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ORIGINAL ARTICLE

Maternal depression trajectories from pregnancy to 3 years postpartum are associated with children's behavior and executive functions at 3 and 6 years

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Abstract
The objective of this study was to investigate how patterns of maternal depressive symptoms from mid-pregnancy to 3 years postpartum are associated with children's behavior at age 3 years and executive functions. Maternal depressive symptoms were measured from mid-pregnancy to 3 years postpartum. Growth mixture modeling was used on standardized maternal depression scores ($n = 147$) to identify trajectories. Children's behavioral problems and mental health symptomatology (internalizing, externalizing, and attention deficit hyperactivity disorder) were obtained at 3 and 6 years. EFs were assessed by a laboratory-based computerized task and maternal-report at 6 years. Multivariable linear regressions of children's outcomes against maternal depressive symptom trajectories were conducted ($n = 103$). Three distinct patterns of maternal depressive symptom trajectories were identified: low ($n = 105$), increasing ($n = 27$), and decreasing ($n = 15$). Children of mothers whose depressive symptoms increased reported more problem behaviors at 3 years and poorer EFs at 6 years as assessed by both instruments, but no significant differences in mental health symptomatology at 6 years, relative to those whose mothers had consistently low depressive symptoms. Children whose mothers became less depressed over time had comparable levels of behavioral problems at age 3, executive functions, and internalizing and externalizing scores at age 6; and fewer reported ADHD behaviors at age 6, than those whose mothers remained less depressed over time. If mothers' depressive symptoms improve over the first 3 years postpartum, their children's outlook may be comparable to those whose mothers had consistently low depressive symptoms.

Keywords Maternal depression · Prenatal · Postpartum · Postnatal · Trajectories · Child development · Executive functions · Child behavior · Child mental health

Introduction

Depression among mothers and pregnant women is prevalent (Underwood et al. 2016) and carries dual concerns regarding the health of the mother and the developing child. Evidence suggests that exposure to maternal depression, both pre- and post-natally, shapes pathways to health and disease for offspring throughout life. Exposure to depression in utero is associated with increased risk of preterm birth and low birth weight (Jarde et al. 2016). Continued exposure to maternal depression in early life remains an independent risk factor for poorer cognitive, behavioral, and emotional development throughout childhood (Sohr-Preston and Scaramella 2006; Suri et al. 2014). Notably, these effects appear to persist even when controlling for obstetric risk, psychosocial disadvantage, and mother's postnatal mood, thereby suggesting that maternal depression may have an early "fetal programming" effect on the developing brain (Glover et al. 2010).

Despite strong evidence supporting an adverse developmental impact of perinatal maternal depression, disentangling the effect of prenatal versus postnatal maternal depressive

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symptoms remains challenging. A recent review of population-based longitudinal studies on maternal depression found a substantial number of individuals alternated between being classified as depressed or non-depressed across pre- and post-natal periods, and suggested that postpartum depression may represent a continuation of prenatal depression (Underwood et al. 2016). Moreover, it may be the severity and/or chronicity of maternal depression, rather than timing of exposure, that plays a critical role in influencing children's mental health and development (Brennan et al. 2000; Hammen and Brennan 2003).

Traditional approaches to studying the effects of maternal depression on children have focused on depression at specific time points or have used predefined cut-points to assess severity and chronicity when using longitudinal data (Brennan et al. 2000; Hammen and Brennan 2003; O'Donnell et al. 2014). However, these methods cannot separate the timing, severity, and chronicity of maternal depressive symptoms (Cents et al. 2013). To overcome these limitations, recent research efforts have identified trajectories of maternal depression using longitudinal data. Trajectory-based approaches are advantageous as they are able to capture the heterogeneity of depressive symptoms over time (Jung and Wickrama 2008) and may thus better represent a child's exposure to his or her mother's depression across key developmental periods.

To date, several studies have modeled maternal mental health trajectories and their impact on children (Betts et al. 2014; Betts et al. 2015; Campbell et al. 2007; Campbell et al. 2009; Cents et al. 2013; Cox et al. 1987; Guyon-Harris et al. 2015; Matijasevich et al. 2015; van der Waerden et al. 2015) and have demonstrated that modeling trajectories provides additional predictive value compared to traditional approaches. However, only a subset of these studies has examined trajectories starting during pregnancy (Betts et al. 2014; Betts et al. 2015; Cents et al. 2013; Guyon-Harris et al. 2015; van der Waerden et al. 2015), which as a critical period of development, should be included when determining the impact of maternal depression. Moreover, these studies have all assessed outcomes in childhood at just one point in time, although tracking outcomes as children age is important, as disturbances may arise differently depending on developmental status (Beck et al. 1961).

Conflicting findings have emerged from this body of work. Some studies have found that maternal mental health trajectories characterized by consistently high symptoms are especially harmful for children's outcomes (Cents et al. 2013; van der Waerden et al. 2015), while others have found that adverse effects on offspring are seen only when the timing of symptoms occurs during gestation (Betts et al. 2014; Betts et al. 2015). Finally, there have been no reports of the impact of maternal depression trajectories on children's executive functions despite the consistent finding that cognitive function is affected (Sohr-Preston and Scaramella 2006). Of important consideration regarding executive functions is that they may be particularly sensitive to maternal depression due to their vulnerability to environmental inputs (McEwen and Morrison 2013).

The current study focused on identifying distinct trajectories of maternal depressive symptoms from pregnancy through the next 3 years, identifying whether maternal characteristics differ across different depressive trajectories, and investigating how these identified trajectories relate to children's behavior at age 3 years and children's mental health symptomatology and executive functions at 6 years of age. We expected that children of mothers whose trajectories reflected higher persistent or even variable levels of depressive symptoms relative to that with the least depressive symptoms would exhibit poorer behavioral, cognitive, and mental health outcomes at both 3 and 6 years.

Methods

Study design

One hundred ninety-one women were recruited (from 258 approached) during their second trimester of pregnancy to participate in a prospective cohort study of the developmental impact of in utero selective serotonin reuptake inhibitor (SSRI) antidepressant exposure and maternal mental health. Women were physician- or self-referred from the Reproductive Mental Health Program at the British Columbia Women's Hospital and Health Centre, family physician practices, and community midwife clinics in the Vancouver Metropolitan area in British Columbia, Canada. The Reproductive Mental Health Program provides specialized perinatal psychiatric services for women who have been referred to the program by a physician, nurse practitioner, or midwife due to mental health concerns. Given the convenience sampling strategy and the fact that the study aimed to investigate the effects of prenatal exposure to SSRIs and maternal mood disorders on offspring, study participants were over-sampled from women at high risk for mental disorders. Criteria for inclusion in the study included singleton pregnancy, confirmed gestational age at birth, and lack of fetal anomalies as detected by ultrasound. Exclusion criteria included the presence of maternal bipolar disorder or drug abuse, obstetrical complications (i.e., diabetes, hypertension), or fetal conditions (e.g., preterm birth, anencephaly). Data were collected over two waves of recruitment from January 2002 until April 2015.

Measures

Maternal depression

The Hamilton Depression Rating Scale (Hamilton 1960) (HAMD) and the Edinburgh Postnatal Depression Scale (Cox et al. 1987) (EPDS) were used to assess maternal depressive symptoms during the second and third trimesters of pregnancy, and at 6 weeks, 3 months, 6 months, and 10 months. The Beck Depression Inventory (Beck et al. 1961) (BDI) was used at the 3-year follow-up, and the HAMD was used at the 6-year follow-up. The HAMD is a 21-item clinician-rated scale with a range of 0 to 63; all assessments were performed by trained research assistants. The BDI and EPDS are self-report questionnaires, the former with 21-items and a range of 0 to 63, and the latter with 10-items with scores from 0 to 30. All three instruments measure the existence and severity of depression symptoms. Cut-off scores signifying risk of meeting criteria for a major depressive episode for the HAMD, EPDS, and BDI, respectively, are 17, 8, and 13 (Lasa et al. 2000; Matijasevich et al. 2014; Zimmerman et al. 2013). Different waves of the cohort underwent assessments for maternal depression at 6 weeks and 10 months.

Child behavior at age 3 years

The Child Behavior Checklist (Achenbach 1978) (CBCL) was completed by mothers when their children were 3 years old. The CBCL measures the degree of children's emotional, behavioral, and social problems. Sex-specific standardized *T*-scores were used to represent the total score of problem behaviors and internalizing and externalizing subscales, with higher scores indicating more behavioral problems.

Child mental health symptomatology at 6 years

The MacArthur Health and Behavior Questionnaire (Boyce et al. 2002) (HBQ) yielded measures of children's mental health symptomatology by maternal report at 6 years. Designed to map onto the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III diagnostic criteria (Boyle et al. 1993), it has been validated as a sensitive instrument for detecting psychopathology in children (Luby et al. 2002). Subscale scores for three domains of symptomatology are provided: internalizing (symptoms of depression, separation anxiety, and generalized anxiety), externalizing (oppositional defiance symptoms and conduct problems), and attention deficit hyperactivity disorder (ADHD) (inattention, impulsivity, and hyperactivity symptoms).

Child executive functions at 6 years

Two instruments were used to measure executive functions. The parent-report version of the Behavior Rating Inventory of Executive Function (Gioia et al. 2000) (BRIEF) was completed by mothers when their children were 6 years old. The BRIEF yields a score of global executive functions, with higher scores indicating worse outcomes. Children also completed the computerized Hearts and Flowers (HF) task (Davidson et al. 2006) at age 6 years. The HF task is conducted over three blocks and is designed to assess the executive function domains of inhibitory control, working memory, and cognitive flexibility. A stimulus appears to the right or left of a computer screen on every trial. On block 1 of the task (the congruent block), participants have only to do what comes naturally (i.e., pressing on the same side as the stimulus); executive functions are not taxed. On block 2 (the incongruent block), participants have to resist that prepotent response and instead press on the side opposite the stimulus. On block 3 (the mixed block), the two types of trials are randomly intermixed, requiring remembering both rules, mentally translating "same [or opposite] side" into "right [or left] hand," and flexibly switching between the two rules, inhibiting one to apply the other.

Children arrived at the study center in the morning and were oriented to the task and computerized set-up by performing a simple choice reaction time task. They were also given practice trials to make sure they understood the task demands. Reaction time and percent accuracy were computed for each block, with calculations performed as previously described (Weikum et al. 2013). Given past work suggesting that meaningful differences on the HF task among normative populations emerge in the most demanding block (Weikum et al. 2013), percent accuracy in the third block was used as an outcome measure in this study.

Cohort characteristics

Maternal age, education, alcohol consumption, SSRI use, and child demographic factors were recorded as previously described (Hanley et al. 2015). SSRI medications that were taken prenatally by mothers included paroxetine, fluoxetine, sertraline, venlafaxine, and citalopram. Minority status was coded as "yes" or "no" based on whether participants identified as Caucasian/white or another ethnicity. Maternal history of depression was based on any prior diagnosis of major depression. Maternal history of mental disorders was based on any prior diagnoses of the following: major depression, substance abuse, mania, obsessive compulsive disorder, anxiety or panic attacks, eating disorders, and suicide attempts. Number of previous mental disorders was recorded as the total number of the previously listed conditions that had been diagnosed. Other psychotropic drug use was classified as "yes" or "no"

based on whether mothers were taking other psychotropic medications in addition to SSRIs while pregnant, and included the following drugs: clonazepam, ativan, imovane, seroquel, stemetil, and loxepine.

Statistical analyses

Analytic samples

From the overall cohort, we derived two study samples to conduct our analyses. The first analytic sample consisted of mothers with complete data on maternal depressive symptoms at the 3-year time point ($n = 147$), and this sample was used to compute maternal depression trajectories. The second and final analytic sample was composed of the subset of mother-child dyads with complete data on child outcomes at ages 3 and 6 years ($n = 103$); this sample was used to calculate associations between maternal depression trajectories and child outcomes. Comparison of prenatal maternal depression scores from the original cohort ($n = 182$ with HAMD scores, HAMD = 8.8) compared to our final analytic sample ($n = 103$, HAMD = 7.9) suggested that although selection bias may have been introduced by more depressed women dropping out of the study, differences in illness severity were minimal and not clinically meaningful. Comparisons of maternal age and education also showed minimal differences between the original cohort ($n = 182$ with data, mean age = 33.3 years, education = 17.1 years) and final analytic sample ($n = 103$, mean age = 33.2 years, education = 17.3 years).

Data imputation

Mothers with complete data on maternal depressive symptoms at the 3-year time point ($n = 147$) comprised the sample used to compute trajectories. Three mothers had missing information on alcohol consumption and one on maternal education; the means of these variables were used to impute and replace missing values. These imputed values were carried over into the next set of analyses conducted on the subset of mother-child dyads with complete data on maternal depressive symptom trajectories and child outcomes at 3 and 6 years ($n = 103$).

Growth mixture modeling

Our first step was to compute trajectories of maternal depressive symptoms from the second trimester of pregnancy until 3-year post-birth. To meaningfully compare the different depression measures, scores at each time point were standardized to produce *Z*-scores and were averaged when there were multiple measurements per time point. We applied growth mixture modeling (GMM) to these scores using the "lcmm" package in R (Proust-Lima et al. 2017). GMM is a person-centered analytic method that allows for the detection of unobserved yet distinct trajectories within a population (Jung and Wickrama 2008; Muthén and Muthén 2000). We expected to identify latent classes that captured the overall meaning and direction of unique trajectories within the data (Muthén and Muthén 2000).

Missing data on maternal depressive symptoms (prenatal prior to 3 years postpartum) were handled under the missing at random assumption. The Bayesian information criterion (BIC) and mean posterior probabilities of group membership for all groups were examined to guide model selection (Nylund et al. 2007). Analyses were successively re-run with data omitted from the 6-week and 10-month follow-up time points, as these data were only captured in alternating waves of the cohort, to assess the robustness of identified trajectories.

Identifying factors associated with maternal depressive symptom trajectories

Our second step was to identify characteristics associated with maternal depressive symptom trajectories. Differences between trajectory groups with respect to continuous and categorical variables were compared using analysis of variance (ANOVA) and chi-square tests; significant differences were analyzed using pairwise post-hoc tests (Tukey's honest significant difference test or pairwise chi-square tests with a family-wise error rate of $p < 0.05$ to detect statistical significance).

Multivariable linear regression analyses

The third stage of our analysis was to estimate associations between maternal depressive symptom trajectories and child outcomes using multivariable linear regressions. We first estimated the association between maternal trajectories and child behavioral problems at 3 years, then estimated associations with children's internalizing, externalizing, and ADHD symptoms, and executive functions on the BRIEF and HF task, at 6 years. Two models were fit for each outcome: unadjusted and adjusted. Adjusted regression models included potential confounding variables selected based on previous literature: child's sex, age, gestational age at birth, birthweight, prenatal SSRI antidepressant exposure, maternal history of depression, maternal education, and maternal minority status. Concurrent maternal depressive symptoms were included as a covariate in all models examining 6-year outcomes.

Sensitivity analysis

Given the study's small sample size and risk for overfitting based on correlations among confounding variables, we also conducted regression analyses using a more parsimonious model that excluded gestational age at birth and maternal history of depression as covariates.

Results

Identification of maternal depressive symptom trajectories

A model with three trajectories of maternal depressive symptoms from the second trimester of pregnancy until 3 years postpartum demonstrated the best fit relative to models with two or four trajectories (BIC as the number of trajectories increased from two to four was 1905.3, 1882.7, and 1897.7). For the three-trajectory model, the mean posterior probability of being assigned to each trajectory was high for all groups (range 0.84–0.96) and above the recommended threshold of 0.8 (Wang and Bodner 2007). Analysis of the dataset excluding the 6-week and 10-month time points also yielded results consistent with a three-trajectory model demonstrating the best fit.

The three maternal depressive symptom trajectories are represented in Fig. 1. Mean depressive scores at each time point per trajectory can be found in Table 1. The "low" trajectory represented 71.4% ($n = 105$) of mothers and was characterized by consistently low depressive symptom scores. The "increasing" trajectory consisted of 18.4% ($n = 27$) of mothers and reflected a pattern of moderate depressive symptoms during pregnancy with increasing symptomatology over time. The "decreasing" trajectory, comprising 10.2% of mothers ($n = 15$), was characterized by high levels of depressive symptomatology during pregnancy that subsequently decreased. Notably, most moms in our sample were in the low group, a finding consistent with previous research (Campbell et al. 2009; Cents et al. 2013).

Maternal characteristics by trajectory group

Women in the low trajectory group had completed more years of education than women in the increasing group (Table 2); they also had lower proportions of prior diagnoses of depression or history of mental disorders, plus the lowest mean number of previous mental disorders, relative to those in the increasing and decreasing groups (Table 2). Women in the low group were less likely to have taken SSRIs during pregnancy than those in the other groups. This difference was still present between women in the low and increasing groups at 3 years postpartum (Table 2). Mean maternal age at child's birth, minority status, alcohol consumption during pregnancy, and method of delivery did not significantly differ across trajectory groups (Table 2).

Child characteristics by mother's depressive symptom trajectory

Child sex, age, minority status, gestational age, and birth weight were not differentially distributed among maternal depressive symptom trajectories (Table 3). However, children in the low group were exposed to fewer maternal depressive symptoms than those in either the increasing or decreasing groups (Table 3).

Maternal depressive symptom trajectories and child behavior at 3 years

At 3 years of age, children of mothers who had increasing depressive symptoms over time showed more behavior problems overall and more evidence of both internalizing and externalizing behaviors than children of mothers in the low group ($\beta = 10.3$, $p < 0.001$; $\beta = 9.1$, $p < 0.01$; $\beta = 9.7$, $p < 0.001$, respectively; Table 4). In contrast, the level of problem behaviors at age 3 was comparable between children of mothers in the low and decreasing trajectory groups, as were their levels on the internalizing and externalizing subscales (Table 4).

Maternal depressive symptom trajectories, child behavior, and executive functions at 6 years

At 6 years of age, maternal depressive symptom trajectories were unrelated to children's internalizing and externalizing symptomatology. However, children whose mothers became less depressed over time had lower reported levels of ADHD symptoms than those whose mothers had consistently few depressive symptoms ($\beta = -0.4$, $p = 0.006$). ADHD symptomatology did not differ between children of mothers in the increasing and low trajectory groups (Table 4).

Turning to executive functions, children of mothers in the low and decreasing trajectory groups showed similar levels of executive functions as assessed by the BRIEF and HF task (Table 4). However, children of mothers in the increasing trajectory group had poorer executive functions at age 6 than those of mothers in the low group, as assessed by both the BRIEF ($\beta = 5.2$, $p = 0.05$) and accuracy on the HF task ($\beta = -0.1$, $p = 0.03$; Table 4).

Results from sensitivity analyses were consistent with those from fully adjusted models (data not shown).

Discussion

We identified three distinct trajectories of maternal depressive symptoms from the second trimester of pregnancy through the first 3 years of a child's life that corresponded to low, increasing, and decreasing patterns over time. We found that children whose mothers' moods improved during this period (the decreasing trajectory group) showed similar internalizing and externalizing scores at 3 and 6 years of age, comparable executive functions, and even less evidence of ADHD-related symptoms when they were 6 years old than children whose mothers had little

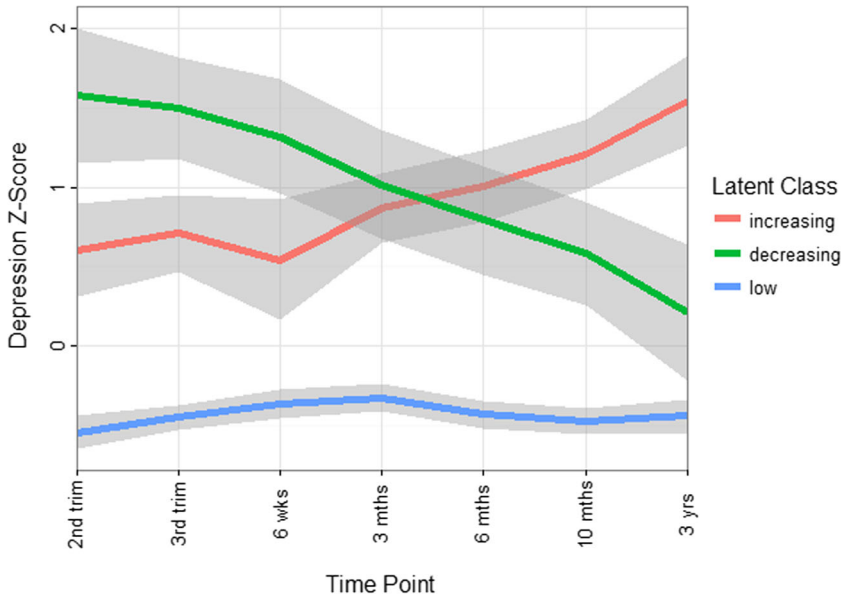

Fig. 1 Maternal depression trajectory groups. Trajectories were visualized using a locally weighted regression smoothing approach. Shaded bars represent 95% confidence intervals

depressive symptoms over time, despite mothers in the decreasing group remaining more symptomatic throughout than those who consistently showed few depressive symptoms. In contrast, children of mothers who had a trajectory of becoming increasingly depressive (i.e., the increasing group) showed more internalizing and externalizing behavior problems at age 3 and poorer executive functions at age 6 than children of mothers who had few depressive symptoms. Our findings on executive functions were consistent across maternal report and an objective, laboratory-based measure and hence are unlikely to be due to maternal reporting bias. Moreover, our analyses controlled for concurrent maternal depressive symptoms at age 6 years, suggesting a persistent effect of exposure to patterns of maternal depressive symptoms during the first 3 years of life on executive functions later in childhood.

It is notable that at no time during the child's first 3 years were the mean depression scores for mothers in the increasing or decreasing trajectory groups ever as low as for mothers in the low group. In fact, when we looked beyond the period of time covered by the trajectories, at 6 years postpartum, women in the decreasing group had even more depressive symptoms than women in the increasing group (Table 3). This pattern of recurring symptoms concurs with the observation of a high relapse rate of depression among mothers (Underwood et al. 2016). Not surprisingly, women in the low group had the lowest rate of SSRI use. It is possible that the higher SSRI

Table 1 Depression scores by trajectory group from the second trimester of pregnancy to 3 years postpartum for available data

	Low $n = 105$	Increasing $n = 27$	Decreasing $n = 15$
Depression *Z*-score, mean (SD)			
2nd trimester	− 0.52 (0.56)	0.58 (0.75)	1.63 (0.54)
3rd trimester	− 0.51 (0.55)	0.83 (0.64)	1.30 (0.87)
6 weeks	− 0.36 (0.57)	0.54 (0.60)	1.85 (1.46)
3 months	− 0.28 (0.75)	0.87 (0.84)	0.84 (0.89)
6 months	− 0.47 (0.53)	1.12 (0.72)	0.82 (0.63)
10 months	− 0.48 (0.48)	0.74 (1.01)	0.87 (0.55)
3 years	− 0.43 (0.52)	1.61 (0.77)	0.15 (0.96)
Raw depression score, mean (SD)			
2nd trimester (EPDS)	3.63 (3.42)	10.08 (4.77)	15.87 (3.80)
3rd trimester (EPDS)	3.40 (2.91)	9.92 (3.67)	12.14 (4.88)
6 weeks (EPDS)	3.90 (3.12)	7.81 (3.12)	12.17 (5.78)
3 months (EPDS)	3.32 (3.37)	9.81 (4.83)	9.93 (4.33)
6 months (EPDS)	3.41 (3.05)	12.19 (4.30)	9.86 (3.32)
10 months (EPDS)	3.22 (2.74)	8.45 (4.91)	9.88 (2.03)
3 years (BDI)	4.62 (4.36)	21.78 (6.45)	9.53 (8.07)

Missing observations per time point, presented in same order as table: 3, 5, 74, 1, 6, 77, 0

Table 2 Maternal characteristics by depression trajectory group ($n = 147$)

	Low_A $n = 105$	$Increasing_B$ $n = 27$	$Decreasing_C$ $n = 15$	Significant group differences*	Overall test statistic**, p value
Maternal characteristics					
Age at birth (years), mean (SD)	33.5 (±4.8)	32.9 (±5.9)	31.7 (±4.5)		0.9, 0.43
Education (years), mean (SD)	17.9 (±3.6)	15.6 (±2.3)	16.8 (±3.5)	B < A	5.2, 0.007
Minority status, *n* (%)					0.03, 0.98
Yes	19 (18.1%)	5 (18.5%)	3 (20%)		
No	86 (81.9%)	22 (81.5%)	12 (80%)		
History of depression, *n* (%)				A < BC	17.6, < 0.001
Yes	33 (31.4%)	18 (66.7%)	11 (73.3%)		
No	72 (68.6%)	9 (33.3%)	4 (26.7%)		
History of mental disorders, *n* (%)				A < BC	20.6, < 0.0001
Yes	50 (47.6%)	23 (85.2%)	14 (93.3%)		
No	55 (52.4%)	4 (14.8%)	1 (6.7%)		
Number of previous mental disorders, mean (SD)	1.0 (±1.3)	2.0 (±1.3)	2.4 (±1.6)	A < BC	11.1, < 0.0001
Delivery mode, *n* (%)					2.6, 0.27
Vaginal	81 (77.1%)	17 (63.0)	10 (66.7%)		
Cesarean section	24 (22.9%)	10 (37.0%)	5 (33.3%)		
Alcohol consumption during pregnancy, mean (SD)	3.9 (±7.7)	2.4 (±5.2)	4.9 (±6.6)		0.7, 0.52
SSRI use prenatally, *n* (%)				A < BC	21.3, < 0.0001
Yes	30 (28.6%)	20 (74.1%)	9 (60.0%)		
No	75 (71.4%)	7 (25.9%)	6 (40%)		
SSRI use at 3 years, *n* (%)				A < B	13.9, < 0.001
Yes	30 (28.6%)	18 (66.7%)	7 (46.7%)		
No	75 (71.4%)	9 (33.3%)	8 (53.3%)		
Other psychotropic drug use, *n* (%)				A < BC	27.8, < 0.000001
Yes	2 (1.9%)	8 (29.6%)	5 (33.3%)		
No	103 (98.1%)	19 (70.4%)	10 (66.7%)		

*Family-wise error rate of $p < 0.05$

**For ANOVA, F-statistic; for chi-square test, χ^2-statistic

use observed among women in the increasing and decreasing trajectory groups reflects drug failure and raises the need to consider additional treatment modalities for women at-risk of depression.

We identified fewer trajectories than in most previous studies; this is likely due to differences in analytic methods (Muthén and Muthén 2000), sample sizes, and cohort characteristics. Nonetheless, there are areas of convergence between our study and others. Another study that modeled maternal depression trajectories from pregnancy until 27 years later (Najman et al. 2016) identified three groups of women: those with few or no symptoms or high-escalating depressive symptoms over time may correspond to our low and increasing groups. The principal difference was that their third group was women with occasional depressive symptoms, and our third group was women with initially high then decreasing symptoms (though this difference may be reflective of the shorter duration of follow-up in our study). Moreover, the high-chronic trajectories reported in other research (Betts et al. 2014; Betts et al. 2015; Cents et al. 2013; Guyon-Harris et al. 2015; van der Waerden et al. 2015) may correspond to the increasing trajectory we identified.

Based on a "*fetal programming*" hypothesis (Glover et al. 2010), we had predicted that children of mothers in the decreasing trajectory group would look worse on our outcome measures at 3 and 6 years than children of mothers with the least depressive symptoms. Instead, at both ages, children of mothers with decreasing depressive symptoms showed outcomes as good or better than those of mothers who consistently had few depressive symptoms over time. Our findings stand in contrast to other research that has found that prenatal maternal depression independently predicts poorer cognitive development and mental health in offspring (Evans et al. 2012; O'Donnell et al. 2014). Our findings also differ from those of other trajectory-based studies that

Table 3 Child characteristics and outcomes by maternal depression trajectory group (n = 103)

	Low_A $n = 76$	$Increasing_B$ $n = 18$	$Decreasing_C$ $n = 9$	Significant group differences*	Overall test statistic**, p value
Child characteristics					
Sex, n (%)					2.5, 0.28
Male	35 (46.1%)	6 (33.3%)	2 (22.2%)		
Female	41 (53.9%)	12 (66.7%)	7 (77.8%)		
Age at 3 years, mean (SD)	3.6 (± 0.6)	3.8 (± 0.8)	3.6 (± 0.3)		1.3, 0.28
Age at 6 years, mean (SD)	5.9 (± 0.6)	6.1 (± 0.7)	6.1 (± 0.5)		1.3, 0.29
Minority status, n (%)					0.5, 0.77
Yes	16 (21.1%)	4 (22.2%)	1 (11.1%)		
No	60 (78.9%)	14 (77.8%)	8 (88.9%)		
Gestational age at birth (weeks), mean (SD)	39.8 (± 1.4)	39.5 (± 1.8)	38.7 (± 1.7)		2.1, 0.13
Birth weight (grams), mean (SD)	3451.3 (± 489.4)	3217.6 (± 490.9)	3239.8 (± 426.0)		2.2, 0.12
Exposure to maternal depression at 6 years (HAMD), mean (SD)	5.8 (± 5.2)	13.4 (± 5.1)	14.3 (± 7.4)	A < BC	21.2, < 0.0000001
Child outcomes – 3 years					
Total CBCL score, mean (SD)	44.63 (9.76)	55.00 (10.20)	44.44 (4.25)	AC < B	8.85, < 0.001
CBCL score – Internalizing, mean (SD)	45.18 (10.66)	55.44 (9.90)	47.89 (4.37)	A < B	7.43, < 0.001
CBCL score – Externalizing, mean (SD)	44.75 (9.79)	52.89 (10.90)	44.44 (6.06)	A < B	5.22, 0.007
Child outcomes – 6 years					
HBQ – Internalizing, mean (SD)	0.30 (0.22)	0.39 (0.28)	0.29 (0.23)		1.34, 0.27
HBQ – Externalizing, mean (SD)	0.28 (0.23)	0.32 (0.19)	0.26 (0.13)		0.32, 0.73
HBQ – ADHD, mean (SD)	0.63 (0.35)	0.61 (0.42)	0.34 (0.21)		2.6, 0.08
Executive function – Global BRIEF scores, mean (SD)	52.47 (8.35)	58.78 (9.17)	47.44 (7.57)	AC < B	6.30, 0.002
Executive function – HF % correct on block 3, mean (SD)	0.68 (0.23)	0.62 (0.23)	0.64 (0.27)		0.58, 0.56

*Family-wise error rate of $p < 0.05$

**For ANOVA, F-statistic; for chi-square test, χ^2 -statistic

found children of mothers who had elevated depressive, anxious, and stress symptoms only during pregnancy had worse mental health in adolescence and young adulthood (Betts et al. 2014; Betts et al. 2015). These differences in results may be due to methodological differences, specifically in the number of mental health symptoms included when computing the trajectories and the analytic approach taken to statistical modeling.

Indeed, our study findings are in line with recent research that found significant effects of exposure to maternal depression in early childhood, and not perinatally, on child behavioral problems after controlling for confounding by familial environment (Gjerde et al. 2017). Moreover, other studies that solely included depressive symptoms when modeling trajectories have also shown findings consistent with those of our study regarding the influence of the *timing* of maternal mood: a maternal depression trajectory with high depressive symptoms during pregnancy alone was not associated with children's behavior at age 5, (van der Waerden et al. 2015), and an early postnatal trajectory characterized by high levels of maternal depression that subsided by 24 months did not predict poorer behavioral or mental health outcomes when children were 15 years old (Campbell et al. 2009). The effect of postnatal, and not prenatal, maternal depressive symptoms on child outcomes is noteworthy. It is possible that depressed mothers are able to meet children's needs in early life, but that deficits begin to emerge as children age and require more engaged parenting (Gjerde et al. 2017). Additional studies that model maternal depression trajectories longitudinally, beyond the time covered in our trajectories, and continue to track cognitive, behavioral, and mental health outcomes into childhood and beyond are warranted to clarify how the course of pre- and postnatal depression affects child development.

Table 4 Linear regression models estimating the effect of maternal depression trajectories on child outcomes at ages 3 and 6 years

		Low $n = 76$	Increasing $n = 18$			Decreasing $n = 9$		
			β (95% CI)	t value	p value	β (95% CI)	t value	p value
Age 3								
Total CBCL score	Unadjusted	Reference	10.4 (5.4–15.3)	4.2	< 0.0001	− 0.2 (− 6.9–6.5)	− 0.06	0.96
	Adjusted[a]	Reference	10.3 (4.9–15.7)	3.8	< 0.001	− 0.6 (− 7.8–6.6)	− 0.2	0.87
CBCL score – Internalizing	Unadjusted	Reference	10.3 (5.0–15.5)	3.9	< 0.001	2.7 (− 4.4–9.8)	0.8	0.45
	Adjusted[a]	Reference	9.1 (3.4–14.9)	3.1	0.002	2.2 (− 5.6–9.9)	0.6	0.58
CBCL score – Externalizing	Unadjusted	Reference	8.1 (3.1–13.2)	3.2	0.001	− 0.3 (−7.1–6.5)	− 0.09	0.93
	Adjusted[a]	Reference	9.7 (4.2–15.2)	3.5	< 0.001	0.3 (− 7.0–7.6)	0.07	0.94
Age 6								
HBQ – Internalizing	Unadjusted	Reference	0.1 (−0.02–0.2)	1.6	0.11	− 0.002 (− 0.2–0.2)	− 0.02	0.98
	Adjusted[b]	Reference	0.01 (− 0.1–0.2)	0.2	0.81	− 0.07 (−0.3–0.1)	− 0.9	0.39
HBQ – Externalizing	Unadjusted	Reference	0.04 (− 0.1–0.2)	0.7	0.48	− 0.02 (−0.2–0.1)	− 0.2	0.79
	Adjusted[b]	Reference	− 0.003 (− 0.1–0.1)	− 0.04	0.96	− 0.04 (− 0.2–0.1)	− 0.5	0.64
HBQ – ADHD	Unadjusted	Reference	− 0.02 (− 0.2–0.2)	− 0.2	0.86	− 0.3 (− 0.5–− 0.03)	− 2.3	0.03
	Adjusted[b]	Reference	− 0.1 (− 0.3–0.1)	− 1.1	0.29	− 0.4 (− 0.7–− 0.1)	− 2.8	0.006
Executive function – Global BRIEF scores	Unadjusted	Reference	6.3 (1.9–10.7)	2.8	0.005	− 5.0 (− 10.9–0.9)	− 1.7	0.09
	Adjusted[b]	Reference	5.2 (− 0.04–10.3)	2.0	0.05	− 6.5 (− 13.2–0.2)	− 1.9	0.06
Executive function – HF % correct on block 3	Unadjusted	Reference	− 0.06 (− 0.2–0.1)	− 1.0	0.31	− 0.03 (− 0.2–0.1)	− 0.5	0.64
	Adjusted[b]	Reference	− 0.1 (− 0.2–− 0.009)	− 2.1	0.03	− 0.06 (− 0.2–0.09)	− 0.9	0.39

[a] Adjusted for child sex, age, gestational age at birth, birth weight, prenatal SSRI exposure, maternal depression prior to pregnancy, maternal minority status, and maternal education

[b] Adjusted for all of the above, and maternal depression at 6-year follow-up

Overall, an adverse and persistent effect of an increasing trajectory of maternal depressive symptoms on children's behavior is consistent with previous findings (Campbell et al. 2009; Cents et al. 2013; van der Waerden et al. 2015). Our results extend these findings by suggesting that early behavioral disturbances seen in relation to chronic, increasing maternal depression may subsequently manifest in later childhood as disruptions in executive functions. One explanation for these results implicates the role of parental behaviors. Prior research has shown that postpartum depression results in poorer parenting behaviors specifically within domains that encourage the development of children's emerging cognitive skills such as play, talking, singing, and reading (McLearn et al. 2006; Paulson et al. 2006). In turn, children exposed to poorer parenting during infancy and toddlerhood have worse executive functions starting as young as 18 months (Bernier et al. 2010; Hughes and Ensor 2009). Another possible pathway by which maternal depression may lead to worse executive functions in children is via the development of less secure attachment styles and poorer socio-emotional regulation (Maughan et al. 2007; Toth et al. 2009).

As executive functions are especially vulnerable to adverse environmental impacts, such as stress or lack of social connection (Diamond 2013), it is plausible that increasing maternal depressive symptoms would selectively and disproportionately affect executive functions. As impairments in executive functions have also been widely observed in mental and physical illness (Snyder 2013), understanding the risk factors associated with poorer executive function and intervening to improve executive functions in preschoolers or earlier holds promise for reducing inequalities in health, wealth, and quality of life, and for positioning children to have better lifelong outcomes (Diamond 2016; Moffitt et al. 2011).

A number of limitations should be mentioned in conjunction with our study results. As our cohort was over-sampled from women at high risk for mental illness, our results may not be generalizable to other populations. While we detected statistically significant differences in our outcome measures, our cohort size was limited, and our findings require replication in independent studies. The loss to follow-up in the study cohort is also a limitation as it may have introduced a form of selection bias, with more depressed mothers dropping out of the study. Though we found minimal evidence of selection bias due to illness severity, it is possible (and likely) that there are sources of selection bias that we did not capture. A related limitation is that we assumed data were missing at random in the computation of our trajectories; yet, this may not be the case as more depressed women may be more likely to miss a study assessment. Maternal reporting bias is also a concern

(Najman et al. 2001); however, it cannot explain our results as mothers in the increasing and decreasing groups had similarly high levels of depressive symptoms when their children were 6 years old; yet, the latter group reported better executive functions in their children than the former. Additional limitations are the use of different measures of depressive symptoms at different time points and that we were unable to assess the influence of other parental figures on children. Finally, we cannot rule out the possibility that our findings reflect heritability, though we attempted to address this issue by including maternal history of depression in our analyses, other sources of unmeasured confounding, or reverse causality.

To conclude, our study reports that long after pregnancy, there are women who continue to have high and increasing depressive symptoms, and that these mood patterns have an impact on their children. The impact appears to be higher internalizing and externalizing behaviors at age 3 years that emerge as poorer executive functions at age 6 years. Our study also identified a group of women whose depressive symptoms decreased over pregnancy and the following 3 years. Even though these mothers' moods remained consistently worse than those of low-depression mothers, associations between their children's behavioral outcomes at 3 years, and mental health indicators and executive functions at 6 years, in relation to exposure to maternal depressive symptom trajectories, were comparable between both groups. Our findings provide insight into the developmental sequelae of exposure to different trajectories of maternal depressive symptoms from pregnancy into early childhood. Importantly, our study suggests that if mothers with initially high levels of depressive symptoms experience even partial remission of symptoms during their child's first 3 years of life, their children's emotional, cognitive, and behavioral development remain unaffected. Our findings provide impetus to monitor and treat maternal depression, even years after birth, for the benefit of both mother and child.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethics statement Ethical approval for the study was obtained from the University of British Columbia Ethics Board and the Children's and Women's Health Centre of British Columbia Research Review Committee.

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