Research report

Do early-life eating habits predict later autistic traits? Results from a population-based study

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**ABSTRACT**

Eating problems are common among children with Autism Spectrum Disorder (ASD), but it is unknown to what extent infant eating behavior is associated with later autistic traits. As eating behavior is currently not included in ASD screening instruments, it is important to evaluate whether infant eating behavior predicts later autistic traits and might therefore be used to enhance the early detection of ASD. We investigated the association of breastfeeding and eating behavior during infancy with later autistic traits in the population-based Generation R cohort. We included 3546 mother-child dyads with maternal reports on feeding and eating at age two months and autistic traits at six years. Eating behavior was assessed with seven items on specific eating habits and the Social Responsiveness Scale was used to evaluate autistic traits. Covariates included child sex, and maternal psychopathology and autistic traits. Linear regression analyses showed that being formula fed at two months was associated with a higher autistic trait score at six years (adjusted B = 0.07; 95% CI: 0.00-0.14). Children who were drinking only small quantities (adjusted B = 0.17, 95% CI: 0.04-0.30) and were hungry/not satisfied (adjusted B = 0.23, 95% CI: 0.08-0.39) at age two months also had a higher autistic traits score at age six years. We found no interactions with sex or breastfeeding. This study shows that eating behavior during infancy is related with autistic traits in childhood. Although the associations were fairly small, these findings suggest that early-life eating problems might be relevant for early detection of ASD and a potential addition to ASD-specific screening instruments.

1. Introduction

Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder that is present from early life onwards. It is characterized by persistent deficiencies in communication and social interaction, and restricted, repetitive patterns of behaviors, interests and activities. Although several symptoms are already present in the early developmental period, some symptoms manifest itself only later in life (American Psychiatric Association, 2013). ASD can be reliably diagnosed as young as 24 months (Johnsson & Myers, 2007), but the current mean age at diagnosis ranges from 38 to 120 months (Daniels & Mandell, 2014). There is an urgency to identifying children with ASD, as particularly early interventions can improve language and cognitive abilities (Dawson & Burner, 2011) and result in better long-term outcomes across the school age years (Clark et al., 2018) compared to interventions at a later stage. Detection of the earliest signs of ASD can enhance timely identification and diagnosis, which then permits early treatment to achieve the most optimal long-term outcomes for children with ASD.

There are several widely used instruments available for ASD screening. The Modified Checklist for Autism in Toddlers (M-CHAT(R)/

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study (Fig. 1). We excluded children with missing data on eating behavior (n = 1779) or breastfeeding (n = 69) at two months and those without information on autistic traits at 6 years (n = 1231). This resulted in a study sample of 3546 mother-child dyads.

2.3. Measures

2.3.1. Breastfeeding

Information about feeding mode was obtained by a maternal postal questionnaire when children were two months old. We assessed if infants were breastfed (yes/no) and whether they received breastfeeding only, a combination of breast- and formula feeding, or formula feeding only at the time the questionnaire was filled out.

2.3.2. Eating behavior

Eating behavior at age two months was assessed in the same maternal questionnaire using seven single items related to eating and feeding difficulties. These assessed relatively common difficulties and behavior, and were partly based on previous studies that also used single items on infant feeding (Micali et al., 2009; Wolke et al., 1994). Parents (mostly mothers, 93.7%) responded; they were asked if their infant exhibited one or more of the following feeding habits: ‘Drinks slowly’, ‘Drinks only small quantities’, ‘Drinks very greedily’, ‘Is hungry or not satisfied’, ‘Spits up a lot,’ Regurgitates mouthfuls of food’ and ‘Refuses breastfeeding’. Response options were Yes or No.

2.3.3. Autistic traits

Autistic traits were assessed using maternal reports of the validated Social Responsiveness Scale (SRS) (Constantino, 2002) when children were six years old. The SRS is an autism screening questionnaire providing a quantitative measure of (sub)clinical autistic traits related to social cognition and communication. The psychometric properties are...
good, including a test-retest reliability of 0.88 and a two-year stability correlation of 0.83 (Constantino et al., 2003). The original questionnaire was reduced to an 18-item shortened SRS to minimize subject burden, with selected items encompassing all DSM-IV autism domains. The shortening was done in consultation with the SRS test developer, as described previously (Román et al., 2013). Our SRS short form consists of the Social Cognition (5 items), Social Communication (8 items) and Mannerism (5 items) subscales. Items assessed traits in the past three months and were scored on a 4-point scale (not true, sometimes true, often true, almost always true). The 18-item shortened SRS shows high rates of 70–80% (Hampton & Strand, 2015).

To identify children with an ASD diagnosis, we examined medical records using a multifaceted screening procedure (White et al., 2019). First, cut-off scores for the SRS were used to identify children with elevated ASD traits. Second, to rule out false-positives, children scoring in the top 15% of the total score of the Child Behavior Checklist (CBCL/1–5) (Achenbach & Rescorla, 2001) at age six years were then screened using the 40-item Social Communication Questionnaire (SCQ), as reported by a parent (Berument et al., 1999). Additionally, psychiatric diagnoses and treatment were routinely assessed at all contact moments between ages 6–9 years (health center visits and questionnaires). If children scored positive in one or more of these three information sources, the medical records at their general practitioners were examined. If an ASD diagnosis was confirmed through the medical records, the child was considered to be a clinically confirmed case of ASD.

2.3.4. Covariates

We included several child and family covariates based on previous studies (Blanken et al., 2015; Cardona Cano et al., 2016; Jansen et al., 2012). Information about sex, birth weight and gestational age at birth was obtained from midwife- and hospital registries. Maternal age, educational level and ethnicity were obtained by postal questionnaire. We used the Brief Symptom Inventory (BSI) to assess maternal psychopathology during pregnancy. The BSI is a validated 53-item self-reported questionnaire assessing diverse psychiatric problems (Derogatis & Melisaratos, 1983). We also used the Autism-Spectrum Quotient (AQ-short) to assess maternal autistic traits. Although this questionnaire was distributed when the children were 9 years old, we assumed that maternal autistic traits were fairly stable across adulthood. The AQ-short is a 28-item self-report assessing autistic traits on the scales ‘social behavioral difficulties’ and ‘fascination for numbers/patterns’, which sum into a total score (minimum = 28, maximum = 112). A cut-off score of >65 is suggested for a quick screening of autistic traits in a clinical setting (Hoekstra et al., 2011).

2.4. Statistical analyses

First, separate linear regressions were conducted to evaluate the relationship between breastfeeding at two months and autistic traits at six years. Three models were evaluated: model 1 was an unadjusted model, model 2 included the covariates maternal age, education and psychopathology, and model 3 additionally included measures of maternal autistic traits. Only covariates that altered the unadjusted beta by more than 10% were included in model 2. Maternal autistic traits were included to demonstrate the possible influence of a familial predisposition for ASD. We also tested sex interactions and finally evaluated the association between breastfeeding at two months and clinically confirmed ASD diagnosis by logistic regression.

In a second set of analyses, linear regressions were conducted to evaluate the relationship between eating behavior at two months and autistic traits in six years, with separate regressions for each type of eating behavior. The same three adjusted and unadjusted models were evaluated for each eating behavior, using a similar method to that described above. We tested for possible interactions of sex with eating behavior, as well as for breastfeeding with eating behavior.

We estimated missing values on confounders (ranging from 0% missing for sex to 32.1% for maternal autistic traits) using multiple imputation techniques. All variables included in the analyses were used to estimate the missing values (Graham, 2009). Regressions were conducted on the imputed data and reported estimates are the pooled results of 30 imputed datasets. All statistical analyses were performed with SPSS 21.

3. Results

3.1. Non-response analyses

We compared the characteristics of participating mother-child dyads (n = 3546) with those excluded from the study due to missing data on determinants or outcome (n = 3079). Data were more often missing in mothers who were younger, had a lower education level, were of non-Dutch ethnicity, and who had higher psychopathology and autistic traits scores (all p-values <.01). Excluded children had a lower birth weight, were more often boys, and more often received no breastfeeding than included children (all p-values <.01).

3.2. Sample characteristics

Child and maternal characteristics of the study sample are presented in Table 1. In total, 51.0% of children were girls and 68.8% received

| Table 1 | General characteristics of parent-child dyads from Generation R cohort (n = 3546). |
|---------|-------------------------------------------------------------------------------------|
|         | Percentage or median^ | % missing |
| Child characteristics | | |
| Sex | | 0.0 |
| Girl, % | 51.0 | |
| Age at assessment (months) | 2.8 (0.4–6.0) | 7.4 |
| Social Responsiveness Scale | 71.8 (58.7–106.8) | 0.0 |
| Gestational age at birth | 40.1 (27.1–43.4) | 0.0 |
| Birth weight (grams) | 3480 (780–5610) | 0.0 |
| Breastfeeding at 2 months | 68.0 | 0.0 |
| Yes, % | | |
| Breastfeeding type at 2 months | | |
| Breastfeeding only, % | 41.2 | |
| Breastfeeding & formula feeding, % | 27.7 | |
| Formula feeding only, % | | |
| Eating behavior at 2 months | | |
| Drinks slowly, % | 13.9 | |
| Drinks only small quantities, % | 6.0 | |
| Drinks very greedily, % | 39.1 | |
| Is hungry or not satisfied, % | 3.9 | |
| Spits up a lot, % | 12.2 | |
| Regurgitates mouthfuls of feed, % | 32.0 | |
| Refuses to breastfeed, % | 1.7 | |
| Autistic traits at 6 years | 0.2 (0.0–2.5) | 0.0 |
| Maternal characteristics | | |
| Age at intake (years) | 31.9 (15.3–45.4) | 0.0 |
| Ethnicity | | 0.2 |
| Dutch, % | 68.0 | |
| Other, % | 31.9 | |
| Education | | 2.7 |
| Higher vocational education/ university, % | 59.5 | |
| Lower vocational education, % | 26.0 | |
| Less than high school, % | 11.8 | |
| Psychopathy score | 0.0 (0.0–2.7) | 15.9 |
| Autism traits score | 50.0 (28.0–84.0) | 32.1 |

^ Values are percentages for categorical variables and medians (range) for continuous non-normally distributed variables.
breastfeeding at two months. More than two-thirds (68.0%) of the mothers had a Dutch background. The study sample included 50 children (1.4%) who had a GP-confirmed diagnosis of ASD. Of the mothers, 5.9% showed elevated levels of autistic traits (AQ-short score >65).

3.3. Prospective relationship between breastfeeding and autistic traits

Table 2 shows that receiving formula feeding at two months was associated with a higher autistic traits score at six years (confounder adjusted $B = 0.07; 95\% CI: 0.00 to 0.14$) than when receiving breastfeeding. Particularly receiving only formula feeding was associated with a higher autistic traits score at six years (confounder adjusted $B = 0.08; 95\% CI: 0.00 to 0.15$), while receiving mixed formula and breastfeeding was not significantly associated with autistic traits score. Adjustment for maternal age, education and psychopathology led to a change in the association between breastfeeding and autistic traits of more than 10%, while the additional inclusion of maternal autistic traits in the model did not notably affect this association. We found no interactions of breast-feeding and sex on autistic traits.

Sensitivity analyses showed that children who were breastfed at two months did not differ in their odds of a later ASD diagnosis, compared with children who were not breastfed ($OR = 0.81; 95\% CI: 0.44 to 1.48$, $p = .50$).

3.4. Prospective relationship between eating behavior and autistic traits

Table 3 indicates that infants who drank only small quantities at two months had a higher autistic traits score at six years (confounder adjusted $B = 0.17; 95\% CI: 0.04 to 0.30$) compared to infants who did not drink small quantities. Results further show that the infant eating behavior ‘being hungry or not being satisfied’ at two months was associated with later autistic traits (confounder adjusted $B = 0.23; 95\% CI: 0.08 to 0.39$). The inclusion of maternal autistic traits in the models did not notably affect the association between infant eating behavior and later autistic traits. The other eating behaviors were not associated with later autistic traits. No interaction of sex or breastfeeding with eating behavior was found.

4. Discussion

This study—in a general population sample—shows that infants who were formula fed, drank only small quantities, or who were often hungry or not satisfied at the age of two months had a higher autistic traits score in childhood at age 6 years.

Table 2
Prospective association between breastfeeding and child autistic traits ($n = 3546$).

|                          | B for SRS total score at six years (95% CI) |
|--------------------------|--------------------------------------------|
|                          | Model 1 | Model 2 | Model 3 |
| Breastfeeding at 2 months |          |          |         |
| (reference response = yes) | 0.15 (0.02; 0.22)** | 0.07 (0.00; 0.14)* | 0.07 (0.00; 0.14)* |
| Type of feeding at 2 months |          |          |         |
| Breastfeeding only      |          |          |         |
| Breastfeeding formula & feeding |          |          |         |
| Reference               | 0.05 (–0.02; 0.03) | 0.02 (–0.05; 0.02) |          |
| Reference               | 0.13 | 0.10 | 0.09 |
| Formula feeding only   |          |          |         |
| Reference               | 0.17 (0.10; 0.24)** | 0.08 (0.01; 0.16)* | 0.08 (0.00; 0.15)** |

Model 1: unadjusted.
Model 2: adjusted for maternal age, education and psychopathology.
Model 3: adjusted for maternal age, education, psychopathology and autistic traits.

Note: We found no significant interaction with sex.

4.1. Breastfeeding

Our results on breastfeeding are in line with previous studies suggesting a negative association between breastfeeding and later ASD (Tseng et al., 2019). Our study contributes to the clinical findings that breastfeeding is associated with a lower degree of autistic traits at a subclinical level in a large general population sample. Although in our subgroup of children with an ASD diagnosis the association pointed in the same direction, caution is needed in drawing firm conclusions since this result was not significant, mostly likely due to the small number of children with a clinically confirmed ASD diagnosis ($n = 50$).

Although it is often suggested that breastfeeding and ASD are causally linked, these potential causal pathways are still quite hypothetical. Genetic factors may well be implicated since autism has a strong genetic basis, as illustrated by a high concordance rate (64–91%) seen in twin studies (Tick et al., 2016). Moreover, literature indicates that other maternal factors may also play a role in the association between ASD and breastfeeding. Multiple studies indicated that general maternal psychopathology is associated with shorter breastfeeding duration (Boucher et al., 2017; Tavoulari et al., 2016). Also, the broader autism phenotype is related to elevated depressive symptomology (Ingersoll & Hambrick, 2011) and socio-affective impairment (Bertozzi et al., 2013) which can negatively affect breastfeeding duration (Falsetti et al., 2019; Henderson et al., 2003). Nonetheless, our results show that psychopathology and particularly the level of autistic traits of mothers only explain a small part of the association between breastfeeding and later autistic traits in children. This is in line with a previous study indicating that the broader autism phenotype does not fully explain the association between breastfeeding and ASD (Soke et al., 2019). We should also consider the possibility of residual confounding. For example, maternal under- and over-responsivity to sensory stimuli—which are common in people with ASD (Lai et al., 2011) and influence the duration that people with ASD (Lai et al., 2011) and influence the duration that
of breastfeeding, suggesting a reverse causal pathway. This may be due to the fact that breastfeeding provides a richer variation in oral sensory stimulation (taste) compared to formula milk (Beauchamp & Mennella, 2011), because the taste of breastmilk (e.g. bitterness) is affected by the mother’s consumption (Mastorakou et al., 2019). Also, compared to other feeding methods, breastfeeding provides more close skin-to-skin contact (Liu et al., 2013) and frequent touch by the mother (Kuzela et al., 1990) which are possibly less pleasant for children with sensory problems. Finally, a disrupted breastfeeding pattern of endless sucking in children with ASD (Lucas & Cutler, 2015) may lead to sore nipples and breastfeeding discontinuation (Ahluwalla et al., 2005; Li et al., 2008).

4.2. Eating behavior

The current study showed that specific infant eating problems—particularly drinking only small quantities and being hungry or not satisfied—were associated with a higher autistic traits score later in childhood. This is in line with our previous study across middle childhood: in that study we found that autistic traits at six years were prospectively associated with elevated levels of picky eating and food responsiveness at ten years in both boys and girls. Among girls only, autistic traits at six years were also associated with elevated levels of emotional over- and undereating at ten years (van ’t Hof et al., 2019). Our current results add to the literature that the association between eating behavior and autistic traits seems to be present even from very early infancy. It is, however, important to emphasize that, although both studies show a prospective association between eating behavior and autistic traits, based on these findings we cannot draw any conclusions on causality.

There are several possible explanations for the reported association. Drinking only small quantities and being hungry or not satisfied are both linked with appetite self-regulation. Typically developing children show good self-regulation, also in feeding (Saltzman et al., 2018), but self-regulation difficulties have been reported among children with ASD (Gomez & Baird, 2005; Jahromi, 2017). It is possible that infant eating problems are an early expression of the self-regulation difficulties typically seen in ASD.

Delays in the development of early motor skills are also often reported in children with ASD (Chinello et al., 2018) and can be related to eating behavior problems in infancy. Specific impairment in oral motor function can affect eating behavior by limited bolus control, and/or manipulation and transit of liquids and solids (Weir et al., 2007), while impairments in oral and pharyngeal sensory-motor functioning may also inhibit feeding skills (Goday et al., 2019). Finally, sensory processing deficits are another common problem in children with ASD (Leekam et al., 2007) and these have been linked to eating problems in ASD (Nadon et al., 2011).

In contrast to our previous study evaluating the association between eating behavior and autistic traits in middle childhood (van ’t Hof et al., 2019), we found no sex differences in the current study. This is most likely because sex differences were previously found solely in the association between emotional eating and autistic traits (van ’t Hof et al., 2019). Emotional eating, however, is mostly shaped by shared environmental factors rather than genetic risk (Herle et al., 2018) and develops during childhood. So, potentially emotional eating problems are not yet present in infants, and even if they were present, such eating behavior would be very difficult to assess at a very young age.

4.3. Implications

Information on eating problems in infancy can potentially be used by professionals as part of the screening for ASD in the general population. Although most early signs of ASD can only reliably be observed from age 1–2 years onwards, previous research has indicated several possible biological and behavioral markers of ASD in infancy. Research on biological markers found that early brain development (Hazlett et al., 2017) may be indicative of ASD as early as six months of age. Furthermore, infant gaze patterns (Shic et al., 2014), reduced looking time (Falck-Ytter et al., 2013), less alternating gaze during interaction with adults (Thorup et al., 2018), and a decline in eye fixation (Jones & Klin, 2013) have all been identified as early behavioral markers of ASD using eye-tracking techniques.

However, these early biological and behavioral markers require expensive and invasive brain imaging and eye-tracking techniques that cannot be easily used for widespread screening of ASD. Our current results suggest that the addition of certain eating behaviors to ASD-specific screening instruments like the M-CHAT, SCQ and the CoSoS might be helpful in providing a more complete ASD phenotype. Such addition might also enhance the validity, and with that the screening properties, of these instruments. In addition, we suggest the standardized monitoring of infant eating behavior in well-baby clinics to increase the identification of eating and feeding problems by using standardized questionnaires such as the BEBQ or by the inclusion of eating behavior items in developmental screening instruments.

4.4. Strengths and limitations

This study has several strengths. First, the large data set enabled us to assess the association between infant eating behavior and autistic traits prospectively and to control for possible confounding factors. We were also able to use validated instruments to assess child (SRS) and maternal (AQ-short) autistic traits in a general population setting, thereby optimizing validity and minimizing measurement bias. However, as infant eating behavior questionnaires, like the Baby Eating Behavior Questionnaire (BEBQ) (Llewellyn et al., 2011), were not available when the children in this study were 2 months old, we assessed a limited number of different eating behaviors using unvalidated, single items. Furthermore, we also did not assess the reasons why mothers stopped breastfeeding their child. More detailed information on eating and feeding behaviors could help us to better understand the underlying mechanisms.

Another limitation of our study was that mothers with a higher psychopathology and autistic traits score were more likely to be lost for follow-up. Considering the genetic component in ASD, children with relatively high levels of autistic traits may also have dropped out selectively. Although no data on autistic traits were available for the excluded sample, we expect the effects of drop-out to be fairly small based on results from another large cohort study (Nilsen et al., 2009). A final limitation was that although the prevalence of children in this study with an ASD diagnosis (1.4%) was comparable to the prevalence found in the United States (one in 59 children, 1.7%) (Baio et al., 2018), the number of children with a confirmed ASD diagnosis in the sample was still small, meaning we had insufficient power to detect statistically significant differences.

5. Conclusions

Our study shows that infant eating problems and the absence of breastfeeding at two months of age are associated with a higher autistic traits score in later childhood. Although the associations were fairly small, these findings suggest that efforts to detect autism at an early stage might benefit from assessing early-life eating problems, alongside other factors like social interaction deficits. We recommend complementing ASD-specific screening instruments with an assessment of early-life eating habits.

Authors’ contributions

This study was conceived and designed by MH, WE, MHJH, HH and P.J. Analyses were performed and interpreted by MH, WE and P.J. MH, WE and P.J prepared the draft manuscript with input from IO, MHJH, HH. All authors read and approved the final manuscript.
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Ethical statement

Ethics approval and consent to participate

Written informed consent was obtained from all participants. The study was approved by the Medical Ethical Committee of the Erasmus Medical Center, Rotterdam.

Declaration of competing interest

PWJ received support from ZonMW (Mental Health Care Research Program, Fellowship 636320005). The authors declare that they have no further competing interest.

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