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# Association between Hyperemesis Gravidarum in pregnancy on postnatal ability of infants to attend to a play task with their mother

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ABSTRACT

Research indicates a higher prevalence of attention deficits in children exposed to HG in utero compared to controls with some claiming that the deficit is due to prenatal effects of malnutrition in HG mothers and others that it is due to maternal mental health after birth. The current study examines the effect of hyperemesis gravidarum (HG) diagnosis during pregnancy on infant attention controlling for maternal stress, depression anxiety and attachment. Thirty-eight infants mean age 4 months were videotaped with their mothers (19 mothers with a hyperemesis diagnosis and 19 controls) during play with a soft toy and looking at a picture book. Infant attention was operationalized as gaze direction towards the play activity, mother, and 'distracted' (indicated by looking away from play or mother). Mothers completed stress, depression, anxiety, and attachment questionnaires. HG exposed infants attended for significantly less time during play with a book or soft toy compared to controls. Maternal stress, depression, anxiety, and attachment did not differ in HG mothers and controls. Infant ability to attend to the toy, book, mother or being distracted did not relate to maternal postnatal attachment, or mental health. These results suggest that the prenatal environment, especially exposure to HG might be associated with reduced infant attention abilities independent of maternal postnatal health.

## 1. Introduction

Hyperemesis gravidarum (HG) defined as severe, prolonged, and persistent vomiting leading to dehydration (Goodwin, 2008) is a primary cause for hospital admission during pregnancy and affects 1.5% of UK (United Kingdom) women and 1.1% worldwide (Fiaschi, Nelson-Piercy, & Tata, 2016; Einarson, Piwko, & Koren, 2013). Research indicates that HG can result in fetal compromised development including Wernicke's encephalopathy (Oudman et al. 2019), pre-renal dysfunction (Hussein & Lafayette, 2014), pre-eclampsia and thromboembolism (Fiaschi, Nelson-Piercy, Gibson, Szatkowski, & Tata, 2018), low birth weight (Fejzo et al., 2009, 2013), and needing neonatal intensive care treatment (Fiaschi et al. 2018).

Apart from the physical health risks identified, HG experiences can affect maternal psychological health (Simpson et al. 2001) including suicidal thoughts and depression (Poursharif et al., 2008; Glover, Bergman & O'Connor, 2008) and anxiety (King, Chambers,

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& O'Donnell, 2010; Glover, Bergman, & O'Connor, 2008, Glover, 2011; O'Connor et al., 2022) and can be long lasting with women reporting acute stress and post-traumatic stress symptoms 12 months after birth (Meltzer-Brody et al. 2017; Kjeldgaard et al. 2019). These long-term effects of maternal anxiety, depression and stress during pregnancy are seen in their offspring's later psychopathology (Glover, O'Donnell, & Fisher, 2018).

Regarding the effects of HG specifically, in addition to medical issues, maternal reports of 12-year-old children suggest higher prevalence of developmental issues, including attention deficits, in HG exposed children compared with controls at 12 years (Fejzo, Kam, Laguna, MacGibbon, & Mullin, 2019). Wang et al. (2020) assessed not only cognitive and psychiatric problems in offspring at 9–11 years but also brain morphology, and they found significant effects of HG in all measures. Research on effects of HG in infancy using maternal reports indicates temperamental differences between HG exposed and control infants (Mullin et al. 2012). Identification of attention deficits at an earlier age can aid our understanding of the prognosis of outcomes because attention and task persistence during infancy are good predictors of later developmental outcome (Lucca & Sommerville, 2018). The current study was designed to test infant attentional abilities in relation to HG exposure using behavioural methods.

The effects of HG on negative neurodevelopmental outcomes in children are unclear. One hypothesis relates to brain function development depending on micronutrients such as Thiamine (e.g., Prado et al., 2018; Reissland, et al. 2020) which are lacking in mothers with HG affecting development from conception. (For a review see Nijsten, et al. 2022). Both prenatal and postnatal effects have been attributed to hyperemesis (Fejzo, et al. 2019). Although micronutrients have been implicated, macronutrients are also essential for healthy fetal and infant development (Persson, 2017; Austin,Wilson, & Saha 2019). Additionally, research has found that HG can result in severe weight loss and malnutrition, and these factors have been linked to cognitive deficits and restricted fetal brain development (Koren, Ornoy, & Berkovitch, 2018). Furthermore, previous research has demonstrated that maternal stress in pregnancy affects fetal movement profiles reflecting variations in neurodevelopment (Reissland, Aydin, Francis, & Exley, 2015) and alteration of hypothalamic–pituitary–adrenal axis development (Lanzski, Shea & Steiner, 2008). Although research so far has indicated that prenatal stress and depression affect postnatal health outcomes (e.g. Glover et al., 2008; O'Connor et al., 2022) and it is indicated that prenatal HG has an effect of fetal movement profiles at 32 weeks gestation controlling for stress, depression and anxiety (Reissland et al. 2020), it is unclear whether negative cognitive outcomes are due to the impact of HG in pregnancy or maternal postnatal mental health on child attention abilities.

The current study tested the effects of HG exposure on infant attention abilities controlling for maternal postnatal stress, depression, anxiety, and attachment difficulties. We expected infants in the HG group would be less attentive during play with two toys and show more distraction by disengaging with the tasks compared to infants not exposed to HG rather than maternal mental health factors.

## 2. Material and methods

### *2.1. Participants*

Nineteen mothers who had been diagnosed with HG and 19 control mother-infant dyads were recruited from across the UK. Infants were aged between 1.2 and 7.1 months at time of testing ($M = 3.95$, $SD = 1.51$).

Inclusion criteria for the HG group included women having received a medical diagnosis of HG during their pregnancy and having lost > 5% of their pre-pregnancy body weight during the first trimester (Goodwin, 1998). All HG women had symptoms severe enough to need medical treatment. Matched controls were recruited based on having infants of the same age, living in the same area as the experimental group and having experienced little or no sickness during their pregnancy. All mothers were over 18 years old and healthy.

### *2.2. Procedure*

#### *2.2.1. Ethics*

Participants were recruited for this cross-sectional observational study via social media and baby groups. After explaining the procedure and ethical practices informed consent was obtained. This study was conducted in accordance with the Declaration of Helsinki. Ethical permission for this study was granted (PGT2018-NNR21 2019–02–28.docx).

#### *2.2.2. Data collection*

Infants sat in a bouncer or chair opposite their mother so that her face was always visible to the infant. A video camera was directed towards participants placed approximately 1 m away. In the semi-structured play paradigm mothers and their infants were recorded for offline analysis for 10 min while performing two different tasks. The video recordings were coded second by second for gaze direction at mother, toys or other. Participants first completed a reading task which involved mothers reading a book to their infant (*That's not my chick…*, Watt, 2018) 'how they usually would' for 5 min. In the unstructured toy-play condition the mother and infant interacted with a soft toy dog for a further 5 min. Mothers were reminded they could stop procedure at any time. "Toy" is used here when infants were looking at the book or the soft toy (whatever was used by the mother for play).

Gaze direction was coded as this develops early in infancy and remains stable across the first three years of life (Farran, Hirschbiel, & Jay, 1980). Coding was done on videos with superimposed time stamps. The video recordings varied in length because of the quality of the videos. Thus, seconds spent looking at toys (book/soft toy), mother, and distracted (looking away from the toy/ mother) were calculated in terms of duration of gaze direction divided by time of the length of the videotaped observation. Percentage of time infants spent looking anywhere other than directly at the toys or their mother was defined as distraction, an indication of infant attention skills (Richards & Casey, 1992). For one HG pair, eye gaze direction of infant could not be ascertained as despite being awake the infant's eyes appeared shut during the task. A second rater confirmed data could not be analysed for this participant. Reliability of child looking direction coding was assessed using Cohen's Kappa (κ). 10% of video footage was assessed independently by a second coder blind to the hypothesis. Cohen's Kappa classification indicates substantial agreement, $\kappa = .728$, $p < .001$.

#### 2.2.3. Maternal stress

Postnatal stress was assessed using the Perceived Stress Scale (PSS-10; Cohen, Kamarck, & Mermelstein, 1994), a 10-item scale assessing feelings of general stress over the last month. It has moderate criterion validity and good internal consistency (Lee, 2012).

#### 2.2.4. Attachment

The Maternal Postnatal Attachment Scale (Condon, 2015) is a 19-item scale assessing mother-to-infant attachment. It has good levels of test-retest reliability and internal consistency (Condon & Corkindale, 1998). Scores range from 19 to 95 whereby higher scores indicate stronger feelings of attachment.

#### 2.2.5. Maternal depression

Mothers also completed the Edinburgh Postnatal Depression Scale (EPDS; Cox, Holden, & Sagovsky, 1987), a 10-item self-report scale designed to screen for postnatal depression. The scale has high sensitivity across clinical and general populations (Eberhard-Gran, Eskild, Tambs, Opjordsmoen, & Ove Samuelsen, 2001). It also has good construct validity and internal reliability (Small, Lumley, Yelland, & Brown, 2007).

#### 2.2.6. Maternal anxiety

Mothers completed the anxiety scale of the validated and reliable Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) to ascertain their anxiety levels. A score of 0–7 is in the normal range, with a score of 11 or higher indicating probable presence of an anxiety disorder, and a score of 8–10 suggesting the presence of anxiety.

## 3. Results

### 3.1. Demographics

No significant group differences were identified (see Table 1). Infant age was not significantly different across experimental and control groups ($t = 0.67$, $p = 0.506$). More male than female infants participated, however, this was similar for both groups ($X^2 = 0$, $p = 1.000$).

### 3.2. Reading picture book and soft toy-play conditions

Percentage time infant spent looking at toys, mother or distracted were calculated for both reading and soft toy-play conditions. While infants show a heterogeneous pattern of looking times across play conditions, the time spent with looking at their mothers is similar across groups and short in most cases (Fig. 1).

### 3.3. Looking time differences

Independent samples t-tests were conducted to identify group differences for infant percentage looking times. Infants of control

**Table 1**
Demographic variables for HG and Control groups.

| | HG number | Control number | Chi Square | *p* values |
|---|---|---|---|---|
| Sample | 19 | 19 | | |
| Married/cohabiting | 19 | 17 | 2.11 | $p = .146$, ns |
| single | | 2 | | |
| Child gender | 11 | 12 | 0.11 | $p = .739$, ns |
| Male | 8 | 7 | | |
| Female | | | | |
| GCSE | 2 | 2 | 1.07 | $p = .782$, ns |
| A Level | 4 | 3 | | |
| Degree level | 7 | 5 | | |
| Postgraduate | 6 | 9 | | |
| | HG (mean) | Control (mean) | *t*-test | *p* values |
| Maternal age (years) | 31.94 | 31.31 | .34 | $p = .730$, ns |
| Infant age (months) | 3.82 | 4.11 | .58 | $p = .560$, ns |
| Number of children | 1.66 | 1.42 | 1.08 | $p = 2.860$, ns |

ns= non significant.

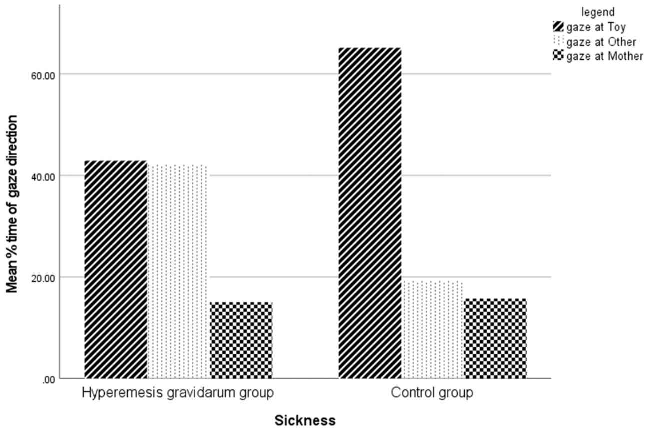


**Fig. 1.** Mean percentage of gaze direction by infants of mothers with HG and controls.

group mothers spent significantly more time looking at the toy during the observation period ($M = 66.01\%$, $SD = 14.93$) compared with HG exposed infants ($M = 43.20\%$, $SD = 19.07$, $t = 4.04$, $p < .001$). Infants exposed in utero to HG instead spent more time distracted ($M = 40.78\%$, $SD = 16.93$) in comparison to control infants ($M = 19.17\%$, $SD = 12.24$, $t = 4.43$, $p < .001$). In contrast, infants in both groups spent similar amounts of time looking at their mothers ($p > .500$). As percentage time distracted is of particular interest to our research objectives, distraction data is the focus of further analyses (see Fig. 1).

### 3.4. Maternal mental health and infant distraction

An independent samples t-test indicates HG mothers did not score significantly higher on the PSS-10 ($M = 15.0$, $SD = 7.54$) than control mothers ($M = 11.16$, $SD = 4.00$, $t = 1.96$, $p = .060$). HG mothers and controls did not show any differences in terms of depression (HG: $M = 8.05$, $SD = 4.98$; Control: $M = 6.89$, $SD = 4.85$, $t = -0.73$, $p = 0.473$) or anxiety (HG: $M = 7.21$, $SD = 4.25$; Control: $M = 6.05$, $SD = 3.14$, $t = 0.96$, $p = 0.346$), and both groups scored similarly on the Maternal Postnatal Attachment Scale (HG: $M = 82.48$, $SD = 6.53$; Control: $M = 82.79$, $SD = 5.65$, $t = 0.16$, $p = 0.876$).

Mental health scales were strongly correlated between each other ($p < .001$) but did not show any correlation with the percentage of distracted looking time when using $p < .05$ as the cut-off for significance (see Table 2).

### 3.5. Covariate effects on looking time proportions

The effects of HG on the different gaze categories are summarized in Table 3. This table gives the t- and p-values of the coefficient of HG from logistic regression models for looking times at Toy, Mother, and Distracted (Other). Each cell of the table corresponds to a fitted logistic regression model, with the response variable given by the relative looking time to the configuration described in the row and column headings of the table and all variables in Table 1 as covariates. The first row gives the results when considering data arising from either of the toys, the second row gives the results when considering book only, and the final row when considering play with the soft toy only. Positive t-values correspond to positive effects of HG; for instance, the value $t = 3.537$ in the "Book only/Other" cell means that, when considering the book only, looking time into a distracted direction increased significantly ($p = 0.002$) for HG mothers.

In sum, (1) Infants of mothers who experienced HG spent less time looking at both toys ($p = 0.003$ across both toys, $p = 0.008$ when using book only, $p = 0.024$ for soft toy only; see t-values in Table 3) and tended to be distracted more ($p = 0.002$ across both toys, $p = 0.002$ when using book only, $p = 0.037$ for soft toy only) compared to infants whose mothers did not experience HG.

(2) The HG status of the mother only related to reduced attention paid to the toy and being distracted; it did not change the amount of attention given to the mother ($p = .573$ across both toys, $p = 0.736$ when using book only, $p = 0.493$ for soft toy only).

(3) The attention given to the mother appears to be influenced by infant age, in that younger infants in the group tend to look more at the mother. This significant effect has been observed across both toys ($t = -2.42$, $p = 0.0024$) and when using a book ($t = -2.708$, $p = 0.013$), but not when using a soft toy ($t = -1.52$, $p = 0.144$). Furthermore, Participant age has a significantly positive effect on

**Table 2**
Matrix of Pearson correlation coefficients between percentage time distracted and the mental health scores.

| | Distracted | Depression | Anxiety | Stress |
|---|---|---|---|---|
| Distracted | 1.00 | | | |
| Depression | 0.24 ($p = 0.150$) | 1.00 | | |
| Anxiety | 0.21 ($p = 0.210$) | 0.81 ($p < 0.001$) | 1.00 | |
| Stress | 0.30 ($p = 0.070$) | 0.79 ($p < 0.001$) | 0.82 ($p < 0.001$) | 1.00 |

**Table 3**
The p- and t-values for the effect HG on three gaze directions, considering both toys, book only, and soft toy only.

| Gaze to | Toy | Mother | Other |
|---|---|---|---|
| Both toys | $t = -3.36$<br>$p = 0.003$ | $t = -0.57$<br>$p = 0.573$ | $t = 3.55$<br>$p = 0.002$ |
| Book only | $t = -2.88$<br>$p = 0.008$ | $t = 0.34$<br>$p = 0.736$ | $t = 3.54$<br>$p = 0.002$ |
| Soft Toy only | $t = -2.41$<br>$p = 0.024$ | $t = -0.70$<br>$p = 0.493$ | $t = 2.22$<br>$p = 0.037$ |

Negative signs of the t-value mean that HG is associated with reduced looking time for this direction and toy configuration.

looking times to the toy when a soft toy is used ($t = 2.45$, $p = 0.022$). All other effects, over all nine fitted models and all involved covariates, were insignificant, and hence no explicit table is provided for these.

(4) Stress, Depression, Attachment, and Anxiety, as well as mother's education level, never played any role ($p > .05$) in terms of the attention given to either toy, mother, or distracted, irrespectively of the type of toy used.

## 4. Discussion

Overall, infants in the HG groups showed more distracted attention by looking away from the toys compared to control pregnancies. This pattern held above and beyond possible differences. Our results indicate that infants born to mothers who experienced HG displayed increased distraction across both play conditions but especially the reading-play condition. Given that joint attention during toy play but specifically during book reading fosters both language and socioemotional outcomes (O'Farrelly, Doyle, Victory, & Palamaro-Munsell, 2018), infants not attending to the play with the book might have a longer-term effect.

The findings of the current study that infants exposed to HG have attention difficulties is supported in the literature. Nulman, Maltepe, and Farine (2015) reported that children assessed with the Wechsler Intelligence scale showed deficits in several domains including verbal abilities and full-scale IQ (Intelligence Quotient). Large-scale survey data has shown a 3.28-fold increase in risk of a HG women's child having neurodevelopmental problems such as attention deficits in comparison to control groups at 8 years old (Fejzo, Magtira, Schoenberg, Macgibbon, & Mullin, 2015) and a 3 times fold increase at 12 years (Fejzo, et al. 2019). Behavioural disorders in HG exposed individuals have also been evidenced as significantly higher than control groups through to adulthood (Mullin et al. 2011). Identification of attention deficits during infancy can help to increase targeted intervention. Use of preventive action such as parent training can help reduce child attention deficits if administered early in childhood (Siegenthaler-Hierro, Presentación-Herrero, Colomer-Diago & Miranda-Casas, 2013). Thus, implementing postnatal support to mothers on training their infant's attention skills may be useful in preventing negative outcomes.

Hypothesised pathways of how HG may impact long-term infant outcomes include postnatal maternal difficulties and prenatal effect on fetal development (Fejzo, et al. 2019, Mullin et al. 2011). Current findings indicate that postnatal attachment issues are unlikely the cause of infant attention problems which is supported by Garvin (2019) reporting that mothers with HG were not less attached to their children post birth than mothers with healthy pregnancies. Furthermore, postnatal stress was similar in both groups and taken together with the findings of results of the effects on the fetus of maternal stress during pregnancy compared to HG effects (Reissland et al. 2020) our findings support the claim that child attention outcomes are at least in part due to impact of HG on fetal neurodevelopment. In support, timing of sickness during pregnancy has been related to severity of outcomes (Martin, Wisenbaker, & Huttunen, 1999). Starvation may lead to numerous shortages of nutritional elements necessary for fetal brain development (Eric, 2017). An interesting and not yet tested speculation could relate to the ideas proposed by Haig (1993) in terms of epigenetic modifications in the fetus because of maternal effort to preserve her own health. This speculation has been tested in terms of nutrition by Ayyavoo et al. (2013) who reported that altered maternal nutrition during pregnancy in mothers with HG had long-term effects on offspring metabolism. In the present study, both HG and control group mothers showed similar levels of stress, depression, anxiety and attachment, indicating that postnatal maternal mental health was unlikely the cause of long-term attention deficits in children exposed to HG. Instead, our results support the assertion by Fejzo et al. (2019), and Mullin et al. (2011) that HG might have an impact on fetal brain development which affects their cognitive functioning after birth.

There are potentially important implications of this research given that attention abilities are essential for cognitive development and have long term effects (e.g., Galler et al. 2012). Our findings indicate that more research is needed to examine how early interventions might prevent long-term attention problems. Additionally, determination of optimal care during pregnancy is necessary until better understanding of HG aetiology is achieved. Thus, our results have important implications for maternal experiences as well as infant life-long outcome.

In the current study we assessed infant reactions which indicated that infants in both groups looked at their mothers with equal frequency arguably indicating that mothers behaved similarly in both groups. This interpretation is arguably supported by previous research which showed that mothers vary their pitch of voice depending on infant gaze direction in a play situation (e.g. Reissland & Shepherd, 2001). Hence, future research needs to test not only maternal mental health, attachment status and infant reactions to their mothers but also potential other more subtle variables, not observed in the current set up, which might discriminate between mothers with and without HG. Additionally, as with most of HG research the current sample has poor ethnic diversity. 97% of the participants were Caucasian limiting generalisability of findings. This is especially important as being Black or Asian is associated with increased risk of HG related hospital admission and extreme weight loss (Fiaschi, et al. 2016). Future research should increase ethnic diversity to ensure findings inform treatment of all HG women and their babies.

Although we did not measure prenatal stress, anxiety and depression that the effects are at least in part due to HG is supported by a study ( Reissland et al. 2020) which examined a group of fetal movement profiles at 32 weeks and found that after adjusting for stress, anxiety, and depression, the movement rate for the fetuses of mothers who experienced HG was significantly larger for the HG group compared with the control group Hence our results are likely affected by HG status over and above the effects of maternal psychological state. Mothers in both groups showed comparable results in terms of postnatal depression, stress, anxiety and attachment and hence postnatal effects cannot explain the current findings.

## 5. Conclusion

Current findings show that HG exposed infants display attention deficits across play tasks in comparison to controls. Specifically, a lack of gaze avoidance by infants of mothers in the HG group indicates that attachment problems are unlikely (Esser et al. 1996). Furthermore, lack of attention to the toys appears unrelated to maternal postnatal mental health refuting the hypothesis that maternal postnatal mental health of mothers who had suffered from HG during their pregnancy causes long-term attention difficulties in children. Instead, we argue that in utero effects of HG on fetal brain development may account for negative outcome in the offspring. Future research needs to test whether early infant intervention can prevent long-term negative outcomes.

## Ethical Statement

Ethical permission for this study was granted from Durham University, United Kingdom (PGT2018-NNR21 2019–02–28.docx).

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No funding was provided for the current project.

## CRediT authorship contribution statement

**Jennifer A. Matthewson**: Conceptualization, Methodology, Investigation, Project administration, Data curation, – original draft. **Nadja Reissland**: Conceptualization, Methodology, Writing, Supervision, Writing – review & editing, Revision. **Jochen Einbeck**: Statistical analysis.

## Conflict of interest

The authors report no conflict of interest.

## Data availability

The authors do not have permission to share data.

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*Data statement*

We do not have permission to share the data.

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