT authorship contribution statement

Erika Kuzminskaite: Conceptualization, Data Analysis, Writing - Original Draft, Writing - Review & Editing. **Christiaan Vinkers:** Conceptualization, Supervision, Writing - Review & Editing. **Yuri Milaneschi:** Data Analysis, Writing - Review & Editing. **Erik J. Giltay:** Writing - Review & Editing. **Brenda W. J. H. Penninx:** Conceptualization, Supervision, Writing - Review & Editing.

Conflict of interest

All authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2022.06.057.

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