Research paper

Maternal perinatal depressive symptoms trajectories and impact on toddler behavior – the importance of symptom duration and maternal bonding

Emma Fransson[a,b,#,*], Ferdinand Sörensen[c,d,#], Theodora Kunovac Kallak[a], Mia Ramklint[e], Patricia Eckerdal[a], Magdalena Heimgärtner[c], Ingeborg Krägeloh-Mann[c], Alkistis Skalkidou[a]

[a] Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden
[b] Department of Microbiology, Tumor and Cell Biology, Karolinska Institutet, Stockholm, Sweden
[c] Pediatric Neurology & Developmental Medicine, University Children's Hospital Tübingen, Germany
[d] Eberhard Karls University Tübingen, Werner Reichardt Centre for Integrative Neuroscience, Germany
[e] Department of Neuroscience, Psychiatry, Uppsala University, Uppsala, Sweden

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ABSTRACT

Background: Maternal perinatal depression is a public health problem affecting mothers and children worldwide. This study aimed to increase the knowledge regarding the impact of timing of maternal depression on child behavioral difficulties at 18 months, taking into consideration child gender and maternal bonding.

Methods: Data from a Swedish population-based longitudinal mother-infant study (n = 1,093) were used for linear regression modeling. Associations between antenatal depression, postpartum depression, persistent depression and child behavioral problems were assessed.

Results: Maternal antenatal and persistent depression were associated with higher Child Behavior Checklist scores. Girls were affected to a greater degree. Postpartum bonding mediated most of the negative effects of postpartum and persistent depression on child behavior; not the effects of antenatal depression, however.

Limitations: Child behavioral problems were reported by the mother. Information regarding paternal depressive symptoms was lacking.

Conclusion: Different onset and timing of maternal depression showed distinct associations with child behavioral problems. The effects of antenatal depression were not mediated by maternal bonding, indicating underlying mechanisms possibly related to fetal programming. Screening of depressive symptoms even during pregnancy would be important in routine care in order to early identify and treat depression.

1. Introduction

Increasing numbers of children and youths seek psychiatric care; worldwide, 10–20% of children and adolescents currently experience mental disorders (WHO, 2018). Antenatal and neonatal complications are established risk factors for the development of child psychopathology, representing somatic and intrauterine environmental factors (Boney et al., 2005), as well as parental psychological factors (Glover, 2014; Stein et al., 2014).

Maternal perinatal depression is a common public health problem that affects not only mothers worldwide, but also their children. Antenatal depression prevalence ranges from 4% to 29% (Szegda et al., 2014), and postpartum depression is estimated to affect between 10% and 20% of all mothers (Woody et al., 2017), with about 10–15%

having persistent depressive symptoms during the perinatal period (Denckla et al., 2018). The importance of maternal depressive symptoms for the offspring has been emphasized (Stein et al., 2014) and problems such as insecure attachment, internalizing and externalizing problems, and cognitive difficulties have been reported in offspring of depressed mothers (Goodman et al., 2011; Wolford et al., 2017). In fact, there is evidence that a broad range of negative child outcomes persist into late adolescence (Stein et al., 2014). Sex-specific effects of maternal depression in child development have been indicated in many studies, however, different outcomes are impacted depending on child gender (cf. the meta-analytic review by (Chaplin and Aldao, 2013)), for instance IQ in adolescent boys and emotional problems in adolescent girls (Hay et al., 2008).

More recently, the need to further investigate the complexity of

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Abbreviations

BASIC -	Biology, Affect, Stress, Imaging and Cognition in pregnancy and puerperium;
CBCL -	The Child Behavior Checklist;
EPDS -	Edinburgh Postnatal Depression Scale

maternal depression trajectories, in order to increase the understanding of maternal risk factors and prognosis, has been emphasized (Putnam et al., 2017; Wikman et al., 2019). Variations in depression trajectory regarding time of onset, length, and intensity may also have different consequences for the offspring (Kingsbury et al., 2015; Guyon-Harris et al., 2016; Park et al., 2018). For example, antenatal depression might differ in consequences for the infant compared with depressive symptoms with onset in the postpartum period and is likely to act on distinct mechanistic pathways that affect child development (Stein et al., 2014).

For child psychopathology, increased odds for depression and anxiety in the child have been suggested for offspring of antenatally depressed mothers (e.g. Goodman et al. (2011)), as have symptoms of aggressive or hyperactive behaviors, and conduct disorders (Hay et al., 2011; Wolford et al., 2017). In utero, the environment and the biological pathways are intertwined. Apart from genetic predisposition, maternal antenatal depression could impact on child development through epigenetic, hormonal, immune, and nutrient pathways, many of which could be mediated through placental function (Monk et al., 2012).

Postpartum, the child's environment expands to include physical stimulation, nurture, and interaction with parents and the entire family system. Parental sensitivity has been proposed as an important mechanism for child development (Behrens et al., 2016). Postpartum depression during the first six months has been associated with lower quality of maternal bonding as well as with poor maternal sensitivity (Moehler et al., 2006; Hakanen et al., 2019). Furthermore, maternal postpartum depression has been associated with poor attachment quality in children (for a review, see Lefkovics et al. (2014)). Children of mothers suffering from postpartum depression are also at risk of internalizing and externalizing problems, as well as suboptimal cognitive functioning and delayed language development (Quevedo et al., 2011). Notably, many studies on postpartum depression do not adjust for antenatal depressive symptoms. Overall, there is a need to increase knowledge regarding the associations between different trajectories of depression, parental sensitivity, and child behavioral development. Previous studies have often focused on antenatal or postpartum depression (Stein et al., 2014). In a rather new field for peripartum depression research, distinct depression trajectories have often been based on symptom intensity, rather than timing (Park et al., 2018). Studies investigating depression trajectories as the exposure have thus often used group-based modeling techniques, categorizing depressive symptoms based on their severity levels; symptom onset and its relation to child outcome have been less in focus. To what extent sex differences exist in association with maternal depression trajectories remains unclear.

In this study, the aim was to investigate the association between different maternal depression trajectories (antenatal depression, postpartum depression, both antenatal and postpartum depression (referred to as persistent depression) and no depressive episodes) and early behavioral difficulties in the offspring, assessed at 18 months of age, using data from a population-based mother-infant cohort in Uppsala, Sweden. Secondary aims were to investigate the importance of child gender and the potential mediating role of maternal bonding.
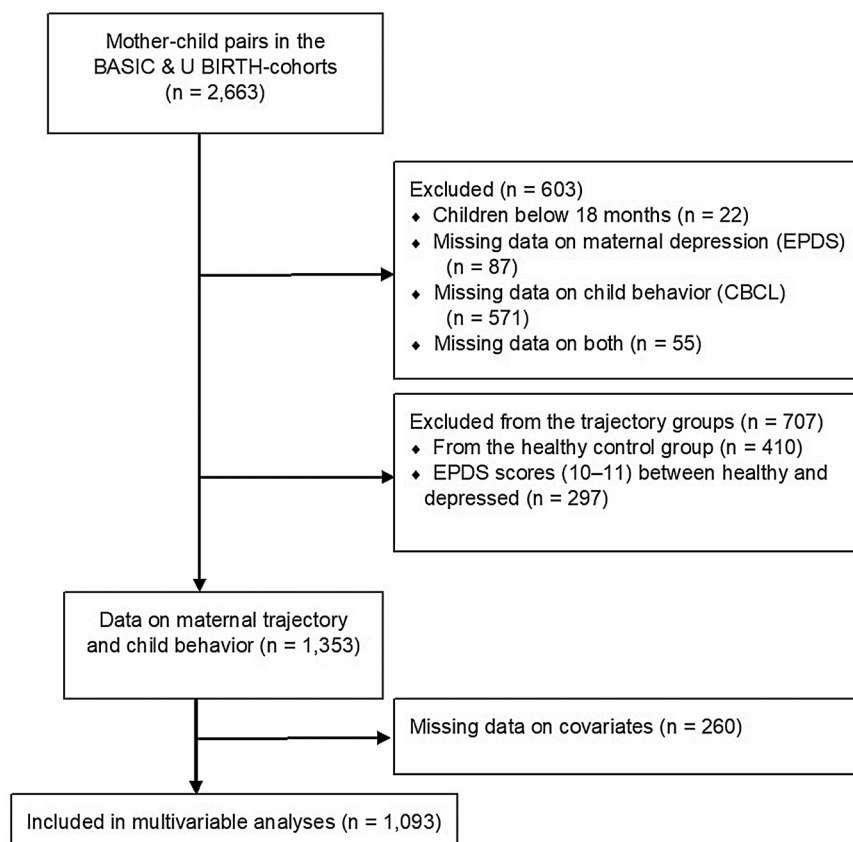

Fig. 1. Overview of the study sample of children and mothers included in the BASIC study, who also agreed to participate in the U BIRTH-follow-up. EPDS = Edinburgh Postnatal Depression Scale. CBCL = Child Behavior Checklist.

2. Method

2.1. Data source and procedures

This study is based on a population-based mother-infant cohort at the Department of Obstetrics and Gynecology at Uppsala University, Sweden; consisting of the cohort from the BASIC Study ("Biology, Affect, Stress, Imaging and Cognition in pregnancy and puerperium") (Axfors et al., 2019), a longitudinal study that started in 2009 to enhance the understanding of peripartum depression, and the child follow-up study (U-BIRTH), which was initiated in 2012.

All Swedish-speaking women over the age of 18 years, who were scheduled for a routine ultrasound at mid-pregnancy at Uppsala University Hospital, received a letter with an invitation to participate in the BASIC study. Women diagnosed with a pathological pregnancy or blood-borne disease, who did not speak Swedish, or who had protected personal data, were excluded. The participation rate was estimated to be 22% of all women giving birth in Uppsala county (Axfors et al., 2019). Participants completed web-based questionnaires during gestational weeks 17 and 32, and postpartum at six weeks, six months, and 12 months. Mothers who consented to participate in the follow-up study (U-BIRTH) received a questionnaire when their child was 18 months old. Participants included in the present study were recruited to the BASIC study from May 2010 to September 2016. A flowchart of the participants is presented in Fig. 1.

3. Measures and instruments

3.1. Maternal measurements

3.1.1. Depressive symptoms

The Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987), a ten-item screening tool for perinatal depressive symptoms, was filled out in gestational weeks 17, 32, and postpartum week six and month six. The EPDS was not included in the 12-month follow-up. Each item is scored from 0 to 3, with total scores ranging from 0 to 30. Scores of ≥ 12 on the EPDS indicate clinically relevant depressive symptoms, as previously validated in Swedish samples, and were used as cut-offs for the analyses (Wickberg and Hwang, 1997). If one out of ten answers on the EPDS was missing, mean imputation was conducted.

A subset of women with a healthy versus a depressed profile, respectively, according to the EDPS, were invited to take part in a sub-study at the research laboratory of the Women's Clinic at the Uppsala University Hospital, in approximately gestational week 38 or at eight weeks postpartum or both. The EPDS was filled out once more, and women were screened using the structured interview Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) by research staff with BASIC training. MINI diagnoses were only available for a subset of participating mothers, during pregnancy (n = 59) and postpartum (n = 94). A depressive episode antenatally was diagnosed in 13 women and postpartum depression in 17 women.

The Depression Self-Rating Scale (DSRS) (Svanborg and Ekselius, 2003), a self-rating scale based on DSM-IV criteria for major depressive disorder, was filled out at 18 months postpartum. Women who were positive on the $A + C$ criteria were considered to suffer from depression (criterion A is specific symptoms of depression; criterion C is impaired function due to depressive symptoms).

3.1.2. Psychological covariates

Anxiety was measured dimensionally. The State-Trait Anxiety Inventory (Spielberger et al., 1983) was used at gestational weeks 17, 32, and six weeks and six months postpartum; for participants answering in 2011–2013, and the Beck Anxiety Inventory (Beck et al., 1988) for answers recorded from 2013. For participants with missing answers, anxiety was calculated using the EPDS anxiety subscale (Jomeen and Martin, 2005). For all three scales, the highest quartile was used as cut-off score and scores in the highest quartile at one time point or more were coded as indicating significant anxiety symptoms.

3.1.3. Socio-demographics and pregnancy-related variables

Maternal sociodemographic data was collected from the web-based questionnaires. At gestational week 17, participants reported their age, country of birth, education, and employment. Participants also reported on their history of depression, as well as providing information about experience of intimate partner violence in current or previous relationships and smoking history. Surveys in postpartum week six and month six included a question on the partner's support with the infant, and questions about stressful life events on the Rosenberg Life Event Scale (Rosengren et al., 1993). Information about pregnancy length and mode of delivery was retrieved from medical records.

3.1.4. Maternal bonding

Participants filled out the Postpartum Bonding Questionnaire (PBQ) (Brockington et al., 2001) at six months postpartum. The PBQ includes 25 questions validated for detection of disorders of the mother-infant relationship, showing high sensitivity for the included constructs (Brockington et al., 2006) and a retest-reliability of 0.95 (Person's product moment correlation coefficient) for the subscales bonding disorders and severe maternal mental disorders; 0.93 for the anxiety subscale and 0.77 for the child abuse subscale (Brockington et al., 2001). The PBQ has been used previously in Scandinavian countries (Høivik et al., 2013). Scores range from 0 to 125, with higher scores indicating more bonding difficulties, as perceived by the mother.

3.2. Child measures

At child age 18 months, participating mothers filled out the Child Behavior Checklist (CBCL) 1½-5 (Achenbach and Rescorla, 2000). The CBCL is used for self-administration by the caregiver(s). It contains 100 questions describing problematic child behavior. The CBCL includes 3 scales: total problem score (0 to 200), internalizing (0 to 72) and externalizing child problems (0 to 48). Higher scores indicate more problematic behavior (Achenbach and Rescorla, 2000). Information about child gender, birth weight, APGAR score at five minutes, and head circumference was retrieved from medical records.

3.3. The depression trajectory measure

Trajectories of maternal depression were determined based on the antenatal or postpartum onset and duration of depressive symptoms during the peripartum period. Significant depressive symptoms were defined as scores above the cut-off ≥ 12 on the EPDS (Murray and Cox, 1990; Wickberg and Hwang, 1997). Participants with scores of 10 and 11 were excluded to enhance diagnostic discriminatory power.

Antenatal depression was defined as EPDS score ≥ 12 at any time point during pregnancy or having a depressive episode, according to MINI, at week 38 or both and no EPDS scores of ≥ 10 postpartum. Depression postpartum was defined as EPDS score ≥ 12 at any time point postpartum or a depressive episode, according to MINI, postpartum, or both, and no EPDS score of ≥ 10 during pregnancy. Persistent depression was defined as EPDS score ≥ 12 at least once during pregnancy or a depressive episode, according to MINI, or both, and at least once postpartum. Participants displaying subclinical values of 10 to 11 once during pregnancy and one EPDS score ≥ 12 or depressive episode, according to MINI, postpartum, or vice versa, were also included.

The "no depressive episode group" included women with EPDS scores ≤ 9 at all time points, as well as no depressive episode during pregnancy or postpartum, based on the MINI interview (if available), no anxiety and no selective serotonin reuptake inhibitor use.

3.4. Statistical analyses

Possible confounding and mediating factors were identified based on previous literature (Robertson et al., 2003; Howard et al., 2014; Stein et al., 2014; Silverman et al., 2017) and tested in univariable models. Univariable linear regressions were applied for each factor to assess its association with the three CBCL subscales (total, internalizing and externalizing problem scores) and chi-square or ANOVA tests were applied, for the association with the maternal depression trajectories. Factors that showed a significant association in the univariable analyses ($p < 0.05$) were used in the multivariable regressions if groups were larger than ten individuals.

The regression models were performed in steps. Model 1 was adjusted for child gender (girl vs. boy); model 2 also for birth order (first-born vs. not first-born) and maternal variables: age in years, pregnancy length in days, delivery mode (spontaneous vs. instrumental), education (university level vs non-university level), employed (vs. unemployed or on sick leave), experience of intimate partner violence (no vs. at least one violent relationship), smoking history (at least once before vs. never), partner support with the infant (yes vs. no or little) and history of depression (no vs. yes). Model 3 was adjusted for all of the above and for maternal bonding (PBQ scores). No significant collinearity or autocorrelation was found. Due to non-normal distribution of residuals, bootstraps were used for the multivariable regression (bias-corrected and accelerated, 2000 resamples). The multivariable regression analyses were then repeated, a) changing reference category from children of healthy mothers to other groups in order to compare the depression trajectories with each other, and b) stratified for child gender.

Path analysis was performed using structural equation modeling to test maternal bonding (PBQ scores) as a mediator between maternal depression and child outcomes, through use of the PROCESS macro (Hayes, 2013) and AMOS 25. All other statistical analyses and procedures were conducted with SPSS 25.

3.5. Sensitivity analyses

To exclude a possible state effect of maternal depression at the time of the evaluation of child behavioral problems at 18 months, additional regression analyses with bootstraps (bias-corrected and accelerated, 2000 resamples) were performed including only children born to mothers without current depression at the time of the child assessment, using the DSRS diagnosis ($n = 1002$). Children of mothers who did not report on this scale ($n = 42$) and those born to mothers who scored in the depression range at child age 18 months ($n = 49$) were excluded.

In a second sensitivity analysis, the possible influence of depressive symptoms on maternal reports of bonding problems (PBQ scores) at six months postpartum was accounted for. The analysis included only children born to mothers without concurrent depressive symptoms at the time of bonding assessment ($n = 910$), excluding mothers displaying depressive symptoms at six months postpartum (EPDS > 9, $n = 183$), to test if bonding was still a mediator between maternal depression and child behavioral problems.

Table 1
Characteristics of participating children and mothers, presented as numbers (n) and percentages (%), or mean scores and standard deviations (SD) when appropriate.

	Children of mothers with *No depressive symptoms* [a]	Children of mothers with *Antenatal depression*	Children of mothers with *Postpartum depression*	Children of mothers with *Persistent depression*	p values	Missing
N = 1353	**n = 870 (64.3%)**	**n = 114 (8.4%)**	**n = 152 (11.2%)**	**n = 217 (16.0%)**		
Child variables						
Gender: girl	403 (47.5%)	63 (58.3%)	69 (47.3%)	102 (49.0%)	0.199	42 (3.1%)
Birth weight (kg), mean (SD)	3.6 (0.5)	3.6 (0.6)	3.6 (0.6)	3.6 (0.6)	0.580	69 (5.1%)
First-born	406 (47.9%)	44 (40.7%)	78 (53.4%)	98 (46.9%)	0.253	43 (3.2%)
Head circumference (cm), mean (SD)	35.1 (1.7)	34.8 (1.8)	35.0 (1.7)	34.8 (1.7)	0.222	59 (4.4%)
APGAR score at five minutes, mean (SD)	9.6 (0.9)	9.6 (0.7)	9.6 (0.7)	9.5 (1.29)	0.182	46 (3.4%)
Child Behavior Checklist						0
Total problem score, mean (SD)	11.9 (8.8)	15.6 (10.3)	14.3 (9.1)	17.1 (13.0)	0.000	
Internal. problem score, mean (SD)	3.1 (3.3)	4.3 (3.9)	4.0 (3.3)	5.0 (5.7)	0.000	
External. problem score, mean (SD)	6.8 (5.3)	8.8 (6.3)	7.9 (6.0)	9.3 (6.9)	0.000	
Maternal variables						
Age (years), mean (SD)	31.9 (4.3)	30.9 (4.4)	32.5 (4.5)	31.3 (4.8)	0.006	0
Born in Scandinavia	819 (94.5%)	100 (95.2%)	125 (89.9%)	197 (93.4%)	0.193	31 (2.3%)
Pregnancy length (days), mean (SD)	279.9 (10.7)	275.6 (15.2)	276.6 (13.1)	278.1 (11.7)	0.000	41 (3.0%)
Spontaneous vaginal delivery mode	685 (78.9%)	87 (77.7%)	95 (62.9%)	164 (75.9%)	0.000	6 (0.4%)
Education at university level	752 (86.7%)	74 (69.2%)	121 (86.4%)	157 (74.4%)	0.000	28 (2.1%)
Employed	846 (97.4%)	93 (88.6%)	130 (92.9%)	186 (88.2%)	0.000	28 (2.1%)
Experience of intimate partner violence	54 (6.4%)	15 (14.4%)	15 (11.1%)	40 (19.5%)	0.000	62 (4.6%)
Smoking at least once before	198 (22.9%)	39 (36.1%)	45 (32.4%)	92 (43.8%)	0.000	31 (2.3%)
Stressful life events: 3–10	22 (2.6%)	6 (5.8%)	7 (4.8%)	19 (9.0%)	0.000	48 (3.5%)
Partner support with infant: no/ little	409 (48.9%)	55 (55.6%)	71 (51.8%)	121 (60.2%)	0.028	79 (5.8%)
History of depression	306 (35.4%)	82 (75.9%)	100 (72.5%)	174 (82.9%)	0.000	33 (2.4%)
Postpartum bonding, mean (SD)	6.3 (4.7)	7.5 (5.5)	10.6 (7.2)	12.6 (8.8)	0.000	126 (9.3%)

[a] ***No depressive symptoms***: EPDS scores at all time points, no anxiety indication at all time points, no MINI interview diagnosis and no intake of selective serotonin reuptake inhibitors. Antenatal depression: EPDS values ≥ 12 at any time point during pregnancy/MINI diagnosis of depression and postpartum EPDS values ≤ 9 postpartum/no MINI diagnosis of depression. Depression postpartum: EPDS values ≤ 9/no MINI diagnosis of depression during pregnancy and postpartum one EPDS value ≥ 12 at any time point postpartum or MINI diagnosis of depression. Persistent depression: EPDS scores ≥ 12/MINI diagnosis of depression at least once during prenatal period and at least once during the postpartum period, and participants displaying subclinical EPDS scores of 10 to 11 during pregnancy/postpartum and at least one EPDS value ≥ 12 during pregnancy/postpartum.

4. Results

4.1. Sample characteristics

As shown in Table 1, the participants in the different trajectory groups were comparable regarding the distribution of birth weight, birth order, head circumference, APGAR scores at five minutes, maternal age, and country of birth. While not significantly different, the ratio of girls was higher in the antenatal depression group. The antenatal and postpartum depression groups had shorter pregnancy length. Univariable associations between covariates and the parent-reported CBCL scores are presented in Supplementary Table 1. Birth order, maternal age, maternal education, and bonding were associated with all CBCL problem scale scores. Maternal previous or current intimate partner violence displayed an association with total and internalizing problem scores, whereas maternal employment showed a significant association with total and externalizing problem scores. Maternal report of no or little partner support and help with the infant was associated with internalizing problem scores.

Children of mothers from the persistent depression group displayed the highest mean values on all three CBCL problem scores (see Table 1, Supplement Fig. 1 and also the figures for internalizing and externalizing problem scores in the supplement (Supp. Figures 2 & 3)).

4.2. Child behavioral problems by maternal depression trajectories

As shown in Table 2, children of mothers in all three maternal depression trajectories had significantly higher CBCL total problem scores, as reported by the mother, compared with children of mothers in the no depressive symptoms group. In models 1 and 2, the effect sizes remained at a similar level. After adding maternal bonding (model 3), only antenatal depression was still statistically significantly associated with child behavioral problems, in comparison to the control group. Higher maternal age was related to lower CBCL total problem scores. Similarly, non-first-born children showed fewer behavioral problems compared with first-born children.

Furthermore, children in all three maternal depression trajectories had significantly higher CBCL internalizing problem scores compared with children of mothers with no depressive symptoms, even if the associations were attenuated after adjustment (Table 3). After including

maternal bonding (model 3), the associations were no longer statistically significant. Non-first-born children and children born to older mothers were reported to have less internalizing problem scores. Little or no support with the infant by the partner was associated with higher internalizing problem scores and was not mediated by postpartum bonding (model 3). No other covariates showed any significant association with internalizing child behavioral problems.

Likewise, children in all three maternal depression trajectories showed significantly higher externalizing problem scores compared with children of mothers without a depressive episode (model 1 and 2 in Table 4). In model 3, children of mothers in the antenatal depression trajectory still showed significantly higher externalizing problem scores compared with children of mothers with no depressive symptoms. Being a boy was significantly associated with higher CBCL externalizing problem scores. Higher maternal age and not being first-born showed associations with lower externalizing problems.

Separate analyses, comparing the CBCL scores of children born to mothers with different onsets of peripartum depression, with each other and not only with children of non-depressed mothers, revealed significant differences only for the externalizing problem scale. Comparing antenatal depression as reference category, which was associated with higher externalizing problem scores, with postpartum ($\beta_{postpartum\_external} = -1.751$, CI $= -3.15, -0.52$) and persistent depression ($\beta_{persistent\_external} = -1.537$, CI $= -3.02, -0.05$).

4.3. Mediation analysis

Mediation analysis was conducted, with postpartum bonding hypothesized to be a mediator in the association between maternal depression trajectory group and child behavior. The analysis showed that this association was mediated by maternal reports of postpartum bonding to a varying degree. Maternal persistent and postpartum depression showed a relatively high indirect effect on all three child behavioral scales (see Fig. 2 and Supp. Figures 4 & 5), whereas antenatal depression displayed a remaining strong direct effect on all three CBCL scales.

4.4. Child behavior problems stratified by gender

The stratified regression analyses revealed more significant

Table 2

CBCL total scores by maternal depressive trajectories, accessed via multivariable linear regression-derived beta coefficients (B) and confidence intervals (CI), bootstrapped regression with 2000 resamples, bias-corrected accelerated (BCa).

Factor	Model 1 B	95% CI		Model 2 B	95% CI		Model 3 B	95% CI	
Maternal depression trajectory									
No depressive episode	Ref.			Ref.			Ref.		
Antenatal depression	**4.275*****	2.05,	6.50	**3.761****	1.47,	6.05	**2.975****	0.77,	5.17
Postpartum depression	**2.918****	1.02,	4.81	**2.557***	0.61,	4.50	0.488	−1.41,	2.39
Persistent depression	**5.054*****	3.42,	6.68	**4.475*****	2.73,	6.21	1.334	−0.44,	3.11
Child gender (girl vs. boy)	0.853	−0.28,	2.00	0.739	−0.39,	1.87	0.758	−0.32,	1.84
First-born (vs. not first-born)				**−2.870*****	−4.15,	−1.59	**−2.603*****	−3.83,	−1.37
Maternal age				**−0.199***	−0.34,	−0.06	**−0.197****	−0.33,	−0.06
Pregnancy length				0.007	−0.04,	0.06	−0.005	−0.05,	0.05
Spontaneous vs. instrumental delivery mode				−0.040	−1.42,	1.34	0.012	−1.31,	1.34
Education at university level (vs. non-university level)				0.467	−1.14,	2.08	1.181	−0.36,	2.73
Employed (vs. unemployed or on sick leave)				1.049	−1.58,	3.68	1.059	−1.46,	3.58
No experience of intimate partner violence (vs. at least one experience)				1.165	−0.86,	3.19	1.477	−0.46,	3.42
Smoking at least once before (vs. never)				−0.454	−1.77,	0.87	−0.694	−1.95,	0.57
Partner support with infant (vs. no/little support)				0.807	−0.33,	1.95	0.790	−0.30,	1.89
No history of depression (vs. history of depression)				0.054	−1.18,	1.29	−0.125	−1.31,	1.06
Postpartum bonding (PBQ scores)							**0.469*****	0.37,	0.56

Significance levels: *$p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

Model 1 is adjusted for: child gender. Model 2 also for birth order (first-born vs. not first-born), maternal age, pregnancy length, delivery mode, maternal education, maternal employment (employed vs. unemployed or on sick leave), intimate partner violence, maternal smoking, partner support with the infant, history of depression. Model 3 is adjusted for all of the above and postpartum bonding. $N = 1093$.

Table 3

CBCL Internalizing problem scores by maternal depressive trajectories, accessed via multivariable linear regression-derived beta coefficients (B) and confidence intervals (CI), bootstrapped regression with 2000 resamples, bias-corrected accelerated (BCa).

Factor	Model 1 B	95% CI		Model 2 B	95% CI		Model 3 B	95% CI	
Maternal depression trajectory									
No depressive episode	Ref.			Ref.			Ref.		
Antenatal depression	**1.110***	0.32,	1.99	**0.891***	0.08,	1.76	0.673	−0.13,	1.55
Postpartum depression	**0.917****	0.28,	1.57	**0.756***	0.02,	1.46	0.183	−0.55,	0.91
Persistent depression	**1.795*****	1.03,	2.70	**1.552*****	0.76,	2.40	0.682	−0.12,	1.54
Child gender (girl vs. boy)	0.224	−0.21,	0.65	0.166	−0.28,	0.61	0.171	−0.27,	0.62
First-born (vs. not first-born)				**−1.097*****	−1.64,	−0.59	**−1.023*****	−1.53,	−0.56
Maternal age				**−0.064***	−0.12,	−0.01	**−0.064***	−0.12,	0.00
Pregnancy length				0.007	−0.01,	0.02	0.004	−0.01,	0.02
Spontaneous vs. instrumental delivery mode				0.158	−0.37,	0.70	0.172	−0.33,	0.70
Education at university level (vs. non-university level)				0.355	−0.26,	0.97	0.553	−0.04,	1.17
Employed (vs. unemployed or on sick leave)				0.096	−0.86,	1.11	0.099	−0.82,	1.07
No experience of intimate partner violence (vs. at least one experience)				0.649	−0.45,	1.98	0.735	−0.35,	2.01
Smoking at least once before (vs. never)				0.086	−0.42,	0.64	0.019	−0.45,	0.56
Partner support with infant (vs. no/little support)				**0.503***	0.05,	0.98	**0.499***	0.06,	0.97
No history of depression (vs. history of depression)				0.106	−0.34,	0.59	0.057	−0.38,	0.53
Postpartum bonding (PBQ scores)							**0.130*****	0.09,	0.17

Significance levels: *$p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.
Model 1 is adjusted for: child gender. Model 2 also for birth order (first-born vs. not first-born), maternal age, pregnancy length, delivery mode, maternal education, maternal employment (employed vs. unemployed or on sick leave), intimate partner violence, maternal smoking, partner support with the infant, history of depression. Model 3 is adjusted for all of the above and postpartum bonding. $N = 1093$.

Table 4

CBCL externalizing problem scores by maternal depressive trajectories, accessed via multivariable linear regression derived beta coefficients (B) and confidence intervals (CI), bootstrapped regression with 2000 resamples, bias-corrected accelerated (BCa).

Factor	Model 1 B	95% CI		Model 2 B	95% CI		Model 3 B	95% CI	
Maternal depression trajectory									
No depressive episode	Ref.			Ref.			Ref.		
Antenatal depression	**2.498*****	1.04,	4.06	**2.313****	0.85,	3.81	**1.834****	0.51,	3.20
Postpartum depression	**1.412***	0.21,	2.62	**1.344***	0.12,	2.56	0.083	−1.12,	1.31
Persistent depression	**2.403*****	1.29,	3.50	**2.211*****	1.06,	3.35	0.297	−0.78,	1.42
Child gender (girl vs. boy)	**0.748***	0.06,	1.40	**0.703***	0.01,	1.39	**0.714***	0.03,	1.41
First-born (vs. not first-born)				**−1.037****	−1.86,	−0.25	**−0.875***	−1.67,	−0.09
Maternal age				**−0.131****	−0.22,	−0.04	**−0.129****	−0.21,	−0.04
Pregnancy length				0.003	−0.02,	0.03	−0.004	−0.03,	0.02
Spontaneous vs. instrumental delivery mode				−0.142	−1.01,	0.71	−0.110	−0.92,	0.75
Education at university level (vs. non-university level)				0.193	−0.81,	1.25	0.627	−0.31,	1.65
Employed (vs. unemployed or on sick leave)				0.282	−1.62,	2.27	0.288	−1.51,	2.20
No experience of intimate partner violence (vs. at least one experience)				0.062	−1.31,	1.46	0.252	−0.99,	1.53
Smoking at least once before (vs. never)				−0.565	−1.41,	0.25	−0.712	−1.48,	0.07
Partner support with infant (vs. no/little support)				0.276	−0.42,	0.97	0.266	−0.39,	0.90
No history of depression (vs. history of depression)				−0.139	−0.88,	0.62	−0.247	−0.94,	0.45
Postpartum bonding (PBQ scores)							**0.286*****	0.22,	0.35

Significance levels: *$p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.
Model 1 is adjusted for: child gender. Model 2 also for birth order (first-born vs. not first-born), maternal age, pregnancy length, delivery mode, maternal education, maternal employment (employed vs. unemployed or on sick leave), intimate partner violence, maternal smoking, partner support with the infant, history of depression. Model 3 is adjusted for all of the above and postpartum bonding. $N = 1093$.

associations between maternal depression and child behavior in girls, compared with in boys (Supp. Tables 2–4). Girls of mothers with any depression trajectory displayed higher risk of elevated scores on total and internalizing behavioral problem scales compared with children of non-depressed mothers, after adjusting for confounders (for total problem scores: $\beta_{G\_antenatal\ total} = 4.486$, CI = 1.54, 7.56; $\beta_{G\_postpartum\ total} = 3.731$, CI = 0.78, 6.87; $\beta_{G\_persistent\ total} = 5.504$, CI = 2.50, 8.91), but only for antenatal and persistent maternal depression and externalizing child problems. After adjusting for confounders, boys of persistently depressed mothers showed significantly elevated CBCL total ($\beta_{B\_persistent\ total} = 3.549$, CI = 0.86, 6.10) and internalizing ($\beta_{B\_persistent\ internal} = 1.055$, CI = 0.11, 1.96) problem scores.

When adding maternal bonding to the regression analysis (model 3), girls of antenatally depressed mothers still showed significantly higher risk of behavioral problems for total problem scores ($\beta_{G\_antenatal}$

$_{total} = 3.772$, CI = 0.98, 6.53), while girls of persistently depressed mothers showed an elevated risk only for internalizing problems ($\beta_{G\_persistent\ internal} = 1.265$, CI = 0.18, 2.60). For boys, however, the previous differences were no longer significant.

4.5. Sensitivity analyses

A sensitivity analysis of the potential influence of current depression on maternal evaluation of child behavioral problems at postpartum month 18 was assessed using linear regression models 1–3 with bootstraps (bias-corrected and accelerated, 2000 resamples), using a second depression measure (DSRS) from the same time point, excluding children of mothers with depression ($n = 49$) and of mothers who did not report on the DSRS ($n = 42$). The results ($n = 1002$) displayed similar significant effect sizes for CBCL total problem scores as previously seen
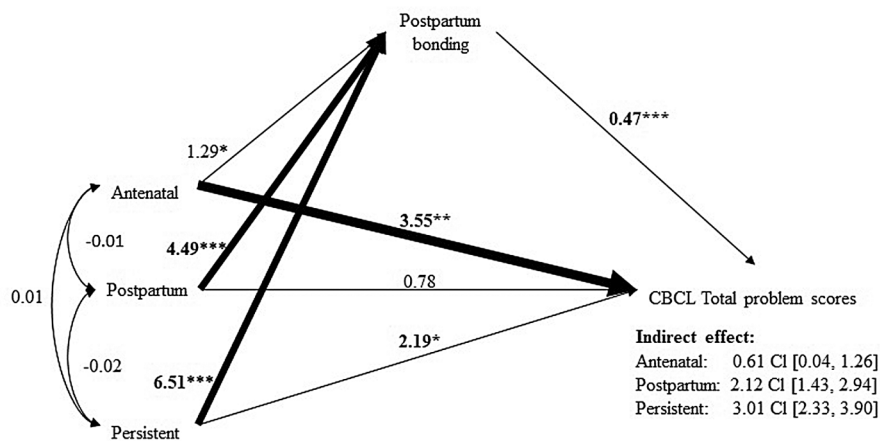
Fig. 2. Path analysis for CBCL total problem scores; direct and indirect association of maternal depression trajectories with child problem scores. Bootstrap (5000 resamples, Andrew Hayes's mediation model 4 & AMOS 25). Coefficients are displayed with significance levels: $*p \leq 0.05$; $** p \leq 0.01$; $*** p \leq 0.001$ for the direct effect (postpartum bonding as a factor) or confidence intervals for the indirect effect indicating the effect of the depressive trajectories on the CBCL via postpartum bonding.

for antenatal ($\beta_{antenatal\_total} = 4.105$ CI = 1.77, 6.52), postpartum ($\beta_{postpartum\_total} = 3.510$ CI = 1.56, 5.58), and persistent depression ($\beta_{persistent\_total} = 3.803$ CI = 1.91, 5.75) (model 1). In the fully adjusted model 2, children of mothers with antenatal depression ($\beta_{antenatal\_internal} = 0.877$ CI = −0.01, 1.87) did not have significantly higher risk of internalizing behavioral problems. This was the only significant result that changed to non-significant when including the DSRS measure and excluding mothers with an indication of depression and missing values on this scale.

Furthermore, a stratified linear regression analysis was used to correct for the influence of concurrent depression on bonding scores (PBQ). Mothers with depressive symptoms at six months postpartum ($n = 130$) were excluded. Among mothers who displayed no depressive symptoms when filling out the CBCL ($n = 910$), there was still a significant association between postpartum bonding and CBCL total ($\beta_{PBQ\_total} = 0.537$ CI = 0.42, 0.66), internalizing ($\beta_{PBQ\_internal} = 0.159$ CI = 0.11, 0.21) and externalizing ($\beta_{PBQ\_external} = 0.309$ CI = 0.24, 0.38) problem scores, when adjusted for confounding factors (model 3).

5. Discussion

This study set out to investigate the potential associations between different maternal perinatal depression trajectories and child behavioral problems assessed at 18 months of age. Children of mothers in the different trajectory groups were found to exhibit different risks for behavioral problems. Regarding total behavioral problem scores in children, the risk was increased for all groups compared with children of mothers with no depressive symptoms. The largest adjusted effect sizes were observed for children of mothers with depression during both the antenatal and the postpartum period, followed by children of mothers with only antenatal depression. Most previous studies regarding maternal depression trajectories and offspring development have investigated high maternal depressive symptom levels versus lower levels, and have similarly reported that offspring of mothers with prolonged high symptom levels are at increased risk of negative affect (Ashman et al., 2008; Kingsbury et al., 2015; Guyon-Harris et al., 2016). Somewhat similarly to our general findings, Kingston et al. (2018) showed that not only high levels, but also persistent moderate maternal symptoms, were associated with both externalizing and internalizing problems in children's behavior. Our study shows that antenatal depression is also associated with a higher risk of behavioral problems in children. A study conducted in the U.S., investigating timing of symptoms, showed that particularly children of mothers with symptoms that increased over time from pregnancy to child age two years, were reported to have more emotional (internalizing) problems at two years of age (Guyon-Harris et al., 2016). However, in the present study, externalizing problems displayed the

largest effect size in association with antenatal depression.

Looking at the impact of maternal depression, stratified modeling revealed more significant associations between maternal depression trajectory and behavioral problems in girls. This finding is somewhat in line with some earlier studies, as summarized by Hicks et al. (2019), suggesting that girls tend to be more vulnerable to antenatal stress, mediated both through larger alterations of the HPA axis and a higher risk of altered placental functions in girl pregnancies, eventually leading to a higher prevalence of internalizing problems. Moreover, maternal stress has been associated with stronger functional amygdala connectivity in girls but not in boys (Sandman et al., 2018) and with increased internalizing behaviors and negative emotionality in girls only (Graham et al., 2019). Future studies might also consider including assessment of maternal and child biomarkers in order to further elucidate the mechanisms involved.

Maternal sensitivity to the infant has been proposed as a possible modifier of the effects of fetal programming (Kaplan et al., 2008), and effect sizes for antenatal depression in our study were indeed attenuated when adding the mothers' perceptions of the relationship with their infant to the model. Furthermore, as the association between antenatal depression and child behavior was still significant, in particular for girls, there might also be a direct effect of antenatal depression on child development which in this sample was not reversed through normal bonding. However, the long-term effects were not investigated in our study. Previous results have indicated that if mothers' depressive symptoms improve over the first three years postpartum, child outcomes could be comparable to that of children to non-depressed mothers (Park et al., 2018). Notably though, in the study by Park et al., antenatal depression was not clearly distinguished from that of postpartum onset. The mediating role of postpartum bonding was particularly pronounced in postpartum and persistent depression, indicating its importance in transmitting the effects of depression to the offspring. Glover (2014) proposes that antenatal exposure to maternal depression and or anxiety may contribute 10–15% of the emotional and behavioral outcomes.

Maternal history of depression does not display any significant independent association in the multivariable model, indicating that perinatal depressive symptoms are more important than previous history of depression, rendering thus an eventual genetic component less important for early childhood symptoms compared with perinatal exposures and possible epigenetic changes. Furthermore, it could be speculated that persistently depressed mothers have an impaired self-esteem, low energy and their interactions with the child may have an impact on the child's behavior through learning processes.

An important consideration relates to the depression-distortion hypothesis (Richters, 1992), which describes a negative bias of a depressed mother's ratings of her children. To make sure that the parent-

reported behaviors were not solely resulting from maternal mood problems, maternal depressive symptoms (measured with DSRS) at child age 18 months was used in a sensitivity analysis where mothers indicating depressed mood were excluded. Most results, except the association between antenatal depression and internalizing problem scores ($p = 0.07$), stayed significant. It should be pointed out that even a negatively distorted maternal perception of the child has consequences, for instance via the negatively affected mother-child interaction (Lee and Hans, 2015). Importantly, previous studies have given evidence of the reverse relation; that mothers of children displaying high negative affect are at increased risk of depression (Baker et al., 2019). Furthermore, the risk of a state effect of postpartum depression on maternal bonding was also examined. Maternal bonding scores from six months postpartum were still significantly associated with CBCL scores at 18 months of age, even after excluding mothers with high EPDS scores at the time of bonding reports.

Apart from depression and postpartum bonding, lower maternal age and being first born were also significantly associated with child behavior problems (all CBCL scores) along with no or little partner support with the infant (internalizing problem scores), even after introducing postpartum bonding to the model. Such associations could be expected, as similar results have been reported previously (Robertson et al., 2003; Stein et al., 2014). In general, however, the associations between maternal postpartum depression and child outcomes were weaker in the present study, compared with results for the antenatal and persistent symptom trajectories. In speculation, the results might have been different had we studied another outcome, such as cognitive functioning (Grace et al., 2003; Hay et al., 2008). Our results show that total, as well as internalizing, and externalizing problems in the 18-month-old child were better explained by maternal bonding difficulties than by depression alone, pointing at a mediating role for postpartum bonding difficulties. This might be especially valid for the impact of postpartum and persistent depression on child behavioral problems.

5.1. Limitations

The results are based on maternal ratings and might have been different if paternal ratings had been included. However, mother and father ratings of child behavioral problems are usually highly correlated, in particular regarding externalizing and total behavior problems in children, and moderately correlated regarding internalizing problems (Duhig et al., 2000).

There is also a possibility that some gender differences could be due to bias, i.e., that the mothers were stricter in their assessments of daughters. Indeed, toddler behaviors are often viewed with gender bias, but the actual behavior of boys and girls may differ already at early ages (Keane and Calkins, 2004). However, the young age per se might be of a larger importance, as depressive and anxious symptoms are more expressed at older age (Bongers et al., 2003) and therefore the discriminative power of the CBCL has been reported to be better for externalizing problems than for internalizing problems at younger ages (La Osa et al., 2016). It is also important to note that these results do not pertain to outcome measures such as language development or cognition.

The results of the present study relate to maternal ratings of child behavior problems at 18 months of age, and detection of problems at this age would enable early interventions. A smaller study of maternal depression trajectories suggests that if maternal depressive symptoms improve over the first three years postpartum, children's outlook may be comparable to that of those whose mothers were non-depressed (Park et al., 2018). A limitation of the current study is that we did not control for contextual factors, such as parental relationship quality, parenting style or other family factors after child age of six months. A British study showed that only children exposed to both antenatal depression and later childhood maltreatment were at risk of developing psychopathology (Pawlby et al., 2011). The present study did not

investigate psychopathology, but only rather mild behavioral symptoms.

The first strength of this study is that it addresses and distinctly studies the impact of different antenatal, postpartum, and persistent depression trajectories, which, when separated, exhibit rather distinct patterns of association with child outcomes. Furthermore, the study included assessments of the role of gender and mediating role of bonding, is population-based, prospective, included a rather large number of participants and has assessed a large number of relevant variables that were controlled for, as confounders or mediators. On the other hand, only 10% of the background population took part in the study, impacting on the generalizability of the results. The homogenous and highly educated community sample included a large majority of mothers with no depressive symptoms and few children having CBCL scores in the clinical range (Achenbach and Rescorla, 2000). The effect sizes might be therefore lower than the ones expected in clinical or population representative samples, and child development problems might be underestimated. Due to low numbers of severely depressed mothers in our sample, we could not compare high symptom severity with moderate severity at each time point. On the other hand, the homogeneity of the sample reduces the impact of eventual confounders; and it is of note that a large number of confounders were recorded and controlled for.

5.2. Conclusion

In conclusion, our study shows that different onset and duration of maternal depression seems to have a differential impact on the child's behavioral development, detectable even in a relatively healthy, well-educated sample. The mother's own perception of bonding quality was identified as an important mediator, especially in the group with postpartum symptom onset. The results contribute to increased knowledge on the various mechanisms of transgenerational transmission, emphasizing the impact of the different time points of depressive symptom onset, child gender, previous history of depression, and maternal bonding. It is important to note that most children are perceived to have behavior within the normal range. Still, the results suggest that depressive symptoms, especially in the antenatal period, might play a role in fetal programming, but they also support a role for potential targeted preventive interventions, such as supporting mothers with bonding difficulties.

Contributions

A.S. and M. R. conceived the idea. P. E. and T.K-K. were involved in data collection and data management. E.F., A. S. and I. K-M. were involved in planning and supervised the work, F. S. performed the data analyses. E. F. and F. S. drafted the manuscript. F. S. designed the figures. M. H. aided with the manuscript and evaluation of the CBCL values. All authors have critically revised the manuscript and approved the final version.

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Declaration of Competing Interest

All authors declare to have no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2020.04.003.

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