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# Associations between prenatal exposure to second hand smoke and infant self-regulation in a New York city longitudinal prospective birth cohort

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ABSTRACT

*Background:* Prenatal exposure to active or passive maternal smoking –also referred to as second hand smoke (SHS) exposure – are associated with externalizing behaviors, hyperactivity and attention deficit hyperactivity disorder, problems which derive in part from altered self-regulation.

*Objectives:* Determine the influence of prenatal SHS on infant self-regulation using direct measures of infant behavior in 99 mothers from the Fair Start birth cohort followed at the Columbia Center for Children's Environmental Health.

*Methods:* Self-regulation was operationalized with self-contingency, the likelihood of maintaining/changing behavior from second-to-second, measured via split-screen video recordings of mothers playing with their 4-month infants. Mother and infant facial and vocal affect, gaze-on/-off partner, and mother touch were coded on a 1 s time-base. Third trimester prenatal SHS was assessed via self-report of a smoker in the home. *Weighted-lag* time-series models tested conditional effects of SHS-exposure (vs. non-exposure) on infant self-contingency for eight modality-pairings (e.g., mother gaze-infant gaze). *Individual-seconds* time-series models and *analysis of predicted values* at $t_0$ interrogated significant weighted-lag findings. Because prior findings link developmental risk factors with lowered self-contingency, we hypothesized that prenatal SHSSHS would predict lowered infant self-contingency.

*Results:* Relative to non-exposed infants, those who were prenatally exposed to SHS had lower self-contingency (more variable behavior) in all eight models. Follow-up analyses showed that, given infants were likely to be in the most negative facial or vocal affect, those with prenatal SHS were more likely to make larger behavioral changes, moving into less negative or more positive affect and to alternate between gaze-on and off mother. Mothers who were exposed to SHS during pregnancy (vs. non-exposed) showed a similar, albeit less prevalent, pattern of larger changes out of negative facial affect.

*Conclusion:* These findings extend prior work linking prenatal SHS with youth dysregulated behavior, showing similar effects in infancy, a critically important period that sthe stage for future child development.

## 1. Introduction

Growing evidence suggests that prenatal second-hand smoke [SHS] exposure, sometimes referred to as environmental tobacco smoke exposure (ETS), increases risk for a range of children's neurodevelopmental problems (Cho et al., 2013; Guillette, 2000; He et al., 2018; Lee et al., 2009; Polanska et al., 2017; Weiss, 2000; Yolton et al., 2005). Nonetheless, 12 U.S. states lack public smoking laws (STATE System Smokefree Indoor Air Fact Sheet, 2022). Nicotine crosses the placenta (Luck et al., 1985; Slotkin, 1998) to bind with nicotinic receptors, affecting the development and function of cholinergic and dopaminergic systems (Smith et al., 2010) and causing changes in

*Abbreviations:* second hand smoke, (SHS); Columbia Center for Children's Environmental Health, (CCCEH).

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inhibitory control, hyperactivity, and attention in rodents (Bryden et al., 2016). SHS also contains heavy metals including lead (Apostolou et al., 2012), which has been associated with altered self-regulation in children (Gump et al., 2017). Paralleling these findings, active maternal smoking in pregnancy has been linked with children's self-regulation difficulties, e.g., attention problems and risk for attention deficit hyperactivity disorder (Ekblad et al., 2017; Kovess et al., 2015; Sourander et al., 2019), neonatal irritability (Stroud et al., 2009), and altered structure and function of neural circuitry serving self-regulatory capacities in childhood (Bennett et al., 2009; El Marroun et al., 2014; Holz et al., 2014; Longo et al., 2013; Toro et al., 2008). Notably, prenatal and early life exposure toSHS has also been linked with altered function of frontostriatal circuits during cognitive control (Margolis et al., 2021) as well as with externalizing behaviors and increased hyperactivity in 5–6 year olds and preschool-age children (Lin, 2017; Liu et al., 2013). Although these studies document the effects of prenatal SHS exposure on externalizing behaviors in children as young as preschool-age, how early these effects manifest and whether or not these patterns are detectable in infancy remains unknown. Herein we address this gap in knowledge by examining the effects of prenatal SHS-exposure on infant behavioral self-regulation during mother-infant face-to-face interaction in a community sample.

Self-regulation is an important cross-domain dimension of development (Wakschlag et al., 2020, 2019) that reflects the capacity to control one's thoughts, behaviors, and emotions (Margolis et al., 2016). Age-sensitive measurement approaches are required in order to accurately capture an individual's self-regulatory capacity (Diamond, 2020). We operationalize infant self-regulation via infant behavioral self-contingency, the degree to which prior behavior predicts current behavior: the degree of stability/variability within an individual's own rhythms of behavior (Beebe et al., 2016; Messinger et al., 2012). Infants are adept at processing sequences and contingencies of behavior and developing expectancies based on these contingencies (Haith et al., 1988; Tarabulsy et al., 1996). Across cognitive and social domains, typically-developing infants have predictable self-contingency patterns of attention (Beebe et al., 2016; Margolis et al., 2019; Messinger et al., 2012), emotion (Beebe et al., 2016; Margolis et al., 2019), head orientation and infant-initiated touch (Beebe et al., 2016). Herein we examine self-contingency in the context of mother-infant face-to-face interaction, a foundational aspect of infant future social and cognitive development.

Self-contingency itself is neutral: higher and lower degrees of self-contingency acquire meaning only in relation to a context or outcome (Tarabulsy et al., 1996). Lower self-contingency indexes a less predictable, more varying process; higher self-contingency indexes a more predictable, less varying process. Our prior work on 4-month mother-infant interaction identified patterns of lowered gaze and vocal affect self-contingency in infants who were exposed to risk factors, specifically, infants who were in utero when mothers were pregnant and widowed on 9/11 (Beebe et al., 2020) and infants of mothers who reported depression at 6 weeks postpartum (Beebe et al., 2008).

In the current study we address an important gap in understanding early-life effects of prenatal SHS exposure on infant self-regulation. We examined 4-month infant self-regulation via infant self-contingency analyzed by time-series models using data derived from second-by-second video microanalysis. In primary analyses, we investigated whether lowered infant self-contingency was associated with prenatal SHS exposure. Given prior findings (Beebe et al., 2008, 2020), we hypothesized that prenatal SHS exposure would be associated with lowered self-contingency, measured in seven communication modality pairings with mother (i.e., infant facial affect-mother touch) and the cross-modal self-contingency of infant facial and vocal affect. Exploratory analyses examined if SHS exposure during pregnancy was associated with lowered maternal self-contingency and if exposure was associated with mother-infant interactive contingency.

## 2. Methods

### 2.1. Participants

Participants are a subset of the Fair Start birth cohort followed at the Columbia Center for Children's Environmental Health (CCCEH). The Fair Start Study began recruiting pregnant women receiving prenatal care in two sites within the care network of New York Presbyterian Hospital in 2015. All the women are age 18+, speak either English or Spanish, and 90% self-identify on survey as Hispanic. The Fair Start Study recruits from this population of women because they are at high risk for exposure to environmental neurotoxicants given the neighborhoods in which they live; the study aims to investigate effects of exposure on infant and child development thereby addressing issues of environmental injustice and mental health disparities in this population.

Beginning in the spring of 2016, sequentially enrolled participants were invited to a study visit assessing mother-infant interaction at infant age 4 months. The current study includes the first 99 mother-infant dyads who completed the 4-month visit and had available environmental tobacco smoke exposure data.

Ethical Considerations: The study was conducted according to guidelines in the Declaration of Helsinki, with written informed consent obtained from the parent before any data collection. The Institutional Review Boards at New York State Psychiatric Institute and Columbia University Medical Center approved all study procedures.

### 2.2. Second hand smoke (SHS) exposure assessment

SHS exposure was assessed via participant self-report of smoker in the home during pregnancy. The self-report questionnaire was completed by mothers during the prenatal visit. A positive answer to the "*In the last 2 years, has a household member or regular visitor to your home/apartment smoked cigarettes, pipes, marijuana, or cigars in your home?*" item of the questionnaire led to the classification of the respective mother and infant as "exposed" and a no response to the dyad being classified as non-exposed. In a separate birth cohort followed at CCCEH, cotinine, a metabolite of nicotine found in maternal blood within two days of delivery, and in cord blood, correlated highly with self-report of a smoker in the home during pregnancy (Rauh et al., 2004).

### 2.3. Infant or mother self-regulation

Self-regulation was operationalized by behavioral self-contingency, the degree to which prior behavior predicts current behavior i.e., the degree of stability/variability within an individual's behavior (Beebe et al., 2016; Messinger et al., 2012). The second-by-second time series of behavior quantifies self-contingency within an individual's behavior. Lower self-contingency indexes a less predictable, more varying process; higher self-contingency indexes a more predictable, less varying process.

### 2.4. 4-Month mother-infant face-to-face interaction

Four months is a window of opportunity for assessing infant social development (Feldman, 2007). By this age, infant social capacities flower, the ability to regulate states of arousal has matured, the capacity to engage/disengage social attention has developed, and a sustained face-to-face encounter is possible (Stern, 1985; E. Z. Tronick, 1989). Mothers were instructed to play with infants as they would at home, but without toys, for approximately 10 min. The infant was in an infant seat, mother seated opposite, as 2 video cameras (mounted on opposite walls) generated a split-screen view of upper torsos, including hands.

### 2.5. Video coding of behavior

The first 2.5 min of continuous uninterrupted videotaped play was coded on a 1s time-base, for mother and infant separately, by coders blind to SHS status. Samples of mother-infant face-to-face interaction of 2–3 min are stable, with robust session-to-session reliability, and standard in the literature (Beebe et al., 2010; E. Tronick, 2007). Behaviors were coded with ordinal scales ordered from high to low (except gaze on/off (Beebe et al., 2010);). We examined 3 communication modalities for infants (gaze, facial affect, and vocal affect) and 3 for mothers (gaze, facial affect, and touch). Inter-rater reliability of coding (mean Cohen's Kappa) on 20% of the data follows: (a) *infants:* gaze 0.86, facial affect 0.84, vocal affect 0.88; (b) *mothers:* gaze 0.89, facial affect 0.86, touch 0.85.

### 2.6. Time-series models

Traditional time-series approaches model each dyad individually and enter model coefficients into analyses of variance. Multi-level time-series approaches (Chen et al., 2007; Littell et al., 2006; Singer and Willett, 2003) model the group as a whole, creating estimates of fixed effects across the sample (group-level), and random effects (individual variation in those effects). Random effects include variation in the mean and the variance of the dependent variable across observations, variation in the linear change in the dependent variable over time, and between-dyad variation in the auto-regressive effect.

Advantages of multi-level modeling include more appropriate statistical assumptions; more accurate estimates of parameters by empirical Bayesian (maximum likelihood) techniques (rather than Ordinary Least Squares); multiple time-series (in our case, self- and interactive contingency) can be modeled simultaneously; and increased power. These models are designed to quantify patterns over time, here the course of behavior second-by-second, within individuals (self-contingency), and between two individuals (interactive contingency; (Beebe et al., 2020, 2007, 2016).

R-package 'lme4' was used to estimate random and fixed effects on the pattern of self- and self-with-other behavior over 150 s. We tested conditional effects of presence/absence of SHS exposure on self- and interactive contingency for 7 mother-infant modality-pairings, e.g., infant gaze paired with mother gaze, and an 8th for infant-infant cross-modal facial and vocal affect. Beta values are standardized and thus represent effect sizes.

### 2.7. Weighted-lag time-series analysis

Consistent with our previous studies, we used a weighted-lag approach to time-series modeling (Beebe et al., 2020, 2010, 2016). Each model predicted one partner's self-and interactive contingency, where estimated coefficients of one form of contingency controlled for the other (see Supplemental Methods). Using a moving 4s window, the prior 3s of self and partner behavior, lags 1, 2 and 3 (L1, L2, L3), were used to predict $t_0$, the current second of behavior of one partner. All 3 prior seconds were condensed to one assessment ("weighted-lag") by weighting each prior second by its relative association with $t_0$. For each dependent variable, measures of prior self or partner behavior ("lagged variables") were computed as a weighted average of the prior 3s, based on these models. The estimated coefficient for the effects of these lagged variables on $t_0$ over the duration of the interaction (150 s) indicates the level of self- or interactive contingency of one partner: the larger the coefficient, the stronger the contingency. Choice of a 4s window size (3 prior seconds predict $t_0$) was based on prior work (Beebe et al., 2007, 2010, 2016) in which we estimated the number of seconds over which lagged effects were significant and their magnitude for the pairs as a whole (fixed model estimates). Typically, the prior 3 s sufficed to account for these lagged effects on the subsequent behavior ($t_0$) (see (Beebe et al., 2007, 2010)).

### 2.8. Individual-seconds time-series models

To further understand the weighted lag time-series models, we also ran individual-seconds time-series models (where again each model predicted one partner's self- and interactive contingency, and estimated coefficients of one form of contingency controlled for the other). These models identify specific patterns of behavioral predictors in L1, L2, and L3 that contribute to any significant group differences at $t_0$ (Beebe et al., 2020, 2018). Three prior lags are evaluated for each second's association with the current moment (L1 → $t_0$; L2 → $t_0$, L3 → $t_0$) in one model, where each lag controls for the other two. A key difference between individual-seconds and weighted-lag models is that lags in the former are simply the values of the prior 1s, 2s, and 3s, whereas lags in the latter are calculated in relation to $t_0$ ("weighted lag"). The weighted-lag approach detects differences between groups using the prior 3s collectively; the individual-seconds approach detects differences which are located in a particular second of the prior 3s (Beebe et al., 2018). Thus, one approach may yield significant differences between groups when the other does not.

### 2.9. Descriptive explication of weighted-lag models using individual-seconds time-series models: analysis of predicted values

Multi-level time-series analyses identify overall group differences in contingency levels but cannot tell us where differences in specific behaviors lie. For example, lowered (more variable) infant gaze self-contingency may indicate greater likelihood of gaze-off to gaze-on, or the opposite. Post-hoc *descriptive explication* is required (see Supplemental Methods). The individual-seconds time-series approach is valuable in such descriptive explication. We use *analysis of predicted values* generated from individual-seconds time-series models to explicate patterns that underlie significant group differences identified in weighted-lag models.

*Analysis of Predicted Values.* Using the individual-seconds time-series models, we computed *predicted values* at $t_0$ for SHS-exposure groups (presence/absence) for each significant weighted-lag finding. To identify sources of significant differences between groups, per modality-pairing, we generated every possible combination of the behavioral codes for mother at L1, L2, L3, and infant at L1, L2, and L3, in relation to the behavior predicted at $t_0$. The resulting value was the predicted level of the behavioral code at $t_0$ for ordinal behavioral scales, and the predicted probability of gaze-on at $t_0$ for gaze (binary). For each modality-pairing, the significant difference in predicted value of $t_0$ indicates that, although the groups with and without SHS exposure behaved in the same way over the prior 3s, they behaved differently at $t_0$. We identified the absolute value of the difference of the predicted values for the two groups and ranked absolute differences from largest to smallest. To ascertain where groups most differed, we examined behavior combinations with the 10 highest differences in predicted value at $t_0$ (see Supplemental Materials).

### 2.10. Further post-hoc descriptive explication: behavioral frequencies

To further understand the findings from significant time-series models, we examined frequencies of behavior. Chi-square tests examined differences between groups (SHS-exposed versus non-exposed) in frequencies of behaviors within each level of a behavioral code (e.g., vocal affect levels: high positive to cry). Because seconds of the time-series are highly intercorrelated, we conservatively interpreted only tests surpassing alpha = .0001, the count relative to the total seconds exceeding 5 percent, and the difference in proportions between groups exceeding 5 percent.

### 2.11. Hypothesis testing

The conditional effects of prenatal SHS-exposure on infant self-regulation was tested using weighted-lag time-series models. SHSAs described in 2.3, self-regulation was operationalized by self-contingency. Primary analyses tested the conditional effects of prenatal SHS-exposure on infant self-contingency in seven communication-modality pairings and in infant intrapersonal cross-modal contingency of facial and vocal affect using the weighted lag time-series model. We further explored conditional effects of prenatal SHS-exposure on other aspects of dyadic regulation: mother self-contingency as well as infant and mother interactive contingency, using weighted lag time-series models. Follow-up analyses used the individual-seconds time-series models to generate *analysis of predicted values* for all significant findings from weighted-lag models. When a weighted lag model is significant but no one individual second in the individual-seconds model produces a unique result, we interpret the change across all 3 individual prior seconds. When a weighted lag model is significant and the individual-seconds model produces a discrepant sign in results, we interpret the sign of the weighted lag model. For completeness, we explore instances when a weighted-lag model is not significant, but the individual-seconds model is significant, and again use *analysis of predicted values* to further understand group differences in behavior.

All time-series models included infant sex assigned at birth, maternal education, age, marital status, income-to-needs ratio (middle value of $10,000 income bin divided by the number of people living in the home), and first-born vs. other-born as co-variates. Primary hypothesis-testing used weighted lag models, fixed effects (presence vs. absence of prenatal SHS exposure groups). In addition to the intercept, fixed effects included: (1) lagged effects of self- and partner behavior (self- and interactive contingency); (2) differences in behaviors associated with groups; (3) differences in self- and interactive contingency associated with groups. After removing nonsignificant terms, the final model was the simplest consistent with the data. The significance level was set at 0.05 (2-tailed). We had 99 dyads with 150 s observations per dyad to detect effects.

## 3. Results

### 3.1. Participant demographics

Ninety-nine mother-infant dyads completed the 4-month face-to-face visit and had prenatal SHS data. Mothers were Latina and/or black (Table 1). There were no differences between exposed and non-exposed mothers in demographic factors nor between mothers who completed the study and those who did not participate in the study (n = 35; all p's > 0.2).

### 3.2. Prenatal SHS-exposure and infant self-contingency

In primary analyses infant self-contingency was lower (more variable) in infants with prenatal SHS exposure (vs. non-exposure) across all 7 modality pairings (Table 2): Infant facial affect (analyzed in relation to mother [M] facial affect), $\beta = -0.037$, $p = .028$ (Supplement Table S1a); Infant vocal affect (M facial affect) $\beta = -0.076$, $p < .001$ (Table S2a); Infant gaze (M-gaze) $\beta = -0.255$, $p < .001$ (Table S3a); Infant vocal affect (M touch) $\beta = -0.078$, $p < .001$ (Table S4a); Infant vocal (M gaze) affect $\beta = -0.077$, $p < .001$ (Table S5a); Infant gaze (M face) $\beta = -0.256$, $p < .001$ (Table S6a); Infant gaze (M touch) $\beta = -0.247$, $p < .001$ (Table S7a). Individual seconds models (Tables S1b–S7b) and probability explication (Tables S1c, S2c, S4c, S5c) showed that, given that both groups of infants were likely to be in the most negative facial or vocal affect codes, infants with prenatal SHS exposure (vs. non-exposed) were more likely to transform to less negative facial (or vocal), or more positive vocal affect codes. Additionally, when gaze-off, infants with prenatal SHS exposure (vs. non-exposed) had a higher probability of moving to gaze-on (infant gaze-mother-gaze, Table S3c; infant gaze-mother touch, Table S7c). When gaze-on, however, infants with prenatal SHS exposure (vs. non-exposed) had a higher probability of moving to gaze-off (infant gaze-mother facial affect, Table S6c). infants with prenatal SHS exposure (vs. non-exposed) also had lower (more variable) cross-modal contingency in facial affect predicting vocal affect, $\beta = -0.071$, $p = .001$ (Table S8a).

**Table 1**
Sociodemographic data for mothers and infants with and without prenatal SHS exposure.

| Factor | Non-exposed (n = 74) | SHS-exposed (n = 25) | Chi-square | *p*-value |
|---|---|---|---|---|
| Maternal Ethnoracial Background | | | $\chi^2 = 1.313$ | *p* = .519 |
| Black/Latinx | 4 (5.4%) | 1 (4.0%) | | |
| Black/non-Latinx | 2 (2.7%) | 2 (8.0%) | | |
| Non-Black/Latinx | 65 (87.8%) | 22 (88.0%) | | |
| Not available | 3 (4.1%) | 0 (0.0%) | | |
| Maternal education | | | $\chi^2 = 9.063$ | *p* = .248 |
| Less than high school | 3 (4.1%) | 0 (0.0%) | | |
| Some high school | 13 (17.6%) | 6 (24.0%) | | |
| High school diploma | 12 (16.2%) | 6 (24.0%) | | |
| GED | 1 (1.4%) | 0 (0.0%) | | |
| Some college | 15 (20.3%) | 5 (20.0%) | | |
| 2yr college degree | 8 (10.8%) | 6 (24.0%) | | |
| 4yr college degree | 11 (14.9%) | 2 (8.0%) | | |
| 4+ yrs. of college | 11 (14.9%) | 0 (0.0%) | | |
| Marital status | | | $\chi^2 = 3.021$ | *p* = .554 |
| Divorced | 5 (6.8%) | 1 (4.0%) | | |
| Married | 27 (36.5%) | 9 (36.0%) | | |
| Never married | 34 (45.9%) | 11 (44.0%) | | |
| Partner_7yrs | 5 (6.8%) | 4 (16.0%) | | |
| Separated | 3 (4.1%) | 0 (0.0) | | |
| Infant sex | | | $\chi^2 = 1.472$ | *p* = .254 |
| Male | 37 (50.0%) | 16 (64.0%) | | |
| Female | 37 (50.0%) | 9 (36.0%) | | |
| First born/not first born | | | $\chi^2 = 1.545$ | *p* = .246 |
| First born | 28 (37.8%) | 13 (52.0%) | | |
| Not first born | 46 (62.2%) | 12 (48.0%) | | |
| Prenatal maternal demoralization | | | *t*-test *t* = -1.445 | *p* = .152 |
| N | 72 | 25 | | |
| Mean (SD) | 21.56 (15.50) | 27.00 (18.23) | | |
| Std. Error Mean | 1.827 | 3.645 | | |
| Average income to needs | | | *t* = -0.883 | *p* = .38 |
| N | 68 | 25 | | |
| Mean (SD) | 8576.59 (6972.31) | 10050.00 (7578.03) | | |
| Std. Error Mean | 845.52 | 1515.61 | | |
| Maternal age | | | *t* = 1.547 | *p* = .125 |
| N | 74 | 25 | | |
| Mean (SD) | 29.41 (6.287) | 27.24 (5.262) | | |
| Std. Error Mean | 845.52 | 1515.61 | | |

*Notes.* Data was missing for neonatal maternal demoralization (N = 2) and average income to needs (N = 6).
% = percent of total dyads with count of no (yes) within non-exposed (n = 74) and SHS-exposed (n = 25).

### 3.3. SHS exposure during pregnancy and maternal self-contingency

Self-contingency was lower (more variable) in mothers who had SHS-exposure during pregnancy (versus non-exposed) in 2 modality

**Table 2**
Summary of effects of prenatal maternal environmental tobacco smoke (SHS) on 4-month self- and interactive contingencies: Weighted lag time-series models.

| Interpersonal Models | | | | | |
|---|---|---|---|---|---|
| **Infant** | **Mother** | I→I | M→I | M→M | I→M |
| (1) Facial Affect | Facial Affect | ↓ | | | |
| (2) Vocal Affect | Facial Affect | ↓ | | ↓ | |
| (3) Gaze | Gaze | ↓ | | | |
| (4) Vocal Affect | Touch | ↓ | | | |
| (5) Vocal Affect | Gaze | ↓ | | | |
| (6) Gaze | Facial Affect | ↓ | | ↓ | |
| (7) Gaze | Touch | ↓ | | | |
| Intrapersonal Infant Cross-Modal Model | | | | | |
| **Infant** | **Infant** | V→V | F→V | F→F | V→F |
| (8) Vocal Affect (V) | Facial Affect (F) | ↓ | ↓ | | |

Notes.
1. I → I = Infant Self-Contingency. M → I = Infant Interactive Contingency.
2. Models controlled for infant sex, first-born (vs. not first-born), maternal education, age, marital status, income-to-needs ratio.
3. Entries = contingency is increased ↑ or decreased ↓ with (SHS).

pairings (Table 2) using weighted-lag models: Mother facial affect analyzed in relation to infant vocal affect ($\beta = -0.037$, $p = .027$, Table S2a) and in relation to infant gaze ($\beta = -0.034$, $p < .043$, Table S6a). Probability explication showed that, given that both groups of mothers were likely to be in the most negative facial affect code, in both findings mothers who had SHS-exposure during pregnancy (versus non-exposed) were more likely to transform to less negative/more positive facial affect (Tables S2d and S6d).

In two additional individual-seconds time-series models, mother self-contingency was higher (less variable) in mothers who had SHS-exposure during pregnancy (versus non-exposed): Mother touch analyzed in relation to infant-vocal affect ($\beta = 0.046$, $p = .018$, Table S4b) and in relation to infant gaze ($\beta = 0.047$, $p < .018$, Table S7b). Probability explication for both findings showed that, given that both groups of mothers were likely to be in the most positive touch code at 3s prior, both groups transformed toward midrange values, but mothers who had SHS-exposure during pregnancy (versus non-exposed) changed less, more likely to stay in more positive values (Tables S4d and S7d).

### *3.4. Prenatal SHS exposure and mother-infant interactive contingency*

Weighted-lag models did not detect any significant conditional effects of SHS exposure on infant or mother interactive contingency. In two individual-seconds models, infant interactive contingency was higher (more reactive) in infants with prenatal SHS exposure (vs. non-exposed): infant gaze analyzed in relation to mother-facial affect ($\beta = 0.141$, $p = .014$, Table S6b) and in relation to mother touch ($\beta = 0.143$, $p = .042$, Table S7b). Given that mothers in both groups were likely to be in the most negative facial affect codes 1s prior, infants with prenatal SHS exposure (vs. non-exposed) were less likely to be gaze-on mother (Table S6c). Given that mothers in both groups were likely to be in the most positive touch codes 3s prior, infants with prenatal SHS exposure (vs. non-exposed) were more likely to be gaze-on mother (Table S7c).

Mother interactive contingency was higher (more reactive) in mothers who had SHS-exposure during pregnancy (versus non-exposed) in two modality pairings using individual-seconds models: mother facial affect analyzed in relation to infant vocal affect (L1 $\beta = 0.052$, $p = .025$; L2 $\beta = -0.059$, $p = .021$, Table S2b); mother-touch in relation to infant gaze (L3 $\beta = -0.072$, $p = .043$, Table S7b). When infants were in the most positive vocal affect codes 1s prior, or in mid-range vocal affect codes (toward no-vocalization) 2s prior, mothers who had SHS-exposure during pregnancy (versus non-exposed) were more likely to be in more positive, but still mild-negative, facial affect codes (Table S2d). Given that infants were gaze-off 3s prior, mothers who had SHS-exposure during pregnancy (versus non-exposed) were more likely to be in more positive touch codes (Table S7d).

### *3.5. Prenatal SHS-exposure and behavioral frequencies*

Infants with SHS exposure were more vocally silent than non-exposed infants (Table S9 for code, S10, 1 of 14 tests). Mothers with SHS-exposure used 'mild smile' (smile 1) more and 'interest increment' less (Tables S9, S10, 2 of 30 tests).

## 4. Discussion

To our knowledge this is the first study to examine the effects of prenatal SHS exposure on infant behavior, and specifically the effects on self-regulatory capacity. Prenatal SHS-exposure was robustly associated with lower infant self-contingency – more variability of behavior – consistent with our hypothesis that prenatal SHS exposure would be associated with altered infant self-regulation. In eight of eight models testing different behavioral pairings, relative to non-exposed infants, those with prenatal SHS exposure showed greater magnitude of change in behavior. In exploratory analyses, mothers who were SHS-exposed during pregnancy (versus non-exposed) showed a similar, albeit less prevalent pattern of greater magnitude of change in behavior. Critically, whereas frequencies of infant behaviors did not distinguish between exposed and non-exposed infants, the contingencies of infant behavior were sensitive to exposure, underscoring the importance of using granular and time-varying measures of behavior to understand complex effects of environmental risk factors.

Infants with prenatal exposure to SHS showed lower, more variable affective self-contingency than non-exposed infants. Relative to non-exposed infants, infants with prenatal SHS exposure made larger shifts in behavior in response to their own negative affect. Our results are consistent with prior findings showing lowered self-contingency in infants exposed to risk factors such as maternal perinatal depression or trauma during pregnancy (Beebe et al., 2020, 2008). Specifically, infants of mothers pregnant and widowed on 9/11 also showed larger shifts out of negative affect. Notably, there were no differences between infants with or without exposure or between mothers with or without exposure in the frequency of negative affect as measured by second-by-second behavioral coding. Significant effects of exposure on affect self-contingency, but not on frequencies of behavior, suggests that SHS exposure alters the regulation of negative affect rather than its prevalence.

Self-contingency of infant intrapersonal cross-modal affect was also sensitive to prenatal SHS exposure. This measure indexed the infant's coordination across facial affect and vocal affect channels and was more discrepant in infants who were exposed to prenatal SHS than those who were not. Similar to the findings for facial and vocal affect in the context of maternal behavior, infants with prenatal SHS exposure had more variability in coupling their own facial and vocal affect and this was specific to moving out of negative affect. Given prior findings showing that concordance between infant facial and vocal affect reflects typical maturation (Jhang and Oller, 2017; Parladé and Iverson, 2011) our findings point to a slower maturing and dysregulated affect system in infants who are prenatally exposed to SHS.

Relative to non-exposed infants, those with prenatal SHS exposure also showed lowered self-contingency in gaze behavior which is theorized to reflect infant attention. Infants with prenatal SHS exposure had a greater likelihood of changing gaze both from 'off' to 'on' and from 'on' to 'off' the mother's face. Because looking is arousing, and looking away is a central means of infant regulation of arousal as measured by heart rate (Field, 1981), greater likelihood of transitioning to looking suggests likelihood of greater arousal; greater likelihood of transitioning to looking away suggests greater need for down-regulation of arousal. One recent study showed that infant gaze-shifts on and off of mother during a social interaction are normative but were not associated with current or future attention capacity (Niedźwiecka et al., 2018). These authors argue that shifts in gaze reflect practice with attentional disengagement. Taken together these findings suggest a u-shaped curve such that more gaze shifts may be optimal within a normative range and beyond that too many shifts may reflect impaired self-regulation.

Our findings of altered infant self-regulation in infants with prenatal SHS exposure are consistent with prior studies reporting increased arousal and activity in infants prenatally exposed to nicotine via active maternal smoking (Law et al., 2003; Stroud et al., 2018). Additionally, maternal smoking during pregnancy has been linked to attenuated methylation of the placental glucocorticoid receptor gene NR3C1 (Stroud et al., 2014), which has been linked with decreased self-regulation (Stroud et al., 2016). Animal models and human neuroimaging studies also document effects of prenatal exposure to SHS on the function of cognitive control circuits that support self-regulatory capacity (Bryden et al., 2016; Margolis et al., 2021; Schneider et al., 2011; Slotkin, 1998; Yochum et al., 2014). These circuits rely on thalamocortical processing which is putatively involved in efference copies (Sherman, 2016). This theory suggests a process to allow for anticipation of impending self-generated behavior by sending information from motor cortex back to the sensory processing stream (Sommer and Wurtz, 2008). Such processes could explain our findings of lowered self-contingency in infants with prenatal SHS exposure such that lowered self-contingency may index lower ability to anticipate one's own behavior.

Exposure to SHS during pregnancy also was associated with altered maternal self-contingency. Mothers with SHS exposure during pregnancy showed a pattern of lowered self-contingency in facial affect, with a larger response to their own negative affect. They also were also more likely to stay in positive touch codes than non-exposed mothers. Our findings are consistent with prior findings showing associations between SHS and cognitive function in adults (Ling and Heffernan, 2016; Llewellyn et al., 2009), but counter to prior findings that SHS exposure is not associated with altered brain function during inhibitory control in non-smoking adolescents (Boormans et al., 2021; Dieleman et al., 2020, 2022). SHS exposure in adults, however, may be different than in adolescents. Furthermore, chemical exposures have been shown to differentially and adversely impact females during pregnancy (Fleisch et al., 2022; Holtcamp, 2012). Such differences may explain effects of exposure on maternal behavior.

Whereas self-contingency (auto-correlation) measures the individual's likelihood of maintaining (or changing) behavior from moment-to-moment, interactive contingency (lagged cross-correlation) measures adjustments the individual makes in response to the partner's prior behavior. Interactive contingency was not sensitive to SHS exposure using the primary weighted-lag models. However, in the individual seconds models, infant and mother interactive contingency was higher (more reactive) with SHS exposure. In dyads with SHS exposure, infants were more likely to look at mother's face when mother used positive touch and to look away when mothers showed negative facial affect. Additionally, mothers were more likely to use positive touch when infants were gazing away and to be facially positive when infants showed positive vocal affect or were silent. These findings parallel the self-contingency findings in that each partner tended toward positive, and away from negative, behavior. Considering the gaze and affect findings together suggests a possible sequence of events: when mothers showed negative facial affect, infants were more likely to look away, but when infants looked away, mothers were likely to engage in more positive touch, in which case infants were more likely to look at mothers.

Our study is limited in several ways. First, our relatively small sample size requires replication as we are underpowered to test sex-specific effects of SHS in self-regulation. Further, our measure of SHS via self-report is not validated by biomarker data such as cotinine, although associations between cotinine and self-report are high in similar cohorts (Rauh et al., 2004). Finally, we are unable to control for some potential cofounds including postnatal SHS exposure (occurring in the first four months of life rather than in utero) as well as pre- or postnatal exposure to ambient or household air pollutants which also are associated with self-regulation (Margolis et al., 2016; Guxens et al., 2018).

## 5. Conclusions

Our novel findings about a potential source of infant dysregulation, prenatal SHS exposure, are generated by the integration of two distinct fields of study: developmental psychology and environmental health science/epidemiology. We have linked an established behavioral marker of development with a chemical exposure, yielding a powerful tool for probing typical and atypical developmental trajectories. Because self-regulation is a transdiagnostic marker of future psychiatric problems, linking it to a prenatal chemical exposure provides strong evidence for increasing public health prevention programs that may reduce these exposures. These kinds of interdisciplinary approaches to understanding the chemical and social environment are needed in order to optimize infant development and best protect children's mental health outcomes.

## Credit statement

Amy E. Margolis: Conceptualization, Methodology, Funding acquisition, Writing- Original draft preparation. Sang Han Lee: Formal analysis. Ran Liu: Investigation. Lindsay Goolsby: Project administration, Data curation. Frances Champagne: Conceptualization, Funding acquisition. Julie Herbstman: Conceptualization, Funding acquisition, Writing – review & editing. Beatrice Beebe: Conceptualization, Methodology, Funding acquisition, Writing – review & editing.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

Data will be made available on request.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2023.115652.

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