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Role of maternal alcohol intake during pregnancy in early-life child neurodevelopment: results of the Italian PHIME cohort

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ABSTRACT

Introduction Prenatal alcohol exposure (PAE) is a well-established risk factor for adverse neurodevelopmental outcomes, particularly at high levels of consumption. The impact of low-to-moderate PAE remains unclear, with mixed results reported. This study investigates the effects of low-level PAE on neurodevelopmental outcomes at 18 months in Italian mother-child pairs enrolled in the Italian Northern Adriatic Cohort II, a part of the 'Public health impact of long-term, low-level, mixed element exposure in susceptible population strata' project PHIME.

Methods The study population consisted of 632 children, and their mothers, who were tested with the Bayley Scales of Infant and Toddler Development third edition (BSID-III) at 18 months of age. PAE, socio-demographic and lifestyle information was collected through questionnaires at different phases of follow-up. We analysed 605 children born at term (≥37 weeks) with BSID-III data and maternal pregnancy alcohol intake estimates. Multiple linear regression assessed associations between each BSID-III composite score (cognitive, motor, language) and PAE.

Results Mothers' alcohol consumption was very low. The median (25th percentile to 75th percentile) of the weekly alcohol intake of the 605 mothers was 0.3 (0–1.4) drinks and of the children's cognitive, language and motor composite score were 105 (100–110), 97 (91–103) and 100 (97–107), respectively. No significant association was found between maternal alcohol intake and BSID-III cognitive nor language scores. Only a suggestive, non-consistent, inverse association was found between PAE and motor neurodevelopment. Maternal IQ and promotion of child autonomy were directly associated with all neurodevelopmental outcomes.

Conclusion Low levels of PAE were not associated with neurodevelopmental impairment at 18 months, except for possible motor impairment at higher exposures: our findings highlight the predominant influence of maternal IQ and the home environment. Further research, including a broader range of alcohol exposure, is needed to better define potential safety thresholds of PAE on early-life neurodevelopment.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Prenatal alcohol exposure (PAE) is a well-established risk factor for adverse neurodevelopmental outcomes, particularly at high levels of consumption.
⇒ The impact of low-to-moderate PAE on early-life neurodevelopment remains unclear.

WHAT THIS STUDY ADDS

⇒ Low levels of PAE are not associated with cognitive nor language neurodevelopment impairment at 18 months.
⇒ The possible detrimental role of PAE on early-life motor neurodevelopment warrants further scientific investigation.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study confirms the importance of maternal cognitive abilities and the home environment in early-life neurodevelopment: support for families and early parenting environments should be prioritised.

INTRODUCTION

The consumption of alcohol during pregnancy is widely recognised for its detrimental impacts on fetal growth and overall development.[1] Prenatal alcohol exposure (PAE) has long-lasting effects on neurodevelopment that may lead to fetal alcohol spectrum disorders (FASDs).[1 2] Growing evidence links prenatal alcohol exposure to poor developmental outcomes, including motor, learning, attention, processing speed, language and executive function deficits.[2 3]

The WHO states that no level of alcohol consumption is safe. Terms like 'low' and 'moderate' are often used interchangeably. Some guidelines set limits: the US Centers for Disease Control and Prevention defines low-to-moderate drinking for women as≤1 drink per day, while many European countries consider up to 10g of pure alcohol per day (≈one drink) low risk. The National Institute on Alcohol Abuse and Alcoholism defines 'low intake' typically in terms of up to one standard drink per day (eg, 355mL of beer—about 5% alcohol; 148mL of wine—about 12% alcohol; 44mL of distilled spirits—about 40% alcohol, such as gin, rum, vodka, whiskey)[4] and no more than seven drinks per week, and defines heavy drinking for women as consuming eight or more drinks per week. However, the WHO and a number of other countries[5] advise that pregnant, lactating and seeking to become pregnant women should abstain from alcohol consumption to prevent baby adverse outcomes such as FASDs. While heavy prenatal alcohol use is known to be harmful on child development, the effects of low-to-moderate use are unclear and safe levels remain debated. Low-to-moderate alcohol exposure has been sometimes linked to deficits in executive functioning, attention and motor skills in children, though findings remain inconsistent due to methodological variations across studies. Human research to date has provided mixed evidence on the potential effects of low to moderate PAE on child neurodevelopmental outcomes, with a recent systematic review reporting adverse effects in six studies, no effect in five studies and a weak positive effect in two.[6] The conflicting findings of these studies may in part be due to limitations in exposure measurement, a lack of sensitivity for detecting impairments for some neurodevelopmental outcomes and inadequate accounting for confounding by environmental and social factors.[6 7] Most recently, Jacobson and colleagues[8] conducted a large dose–response analysis across six US longitudinal cohorts, showing that while overall effects of average daily intake on cognition appeared linear, stronger adverse effects emerged when considering drinking pattern, particularly higher doses per occasion and frequent drinking. These findings underscore the importance of considering not only quantity but also drinking patterns when evaluating the potential impact of PAE on child neurodevelopment.

Beyond alcohol exposure, socioeconomic status (SES) plays a critical role in shaping developmental trajectories. SES, often defined by parental income, education and occupation, is closely intertwined with access to resources and early life experiences essential for cognitive and emotional development. Low SES has been associated with adverse outcomes such as reduced language and executive function skills,[9 10] and in children exposed to alcohol prenatally, these challenges may compound or moderate neurodevelopmental outcomes. The home environment plays a pivotal role in early neurodevelopment—encompassing motor, language and cognitive domains—and can significantly confound the observed effects of PAE. A nurturing and stimulating home environment is fundamental to a child's neurodevelopment.[11] Studies have shown that children raised in enriched environments exhibit enhanced cognitive and language skills, whereas those in deprived settings may experience developmental delays. These environmental factors can either mitigate or exacerbate the effects of PAE.[12 13] Most of the studies pointed out that child cognitive development is strongly influenced by parental IQ, socioeconomic status, home environment and sibling relationship.[13] Understanding these combined effects can help refine early intervention strategies, particularly in resource-constrained settings, where children face heightened vulnerability. This study aims to explore the role of low PAE in early-life development in Italian mother-child pairs enrolled in the Northern Adriatic Cohort II (NAC-II). The Italian NAC-II is part of the Mediterranean cohort involved in the 'Public health impact of long-term, low-level, mixed element exposure in susceptible population strata' (PHIME) project.[14]

MATERIALS AND METHODS

Study population

A detailed description of the study protocol, inclusion and exclusion criteria and power's calculation has been published elsewhere[14] and detailed in online supplemental material. Briefly, recruitment and follow-up took place at the Institute for Maternal and Child Health IRCCS Burlo Garofolo. At recruitment from April 2007 to April 2009, eligible pregnant women, between 20–22 gestational weeks, filled in a short questionnaire to identify any excluding conditions and to provide some brief information on the family and a quick assessment of maternal consumption of some category of food (vegetables; milk and milk products; eggs; meat; fresh, frozen and canned fish; and alcoholic beverages) between 20 and 22 gestational weeks. At 20–32 gestational weeks, pregnant women enrolled in the study were tested with the Standard Progressive Matrices (SPM),[15] a version of the Raven's Progressive Matrices, to estimate the maternal IQ. At 1month after delivery, mothers filled in a detailed, long questionnaire to collect information on demographic, socioeconomic and health status on pregnancy and delivery, on lifestyles and on detailed dietary and alcoholic habits during the whole pregnancy.

At 18 months after delivery, mothers completed a supplementary questionnaire to detect changes in sociodemographic information and SES, and children were tested by the Bayley Scales of Infant and Toddler Development third edition (BSID-III).[16]

Starting from 18 months after delivery, a home environment evaluation was conducted using the Italian "Affetto, Incoraggiamento, Rispetto, clima Emotivo" instrument (AIRE),[17] an adaptation of the Home Observation for Measurement of the Environment model.[18] The AIRE visit at home lasted 30–40min. The AIRE, SPM and BSID-III tests were conducted by trained psychologists.

Exposures

The mother's habitual alcohol consumption during the whole pregnancy was collected soon after delivery using a questionnaire adapted from a validated Food Frequency Questionnaire.[19–21] Within this long questionnaire, six quantitative questions were related to frequency of consumption of alcoholic beverages. Considering the different ethanol concentrations, one alcoholic drink corresponded approximately to 12 g of ethanol in the following alcoholic beverages: one 125 mL glass of white, red wine or aperitif (eg, Campari, Marsala, Vermouth); one 330 mL can or bottle of beer; and one 30–40 mL small glass of hard liquor. As was done in previous analyses, for each alcohol item, conversion from categories of consumption into continuous intakes of alcohol servings was done by assigning to each category a consumption level equal to the median value for that category (eg, two to four times per week became three times per week).[22] Total alcohol intake was calculated by summing the estimated weekly drinks of all alcoholic beverages reported.

Outcome definition and measurement

Children at 18±2 months of age underwent the BSID-III neurodevelopment test which measures the major areas of child development. The sum of the number of points obtained for a subtest, named raw scores, was converted to scaled score. The scaled scores, which represented a child's performance on a subtest relative to his/her same age peer, were derived from the standardisation of total raw score for child's age in days at test administration. For each composite score, the distribution of scaled score (or the sum of scaled score for language and motor scales) was used to derive corresponding percentiles which were converted to composite scores. Composite scores had an average of 100, a SD of 15 and a range from 40 to 160. The higher the composite score, the better the child's performance. Cognitive, language and motor composite scores were considered as study outcomes.

Potential confounders

The following list of covariates was considered for estimating the effect of maternal alcohol intake during pregnancy on child neurodevelopment. During pregnancy: the smoking habits (people who have never smoked, people who have quit smoking and people who smoke) and the smoking passive exposure at home and at work (Yes/No), maternal IQ. At delivery: mother's age, size of the home as socioeconomic factor and the socioeconomic index of family (SES index) adapted from Bennett and colleagues.[23] The SES index was built taking into account the following parameters: parents' occupation (1=yes vs 0=no), type of employment (1=white collar vs 0=blue collar following the Hollingshead classification), educational level (0=up to middle school, 0.5=high school, 1=university degree) and homeownership (1=yes). Finally, the scores were summed (for type of employment and educational level the mean between parents was used). In addition, the AIRE's scores were considered. The range of AIRE's score is 0–20 for each of the following subscales: communication and affective relation between parents and child (AIRE_Comm); promotion of child autonomy alone; respect for the child and implementation of rules; emotional atmosphere. The higher the scores, the better the home environment evaluation.

Statistical analysis

Consistent with previous analysis performed in the Italian and Mediterranean cohort,[22 24–26] only children born during or after week 37 of gestation who underwent the BSID-III at 18±2 months and for whom self-reported weekly alcohol intake during pregnancy by mothers was included in the analysis of the present research.

We described mother–child characteristics using mean, SD and median for continuous variables, and frequency and percentage for categorical variables. The percentage distributions of each item concerning mother's alcohol intake during pregnancy included in the short and the long questionnaires were calculated and the Pearson's correlation between the two questionnaires was tested. We estimated minimum, maximum and selected percentiles (1st, 5th, 10th, 25th, 75th, 90th, 95th, 99th) for composite scores and weekly alcohol intake during pregnancy (long questionnaire).

Simple and multiple linear regressions were performed to study the relation between neurodevelopmental composite scores and maternal alcohol intake during pregnancy. In a multiple regression model, VanderWeele's automatic selection method[27] was applied and only potential confounders with p≤0.15 were included in the final model. The robust MM-estimator[28] was used due to violations of the standard ordinary least squares assumptions. Beta (β) and the 95% CI of each multiple linear regression, based on the approach of MM-estimation, are presented in tables. For each composite score, the interaction between maternal alcohol intake during pregnancy and each confounder selected in the final model was assessed.

Statistical analyses were carried out using SAS software V.9.4 (SAS Institute, Cary, North Carolina, USA).

RESULTS

In the recruiting period, 900 pregnant women were enrolled in the cohort; 767 (85%) of these remained in the study at delivery and 632 children, the 82% of those born within cohort, underwent BSID-III testing at 18 months. The mothers of children lost to follow-up had significantly lower IQs (median 118 vs 125, p=0.002) and were less frequently married (85.5% vs 90.4%) and more frequently separated (8.4% vs 3.3%, p=0.04) than the mothers of children still within the study at the age of 18 months. Age at delivery and employment status in the two groups of mothers, on the other hand, did not differ significantly. Maternal alcohol intake during pregnancy differed significantly in the two groups of mothers: the mothers lost to follow-up had a significantly lower intake (median=0.35 vs 0.23 weekly alcohol drinks, p=0.03) than those still within the study.

After excluding preterm births, 605 children, who underwent the BSID-III at 18±2 months and for whom maternal alcohol intake during pregnancy was measured, were used in the final analysis. The main characteristics of the 605 mothers and 605 children included in the

Table 1 Main characteristics of mothers (n=605)

Main characteristics of mothers	
Mother's age at delivery, mean±SD (median), n=605	33.3+4.3 (33.0)
Maternal BMI before pregnancy, mean±SD (median), n=605	22.8±3.8 (22.2)
Maternal IQ, mean±SD (median), n=605	119±11 (125)
Mother's occupation, n (%)	
Employed on maternity/paternity	456 (76.4)
Employed worker	52 (8.7)
Housewife/househusband	47 (7.9)
Other condition	42 (7.0)
Mothers' marital status, n (%)	
Married/living together	540 (90.3)
Widow/single/never married/separated/divorcing	58 (9.7)
Mother's educational level, n (%)	
Elementary and middle school	100 (16.6)
High school	291 (48.3)
University degree	212 (35.2)
Home size, n (%)	
<50 mq	41 (6.8)
50–100 mq	405 (67.6)
>100 mq	153 (25.5)
Smoking habits during pregnancy, n (%)	
People who have never smoked	354 (59.3)
People who have quit smoking	195 (32.7)
People who smoke	48 (8.0)
Exposure to passive smoke during pregnancy, n (%)	
No (2)	473 (78.3)
Yes (1)	131 (21.7)
Alcoholic drinks per week during pregnancy, mean±SD (median), n=605	1.6±3.3 (0.3)
SES index, mean±SD (median), n=597	
SES index in categories, n (%)	
Low (≤1)	52 (8.7)
Medium (2)	285 (47.7)
High (≥3)	260 (43.6)
Folic acid use in the 3 months preceding the pregnancy	
No (2)	371 (61.6)
Yes (1)	231 (38.4)

BMI, body mass index; SES, socioeconomic status.

Table 2 Main characteristics of children (n=605)

Main characteristics of children	
Children's sex, n (%)	
Male (1)	305 (50.4)
Female (2)	300 (49.6)
Birth weight (g), mean±SD (median), n=604	3421.5±452.3 (3405.0)
Breastfeeding, n (%)	
No (0)	37 (6.4)
Yes (1)	542 (93.6)
Duration of breastfeeding (months), mean±SD (median), n=579	10.1±5.9 (10.0)
Child's consumption of homogenised fish (number of months with at least one portion of fish per week), mean±SD (median), n=579	2.7±4.5 (0)
Child's consumption of fresh fish (number of months with at least one portion of fish per week), mean±SD (median), n=579	9.1±4.0 (10.0)
AIRE scores	
Communication and affective interaction between parents and child, mean±SD (median), n=496	18±2 (19)
Promotion of child autonomy alone, mean±SD (median), n=496	19±1 (19)
Respect for the child and implementation of rules, mean±SD (median), n=496	16±2 (17)
Emotional atmosphere, mean±SD (median), n=496	17±2 (17)
Bayley at 18 months	
Cognitive composite score, mean±SD (median), n=602	106±8 (105)
Language composite score, mean±SD (median), n=602	98±9 (97)
Motor composite score, mean±SD (median), n=602	101±6 (100)

AIRE scores, The Italian "Affetto, Incoraggiamento, Rispetto, clima Emotivo" instrument.

present research are shown in tables 1 and 2, respectively. The percentage distribution of each item concerning the mother's alcohol intake during pregnancy included in the questionnaires is shown in table 3 and online supplemental table S1, respectively. Pearson's correlation between mother's weekly alcohol intake during pregnancy measured at recruitment and 1 month after delivery was 0.6 (p≤0.001). The distribution of composite scores and weekly alcohol intake during pregnancy is shown in online supplemental table S2.

Subgroup analyses show some alcohol intake heterogeneity as described in detail in online supplemental materials. According to Pearson's correlation test, alcohol intake during pregnancy was directly correlated with mother's age at delivery (0.11, p<0.01), and inversely correlated with motor composite score (−0.11, p=0.01). No Pearson's correlation was found between mother's weekly alcohol intake and SES index, AIRE scores, mother's IQ, cognitive and language composite score.

The results of multiple linear regressions, based on the approach of MM-estimation, between composite scores and the weekly alcohol intake during pregnancy,

Table 3 Percentage distribution of the quantitative question on overall alcohol intake frequency included in the questionnaire at 20–22 gestation weeks of pregnancy (recruitment) (n=603)

Alcoholic beverage, one serving*	%
Never	58.5
Less than once per week	10.6
1–3 per month	10.9
1 per week	9.6
2 per week	3.6
3 per week	1.8
4 per week	0.8
5 per week	0.3
6 per week	1.5
At least once per day	2.2

*One serving=one glass of wine (125 mL) or one can of beer or one small glass of spirits (30 mL).

controlling for the selected potential confounders, are shown in table 4. A total of 495 mother-child pairs were left for the multiple linear regression analyses. Overall, no clear inverse associations were found between mother's alcohol intake during pregnancy and BSID-III neurodevelopmental scores, while direct associations were found with AIRE's subscale Promotion of child autonomy and with mother's IQ.

Interaction effect

Only the interaction between the weekly alcohol drinks consumption during pregnancy and the AIRE_Comm on motor composite score was found. In terms of the main effect, the coefficient for weekly alcohol drinks was −2.05 ($p<0.001$), which means that, for a given value of AIRE_Comm, a one-unit increase in weekly alcohol drinks is associated with a −2.05-unit decrease in motor composite score on average. The AIRE_Comm also had a negative coefficient equal to −0.39 (p=0.01).

The coefficient for the interaction is 0.10, which means that the effect of weekly alcohol drinks on motor score increases by 0.10 units for every one-unit increase in AIRE_Comm on average. In other words, weekly alcohol drinks had a more negative impact on motor composite score in children with lower home environment evaluation than in children with higher evaluation. The interaction effect between weekly alcohol consumption during pregnancy and parent–child communication (AIRE_Comm) on motor composite scores is illustrated in figure 1. For children with low levels of communication ($\mu - 1$ SD=16, blue solid line), higher maternal alcohol intake was associated with a steeper decline in motor scores compared with children at average levels of communication (μ=18, red dashed line) or at high levels of communication (μ+1 SD = 20, green dash-dotted line).

DISCUSSION

In this study, we analysed the relationship between PAE and early-life child neurodevelopment in an Italian birth cohort that was evaluated previously in relation to chemical exposures.[24–26] In our cohort, 41.5% of women reported having consumed one serving of alcohol, between 20 and 22 gestational weeks, of which 20.5% at least four servings per month and 2.2% at least once per day. In our cohort, low levels of alcohol consumption during pregnancy were confirmed, with a mean of 1.6 alcoholic drinks per week (SD=3.3) and a median of 0.3, consistent with several studies that indicate a low prenatal alcohol consumption up to one to two drinks per week.[29 30] A 2022 survey by the Italian National Institute of Health found that in Friuli Venezia Giulia, 20.7% of pregnant women reported drinking alcohol at least one to two times per month, and 4.0% at least three to four times per month.[31] The same survey shows that alcohol consumption during breastfeeding is more common than during pregnancy: in Friuli Venezia Giulia Region, the proportion who reported having consumed alcohol at least three to four times between months 2 and 5 of lactation is 9.1%, increasing to 16.6% during months 11 and 15 of lactation. A higher prevalence is confirmed in the Central and Northern regions.[31]

Our results conformed to no link between low prenatal alcohol exposure and cognitive or language development at 18 months, consistent with studies using large population samples.[6 8] On the other hand, we found a suggestive although non-consistent inverse association between

Table 4 Associations—beta and 95% CI of multiple robust regressions—between each composite score and the weekly alcohol intake during pregnancy by mothers adjusted for the selected potential confounders (n=495)

	Adjusted beta (95% CI)		
	Cognitive composite score	Language composite score	Motor composite score
Weekly alcohol drinks during pregnancy by mothers	−0.05 (−0.28 to 0.18), p=0.68	−0.09 (−0.32 to 0.14), p=0.44	−0.13 (−0.31 to 0.05), p=0.14
Communication and affective interaction between parents and child	−0.31 (−0.75 to 0.12), p=0.15	–	−0.28 (−0.57 to 0.02), p=0.07
Promotion of child autonomy alone	0.84 (0.20 to 1.47), p=0.01	0.71 (0.17 to 1.26), p=0.01	0.44 (0.02 to 0.87), p=0.04
Mother's IQ	0.08 (0.01 to 0.15), p=0.02	0.12 (0.05 to 0.19), p=0.01	0.06 (0.01 to 0.10), p=0.02

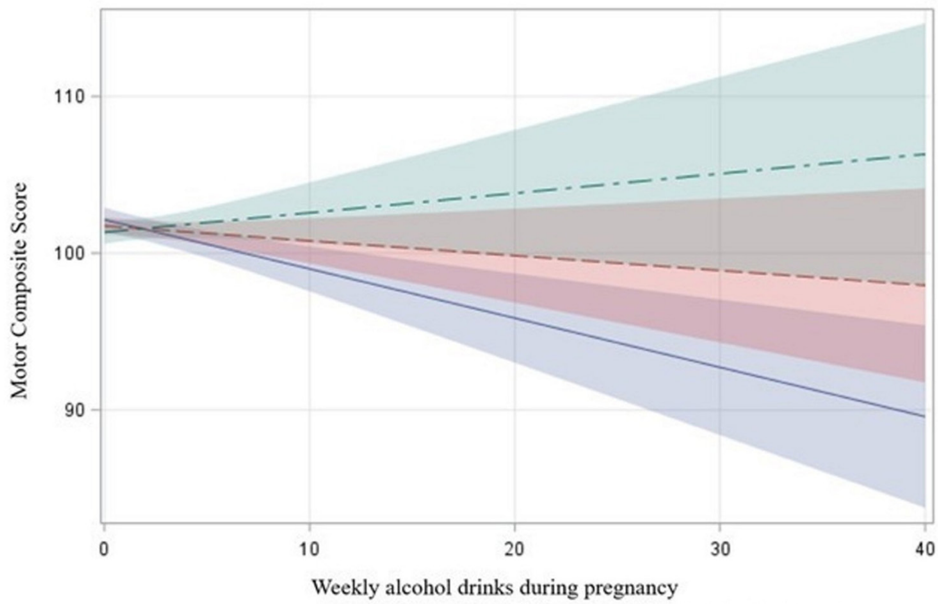

Figure 1 Interaction plot for the effect of weekly alcohol drinks and the Italian "Affetto, Incoraggiamento, Rispetto, clima Emotivo" (AIRE) score 'communication and affective relation between parents' (AIRE_Comm), on motor composite score.

PAE and motor neurodevelopment, with a more negative impact on motor composite score in children with lower home environment evaluation: the potential effect observed in our results remains small, indicating that, assuming a linear dose-response relationship between PAE and motor development, each additional alcoholic drink consumed per week during pregnancy is associated with an estimated 0.13-point decrease in the BSID-III motor score at 18 months. Few studies suggest that moderate prenatal alcohol exposure, well below levels linked to fetal alcohol syndrome, may affect children's psychomotor development.[32] Various physio-pathological mechanisms may underlie motor system susceptibility to PAE, including structural and functional changes in the cerebellum, basal ganglia, sensorimotor networks, neuromuscular junctions and spinal motoneurons, leading to lasting motor coordination and processing deficits.[33] Nevertheless, the impact of low prenatal alcohol exposure on early motor development remains unclear, with no strong evidence of significant impairments.[3 34]

Our findings confirm the predominant influence of environmental and maternal factors—particularly maternal IQ, promotion of child autonomy and the quality of parent–child interaction—on early child neurodevelopment.[35] In previous research on this PHIME cohort, maternal IQ was linked to SES, with home environment fully mediating effects on cognitive and language outcomes; maternal IQ also directly influenced motor development, partly mediated by home environment.[35]

In terms of external consistency, maternal IQ has been consistently associated with children's cognitive outcomes, not only due to potential genetic heritability but also through enriched language exposure, problem-solving support and overall cognitive stimulation in the home environment.[36] Higher maternal IQ often corresponds with better parenting practices and more cognitively stimulating home environments, both of which promote early developmental gain. Beyond maternal IQ, fostering child autonomy—such as encouraging independent exploration—benefits executive function and adaptive behaviours.[37] Additionally, the quality of parent–child communication and affective interaction plays a vital role in shaping emotional security, language development and cognitive functioning.[38] Although prenatal exposures like nutrition and low alcohol use may affect some neurodevelopmental areas, our results confirm maternal IQ and early caregiving have a stronger, lasting impact on early-life development trajectories.

Our study has several limitations. PAE was not the original main exposure of interest of the study and its effect on neurodevelopment was not the main hypothesis. As a consequence, PAE assessment may lead to an incomplete assessment of alcohol consumption, potentially resulting in misclassification and imprecise estimates. Furthermore, alcohol intake as well as covariates used in final analyses were not based on objective assessment but on self-reported questionnaires. Self-report of alcohol intake is known to be prone to under-reporting, as shown for example by discrepancies between maternal self-report and alcohol-positive newborn blood spots, or between population-level self-report and alcohol sales. Maternal under-reporting of exposures may have caused misclassification or bias, likely weakening associations and contributing to the lack of observed effect. In addition, the vast majority of women in our cohort reported very low alcohol consumption (median 0.3 drinks per week, with nearly 60% never consuming and only 6.8% drinking≥4 times per week). As a result, our study may be underpowered to assess effects of moderate or higher PAE, and conclusions are therefore limited to low-level exposures. Nevertheless, regarding maternal alcohol intake during pregnancy, the Pearson's correlation between the two measurements obtained, at recruitment and 1 month after delivery, was rather high, iethat is, 0.6 (p≤0.001). Despite the very low alcohol consumption reported, our data show a higher level of alcohol consumption during pregnancy than the survey conducted by the National Institute of Health,[31] probably as a consequence of nationwide 'no-alcohol during pregnancy' prevention strategies implemented over the years. Despite adjusting beta coefficients for several covariates in our final analysis, neurodevelopment is shaped by a complex interplay of factors and may also be influenced by unmeasured or currently unknown variables, including potential genetic susceptibility.[39] Furthermore, the study was not originally powered to detect potential effects of PAE on neurodevelopment, so the lack of significant associations, apart from a borderline, suggestive link with motor scores, may be attributable to random variation. This study also presents several strengths. By evaluating three distinct domains of neurodevelopment at 18 months, we were able to explore how prenatal alcohol exposure may differentially affect various developmental outcomes. Additionally, we controlled for multiple potential confounders and assessed neurodevelopment using standardised tools administered by two trained psychologists, whose evaluations demonstrated a high level of inter-rater reliability.[40] The prospective nature of the study reduces recall bias and allows for temporal relationships between prenatal exposure and outcomes to be more accurately assessed, and including a large sample size population with neurodevelopmental evaluation provides substantial statistical power for many comparisons, especially in early childhood studies. Furthermore, limiting the analysis to term-born children reduced confounding due to prematurity-related developmental impairments.

In conclusion, in our study, low levels of prenatal alcohol exposure were not associated with neurodevelopmental impairments at 18 months of age. Our findings emphasise that maternal cognitive abilities and home environment, particularly maternal IQ and parent–child interaction, strongly influenced early developmental outcomes. These environmental influences appeared to have a stronger impact on neurodevelopment than low-level prenatal exposures. Future studies should include more detailed monitoring of alcohol exposure during preconceptional and periconceptional times, and through pregnancy and lactation and longer follow-up periods to more precisely determine potential thresholds of risk for prenatal alcohol exposure on early-life neurodevelopment.

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