

Challenging the Sensitive Window Hypothesis: Timing Effects of Maternal Depressive Symptoms on the Intergenerational Transmission of Maltreatment and Psychopathology in the Next Generation

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Keywords

Maternal depression · Timing effects · Child abuse potential · Child behaviour problems · Intergenerational transmission of childhood maltreatment

Abstract

Objective: The current study explored the role of maternal depressive symptoms in the intergenerational transmission of childhood maltreatment and developmental psychopathology. Based on the sensitive window hypothesis, the effects of earlier versus later maternal depression symptoms on child development were analysed. **Method:** Ninety-nine mother-child dyads, 65% of which had high-risk teenage mothers, participated in a longitudinal study with three assessments in the first 18 months of the child's life (T1–T3) and a 4th reassessment (T4) at the child's preschool age. Using serial mediation analyses, we tested whether the relationship between the mother's own maltreatment history (Childhood Experience of Care and Abuse Questionnaire) and the child's psychopathological outcome at preschool age was mediated in a causal effect chain by maternal depression in the first 2 years of life, by current maternal depression (Beck

Depression Inventory-II) and by current maternal child abuse potential (Child Abuse Potential Inventory). The children's emotional problems and externalizing symptoms were assessed at preschool age by parent or teacher Strengths and Difficulties Questionnaire ratings. **Results:** The results indicated that especially later maternal depression mediated the relationship between maternal childhood maltreatment and negative developmental outcomes in the next generation. The effects of maltreatment type on maternal depression were rather nonspecific. However, mental abuse affected existing risk factors more directly over time compared to physical and sexual abuse. Additionally, the impact of early life maltreatment and maternal depression on child psychopathology varied by rater. The pathway to externalizing symptoms was significant only in teacher ratings and for the pathway to emotional problems only in maternal ratings. **Conclusions:** The present findings suggest that early maternal depression followed by ongoing maternal depression plays a mediating role in the intergenerational cycle of maltreatment. Therefore, in the future, interventions should be offered at an early stage, but also extend well beyond the first 2 years of a child's life, addressing maternal depression and trauma.

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Published by S. Karger AG, Basel

Introduction

Sensitive periods are time windows in which experiences have a particularly large impact on neural brain development [1]. In particular, perceptual, cognitive, and emotional capabilities are shaped during these sensitive periods. The successful accomplishment of developmental tasks at certain times lays the foundation for proper social and emotional development in individuals. Therefore, adequate maternal caregiving plays an important role in supporting the typical development of neural circuits in offspring. If the developmental task is not learned or experienced within the sensitive time window, development is affected in the long term [2]. Maternal psychopathology and emotional functions have been linked consistently to children's social-emotional development, particularly in early life [3]. In humans, evidence for exactly defined time windows for social-emotional outcomes is lacking. However, the first 2 years of life are considered the most plastic and critical period of postnatal brain development [4]. During this period, the developing brain is especially responsive to environmental and experiential input, particularly to dyadic social interactions (sensitive window hypothesis) [5, 6]. Infants are born with a limited capacity to regulate their behaviours or their physiological and emotional states [7] and thus must develop the capacity for self-regulation over time. This social-emotional development is deeply embedded in the quality of the early dyadic interactions with their primary caregiver(s) [8]. More specifically, early in life, sensitive mothers coregulate their infant's stress responses by attending promptly, appropriately, and contingently to their infant's distress signals [9]. There is extensive literature showing that high-quality early mother-child interactions may promote positive child development, facilitating better outcomes related to emotion regulation and stress reactivity [10–13] and laying the biobehavioural foundation for adaptive psychosocial functioning and emotional well-being across the lifespan [14].

Children of mothers with subclinical depressive symptoms, however, are at increased risk of negative developmental outcomes, with consistent evidence indicating that depressed mothers are less sensitive to their infants' cues, resulting in a poorer quality of the dyadic interaction [15–18]. Research has long focused on the impact of maternal depression on early childhood, namely, the first 1 to 2 years of life, which is in line with the sensitive window hypothesis. Bagner et al. [19], for instance, showed that maternal depression during the child's first year of life was a specific predictor of internalizing, externalizing,

and total behaviour problems in the offspring. However, maternal depression prior to pregnancy and during the prenatal period had no effects on later child psychopathology, suggesting that the effect was specific to the first year of life. In line with this, Bureau et al. [20] also explored the timing of exposure to maternal depressive symptoms and child depressive symptoms later in life. In this longitudinal study, maternal depressive symptoms during the child's first years of life contributed to the likelihood of child depressive symptoms at age 8, even after controlling for concurrent maternal depressive symptoms. However, more recently, the sensitive window hypothesis has been challenged by findings indicating an even stronger impact of the mother's later depression beyond the sensitive period on the child's developmental outcomes [21, 22]. In a birth cohort of 1,707 children and their mothers, Agnafors et al. [21] showed that recurrent and ongoing maternal depressive symptoms significantly increased the risk of child behaviour problems in 12-year-olds, while symptoms of postpartum depression (3 months after birth) did not result in an increased risk of behavioural problems [23]. Furthermore, a systematic review conducted in 2015 concluded that postnatal depression increases risk vulnerability in the presence of recurrent maternal depression but that the latter factor may be the stronger predictor [24].

A prominent risk factor for clinical (and subclinical) depression in mothers, in general, is early life maltreatment (ELM) experiences [25–27]. During the postpartum period, mothers with high levels of ELM may be particularly overwhelmed by the heightened demands of caregiving and by bad memories of how they grew up themselves [27]. Thus, mothers with ELM are at greater risk for the development of postnatal depression [28] and for transmission of early adversity into the next generation [28]. Thus, parents who experienced maltreatment in childhood are at an increased risk for abusive or neglectful parenting behaviour towards their own children [29]. Overall, previous studies show inconsistent findings regarding the consequences of specific ELM types. A meta-analysis examining specific effects of childhood maltreatment type on major depression revealed associations for each investigated type of maltreatment (antipathy, neglect, physical abuse, sexual abuse, and psychological abuse) and depressive symptomatology [30]. However, these findings also indicate that psychological abuse and neglect were most strongly associated with the outcome of depression, thus highlighting the potential impact of the more "silent" types of childhood maltreatment. Regarding the intergenerational transmission of abuse and

neglect in the past, women who experienced sexual abuse had increased child abuse potential [31]. A systematic review reported that various types of maternal ELM were associated with internalizing and externalizing problem behaviour in the offspring with a more tenuous association documented for internalizing difficulties [32]. To summarize, only few studies have examined the specific effects of different types of childhood abuse on outcomes, such as depression, child abuse potential, or child problem behaviour. A reason might be that maltreatment subtypes often co-occur and are therefore difficult to examine in isolation.

In a recent large-scale Environmental Risk (E-Risk) Longitudinal Twin Study [33] the role of maternal depression in the intergenerational transmission of childhood maltreatment and its psychological consequences for the next generation were analysed in greater detail. The study findings suggested that mothers who had been maltreated as children were at increased risk for postpartum depression during their child's first year of life. In turn, postpartum depression predicted children's exposure to maltreatment, followed by more emotional and behavioural problems of the child. Indirect effects of maternal childhood maltreatment on child outcomes were robust across child gender and supported significant mediation through postpartum depression; however, the results indicated that the mediating effect of postpartum depression from maternal childhood maltreatment on child harm and subsequent outcomes was carried out by *later* maternal depression (between one and 10 years of age). However, in this study, the assessment of maternal postpartum depression was carried out retrospectively. Therefore, it is likely that the assessment of prior depressive symptoms was biased by the current symptomatology. Additionally, the severity of postpartum depression was not assessed. Thus, prospective studies are necessary to better understand the effects of postpartum depression and later depression on child outcomes. Finally, as the E-Risk study was conducted in families with twins in the United Kingdom, the replicability of findings in other health settings and with non-twin families is important.

Overall, mixed findings have been reported with respect to the timing effects of maternal depression as a mediator in the intergenerational transmission of child psychopathology and maltreatment. Identifying vulnerable time windows would allow interventions to be offered at precisely the time when they are most effective. In addition, research findings that explore the consequences of postpartum depression and ongoing/later maternal depression in prospective studies with dimensional assess-

ments of psychopathological symptoms are scarce. Furthermore, little is known about the potential impact of specific maternal maltreatment types on maternal and child psychopathology and whether children are affected more by internalizing or externalizing symptoms [31].

Study Goals

Based on the research findings outlined above, the goals of the current longitudinal study were to investigate whether maternal depressive symptomatology and a child's abuse potential mediate the relationship between maternal childhood maltreatment and negative developmental outcomes in the next generation, specifically the child's internalizing and externalizing symptoms.

This study included a longitudinal high-risk sample with approximately 35% of the sample being teenage mothers (aged below 21 years at the time of the child's birth). Dense and extensive assessments in the first 18 months (T1–T3) of each child's life were carried out, including detailed assessments of each mother's own childhood maltreatment experiences, and a fourth reassessment of the mother-child dyad at the child's preschool age (between 3.0 and 5.9 years) was performed. This approach allowed us to analyse more detailed mechanisms of the intergenerational cycle of maltreatment.

Given the inconsistent findings in previous studies [21, 32, 34], we were particularly interested in the effects of early versus later maternal depressive symptoms on child psychopathology (*Research Question 1*). Based on the assessment schedule in the current study, we defined the early sensitive period as the first 2 years of life (with assessments taking place on average between 3 [T1] and 18 months [T3] of the child's life), whereas "later" refers to maternal depression at the time of a child's preschool age (T4). We were also interested in the specificity of these effects on internalizing versus externalizing symptoms (*Research Question 2*). Specifically, we hypothesized that later maternal depressive symptoms, in particular, mediate the intergenerational transmission of childhood maltreatment and its psychological consequences for the offspring.

As parent and teacher ratings of children's emotional/behavioural problems typically differ [35] and maternal reports might be biased by their own depressive symptoms [36], we analysed the children's psychopathology separately based on teacher or maternal ratings. Furthermore, to evaluate the relative impact of specific forms of maternal childhood maltreatment on developmental outcomes, we explored the effects of mental abuse (antipathy and neglect) and of physical and sexual abuse on child-

Table 1. Descriptive statistics including means and standard deviations and amount of clinically abnormal data

	T1	T2	T3	T4
<i>N</i>	99	74	72	59
Sociodemographic characteristics				
Child's age, months, M (SD)	5.62 (1.65)	12.39 (8.66)	18.60 (9.138)	47.8 (10.53)
Mother's age, years, M (SD)	23.05 (5.83)	23.62 (5.84)	24.14 (5.84)	26.57 (5.79)
Sex of infant (m/w)	(55/44)	(39/35)	(39/33)	(37/22)
Mother's characteristics after imputation				
<i>N</i> after imputation	99	99	99	99
BDI, M (SD)	7.82 (5.58)	9.17 (6.28)	8.31 (4.75)	9.42 (6.73)
Mild symptoms ≥ 13 , <i>n</i> (%)	18 (18.2)	13 (13.1)	18 (18.2)	17 (17.2)
Moderate symptoms ≥ 20 , <i>n</i> (%)	3 (3.0)	7 (7.1)	1 (1.0)	4 (4.0)
Severe symptoms ≥ 29 , <i>n</i> (%)	0 (0.0)	1 (1.0)	0 (0.0)	1 (1.0)
CECA.Q				
Mental abuse, M (SD)	16.64 (5.90)			
Mother antipathy ≥ 25 , <i>n</i> (%)	18 (18.8)	–	–	–
Mother neglect ≥ 22 , <i>n</i> (%)	12 (12.1)	–	–	–
Mother physical abuse, <i>n</i> (%)	10 (10.1)	–	–	–
Father antipathy ≥ 25 , <i>n</i> (%)	17 (17.17)	–	–	–
Father neglect ≥ 24 , <i>n</i> (%)	16 (16.16)	–	–	–
Father physical abuse, <i>n</i> (%)	3 (3.03)	–	–	–
Sexual abuse, <i>n</i> (%)	23 (23.2)	–	–	–
Child's characteristics after imputation				
CAPI, M (SD)	–	–	–	40.01 (7.575)
CAPI ≥ 60 , <i>n</i> (%)	–	–	–	3 (3.03)
SDQ teachers emotional, M (SD)	–	–	–	1.76 (1.078)
Borderline = 5, <i>n</i> (%)	–	–	–	3 (3.03)
Abnormal >5 , <i>n</i> (%)	–	–	–	0 (0)
SDQ teachers behavioural, M (SD)	–	–	–	2.36 (1.141)
Borderline = 3, <i>n</i> (%)	–	–	–	6 (6.06)
Abnormal >3 , <i>n</i> (%)	–	–	–	3 (3.03)
SDQ parents emotional, M (SD)	–	–	–	2.13 (1.839)
Borderline, <i>n</i> (%) = 4	–	–	–	5 (5.05)
Abnormal, <i>n</i> (%) > 4	–	–	–	9 (9.09)
SDQ Parents behavioural, M (SD)	–	–	–	2.52 (1.464)
Borderline, <i>n</i> (%) = 3	–	–	–	34 (34.3)
Abnormal, <i>n</i> (%) > 3	–	–	–	20 (20.2)

BDI, Beck Depression Inventory; CECA.Q, Childhood Experience of Care and Abuse Questionnaire; CAPI, Child Abuse Potential Inventory; SDQ, Strengths and Difficulties Questionnaire.

hood development (*Research Question 3*). In line with previous literature [31], we hypothesized that both types are risk factors for the development of depressive symptomatology, with mental abuse being particularly harmful.

Materials and Methods

Study Design

Data were collected as part of the multicentre project “Understanding and Breaking the Intergenerational Cycle of Abuse” in the area of three German cities (Aachen, Heidelberg, and Berlin).

The subproject in Aachen examined 99 mother-child dyads in a longitudinal design with three assessments (T1–T3). After the end of the study, participants were invited to take part in a follow-up study, which comprises a fourth assessment (T4). Mother-child dyads were invited to the lab to assess primary and secondary outcome measures when children were aged between 3 and 6 months before the start of the intervention (baseline, T1), after the 9 months of intervention (post-intervention, T2), and 6 months after the end of the intervention (follow-up, T3).

After T1, approximately half of the participants ($n = 56$) were randomized to receive an intervention (STEEP-b intervention) in addition to standard care (with standard care only as the control condition). As part of the STEEP-b intervention, video feedback was used to teach parents to perceive the signals and needs of their

Table 2. Amount of missing data for all main variables

	T1	T2	T3	T4
	99	74	72	59
Amount of missing data				
CECA.Q, <i>n</i> (%)	7 (7.07)	–	–	–
BDI, <i>n</i> (%)	0 (0)	26 (26.26)	27 (27.27)	37 (37.37)
CAPI, <i>n</i> (%)	–	–	–	38 (38.38)
SDQ _{parent} , <i>n</i> (%)	–	–	–	38 (38.38)
SDQ _{teacher} , <i>n</i> (%)	–	–	–	63 (63.63)

CECA.Q, Childhood Experience of Care and Abuse Questionnaire; BDI, Beck Depression Inventory; CAPI, Child Abuse Potential Inventory; SDQ, Strengths and Difficulties Questionnaire.

children and react sensitively to them. Adolescent mothers were visited biweekly by the same adviser over a period of 9 months. There were a total of four modules that specified the content of the sessions: child development, maternal sensitivity, frightening and intrusive behaviours, and sensitive discipline. Participants who were assigned to the control condition were not allowed to receive any intervention using video feedback but were allowed to receive the standard support of the welfare system (for more information, see [37]).

Since the intervention did not reveal any significant group differences in the primary outcome variables of the study at any of the measurement time points [38], the intervention was not considered in the current analyses. This procedure was supported with a post hoc test of one-way ANOVA using Scheffe's method for controlling the family wise error rate to investigate the influence of the treatment groups on the relevant variables. The results revealed that the initial treatment in the adolescent group did not influence any of the study variables but that maternal age should be included as a control variable.

The study was approved by an independent Ethics Committee of the Medical Faculty of RWTH Aachen University (EK144/12). All mother-child dyads received financial compensation for the assessments and travel expenses. Children received small presents. For more information on the Understanding and Breaking the Inter-generational Cycle of Abuse project, see <https://www.ubica.site>.

Sample

Mother-child dyads were recruited via advertisements in a local newspaper, obstetric clinics, midwife practices, and paediatrician practices. Caucasian adolescent (<21 years) and adult primiparous mothers (>25 years) with children between 3 and 6 months were included in the study. Mothers whose children were born preterm (<36 weeks of gestation) with serious medical problems or genetic syndromes were not included in the study. Maternal exclusion criteria included current substance abuse, current suicidal ideation, psychotic disorders, or separation from the child for longer than 3 months. Further, only mothers of European descent were included since genetic data were collected as part of the larger project (see [37]).

The initial study sample consisted of 99 mother-child dyads (64 adolescent mothers and 35 adult mothers). Of these, 25 dropped out of the study after T1, and two dropped out after T2. The remaining mother-child dyads were invited to participate in the fol-

low-up study at T4 (the exclusion criteria were identical). Of these, *n* = 59 participated at T4, *n* = 12 no longer met the inclusion criteria (e.g., out-of-home placements), *n* = 14 could not be reached by telephone or postal form, *n* = 10 denied re-participation due to time constraints or personal reasons, and *n* = 1 had to be excluded from the analysis due to a newly diagnosed neurological disorder of the child. The demographic variables of the sample are presented in Table 1. Those who remained in the study and those who dropped out did not differ on any of the study variables at T1, Childhood Experience of Care and Abuse Questionnaire (CECA.Q) mental abuse: ($t(97) = 0.17, p = 0.866$); CECA.Q physical/sexual abuse: $\chi^2(3, 99) = 4.74, p = 0.192$; Beck Depression Inventory (BDI): ($t(97) = 1.62, p = 0.109$); Child Abuse Potential Inventory (CAPI): ($t(97) = 0.35, p = 0.362$), demographic variables (child's age: ($t(97) = 0.86, p = 0.393$); socioeconomic status: $\chi^2(3, 99) = 4.68, p = 0.197$), except for maternal age ($t(97) = -2.91, p = 0.005$). Adolescent mothers dropped out of the study significantly more frequently than adult mothers. Due to the longitudinal study design, there were missing data; therefore, multiple imputation (MI) was used (for more information, see Statistical Analysis section below and Table 2). A total of 57 out of 99 participants had a full dataset that included all relevant variables from T1 to T3. Of the 59 subjects who participated again at T4, 42 participants had a complete dataset with respect to the parent report outcome variable and 28 participants with respect to the teacher report.

All main analyses were conducted across all parent-child dyads (including both adolescent and adult mothers), as the risk factors considered in this paper do not apply to teenage mothers only [1, 39]. Therefore, maternal age was included as a dichotomous control variable for the main analyses (0 = adolescent, 1 = adult).

Measurements

Childhood Experience of Care and Abuse Questionnaire

Maternal ELM experiences were assessed at T1 using the German version of the CECA.Q, a retrospective questionnaire on parents' behaviours towards children up to an age of 17 years [40]. The questionnaire assesses mental, physical, and sexual abuse. Mental abuse is assessed by 16 items related to parental care (8 items for antipathy and 8 for neglect) separately for mother and father, leading to a total of four scales for mental abuse. All items are rated on a five-point Likert scale from "1 = yes definitely" to "5 = not at all," which are then added to a sum score after certain items were reversed (total score 16–80). A total score above 25 is considered the

cut-off value for the mother's and father's antipathy scales. Total scores above 22 and 24 are considered the cut-off values for the mother's and father's neglect scales, respectively. The presence of physical and sexual abuse is measured by a single "yes" or "no" question. For the mental abuse scales, Cronbach's alpha in the current sample was acceptable ($\alpha = 0.737$). To compare the effects of mental versus physical/sexual abuse, the four parental care scales of the CECA.Q (mother's and father's antipathy and neglect) were averaged and considered a measure of mental abuse in the current analyses (for a similar approach, see Lehl [41] and Li et al. [42]). The variable "presence of physical and/or sexual abuse" was dichotomized (1 = if physical and/or sexual abuse has occurred by the mother and/or father, or, in the case of sexual abuse by others and 0 = if participants had not experienced physical or sexual abuse at all).

Beck Depression Inventory

The German version of the BDI-II was used to assess maternal depression symptoms within the past 2 weeks via self-report [43] at T1, T2, T3, and T4. The BDI-II consists of 21 items (answered on a four-point Likert scale from zero to three), which are summed up to a total score (possible range: 0–63). A total score of zero to 12 suggests no depressive symptomatology, 13–19 suggests mild, 20–28 moderate, and 26–63 severe depressive symptomatology. In the present study, the internal consistency, as assessed by Cronbach's alpha, was acceptable to good ($\alpha = 0.795$). To examine the effects of early versus late maternal depression, BDI T1, T2, and T3 values were averaged as a measure of early depression (BDI_{T1-T3}), whereas BDI T4 scores served as a measure of late or ongoing depression. A bivariate correlation analysis revealed a strong, significant correlation between the three averaged time points (T1, T2, and T3; the correlation of maternal BDI scores at the different time points was between $r = 0.47$ and $r = 0.66$).

Strengths and Difficulties Questionnaire

The Strengths and Difficulties Questionnaire (SDQ) [44, 45] is a behavioural screening questionnaire that consists of 25 items and was assessed only at T4 by the mother and the child's teacher. For the present study, two different versions were used depending on the age of the child (2–4-year-old vs. 4–17-year-old). The 25 items are answered on three-point Likert scales (0 = "not true," 1 = "somewhat true," 2 = "certainly true") and assigned to five subscales with five items each: emotional problems, behavioural problems, hyperactivity, behavioural problems with peers, and prosocial behaviour. For the current analysis, only the emotional and behavioural problems' subscales were included to provide a measure of internalizing and externalizing problem behaviour, respectively. The subscales' scores can be categorized as "normal" (emotional problems = <5, behavioural problems = <3), "on the borderline" (emotional problems = 5, behavioural problems = 3), or "abnormal" (emotional problems = >5, behavioural problems = >4). Cronbach's alpha was acceptable to good both for the teacher report (emotional problems: $\alpha = 0.684$; behavioural problems: $\alpha = 0.714$) and for the parent report (emotional problems: 0.713; behavioural problems: $\alpha = 0.614$).

Child Abuse Potential Inventory

The German version of the CAPI is a factor-analytically abbreviated and newly validated version of the CAPI by Milner [46]. It includes a 63-item self-report screening tool for the detection of

child abuse that is answered in an agree/disagree, forced-choice format. The CAPI records the degree of stress faced by parents as an indicator of the extent of possible risk to the child's well-being. The procedure is divided into a primary clinical scale for recording the parental stress level and three validity scales for recording specific tendencies of response bias (social desirability, unreflected response behaviour, inconsistent response behaviour). In the current study, five subjects exceeded the cut-off for the validity scales. Excluding the participants did not change any of the main results, thus, results are reported for the complete sample. The raw values can then be converted into *T* values (for risk and non-risk samples) using norm tables. *T* scores were included in all analyses for the current study. Cronbach's alpha for the parental stress scale of the German version of the CAPI was good ($\alpha = 0.882$) in the present sample.

Statistical Analysis

Data analyses were conducted in IBM SPSS Statistics 25 (IBM corp., Armonk, NY, USA). All statistical tests were two-tailed, and *p* values <0.05 were considered statistically significant.

Due to the longitudinal design and inclusion of different raters, there were missing data (see Table 2). Missing data analyses were conducted to map the amount and pattern of missing data. For all measures, the patterns of missing data were completely random at all measurement time points, as indicated by little's MCAR test. Missing values were imputed using MI, which has been shown to be beneficial even if the number of missing values, especially in the outcome variable, is high [47, 48]. Based on the recommendation by Asendorf et al. [49], 20 datasets were imputed. These were then recombined into one single dataset in which each missing value was replaced by the average of the $n = 20$ imputed values.

To address our main research questions, serial mediation analyses were run using the PROCESS macro for SPSS [50] (for a similar approach, see [51]) to explore whether the link between maternal ELM experiences and children's internalizing and externalizing problem behaviour was mediated by early or late maternal depression as well as by the child's abuse potential. The independent variables were the maternal mental abuse and physical and sexual abuse scales of the CECA.Q. Mediator variables were the BDI-II T1–T3 (mediator 1, M1), BDI-II T4 (mediator 2, M2), and the CAPI measured at T4 (mediator 3, M3). Dependent variables were the teacher and maternal ratings on the SDQ, measured at T4 (see Fig. 1). In total, eight models were calculated, four for the CECA.Q mental abuse scale and all four possible dependent variables (SDQ emotional problem and behavioural problem scales for teachers and parents) and four for the CECA.Q physical/sexual abuse scale and all four dependent variables. Indirect effects were tested by bias-corrected bootstrapping of the 95% confidence interval ($n = 5,000$ runs). A post hoc power analysis revealed a satisfactory power of 81% for the current study (parameters: $\alpha = 0.05$, total sample size = 99, number of predictors = 6, effect size $f^2 = 0.15$).

Results

Descriptive Analyses

Descriptive statistics for the entire sample are presented in Table 1. Overall, 43% of all mothers reported any

Fig. 1. Mediation model with maternal depression and child abuse potential as mediators.

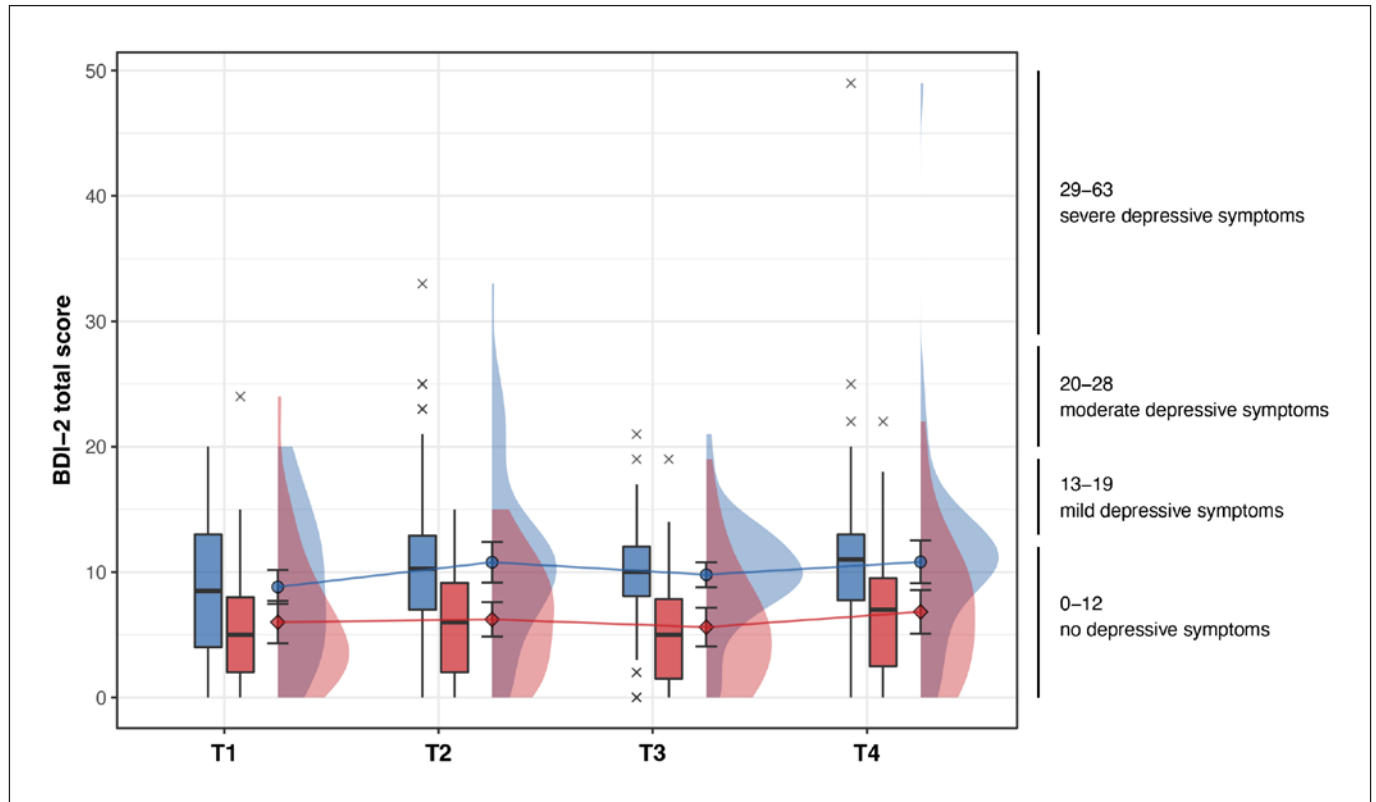
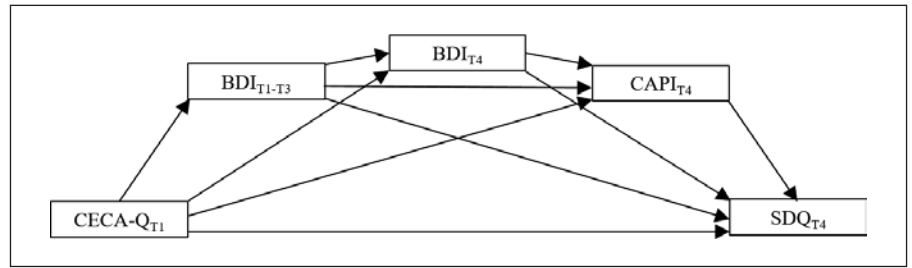


Fig. 2. Visualization of the course of depressive symptoms (as assessed by the BDI-II) for all assessments and separately for adolescent versus adult mothers. Red, adolescent mothers; blue, adult mothers.

type of ELM. Nineteen percent reported two or three types and 24% reported one type of ELM. Nineteen to 22% of all mothers reported at least mild depressive symptoms between T1 and T4. According to teacher ratings, 3% of all children had clinically relevant emotional problems and approximately 9% had clinically relevant behavioural problems. In contrast, according to the maternal ratings, 45.4% of the children scored in the borderline or abnormal SDQ ranges for emotional problems and 54.5% for behavioural problems.

Adolescent versus Adult Mothers

Adolescent mothers reported retrospectively that they had experienced more mental abuse by their mothers ($t(97) = 2.61, p = 0.011, d = -0.512$), whereas the amount of mental abuse by fathers and the amount of physical and sexual abuse did not differ between age groups (mental abuse by fathers: ($t(97) = 0.99, p = 0.325$); physical/sexual abuse: ($t(97) = 1.55, p = 0.125$)). The number of mothers who had clinically relevant BDI-II scores can be found in Table 1 and is visualized in Figure 2. The differences in symptom expression for adolescent versus adult mothers

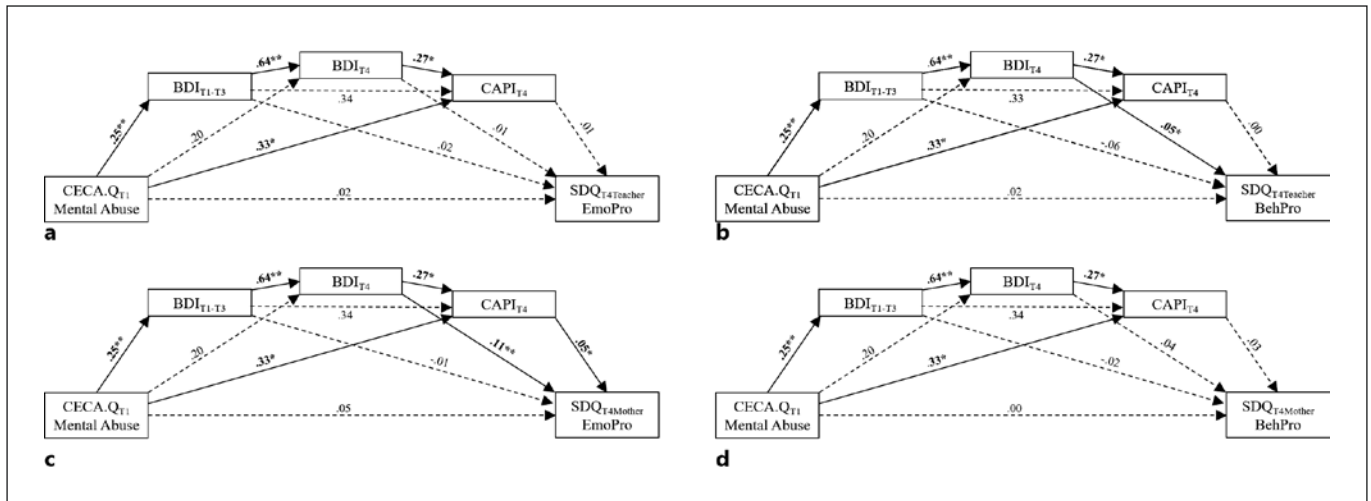


Fig. 3. a Serial mediation model for the relationship between maternal early life maltreatment, namely parental mental abuse and the offspring’s emotional problem behavior (EmoPro) rated by teachers. Mediators include early maternal depression (mediator 1; BDI_{T1-T3}), later maternal depression (mediator 2; BDI_{T4}) and child’s abuse potential (mediator 3; CAPI_{T4}). Unstandardized coefficients are depicted. * $p < 0.05$, ** $p < 0.01$. Overall model significance R^2 for model **a** was 0.05. **b** Serial mediation model for the relationship between maternal early life maltreatment, namely parental mental abuse and the offspring’s behavioral problems (BehPro) rated by teachers. Mediators include early maternal depression (mediator 1; BDI_{T1-T3}), later maternal depression (mediator 2; BDI_{T4}) and child’s abuse potential (mediator 3; CAPI_{T4}). Unstandardized coefficients are depicted. * $p < 0.05$, ** $p < 0.01$. Overall model significance R^2 for model **b** was 0.21. **c** Serial me-

diation model for the relationship between maternal early life maltreatment, namely parental mental abuse and the offspring’s emotional problem behavior (EmoPro) rated by mothers. Mediators include early maternal depression (mediator 1; BDI_{T1-T3}), later maternal depression (mediator 2; BDI_{T4}) and child’s abuse potential (mediator 3; CAPI_{T4}). Unstandardized coefficients are depicted. * $p < 0.05$, ** $p < 0.01$. Overall model significance R^2 for model **c** was 0.30. **d** Serial mediation model for the relationship between maternal early life maltreatment, namely parental mental abuse and the offspring’s behavioral problems (BehPro) rated by mothers. Mediators include early maternal depression (mediator 1; BDI_{T1-T3}), later maternal depression (mediator 2; BDI_{T4}) and child’s abuse potential (mediator 3; CAPI_{T4}). Unstandardized coefficients are depicted. * $p < 0.05$, ** $p < 0.01$. Overall model significance R^2 for model **d** was 0.05.

were significant for all four assessments; adolescent mothers had higher BDI-II scores, indicating more depressive symptomatology. A repeated-measures ANOVA revealed only a significant group effect with adolescent mothers having higher BDI-II scores than adult mothers across all time points ($F(1, 97) = 19.42, p < 0.001, \eta^2 = 0.16$).

Parents versus Teacher Reports

Parent and teacher reports for the child’s emotional ($r = 0.17, p = 0.09$) and behavioural problems ($r = -0.04, p = 0.70$) were not significantly associated with each other. However, teacher reports for the child’s behavioural and emotional problems correlated positively with each other ($r = 0.37, p < 0.001$), which was not the case for the maternal reports of their children’s difficulties. Teacher reports significantly differed between children of adolescent and adult mothers with respect to the behavioural problem scale ($t(97) = 3.43, p = 0.001, d = -0.794$), but not for the emotional problem scale ($t(97) = 1.13, p = 0.262$).

Children of adolescent mothers were rated higher by the teacher on the SDQ behavioural problem scale indicating more problem behaviour. For the maternal reports, on the other hand, there was a significant difference between children of adolescent and adult mothers for the emotional problem scale ($t(97) = 2.57, p = 0.012, d = -0.391$), but not for the behavioural problem scale ($t(97) = 2.57, p = 0.012, d = -0.542$), with children of adolescent mothers being rated higher on the emotional problem scale.

Mediation Analysis

We ran eight mediation analyses to explore whether the links between maternal ELM experiences and the child’s internalizing and externalizing problem behaviour were mediated by early (within the first 2 years after the child’s birth) or later maternal depressive symptoms as well as maternal child abuse potential. Analyses were conducted with maternal age (adolescent vs. adult mothers) as a covariate to control for maternal age. The cor-

Table 3. Pearson correlations for the SDQ subscales with the main study variables

	Emotional problems teacher	Behavioural problems teacher	Emotional problems mother	Behavioural problems mother
CECA.Q _{mental abuse}	0.178	0.194	0.214*	0.030
CECA.Q _{physical/sexual abuse}	0.083	0.061	0.124	0.006
BDI T1–T3	0.176	0.103	0.317**	0.075
BDI T4	0.154	0.303**	0.510**	0.184
CAPI	0.103	0.142	0.358**	0.166

EmoPro, emotional problems on SDQ; BehPro, behavioural problems on SDQ; BDI, Beck Depression Inventory; CECA.Q, Childhood Experience of Care and Abuse Questionnaire; CAPI, Child Abuse Potential Inventory; SDQ, Strengths and Difficulties Questionnaire. * $p < 0.05$. ** $p < 0.01$.

Table 4. Overview of all statistical results for mediation analysis

	Emotional problems teacher		Behavioural problems teacher		Emotional problems mother		Behavioural problems mother	
	<i>b</i>	95% CI	<i>b</i>	95% CI	<i>B</i>	95% CI	<i>b</i>	95% CI
Mental abuse								
Total effect	0.01	−0.007; 0.030	0.00	−0.015; 0.024	0.06	0.015; 0.122	0.02	−0.012; 0.057
Direct effect	0.02	−0.022; 0.055	0.02	−0.020; 0.057	−0.01	−0.074; 0.114	−0.02	−0.077; 0.038
Indirect effect 1	0.00	−0.012; 0.021	−0.01	−0.033; 0.000	−0.00	−0.038; 0.018	−0.01	−0.029; 0.016
Indirect effect 2	0.00	−0.013; 0.024	0.01	−0.001; 0.026	0.02	−0.002; 0.054	0.01	−0.007; 0.028
Indirect effect 3	0.00	−0.006; 0.009	0.00	−0.012; 0.013	0.02	−0.002; 0.046	0.01	−0.008; 0.031
Indirect effect 4	0.00	−0.003; 0.009	0.01	0.001; 0.019	0.02	0.002; 0.045	0.01	−0.005; 0.022
Indirect effect 5	0.00	−0.004; 0.004	0.00	−0.004; 0.004	0.00	−0.001; 0.013	0.00	−0.002; 0.010
Indirect effect 6	0.00	−0.001; 0.004	0.00	−0.003; 0.003	0.00	−0.001; 0.010	0.00	−0.002; 0.007
Indirect effect 7	0.00	−0.002; 0.003	0.00	−0.002; 0.002	0.00	−0.001; 0.009	0.00	−0.001; 0.006
Physical and/or sexual abuse								
Total effect	0.19	−0.096; 0.532	0.13	−0.160; 0.441	0.98	0.113; 2.278	0.26	−0.247; 0.994
Direct effect	0.11	−0.856; 1.084	−0.10	−1.069; 0.871	−0.24	−1.789; 1.315	−0.29	−1.735; 1.152
Indirect effect 1	0.09	−0.291; 0.409	−0.26	−0.651; 0.063	−0.05	−0.733; 0.438	−0.12	−0.563; 0.355
Indirect effect 2	0.03	−0.138; 0.186	0.19	−0.019; 0.544	0.44	−0.067; 1.320	0.14	−0.110; 0.720
Indirect effect 3	−0.01	−0.149; 0.155	−0.00	−0.095; 0.161	−0.03	−0.331; 0.367	−0.01	−0.196; 0.247
Indirect effect 4	0.03	−0.068; 0.225	0.17	0.018; 0.441	0.39	0.037; 1.027	0.13	−0.147; 0.457
Indirect effect 5	0.03	−0.085; 0.114	0.01	−0.081; 0.112	0.11	−0.015; 0.322	0.06	−0.069; 0.233
Indirect effect 6	0.01	−0.044; 0.116	0.01	−0.050; 0.090	0.06	−0.022; 0.260	0.03	−0.058; 0.144
Indirect effect 7	0.01	−0.043; 0.087	0.01	−0.048; 0.062	0.05	−0.006; 0.223	0.03	−0.038; 0.147

Results written in bold are statistically significant with at least a $p < 0.05$.

relations of the SDQ scales with the main study variables can be found in Table 3. The effects reported below are visualized in Figure 3a–d (models 1–4 with maternal mental abuse) and Figure 4a–d (models 5–8 with maternal physical and/or sexual abuse).

For model 1 (Fig. 3a) and model 4 (Fig. 3d), all indirect mediation pathways were not significant (Table 4). However, mental abuse was significantly associated with early

maternal depressive symptoms (averaged across T1–T3) ($b = 0.25$; 95% CI [0.117; 0.392], $p = 0.000$) and child abuse potential at T4 ($b = 0.33$; 95% CI [0.077; 0.580], $p = 0.011$). Early maternal depression was strongly associated with later maternal depression ($b = 0.64$; 95% CI [0.356; 0.933], $p = 0.000$). Additionally, later (T4) ($b = 0.27$; 95% CI [0.031; 0.512], $p = 0.028$), but not early maternal depressive symptoms ($b = 0.34$; 95% CI [−0.034; 0.712]) were

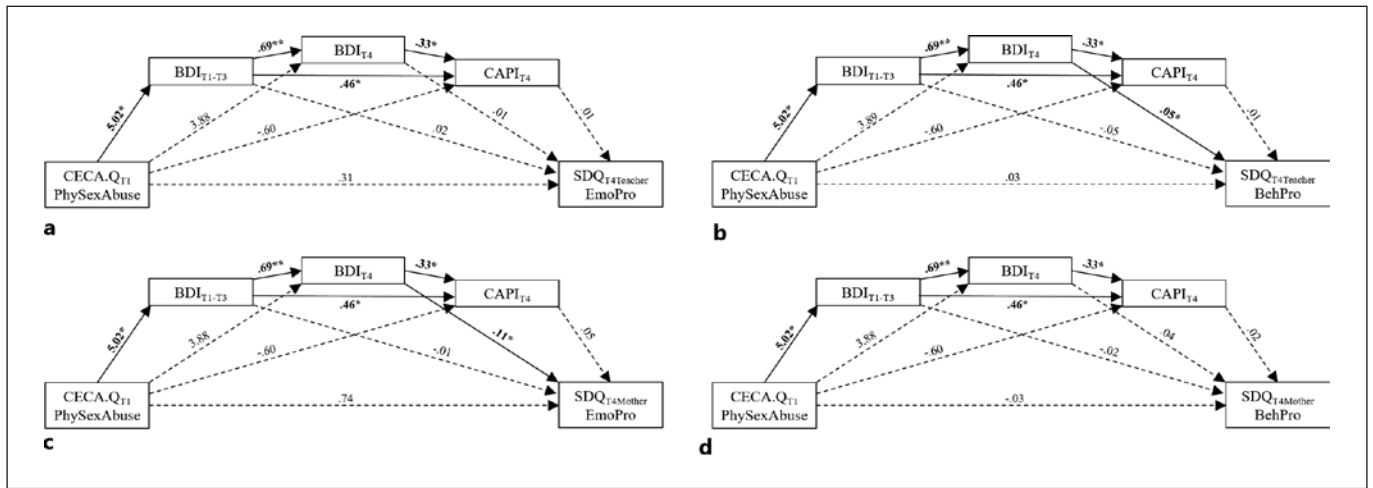


Fig. 4. **a** Serial mediation model for the relationship between maternal early life maltreatment, namely physical and sexual abuse (PhySexAbuse), and the offspring's emotional problem behavior (EmoPro) rated by teachers. Mediators include early maternal depression (mediator 1; BDI_{T1-T3}), later maternal depression (mediator 2; BDI_{T4}) and child's abuse potential (mediator 3; CAPI_{T4}). Unstandardized coefficients are depicted. * $p < 0.05$, ** $p < 0.001$. Overall model significance R^2 for model **a** was 0.13. **b** Serial mediation model for the relationship between maternal early life maltreatment, namely physical and sexual abuse (PhySexAbuse), and the offspring's behavioral problems (BehPro) rated by teachers. Mediators include early maternal depression (mediator 1; BDI_{T1-T3}), later maternal depression (mediator 2; BDI_{T4}) and child's abuse potential (mediator 3; CAPI_{T4}). Unstandardized coefficients are depicted. * $p < 0.05$, ** $p < 0.01$. Overall model significance R^2 for model **b** was 0.12. **c** Serial mediation model for the

relationship between maternal early life maltreatment, namely physical and sexual abuse (PhySexAbuse), and the offspring's emotional problem behavior (EmoPro) rated by mothers. Mediators include early maternal depression (mediator 1; BDI_{T1-T3}), later maternal depression (mediator 2; BDI_{T4}) and child's abuse potential (mediator 3; CAPI_{T4}). Unstandardized coefficients are depicted. * $p < 0.05$, ** $p < 0.01$. Overall model significance R^2 for model **c** was 0.30. **d** Serial mediation models for the relationship between maternal early life maltreatment, namely physical and sexual abuse (PhySexAbuse), and the offspring's behavioral problems (BehPro) rated by mothers. Mediators include early maternal depression (mediator 1; BDI_{T1-T3}), later maternal depression (mediator 2; BDI_{T4}) and child's abuse potential (mediator 3; CAPI_{T4}). Unstandardized coefficients are depicted. * $p < 0.05$, ** $p < 0.01$. Overall model significance R^2 for model **d** was 0.07.

significantly associated with child abuse potential at T4. All other mediation pathways were not significant (Table 4).

For model 2 (Fig. 3b), indirect effect four (see Fig. 5) of mental abuse on the child's behavioural problems assessed by the teacher ratings ($b_{\text{indirect}4} = 0.01$; 95% CI [0.001; 0.019]) was significant in the full model. All other mediation pathways were not significant (Table 4). Analogous to models 1 and 4, additionally mental abuse ($b = 0.33$; 95% CI [0.077; 0.580], $p = 0.011$) and later (T4) maternal depression ($b = 0.27$; 95% CI [0.031; 0.511], $p = 0.028$), but not early depressive symptoms ($b = 0.34$; 95% CI [-0.034; 0.712]), were significantly associated with child abuse potential at T4.

For model 3 (Fig. 3c), again, indirect effect four (see Fig. 5) of mental abuse on the child's behavioural problems assessed by the mother's ratings ($b_{\text{indirect}4} = 0.01$; 95% CI [0.001; 0.019]) was significant in the full model. Furthermore, the total effect of maternal ELM (mental abuse)

on the child's emotional problems, rated by the mother, was significant ($b_{\text{total}} = 0.06$; 95% CI [0.015; 0.122]). All other mediation pathways were not significant (Table 4). Analogous to models 1, 2, and 4, mental abuse ($b = 0.33$; 95% CI [0.077; 0.580], $p = 0.011$) and later (T4) maternal depression ($b = 0.27$; 95% CI [0.031; 0.511], $p = 0.028$), but not early depressive symptoms ($b = 0.34$; 95% CI [-0.034; 0.712]) were significantly associated with child abuse potential at T4. Additionally, child abuse potential at T4 was significantly associated with child's emotional problems rated by the mothers ($b = 0.05$; 95% CI [0.001; 0.098], $p = 0.046$).

For model 5 (Fig. 4a) and model 8 (Fig. 4d), all indirect mediation pathways were not significant (Table 4). However, physical and/or sexual abuse was significantly associated with early ($b = 5.02$; 95% CI [1.166; 0.8.872], $p = 0.011$), but not with later maternal depressive symptoms ($b = 3.88$; 95% CI [-1.664; 0.9.424]). Early maternal depression was strongly associated with later mater-

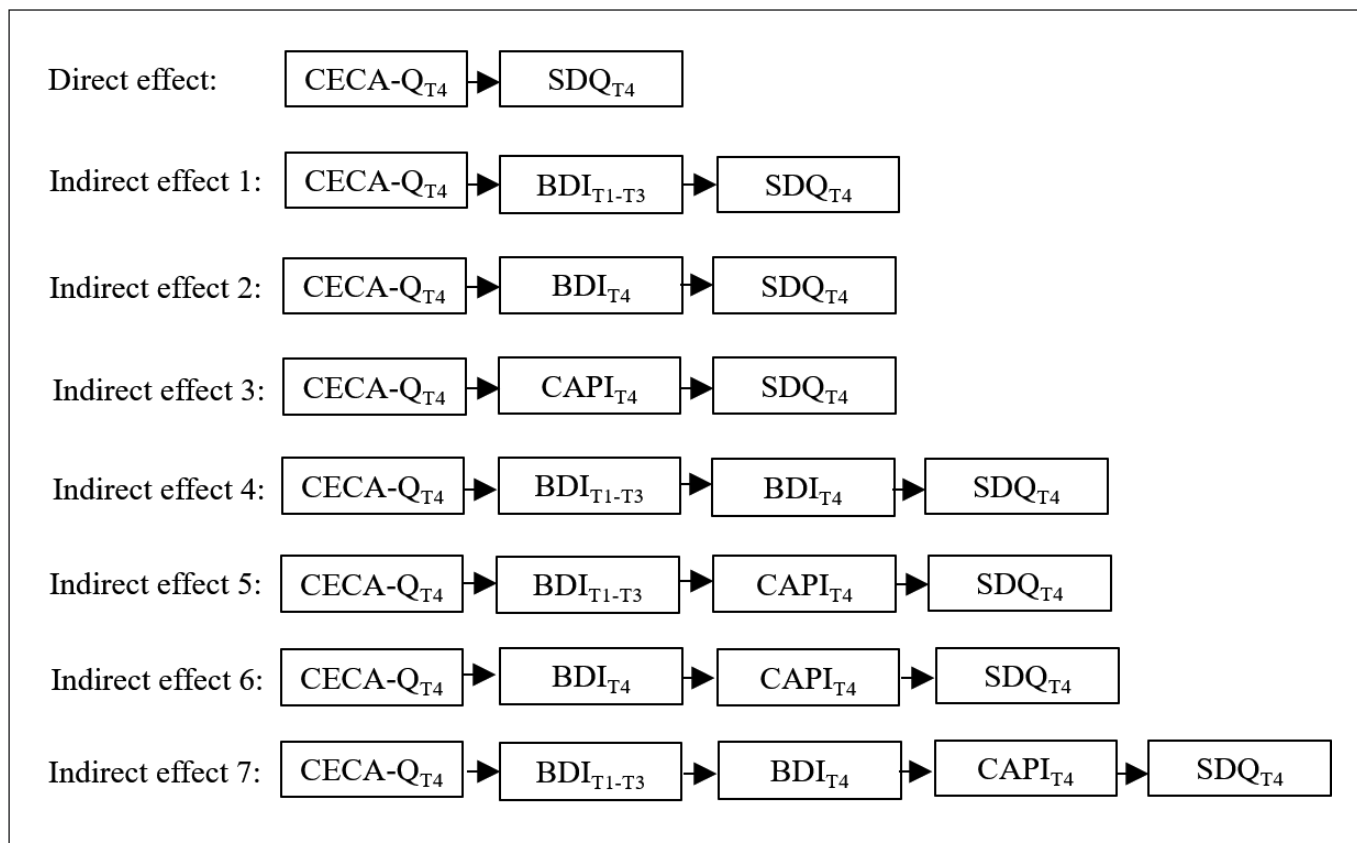


Fig. 5. Visualization of direct and indirect mediation pathways.

nal depression ($b = 0.69$; 95% CI [0.412; 0.974], $p = 0.000$). In contrast to models 1–4, physical and/or sexual abuse was not associated with child abuse potential at T4 ($b = -0.60$; 95% CI [-7.368; 6.163]) but early ($b = 0.46$; 95% CI [0.077; 0.838], $p = 0.019$) and late maternal ($b = 0.33$; 95% CI [0.089; 0.581], $p = 0.008$) depression were. All other mediation pathways were not significant (Table 4).

Analogous to the models for mental abuse, for model 6 (Fig. 4b), indirect effect four (see Fig. 5) of physical and/or sexual abuse on children’s behavioural problems assessed by teacher ratings ($b_{\text{indirect4}} = 0.17$; 95% CI [0.018; 0.441]) was significant in the full model. All other mediation pathways were not significant (Table 4). Additionally, early ($b = 0.46$; 95% CI [0.077; 0.838], $p = 0.019$) and later maternal depression ($b = 0.33$; 95% CI [0.089; 0.581], $p = 0.008$) were significantly associated with child abuse potential at T4.

For model 7 (Fig. 4c), indirect effect four (see Fig. 5) of physical and/or sexual abuse on children’s emotional problems assessed by the maternal ratings ($b_{\text{indirect4}} =$

0.39; 95% CI [0.037; 1.027]) was significant in the full model. Furthermore, the total effect of maternal ELM (physical and/or sexual abuse) on the child’s emotional problems, rated by the mother, was significant ($b_{\text{total}} = 0.98$; 95% CI [0.113; 2.278]). All other mediation pathways were not significant (Table 4). Additionally, early ($b = 0.46$; 95% CI [0.077; 0.838], $p = 0.019$) and later maternal depression ($b = 0.33$; 95% CI [0.089; 0.581], $p = 0.008$) were significantly associated with child abuse potential at T4.

Discussion

Regarding *Research Question 1* (What are the effects of early vs. later maternal depressive symptoms on child psychopathology?), we hypothesized that postpartum depression followed by later maternal depression plays a mediating role in the intergenerational transmission of maltreatment and psychopathology. As expected, maternal depressive symptoms mediated the transgenerational

transmission of child neglect and abuse accompanied by increased emotional and behavioural problems in the offspring. The latter, however, depended on the rater. Examining *Research Question 1*, substantial differences in early versus late maternal depressive symptoms and their mediating role in the relationship between maternal childhood maltreatment and negative developmental outcomes in the next generation were found. Regardless of the maltreatment type and the child's outcome, early maternal depressive symptoms of the mother were a risk factor only for later maternal depressive symptoms and were not directly linked with the child's development. However, later occurring depressive symptoms in mothers were directly related to increased behavioural or emotional problem behaviour in the child, as well as to a heightened potential for child abuse. This finding is contrary to the sensitive window hypothesis [19, 32] and in line with more recent research [21, 22, 33]. Wiersma et al. [52] found that the chronicity of depression was associated with a higher prevalence of childhood trauma. Furthermore, there is already consistent evidence that current depressive episodes are well-predicted by earlier depressive episodes [53]. Our findings are in line with these previous studies showing that even in samples with maximally mild to moderate depressive symptoms, ELM was a predictor for depressive symptom expressions in mothers across all time points (after delivery until the child's preschool years). In addition, we also found evidence in the current sample for high stability of BDI scores across the four time points. However, later or chronic maternal depressive symptoms, possibly beginning during the sensitive window, were found to have the strongest effects on the development of externalizing and internalizing problem behaviour in offspring. Such strong effects might be explained by "more concurrent" assessments of mother's and child's psychopathology at T4. Second, it could be that cumulative maternal depressive symptoms are especially harmful to the development of the child. An additional explanation would be that early depressive symptoms harm early child development but that this is sustainable only if ongoing depression occurs [33]. The results imply that not only postpartum depression but also ongoing maternal depression is an important risk factor for child psychopathology. At present, ongoing maternal depression is usually treated in isolation from the child, if at all, as part of individual psychotherapy or pharmacotherapy. Since maternal depression has a major impact on parenting skills [54], this study's findings should be taken into account in future intervention programs.

Regarding *Research Question 2* (Are the consequences of ELM and maternal depression for child development

specific in the sense that they tend to contribute to internalizing or externalizing problem behaviour?), we hypothesized that the effects were rather unspecific. A specific link between ELM, maternal depressive symptoms, and the development of either externalizing or internalizing symptoms in the next generation could not be clearly identified. As expected, our results were strongly dependent on the rater of the child's SDQ. In a previous systematic review, associations between maternal ELM and all three domains of the child's problem behaviour (total, externalizing, and internalizing problems) were found [32]. Thus, it seems as if ELM has rather unspecific effects on the development of internalizing and externalizing symptoms in the next generation. However, interestingly, the rater-dependent patterns observed in our study (pathway to externalizing symptoms significant only in teacher ratings and vice versa for emotional problems based only on maternal reports) were identical to those previously reported in the large twin study [33]. Thus, such differential pathways might result from the fact that externalizing symptoms are much more obvious across different settings, while mothers may be more likely than teachers to observe subtle internalizing symptoms of their children in daily life at home. Of note, mothers rated their child's behaviour as clinically abnormal more often than teachers did. This finding could be explained by the fact that more depressed mothers were more stressed and had fewer resources in everyday dealings with their children due to their own depressive symptomatology. As a result, their ratings of their child's behaviour might have been biased and shifted towards clinically abnormal rating scores [36]. The teachers, on the other hand, rated the children's behaviour as less clinically abnormal, especially with respect to emotional problems. In contrast to mothers with high levels of ELM, trained teachers may have more resources to deal with sometimes difficult but age-appropriate behaviour patterns of the children. However, it could also be that internalizing problems may be more easily overlooked by the teachers, since children with internalizing problems typically have fewer demands on pedagogical guidance and, thus, emotional problems are known to be under-reported in educational contexts [55]. This also fits well with the high association between the teachers' ratings of the child's emotional and externalizing problem behaviours, indicating a rather "global and less differential rating" reflected in teacher ratings of preschool-aged children. However, the link between internalizing problems rated by the mothers might possibly be overestimated due to a genetically determined transmission of internalizing psychopathology from generation to generation [56].

Regarding *Research Question 3* (Do different types of maternal childhood maltreatment contribute to specific developmental outcomes?), we hypothesized that both types are risk factors for the study variables (maternal depression independent of timing, child abuse potential, and child psychopathology) in the model, with mental abuse being particularly harmful. We analysed two different subtypes of maltreatment (mental vs. physical/sexual abuse) and found that both were associated with maternal depressive symptoms indicating that ELM represents a significant risk factor for depression, independent of the type of ELM. However, interestingly, mental abuse affected existing risk factors more directly over time. For instance, mental abuse was linked to early depressive symptoms in mothers as well as to increased child abuse potential later in life, whereas physical and sexual abuse in mothers had primarily direct effects on early maternal depression and only indirect effects on the other risk factors, which can still be considered as meaningful. The former finding illustrates that it might indeed be very hard to break the cycle of transgenerational transmission via prevention and intervention programs targeting primarily maternal depression. This also suggests that experiences of mental abuse in childhood might be even more harmful in the intergenerational transmission of maltreatment, which is also in line with Infurna et al. [30], who conducted a meta-analysis to examine the specific effects of various types of childhood abuse and neglect on depression. Although only studies with clinically relevant depressive disorders were considered in the meta-analyses, the results also confirmed that psychological abuse and neglect were most strongly associated with the outcome of depression, while sexual abuse, although significant, was less strongly related.

Strength and Limitations

By addressing the impact of early versus late maternal depressive symptoms on intergenerational transmission processes, the current findings contributed new insights into vulnerable periods, challenging the sensitive window hypothesis. The longitudinal study design allowed us to examine maternal depressive symptoms over the first 4 years of the child and their consequences on the child's development. In contrast to previous studies [33], dimensional measures of maternal depression and the child's problem behaviour symptoms (the latter based on two raters) were taken into account, resulting in differentiated pathways across the whole spectrum of normal and deviant symptomatology. Regardless of this study's strength, several limitations may be considered. First, the BDI-II can overestimate maternal depression in the postnatal period [57], but postpartum-specific measures such as the

“Edinburgh Postnatal Depression Scale” (EPDS) were not available for this study. Second, our sample, although including a high-risk group of adolescent mothers, might not be representative of other dyads at risk (e.g., it included only Caucasian mothers); thus, our findings require replication in independent samples. Second, although MIs have been shown to be beneficial compared to analyses of incomplete longitudinal datasets [48], high amounts of missing data can still be seen as a limitation [58]. Third, although we included high-risk dyads, some of our ratings showed limited variance (e.g., the teacher ratings for the child's emotional problems), limiting the power to detect significant associations and to identify relevant predictors of developmental outcomes. Maternal ELM was assessed using retrospective instruments, which could lead to under-reporting [59], although CECA.Q in general shows good psychometric criteria [60]. Furthermore, there was a potential bias since mothers reported on their own ELM, depression, and later risk for child abuse [61]. Therefore, future studies should aim to assess risk factors via more objective diagnostic instruments. In addition to the type of ELM, the severity and frequency of ELM should be considered to more accurately predict negative outcomes across generations. However, it is very difficult to assess ELM precisely in a maltreatment type-, time-, and severity-specific manner by using retrospective self-report measures (see Teicher and Parigger [62] for a more extensive discussion). Furthermore, future research would benefit from even more detailed analyses including not only different types of ELM but also its severity and frequency, a variety of maternal mental health issues and their characteristics as well as possible resilience and protective factors.

Conclusion

The present findings suggest that early maternal depression, especially when followed by ongoing depressive symptomatology, plays a mediating role in the intergenerational cycle of maltreatment. Mothers with ELM experiences are at an increased risk for depression after childbirth and later in life. The offspring are exposed to these risk factors which are accompanied by increased abuse potential and increased risk of developing internalizing and externalizing problem behaviours. Therefore, interventions should be offered at an early stage but should also go far beyond the child's first 2 years of life. Additionally, to interrupt the intergenerational cycle of maltreatment, future interventions should address both depression and trauma, since mental abuse was a direct predictor of an increased potential for child abuse.

Acknowledgements

This study was performed within the consortium of UBICA (Understanding and Breaking the Intergenerational Cycle of Abuse) – a research association for investigating the influence of maternal early trauma, neglect, and abuse on child development. The authors would like to thank the participants and all researchers involved in the data collection, in particular Lea Jahnen.

Statement of Ethics

The study protocol was approved in accordance with the World Medical Association Declaration of Helsinki by an independent Ethics Committee of the Medical Faculty of RWTH Aachen University (EK144/12). Written informed consent was obtained from participants, their parents, or legal guardian. The trial is registered at German Clinical Trials Register, number (1). Full details of the trial protocol can be found at https://www.drks.de/drks_web/.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Funding Sources

This study is financially supported by a grant awarded to B.H.-D. and K.K. by the German Ministry for Research and Education (BMBF No. 01KR1207B and 01KR1803A). The study is further sponsored by the Clinical Trials Center Aachen (CTC-A). The sponsor and funding source had no role in the design of the study and will not have any role during its execution analyses, interpretation of the data, or decision to submit results.

Author Contributions

K.K. and B.H.-D. conceived the research project and acquired funding. D.D., C.F., and B.D. contributed to the data collection and study administration. D.D. analysed the data with support of V.R. and C.B. and wrote the manuscript with support of K.K. and V.R. All authors have discussed the results and have revised the manuscript.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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