Early Human Development 115 (2017) 51–59

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

The effect of prenatal substance use and maternal contingent responsiveness on infant affect

Jean Lowe[a], Fares Qeadan[b], Lawrence Leeman[c,d], Shikhar Shrestha[e], Julia M. Stephen[f], Ludmila N. Bakhireva[b,c,e,*]

[a] Department of Pediatrics, University of New Mexico, Albuquerque, NM, USA
[b] Division of Epidemiology and Biostatistics, Department of Internal Medicine, University of New Mexico, Albuquerque, NM, USA
[c] Department of Family and Community Medicine, University of New Mexico, Albuquerque, NM, USA
[d] Department of Obstetrics and Gynecology, University of New Mexico, Albuquerque, NM, USA
[e] Department of Pharmacy Practice and Administrative Sciences, University of New Mexico College of Pharmacy, Albuquerque, NM, USA
[f] The Mind Research Network and Lovelace Biomedical and Environmental Research Institute, Albuquerque, NM, USA

ARTICLE INFO

Keywords:
Infant affect
Stress reactivity
Maternal contingent responsiveness
Alcohol
Opioids

ABSTRACT

Background: The effects of prenatal substance exposure on neurobehavioral outcomes are inherently confounded by the effects of the postnatal environment, making it difficult to disentangle their influence. The goal of this study was to examine the contributing effects of prenatal substance use and parenting style (operationalized as contingent responding during the play episodes of the Still-face paradigm [SFP]) on infant affect.

Methods: A prospective cohort design was utilized with repeated assessment of substance use during pregnancy and the administration of the SFP, which measures infant response to a social stressor, at approximately 6 months of age. Subjects included 91 dyads classified into four groups: 1) Control (n = 34); 2) Medication assisted therapy for opioid dependence (MAT; n = 19); 3) Alcohol (n = 15); 4) Alcohol + MAT (n = 23). Mean % of positive infant affect and mean % of maternal responsiveness (watching, attention seeking, and contingent responding) was compared among the five SFP episodes across the four study groups by MANOVA. Mixed effects modelling was used to estimate the contributing effects of the study groups and maternal responsiveness on infant affect.

Results: Maternal contingent responding was associated with increase ($\hat{\beta} = 0.84$; $p < 0.0001$) and attention seeking with decrease ($\hat{\beta} = -0.78$; $p < 0.0001$) in infant positive affect. The combined effect of prenatal exposures and covariates explained 15.8% of the variability in infant positive affect, while the model including contingent responding and covariates explained 67.1% of the variability.

Conclusions: Higher maternal responsiveness was a much stronger predictor of infant behavior than prenatal exposures, providing the basis for future intervention studies focusing on specific parenting strategies.

1. Introduction

Substance use disorders are a complex and prevalent public health problem which affects all segments of the population, including vulnerable groups such as pregnant women. It is estimated that 5.4% of pregnant women use illegal drugs and 10.8% use alcohol [1]. The effects of maternal drug exposure on neurocognitive outcomes in prenatally-exposed infants are complex and vary by the substance of abuse, timing of exposure, patterns of administration, and frequency of use [2]. The devastating effects of prenatal alcohol exposure (PAE), collectively known as Fetal Alcohol Spectrum Disorders (FASD), are well described [3]. Ongoing attention problems [4], poor memory and executive functioning skills [5], and deficits in verbal comprehension, working memory, and full-scale IQ [6] are associated with PAE and often result in learning disabilities in affected children [7]. Neurodevelopmental outcomes commonly associated with PAE might be mediated, at least in part, by hypothalamic-pituitary-adrenal (HPA) dysregulation [8] leading to increased stress reactivity and poor stress regulation in PAE children [9]. Alternatively, HPA dysregulation and increased stress reactivity in children affected by PAE might be the basis for some of the PAE-induced behavioral deficits [10] and increased vulnerability to secondary psychopathologies, such as mental health problems, inappropriate sexual behavior, and learning disabilities [11].

* Corresponding author at: University of New Mexico College of Pharmacy, 1 University of New Mexico, MSC 09 5360, Albuquerque, NM 87131, USA.
E-mail address: lbakhireva@salud.unm.edu (L.N. Bakhireva).

http://dx.doi.org/10.1016/j.earlhumdev.2017.09.013
Received 10 April 2017; Received in revised form 24 July 2017; Accepted 5 September 2017

Opioid use disorder has reached epidemic proportion in the United States [12] with an accompanying four-fold increase in antepartum maternal opiate use from 2000 to 2009. As a result, neonatal abstinence syndrome (NAS) now affects 5.8 per 1000 hospital births [13]. Emerging evidence suggests that consequences of NAS beyond the neonatal period might include impaired cognitive and language development [14], increased risk of developing attention deficit/hyperactivity disorder, diagnoses of disruptive behaviors [15], and parent-reported behavior problems [16]. A recent study reported less "positivity" (lower scores for smiling and laughter) among opioid-exposed infants and lower responsiveness to soothing [17], suggesting that prenatal opioid exposure might affect infant emotional reactivity and maternal-infant interaction. Finally, polysubstance use may present the greatest risk to the developing fetus [18], while little is known about the effect of polysubstance use on stress reactivity and regulation in young children.

The long-term effects of prenatal drug and/or alcohol exposure on neurocognitive and behavioral outcomes are inherently confounded by the effects of the postnatal environment, making it difficult to disentangle the influence of prenatal and postnatal factors. The '*nature* vs. *nurture*' concept is not new, but continues to present a challenge for the interpretation of perinatal epidemiology and substance use research. The importance of postnatal factors was demonstrated in a study of children exposed to heroin during pregnancy, which found that children adopted at a young age had intellectual skills similar to non-exposed controls; however, heroin-exposed children who remained with their biological parents had lower intellectual test scores compared to non-exposed controls [19]. In another study, toddlers prenatally exposed to polysubstance use were found to have adverse outcomes, such as lower self-regulation and increased externalizing problems at 3 years of age, when their mothers were observed using harsh behaviors during a video-taped free play paradigm [20]. Heightened infant reactivity and distress, mother-infant attachment disorders, and decreased sensitivity and responsiveness towards the child have been associated in research with parenting practices among mothers with various substance use disorders [21–26]. Substance-using mothers of children with prenatal exposures have been shown to perform poorer than non-using caregivers of children with prenatal exposures on caregiver-child interaction assessments, highlighting the particular vulnerability of the maternal-child relationship when maternal substance use is present [27]. Despite these reports suggesting that the quality of maternal-infant interaction might be an important factor that may impact child psychopathology, we are not aware of any studies directly assessing the role of prenatal substance use versus supportive parenting style on infant emotional regulation.

Emotional regulation has been conceptualized as the ability to control the response to an environmental stressor and the ability to recover from the distressful situation [28]. Difficulty with emotional regulation has been associated with later externalizing behavioral problems [29,30] and impairments in executive functioning [31]. Emotional regulation in infancy is often measured by infant positive and negative affect in relation to a social stressor [32]. The Still-face paradigm (SFP) is an established experimental procedure that measures an infant's reaction to the introduction of a disruptive event, specifically to their mother's 'still-face' - a social stressor which indicates a mismatch or non-responsiveness in the communication between mother and infant [33]. The SFP effect is robust and results in a pattern of reduced positive affect and increased negative affect during the 'still-face episodes' and increased positivity during the reunion or play episodes [34]. Meta-analyses also reveal that higher maternal responsiveness or sensitivity predicts higher infant affect, and the maternal-infant interaction during the SFP are predictive of secure attachment at 1 year of age [34]. Our earlier study found that PAE infants had increased cortisol reactivity, elevated heart rate, and increased negative affect during the stressor episodes of the SFP [35]. Infants with moderate to heavy PAE have been found to have greater physiologic stress reactivity between 6 and 15 months as measured by salivary cortisol during the SFP, compared to infants with mild or no PAE exposure [36].

The specific aims of this prospective cohort study were to examine: 1) the differences in maternal behavior styles during the SFP between women who used alcohol, opioids, both substances in combination, or abstained from alcohol and illicit drugs during pregnancy; 2) the contributing effects of prenatal substance use and parenting style (operationalized as maternal contingent responding) on infant positive affect during maternal-infant play episodes of the SFP. We hypothesized that substance using women will be less likely to engage in contingent responding behavior style, and that maternal contingent responding would be an equally important predictor of infant affect as prenatal exposure to substances of abuse.

2. Methods

2.1. Study design and population

Data were derived from two consecutive prospective cohort studies conducted at the University of New Mexico (UNM) with the same study population. The UNM Human Research Review Committee approved both studies and patients gave written informed consent. The *Biomarkers*, *Infant Neurodevelopment*, *and Growth* (*BINGO*) study (PI: Bakhireva, supported by NIAAA 1R03AA020170 and 1P20 AA017608 grants) was conducted at UNM in 2011–2012 and served as a pilot study to the larger, ongoing *Ethanol*, *Neurodevelopment*, *Infant and Child Health* (*ENRICH*) cohort study (MPIs: Bakhireva, Stephen; supported by NIAAA R01 AA021771), which began in 2013. Participants were recruited from UNM-affiliated prenatal care clinics. Both studies included three visits: 1) prenatal, during one of the first prenatal care appointments; 2) early postpartum, during the hospital stay after labor and delivery; and 3) neurodevelopmental and SFP assessment of children at ~6 months of age. The following eligibility criteria were applied to all participants: 1) at least 18 years old; 2) singleton pregnancy; 3) currently residing and planning to stay in the Albuquerque metropolitan area to complete all study visits; 4) ability to give informed consent in English; and 5) no fetal diagnosis of a major structural anomaly.

Pregnant women in both cohort studies were recruited into one of four mutually exclusive study groups, as follows: participants 1) without perinatal substance exposures (Control); 2) with opioid use disorder who prenatally received medication assisted therapy (MAT; either methadone or buprenorphine) and did not use alcohol in pregnancy; 3) with alcohol use during pregnancy (Alcohol); and 4) with MAT and alcohol use during pregnancy (Alcohol + MAT). While the focus of both cohorts was to ascertain the effects of prenatal alcohol exposure on infant outcomes, MAT and Alcohol + MAT groups were included, in addition to unexposed controls, to better match pre- and post-natal environmental factors across groups. Participants classified into the control group needed to 1) be a lifetime abstainer of illicit drugs and tobacco products (reported use of ≤ 100 cigarettes in lifetime); and 2) abstain from alcohol use since the last menstrual period (LMP) and be no more than a light alcohol user (≤ 2 standard drinks/week on average) before the LMP. Participants classified into the alcohol-exposed groups (Alcohol, Alcohol + MAT) had to 1) self-report at least moderate levels of drinking [37] in the periconceptional period (≥ 3 drinks per week or ≥ 2 binge drinking episodes ['binge' defined as ≥ 4 drinks per occasion] during the month surrounding the LMP) using the Timeline Follow-Back assessment method; and 2) continue drinking during pregnancy, as confirmed by self-report or positive ethanol biomarker. The self-reported cutoffs for risky alcohol use employed in this study and our conjunctive use of ethanol biomarkers in pregnancy are rigorous and well-supported by the literature [37–41]. The final sample size for this analysis was 91 maternal-infant pairs who had completed the three study visits as of January 2017.