



## Brief communication

Physiological reactivity during object manipulation among cigarette-exposed infants at 9 months of age<sup>☆</sup>

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## ABSTRACT

The purpose of this study was to examine the association between prenatal exposure to cigarettes and heart rate during an object manipulation task at 9 months of age. Second-by-second heart rate was recorded for 181 infants who were prenatally exposed to cigarettes and 77 nonexposed infants during the manipulation of four standardized toys. A series of longitudinal multilevel models were run to examine the association of prenatal smoking on the intercept and slope of heart rate during four 90-second object manipulation tasks. After controlling for maternal age, prenatal marijuana and alcohol use, duration of focused attention and activity level, results indicated that the heart rates of exposed infants significantly increased during the object manipulation task. These findings suggest casual rather than focused attention and a possible increase in physiological arousal during object manipulation.

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## 1. Introduction

Despite well-documented concerns about health risks and adverse developmental outcomes as a result of prenatal tobacco exposure (PTE), approximately 13.8% of mothers continue to smoke cigarettes during pregnancy (Tong et al., 2009). PTE is consistently associated with adverse perinatal outcomes such as lower birth weight, shorter gestations and decreased head circumference at birth (Fried and O'Connell, 1987; Zaren et al., 2000) and with disruptions in autonomic nervous system (ANS) functioning (Fried and Makin, 1987; Jacobson et al., 1984; Schuetze and Eiden, 2006; Schuetze and Zeskind, 2001), including altered heart rate (HR) and increased tremors, arousal and irritability. HR is an index of functioning in both the sympathetic and

parasympathetic branches of the ANS (e.g., Richards, 2001). Thus, HR responses to environmental stimulation may be particularly useful measures of autonomic functioning among infants with PTE.

The direction of cardiac responses has long been used to indicate either an attentional or orienting (deceleration in HR) or defensive (acceleration) reaction to external stimulation (Graham and Clifton, 1966; Lewis et al., 1966). Increases in HR are associated with environmental stimulation requiring motor activity and affective responses and indicate increased arousal (Graham and Clifton, 1966; Pomerleau and Malcuit, 1980). Decreases in HR, on the other hand, are associated with environmental stimulation requiring information processing such as focused and sustained attention (Lansink and Richards, 1997). Richards and colleagues demonstrated that infants, when orienting to an external stimulus, typically show a significant decrease in HR, followed by a period of sustained lowered HR (Richards and Casey, 1991). Heart rate responses can be used to assess attentional and affective processes in infancy, including the infant's ability to regulate arousal and control attention (Colombo and Cheatham, 2006) in the presence of external stimuli. Previous research with infants has shown that a single stimulus can elicit both cardiac acceleration with an approach motor response, indicating that the infant has enough information for a somatic response, and cardiac deceleration without observable motor responses, indicating that the infant is engaged in observation and information gathering (Pomerleau and Malcuit, 1980). Concurrently, infants are developing the ability to and interest in manipulating small objects (Richards, 2008). Thus, the

**Abbreviations:** PTE, prenatal tobacco exposure; ANS, autonomic nervous system; HR, heart rate; NE, nonexposed; TLFB, Timeline Followback Interview; ELISA, enzyme-linked immunosorbent assay; LC-MSMS, liquid chromatography-tandem mass spectrometry; HLM, hierarchical multilevel model; FA, focused attention; BW, birth weight; HC, head circumference.

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primary goal of this study is to examine the HR responses of infants with PTE during object manipulation.

Attentional and arousal processes are both sensitive to biological risk (e.g., Ruff and Lawson, 1990) such as prenatal exposure to substances. Existing studies with PTE infants found associations between PTE and HR. During the neonatal period, PTE was associated with higher HR during quiet and active sleep, and with lower long-term HR variability (Schuetze and Zeskind, 2001). In early infancy, PTE was associated with disturbances in ANS functioning using spectral analysis of HR during sleep (Franco et al., 2000) and with higher HR during sleep (Schuetze and Eiden, 2006). Although numerous studies examined autonomic functioning during affect-eliciting tasks among cigarette-exposed infants, less is known about how these infants respond physiologically during an object manipulation task. This is particularly important given that numerous studies documented an association between PTE and attentional difficulties in older children (Linnett et al., 2003), with less information on attentional processes during infancy in this population. Object manipulation tasks are frequently employed to assess behavioral and physiological responses reflecting attention in older infants (Lansink, Mintz & Richards, 2000). Thus, the purpose of this study was to examine the association between PTE and HR during an object manipulation task at 9 months of age. Given findings of attentional deficits in older PTE children, we hypothesized that infants with PTE would not have the decreased HR associated with sustained attention and, instead, may have an increased HR indicative of altered autonomic functioning during environmental stimulation.

## 2. Method

### 2.1. Participants

Participants were 181 PTE and 77 nonexposed (NE) infants in an ongoing longitudinal study. The smoking group was oversampled, to allow for a wide range of maternal smoking from light–heavy, such that one non-smoker was recruited for every two smokers. Groups were matched on maternal age and education. The sample was primarily single (55%), minority (70%) women with a high school diploma or less (58%).

### 2.2. Procedures and instruments

Mothers were screened at their first prenatal appointment. Interested/eligible mothers were asked to sign consent. After birth, dyads were maintained in the sample if the infant could medically comply with procedures. Assessments were conducted once per pregnancy trimester, and at 2 ( $M = 2.51$ ,  $SD = .41$ ) and 9 ( $M = 8.81$ ,  $SD = .87$ ) months of age. The study received Institutional Review Board approval.

### 2.3. Substance use

PTE was assessed by maternal report during pregnancy, using the Timeline Followback Interview (TLFB; Sobell and Sobell, 1995), infant meconium and maternal salivary analysis. The TLFB conducted at each prenatal visit yielded data about average number of cigarettes smoked per week during pregnancy, as well as daily alcohol (standard drinks) and marijuana use (joints) during pregnancy. Maternal saliva was collected at each prenatal lab visit and analyzed for cotinine, the primary nicotine biomarker, with enzyme-linked immunosorbent assay (ELISA) or liquid chromatography-tandem mass spectrometry (LC-MSMS) at 10 ng/ml cutoff. Infant meconium, the gold standard for fetal exposure, was assayed with a validated LS-MSMS method for nicotine, cotinine, and trans-3'-hydroxycotinine (OHCOT) (Gray et al., 2009). Infants were included in the PTE group if any prenatal indicator of PTE was positive.

### 2.4. Birth outcomes

Measures of birth weight (BW:kg), birth length (BL:cm), and head circumference (HC:cm) were taken from medical charts. Gestational age was calculated by maternal report of last menstrual period.

### 2.5. Object manipulation task

Between 34 and 40 weeks of age, corrected for prematurity, infants were presented with a four novel toys in a specific order. Mothers were seated next to the infant and asked not to interact with the infant. The assessor presented each toy for 90 s with no overlap of toys and no intervals between toys. Toy1 was a plastic block with various colors and textures. Toy2 was a blue ball, within a yellow casing, that moved and made noise. Toy3 was a cylinder containing small beads which, when moved, slid from side to side. Toy4 consisted of three handles that moved and made noise when cranked.

### 2.6. Physiological reactivity

Recording of HR began once the child was in a stable, quiet alert state (baseline) and was continuously recorded throughout the presentation of the four toys. First, electrodes were triangulated on the infant's chest. IBI Analysis software (James Long Company, 1999) processed the HR data. HR samples, collected every 10 ms, were used to calculate mean HR. A level detector was triggered at the peak of each R-wave. Intervals between sequential R-waves were calculated to the nearest millisecond. Data files of R-wave intervals were later manually edited to remove incorrect detections of R-waves or movement artifacts that occurred in less than 2% of cases. Resulting output for HR was recorded for each second of data collection. An event marker was used to indicate each toy presentation.

### 2.7. Behavioral measures

Videotapes of object manipulation were coded by research assistants, blind to group status. Behavioral state (1 = drowsy, 2 = quiet/alert, 3 = active/alert, 4 = fussy, 5 = crying), was assessed immediately prior to the toy presentations (baseline state) and during each toy presentation. Behaviors during each toy presentation were also rated on vigor of movement (activity level), number of times the toy was thrown or dropped, duration of focused attention (FA), and latency to look at object. Inter-rater reliability, conducted on 12% of tapes, ranged from an intra-class correlation of .83–.94.

### 2.8. Data analytic strategy

The main study variables were initially examined descriptively in SPSS 21 (IBM, 2013). Hypothesis testing was then conducted using PROC MIXED in SAS 9.3 to examine a three-level hierarchical multilevel model (HLM) predicting the intercept and slope of HR during baseline and over each of the 4 trials. A total of four models were run. Model 1 had no predictors of the variance in the slope. The only predictors are the predictors of the intercept. Model 2 included prenatal smoking as a predictor of the slope in the model. Model 3 includes activity level as a predictor of the slope on the model. Model 4 includes both prenatal smoking and activity level as predictors of the slope in the model. Given that the longitudinal data had a three-level hierarchical structure with time-varying HR (Level 1) nested within trial (Level 2) nested within persons (Level 3), we accounted for the within-person autocorrelation of HR (sampled once per second over each 90 second trial) using an autoregressive covariance matrix. In order to maximize power, only those variables that were significantly associated with either the main independent variable, prenatal smoking, or main dependent variable, HR, were included in the HLM analyses.

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