Emotional scars : impact of childhood trauma on depressive and anxiety disorders

Hovens, J.G.F.M.

Chapter 5

Impact of Childhood Life Events and Childhood Trauma on the Onset and Recurrence of Depressive and Anxiety disorders

Jacqueline G.F.M. Hovens, Erik J. Giltay, Philip Spinhoven, Albert M. van Hemert, Brenda W.J.H. Penninx

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Abstract

Objective: To investigate the effect of childhood life events and childhood trauma on the onset and recurrence of depressive and/or anxiety disorders over a 2-year period in participants without current psychopathology at baseline.

Method: Longitudinal data in a large sample of participants without baseline DSM-IV depressive or anxiety disorders (N = 1,167, aged 18 to 65 years; assessed between 2004 and 2007) were collected in the Netherlands Study of Depression and Anxiety (NESDA). Childhood life events and childhood trauma were assessed at baseline with a semi-structured interview. The Composite International Diagnostic Interview, based on DSM-IV criteria, was used to diagnose first onset or recurrent depressive and/or anxiety disorders over a 2-year period.

Results: At baseline, 172 participants (14.7%) reported at least 1 childhood life event, and 412 (35.3%) reported any childhood trauma. During 2 years of follow-up, 226 participants (19.4%) developed a new (N = 58) or recurrent (N = 168) episode of a depressive and/or anxiety disorder. Childhood life events did not predict the onset and recurrence of depressive or anxiety disorders. Emotional neglect and psychological, physical, and sexual abuse were all associated with an increased risk of first onset and recurrence of either depressive or comorbid disorders ($P < 0.001$), but not of anxiety disorders. In multivariate models, emotional neglect was the only significant independent predictor of first onset and recurrence of any depressive or comorbid disorder ($P = 0.02$). These effects were primarily mediated by the severity of (subclinical) depressive symptoms at baseline and, to a lesser extent, by a prior lifetime diagnosis of a depressive and/or anxiety disorder.

Conclusion: Childhood maltreatment is a key environmental risk factor, inducing vulnerability to develop new and recurrent depressive and comorbid anxiety and depressive episodes.

Introduction

Childhood abuse and other adverse childhood experiences have been linked to an increased risk of psychopathology, in particular the emergence of depressive and anxiety disorders in later life (1-6). Although previous research has documented long-term associations, these studies have largely focused on the prevalence of disorders rather than on first onset. Most studies investigating the association between childhood adversities and psychopathology in adulthood used cross-sectional designs (1-6) and were limited to specific trauma domains (7-11). Prospective evidence for childhood adversity predicting incident psychopathology in adulthood is rather limited. Several prospective studies that assessed the risk of depression and anxiety disorders included children exposed to childhood maltreatment and followed them up until (young) adulthood (12-15). Studies on anxiety disorders have been conducted much less often than studies on depressive disorders and have mainly focused on generalized anxiety disorders (14, 15).

In the US National Comorbidity Study, Kessler et al showed that childhood adversities were consistently associated with a higher risk of first onset of depressive episodes (1), and this was confirmed in a replication study (16). This finding, although retrospective, is important to advance our understanding of the chain of events and dynamic relationships between childhood trauma and adult-onset psychopathology. Longitudinal research offers excellent opportunities to predict the development of psychopathology after exposure to childhood trauma and to study its potential mediators.

In this prospective study, the impact of childhood trauma and childhood life events on the occurrence of adult psychopathology is studied in more detail and approached from different points of view to identify: (1) the differential effects on anxiety, depressive and comorbid disorders, (2) the specific effect of various childhood life events and all domains of childhood trauma, (3) whether relationships differed in subjects with and without lifetime psychopathology, and (4) whether clinical factors such as severity of baseline anxiety and depressive symptoms and a prior lifetime diagnosis, are important in mediating the relationship between childhood trauma and the occurrence of depressive and anxiety disorders. To address these topics, a large cohort of subjects without any current depressive and/or anxiety disorder at baseline was followed over a 2-year time period.

Method

Sample

Baseline data were collected between 2004 and 2007 from a longitudinal cohort study including 2,981 participants aged 18 to 65 years from the Netherlands Study of Depression

and Anxiety (NESDA). To represent various settings and stages of psychopathology, NESDA recruited from three different settings: the general population (N = 564), primary care (N = 1,610) and mental health organizations (N = 807), in which persons with depressive and/or anxiety disorders were overrecruited. Since we utilized a sample without current psychopathology in this study, participants came from the general population (N = 380) and primary care settings (N = 787) only, where they were largely recruited through a 3-step screening approach. A detailed description of the study design, its rationale, and methods have been reported elsewhere (17). At baseline, lifetime presence of depressive and anxiety disorders was defined according to DSM-IV criteria and diagnosed with the Composite International Diagnostic Interview, WHO version 2.1 (CIDI), a fully structured diagnostic interview (18, 19). The present study reports on data from baseline and 2-year follow-up assessments.
Of the 2,981 participants in NESDA, we included 1,280 participants (42.9%) without a current depressive and/or anxiety disorder (defined as no disorder within the 6 months preceding baseline), of whom 1,167 (91.2%) participated in the 2-year follow-up interview. The effect of childhood trauma on illness course, in participants with a current depressive and/or anxiety disorder has been described in a previous article (20). Non-response was associated with fewer years of education (P = 0.001) and with reported childhood trauma (P = 0.002).
The sample analyzed in this study constituted a mixture of individuals in remission after a previous episode of anxiety and/or depressive disorders (N = 569) and individuals free of any lifetime anxiety and/or depressive disorders (N = 598).

Trauma assessment
At baseline, childhood life events and childhood trauma were assessed retrospectively by a structured interview, used in the Netherlands Mental Health Survey and Incidence Study (NEMESIS) within the age range 18-64 years (5, 21).

NEMESIS Childhood Trauma Interview (CTI) is a comprehensive trauma interview focused on five areas of childhood interpersonal trauma prior to the age of 16 years: (1) childhood life events defined as separations and losses, (2) emotional neglect, (3) psychological abuse, (4) physical abuse, and (5) sexual abuse. This instrument measures trauma with a continuous scoring system, which is advantageous from a clinical and statistical perspective, rather than dichotomous ratings of trauma (22).

Childhood life events. Participants were asked if any of the following life events had happened before the age of 16 years: death of either biological father or mother, divorce of the parents or being placed in care (defined as children's home, juvenile prison or foster family). Each childhood life event was coded in a dichotomous format (0 absent / 1 present). The childhood life events were analyzed for each separate item, as well as cumulative. The childhood life event score, a cumulative index ranging from 0 to 3, reflects the number of life events experienced (5, 21).

Childhood trauma. The definition of *emotional neglect* included lack of parental attention or support and parental ignorance of the child's problems and experiences. *Psychological abuse* was defined as being verbally abused, being given undeserved punishment, being subordinated to siblings, and being blackmailed. *Physical abuse* was defined as being kicked or hit with hands or an object, being beaten up or subjected to physical abuse in any other way. *Sexual abuse* was defined as being sexually approached against their will, meaning being touched or having to touch someone in a sexual way. Participants were asked to give an indication about the frequency on a five-point scale (i.e. once, sometimes, regularly, often and very often). In the analyses, the frequencies were categorized into three groups (0: absent, 1: once or sometimes, 2: regularly, often and very often). A *cumulative childhood trauma score*, defined as the sum of the frequency scores ranging from 0 to 8, was created, with a higher score indicating more types and a higher frequency of childhood trauma (5, 21).

Two-year occurrence of depressive and anxiety disorders

At the 2-year follow-up assessment, the CIDI was repeated to assess the occurrence of depressive and/or anxiety disorders since the baseline interview. Occurrence of a disorder was defined as either first onset or recurrence of the disorder anytime between baseline and 2-year follow-up assessment. Various disorder groups were identified: no occurrence, occurrence of depressive disorder, occurrence of anxiety disorder, and occurrence of comorbid depressive and anxiety disorder, defined as both disorders occurring at any time within the 2-year of follow-up.

Determinants of 2-year course

Sociodemographics. Demographic data used in our study were gender, age and years of education attained. Since gender, age and education were significantly associated with the childhood life-event or trauma score (Table 1), we included these demographic variables as covariates. The presence of lifetime alcohol abuse and/or dependence was diagnosed with the CIDI and used as a covariate (18, 19). The number of participants who abused substances other than alcohol was almost negligible and therefore not tested for.

Clinical characteristics. Previous NESDA studies showed that a psychiatric history and subthreshold depression and anxiety independently predict the subsequent occurrence of depressive or anxiety disorders (23) and that childhood trauma is associated with higher severity of depressive and anxiety symptoms (20). Therefore, subtreshold symptoms of depression and anxiety and a lifetime history were used to assess their potential role as mediators. Severity of depressive symptoms was measured with the 30-item Inventory of Depressive Symptomatology-Self Rated (IDS-SR) (24). Severity of anxiety symptoms was measured using the 15-item Fear Questionnaire (25) and the 21-item Beck Anxiety Inventory (26). Lifetime diagnosis was defined as the presence of an earlier episode of a depressive and/or anxiety disorder at any time during the individual's lifespan, with the exception of the 6 month period preceding baseline.

Table 1. Baseline characteristics according to the childhood life-event score and the childhood trauma score in participants without a baseline diagnosis of depressive or anxiety disorder (N=1,167).

	Childhood life-event score			
	0	**1**	**2 to 3**	***P*-value[a]**
No. of participants	996	156	15	
Age (years, ± SD)	42.9 ± 13.9	40.5 ± 14.0	45.0 ± 11.8	0.17
Female gender	66.3%	64.1%	46.7%	0.20
Education level attained (years, ± SD)	12.9 ± 3.2	12.3 ± 3.4	10.1 ± 2.7	0.001
IDS-SR (score, ± SD)	10.8 ± 8.3	12.2 ± 8.8	17.6 ± 11.8	0.002
BAI (score, ± SD)	5.4 ± 5.8	5.7 ± 5.2	8.2 ± 7.8	0.15
FQ (score, ± SD)	0.9 ± 0.9	1.0 ± 0.9	1.3 ± 1.6	0.02
Lifetime diagnosis:				
No lifetime psychopathology	51.6%	48.7%	53.3%	0.63
Depressive disorder	21.3%	21.2%	20.0%	0.91
Anxiety disorder	8%	9.0%	6.7%	0.93
Comorbid depressive and anxiety disorder	18.3%	21.2%	20.0%	0.42

	Childhood trauma score			
	0	**1 to 3**	**4 to 8**	***P*-value[a]**
No. of participants	755	303	109	
Age (years, ± SD)	40.9 ± 14.4	44.4 ± 12.9	49.4 ± 9.7	< 0.001
Female gender	61.6%	75.2%	67.9%	0.002
Education level attained (years, ± SD)	12.7 ± 3.2	12.9 ± 3.2	12.2 ± 3.5	0.5
IDS-SR (score, ± SD)	9.4 ± 7.8	13.4 ± 8.5	16.5 ± 9.5	<0.001
BAI (score, ± SD)	4.5 ± 5.1	6.8 ± 5.9	8.4 ± 7.4	<0.001
FQ (score, ± SD)	0.8 ± 0.8	1.1 ± 1.0.	1.1 ± 1.0	<0.001
Lifetime diagnosis:				
No lifetime psychopathology	60.5%	36.6%	27.5%	<0.001
Depressive disorder	19.7%	23.4%	25.7%	0.08
Anxiety disorder	8.1%	10.9%	8.3%	0.43
Comorbid depressive and anxiety disorder	11.7%	29.0%	38.5%	<0.001

[a] *P* values by analysis of variance (ANOVA) linear term or X^2 tests (for linear association).
Abbreviations: BAI=Beck Anxiety Inventory; DSM-IV= Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; FQ=Fear Questionnaire; IDS-SR, Inventory of Depressive Symptoms Self Report.
Data are numbers, percentages or mean (± SD).

Statistical analyses

Baseline characteristics were compared across the childhood life event and childhood trauma indices, using analysis of variance for continuous variables and chi-square tests (for linear by linear association) for categorical variables. Multinomial logistic regression analysis was used to calculate odds ratios (ORs with 95% confidence intervals [CIs]) for the 2-year occurrence rates of depressive and/or anxiety disorders, according to childhood trauma domains and childhood trauma score, adjusted for age, gender, and education (Model 1).

In an extra multivariable model (Model 2), all childhood trauma domains were included in 1 model to determine the independent predictors for 2-year occurrence of anxiety and depressive disorders. Next, the childhood trauma score was considered a continuous variable ranging from 0 to 8, in which the "no diagnosis" group was regarded as reference group. Post-hoc analyses were done in subgroups of separate anxiety disorders. *P*-values were derived from likelihood ratio tests.

The interaction term of a lifetime diagnosis x trauma (based on childhood trauma score) was added to the analyses to assess potential moderators. To examine the mediation effects of baseline clinical characteristics on the relationship between childhood trauma score and 2-year occurrence rates, a multiple mediation model by Preacher and Hayes (27) was used. Mediation was investigated by directly testing significance of the indirect effect of the independent variable (IV) on the dependent variable (DV) through the mediator (M) quantified as the product of the effects of the IV on M (a) and the effect of M on DV (b), partialling out the effects of the IV. The indirect effect is the product a x b, and this is about equivalent to c minus c' (ie, the difference between the total effect and the direct effect). The 95% percentile-based CIs were computed using the cut-off values for the 2.5% highest and lowest scores of the empirical distribution. A 2-tailed $P < 0.05$ was considered statistically significant; the statistical software used was SPSS 18.0 (SPSS Inc., Chicago, Illinois).

Results

Sixty-six percent of the study population was female, the mean age was 42.6 years (standard deviation [SD] = 13.9). At baseline, 14.7% reported at least 1 childhood life event and 35.3% any childhood trauma. A lifetime diagnosis of a depressive and/or anxiety disorder was present in 569 of the participants (48.8%). Sample characteristics at baseline are shown in Table 1. A higher childhood life-event score was associated with a lower level of education and higher severity scores for both anxiety and depressive symptoms. A higher childhood trauma score was associated with being older, being female, higher severity scores for both anxiety and depressive symptoms, and a positive lifetime history of a depressive and/or anxiety disorder.

The 2-year occurrence rates of depressive and/or anxiety disorders are presented in Table 2: 941 (80.6%) of the 1,167 participants remained without a disorder, 66 (5.7%) had a pure anxiety disorder, 97 (8.3%) had a pure depressive disorder, and 63 (5.4%) had a comorbid disorder. Of the 569 participants with a baseline lifetime diagnosis of a depressive and/or anxiety disorder, 168 (29.5%) reported any disorder since baseline, compared to 58 (9.7%) of the 598 participants without a lifetime diagnosis at baseline ($P < 0.001$). Thus, within the 2-year follow-up period, 25.7% experienced first episodes and 74.3% recurrent episodes.

Table 2. Contributions of childhood life events and trauma score to the occurrence of depressive and/or anxiety disorders, in participants without a baseline diagnosis of depressive or anxiety disorder (N=1,167).

	Diagnosis between baseline and 2-year follow-up[a]				
	No disorder	**Anxiety disorder**	**Depressive disorder**	**Comorbidity**	***P* value[b]**
	N=941	N=66	N=97	**N=63**	
Childhood life events:					
Divorce parents	99 (10.5%)	6 (9.1%)	11 (11.3%)	10 (15.9%)	0.36
Early parental loss	61 (6.5%)	7 (10.6%)	7 (7.2%)	3 (4.8%)	0.77
Placed in care	45 (4.8%)	3 (4.5%)	7 (7.2%)	5 (7.9%)	0.29
Childhood life event score:					
0	808 (85.9%)	58 (87.9%)	80 (82.5%)	50 (79.4%)	0.20
1	122 (13.0%)	7 (10.6%)	16 (16.5%)	11 (17.5%)	
2 to 3	11 (1.2%)	1 (1.5%)	1 (1.0%)	2 (3.2%)	
Childhood trauma:					
Emotional neglect:					
Once or sometimes	107 (11.4%)	14 (21.2%)	20 (20.6%)	15 (23.8%)	
Regularly or very often	101 (10.7%)	10 (15.2%)	18 (18.6%)	15 (23.8%)	<0.001
Psychological abuse:					
Once or sometimes	80 (8.5%)	6 (9.1%)	11 (11.3%)	10 (15.9%)	
Regularly or very often	48 (5.1%)	4 (6.1%)	7 (7.2%)	13 (20.6%)	<0.001
Physical abuse:					
Once or sometimes	46 (4.9%)	3 (4.5%)	7 (7.2%)	3 (4.8%)	
Regularly or very often	20 (2.1%)	2 (3.0%)	6 (6.2%)	8 (12.7%)	<0.001
Sexual abuse:					
Once or sometimes	61 (6.5%)	4 (6.1%)	7 (7.2%)	2 (3.2%)	
Regularly or very often	56 (6.0%)	4 (6.1%)	12 (12.4%)	12 (19.0%)	0.003
Childhood trauma score:					
0	640 (68.0%)	38 (57.6%)	53 (54,6%)	24 (38.1%)	<0.001
1 to 3	227 (24.1%)	21 (31.8%)	30 (30.9%)	25 (39.7%)	
4 to 8	74 (7.9%)	7 (10.6%)	14 (14.4%)	14 (22.2%)	

[a] Values are N (%)
[b] *P* value by X^2 test

Childhood life-events and incidence of depressive and anxiety disorders

Neither specific childhood life events nor the childhood life event score showed statistically significant associations with the occurrence of psychopathology within a 2-year follow-up period (Table 2).

Childhood trauma and incidence of depressive and anxiety disorders

Emotional neglect and psychological, physical, and sexual abuse were all associated with the 2-year occurrence rates of depressive, anxiety and comorbid disorders (Table 2).

The presence of all childhood abuse domains (regularly or very often) gradually increased in the following order: from no disorder, anxiety disorder, depressive disorder, to a comorbid disorder. The cumulative childhood trauma score followed the same pattern (P <0.001).

Odds ratios for the 2-year occurrence of any depressive and/or anxiety disorder are listed in Table 3. Multivariate regression analyses, adjusted for age, gender, and education (Model 1), showed that the occurrence of any disorder was predicted by all trauma domains. The effect of childhood trauma on the occurrence of anxiety, depressive or comorbid disorders was investigated (Model 1). Regularly or frequent emotional neglect, physical abuse, and sexual abuse were associated with an increased risk of occurrence of depressive disorders. An even stronger association was found between emotional neglect and psychological, physical, and sexual abuse and the occurrence rate of comorbid disorders within a 2-year period. None of the childhood trauma domains were significantly associated with the risk of anxiety disorders, except for the relationship with emotional neglect (but only for the "once or sometimes" category). In addition, multivariate analyses were done, in which all separate childhood trauma domains were entered simultaneously to investigate which trauma domains were independent predictors (Model 2). Emotional neglect was the only significant independent predictor of 2-year occurrence rates for depressive and comorbid disorder (P = 0.002). Severe psychological and sexual abuse did independently predict the occurrence of comorbid disorders. The effect of childhood trauma on incident anxiety and depressive disorders did not change when we added baseline alcohol abuse or dependence as a covariate in the model (Table 3). The number of participants who abused substances other than alcohol was almost negligible and therefore not tested for.

Figure 1 graphically displays the childhood trauma score with OR's for occurrence of disorders. An increased score for childhood trauma corresponded in a dose-response manner with a higher likelihood of having a depressive (P < 0.001) and a comorbid disorder (P < 0.001) within 2 years, but not for having an anxiety disorder.

Finally, to determine the possible moderating effect of a lifetime diagnosis at baseline, the interaction term of a lifetime diagnosis x trauma was added to the analyses. In all trauma domains, no significant moderating effect of lifetime psychopathology at baseline was found in predicting the occurrence of any depressive and/or anxiety disorder in the 2-year follow-up period. This finding suggests that the predictive effects of childhood trauma were of similar strength among subjects with and without lifetime psychopathology.

We further analyzed whether the relationship between childhood trauma score (IV) and 2-year occurrence rates of depressive and anxiety disorders (DV) could be explained by baseline clinical characteristics as mediating variables (M). Table 4 presents the results of mediation analyses: all clinical characteristics demonstrated significant indirect effects (a x b effects) in

Table 3. Odds ratios adjusted for sociodemographic covariates for the occurrence of depressive and/or anxiety disorders, in participants without a baseline diagnosis of depressive or anxiety disorder (N=1,167).

		Model [b]	Any disorder	Anxiety disorder	Depressive disorder	Comorbid disorder
Childhood trauma scorea score[a]		Model 1	1.25 (1.15-1.36)**	1.09 (0.93-1.27)	1.25 (1.11-1.40)**	1.41 (1.25-1.60)**
Emotional neglect:	Once or sometimes	Model 1	2.66 (1.79-3.95)**	2.26 (1.18-4.33)**	2.64 (1.51-4.61)**	3.23 (1.67-6.24)**
		Model 2	2.71 (1.75-4.21)**	2.76 (1.37-5.57)**	2.76 (1.50-5.10)*	2.44 (1.13-5.28)*
	Regularly or very often	Model 1	2.47 (1.64-3.73)**	1.72 (0.83-3.57)	2.51 (1.40-4.49)**	3.42 (1.77-6.63)**
		Model 2	2.06 (1.23-3.44)**	2.21 (0.94-5.21)	2.48 (1.22-5.04)*	1.39 (0.56-3.46)
Psychological abuse:	Once or sometimes	Model 1	1.63 (1.01-2.62)*	1.06 (0.44-2.56)	1.55 (0.78-3.07)	2.63 (1.25-5.55)*
		Model 2	0.82 (0.47-1.45)	0.61 (0.22.-1.68)	0.63 (0.28-1.42)	1.61 (0.65-4.01)
	Regularly or very often	Model 1	2.42 (1.43-4.11)*	1.21 (0.42-3.53)	1.59 (0.69-3.68)	5.96 (2.91-12.20)*
		Model 2	1.20 (0.59-2.44)	0.73 (0.20-2.72)	0.56 (0.19-1.69)	4.36(1.55-12.28)*
Physical abuse:	Once or sometimes	Model 1	1.33 (0.70-2.53)	0.97 (0.29-3.22)	1.72 (0.75-3.97)	1.16 (0.35-3.89)
		Model 2	0.79 (0.39-1.60)	0.77 (0.21-2.86)	1.23 (0.48-3.13)	0.38 (0.10-1.44)
	Regularly or very often	Model 1	3.48 (1.76-6.87)*	1.39 (0.32-6.10)	3.14 (1.22-8.09)*	6.50 (2.70-15.62)*
		Model 2	1.81 (0.79-4.13)	1.15 (0.21-6.19)	2.35 (0.73-7.60)	1.60 (0.52-4.87)
Sexual abuse:	Once or sometimes	Model 1	0.96 (0.51-1.80)	0.87 (0.30-2.50)	1.35 (0.59-3.07)	0.53 (0.13-2.26)
		Model 2	0.89 (0.47-1.70)	0.84 (0.29-2.43)	1.27 (0.55-2.93)	0.43 (0.10-1.89)
	Regularly or very often	Model 1	2.15 (1.32-3.51)*	0.91 (0.32-2.61)	2.42 (1.23-4.75)*	3.29 (1.63-6.61)*
		Model 2	1.60 (0.94-2.70)	0.76 (0.26-2.26)	1.75 (0.86-3.59)	2.27 (1.05-4.90)*

[a] The childhood trauma score was considered a continuous variable ranging from 0 to 8.
[b] Model 1: odds ratios (with 95% confidence intervals) by multinomial logistic regression analysis, adjusted for gender, age, and education. Model 2: additionally adjusted for all other childhood trauma domains.
P-value by X^2 test (*: $P<0.05$, **: $P<0.001$)

univariate regression analyses. In multivariate regression analyses, the indirect effects of the IDS-SR score and an earlier diagnosis before baseline remained significant, suggesting that they are important in mediating the association between childhood trauma and 2-year occurrence of depressive and/or anxiety disorders. When all the mediating variables were added into the model, the direct effect (c') between trauma and 2-year occurrence of depressive and/or anxiety disorders was no longer statistically significant (0.078 of total effect, approximately 36%).

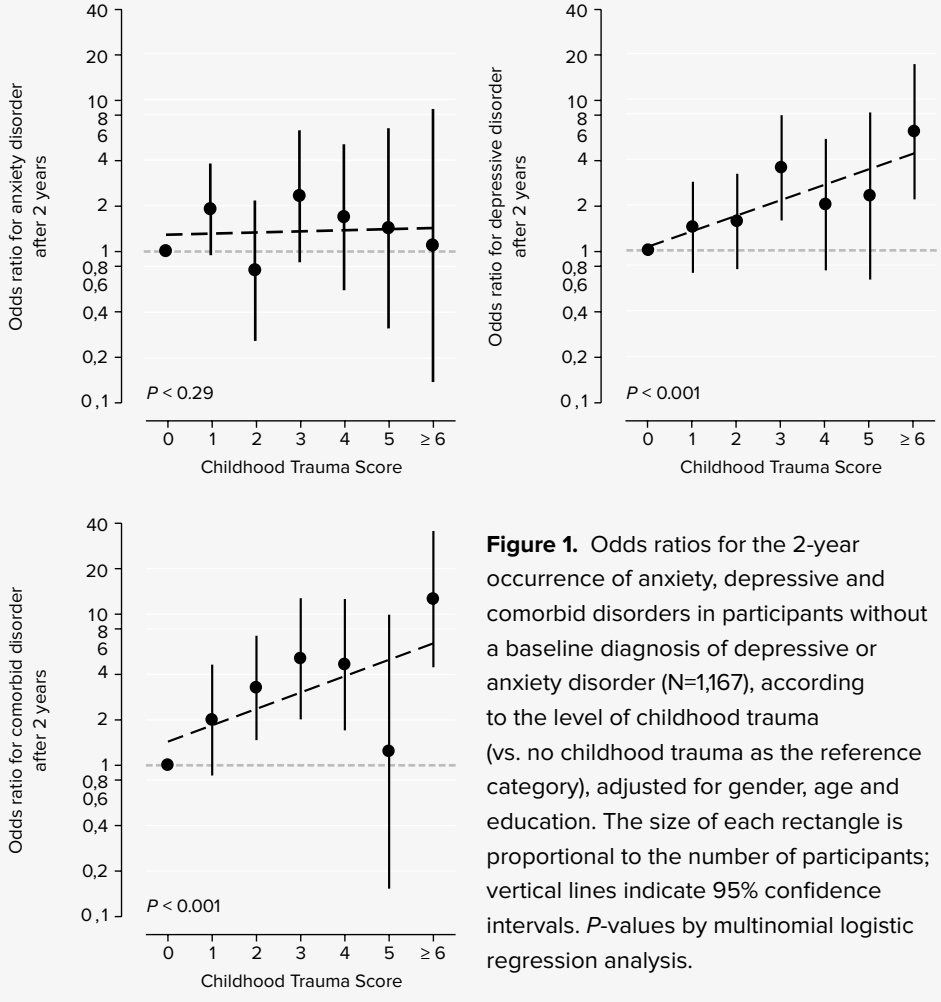

Figure 1. Odds ratios for the 2-year occurrence of anxiety, depressive and comorbid disorders in participants without a baseline diagnosis of depressive or anxiety disorder (N=1,167), according to the level of childhood trauma (vs. no childhood trauma as the reference category), adjusted for gender, age and education. The size of each rectangle is proportional to the number of participants; vertical lines indicate 95% confidence intervals. *P*-values by multinomial logistic regression analysis.

Table 4. Mediation analysis of baseline disease characteristics on the relationship between the childhood trauma index (IV) and occurrence of a diagnosis within 2 years (DV) in participants without a baseline diagnosis of depressive or anxiety disorder (N=1,167).

Mediating variable (M)	No. DV / reference	Effect of trauma on M (a)	Effect of M on DV (b)	Mediating effect[a] (a x b; 95% CI)	Direct effect of trauma on DV (c')	Total effect (c)
IDS-SR	226 / 941	1.528	0.102	**0.156 (0.114; 0.202)**	0.116	0.217
BAI	226 / 941	0.825	0.113	**0.094 (0.061; 0.135)**	0.163	0.217
Fear Questionnaire	226 / 941	0.082	0.422	**0.035 (0.016; 0.060)**	0.198	0.217
Earlier diagnosis before baseline	226 / 941	0.075	1.288	**0.097 (0.063; 0.134)**	0.161	0.217
All mediating variables combined:	226 /941					
– IDS-SR		1.528	0.077	**0.117 (0.077; 0.173)**	0.078	0.217
– BAI		0.825	0.029	0.024 (-0.005; 0.063)		
– Fear Questionnaire		0.082	0.061	0.005 (-0.009; 0.022)		
– Lifetime diagnosis before baseline		0.075	0.961	**0.072 (0.042; 0.108)**		

[a] Mediating effects were considered as significant when the bias corrected and accelerated confidence interval did not include zero (indicated in bold).
Abbreviations: a=effect of IV on M, a x b = indirect effect, b = effect of M on DV, BAI = Beck Anxiety Inventory, c = total effect, c' = direct effect, DV = dependent variable, IDS-SR = Inventory of Depressive Symptoms Self Report, IV = independent variable, M = mediating variable.

Discussion

In our present study, we examined whether childhood trauma and childhood life events were predictive for the occurrence of depressive and/or anxiety disorders over a 2-year period in a large cohort of subjects without any current depressive and/or anxiety disorder at baseline. We demonstrated that childhood life events did not predict the occurrence of depressive or anxiety disorders, whereas a history of childhood trauma did predict the occurrence of depressive disorders and comorbid disorders. In particular, of all trauma domains emotional neglect was the main independent predictor. These associations were mediated through a higher severity of depressive symptoms at baseline and the presence of a prior history of a disorder at baseline, indicating that the increased onset of (comorbid) depressive disorders among individuals with childhood trauma is partially due to their already mildly elevated depressive symptom levels at baseline and earlier episodes of anxiety and/or depression.

Our findings are consistent with the results of previous prospective studies of children, exposed to maltreatment, who were followed until (young) adulthood. Childhood neglect and physical abuse were associated with an increased risk of lifetime major depression (13). A 45-year prospective study of a large British birth cohort (N = 9,337), showed that

cumulative adversity and physical and sexual abuse were significantly associated with mid-life psychopathology (ICD-10 depressive and anxiety disorders) (15). In the Dunedin birth cohort (N = 1,037) (14), the group that developed comorbid major depression *plus* generalized anxiety disorder reported significantly higher levels of childhood adversities. Both studies support our finding of a dose-response relationship between childhood trauma score and likelihood of developing a depressive and a comorbid disorder within a 2-year period. The lack of a significant association between childhood trauma and anxiety disorders in adulthood suggests that causal pathways to the development of anxiety disorders are less vulnerable to the impact of childhood trauma.

Among the specific effects of childhood trauma, emotional neglect was the most important predictor of the occurrence of psychopathology in adulthood at 2-year follow-up, suggesting that the relationship between childhood trauma and psychopathology is predominantly driven by emotional neglect. In a recent systematic review assessing the association between child maltreatment and mental health outcome, a 3-fold higher risk of developing a depressive disorder was found among emotionally abused individuals than non-abused individuals (28). Although emotional neglect is a major public health problem, its serious lifelong consequences and impact on adult psychopathology have not been recognized for a long time. Previous prospective studies were usually conducted in non-representative samples. Childhood abuse data were often drawn from official court records and/or behavioral observations and most likely represent the most extreme cases processed in the system and were skewed towards the lower end of the socio-economic spectrum. *Childhood neglect* was defined as lack of child care and emotional abuse was often not specifically asked for, and thus, underreported. In 2 prospective studies, physical and sexual abuse was added later, based on retrospective reports during adulthood (14, 15).

We provide new evidence that in all trauma domains, no significant moderating effect of lifetime psychopathology at baseline was found in the occurrence of any depressive and/or anxiety disorder in the 2-year follow-up. The relative effects of childhood trauma were of similar strength in patients with and without lifetime psychopathology, which demonstrates that childhood trauma is associated with both onset and recurrence of psychopathology.

We found that more unfavorable clinical disease characteristics at baseline, such as severity of subsyndromal depressive symptoms and presence of lifetime psychopathology, mediated the differences such that the direct relationship between childhood trauma and psychopathology became non-significant. Patients with a history of childhood trauma had a higher severity of anxiety and depressive symptoms at baseline, in the absence of a depressive or anxiety disorder. We speculate that these subsyndromal symptoms increase vulnerability for additional exposure to stressful life events, which subsequently predispose to disorder onset (29). Clark et al. (15) found that psychopathology at 23 years, but not at 16 years, partially

mediated the associations of physical and sexual abuse and cumulative adversity with mid-life disorder. This finding is congruent with the importance of our finding of lifetime psychopathology as a potential mediator. These mediation analyses are demonstrating the lifelong influence and mechanisms through which childhood trauma may affect psychopathology throughout the lifespan. Our results feed into the enduring effect model, which assumes that early experiences continue to influence the outcome over time as recently described by Fraley et al. (30). This model is represented by a remaining direct path (about 36%) after the mediating factors have been taken into account. In other words, childhood trauma is a key environmental risk factor triggering a chain of risks, such as recurrent depressive episodes that may enhance the vulnerability to develop further depressive disorders.

Our findings are in agreement with the hypothesis that patients with childhood trauma represent a vulnerable group with long-term psychopathology, characterized by a course of chronic waxing and waning of the mental disorder. On the other hand, the association between childhood adversity and occurrence of adulthood psychopathology may also refer to the “kindling hypothesis”, assuming that with each previous episode, less stressful life events are needed to elicit a subsequent episode (31, 32).

The findings of this study have implications for clinical practice. Information about a history of childhood maltreatment helps to identify individuals who are at high risk of developing recurrent and chronic subtypes of depression. The ability to predict which traumatized individuals will develop a depressive and/or anxiety disorder in the near future will provide more insight into the mechanisms of psychopathology related to childhood trauma. Clinicians should, therefore, routinely inquire about childhood trauma, which can add important prognostic information to update risk assessment and provide opportunities for preventive interventions.

The strength of this study is the prospective design and large sample of midlife participants without a baseline diagnosis of depressive and/or anxiety disorder. All childhood trauma domains and childhood life events were considered. Furthermore, outcome measures were based on structured diagnostic interviews, and important baseline clinical characteristics were taken into account as potential mediators. Methodological limitations include the retrospective trauma assessment at baseline, although participants were not suffering from any anxiety and/or depressive disorder at the time of the interview. Our findings cannot be extrapolated to psychiatric disorders that were not assessed in this study, which may be of particular importance to post-traumatic stress disorder. Given the long time elapsed between childhood trauma and adult psychopathology, we were not able to consider the multifaceted mediating mechanisms that have largely occurred before the NESDA baseline wave.

We could test only a crude mediation model, while a more complex interplay between the family context and psychosocial resources and vulnerabilities should be the perspective of further research. The chain of events linking childhood adversities to psychopathology in adulthood involves a highly complex interplay of multiple psychological vulnerabilities and environmental factors (33, 34). Our 2-year follow-up period is a very short period considering the length of time elapsed between the exposure of childhood trauma and baseline assessments of adult participants and all the additional events that may have occurred since childhood, which we could not grasp with our current design. Nevertheless, significant effects of childhood trauma on incident adult psychopathology were found within this relative short follow-up period.

In conclusion, we found that all childhood trauma domains predicted the occurrence of either depressive or comorbid disorders within 2 years in adults without current psychopathology at baseline. Part of the impact of childhood trauma on the occurrence of depressive and comorbid disorder after 2 years of follow-up was found to be mediated through the severity of subsyndromal depressive symptoms and a prior history of psychopathology. Childhood maltreatment is a key environmental risk factor, which contributes to a course of chronic waxing and waning of depressive and comorbid disorders.

Clinical points

- A history of childhood trauma predicts the development of new and recurrent depressive and comorbid disorders in patients without a current depressive/anxiety disorder.
- Emotional neglect in childhood is the main independent predictor of all trauma domains.
- Higher severity of depressive symptoms and the presence of an earlier history of a disorder at baseline are important mediators between childhood trauma and the onset/recurrence of depressive and comorbid disorders.

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