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ORIGINAL ARTICLE

Depression during gestation in adolescent mothers interferes with neonatal neurobehavior

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Objective: To compare the neurobehavior of neonates born to adolescent mothers with and without depression during gestation.
Methods: This prospective cross-sectional study included healthy term neonates born to adolescent mothers with untreated depression during gestation, without exposure to legal or illicit drugs, and compared them with infants born to adolescent mothers without psychiatric disorders. Maternal psychiatric diagnoses were assessed by the Composite International Diagnostic Interview (CIDI 2.1) and neonatal neurobehavior by the Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS) at 24 to 72 hours of life. Neurobehavioral outcomes were analyzed by ANOVA adjusted for confounders.
Results: 37 infants born to mothers with depression during gestation were compared to 332 infants born to mothers without psychiatric disorders. Infants of mothers with depression had smaller head circumferences. Significant interactions of maternal depression and male gender, gestational age > 40 weeks, regional anesthesia during delivery, vaginal delivery, and infant head circumference $\geqslant 34$ cm were found. Worse performance was noted in the following neonatal neurobehavioral parameters: arousal, excitability, lethargy, hypotonicity, and signs of stress and abstinence.
Conclusion: Infants born to adolescent mothers with depression exhibit some behavioral changes in the first days of life. These changes are associated with infant sex, gestational age, type of anesthesia, mode of delivery, and head circumference.

Keywords: Depressive disorder; pregnancy in adolescence; infant behavior

Introduction

Pregnancy during adolescence is a public health problem. In Brazil, in 2010, 19.3% of all births occurred in mothers aged 10-19 years.[1] In the United States, in the same year, 9.3% of all births were from adolescent mothers.[2] Most adolescent mothers are psychologically and emotionally immature,[3] which poses a risk to mother-infant bonding.[4]

Depression is frequent during gestation. A study of 1,795 pregnant women aged 29±5 years in the second trimester of gestation showed that 14% had one or more psychiatric disorders, and depression was observed in 10% of the participants.[5] Adolescence is a transitional developmental period, which is plastic from neurobiological, behavioral, and psychological perspectives. There is a high prevalence of depressive, emotional, and behavioral disorders, including substance abuse, among adolescents.[6] In São Paulo, Brazil, 1,000 pregnant adolescents were evaluated by the Composite International Diagnostic Interview (CIDI 2.1),[7] and 28% were found to have one or more psychiatric disorders: depression in 13%, post-traumatic stress in 10%, anxiety in 6%, psychotic disorders in 3.5%, and other disorders in 3.7%.[8] Caputo & Bordin, using the Youth Self Report in Brazilian adolescents, showed that pregnant girls, compared with non-pregnant adolescents, reported a higher frequency of anxiety and depression symptoms (24 vs. 15%; $p < 0.001$) and internalizing behavior (13 vs. 5%; $p < 0.001$).[9]

Negative social experiences and emotional states in women can trigger a physiological stress response that influences the risk for poor fetal outcomes. Stress during pregnancy is associated with low birth weight, intrauterine growth restriction, and prematurity.[10] Follow-up of pregnant women that suffered post-traumatic stress disorder after the events of September 11, 2001 showed offspring with smaller head circumference at birth.[11] High levels of depressive symptoms during gestation were associated with premature birth and lower Apgar scores.[12] However, a Swedish study did not show any association between maternal anxiety or depression disorder and adverse newborn outcomes.[13]

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Psychiatric disorders during pregnancy can also interfere with neonatal behavior. Newborns of mothers with antepartum and postpartum depressive symptoms exhibit high urine cortisol and norepinephrine levels, low dopamine levels, electroencephalographic frontal asymmetry, and lower vagal tone.[14,15] They also spend more time in deep sleep and less time in quiet and active alert states, with more state changes and worse performance on the Brazelton Neonatal Behavior Assessment Scale (NBAS).[15] Van der Wal et al. showed that depressive symptoms, anxiety, and stress during gestation are associated with excessive infant crying.[16] Neonates born to mothers who reported more chronic stress during pregnancy had lower scores for orientation and state regulation at NBAS evaluation.[17] On administration of the Neonatal Intensive Care Unit Neurobehavioral Network Scale (NNNS), newborn infants of mothers with depressive symptoms showed lower arousal scores and higher stress scores at 5 days of life as compared to infants born to mothers without depression.[18] Another study comparing infants of mothers who had depression during pregnancy to infants of non-depressed mothers showed poorer self-regulation, more signs of stress, and greater excitability and arousal in the former at 1 month of age.[19] Using the NNNS in the first 3 weeks of life, Salisbury et al. noted that infants of depressed mothers who did not take antidepressants exhibited lower attention scores compared to those whose mothers used antidepressants. In the same study, lower quality of movements and more signals of stress and abstinence were observed in infants of mothers with depression who had not received antidepressant therapy as compared with babies of mothers without depression.[20] However, Suri et al. examined the effects of antidepressants during pregnancy on early infant neurobehavior using the NBAS in the first week of life and, again, at 6 to 8 weeks of age and did not find differences between the neurobehavior of infants of depressed mothers, regardless of exposure to antidepressants, and that of infants born to non-depressed mothers.[21]

The brief description above suggests that depression is more common in adolescents and pregnant women, and that the influence of maternal depression on neonatal neurobehavior is controversial. Therefore, the aim of this study was to ascertain whether prenatal maternal depression interferes with the neurobehavior of neonates born to adolescent mothers, assessed between hours 24 and 72 of life. We hypothesized that newborn infants of adolescent mothers with depression would exhibit poorer neurobehavioral performance in the first days of life as compared with infants of adolescent mothers who did not have psychiatric disorders during pregnancy.

Methods

This prospective cross-sectional study was conducted at Hospital Municipal e Maternidade Escola Mario de Moraes Altenfelder Silva, a tertiary municipal hospital in São Paulo, Brazil, between July 2001 and November 2002. The study was approved by the Ethics Committees of the hospital and of the Federal University of São Paulo and was funded by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP grant no. 00/10.293-5). After birth, one of the investigators explained the study and read the informed consent to each adolescent mother. After addressing any questions, the investigator asked the mother to sign the consent form.

Neonates were included in the study according to the following criteria: signed maternal informed consent; adolescent mothers aged 10 through 19 years, and full-term newborn infants, defined as those with gestational age between 37 weeks and 41 weeks and 6 days, preferably according to obstetric estimates (date of last menstrual period or first trimester ultrasound) or by the New Ballard method.[22] Neonates with conditions that could potentially interfere with their neurobehavioral assessment, such as those whose mothers had positive serology for syphilis, toxoplasmosis, cytomegalovirus, or human immunodeficiency virus; psychiatric disorders, except depression; use of antidepressants during pregnancy, administration of opioids, sedatives, and/or anticonvulsants to mothers during the 24 hours prior to delivery; newborn infants whose mothers received systemic anesthesia for delivery; neonates exposed during pregnancy to tobacco, alcohol, marijuana, cocaine, or other illicit drugs; multiple births; neonates with 1-minute Apgar scores less than 3 or 5-minute Apgar scores less than 7; infants with major congenital malformations or genetic syndromes; and those small or large for gestational age and/or with any clinical problems requiring supportive care (incubator, oxygen, vascular access, orogastric tube, and/or any medications) were excluded from the sample. Maternal psychiatric disorders and use of tobacco, alcohol, marijuana, cocaine, or other illicit drugs during pregnancy were identified by the CIDI 2.1.[7] Marijuana and cocaine use during pregnancy were also identified by toxicological analysis of maternal hair and newborn infant meconium for the whole studied sample. A 3-cm segment of hair collected near the scalp was analyzed by semiquantitative enzymatic immunoassay after initial decontamination. All positive results were confirmed by gas chromatography and mass spectrometry. Meconium samples were collected in the first 48 hours and analyzed by a homogeneous semiquantitative enzymatic immunoassay.

Neonates and their mothers were studied by a team of five neonatologists, three psychologists, and two psychiatrists. This stage of the study comprised the following steps: 1) maternal interview by the neonatologists for collection of sociodemographic and obstetric data; 2) administration of the CIDI 2.1[7] to the mothers by the psychologists; 3) clinical examination of the neonate for collection of data related to birth and clinical course until inclusion in the study; 4) neurobehavioral assessment of the infants by the neonatologists with the NNNS[23]; 5) collection of maternal hair and neonatal meconium samples for analysis regarding the presence of marijuana and cocaine metabolites.

The CIDI is a standardized and structured diagnostic interview that identifies psychiatric disorders according to

ICD-10 and DSM-IV. The tool contains 276 symptom questions, many of which are coupled with probe questions to evaluate symptom severity, as well as questions for assessing help-seeking behavior, psychosocial impairments, and other episode-related questions. It can be used in epidemiological studies of mental disorders, but also for clinical and other research purposes. The test-retest reliability ranges from 81 to 98%, the inter-rater agreement from 97 to 100%, and the diagnostic agreement from 0.76 to 0.84.[24] It can identify psychiatric disorders such as depression, anxiety, PTSD, mania, bipolar, psychotic, dissociative, somatoform or eating disorders, as well as alcohol, tobacco, or illicit drug use, occurring throughout life or in the last 12 months. Neonates of mothers without any psychiatric disorder and those whose mothers were identified as having depression in the last year but had not received antidepressants were studied.

The NNNS evaluates the neurological integrity, behavioral function, and presence of signs of stress and abstinence in newborn infants. The NNNS was administered after the 24th hour of life, when the global stress response to the birth process is already attenuated, and before the 72nd hour of life. The examination was carried out in a specific, warm, quiet, and dimly lit room by one of four previously trained neonatologists. The principal investigator was certified to perform the NNSS in Rhode Island Hospital, Brown University, Providence, RI, according to the Maternal Lifestyle Study.[25] The other three were trained by the principal investigator in the same way. After completion of the NNNS evaluation, the items assessed were grouped into 13 variables according to Boukydis et al.[26] (Table 1).

Maternal and neonatal characteristics and NNNS scores were compared between neonates born to mothers with depression and those born to mothers without any psychiatric disorders by the chi-square test or Student *t*-test. Analysis of variance (ANOVA) was used to compare NNNS scores between infants of mothers with and without depression, adjusted for confounders (anesthesia, mode of delivery, sex, gestational age, head circumference, age of the neonate, and time between last feeding and the NNNS). The interaction between independent factors with the mean scores of the NNNS variables was also tested by ANOVA. The independent variables analyzed were depressive disorder (absent vs. present), anesthesia (absent or local vs. regional), mode of delivery (vaginal vs. cesarean section), sex (female vs. male), gestational age ($<$ or $\geqslant$ 40 weeks), head circumference ($\leqslant$ or $>$ 34 cm), age of the neonate at NNNS administration ($\leqslant$ or $>$ 33 hours), and time between last feeding and the NNNS ($\leqslant$ or $>$ 30 minutes). For the last four variables, cutoffs were chosen according to the median value obtained for the whole studied population.

The sample size needed to detect an average difference of 0.7 points in the 13 items of the NNNS scores between infants of mothers with depression and infants of mothers without any psychopathologic disorder, with a standard deviation of 1.0, an alpha error of 5%, and a power of 80%, was 32 for each studied group. The values used for this calculation were based on the expected NNNS scores obtained for term newborn infants of adolescent mothers.[27] All statistical procedures were performed in SPSS 13.0.

Results

From July 2001 to November 2002, 3,685 infants were born in the study hospital, 928 (25%) of whom were born to adolescent mothers. Among these, 131 were preterm, five were post-term, and 423 met one or more exclusion criteria: positive serology for congenital infections (26);

Table 1 Description of NNNS variables

NNNS variables	Meaning of high scores
Habituation	Good capacity of the infant to protect his or her sleep by progressively tuning out a stimulus, after an initial response.
Attention	Good turning and following on the visual and auditory stimulation, and sustained alertness.
Arousal	Infant who is easily aroused to fuss and cry during the examination, and highly active while being handled and while left alone.
Regulation	Good physiologic, motor, and attentional responses to the demands of the exam.
Handling	Infants who need substantial input from the examiner to elicit orientations.
Quality of movements	Good quality of movements: smooth movement with little or no jitteriness, tremors, or startles, and average amounts of spontaneous and elicited motor activity.
Excitability	Infants who become irritable during the examination, as well as those who remain irritable despite repeated attempts by the examiner to soothe them.
Lethargy	Examiner made efforts to bring the infant to a stable alert state to evaluate his or her response to visual and auditory stimulation.
Non-optimal reflexes	Number of non-optimal responses during reflexes.
Asymmetric reflexes	Number of asymmetric responses during reflexes.
Hypertonicity	Infants with increased tone in arms, legs, trunk, neck, and shoulders.
Hypotonicity	Infants who were consistently hypotonic in arms, legs, truck, neck, and shoulders.
Stress/Abstinence	Infant showed many signs of stress or abstinence during the exam.

NNNS = Neonatal Intensive Care Unit Network Neurobehavioral Scale.

Table 2 Demographic characteristics of adolescent mothers with (n=37) and without (n=332) depression during gestation

	Maternal depression disorder		
	Absent (n=332)	Present (n=37)	p-value
Maternal age*	16.91±0.16	16.92±0.45	0.962
White race, n (%)	170 (51)	19 (51)	0.987
Married, n (%)	211 (64)	24 (65)	0.875
Years in school*	7.19±0.24	7.32±0.76	0.714
Per capita income (US$ per month)*	98.15±7.57	94.20±30.40	0.750
Prenatal care received, n (%)	320 (96)	36 (97)	0.776
Prenatal care visits*	6.75±0.29	7.75±0.76	**0.031**
Vaginal delivery, n (%)	242 (73)	31 (84)	0.152
Regional anesthesia, n (%)	252 (76)	28 (76)	0.975

* Data presented as mean ± 1.96 × standard error.
Significant p-values set in bold type.

maternal use of opioids/sedatives 24 hours prior to delivery (7); any maternal use of tobacco, alcohol, marijuana, and/or cocaine (170); maternal psychiatric disorders, except depression (77); multiple gestation (6); Apgar score < 3 at 1 minute or < 7 at 5 minutes (16); major congenital malformations or genetic syndromes (2); small or large for gestational age (203); or clinical problems (65).

Therefore, 369 infants were studied: 37 infants of mothers with non-treated depression and 332 infants of mothers without any psychiatric disorders. The characteristics of mothers with and without depression during gestation are displayed in Table 2. Mothers with depression during gestation had more prenatal care visits than those without any psychiatric disorder (7.7±2.3 vs. 6.7±2.1; p = 0.031).

Neonatal demographic characteristics and data regarding timing of NNNS administration are shown in Table 3. The neonates of the two groups were similar, except for head circumference; babies of mothers with non-treated depression had smaller head circumferences than those of mothers without psychiatric disorders (33.8±1.1 vs. 34.4±1.1 cm; p = 0.003).

Table 4 shows the neurobehavioral scores of the two studied groups. No differences were observed in NNNS scores between groups with or without adjustment for type of anesthesia, delivery mode, sex, gestational age, age at neurologic exam, exam duration, and time between last feeding and the exam.

For each NNNS variable, interactions between depression and the independent variables were studied. Male infants of mothers with depression had higher arousal (3.95±0.16 vs. 3.49±0.18; F = 4.939; p = 0.027) and excitability scores (3.20±0.41 vs. 2.04±0.47; F = 4.032; p = 0.045) than female infants; these differences were not observed in infants born to mothers without depression. Infants born to mothers with depression at a gestational age of < 40 weeks had higher lethargy scores (5.55±0.56 vs. 3.86±0.80; F = 5.727; p = 0.022) than those with gestational age $\geqslant 40$ weeks; this difference was not observed in infants of mothers without depression. Neonates born to mothers with depression and delivered under regional anesthesia had higher hypotonicity scores than those born from mothers with depression who had not receives anesthesia or who had received only local anesthetics (0.17±0.07 vs. 0.02±0.12; F = 5.727; p = 0.017); this difference was not observed in infants of mothers without depression. Finally, infants born to mothers with depression and with a head circumference > 34 cm had higher stress and abstinence scores than infants with a head circumference $\leqslant 34$ cm (0.09±0.01 vs. 0.03±0.01; F = 8.752; p = 0.003), and infants of mothers with depression who were delivered vaginally had

Table 3 Demographic characteristics and data at NNNS assessment of newborn infants of mothers with (n=37) and without (n=332) depression during gestation

	Maternal depression disorder*		
	Absent (n=332)	Present (n=37)	p-value
Gestational age (weeks)	39.34±0.12	39.31±0.33	0.898
Birth weight (g)	3233.45±31.79	3220.95±91.49	0.807
Length (cm)	48.9±0.16	48.6±0.51	0.298
Head circumference (cm)	34.37±0.12	33.78±0.35	**0.003**
Male sex, n (%)	180 (54)	22 (59)	0.604
Apgar at 1 minute	8.17±0.14	8.05±0.47	0.599
Apgar at 5 minutes	9.57±0.06	9.65±0.20	0.462
Postnatal age (hours)	33.39±0.73	33.52±2.41	0.912
Exam duration (minutes)	22.47±1.12	21.81±1.67	0.465
Time after feeding (minutes)	47.58±5.72	54.59±20.91	0.458
Length of hospital stay (days)	2.46±1.00	2.54±0.33	0.601

NNNS = Neonatal Intensive Care Unit Network Neurobehavioral Scale.
* Data presented as mean ± 1.96 × standard error, unless noted otherwise.
Significant p-values set in bold type.

Table 4 NNNS scores of newborn infants of mothers with (n=37) and without (n=332) depression during gestation in the studied population

	Maternal depression disorder			
	Absent (n=332)	Present (n=37)	p-value	Adjusted p-value*
Habituation	6.95±0.20 (n=197)	6.87±0.72 (n=20)	0.802	0.939
Attention	5.77±0.14 (n=305)	5.46±0.43 (n=34)	0.182	0.180
Arousal	3.71±0.08	3.69±0.25	0.865	0.829
Regulation	6.05±0.08	6.09±0.24	0.747	0.723
Handling	0.36±0.02	0.35±0.08	0.820	0.899
Quality of movement	5.24±0.06	5.28±0.16	0.599	0.409
Excitability	2.70±0.20	2.65±0.59	0.874	0.898
Lethargy	4.55±0.29	5.05±0.86	0.270	0.415
Non-optimal reflexes	9.31±0.14	9.19±0.37	0.581	0.733
Asymmetric reflexes	0.74±0.12	0.59±0.22	0.425	0.413
Hypertonicity	0.17±0.04	0.27±0.14	0.180	0.098
Hypotonicity	0.11±0.04	0.14±0.12	0.658	0.874
Stress/Abstinence	0.067±0.01	0.073±0.02	0.440	0.427

NNNS = Neonatal Intensive Care Unit Network Neurobehavioral Scale.
Data presented as mean ± 1.96 × standard error.
* Adjusted for type of anesthesia, delivery mode, sex, gestational age, age at neurologic exam, time between last feeding and the exam, and head circumference.

higher stress and abstinence scores than infants who were delivered by cesarean section (0.10±0.01 vs. 0.02±0.02; F = 8.579; p = 0.004); these differences were not found between babies of mothers without depression. No interactions were found between the independent variables and the presence of maternal depression on the following NNNS variables: habituation, attention, regulation, handling, quality of movements, non-optimal reflexes, asymmetric reflexes, or hypertonicity.

Discussion

In this study, the neonatal neurobehavior of infants born to adolescent mothers identified by the CIDI as having non-treated depression during gestation and evaluated in the second or third day of life by the NNNS was compared with the neurobehavior of infants born to adolescent mothers without any psychiatric disorders. No between-group differences were found in any of the 13 NNNS parameters (habituation, attention, arousal, regulation, handling, quality of movements, excitability, lethargy, non-optimal reflexes, asymmetric reflexes, hypertonicity, hypotonicity, and signs of stress and abstinence). However, interactions between maternal depression and obstetric/neonatal variables were found. Male infants born to mothers with depression were easily aroused and were more excitable than female neonates. Furthermore, less mature neonates of depressive mothers (gestational age: $37^{0/7}$ to $39^{6/7}$) were more lethargic than those with gestational age $\geqslant$ 40 weeks. Infants born to mothers with depression and delivered under regional anesthesia were more hypotonic than those delivered under local or no anesthesia. Infants born to mothers with depression and with a greater head circumference, or those delivered vaginally, exhibited more signs of stress and abstinence.

Therefore, subtle neurobehavioral performance changes, mainly on items related to self-regulation ability, were noted in infants whose mothers were diagnosed by a structured and validated psychological exam as having depression soon after birth, associated with some neonatal characteristics that may enhance vulnerability to poorer neurobehavioral performance, such as anesthesia during delivery, mode of delivery, sex, gestational age, and head circumference. Similar results were found in other studies. Male healthy term neonates, after a mildly stressful behavioral assessment procedure, the NBAS, exhibited higher cortisol levels and lower motor performance cluster scores than female infants.[28] Infants that were delivered under epidural anesthesia with bupivacaine, compared to those delivered without anesthesia, showed poorer NBAS performance on orientation and motor clusters during the first month of life. Those findings were explained by longer labor, more forceps deliveries, and a greater amount of oxytocin use.[29]

Few studies have analyzed the neurobehavior of neonates born to mothers with depression during gestation. Abrams et al.[30] evaluated 47 newborns of mothers with depression, identified by the Beck Depression Inventory, and administered the NBAS in the first 24 hours after birth. Compared to babies of mothers without depression, the neonates born to mothers with depression had lower scores on the orientation cluster and exhibited less motor tone and activity, more irritability, and less robustness and endurance during the examination. Lundy et al.[31] evaluated 20 full-term infants born to mothers with depression, identified by the Center for Epidemiological Studies Depression Scale, and compared them to 20 neonates born to mothers without depression. The NBAS was administered between hours 24 and 72 of life. Babies born to mothers with depression had lower scores on orientation, motor behavior, more abnormal reflex responses, lower activity levels, lower robustness and endurance scores, and higher excitability scores. The same group of authors studied the neurobehavior of 36 babies born to mothers with depression during the first week of life and reported lower orientation scores, more abnormal reflex responses, higher excitability, and more withdrawal symptoms.[32]

The results of studies that have evaluated the neonatal neurobehavioral performance of infants born to mothers with depression are inconsistent due to methodological differences. These studies used different tools to identify maternal depression, and some studies did not adjust their results for confounders, such as intake of antidepressants, alcohol, tobacco, or illicit drugs during gestation. Furthermore, neonatal neurobehavior was assessed by different tests at different periods, ranging from the first day of life to 6-8 weeks of age. Despite these differences, most studies confirm our results, showing that neonates born to mothers who experienced non-treated depression during gestation exhibit difficulties regarding state regulation, excitability, lethargy, and muscle tone in the first days after birth, especially if maternal depression is associated with biological or environmental risk factors for neonatal behavioral maladaptation, such as gestational age, sex, anesthesia during delivery, and mode of delivery. These findings support the hypothesis of fetal programming by antenatal maternal depression. Maternal psychiatric disorders may provide a prenatal environment that interacts with genetic factors to define phenotype at birth.[33] More studies in this field are needed to clarify the pathways that may explain the influence of depression during gestation on neonatal neurobehavioral performance.

There is evidence that human fetuses develop a range of behavioral responses to stress from, at least, midgestation: habituation to repeated vibroacoustic stimuli,[34] hormonal stress response,[35] and cardiovascular and motor patterns of response to stress.[36] Fetal heart rate variability is an index of the ability of the fetus to self-regulate via autonomic reactivity, and some authors have suggested that these neurobehavioral patterns have predictive value in terms of subsequent infant temperament.[37] Studies have also reported increased arousal in near-term fetuses of women with high stress or anxiety, as reflected by increases in fetal wakefulness, heart rate variability, and percentage of body movements during active sleep (REM).[38] These findings can be explained by the fact that sleep and stress control systems share particular brain loci, namely, the locus coeruleus and forebrain centers.[39]

Behavioral functions are mediated through the prefrontal cortex, which is connected with all sensory systems, cortical and subcortical motor system structures, subcortical arousal and attention functions, and with limbic and midbrain structures involved in affection, memory, and reward.[40] Prenatal programming of the hypothalamic-pituitary-adrenal axis and structure-function relationships, controlled by the prefrontal cortex, may contribute to cognitive, behavioral, and emotional problems in children born to mothers with depression.[41]

The main limitation of this study is its cross-sectional design. It would be interesting to conduct a longitudinal study starting in pregnancy and following the neurobehavioral skills of newborn infants of adolescent mothers with and without depression until adulthood. A single neurobehavioral evaluation should only be used as a screening tool to identify neurobehavioral problems in these groups of newborns.

In summary, despite its limitations, this study showed that infants born to adolescent mothers with depression exhibit worse neurobehavioral performance when maternal depression is associated with male sex, lower gestational age, regional anesthesia, vaginal delivery, and larger infant head circumference. These subtle neurobehavioral changes may put these infants at additional risk, as they may interfere with mother-infant bonding. Prevention, intervention, and support programs to address depressive disorder during pregnancy and their effects on child outcomes should be studied.

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Disclosure

The authors report no conflicts of interest.

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