



## CLINICAL RESEARCH ARTICLE



# Effects of prenatal psychosocial stress and COVID-19 infection on infant attention and socioemotional development

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**BACKGROUND:** The COVID-19 pandemic dramatically altered the psychosocial environment of pregnant women and new mothers. In addition, prenatal infection is a known risk factor for altered fetal development. Here we examine joint effects of maternal psychosocial stress and COVID-19 infection during pregnancy on infant attention at 6 months postpartum.

**METHOD:** One-hundred and sixty-seven pregnant mothers and infants (40% non-White;  $n = 71$  females) were recruited in New York City ( $n = 50$  COVID+,  $n = 117$  COVID-). Infants' attentional processing was assessed at 6 months, and socioemotional function and neurodevelopmental risk were evaluated at 12 months.

**RESULTS:** Maternal psychosocial stress and COVID-19 infection during pregnancy jointly predicted infant attention at 6 months. In mothers reporting positive COVID-19 infection, higher prenatal psychosocial stress was associated with lower infant attention at 6 months. Exploratory analyses indicated that infant attention in turn predicted socioemotional function and neurodevelopmental risk at 12 months.

**CONCLUSIONS:** These data suggest that maternal psychosocial stress and COVID-19 infection during pregnancy may have joint effects on infant attention at 6 months. This work adds to a growing literature on the effects of the COVID-19 pandemic on infant development, and may point to maternal psychosocial stress as an important target for intervention.

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## IMPACT:

- This study found that elevated maternal psychosocial stress and COVID-19 infection during pregnancy jointly predicted lower infant attention scores at 6 months, which is a known marker of risk for neurodevelopmental disorder. In turn, infant attention predicted socioemotional function and risk for neurodevelopmental disorder at 12 months. These data suggest that maternal psychosocial stress may modulate the effects of gestational infection on neurodevelopment and highlight malleable targets for intervention.

## INTRODUCTION

Psychosocial stress during pregnancy is a known risk factor for altered neurodevelopment and risk for psychiatric disorders in later life.<sup>1</sup> In addition, psychosocial stress is also related to higher susceptibility to contracting infections and generally lower quality of physical health.<sup>2–4</sup> Examining the effects of maternal prenatal psychosocial stress and infection on infant outcomes is particularly timely in the context of the COVID-19 pandemic. In the current study, we evaluate the joint influences of maternal prenatal psychosocial stress and COVID-19 infection during pregnancy on objective measures of infant outcomes in a prospective longitudinal study of 167 mother–infant dyads. Specifically, we examine the effects on infant attention at 6 months postpartum, given that early attention is a reliable predictor of cognitive and socioemotional development and long-term neurodevelopmental outcomes.<sup>5–7</sup>

## Attention as a window into understanding the effects of prenatal stress on neurodevelopment

There is a large literature linking prenatal stress to neurodevelopmental outcomes. Multiple meta-analyses have demonstrated robust associations between maternal mental health during pregnancy and delays across infant cognitive and socioemotional outcomes.<sup>8,9</sup> Of relevance to the COVID-19 pandemic, a recent meta-analysis found that stress connected specifically to the occurrence of natural disasters during pregnancy was associated with adverse outcomes across nearly all domains of child development, including cognitive, motor, socioemotional, and behavioral development.<sup>10</sup> Despite this evidence, previous studies examining maternal prenatal stress have largely relied on global measures of cognitive ability (e.g., the Bayley Scales of Infant Development) or on maternal report measures of infant development (e.g., the Ages and Stages Questionnaire) rather than

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objective assessments of specific cognitive domains. While general measures of infant development may be useful for identifying infants at risk for severe developmental delays, there are several limitations to using these global measures, including potential confounds arising from parental or examiner's subjective ratings as well as poor correlations with long-term cognitive outcomes.<sup>11,12</sup>

Behavioral assessments of infant attention, measured through direct, standardized observations of infant looking behavior, may provide a reliable window into the early brain and cognitive development.<sup>13–15</sup> Visual attention is a foundational cognitive capacity that is observable from early infancy and shows rapid developmental change, particularly over the first postnatal year.<sup>15,16</sup> Importantly, animal models have also linked specific aspects of visual attention to key brain networks.<sup>17,18</sup> Beyond serving as a behavioral correlate of brain function, visual attention also predicts cognitive and socioemotional outcomes in later infancy and childhood. Even relatively coarse objective measures of infant attention, such as looking durations, have been shown to predict higher-order cognition in later childhood.<sup>19–22</sup> Atypical patterns of attentional development are also one of the earliest behavioral markers of risk for numerous neurodevelopmental disorders, including autism,<sup>5</sup> attention-deficit disorder,<sup>23</sup> and anxiety disorders.<sup>24</sup> As such, examining individual differences in infant attention may be valuable for predicting subsequent developmental outcomes. Moreover, this capacity is also externally observable from early in postnatal life through measurement of infant looking behavior, allowing for objective assessment of individual differences from early in infancy.

The anatomical connections supporting attentional control and behavioral regulation are established in utero.<sup>25</sup> These cortical connections are thus vulnerable to shaping by environmental signals even before birth.<sup>1</sup> Increasing evidence shows associations between prenatal stress and phenotypic alterations in infant attentional processing using both maternal report measures<sup>26,27</sup> and measurement of infant looking behavior.<sup>28,29</sup> Recent findings point to inflammatory processes as one mechanistic pathway through which maternal prenatal stress may impact fetal development. For instance, elevated psychosocial stress, whether chronic or in response to stressful life events, is linked to elevated levels of pro-inflammatory cytokines, which can cross the placenta during pregnancy and adversely influence fetal outcomes.<sup>30</sup> Moreover, multiple exposures that elevate inflammatory levels during pregnancy, such as from repeated immune activation or chronic stress exposure, may have compounding impacts on neurocognitive development in offspring.<sup>31</sup>

### Possible sequelae of the COVID-19 pandemic on infant developmental outcomes

The COVID-19 pandemic has drawn heightened attention to possible interactions between infection and neuropsychological function. Even relatively minor cases of COVID-19 infection have been shown to predict elevated risk of new-onset mental health problems in the general population,<sup>32–34</sup> and can even lead to more severe psychiatric sequelae.<sup>35</sup> These neurological and psychiatric effects may be related to the peripheral immune response to infection.<sup>36,37</sup> Indeed, COVID-19 infection is associated with elevated inflammatory markers and increased cytokine expression,<sup>38</sup> which can contribute to neurological dysfunction.<sup>39</sup> Thus, it is possible that the peripheral immune response to COVID-19 infection may have downstream impacts on infant neurodevelopmental outcomes.

Knowledge of the impact of the COVID-19 pandemic on infant development is relatively limited. There is some evidence that maternal COVID-19 pandemic-related stress is associated with altered infant temperament, including decreased surgency in 3-month-olds<sup>40</sup> and decreased regulatory capacity at 4 and 6 months of age.<sup>41</sup> However, other research has found that maternal

depressive symptoms measured during the COVID-19 pandemic were not associated with infant temperament,<sup>42</sup> and that exposure to the pandemic in general had no association with infant socioemotional or language outcomes.<sup>43</sup> In regards to direct effects of maternal prenatal SARS-CoV-2 exposure, existing reports, to date, have found no significant associations between maternal prenatal infection and infant outcomes, measured through maternal report at 6 months of age.<sup>44</sup> However, there are likely important individual differences that may modulate individual risk. In particular, the COVID-19 pandemic presented a vast number of psychosocial stressors, even in individuals not directly infected with the virus. Indeed, data from large samples of perinatal individuals across the United States has shown that these psychosocial aspects of the COVID-19 pandemic adversely influenced perinatal mental health and stress levels.<sup>45,46</sup> It is possible that these psychosocial sequelae may modulate individual risk from infection or exert independent effects on early neurodevelopment. However, there is scant evidence examining interactions between prenatal COVID-19 infection and psychosocial stress in predicting infant developmental outcomes.

### The current study

Here we examine whether maternal prenatal psychosocial stress and COVID-19 infection are associated with early infant neurodevelopmental outcomes, using infant attention as a behavioral model. In addition, we also conduct exploratory analyses examining longitudinal associations with socioemotional outcomes and neurodevelopmental risk at 12 months. Understanding individual differences that may influence infant outcomes is key for identifying mothers and infants at increased risk, and may have direct impacts on targeting personalized therapies to support adaptive long-term outcomes.

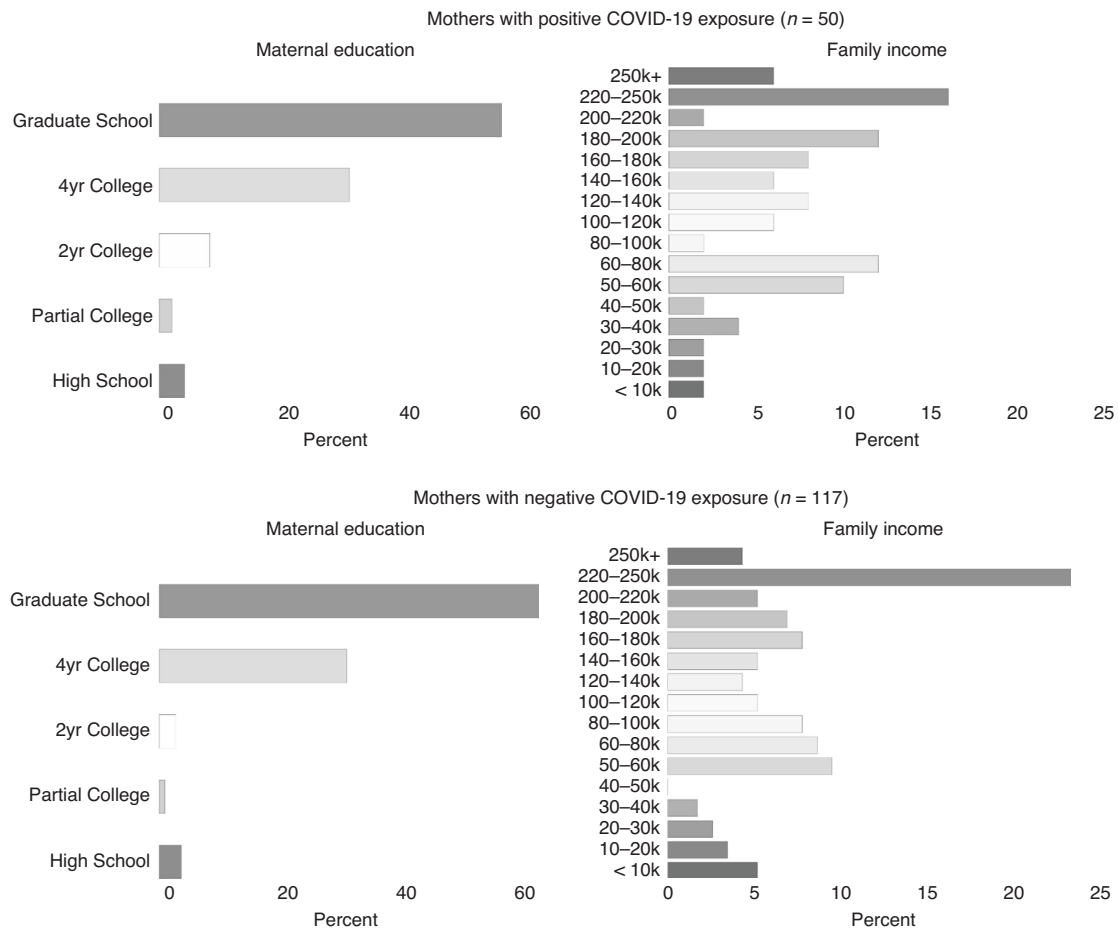
## METHOD

### Participants

The current sample included 167 mothers and their infants ( $n = 71$  females,  $n = 96$  males) enrolled between March 2020 and January 2023. The racial breakdown of infants in the full sample was as follows: 60% White, 17% two or more races, 8% other, 5% Asian, 5% Black, and 5% not reported. In addition, 24% of the sample identified as Hispanic or Latino. Mothers were recruited from NYU Langone Health medical records as part of an ongoing, prospective longitudinal study ( $n = 117$  COVID-negative,  $n = 50$  COVID-positive). Prenatal SARS-CoV-2 exposure was defined based on maternal report of positive COVID-19 infection during pregnancy. This was probed using the COPE: COVID-19 & Perinatal Experiences – Impact Survey<sup>47</sup> and the Novel Coronavirus Illness Patient Report Survey.<sup>33</sup> We verified that there were no differences in sociodemographic characteristics between mothers with positive prenatal COVID-19 exposure and those who were not exposed,  $ps > 0.16$ . Additional sociodemographic information by COVID-19 exposure group is reported in Fig. 1.

### Protocol

Maternal self-reported psychosocial stress and COVID-19 exposure were evaluated during a baseline assessment. When infants were 6 months of age ( $M$  age = 6.64 months,  $SD = 0.70$  months), families then participated in a remote free-viewing visual attention assessment in the home. The remote visual attention task occurred synchronously through Zoom using laptops (71%) or smartphones (29%). A short (80-s) Sesame Street video (Cecile - Up Down, In Out, Over and Under) used in previous in-lab assessments of infant attention<sup>48</sup> was adapted for mobile testing through Zoom.<sup>49</sup> In brief, parents were asked to participate in a quiet area of their home relatively free from distractions and were instructed to hide both their own and the experimenter's video. Experimenters guided parents through positioning their infants so that infants' eye movements to animated cartoons presented on the left, right, bottom, and top of the screen could be clearly seen during a calibration procedure prior to testing. Experimenters recorded the infants for subsequent post hoc analysis of infants' gaze behavior using an online webcam-linked eye tracker (OWLET) developed to analyze infant eye-tracking data collected on personal devices in the home.<sup>50</sup> In addition, caregivers used an 18-inch tape



**Fig. 1 Study sociodemographic characteristics.** Maternal educational attainment and annual family income for the COVID+ and COVID- groups.

measure that was mailed to families prior to participation to measure their distance from the screen during the visual attention task. Caregivers also reported the specific testing device used during the study, which was used to obtain the dimensions of the testing screen. This information was used to estimate the visual angle of viewing. We verified that individual differences in visual angle were not correlated with the total looking time or attention-orienting variables,  $r_s < 0.12$ ,  $p_s > 0.22$ .

Families were invited to participate in a follow-up assessment when infants were approximately 12 months of age. Ninety-nine mothers (60%) completed surveys on infant socioemotional development and neurodevelopmental risk during this follow-up assessment ( $M$  age = 12.32 months,  $SD = 0.53$  months;  $n = 37$  females,  $n = 62$  males;  $n = 71$  COVID-negative,  $n = 28$ , COVID-positive). Attrition from 6 to 12 months occurred due to study dropout ( $n = 36$ ) or due to not completing the survey on infant socioemotional outcomes ( $n = 32$ ). To test for potential attrition-related biases, we ran multiple t-tests to assess for differences in maternal prenatal psychosocial stress levels, COVID-19 exposure, postnatal depression, or family sociodemographic characteristics between 6 and 12 months. Results indicated no differences between families who provided data at both timepoints and those who did not,  $p_s > 0.14$ .

### Maternal measures

**Maternal prenatal psychosocial stress.** Maternal psychosocial distress was measured in pregnant mothers using maternal report of depressive symptoms, anxiety, physical complaints, and post-traumatic stress symptoms. Symptoms of depression, anxiety, and somatic issues were evaluated using the Depression, Anxiety, and Somatic subscales of the Brief Symptom Inventory (BSI-18).<sup>51</sup> In addition, symptoms of post-traumatic stress were assessed using a modified version of the PCL-5 PTSD Checklist for DSM-5.<sup>52</sup> Both the BSI-18 and PCL-5 ask subjects to indicate the distress they have experienced from each symptom in the past two weeks on a 5-point Likert-type scale (1 = not at all;

5 = extremely). The suicidality item from the BSI-18 was omitted. In total, there were five items probing depressive symptoms, six probing anxiety symptoms, six probing somatic symptoms, and ten probing post-traumatic stress symptoms. Scores from each subscale were averaged to generate a total psychosocial stress score. Reliability was high for the overall psychosocial stress measure (Cronbach's alpha = 0.93, 95% CI = [0.92, 0.94]).

### Six-month attention measures

**Looking time and orienting patterns.** Infant total looking time and visual orienting patterns were assessed while infants watched an 80-s Sesame Street video during a remote free-viewing visual attention assessment (see protocol for full administration details). Total looking time was calculated by summing the time that infants' point-of-gaze fell within the screen boundaries during the 80-s video. Infant total looking time was used as a proxy of focused attention and information processing efficiency, consistent with standard approaches.<sup>20,53,54</sup>

Infant attention-orienting patterns were evaluated during segments of the Sesame Street video in which multiple salient regions were present (occurring at approximately 33–37 s, 45–51 s, 56–62 s, and 67–71 s), eliciting competition for attentional resources. Saliency maps were computed for each frame in these segments (at 30 frames per second) using a static saliency model implemented using the OpenCV library in Python.<sup>55</sup> In contrast to more computationally intensive models, the static saliency model does not rely on the linear summation of individual feature maps for color, intensity, motion, or depth.<sup>56</sup> Instead, this algorithm computes saliency maps by evaluating regions of an image that "pop out" from the background by analyzing the log spectrum of an image (see Supplemental Information for heatmaps of the computed saliency maps across the four video segments). Prior work shows that this algorithm approximates human determinations of salient regions and performs equivalently or better than more computationally intensive methods that

rely on the linear summation of feature maps.<sup>55</sup> Infant attention-orienting scores were then computed by analyzing cross-correlations between the coordinates of infants' point-of-gaze and the coordinates with the maximum saliency value on a frame-by-frame basis across these four segments. Higher scores indicate that infants are primarily oriented toward the most visually salient regions across video frames rather than orienting attention amongst multiple competing areas of interest. As such, we use infants' orienting scores as an exploratory index of attentional flexibility.

**Regulatory capacity.** Parental report data on infant attentional control and regulatory function was collected using the revised Infant Behavior Questionnaire – very short form (IBQ-VSF).<sup>57</sup> We use the Regulatory Capacity factor of the IBQ-VSF in the current analysis, which provides a global parent-report measure of infant attentional and regulatory functioning in their everyday environments. This measure captures additional aspects of infant attentional control that may not emerge during a short testing session, and has shown high relation with laboratory measures of attention.<sup>58</sup> Indeed, prior research has found that infant looking behavior is associated with parent-report measures of infant regulatory capacity, with shorter looking times generally predicting higher regulation.<sup>59–61</sup>

### Twelve-month socioemotional measures

Socioemotional outcomes and neurodevelopmental risk were assessed using the Brief Infant-Toddler Social and Emotional Assessment (BITSEA). The BITSEA is a parent-report screening tool designed to identify children with possible deficits or delays in socioemotional and behavioral development. This measure contains 42 questions, each requiring one of three responses (true/rarely, somewhat true/sometimes, or very true/often), and has been validated in infants and toddlers ages 12–36 months.<sup>62</sup> Although this measure is not diagnostic, prior research has found that it has high predictive validity in identifying children at risk for socioemotional delays and neurodevelopmental disorders.<sup>63</sup> The BITSEA yields a Competence Total Score, which indexes normative socioemotional development, a Problem Total Score, which indexes possible socioemotional developmental delays. In addition, the BITSEA also yields an Autism-Competence Risk Score, an Autism-Problem Score, and an Autism Total Risk Score, which is equal to the Autism-Problem Score minus the Autism-Competence Score. Here we use the Autism Total Risk Score as an index of overall neurodevelopmental risk.

### Covariates

**Prior maternal mood/anxiety disorder.** Mothers were asked to report on a binary measure of whether they had previously been diagnosed with a mood or anxiety disorder (yes or no).

**Maternal postpartum depression.** At 6 months postpartum, maternal postpartum depression was assessed using the Edinburgh Postnatal Depression Scale (EPDS).<sup>64</sup> The EPDS consists of 10 items probing the severity of postpartum depression and anxiety symptoms, which are rated on a four-point Likert scale ranging from 0 (not at all) to 3 (very often). Scores were summed across all items.

**Socioeconomic status.** Prior work has indicated associations between socioeconomic status (SES) and infant attention.<sup>6,65</sup> Thus, we used categorical scales of family income as a proxy for SES (Fig. 1).

### Analytical plan

Confirmatory factor analysis (CFA) was used to derive a global measure of infant attention. We modeled infant attention as a latent variable to provide a more comprehensive assessment of attention than any one observed variable by itself could provide. In addition, unlike statistical analyses that focus solely on observed variables, CFA explicitly models measurement error such that observed variables are represented by both the true score and measurement error. Multiple linear regressions were then used to evaluate whether interactions between prenatal SARS-CoV-2 exposure and psychosocial stress predicted individual differences in infant attention. In addition, we also examined exploratory longitudinal associations between infant attention and subsequent socioemotional outcomes and neurodevelopmental risk at 12 months. Missing data were accounted for using full-information maximum likelihood estimation, which generates unbiased estimates for data missing at random and is superior to other methods for handling missing data, including listwise deletion, pairwise

**Table 1.** Descriptive statistics.

Variable	N	M or %	SD
Maternal measures			
Prenatal psychosocial stress (1–5 range)	126	1.56	0.52
Prenatal COVID-19 exposure (% positive)	167	30%	–
Postnatal depression score (0–30 range)	153	11.14	3.54
Mood/anxiety disorder (% with prior history)	167	22%	–
Infant 6-month attention measures			
Regulatory capacity (1–7 range)	151	5.46	0.63
Look duration (s)	151	59.60	18.4
Attention-orienting score (0–1 range)	136	0.31	0.08
Infant 12-month socioemotional measures			
BITSEA Total Competence Raw Score	99	13.69	3.86
BITSEA Total Problems Raw Score	99	7.33	5.28
BITSEA Neurodevelopmental Risk Raw Score	99	–9.74	3.07

deletion, or mean imputation.<sup>66</sup> Little's Missing Completely at Random (MCAR) test indicated that the data fit an MCAR pattern,  $\chi^2 = 107.87$ ,  $p = 0.16$ . Analyses were conducted using MPLUS v.8.

## RESULTS

Descriptive statistics for primary study variables are displayed in Table 1, and correlations among all variables are displayed in Table 2.

### Predictors of prenatal psychosocial stress in mothers exposed to the SARS-CoV-2 virus

Prior to testing primary hypotheses, we first explored interactions between maternal SARS-CoV-2 exposure and relevant socio-demographic variables (income, prior history of mood or anxiety disorder) in predicting maternal prenatal psychosocial stress. In mothers reporting positive SARS-CoV-2 exposure, neither mood/anxiety disorder history,  $\beta = 0.09$ ,  $p = 0.56$ , nor family income,  $\beta = 0.10$ ,  $p = 0.53$ , were predictive of psychosocial stress levels (Fig. 2). In contrast, both mood/anxiety disorder history,  $\beta = 0.33$ ,  $p < 0.01$ , and lower family income,  $\beta = -0.34$ ,  $p < 0.01$ , were significant predictors of psychosocial stress in mothers reporting no SARS-CoV-2 exposure during pregnancy (Fig. 2). These findings provide behavioral evidence in support of the hypothesis that elevated psychosocial stress in individuals experiencing COVID-19 infection may be tied to peripheral effects of infection.<sup>32,35</sup>

### Effects of maternal psychosocial stress and SARS-CoV-2 exposure on infant attention

Next, the effects of maternal prenatal psychosocial stress and SARS-CoV-2 exposure on infant attention were evaluated. A latent measure of infant attention was derived using CFA with the observed attention variables (look duration, attention-orienting score, and regulatory capacity) as indicators. A unidimensional model fit the data, CFI = 1.00,  $\chi^2 = 14.29$ ,  $p = 0.002$ , RMSEA = 0, SRMR = 0, with all factor loadings in the expected direction (look duration:  $\beta = -0.32$ , 95% CI [0.06, 0.45],  $p = 0.02$ ; attention orienting:  $\beta = -0.43$ , 95% CI [0.12, 0.91],  $p = 0.01$ ; regulatory capacity:  $\beta = 0.68$ , 95% CI [0.22, 1.61],  $p = 0.01$ ).

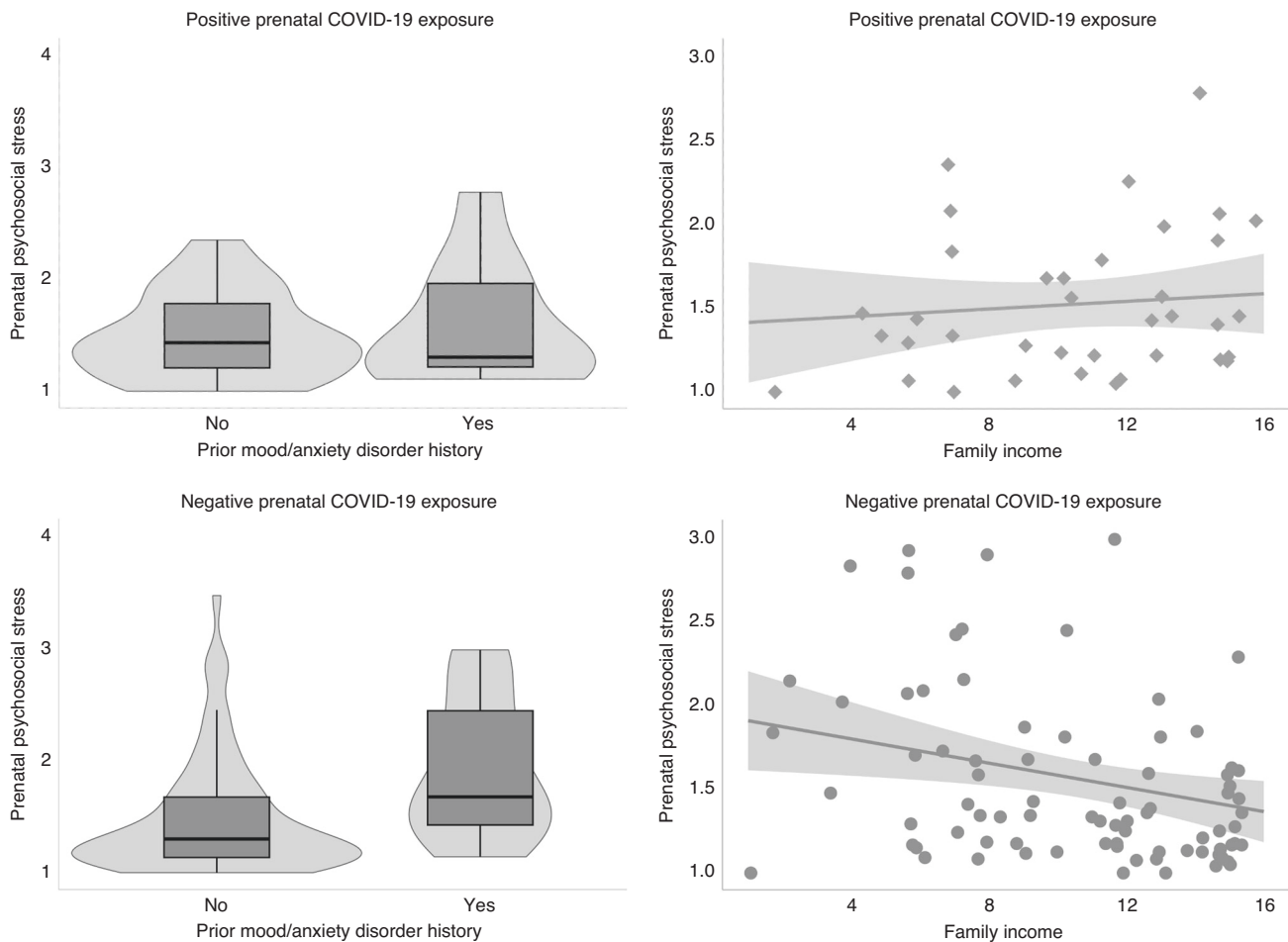
The latent measure of infant attention was regressed onto maternal prenatal psychosocial stress, prenatal SARS-CoV-2

**Table 2.** Bivariate correlations.

Variable	1	2	3	4	5	6	7	8	9	10
1. Family income	1									
2. Prenatal psychosocial stress	<b>-0.18*</b>	1								
3. Postnatal depression	-0.02	<b>0.41**</b>	1							
4. SARS-CoV-2 exposure	0.00	-0.05	0.00	1						
5. Prior mood/anxiety disorder	0.10	<b>0.24**</b>	<b>0.32**</b>	0.04	1					
6. Regulatory capacity	-0.11	-0.08	-0.11	0.09	0.05	1				
7. Looking duration	0.08	-0.01	0.12	-0.08	<b>0.14<sup>+</sup></b>	-0.05	1			
8. Attention-orienting score	0.11	0.07	0.04	-0.07	-0.01	<b>-0.21*</b>	-0.07	1		
9. Socioemotional competence	-0.11	-0.09	-0.10	<b>0.17*</b>	-0.07	<b>0.41**</b>	0.05	0.07	1	
10. Socioemotional problems	-0.12	0.12	<b>0.17<sup>+</sup></b>	-0.07	0.10	-0.12	-0.08	0.11	0.05	1
11. Neurodevelopmental risk	0.02	0.07	0.08	-0.14	0.12	<b>-0.40**</b>	0.04	0.08	<b>-0.85**</b>	<b>0.23*</b>

<sup>+</sup> $p < 0.10$ ; \* $p < 0.05$ ; \*\* $p < 0.01$ .

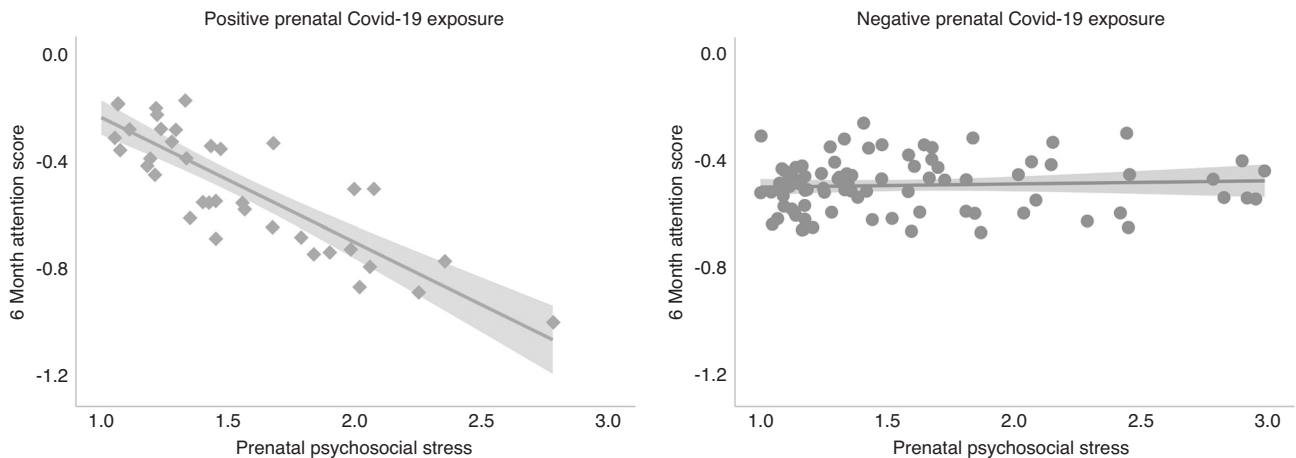
Bold values indicate significant correlations.



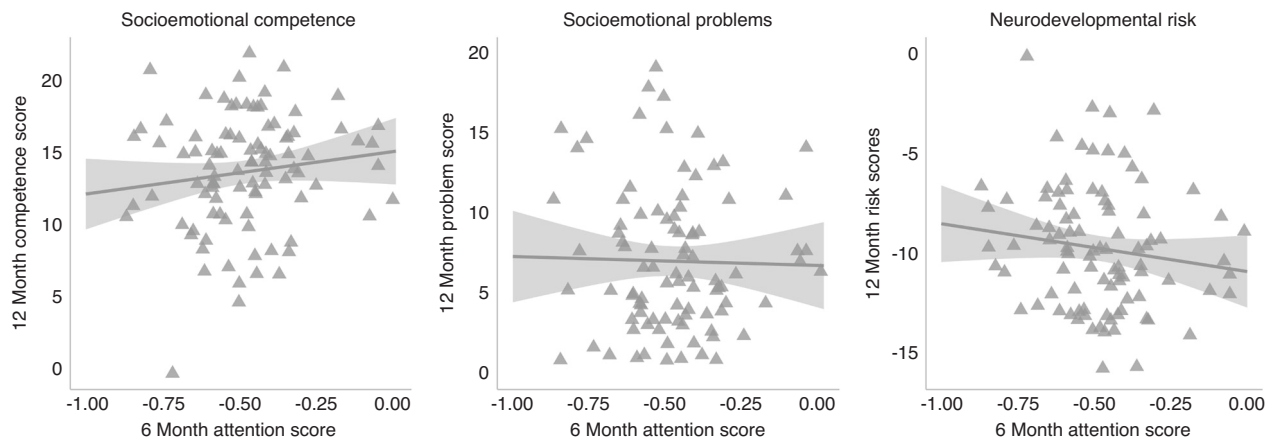
**Fig. 2 Prenatal psychosocial stress.** Family income and self-reported history of a mood/anxiety disorder were associated with psychosocial stress in mothers reporting negative SARS-CoV-2 exposure but not in mothers reporting positive SARS-CoV-2 exposure.

exposure, and the interaction between these variables. Family income, history of a mood/anxiety disorder, and infant age were included as covariates. Results indicated a main effect of prenatal SARS-CoV-2 exposure,  $\beta = 0.60$ , 95% CI [0.46, 0.75],  $p < 0.01$ , but no significant main effect of maternal prenatal psychosocial stress,  $\beta = -0.09$ , 95% CI [-0.27, 0.09],  $p = 0.42$ . Importantly, however, there was an interaction between

prenatal psychosocial stress and SARS-CoV-2 exposure on infant attention,  $\beta = -0.68$ , 95% CI [-0.64, -0.10],  $p < 0.01$ , such that higher psychosocial stress during pregnancy was associated with poorer attention scores in infants of mothers reporting positive prenatal SARS-CoV-2 exposure but not in mothers reporting negative prenatal SARS-CoV-2 exposure (Fig. 3).



**Fig. 3 Infant attention outcomes.** Maternal psychosocial stress moderated the impact of prenatal SARS-CoV-2 exposure on infant attention, such that higher maternal prenatal stress predicted lower infant attention scores in mothers reporting prenatal infection.



**Fig. 4 Associations between infant attention and socioemotional development.** Higher attention scores at 6 months predicted greater socioemotional competence and lower neurodevelopmental risk at 12 months. Infant attention was not associated with socioemotional problems.

We evaluated the robustness of these effects when controlling for maternal depression at 6 months postpartum. The interaction between maternal prenatal psychosocial stress and SARS-CoV-2 exposure on infant attention remained robust,  $\beta = -0.67$ , 95% CI  $[-0.82, -0.52]$ ,  $p < 0.01$ . In addition, infant attention was not predicted by current postpartum depression scores,  $\beta = -0.09$ , 95% CI  $[-0.26, 0.09]$ ,  $p = 0.43$ .

#### Longitudinal associations with infant socioemotional outcomes at 12 months

Finally, we conducted exploratory analyses examining associations between infant attention scores and socioemotional outcomes and neurodevelopmental risk at 12 months of age. Raw total scores for the socioemotional competence, socioemotional problems, and autism risk subscales of the BITSEA were used as dependent variables. Family income, maternal mood/anxiety disorder history, and infant age were included as control variables. There were no interactions between maternal prenatal psychosocial stress and SARS-CoV-2 exposure on infant socioemotional outcomes at 12 months,  $p_s > 0.19$ ,  $\beta_s < 0.17$ . However, higher latent infant attention scores at 6 months were associated with higher socioemotional competence,  $\beta = 0.27$ , 95% CI  $[0.06, 0.49]$ ,  $p = 0.02$ , and lower neurodevelopmental risk,  $\beta = -0.32$ , 95% CI  $[-0.53, -0.11]$ ,  $p < 0.01$  (Fig. 3). There were no significant effects of

infant attention on socioemotional problems at 12 months,  $\beta = -0.10$ , 95% CI  $[-0.33, 0.13]$ ,  $p = 0.39$  (Fig. 4).

#### DISCUSSION

Here we evaluated the impacts of the global COVID-19 pandemic on early neurodevelopment using infant attention as a behavioral model. We examined the psychosocial effects of the pandemic through impacts on maternal prenatal psychosocial stress, as well as the effects of maternal gestational exposure to the novel coronavirus (SARS-CoV-2) on infant attention and socioemotional development.

Our results suggest that maternal self-reported psychosocial stress and SARS-CoV-2 exposure during pregnancy jointly impacted infant attention development at 6 months. In particular, mothers with higher psychosocial stress who were also infected with the COVID-19 virus during the pandemic were more likely to have infants with lower scores on a global latent measure of attention characterized by longer looking times, lower regulatory capacity, and different patterns of attentional orienting during a free-viewing attention assessment. These global patterns of attention, assessed through standardized laboratory assessments, are thought to reflect less efficient information processing and attentional control.<sup>54</sup>

We also conducted exploratory analyses examining longitudinal associations between infant attention and subsequent socioemotional development and neurodevelopmental risk at 12 months. Our results indicated that there were no direct effects of prenatal psychosocial stress or maternal SARS-CoV-2 exposure on infant socioemotional competence. However, we found that higher attention scores at 6 months were correlated with higher socioemotional competence and lower neurodevelopmental risk scores at 12 months of age, regardless of maternal prenatal infection or psychosocial stress exposure.

The different patterns of infant attention, at different ages, observed in the current study may indicate alterations in child neurodevelopmental trajectories. However, it is also possible that observed attention patterns may reflect differences in the conditioning of autonomic responses that facilitate mother–infant attachment, beginning in utero. For instance, calming cycle theory posits that normal gestation and birth results in autonomic co-regulation between the mother and infant, producing physiological and behavioral effects that ensure mutual attraction between the dyad<sup>67</sup>. Disruptions to this autonomic co-regulation, such as due to physiological sequelae of prenatal stress and infection, may result in different patterns of infant attention and orienting behaviors.

Regardless of the underlying mechanisms driving differences in infant attention, these phenotypic alterations could be adaptive across many contexts. For instance, if paired with appropriate caregiver scaffolding, increased attentional orienting to salient stimuli, as captured by the attentional orienting component of our global latent construct of attention, might promote better learning from environmental cues.<sup>68,69</sup> However, these changes may also convey an increased risk for neuropsychiatric or neurodevelopment disorders in some contexts.<sup>70</sup> For instance, prior work has shown that infants subsequently diagnosed with neurodevelopmental disorders, such as autism and ADHD, demonstrate early differences in attentional processing.<sup>5,23,71–73</sup> These findings broadly align with the observed longitudinal associations between infant attention and neurodevelopmental risk in our sample. However, it is important to note that our socioemotional measures relied solely on maternal report, evaluated using the BITSEA questionnaire.<sup>62</sup> While this measure has been found to correlate with objective assessments of socioemotional problems and has predictive validity for neurodevelopmental risk,<sup>63,74</sup> it is not validated to diagnose disorders or delays. We also evaluated socioemotional development and neurodevelopmental risk at an early timepoint during which substantial variability in developmental trajectories is observed. Given this, these individual differences are likely indicative of normative variability in developmental trajectories. As well, attention is highly malleable to early postnatal experience,<sup>75,76</sup> which could additionally buffer or elevate long-term neurodevelopmental risk. Further investigations into both prenatal and postnatal modulators of early attention development, and possible cascading associations with neurodevelopmental outcomes, are needed to shed light on these questions.

Our findings should be interpreted within the limitations of our data. For one, while objective, standardized assessments of attention may be more ecologically valid in the home, it also limits experimenter control over distractions and noise. Proximal aspects of the home environment (e.g., residential crowding, chaoticity, presence of other family members or pets) could contribute to individual differences in infant attentional processing in the moment. Moreover, it is possible that using animated videos to measure infant looking time may increase “attentional inertia”, such that some infants demonstrate longer looking times to television-based programming regardless of attentional capacity.<sup>77</sup> This potential source of noise in video-based measures of looking time highlights an additional benefit of using multiple indicators of attention in a structural equation modeling

framework that accounts for measurement error. Moreover, while assessing attention using standardized tasks facilitates comparisons with existing literature, alternative operationalizations of infant attention that are grounded in the context of the dyadic mother–infant relationship may be more relevant for understanding infant neurodevelopment. For example, recent work proposes that measuring infant orienting responses to socioemotional stimuli<sup>78</sup> or mutual gaze between the mother and infant<sup>79</sup> may be relevant behavioral outputs of infants’ physiological attention and approach systems.

We also relied on maternal report when defining COVID-19 exposure groups and did not have medical records of illness severity. Future work using direct biological markers of maternal infection is needed to confirm these findings and probe the biological factors that may contribute to these effects. In addition, future studies should consider the biological and experiential factors that may buffer maternal psychosocial stress, particularly in the context of stressful life events such as the COVID-19 pandemic. For instance, prior work indicates that anti-inflammatory hormones such as oxytocin, which is involved in regulating childbirth and social bonding<sup>80, 81</sup>, could buffer against adverse downstream impacts of stress or prenatal infection on infant outcomes. Finally, it is important to note that our findings are drawn from infants predominately from families with higher socioeconomic backgrounds in a single geographic region. Future empirical and epidemiological studies are needed to replicate these findings and evaluate long-term outcomes, particularly amongst more socio-demographically diverse samples of families.

In sum, here we find evidence for interactions between prenatal psychosocial stress and maternal COVID-19 infection in predicting individual differences in infant attention, with potential consequences for subsequent socioemotional development. A strength of our study is the use of multiple indices of infant attention that may otherwise be obscured when using single coarse measures of attentional processing, such as measures based solely on caregiver report. In addition, our approach draws both on the ecological validity of caregiver observations across a variety of environments combined with experimental measures of attention that provide a quantitative snapshot of variation in infant response to controlled stimuli. Taken together, these findings may suggest that there are phenotypic adaptations in attention development in infants of mothers most significantly impacted by the COVID-19 pandemic, and highlight the importance of considering individual differences in modulating neurodevelopmental trajectories.

## DATA AVAILABILITY

The data analyzed in the current study are available from the corresponding author upon reasonable request.

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## AUTHOR CONTRIBUTIONS

D.M.W., C.L.H., M.E.T. and N.H.B. conceptualized the study questions. D.M.W. analyzed the data and wrote the manuscript with input from C.L.H., N.H.B. and M.E.T. A.M.H. and M.Z. collected and coded data. D.M.W., C.L.H. and M.E.T. revised the manuscript.

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## COMPETING INTERESTS

The authors declare no competing interests.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Institutional Review Board at NYU Langone Health approved all study protocols, and informed written consent was obtained electronically prior to testing. Each participant provided informed consent prior to participation.

## ADDITIONAL INFORMATION

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