



OPEN Impact of tea and coffee consumption during pregnancy on children's cognitive development

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Evidence on the association between maternal tea/coffee consumption and children's cognitive development is limited. This study included 1423 mother–child pairs from the Chinese National Birth Cohort (CNBC). Maternal tea/coffee consumption status was collected in the 1st, 2nd and 3rd trimesters of pregnancy. Cognitive development was assessed using the Bayley Scales of Infant and Toddler Development III (BSID-III) in children aged averagely 36-months. We utilized group-based trajectory modeling (GBTM) to fit trajectories of maternal tea/coffee consumption across the three trimesters of pregnancy. Linear regression models were used to analyze the association between maternal tea/coffee consumption and children's cognitive development scores. Positive associations between maternal tea consumption during pregnancy and children's cognitive development were observed. Children of mothers who belonged to a continuous tea drinking trajectory throughout pregnancy had higher cognition, fine motor, and gross motor scores than those whose mothers belonged to a trajectory of tea-drinking in the 1st trimester of pregnancy, only. Comparison of tea-drinkers (yes/no) in each trimester separately indicated that tea-drinking in the second and third trimesters were more strongly associated with the outcomes than tea-drinking in the 1st trimester. The second and third trimesters of pregnancy might be key periods regarding maternal tea consumption affecting children's cognitive development. No significant association were found between maternal coffee consumption during pregnancy and children's cognitive development. The GBTM modelling provides clues to truly reflect the status and trajectory of pregnant women's tea and coffee consumption across different trimesters as their lifestyles change dynamically throughout pregnancy, which provides new motivation to investigate the association between maternal life pattern with offspring's cognitive development.

Keywords Pregnancy, Tea, Coffee, Caffeine, Children, Cognitive development

Reproductive-aged women habitually consume tea and coffee; thus, the potential effects of their consumption on women and their children deserve attention¹. The main components of tea are caffeine, polyphenols, flavonoids, and various minerals². The main components of coffee are caffeine, tannic acid, fat, protein, sugar and minerals³. Both tea and coffee contain caffeine but in different amounts. On average, one cup of espresso coffee (60 mL) contains around 80 mg of caffeine, and one cup of filtered coffee (200 mL) contains around 90 mg of caffeine. There are many different types of tea, including black, green, and oolong. The concentration of caffeine in tea ranges from 14 to 61 mg per cup, depending on the type of tea. One cup of black tea (220 mL) contains around 50 mg of caffeine⁴. There is no consistent trend indicating that one type of tea consistently has higher caffeine levels than the others. Generally, green tea contains less caffeine compared to black tea, but the specific amount may vary depending on the tea brand, brewing time, and water temperature⁵. Caffeine readily crosses biological membranes, including the blood–brain barriers and placental barriers, and can enter amniotic fluid and breast milk⁶. Recently, The negative influence of maternal caffeine consumption on pregnancy has been widely reported, focusing on the association between caffeine intake and miscarriage, fetal growth restriction, small-

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for-gestational-age newborns, or preterm birth^{7–9}. However, there is a debate on whether there is an association between maternal caffeine consumption during gestation and offspring's neurodevelopment.

Animal studies have demonstrated a strong correlation between maternal use of caffeine and cognitive deficits in the offspring^{10,11}. The effects of prenatal caffeine intake in rodents may be mediated by a decrease in acetylcholinesterase activity in the brain¹², hippocampal adenosine A receptors¹³ and GABA neurons¹⁴. However, these findings cannot be directly related to humans. In humans, some studies have demonstrated that maternal caffeine consumption is a risk factor for the child neurodevelopment^{15–20}. For example, a French birth cohort found an association between caffeine intake during pregnancy and offspring's impaired cognitive development and suggested that conservative guidelines for caffeine intake are recommended during pregnancy (i.e., 200 mg/day)¹⁵. The Japan Environment and Children's Study also showed that mothers who consumed > 300 mg of caffeine daily had a 1.11-fold increase in gross motor developmental delay odds at 12 months²⁰. In contrast, some studies did not find any association between maternal caffeine intake and the children's neurodevelopment^{21–23}. For example, Loomans et al.²¹ indicated that prenatal caffeine intake does not increase the risk of behavioral problems in 5 to 6-year-old children. In line with this, Barr et al.²² found no association between maternal caffeine intake and impaired neurobehavioral outcomes in 7-year-old children. Likewise, the Norwegian Mother, Father and Child Cohort Study showed that low to moderate coffee drinking during gestational (56 mg/day–172 mg/day) was not associated with any persistent adverse effects concerning the child's neurodevelopment up to 8 years of age, such as negative mood, language difficulties, and gross motor and fine motor deficits²³. Therefore, more epidemiologic investigations are needed to further examine the direction of the association between pregnant women's consumption of tea or coffee (the main source of caffeine) and the offspring's neurodevelopment. At the same time, pregnant women's lifestyles are dynamic throughout pregnancy²⁴, most existing prospective birth cohort studies on maternal tea/coffee and the offspring neurodevelopment include only one or some time points during pregnancy. Whether there is a key tea/coffee intake period on children's cognitive development is unknown.

The aim of the current study was to explore the association between maternal tea/coffee consumption in each trimester, consumption trajectories throughout pregnancy, and children's cognitive development and to reveal possible key periods.

Material and methods

Ethics and compliance statement

All methods were carried out in accordance with relevant guidelines and regulations, and the study has obtained appropriate ethical approval from the relevant committee. We adhered strictly to all research ethical standards involving human subjects. All participants gave informed consent and had the right to withdraw from the study at any time.

Study population

This study was based on the China National Birth Cohort (CNBC). Couples in early pregnancy who came for the first antenatal checkup in the Ma'anshan Maternal and Child Health Center in Anhui Province, China from May 2017 to September 2018 were recruited. The inclusion criteria were as follows: ① maternal age ≥ 18 years; ② spontaneous pregnancy; ③ planning to undergo routine obstetric checkups and delivery at the Center; ④ willingness to undergo follow-up. In total, 1508 families were included in this cohort. After excluding adverse pregnancy outcomes and twin births, finally 1423 families were included in the study. The flowchart of the participants is shown in Fig. 1.

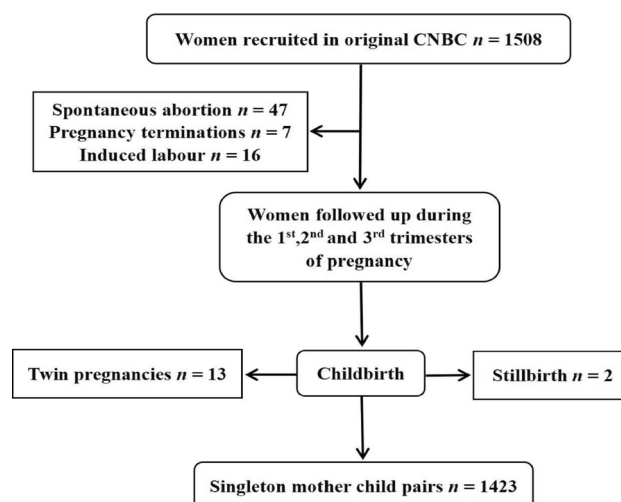


Fig. 1. flowchart of participant selection.

Tea and coffee consumption during pregnancy

In this study, participants were asked about their tea and coffee consumption status during the first, second and the third trimester of pregnancy. The original responses included “Never,” “Once in a while,” “Less than once a month,” “Less than once a week,” and “At least once a day” for the first trimester, and included “Never,” “Yes, no changes,” and “Yes, significantly reduced” for the second and third trimesters. For the separate three trimesters, if a mother reported “Never” for tea consumption, participants were grouped into the no tea drinking group, respectively. In contrast, all participants with other responses were grouped into the tea drinking group. The same grouping rationale was adopted for maternal coffee drinking.

Evaluation of children’s cognitive function

The Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) is a comprehensive scale applicable to infants aged 0 to 42 months²⁵. The Bayley scale was initially developed in 1933 by American psychologist N. Bayley and colleagues. It consists of (i) a motor scale with 81 items to measure gross and fine motor movements; (ii) an intelligence scale with 163 items to measure visual and auditory responses to stimuli, hand–eye coordination, language perception and expression, and cognitive ability; and (iii) a behavioral record with 24 items to record the infants’ emotions, cooperation, response to parents and experimenters, interest, and breadth of attention. BSID-III adds social-emotional and adaptive domains to the above three domains. Cognitive functioning was thus categorized into five dimensions: cognition, receptive language, expressive language, fine motor, and gross motor. Each area yields a standardized composite score with a mean of 100 and a standard deviation (SD) of 15; higher scores indicate better development. A composite score below 70 indicates significant developmental delay, while a score of 70–84 is interpreted as “suspect delay.” A cross-sectional study provided evidence that the Bayley-III cognitive scale is a valid measurement that could be used in the Chinese population, as well as the consideration of sex differences when used in a Chinese context²⁶. The Bayley-III scale is satisfactory in reliability and validity among Chinese children, with a retest reliability correlation of 0.946 and a Cronbach’s coefficient of 0.987²⁷.

Covariates

Confounding factors were identified by the directed acyclic graph (DAG)^{28,29}, including maternal age, pre-pregnancy BMI, maternal occupation before pregnancy, family income, education level, maternal smoking, passive smoking, alcohol consumption, anxiety, depression, stress and pregnancy vomiting. (Fig. S1).

Information on maternal age, maternal occupation before pregnancy, family income, education level, maternal smoking, passive smoking, alcohol consumption, and pregnancy vomiting was collected using questionnaires at the first antenatal checkup. At the same time, pre-pregnancy BMI was calculated using the body weight and height measured by physicians.

Data on the psychosocial status of pregnant women were evaluated using the Center for Epidemiologic Studies Depression Scale (CES-D), 10-item Perceived Stress Scale (PSS-10), and Self-rating Anxiety Scale (SAS). The CES-D scale was developed in 1977 by Sirodff in the U.S. National Institutes of Research consists of 20 questions to screen participants for depressive symptoms³⁰. The CES-D is rated on a scale of 0 to 3, with a total score of 0 to 60. A higher test score represents a worse depression. Its general cutoff score is 16, and it has been widely used in pregnant women. Cohen, S., Kamarch, T. & Mermelstein, R. (1983) proposed the PSS-10 is a 10-question scale. It assesses participants’ feelings, reactions, and levels of identity and measures an individual’s perceived stress³¹. Participants were asked to answer each question on a 5-point Likert scale ranging from 0 (never) to 4 (often). The total scores range from 0 to 40, with higher scores indicating greater stress. A total score of 13 indicates an average stress level, whereas a score of 20 or higher indicates high stress levels. W.K. Zung developed the SAS in 1971. This scale includes 20 projects reflecting feelings of subjective anxiety, and each project is rated on a four-point scale based on the frequency of symptoms³². Women with SAS scores of at least 50 were considered to have anxiety.

Data on pregnancy complications, folic acid consumption, gestational weeks, birth weight, exclusive breastfeeding for six months, developmental behavior of 36-month-old infants and children’s gender were collected for sensitivity analysis. Data on folic acid consumption was collected by questionnaire survey during pregnancy. Based on maternal folic acid consumption, women can be categorized into two groups: those with folic acid intake in at least one trimester (yes) and those without folic acid intake in all three trimesters (no). Information on gestational week, birth weight, and maternal pregnancy complications (including gestational diabetes mellitus and gestational hypertension) was obtained from the medical records. Exclusive breastfeeding for six months and children’s gender were collected from questionnaires completed by the infant’s caregivers.

The Ages and Stages Questionnaire, Third Edition (ASQ-3) was adopted to evaluate children’s developmental behaviors. It was a widely used and validated parent-completed questionnaire for screening children’s communication, gross motor, fine motor, problem-solving, and personal-social delays³³. For each project, three responses were chosen: not yet, sometimes, and yes, scored as 0, 5, and 10, respectively. The overall domain score is obtained from the sum of all items, with a maximum score of 60 for each domain. The higher the score, the better the skills and abilities in the given realm. These realm scores were used to classify children as ‘well-developed’ (i.e., scores not less than the cut-off score) or ‘developmental delay’ (i.e., scores below the cut-off score). The cutoffs for communication, gross motor, fine motor, problem-solving, and personal-social skills were 40, 40, 20, 30, and 30, respectively.

Statistical analysis

Participants’ demographic characteristics were reported as mean \pm standard deviation (SD) or percentage (n %).

The beta coefficient (β) and 95% confidence intervals (CIs) between maternal tea or coffee consumption during pregnancy and children’s cognitive development were calculated using linear regression models, with

or without adjustment for important confounders (Crude models: no covariates were adjusted; Adjusted models: adjusted for maternal age, pre-pregnancy BMI, maternal occupation before pregnancy, family income, education level, maternal smoking, passive smoking, alcohol consumption, anxiety, depression, stress and pregnancy vomiting). We then explored the association between maternal tea or coffee consumption throughout pregnancy and separate maternal tea or coffee consumption in each trimester of pregnancy and cognitive developmental scores in 36-month-aged children. To clearly identify potential key period regarding maternal tea consumption affecting children's cognitive development, we further adjusted for the maternal tea/coffee consumption in the other trimesters when examining the independent effect of tea/coffee consumption in one certain trimester of pregnancy. 1. when investigating the association between maternal tea/coffee consumption in the 1st trimester of pregnancy and children's cognitive development, we have not controlled for the 2nd and 3rd trimester consumption, as tea/coffee consumptions in the 2nd and 3rd trimesters do not affect the 1st trimester consumption levels and are therefore not confounders; 2. when investigating the association between maternal tea/coffee consumption in the 2nd trimester of pregnancy and children's cognitive development, we have controlled for the 1st trimester consumption. This is because that women's consumption in the 1st trimester may influence their consumption levels in the 2nd trimester; 3. when investigating the association between maternal tea/coffee consumption in the 3rd trimester of pregnancy and children's cognitive development, we have controlled for the 1st and 2nd trimester of pregnancy consumption separately. Since women's consumption in the 1st and 2nd trimesters occurs before the 3rd consumption, and may affect their consumption levels in the 3rd trimester. Additionally, considering the possible association between consumptions between the 2nd and the 3rd trimester, we control for the two variables separately.

We had different grouping strategies towards maternal tea/coffee consumption status when examining its potential effect on children's cognitive development. Firstly, we classified women into tea/coffee drinking in at least one trimester vs. no tea/coffee drinking in all three trimesters. To observe the potential key period regarding maternal tea/coffee consumption affecting children's cognitive development, we categorized women into tea/coffee drinking in the first trimester vs. no tea/coffee drinking in the first trimester, tea/coffee drinking in the second trimester vs. no tea/coffee drinking in the second trimester, and tea/coffee drinking in the third trimester vs. no tea/coffee drinking in the third trimester, respectively.

Group-based trajectory modeling (GBTM) was used to fit maternal tea/coffee consumption trajectories according to the incidence of maternal tea/coffee consumption across the three trimesters of pregnancy. The maximum likelihood method was used for parameter estimation and model fitting. Based on recommendations^{34,35}, the detailed selection criteria for the best-fitting model for trajectories were as follows: (1) Bayesian Information Criterion (BIC). The closer the BIC value is to 0, the better the model fit; (2) a higher value of entropy indicates how well the classification distinguishes from one group to another; and (3) the average posterior probability is required to be > 0.7. Finally, two categories of the maternal tea consumption (continuous drinking trajectory and drinking in the first trimester trajectory) (Fig. 2) during the entire pregnancy were fitted. Similarly, two categories of maternal coffee consumption (drinking in the second and third trimester trajectory and drinking in the first trimester trajectory) (Fig. 3) during the entire pregnancy were fitted as well.

Linear regression models were finally used to analyze the association between maternal tea consumption trajectories and coffee consumption trajectories during pregnancy and children's cognitive development.

Four sensitivity analyses were performed in this study: 1. High tea/coffee intake during pregnancy increases the risk of pregnancy complications^{36,37}, and children born to these women have an increased risk of neurodevelopmental delay^{38–40}. Pregnancy complications may mediate the intake of tea/coffee during pregnancy and children's cognitive development and can be further adjusted. 2. Maternal tea/coffee intake during pregnancy may lead to premature birth⁴¹ and low birth weight^{42,43}, which in turn is associated with offspring's neurodevelopment⁴⁴. Gestational age and birth weight may also be potential intermediary factors between tea/coffee consumption and neurodevelopment in offspring. Accordingly, the birth weight z-scores by gestational

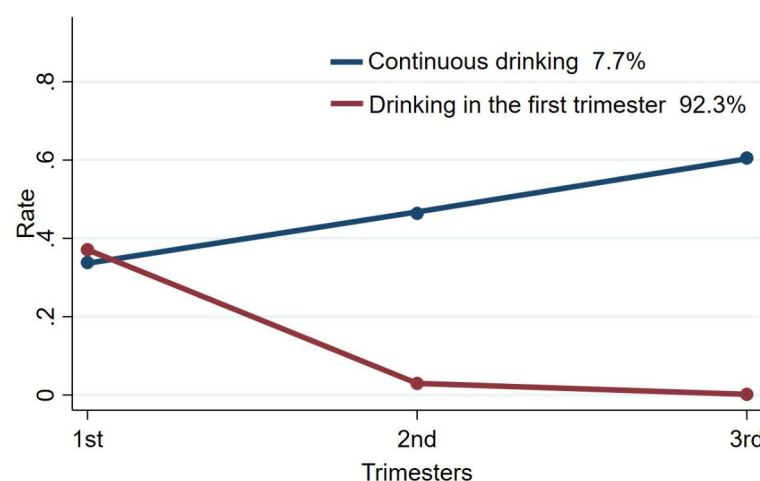


Fig. 2. Maternal trajectories of tea consumption during three trimesters.

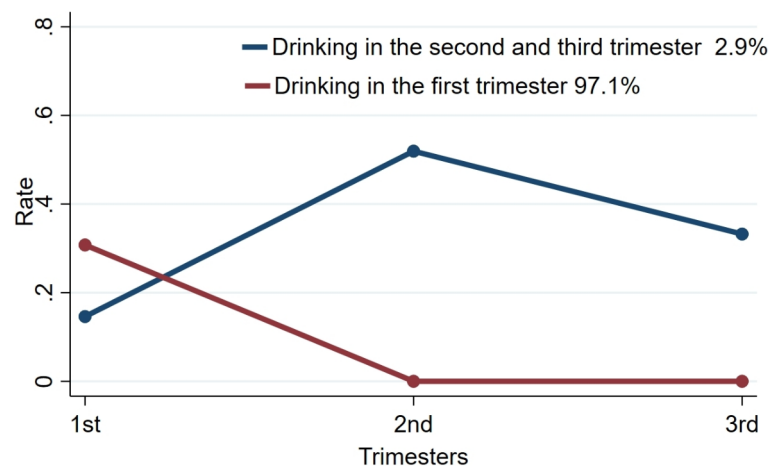


Fig. 3. Maternal trajectories of coffee consumption during three trimesters.

age were further computed and adjusted. Exclusive breastfeeding may be a protective factor for children's cognition^{45,46}. This precise variable requires further adjustments. 3. Additionally, behavioral developmental disorders in young children may be negatively correlated with cognition^{47,48}. Folic acid intake during pregnancy may have potential effects on children's neurodevelopmental outcomes⁴⁹. It may also be the precision variable related to children's cognitive function. Therefore, children's developmental behaviors assessed by ASQ-3, as well as maternal folic acid intake during pregnancy were further adjusted. 4. Finally, children's cognitive development might be gender-specific^{26,50}. Therefore, analyses on additive interaction and multiplicative interaction between children's gender and maternal tea/coffee consumption during pregnancy on children's cognitive function were performed. Children's gender was further adjusted to explore whether gender played a modified effect on the observed associations.

Statistical analysis was performed using SPSS 26.0 and Stata 15.0, and was judged to be statistically significant with a two-tailed value of $p < 0.05$.

Results

Baseline characteristics of participants

Table 1 showed the overall characteristics of the 1,423 participants. The average age of the pregnant women included in this study was 28.7. Most mothers had a BMI within the normal range. Most pregnant women did not smoke or drink alcohol, but 44.5% smoked passively once in a while because their fathers or other family members had a smoking habit. The mean birth weight of children was 3353.2 ± 463.4 g, and the average gestational week was 38.9 ± 1.4 weeks. As presented in Table S1/2, significant differences were observed in breastfeeding practices across different tea trajectory groups. Specifically, the group following the tea drinking in the first trimester trajectory exhibited a higher rate of exclusive breastfeeding (52.9%) compared to the group of continuous tea drinking (41.3%).

Distribution of maternal tea/coffee consumption during pregnancy

As shown in Table S3, the prevalence of maternal tea consumption in the first, second, and third trimesters was 36.8% (523/1423), 6.3% (89/1423), and 4.4% (63/1423), respectively. Furthermore, two tea consumption trajectories [tea drinking in the first trimester trajectory (92.3%) and continuous tea drinking trajectory (7.7%)] were observed.

The prevalence of maternal drinking coffee in the 1st, 2nd, and 3rd trimesters was 30.2% (430/1423), 1.5% (21/1423), and 0.9% (13/1423), respectively. Furthermore, there were two coffee consumption trajectories [coffee drinking in the first trimester trajectory (97.1%) and coffee drinking in the second and third trimester trajectory (2.9%)]. Additionally, the results of the t-test are shown in Figs. 4, 5.

Association between maternal tea consumption during pregnancy and children's cognitive development

The results of the linear regression analysis are presented in Fig. 6/ Table S4-6. After controlling for important confounders, we found that maternal tea drinking in the 2nd trimester was associated with a higher cognitive ($\beta = 0.500$, 95%CI 0.001, 1.007) and fine motor ($\beta = 0.438$, 95%CI 0.023, 0.852) scores in offspring aged 36 months. Maternal tea drinking in the 3rd trimester was associated with a higher cognitive ($\beta = 0.672$, 95%CI 0.044, 1.301) and gross motor ($\beta = 0.443$, 95%CI 0.011, 0.874) scores.

After further adjustment for maternal tea consumption in the 1st trimesters, we have observed a significant association between maternal tea consumption in 2nd trimester of pregnancy and offspring's cognitive development, especially in fine motor ($\beta = 0.436$, 95%CI 0.021, 0.851). After further adjustment for maternal tea consumption in the 1st trimesters, we have observed a significant association between maternal tea consumption in 3rd trimester of pregnancy and offspring's cognitive development, especially in cognition

Characteristics	Distributions
Demographic characteristics	
Maternal educational level [n (%)]	
Junior high school or below	8(0.6)
Senior middle school	507(35.6)
Junior college or above	908(63.8)
Annual household income (million yuan)*[n (%)]	
<5	192(13.5)
5–10	698(49.1)
10–20	412(29.0)
20–30	95(6.7)
>30	24(1.7)
Maternal characteristics	
Maternal age, years (Mean \pm SD)	28.7 \pm 4.0
Body mass index before pregnancy*[n (%)]	
Underweight (BMI < 18.5)	227(16.0)
Normal weight (18.5 \leq BMI < 24.9)	1028(72.2)
Overweight obesity (BMI \geq 24.9)	164(11.5)
Maternal occupation [n (%)]	
Brain work	637(44.8)
Manual work	509(35.8)
Other	88(6.2)
No work	189(13.3)
Smoking during pregnancy*[n (%)]	
Yes	30(2.1)
No	1389(97.6)
Passive smoking*[n (%)]	
Never	450(31.7)
Once in a while	632(44.5)
Nearly everyday	337(23.7)
Alcohol during pregnancy*[n (%)]	
Yes	352(24.7)
No	1067(75.0)
Vomiting during pregnancy*[n (%)]	
Yes	987(69.6)
No	432(30.4)
Folic acid consumption during pregnancy*[n (%)]	
Yes	1091(76.7)
No	307(21.6)
Hypertension during pregnancy*[n (%)]	
Yes	13(0.9)
No	1302(91.5)
Diabetes mellitus during pregnancy*[n (%)]	
Yes	317(22.3)
No	998(70.1)
Pregnancy anxiety level*(Mean \pm SD)	39.5 \pm 8.0
Pregnancy depression level*(Mean \pm SD)	13.7 \pm 7.9
Pregnancy stress level*(Mean \pm SD)	12.8 \pm 5.4
Children's characteristics	
Age*(Mean \pm SD)	2.9 \pm 0.3
Gender*[n (%)]	
Boys	752
Girls	668
Continued	

Characteristics	Distributions
Gestational weeks*(Mean ± SD)	38.9 ± 1.4
Neonatal weight (g)*(Mean ± SD)	3353.2 ± 463.4
Exclusive breastfeeding for 6 months*[n (%)]	
Yes	633(44.5)
No	603(49.4)

Table 1. Baseline characteristics of participants. *Missing data *BMI* body mass index; *SD* standard deviation

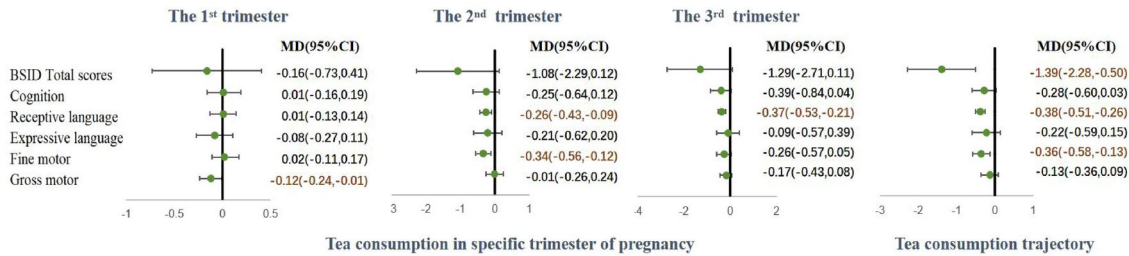


Fig. 4. Independent samples t-test results of maternal tea consumption and cognitive development in 36-month-old children.

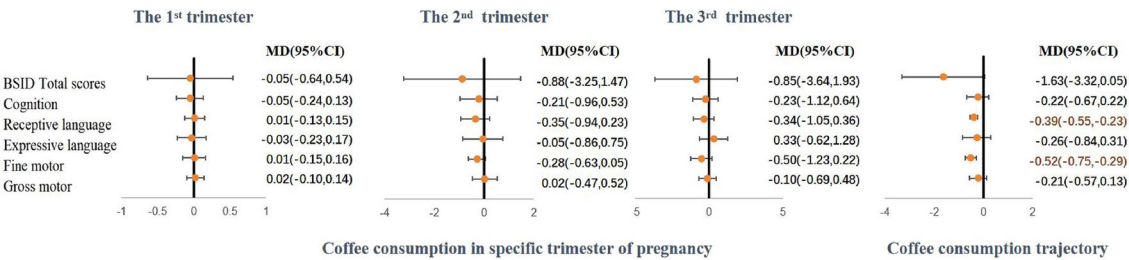


Fig. 5. Independent samples t-test results of maternal coffee consumption and cognitive development in 36-month-old children.

($\beta = 0.678$, 95%CI 0.050, 1.307) and gross motor ($\beta = 0.448$, 95%CI 0.017, 0.880). After further adjustment for maternal tea consumption in the 2nd trimesters, we have observed a significant association between maternal tea consumption in 3rd trimester of pregnancy and offspring's cognitive development, especially in gross motor ($\beta = 0.508$, 95%CI 0.048, 0.967).

Figure 6/ Table S7 showed the results of the linear regressions between the maternal tea consumption trajectory and the cognitive development of 36-month-old children. Compared to mothers who complied with tea drinking in the first trimester trajectory, children of mothers with a continuous tea drinking trajectory had higher cognition ($\beta = 0.701$, 95%CI 0.099, 1.302), fine motor ($\beta = 0.485$, 95%CI 0.003, 0.973) and gross motor ($\beta = 0.429$, 95%CI 0.026, 0.831) scores.

Association between maternal coffee consumption during pregnancy and children's cognitive development

As shown in Fig. 7, Table S4-7. After controlling for important confounders, we did not observe a significant association between maternal coffee drinking during pregnancy and children's cognitive development.

Sensitivity analyses

No significant association between interaction of children's gender and maternal tea/coffee consumption with children's neurodevelopment was observed (Table S8/S9). Our findings remained stable after further controlling for potential intermediary factors and precision variables. (Table S10/S11/S12/S13).

Discussion

Our study supports a positive association between maternal tea consumption during pregnancy and cognitive development in 36-month-old children. Children of mothers with continuous tea drinking trajectory throughout pregnancy had higher cognition, fine motor, and gross motor scores than those with a trajectory of tea-drinking in the 1st trimester of pregnancy. Comparison of tea-drinkers (yes/no) in specific trimester of pregnancy

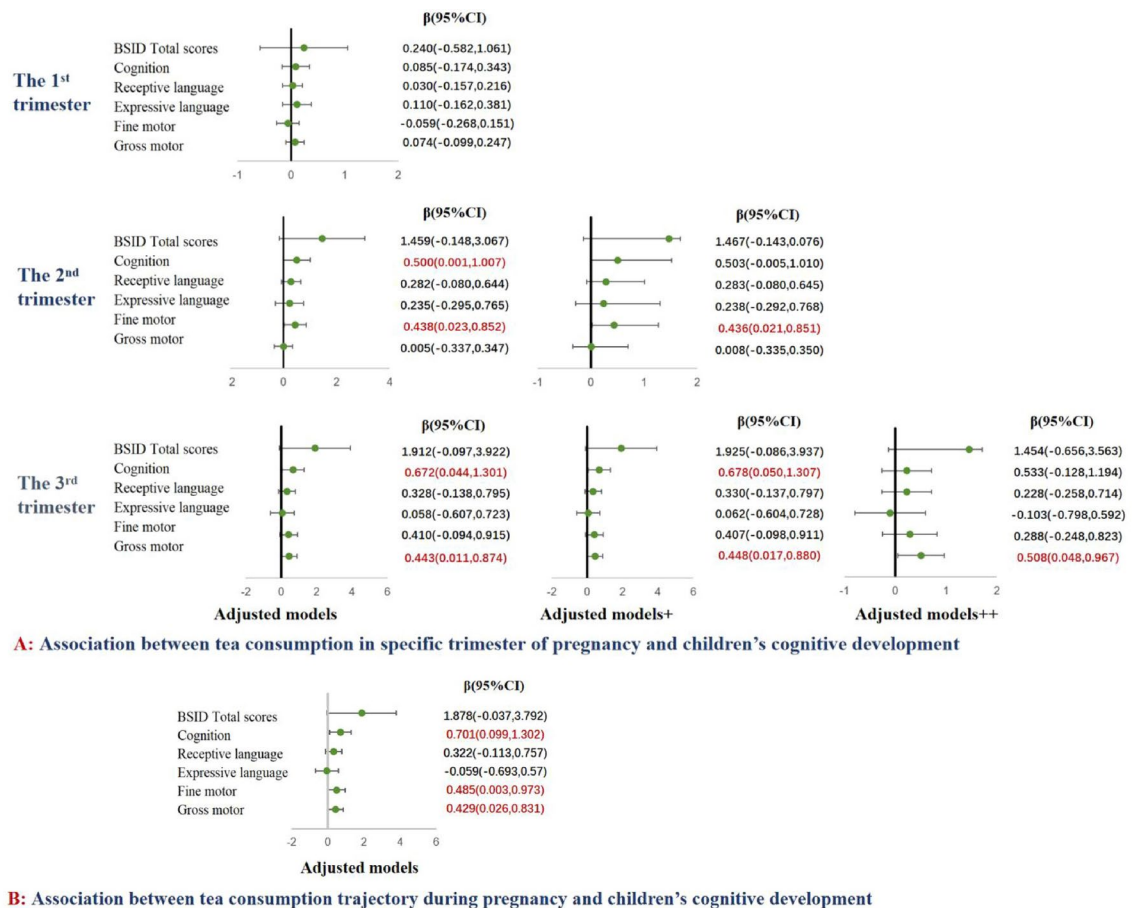


Fig. 6. Linear regression results of the association between maternal tea consumption during pregnancy and children's cognitive development. Adjusted models: Adjusting for the confounding factors such as maternal age, pre-pregnancy BMI, maternal occupation before pregnancy, family income, education level, maternal smoking, passive smoking, alcohol consumption, anxiety, depression, stress, and pregnancy vomiting; Adjusted models + : Further adjusted for Adjusted models + maternal tea consumption in the 1st trimesters; Adjusted models + + : Further adjusted for Adjusted models + maternal tea consumption in the 2nd trimesters.

indicated that tea-drinking in the second and third trimesters were strongly associated with children's cognitive development. No significant associations were found between maternal coffee consumption during pregnancy and children's cognitive development.

For the general population, two previous meta-analyses indicated that moderate consumption of caffeinated tea and coffee may reduce the risk of cognitive impairment^{51,52}. Tea and coffee are essential sources of caffeine (1,3,7-trimethyl xanthine). Caffeine readily crosses biological membranes, including the blood-brain barrier and placental barrier, and can enter the amniotic fluid and breast milk⁶. Epidemiological studies have reported inconsistent findings on the association between maternal caffeine intake and cognitive disorders in children. Most studies have reported the adverse effects of caffeine consumption during pregnancy^{15–20}. Studies have shown that intrauterine caffeine exposure is associated with changes in the cortical network of the visual cortex and deleterious cognitive developmental outcomes, such as externalization, internalization, somatization, abnormal neurodevelopment, inattention, hyperactivity, and daydreaming in children aged 9–10 years¹⁸. In a study based on the Eden mother-child cohort, prenatal caffeine exposure was reported to affect IQ in children aged 5.5 years¹⁵. The Danish National Birth Cohort study also suggested that maternal caffeine consumption during pregnancy may contribute to behavioral disturbances in offspring aged 11 years¹⁶. Marisa et al.¹⁷ indicated that gestational caffeine intake might be a marker of vulnerability to childhood Autism Spectrum Disorder(ASD)-related behaviors. However, results from the Norwegian Mother, Father and Child Cohort study showed that low-to-moderate caffeine intake during pregnancy was not related to any persistent negative influences on behavior, temperament, motor development, or language development in children under eight years of age²³. The effects of caffeine are dose-dependent⁵³. Currently evidence suggests that pregnant women should limit coffee consumption to ensure that daily caffeine intake does not exceed 200 mg/day, in line with recommendations from the European Food Safety Authority (EFSA) and other regulatory bodies^{15,54}. The relevant biological mechanisms involve caffeine as a nonselective antagonist of A1 and A2A adenosine receptors while stimulating cholinergic neurons. Blocking A2A receptors could potentially protect against amyloid- β -induced cognitive deficits⁵⁵, yet excessive or insufficient activation of the adenosine system activity may hinder

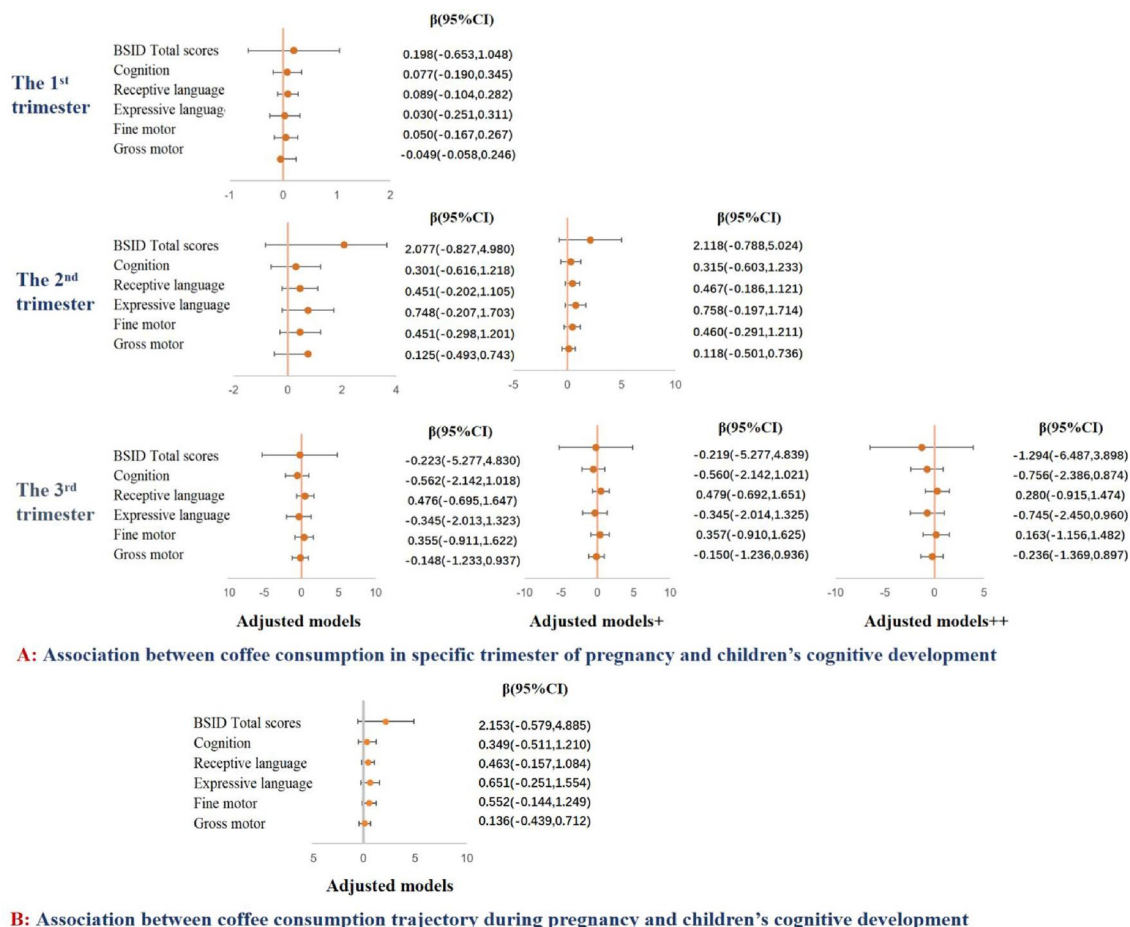


Fig. 7. Linear regression results of the association between maternal coffee consumption during pregnancy and children's cognitive development. Adjusted models: Adjusting for the confounding factors such as maternal age, pre-pregnancy BMI, maternal occupation before pregnancy, family income, education level, maternal smoking, passive smoking, alcohol consumption, anxiety, depression, stress, and pregnancy vomiting; Adjusted models + : Further adjusted for Adjusted models + maternal coffee consumption in the 1st trimesters; Adjusted models + + : Further adjusted for Adjusted models + maternal coffee consumption in the 2nd trimesters.

normal cognitive function⁵⁶. Hence, it is advisable for pregnant women to consume caffeine-containing foods, such as tea and coffee, within the recommended limits, and avoid excessive consumption.

We did not find negative neurodevelopmental outcomes in children caused by maternal coffee intake during pregnancy. The lack of association between maternal coffee consumption and offspring's neurodevelopment warrants further concern, especially given the generally higher caffeine content of coffee compared to tea⁴. It is speculated that caffeine may only be harmful at high doses⁵³. A dose-response meta-analysis of nine cohort studies indicated a "J-shaped" association between coffee consumption and cognitive disorders, with the lowest risk of incident cognitive disorders at a daily coffee intake level of 1–2 cups⁵⁷. While our study did not find an association between coffee intake during pregnancy and adverse neurodevelopmental outcomes in children, it is essential to consider the potential risks associated with high caffeine consumption, as well as individual differences in metabolism.

Owing to the influence of traditional Chinese culture, tea consumption is more widespread among Chinese people than coffee, especially green tea. Another primary ingredient present in tea is polyphenols-catechins, which have neuroprotective effects. The related mechanisms involve the protein-binding action of its component catechins, which prevent abnormal fibrin accumulation⁵⁸. In the present study, we collected different tea types only in early pregnancy; the ratio of green to black tea drinkers during pregnancy was 3:1. We did not observe a significant effect of black or green tea consumption on children's cognitive development compared to pregnant women who drank neither tea nor coffee in the early stages of pregnancy (Table S14). It is reported that, green tea consumption, but not other beverages, such as black tea, is associated with a reduced risk of cognitive decline⁵⁹. A dose-response meta-analysis concluded that the cognitive benefits of green tea consumption increased with daily consumption⁵¹. However, most current studies have focused on the advantages of tea in protecting the cognitive abilities of middle-aged and older adults, including preventing Alzheimer's disease and some degenerative diseases^{60,61}. It is unclear whether tea intake during pregnancy has beneficial effects on cognition in children from prior studies. Our results indicated a potential protective association between maternal tea consumption

and offspring cognitive development, although the effect was relatively small. In addition, we found that the late gestational period is likely the key period for the effect of maternal tea consumption during pregnancy on the offspring's neurodevelopment. This assertion is supported by the understanding that late pregnancy represents a critical phase for human fetal brain development⁶². The fetal nervous system might be more sensitive and easily influenced by the external environment at this stage. Observational studies with larger sample sizes and clinical studies are needed to further confirm the association above, as well as to see whether consuming different types of tea during pregnancy has different effects on offspring's cognitive development.

No significant association between interaction of children's gender and maternal tea/coffee consumption with children's neurodevelopment was observed. Although children's cognitive development might be gender-specific^{25,49}, gender might not play a modified effect in the association between maternal tea/coffee consumption and children's cognitive development.

The present study firstly analyzed the association between maternal tea/coffee consumption trajectories and children's cognitive development at 36 months. Group-based trajectory modeling: GBTM enables longitudinal clustering of indicators by identifying individuals with similar developmental trajectories⁶³. Once pregnant, women often become particularly receptive to making behavioral changes for their baby's health²⁴. Lifestyle, modern food habits and nutrition are dynamic throughout pregnancy. The present study used GBTM to fit trajectories to maternal repeated measures of tea/coffee consumption to better predict child development than using data from only a single pregnancy. We found it interesting that children whose mothers maintained a continuous tea-drinking habit during pregnancy were more likely to have higher cognitive development scores than mothers who drank tea in the 1st trimester and discontinued the habit in the 2nd and 3rd trimester. This study provides new epidemiological evidence for mothers who have a tea-drinking habit during pregnancy, suggesting that it may not be necessary to abandon the original tea-drinking habit completely.

Our study has several strengths. First, we collected information on maternal tea/coffee consumption for three repetitions in the 1st, 2nd, and 3rd trimesters. GBTM was employed to model the tea/coffee consumption trajectory to better reflect pregnant women's tea/coffee intake situation and trends, which provides sufficient motivation to investigate its association with cognitive development. Second, we innovatively found a protective effect of continuous tea-drinking trajectory, which has not been reported in other studies. Our findings also provide an initial evidence-based basis for prenatal lifestyle health education in obstetrics clinics, although a larger sample is needed to confirm this result. Third, our study was based on a prospective birth cohort, and the data used in the analysis were obtained through follow-up questionnaires, including exposure, outcome variables, and confounding factors, which effectively reduced the recall bias. Finally, precision variables affecting cognitive development were considered in the sensitivity analyses to increase the precision of the findings.

There were, of course, some limitations in this study. The specific amounts or cups of coffee and tea that pregnant women have consumed have not been measured. The frequency of drinking, however, does not directly reflect actual intake. The findings on the association between maternal tea/coffee consumption and children's neurodevelopment might be overestimated or underestimated in this study. The relevant components of tea and coffee consumed by pregnant women, such as caffeine and catechins, have not been precisely quantified. Therefore, we could only speculate on the mechanism of association based on previous studies and were not able to determine exactly which ingredient in either tea or coffee was responsible for the findings. Tea categorization was collected only in early pregnancy, but the significance of different tea types for child neurodevelopment may vary. This variation may be attributed to the distinct compositions of different types of tea. For instance, a single cup of black tea (220 mL) typically contains approximately 50 mg of caffeine⁴. Generally, green tea contains less caffeine compared to black tea, but the specific amount may vary depending on the tea brand, brewing time, and water temperature⁵. Differences in tea drinking habits are likely to vary by populations and countries. Approximately 76–78% of the tea produced and consumed worldwide is black tea, 20–22% is green tea, and less than 2% is oolong tea. Black tea is mainly drunk in Europe, North America, and North Africa (except Morocco), whereas green tea is consumed principally in Asia, and oolong tea is popular in southeast China⁶⁴. Our study was based on a cohort study in China, with limitations in extrapolating the results to populations other than Chinese. The overall sample size of this study was limited. Although we tested the robustness of the findings through multiple sensitivity analyses, findings in this study still need to be validated in large study samples. In addition, observational studies are limited in inferring causality, so more in-depth trials are needed to validate the results of this study. Besides the confounders already considered in the analyses, some residual confounders could not be ruled out. For instance, it has been demonstrated that maternal dietary patterns in the second and third trimesters are associated with cognitive development in infants⁶⁵.

Conclusion

This study suggests that maternal tea consumption during pregnancy may be associated with improved cognitive development in children. The second and third trimesters appear to be key periods in this association.

Data availability

The data are not publicly available due to privacy restrictions. If required, the data that support the findings of this study are available on request from the corresponding author.

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Author contributions

JO and KH designed the study. JO, PW and LC designed the analysis plan. JT was involved in the cohort data collection. SY was the cohort leader. FT provided data management. JO, JT processed and analyzed the data. PW involved in the literature collection. JO prepared the first draft of the manuscript. KH was the cohort site leader, reviewed, revised the first draft, supervised, and led the study. JL has provided the Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III) and critically revised important intellectual content. All authors have read and approved the final manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethical approval

This study was approved by the Ethics Committee of Anhui Medical University (Number: 20160270, 30 March 2016).

Informed consent

Informed consent was obtained from all participants involved in the study.

Additional information

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