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Physiological Reactivity during Object Manipulation among Cigarette-exposed Infants at 9 Months of Age

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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.

Keywords

prenatal cigarette exposure; object manipulation; heart rate; physiological arousal; attention

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

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smoke cigarettes during pregnancy (Tong, Jones, Dietz, D'Angelo & Bombard, 2009). PTE is consistently associated with adverse perinatal outcomes such as lower birthweight, shorter gestations and decreased head circumference at birth (Fried & O'Connell, 1987, Zaren, Lindmark & Bakketeig, 2000) and with disruptions in autonomic nervous system (ANS) functioning (Fried & Makin, 1987; Jacobson et al., 1984; Schuetze & Eiden, 2006; Schuetze & 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 & Clifton, 1966; Lewis, Kagan, Campbell, & Kalafat, 1966). Increases in HR are associated with environmental stimulation requiring motor activity and affective responses and indicate increased arousal (Graham & Clifton, 1966; Pomerleau & Malcuit, 1980). Decreases in HR, on the other hand, are associated with environmental stimulation requiring information processing such as focused and sustained attention (Lansink & 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 & 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 & 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 & Malcuit, 1980). Concurrently, infants are developing the ability to and interest in manipulating small objects (Richards, 2008). Thus, the 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 & 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 & 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 & 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, 2001). 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.

2.0 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 & 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 10ng/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 seconds 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, Caroga Lake, NY) 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.

In order to examine whether PTE predicted the slope of HR across baseline and each 90 second trial, interaction terms were computed between each of the trimester smoking variables and the time variable. All of the independent variables were grand mean centered, except for infant gender and small for gestational age status, which were dummy coded. The quadratic term for time was nonsignificant in all analyses, so it was not included in the final models.

3.0 Results

3.1 Descriptive Statistics

We examined the correlations of maternal variables (age, education, prenatal smoking, alcohol and marijuana use), and infant variables (BW, HC, small for gestational age status, gender, behavioral state, FA duration, FA latency, activity level, dropping the toy) with HR during the object manipulation task. Bivariate correlations and means for both demographic and substance use variables for mothers and infants are presented in Table 1. Maternal prenatal smoking was negatively associated with maternal education, and positively associated with prenatal marijuana and alcohol use. FA duration was negatively associated and activity level was positively associated with HR. Consequently, these variables were included as covariates in the HLM models. Analyses of variance were conducted on maternal demographics, maternal substance use during pregnancy, fetal growth and behavioral and physiological measures during the object manipulation task (see Table 1) to examine group differences. The smoking group had significantly lower BW and smaller HC, and significantly higher levels of prenatal smoking, marijuana use, and alcohol use. There were no group differences for any of the behavioral or physiological measures during the object manipulation task.

3.2 Smoking and Heart Rate during Object Manipulation

A three-level longitudinal HLM was run to examine the association of prenatal smoking on HR during baseline and four object manipulation tasks, controlling for maternal age, prenatal marijuana and alcohol use, duration of FA and activity level, with the intercept and slope of HR during baseline and the four 90-second object manipulation tasks (see Table 2). PTE interacted with time in seconds to predict HR (was significantly associated with the slope of HR; See Table 2, Model 2 and Figure 1). Activity level was also significantly associated with the slope of HR (see Model 3). However, PTE remained significantly associated with the slope of HR after controlling for the effect of activity level (see Model 4).

4.0 Discussion

As hypothesized, PTE was not associated with the decrease in HR that would indicate stimulus orientation or sustained focus on the stimulus (Richards & Casey, 1991). Instead, PTE was associated with a significant *increase* in HR during the object manipulation task. These findings mirror those of infants exposed to other substances prenatally (Bandstra, Morrow, Anthony, Accornero & Fried, 2001; Lester, Freier, & LaGasse, 1995; Mayes & Bornstein, 1997) and suggest that the attentional deficits that have been well-documented in PTE children and adolescents may already be present during infancy. It is important to note that the nonexposed infants also did not show a decrease in HR that would be indicative of focused attention. Given that the sample as a whole is at high demographic risk due to poverty and associated cumulative risks, these findings may indicate that attentional processes are impacted for entire sample. However, there seem to be some unique effects of PTE that are exacerbating this risk. Failure to intensively engage with objects during infancy may also have implications for social and cognitive development as these aspects of

development require ongoing engagement with the environment. It is important, however, to note that attention is a multifaceted construct that cannot be fully captured in one task. Furthermore, it is not clear if this pattern of HR functioning during an object manipulation task would still be present beyond the first year of life. Thus, future studies should longitudinally examine autonomic functioning during a variety of attentional tasks and examine if this pattern of acceleration in infancy was predictive of later problems.

Furthermore, the findings of a slight increase in HR for exposed infants during the object manipulation task suggest a possible affective response. Importantly, this finding persisted after controlling for the effect of activity level on HR. Thus, the increase in HR cannot be explained alone by an increase in activity level while manipulating the objects. Instead, the increase in HR may indicate an increase in physiological arousal during the presentation of the toys, suggesting that exposed infants may find an exploratory task to be stressful, relative to nonexposed infants. The increase in behavioral state from baseline provides additional evidence that behavioral arousal increased during this task in the same pattern for both groups of infants. Thus, the increase in physiological arousal among exposed infants, in the presence of behavioral arousal similar to that of nonexposed infants, suggests that HR may be indexing a subtle pattern of physiological stress among PTE infants. Given the developmental significance of this type of exploration during later infancy as well as the frequency with which object manipulation and exploration occur during early childhood, this response can be considered in the context of allostasis and allostatic load (McEwen, 2001). Allostasis is defined as the extent of activity necessary for an infant to maintain a stable state in the presence of stressors-i.e., to adapt (McEwen, 2000). Allostatic load, or “wear and tear,” results with repeated adaptations to stressors. Allostatic load can be characterized as repeated or chronic stress, failure to habituate to repeated challenge, failure to respond appropriately to environmental challenges, or failure to terminate a response once the stressor has subsided (McEwen, 2001). Consequently, hyperresponsivity can lead to allostatic load that may have nonoptimal developmental consequences for infants.

In addition to the limitations noted above, this study has one other important limitation. Accurate assessment of substance use both prenatally and postnatally is difficult. Pregnant and postpartum women are often hesitant to divulge substance use information. One strength of this study is the use of multiple methods to prospectively ascertain prenatal substance use that partially mitigated this limitation. Thus, this study fills an important gap in the literature in the autonomic functioning of infants with PTE during a developmentally significant task. After controlling for confounding factors, we found that the physiological responses of exposed infants to an object manipulation task indicated possible increased arousal rather than sustained attention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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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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Highlights

- This study examined the association between prenatal tobacco exposure heart rate during an object manipulation task at nine months of age. Heart rate was obtained during baseline and during four trials of object manipulation (age appropriate toys).
- 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.

Figure 1. Effect of Prenatal Smoking on Heart Rate During Object Manipulation

Note: Prenatal smoking was measured continuously, so these cigarettes/day values in the figure are for graphing purposes only.

Table 1

Correlations Between Study Variables

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Group Status	
																	Control	Smoking
1. Maternal age	---																23.30 (4.90)	24.34 (4.96)
2. Level of Maternal education	.20**	---															2.39 (1.11)	2.24 (1.10)
3. Gender ^a	-.02	.05	---														.54 (.50)	.45 (.50)
4. Birth weight	.07	.11	-.09	---													3.36 (.55)	3.18 (.58)*
5. Head circumference	.08	.13*	-.10	.64***	---												34.44 (1.83)	33.75 (1.84)*
6. Small for gestational age ^b	.00	.01	.09	-.46***	-.31***	---											.13 (.34)	.14 (.35)
7. Prenatal smoking	.18**	-.11	-.11	-.08	-.08	-.02	---										.00 (.00)	5.07 (4.78)***
8. Prenatal marijuana	-.05	-.13*	.12	-.15*	-.16*	.10	.16*	---									.06 (.30)	.31 (.69)***
9. Prenatal alcohol	.01	.01	.04	-.12	-.07	.06	.18**	.13*	---								.01 (.04)	.08 (.19)***
10. FA global rating	.02	-.04	.04	-.03	.10	.02	-.02	-.14*	-.09	---							2.75 (.63)	2.65 (.53)
11. FA duration	-.02	-.02	.03	-.03	.08	.02	.00	-.13	-.08	.91***	---						34.70 (13.03)	33.93 (12.32)
12. FA latency	-.04	.09	-.13	-.09	-.10	.02	.08	-.07	-.03	-.14*	-.19**	---					.44 (2.77)	.81 (3.44)
13. Activity level	-.03	.01	-.06	.07	.07	-.06	.12	.03	.06	-.38***	-.29***	.00	---				2.29 (.54)	2.28 (.55)
14. Dropped toy	-.01	.04	-.13*	.04	.09	-.03	-.07	-.04	-.03	-.09	-.10	.02	-.00	---			.63 (2.42)	.35 (.55)
15. Baseline behavioral state	-.11	.12	.04	.06	.05	.01	-.06	.06	.04	-.10	-.11	.01	.24***	.00	---		2.61 (.69)	2.56 (.69)
16. Behavioral state during task	.02	.11	-.03	-.02	-.03	-.05	-.02	.03	.03	-.36***	-.34***	.29***	.38***	.11	.24***	---	2.92 (.35)	2.93 (.39)
17. HR during OM	.04	-.05	.09	-.07	-.11	.00	.03	.00	.00	-.12	-.14*	.13	.14*	.11	.12	-.05	129.85 (9.50)	129.42 (11.22)

Notes: HR = Heart Rate; OM= Object Manipulation;

* $p < .05$;** $p < .01$;

0 = Not small for gestational age, 1 = small for gestational age

0 = Male, 1 = Female;

$p < .001$;

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Table 2
Multilevel models with prenatal smoking predicting heart rate during object manipulation

<i>Variables</i>	Model 1	Model 2	Model 3	Model 4
<i>Effects on Intercept</i>				
Intercept	129.908 ^{***}	129.907 ^{***}	129.908 ^{***}	129.736 ^{***}
Maternal Age	.003	.003	.005	.033
Prenatal Smoking	-.009	.033	.001	.065
Prenatal Marijuana	.075	.075	.055	.123
Prenatal Alcohol	.346	.339	.317	.998
FA Duration	-.083 ^{***}	-.083 ^{***}	-.083 ^{***}	-.083 ^{***}
Activity Level	.698 ^{**}	.697 ^{***}	.715 ^{**}	.713 ^{**}
<i>Effects on Slope</i>				
Time	.034 ^{***}	.034 ^{***}	.034 ^{***}	.032 ^{***}
Prenatal Smoking X Seconds		.002 ^{***}		.002 ^{***}
Activity Level X Seconds			.011 ^{**}	.010 ^{**}
BIC	439944.8	439936.5	439935.1	439928.1
Variance in Intercept	87.663 ^{***}	87.621 ^{***}	87.608 ^{***}	87.587 ^{***}
Variance between Trials	8.269 ^{***}	8.261 ^{***}	8.257 ^{***}	8.250 ^{***}
Variance in Slope	.001 ^{***}	.001 ^{***}	.001 [*]	.001 ^{***}
Covariance between Intercept and Slope	.038	.035	.030	.029

Notes: Models 1-4 refer to different iterations of the 3-level MLM. 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.

*
 $p < .05$;

**
 $p < .01$;

 $p < .001$.