BMC Pediatrics

RESEARCH

Open Access

Prenatal risk factors for child executive function at 3–5 years of age: the roles of maternal mood, substance use, and socioeconomic adversity in a prospective cohort study

Yael K. Rayport[1], Santiago Morales[2], Lauren C. Shuffrey[3], Christine W. Hockett[4,5], Katherine Ziegler[4,5], Shreya Rao[1], William P. Fifer[1,6,7], Amy J. Elliott[4,5] and Ayesha Sania[1*]

Abstract

Background A growing body of literature links prenatal mood and substance use to children's cognitive and behavioral development. The relative contribution of these risk factors on children's executive function (EF) in the context of socioeconomic adversities needs further evaluation. To address this gap, we investigated the role of prenatal maternal anxiety and depression on childhood EF, specifically inhibitory control and working memory, within the context of socioeconomic adversities and prenatal substance use. We hypothesized that higher maternal mood symptoms, higher persistent prenatal drinking and smoking, and lower socioeconomic status would be associated with lower EF skills during early childhood.

Methods We used data from 334 mother–child dyads followed prospectively through pregnancy and the offspring's childhood. Prenatal maternal depression and anxiety were assessed via standardized questionnaires. Prenatal alcohol and tobacco consumption were assessed via a timeline follow-back interview. The EF touch battery assessed child inhibitory control and working memory at 3–5 years of age (4.76 ± 0.58 years, 171 females). Separate linear regression models were used to estimate the association of prenatal tobacco, alcohol, anxiety, and depression exposure with our two components of child EF, inhibitory control and working memory, while adjusting for gestational age, sex, and age at assessment. The following variables were also included as covariates: maternal educational achievement, employment status, parity, and household crowding index.

Results Children of mothers with high trait anxiety scores had reduced inhibitory control compared to children of mothers without trait anxiety or depression (β = -0.12, 95% CI:-0.22,-0.01). Children of mothers in the moderate to high continuous smoking group showed lower inhibitory control (β = − 0.19, 95% CI:-0.38,-0.01) compared to children of mothers in the none smoking group. Additionally, lower maternal education and higher household crowding were each associated with reduced inhibitory control. We found no significant association between prenatal maternal depression, anxiety, or socioeconomic factors with working memory.

*Correspondence:
Ayesha Sania
as4823@cumc.columbia.edu
Full list of author information is available at the end of the article

Conclusions These results underscore the need for comprehensive context-specific intervention packages, including mental health support for women to promote healthy inhibitory control development in children.

Keywords Prenatal anxiety, Prenatal depression, Prenatal alcohol and tobacco exposure, Socioeconomic adversity, Executive function, EF touch battery

Background

The development of executive function (EF) in children is influenced by a complex interplay between biological and environmental factors. Maternal mood, including prenatal depression and anxiety, are proximal factors that directly affect childhood EF. A growing body of literature has established a link between variations in prenatal mood and EF difficulties in offspring [1, 2]. Furthermore, prenatal anxiety and depression are often comorbid with substance use, such as alcohol and tobacco, which can independently contribute to adverse outcomes in child EF development [3–5]. Proxies of low socioeconomic status (SES) have also been found to exacerbate maternal mood disruptions and substance use [6, 7], as well as directly impede child EF [8]. Nonetheless, there remains a dearth of research examining the relative contribution of these prenatal exposures within socioeconomically diverse samples.

EF serves as an "umbrella term" for higher-order cognitive processes that regulate cognitive control and goal-directed behavior [9]. Leading frameworks in EF development highlight three primary components [10]. The first is inhibitory control, which involves controlling or restraining one's instinctual responses as well as interference control at the level of perception. The second component is working memory, which comprises the ability to remember and manipulate information during a short period of time without aids or cues. The third component is cognitive flexibility, which is the capability to switch between mental states, rules, or tasks [10, 11]. EFs emerge soon after birth and as children mature, EF components develop, but at different rates [12]. EF skills undergo rapid development between the ages of 3 and 6, with inhibitory control and working memory postulated as the first components to differentiate [11, 13]. EF skills have significant implications on children's success, significantly influencing their physical and mental health, academic achievement, and positive behaviors [14–16].

The prefrontal cortex is considered to be one of the neural substrates through which EF develops [17]. It is one of the last brain regions to fully mature and is therefore considered to exhibit high levels of plasticity throughout childhood and adolescence [18]. The prenatal environment plays a significant role in influencing prefrontal cortex development and, consequently, child EF through various pathways [19–21]. Maternal prenatal anxiety, depression, and substance exposure affect the developing brain via "fetal programming" mechanisms: in-utero exposures that cause the fetus to undergo adaptive responses affecting future behavior and biology [19]. Socioeconomic stressors during pregnancy, such as low household income or higher household crowding indexes, can contribute to maternal inflammatory processes and cortisol production by altering hypothalamic-pituitary axis function. These changes can have downstream effects on child brain development, including brain regions related to EF [20]. Maternal mood disorders also impact child EF development postnatally through parenting behavior and parent–child interactions [21].

Previous studies examining the early life risk factors of EF lack one of these three aspects: 1) studies did not examine the relative contribution of all three prenatal factors, namely maternal mood, substance use, and SES, within an integrated framework. Several previous studies that investigate one or more of these prenatal risk factors, such as the effects of drinking and smoking, tend to be cross-sectional rather than prospective in nature [4, 22, 23]. Moreover, studies exploring maternal anxiety and childhood EF have yet to examine state- and trait anxiety independently. A recent meta-analysis by Delagneau et al. found that prenatal maternal anxiety has a weak negative association with child cognitive development, with the caveat that more research is needed to distinguish between different types of prenatal anxiety (trait anxiety, state anxiety, pregnancy-specific anxiety, or general perceived stress) [24]. 2) Studies examining prenatal risk factors and childhood EF tend to have small sample sizes, ranging between 60–173 children [8, 25]. 3) Lastly, many prior studies have relied on subjective measures of childhood EF (e.g., parent or teacher reports), which can introduce biases [3, 26]. To address these gaps, we investigated the role of prenatal maternal state- and trait anxiety, as well as prenatal maternal depression, on children's EF within the context of socioeconomic adversities and prenatal substance use. We conducted this study among socioeconomically diverse mother–child dyads recruited as part of an *Environmental Influences on Child Health Outcomes* (ECHO) cohort in South Dakota [27, 28]. We assessed children's EF using an objective measure, the EF touch battery, at 3–5 years of age [29]. We hypothesized that higher maternal mood symptoms, higher persistent

prenatal drinking and smoking, and lower socioeconomic status would be associated with lower EF skills during early childhood.

Methods

Study design and participants

From September 2018 through November 2022, 3,312 parent–child dyads were enrolled in the National Institute of Health's (NIH) Environmental influences on Child Health Outcomes (ECHO) Research Program. Participants in the present follow-up study were originally enrolled in the Safe Passage Study conducted by the Prenatal Alcohol and SIDS and Stillbirth (PASS) Network, which recruited 11,892 pregnant women and investigated the effects of prenatal exposure to alcohol and tobacco use in perinatal outcomes and child neurodevelopment [30]. Participants were recruited from clinical sites in the Northern Plains (NP), USA ($N=4,989$) or Cape Town, South Africa ($N=6,903$) at approximately 12–28 weeks of gestation. Eligibility criteria for PASS included being 16 years of age or older at the time of consent and having a fetal gestational age between 6–40 weeks at the time of consent. Exclusion criteria included planned therapeutic abortion, moving from the area prior to the estimated date of delivery, and clinical judgment of medical risk [30].

In the present study, a subset of the PASS participants was followed as part of the ECHO Program from two research sites in South Dakota, USA (Sioux Falls and Rapid City). At 3–5 years of age, children underwent evaluation for EF. To be included in this analysis, participants had to have EF data from both the inhibitory control and working memory EF tasks as well as complete prenatal exposure data which was originally collected as part of PASS ($N=334$). Three hundred thirty-four parent–child dyads were included in the current analysis (Fig. 1).

Sociodemographic information of the study participants is presented in Table 1. The majority of mothers identified as White (75%) or American Indian / Alaskan Native (24%). Most of the mothers had educational achievements beyond high school (79%), were employed (78%), were married (89%), and had a mean (SD) household crowding index of 0.62 (SD 0.46) persons per room. For the majority of women, this was their first or second pregnancy (60%) and the most common pre-pregnancy body mass index (BMI) was obese (40% had a BMI > 30). A small proportion of the women had clinical levels of depression (Edinburgh Postnatal Depression Scale (EPDS) > 13) (6.82%), state anxiety (State-Trait Anxiety Inventory (STAI) > 40) (4.46%), or trait anxiety (STAI > 40) (10.71%). Many of the pregnant women with prenatal alcohol use ceased drinking during the first trimester of pregnancy (43.36%). Pregnant women who smoked tobacco during pregnancy tended to smoke at a low-continuous level (7.31%). The cluster groups for prenatal alcohol and tobacco exposure were derived using the greater PASS cohort, which has previously been described [31]. By using the cluster groups, we can better capture the quantity as well as the timing of substance use during pregnancy. Within the greater cohort, the moderate to high continuous group, the low continuous group, the quit early group, and the non-drinkers group consumed 40.89 (SD = 60.08), 2.41 (SD = 3.83), 8.77 (SD = 7.41), and 0.04 (0.16) drinks in the first trimester, respectively. Regarding smoking in the first trimester, the moderate to high continuous group, the low continuous group, the quit early group, and the non-smoking group, smoked 48.31 (SD 21.71), 15.72 (SD 10.28), 8.81 (SD 9.92), 0.014 (SD 0.08) cigarettes on average per week, respectively [32].

Maternal characteristics

Maternal mood

Maternal prenatal depressive symptoms were measured at 20–24 weeks gestation with the Edinburgh Postnatal Depression Scales (EPDS). The EPDS is a 10-item screening tool assessing depressive symptoms in perinatal women with a higher score indicating more depressive symptoms [33]. An EPDS score ≥ 13 has been shown to be a sensitive and specific indicator of major depression in prior studies [34]. Maternal prenatal anxiety was assessed at 28–32 weeks gestation with the State-Trait Anxiety Inventory Scale (STAI). The STAI comprises two 20-item subscales: state-anxiety (one's current state of anxiety) and trait anxiety (anxiety attributed to one's personality). Higher scores on the STAI indicate more anxiety symptoms [35]. A cut-off score of > 40 on each subscale indicates clinical levels of state or trait anxiety [36]. The STAI has been widely validated to assess anxiety in perinatal women [37]. In this cohort, state and trait anxiety were highly correlated with depression and were therefore analyzed in tandem. Our sample showed lower rates of depressive and anxiety symptoms compared to the larger PASS cohort. Specifically, only 7% of our sample had an EPDS > 13, whereas 32% of the larger cohort exceeded this threshold [38]. Similarly, our sample had a smaller proportion of participants with anxiety than the larger PASS cohort (STAI > 40). Specifically, while 4% of our sample had high state anxiety and 11% had high trait anxiety, the corresponding portions in the greater PASS cohort were 10% and 17%, respectively, suggesting that pregnant women included in our analysis were lower risk.

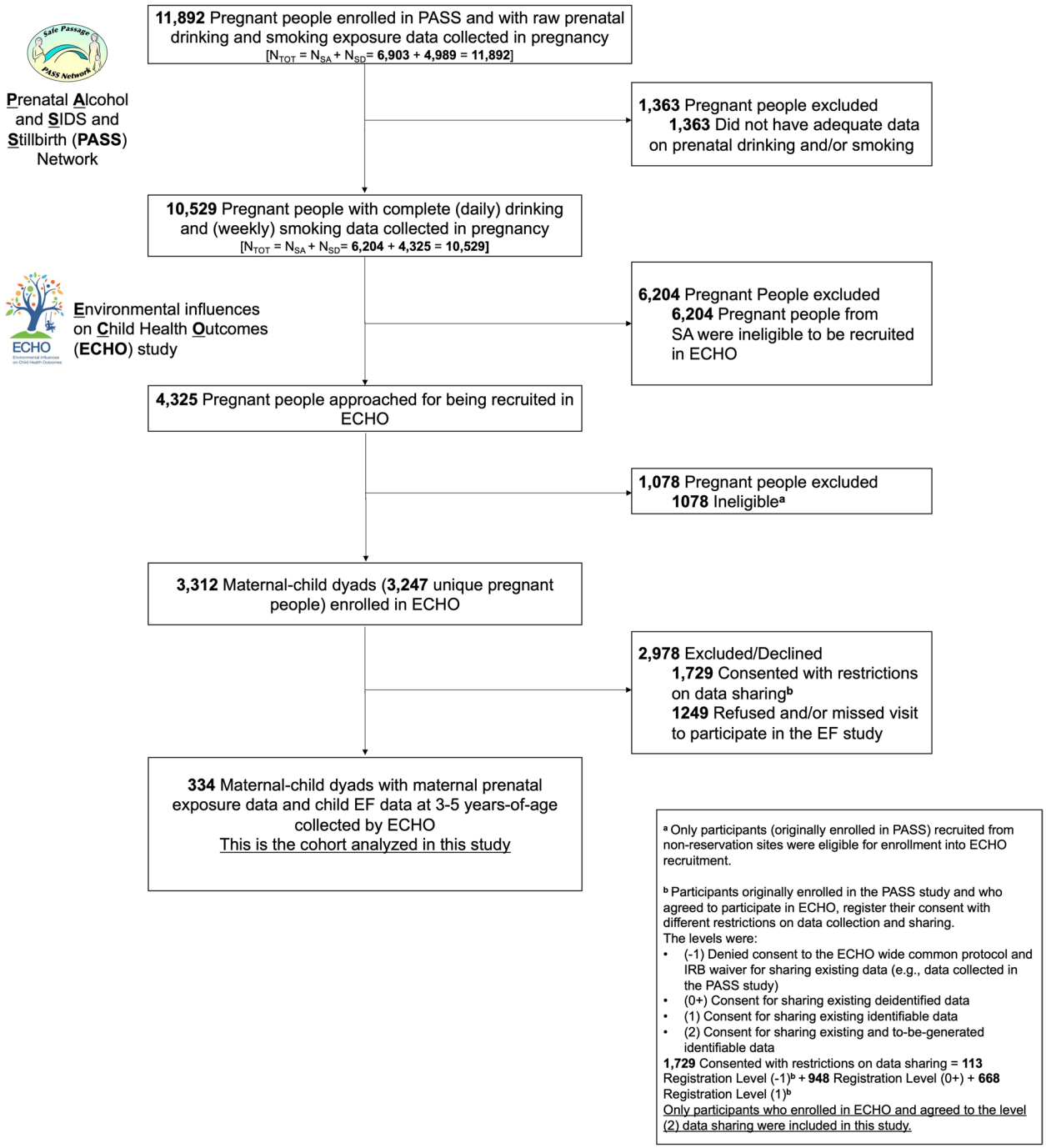

Fig. 1 CONSORT diagram

Substance use

To measure prenatal alcohol and tobacco exposure, a validated modified version of the 30-day timeline follow-back method was used [39]. Up to four times during pregnancy, women reported their most recent drinking or smoking day and the 30-days prior to it. Women described the quantity and frequency of alcohol and cigarette consumption. The information was used to estimate the total number of grams of alcohol consumed per day of pregnancy and the average number of cigarettes smoked per week of pregnancy. Missing alcohol and weekly smoking data was imputed by a nonparametric machine learning algorithm, the k-nearest neighbor approach, where a missing data point was imputed based

Table 1 Sociodemographic maternal and child characteristics

Characteristics	Demographics Variables	N ± SD or N (%)
Maternal	**Age (years)**	29.08 ± 5.03
	Race	
	White	257 (75.15)
	American Indian or Alaska Native	82 (23.98)
	Other/Unknown	3 (0.88)
	Education	
	Primary school education	2 (0.58)
	Some high school education	28 (8.19)
	High school completed	42 (12.28)
	Higher than high school	270 (78.95)
	Employment status	
	Unemployed	76 (22.22)
	Employed	266 (77.78)
	Marital status	
	Unmarried	39 (11.4)
	Married/Cohabiting	303 (88.6)
	Household crowding index (persons/room)	0.62 ± 0.46
	Height (cm)	166.27 ± 7.1
	Pre-pregnancy body mass index	
	< 18.5	6 (1.75)
	18–25	96 (28.07)
	25–30	102 (29.82)
	> 30	138 (40.35)
	Missing	4 (1.17)
	Parity	
	0	98 (28.65)
	1	108 (31.58)
	2	71 (20.76)
	3 or more	65 (19.01)
	Prenatal alcohol use	
	No alcohol	167 (49.26)
	Quit early	147 (43.36)
	Low continuous	7 (2.06)
	Moderate to high continuous	18 (5.31)
	Prenatal tobacco use	
	No smoking	290 (84.8)
	Quit early	16 (4.68)
	Low continuous	25 (7.31)
	Moderate to high continuous	11 (3.22)
	Depression (EPDS > 13)	
	Not clinically depressed	314 (93.18)
	Clinically depressed	23 (6.82)
	Missing	5 (1.46)
	State anxiety (STAI > 40)	
	Low state anxiety	321 (95.54)
	High state anxiety	15 (4.46)
	Missing	6 (1.75)
	Trait anxiety (STAI > 40)	
	Low trait anxiety	300 (89.29)
	High trait anxiety	36 (10.71)
	Missing	6 (1.75)
	Depression and state anxiety (4 group variable)	
	No depression or state anxiety	303 (90.18)
	Depression but no state anxiety	18 (5.36)
	State anxiety but no depression	10 (2.98)
	Depression and state anxiety	5 (1.49)
	Missing	6 (1.79)
	Depression and trait anxiety (4 group variable)	
	No depression or trait anxiety	290 (86.31)
	Depression but no trait anxiety	10 (2.98)
	Trait anxiety but no depression	23 (6.85)
	Depression and trait anxiety	13 (3.87)
	Missing	6 (1.79)
	Anti-depressant medication	
	No	301 (89.58)
	Yes	35 (10.42)
	Missing	6 (1.79)
	Anti-anxiety medication	
	No	326 (97.02)
	Yes	10 (2.98)
	Missing	6 (1.79)
Child	**Sex**	
	Female	170 (49.85)
	Male	171 (50.15)
	Gestational age at birth	38.79 ± 2.15
	Birthweight	
	Low birthweight (< 2500 g)	42 (12.32)
	Normal birthweight (≥ 2500 g)	299 (87.68)
	Birthweight (grams)	3387.09 ± 614.91
	Age at assessment (years)	4.74 ± 0.60
	Inhibitory control score (SSS)	0.7 ± 0.28
	Working memory score (PTP)	0.74 ± 0.11

on data from a participant's own drinking or smoking trajectory and data from similar participants [40]. The PASS cohort ($N = 11{,}083$) was used to derive substance use clusters based on alcohol and tobacco use trajectories [31]. Given the smaller PASS-ECHO cohort, the clusters were collapsed into four alcohol (moderate to high continuous, low continuous, quit early, and no alcohol) and tobacco (moderate to high continuous, low continuous, quit early, and no smoking) groups. Compared to the greater PASS cohort, our sample was considered

low risk for substance use exposure. In our sample, 51% of our participants consumed alcohol and 15% smoked. Meanwhile, in the greater PASS cohort, 61% of participants reported drinking and 56% reported smoking during pregnancy [38].

Demographics

Study specific demographic questionnaires were administered at enrollment to ascertain maternal education level (beyond high school, completed high school, some high school, or some primary school), employment status (employed versus unemployed), marital status (unmarried versus married/cohabitating, household crowding index (ratio of number of people per room in a household), parity (0, 1, 2, 3 or more), and pre-pregnancy BMI (< 18.5, 18–25, 25–30, > 30).

Child characteristics

Child characteristics were collected at birth via medical record chart abstraction. Variables of interest included birth weight, gestational age at birth, and sex. Child age at assessment of executive function was recorded during the laboratory visit.

Executive function

The EF touch battery was administered in a single study visit to children between 3–5 years of age to assess inhibitory control and working memory [29]. This battery is a computerized adaptation of previous EF assessments that were paper–pencil-based [17] and has been validated within low-income populations [41]. Two of the EF touch battery tasks were chosen for this study to capture important components of EF: inhibitory control and working memory. The first EF assessment was the Silly Sounds Stroop (SSS) task which assesses inhibitory control of a prepotent response. In this task, children are presented with two pictures on a tablet—one of a cat and one of a dog. In each trial, either a dog bark or a cat meow is played. The children were instructed to touch the picture of the cat when they heard a dog bark and vice versa. This task required children to overcome a highly learned response. The inhibitory control score was determined by the percentage of trials in which children correctly matched the animal sound with the opposite animal picture.

The other EF assessment was a self-ordered pointing task testing working memory, called Pick the Picture (PTP). In this task, children were shown picture sets, which increased in size (2,3,4,6 pictures). For each set, children were initially instructed to touch any picture. The same set was then presented multiple times, with the pictures' locations randomized each time. Children were instructed to touch a new picture each time, ensuring that "all the pictures get a turn." To successfully complete the task, children were required to recall which pictures they had previously touched and select a new one each time. The working memory score was calculated based on the proportion of series in which a unique picture was selected every time [29]. As programed in the EF touch software, the working memory task (PTP) was always administered prior to the inhibitory control task (SSS).

Statistical analysis

Participant characteristics were examined using descriptive statistics. Multiple linear regression models were employed to evaluate the association between prenatal state-trait anxiety, depression and socio-economic indicators with inhibitory control and working memory scores. State- and trait anxiety were highly correlated with each other and with depression thus a four-category variable was created for each anxiety type. For state anxiety the following groups created were, 1) no depression or state anxiety, 2) state anxiety but no depression, 3) depression but no state anxiety, and 4) depression and state anxiety. The same four groupings were repeated for trait anxiety. In multivariate models, the four-category state anxiety-depression variable was run in a separate model from the four-category trait anxiety-depression variable to avoid representing depression twice in the model. Univariate models were initially conducted to predict EF scores, separately for the two EF tasks (inhibitory control and working memory). Predictor variables significant at $p = 0.2$ in univariate analysis were included in the multivariate models, including the four-category anxiety-depression variable, prenatal alcohol and tobacco use, educational achievement, employment status, parity, and household crowding index. Maternal pre-pregnancy BMI and marital status were not significant at the $p = 0.2$ level and were not including in the multivariate models. This entry criteria of $p = 0.2$ is a standard cutoff in statistical modeling, allowing for a more inclusive approach to variable selection [42]. In the final multivariate model, statistical significance was set at $p < 0.05$. Missing covariate values were replaced with a "missing" indicator and included in the multivariable models. All models were adjusted for biological sex (male or female), gestational age at birth, and age at EF assessment, regardless of p-value. Child sex and age at assessment are known predictors of child EF and hence were covariates in all models [43–45]. All analyses were performed in SAS software version 9.4 (SAS Institute, Cary NC).

Results

Participants in the current analysis consisted of 334 mother–child dyads. For inhibitory control, children's average performance on the task was 0.7 ± 0.28. For

working memory, children's average performance on the task was 0.74 ± 0.11 (Table 1). Previous studies utilizing the EF Touch protocol have reported similar ranges for their respective cohorts [46, 47]. The distribution of performance was normally distributed within age bands. The inhibitory control score was slightly skewed, as more children performed well overall, but the mean and median were similar for inhibitory control (mean = 0.70 (SD = 0.27), median = 0.76) and working memory (mean = 0.73 (SD = 0.10), median = 0.75). Female children tended to perform better than male children on both tasks (inhibitory control Female: 0.71 ± 0.28, Male: 0.69 ± 0.27; working memory Female: 0.75 ± 0.1, Male: 0.72 ± 0.11) (data not shown). EF scores on the inhibitory control and working memory tasks were weakly correlated with each other. A similar correlation effect has previously been found between the inhibitory control and working memory tasks within 5-year-old children [29]. The inhibitory control and working memory scores were moderately positively correlated with child age at assessment (inhibitory control: r(334) = 0.43, $p < 0.0001$; working memory: r(334) = 0.40, $p < 0.0001$). As observed in other studies, EF and age at assessment are correlated [43, 44]. Maternal prenatal depression was moderately correlated with both prenatal state- and trait anxiety. Maternal depression was weakly correlated with child Inhibitory control. Maternal trait anxiety was weakly correlated with child Inhibitory control and working memory. Indicators of SES were also weakly correlated with child inhibitory control, including maternal, employment and household crowding indexes. Maternal sociodemographic, prenatal exposure, and child EF data are described in Table 1. See Table 2 for a correlation table of all the exposure variables.

Maternal mood

We found significant associations between prenatal trait anxiety and childhood EF. Children of mothers with trait anxiety had lower inhibitory control scores compared to children of mothers who did not have trait anxiety nor depression (β = -0.12, CI = -0.23, -0.01, $p = 0.04$) (Fig. 2). In our sample, 11% of mothers met the clinical threshold for trait anxiety [36]. 4.5% of mothers met the clinical threshold for state anxiety and 7% for depressive symptoms. Maternal state anxiety and depression were not associated with inhibitory control or working memory (Table 3).

Maternal substance use

We observed significant associations between prenatal tobacco use and childhood EF, but not alcohol use. Children of mothers in the moderate to high continuous smoking group had lower inhibitory control scores compared to children of mothers in the unexposed group (β = -0.20, CI = -0.39, -0.01, $p = 0.04$) (Fig. 3). Children of mothers in the low continuous (β = -0.01, CI = -0.13, 0.11, $p = 0.85$) or quit early smoking groups performed similarly (β = 0.06, CI = -0.07, 0.20, p = 0.36) on the EF tasks as children of mothers in the none smoking group (Fig. 3). All levels of prenatal smoking were not associated with children's working memory. All levels of prenatal drinking were not associated with children's inhibitory control or working memory (Table 3).

Maternal socio-demographics

Some indicators of maternal socioeconomic status were significantly associated with childhood EF. Children of mothers who did not complete high school education showed a mean reduction in child inhibitory control scores compared to children of mothers who completed more than high school education (some high school: β = -0.25, CI = -0.36, -0.13, $p < 0.0001$; some primary school: β = -0.10, CI = -0.19, -0.01, $p = 0.028$) (Fig. 4). Higher crowding indexes were associated with reduced inhibitory control scores β = -0.07, CI = -0.14, -0.01, $p = 0.038$) (Fig. 4). Employment status and marital status were not significantly associated with childhood EF in the minimally adjusted models and were therefore not included in the multivariate model (Table 3).

Discussion

We examined the effects of prenatal maternal anxiety and depression on early childhood EF in the context of substance use and socioeconomic adversities. Consistent with previous literature, we found that maternal prenatal trait anxiety, moderate to high continuous smoking, lower educational achievement, and higher household crowding were each associated with reduced children's inhibitory control scores at 3–5 years of age measured with the EF touch battery. In contrast to previous literature, maternal prenatal depression, and alcohol use were not significantly associated with child inhibitory control or working memory.

Our study is the first to examine the role of prenatal trait- and state anxiety separately on child EF. We found that trait anxiety, but not state anxiety predicted children's inhibitory control. A recent meta-analysis by Delagneau et al. found that prenatal maternal anxiety has a weak negative association with child cognitive development, with the caveat that more research is needed to distinguish between different types of prenatal anxiety (trait anxiety, state anxiety, pregnancy-specific anxiety, or general stress) [24]. Three studies within the meta-analysis and one additional study have

Table 2 Descriptive statistic correlations

Prob > |r| under H0: Rho = 0

	Maternal depression	Maternal trait-anxiety	Maternal state-anxiety	Inhibitory control (SSS)	Working memory (PTP)	Prenatal alcohol exposure	Prenatal tobacco exposure	Child sex	Gestational age at birth	Birthweight	Maternal education	Maternal employment	Household crowding
Maternal depression													
Maternal trait-anxiety	**0.73**												
	<.0001												
Maternal state-anxiety	**0.52**	**0.73**											
	<.0001	**<.0001**											
Inhibitory control (SSS)	**-0.12**	**-0.14**	-0.09										
	0.03	**0.01**	0.09										
Working memory (PTP)	-0.11	**-0.13**	-0.08	**0.32**									
	0.06	**0.02**	0.15	**<.0001**									
Prenatal alcohol exposure	-0.10	-0.05	0.05	0.04	0.06								
	0.08	0.33	0.36	0.50	0.30								
Prenatal tobacco exposure	**0.18**	**0.16**	**0.14**	-0.08	-0.05	-0.01							
	0.00	**0.00**	**0.01**	0.14	0.39	0.82							
Child sex	0.04	0.06	0.07	0.04	**0.13**	-0.01	-0.05						
	0.47	0.27	0.21	0.50	**0.02**	0.87	0.34						
Gestational age at birth	-0.10	-0.02	-0.03	**0.12**	0.09	0.07	**-0.15**	-0.07					
	0.06	0.75	0.59	**0.02**	0.10	0.23	**0.01**	0.21					
Birthweight	-0.10	0.01	-0.04	-0.05	-0.06	-0.05	**-0.12**	**-0.16**	**0.61**				
	0.06	0.92	0.46	0.35	0.30	0.33	**0.02**	**0.00**	**<.0001**				
Maternal education	**-0.14**	**-0.17**	**-0.17**	**0.33**	0.09	0.06	**-0.13**	-0.08	0.10	0.05			
	0.01	**0.00**	**0.00**	**<.0001**	0.11	0.25	**0.02**	0.14	0.06	0.34			
Maternal employment	**-0.12**	-0.10	**-0.11**	**0.13**	0.11	**0.11**	-0.09	0.00	0.01	-0.01	**0.28**		
	0.03	0.06	**0.04**	**0.01**	0.06	**0.03**	0.08	0.98	0.82	0.90	**<.0001**		
Household crowding	**0.18**	**0.19**	**0.24**	**-0.23**	-0.10	-0.10	**0.23**	-0.02	-0.10	-0.05	**-0.37**	**-0.22**	
	0.00	**0.00**	**<.0001**	**<.0001**	0.06	0.06	**<.0001**	0.69	0.07	0.38	**<.0001**	**<.0001**	

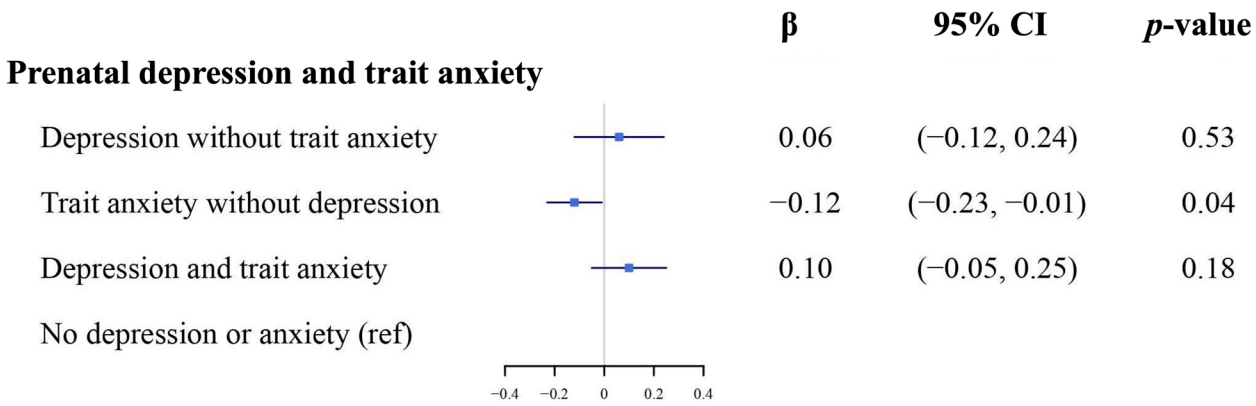

Fig. 2 Association between prenatal maternal depression and trait anxiety with child inhibitory control measured by the EF Touch battery. Each line plot depicts the beta estimates and their 95% CI for inhibitory control (x-axis) and each prenatal maternal trait anxiety and depression group (y-axis). No prenatal maternal depression and trait anxiety served as the reference group. Models were adjusted for prenatal alcohol and tobacco use, educational achievement, employment status, household crowding index, as well as, child biological sex, gestational age at birth, and age at EF assessment

assessed maternal anxiety on childhood EF specifically (i.e., attention shifting, working memory, and inhibition), but only measure general or pregnancy-specific anxiety [1, 48–50]. On the other hand, a few studies have examined separate effects of prenatal trait- and state anxiety on child cognitive development, but not EF [51–53]. The majority of this research was done in high-income urban settings. Thus, our study adds an important contribution to the literature, reporting an association between maternal state-trait anxiety and child EF among children in a socioeconomically diverse population within rural USA.

Contrary to previous findings, our study did not observe a significant association between prenatal maternal depression and childhood inhibitory control or working memory [2]. The vast majority of research examining the association between perinatal depression and child EF, has predominantly focused on the postnatal period [2]. The influence of pre- and postnatal depression on childhood EF are thought to operate through distinct pathways. Postnatal depression is theorized to affect childhood EF through parenting behavior and less secure attachment styles [25]. On the other hand, prenatal depression is hypothesized to impact childhood EF by altering brain development, HPA-axis function, immune function, and autonomic nervous system processes [54]. Existing literature on prenatal depression suggests a dose–response relationship with child EF [54]. In our cohort, only a small percentage (6.8%) of participants met clinical levels of depression, with an average EPDS score of 5.16 ± 4.04, indicating a low-risk cohort. A study with a similar EPDS range of 5.0 ± 3.6 reported no influence of prenatal depression on childhood EF at two-years-of-age [50]. However, another study by Faleschini et al., examining high maternal depressive symptoms during pregnancy, found that exposed children had worse EF [26]. Compared to our cohort, Faleschini et al.'s study had a larger sample of 1225 mother–child dyads, with a higher percentage of the mothers (10%) meeting the threshold for clinical depression (EPDS > 13). Furthermore, in a longitudinal study investigating perinatal depression profiles, it was found that children of mothers in the chronic depression group, experiencing depression both pre- and postnatally, exhibited poorer inhibitory control compared to children of mothers with intermittent or later exposure [54]. Thus, it is possible that we did not observe an effect of prenatal depression on child EF because our cohort had milder depressive symptoms, and symptoms were not assessed postnatally.

Our study confirms previous findings by demonstrating that prenatal maternal smoking has detrimental effects on childhood inhibitory control [4]. In utero tobacco exposure is hypothesized to exert effects on the developing brain via multiple pathways. Nicotine, a key component of tobacco smoke, can disrupt central-nervous system development, particularly neuronal differentiation, thus affecting brain structure and function. Additionally, maternal prenatal smoking can lead to fetal hypoxia, which impairs fetal autonomic function. Another significant pathway involves alterations in DNA methylation and microRNA expression associated with prenatal maternal smoking [55]. These pathways can result in downstream effects on the brain and cognitive processes, potentially influencing the trajectory of EF development in children as they grow older.

A large body of literature has linked prenatal maternal drinking with detrimental effects on childhood EF [5, 56]. These studies, however, include mothers with

Table 3 The association between prenatal maternal mood, substance use, and socioeconomic conditions with child executive function

Predictor	Inhibitory control[a]		Working memory	
	Beta Estimate (95% Confidence Limits)	*P* Value	Beta Estimate (95% Confidence Limits)	*P* Value
Maternal education				
Beyond high school (ref)	-	-	-	-
Completed high school	-0.02 (-0.53, 0.49)	0.93	0.04 (-0.18, 0.25)	0.74
Some high school	-0.25 (-0.36, -0.13)	**< 0.0001**	-0.02 (-0.08, 0.03)	0.35
Some primary school	-0.1 (-0.19, -0.01)	**0.03**	-0.01 (-0.05, 0.03)	0.7
Maternal employment status				
Unemployed (ref)	-	-	-	-
Employed	0 (-0.07, 0.08)	0.94	0.02 (-0.02, 0.05)	0.31
Household crowding index	-0.07 (-0.14, 0)	**0.04**	-0.01 (-0.04, 0.02)	0.69
Parity				
0 (ref)	-	-	-	-
1	-0.03 (-0.11, 0.04)	0.41	-0.03 (-0.07, 0)	**0.04**
2	-0.02 (-0.1, 0.06)	0.67	-0.01 (-0.04, 0.02)	0.58
3 or more	-0.12 (-0.21, -0.04)	**0.01**	-0.02 (-0.06, 0.01)	0.22
Prenatal depression and state anxiety[b]				
No depression or state anxiety (ref)	-	-	-	-
Depression without state anxiety	0.05 (-0.08, 0.18)	0.45	-0.03 (-0.08, 0.03)	0.37
State anxiety without depression	0.07 (-0.1, 0.24)	0.42	-0.04 (-0.11, 0.04)	0.31
Depression and state anxiety	0.21 (-0.02, 0.44)	0.07	0.03 (-0.07, 0.12)	0.6
Prenatal depression and trait anxiety[c]				
No Depression or trait anxiety (ref)	-	-	-	-
Depression without trait anxiety	0.06 (-0.12, 0.24)	0.53	-0.05 (-0.13, 0.02)	0.16
Trait anxiety without depression	-0.12 (-0.23, -0.01)	**0.04**	-0.03 (-0.08, 0.02)	0.25
Depression and trait anxiety	0.1 (-0.05, 0.25)	0.18	0.01 (-0.05, 0.07)	0.72
Prenatal alcohol use				
No alcohol (ref)	-	-	-	-
Quit early drinking	0 (-0.06, 0.06)	0.91	0 (-0.03, 0.03)	0.99
Low continuous drinking	0.05 (-0.14, 0.25)	0.59	0.05 (-0.04, 0.13)	0.3
Moderate to high continuous drinking	-0.03 (-0.16, 0.11)	0.69	-0.02 (-0.07, 0.04)	0.53
Prenatal smoking use				
No smoking (ref)	-	-	-	-
Quit early smoking	0.06 (-0.07, 0.2)	0.36	0.02 (-0.04, 0.07)	0.57
Low continuous smoking	-0.01 (-0.13, 0.11)	0.85	-0.02 (-0.07, 0.03)	0.46
Moderate to high continuous smoking	-0.20 (-0.39, -0.01)	**0.04**	0 (-0.08, 0.08)	0.97
Gestational age at birth	0.01 (-0.01, 0.02)	0.23	0 (0, 0.01)	0.38
Child sex				
Male (ref)	-	-	-	-
Female	0.03 (-0.03, 0.08)	0.35	0.03 (0, 0.05)	**0.03**
Child age at assessment	0.19 (0.14, 0.23)	**< 0.0001**	0.07 (0.05, 0.09)	**< 0.0001**

[a] Separate models were fit with inhibitory control and working memory outcomes

[b] Estimates of the prenatal maternal depression and state anxiety variable were derived from a separate model which included all the covariates other than prenatal maternal depression and trait anxiety

[c] Results presented in Table 3 are derived from the model with prenatal maternal depression and trait anxiety as a covariate because it had a significant association with child EF

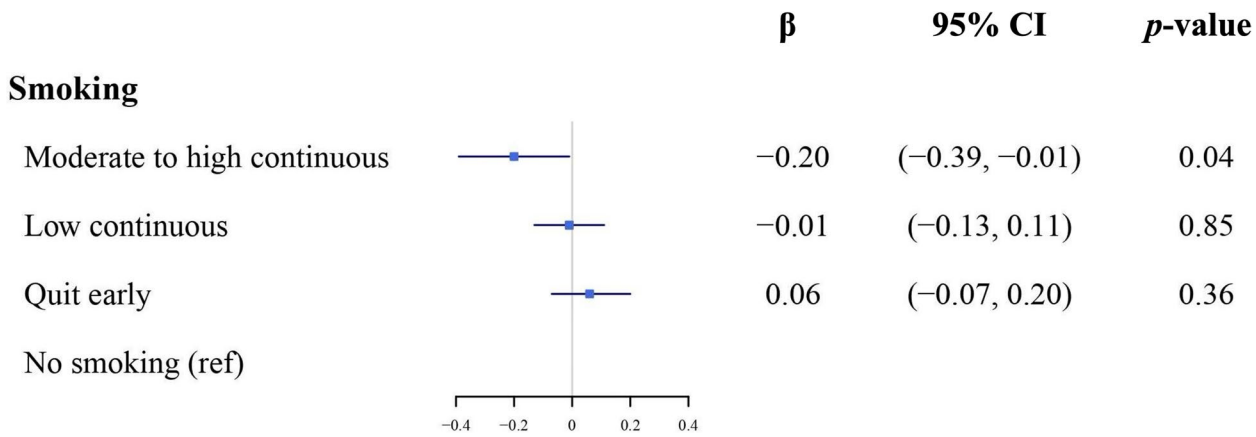

Fig. 3 Association prenatal smoking with child inhibitory control measured by the EF Touch battery. Each line plot depicts the beta estimates and their 95% CI for inhibitory control (x-axis) and each prenatal smoking group (y-axis). No prenatal maternal smoking served as the reference group. Models were adjusted for prenatal trait anxiety and depression, alcohol use, educational achievement, employment status, household crowding index, as well as, child biological sex, gestational age at birth, and age at EF assessment

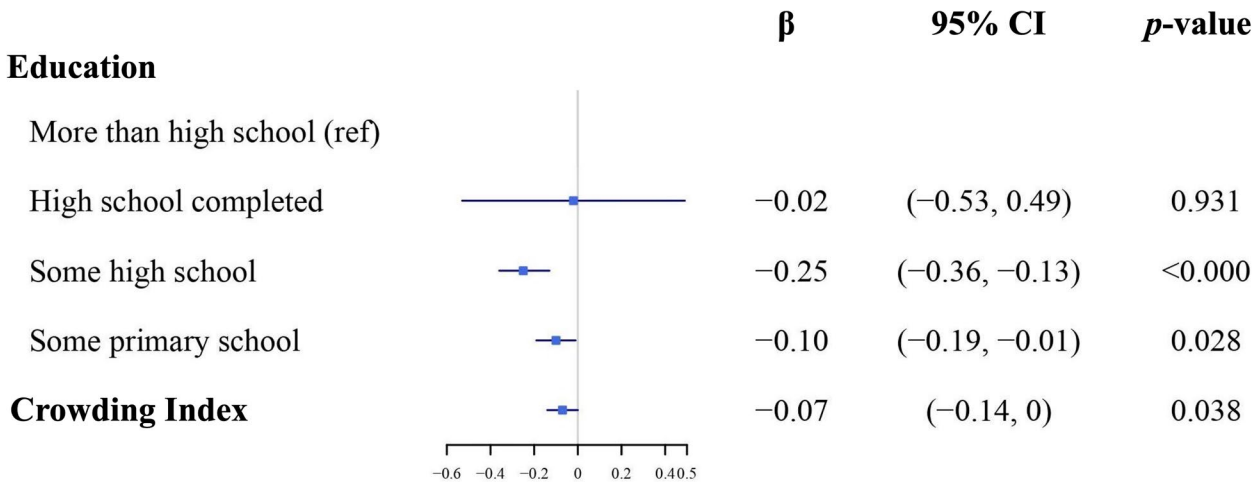

Fig. 4 Association of indicators of SES with child inhibitory control measured by the EF Touch battery. Each line plot depicts the beta estimates and their 95% CI for inhibitory control (x-axis) and maternal education and household crowding (y-axis). For maternal education, an educational achievement of more than high school served as the reference group. Models were adjusted for prenatal trait anxiety and depression, alcohol and tobacco use, employment status, as well as, child biological sex, gestational age at birth, and age at EF assessment

much higher levels of alcohol consumption compared to our cohort. Children exposed to high quantities of alcohol prenatally show deficits in verbal fluency, inhibition, problem solving and planning, concept formation, set-shifting, and working memory [56]. Children with fetal alcohol spectrum disorder are also found to have smaller brain volumes and worse EF, regardless of household SES [57]. In our study, only a small percentage of women (5.3%) fell into the moderate to high continuous drinking category. Even within this group, alcohol consumption was categorized as drinking approximately 3 drinks per week. Other studies with similarly low levels of alcohol exposure have also reported no significant on childhood EF [3, 22]. The relatively low levels of alcohol exposure in our cohort compared to studies demonstrating detrimental effects on child EF may account for our lack of significant findings in relation to prenatal alcohol use and childhood EF.

In this study, we found that two areas of SES had significant implications for childhood inhibitory control. The first aspect is maternal education, which aligns with previous research demonstrating that lower levels of maternal educational attainment are associated with poorer child EF scores, particularly inhibitory control [23, 58, 59]. Maternal education influences child EF through responsive caregiving and parental support

[58]. In our study, we found a dose-dependent response, wherein each level of maternal education completed corresponded to an increase in child EF. The second area of SES associated with child inhibitory control was household crowding. Consistent with existing literature, we found that higher levels of household crowding are associated with worse childhood inhibitory control [60, 61]. Household crowding can also be considered a marker of household chaos, which encompasses factors such as household clutter, ambient noise, crowding, and lack of structure. A meta-analysis investigating the relationship between child EF and household chaos revealed that children residing in more chaotic households exhibited significantly worse EF [60]. Household crowding and maternal education, two relatively accessible measures, could serve as potential screening tools to identify children at risk of poor EF development and be targeted for intervention to improve children's EF.

While our study identified several prenatal risk factors associated with child inhibitory control, we found no such associations with working memory. Previous literature has found associations between prenatal alcohol and tobacco use, maternal depression and anxiety, as well as SES on offspring working memory [1, 4, 8, 54, 56]. Our null results could be attributed to several factors. First, our cohort, although socioeconomically diverse, was relatively low risk. The maternal mood symptoms, substance use, and SES risk factors were less severe compared to studies that identified an effect of prenatal risk factors on child working memory [5, 8, 54]. Another possibility is that working memory is less affected by prenatal risk factors as inhibitory control. For instance, Noble et al. reported a larger effect size of maternal SES on 5-year-old child inhibitory control (Cohen's d = 0.56) than on working memory (Cohen's d = 0.31)[8]. Similarly, Knopik et al. found a stronger association between maternal prenatal smoking and inhibitory control (β = -0.17, SE = 0.07) than spatial working memory (β = -0.13, SE = 0.07) in early-mid adolescents [4]. A further possible explanation for our null findings may be attributed to the typical developmental trajectory of child EF. EF develops in a sequential manner: inhibitory control emerges during infancy, followed by the development of working memory during the preschool years, and finally, cognitive flexibility during childhood, which relies on the maturation of both inhibitory control and working memory [11]. Given that the average age of the children in this study was 4.74 ± 0.60 years, it is plausible that their inhibitory control abilities were more developed, while their working memory skills were still maturing. This could explain why we observed a more pronounced difference in inhibitory control between exposed and unexposed children, as this function was likely more stable. If the study were to be repeated at a later point, when the children's working memory skills have had more time to develop, we might observe differences in this aspect of executive function as well.

Our study demonstrates several notable strengths. First, this study is the first to examine the relative contribution of prenatal maternal mood, substance use, and SES on childhood EF development. Second, this study overcomes potential biases by recruiting participants prospectively, preventing recall bias, and by using an objective assessment of early childhood executive function skills, increasing validity and reliability. Third, participants were recruited from a socioeconomically diverse population which gives more insight into an understudied population in the field of EF as well increases the generalizability of our findings to broader range of individuals. Fourth, our study benefits from a substantial sample size; most studies' using objective measures of EF have samples ranging between 60–173 children [8, 25]. Finally, this study has extensive assessment of prenatal maternal mood, smoking, and drinking allowing us to capture a more comprehensive understanding of the relationships between these factors and childhood EF. Collectively, these strengths advance the understanding of the complex interplay between prenatal factors, SES, and EF.

This study has several limitations. First, the lack of data on responsive parenting behavior and child stimulation is a weakness, as previous studies have established the importance of parenting behavior in shaping child EF [62, 63]. Additionally, the absence of postnatal maternal mood data, including depression and anxiety symptoms, limits our ability to determine the specificity of our findings to the prenatal period. While postnatal measures of maternal mood are likely positively correlated with their prenatal counterparts, we acknowledge that the postnatal period also has a profound impact on childhood EF [2]. Therefore, future research should consider including postnatal measures to disentangle the relative contributions of prenatal and postnatal factors on child EF development. Furthermore, we did not examine the moderating effect of anti- depressant and anxiety medication on the observed associations because we had few mothers taking these medications (N = 7.5% for anti-depressants and 3% for anti-anxiety medication). We also only had categorical data on anti-depressant and anxiety use (yes/no) and lacked information on duration and dosage, precluding further investigation into the moderating effects of antidepressants. Similarly, few participants in the sample used recreational drugs (< 5%) and we could therefore not analyze its effects on childhood EF. Another limitation of our study is the utilization of the timeline follow-back interview method, a self-report measure

that is vulnerable to reporting bias. The timeline follow-back interview, however, is the preferred approach for assessing substance use during pregnancy, as it provides a comprehensive evaluation of exposure while minimizing participant burden [39]. Moreover, our single-time-point measurement of EF, provides only a snapshot of an individual's EF abilities, which may be influenced by various transient factors, such as daily fluctuations in nutrition, familiarity with the assessment tool (e.g., tablets), or other extraneous variables. As such, measurement error may have been introduced in our assessment of child EF. Our sample, recruited from two research sites in the Northern Plains of South Dakota with a high proportion of people identifying as Native American, limits the generalizability of our findings to similar contexts. Despite these limitations, given that few studies have investigated the associations between prenatal maternal exposures and child EF in communities from diverse socioeconomic contexts, our findings contribute valuable insights to the existing literature.

Conclusions

Our study sheds light on the complex interplay among prenatal maternal mood, substance use and SES in shaping children's EF in early years. Our findings demonstrate the adverse effects of maternal trait anxiety on children's inhibitory control, emphasizing the critical need for mental health support for women across the lifespan. Consistent with previous literature, we have demonstrated the adverse consequences of prenatal maternal smoking on childhood EF in a low-exposure sample, underscoring the importance of continued public health interventions targeting smoking during pregnancy. Furthermore, our analyses identify two indicators of SES, maternal education, and household crowding, as having a significant impact on child EF development which could be used to identify high-risk children. Taken together, these findings emphasize the importance of implementing comprehensive intervention packages appropriate for the local context to promote child EF outcomes and have lasting impacts on academic performance.

Abbreviations

EF	Executive function
SES	Socioeconomic status
ECHO	Environmental Influences on Child Health Outcomes
NIH	National Institute of Health's
PASS	Prenatal Alcohol and SIDS and Stillbirth
BMI	Body-mass-index
SD	Standard deviation
EPDS	Edinburgh Postnatal Depression Scale
STAI	State-Trait Anxiety Inventory
SSS	Silly Sounds Stroop
PTP	Pick the Picture

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12887-024-05113-2.

Supplementary Material 1.

Acknowledgements

The authors would like to thank the mothers and children who participated in the study.

Authors' contributions

YKR wrote the initial manuscript, participated in data analysis and interpretation. AS designed and conducted the final analysis, interpreted data, and provided critical input in manuscript writing. AS had full access to all the data, assuming responsibility for data integrity and accuracy in the data analysis. The parent study was designed, and funding was secured by WPF and AJE. The study planning and implementation received scientific, administrative, and technical support from CWH, KZ, AJE. SR contributed to data analysis and figure creation. SM and LCS provided valuable advice and technical input on data processing and analysis, and manuscript drafting. All authors reviewed and approved of the final manuscript.

Funding

The Environmental Influences on Child Health Outcomes (ECHO*) research was supported by a grant (UH3OD023279) from the Office of the Director (OD), NIH. AS is supported by a re-entry supplement (UH3OD023279-05S1) from the OD and Office of Research on Women Health, NIH.

Data availability

De-identified ECHO data is shared on the NICHD DASH platform for public access.

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from all primary caregivers and assent from the children in the PASS-ECHO study. The study protocol was approved by ECHO, Avera Research Institute, Columbia University Irving Medical Center, and New York State Psychiatric Institute Institutional review boards.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Department of Psychiatry, Columbia University Irving Medical Center, New York, NY 10032, USA. [2]Department of Psychology, University of Southern California, Los Angeles, CA 90089, USA. [3]Department of Child and Adolescent Psychiatry, NYU Grossman School of Medicine, New York, NY 10016, USA. [4]Avera Research Institute, Sioux Falls, SD 57108, USA. [5]Department of Pediatrics, University of South Dakota Sanford School of Medicine, Sioux Falls, SD 57105, USA. [6]Division of Developmental Neuroscience, New York State Psychiatric Institute, New York, NY 10032, USA. [7]Department of Pediatrics, Columbia University Irving Medical Center, New York, NY 10032, USA.

Received: 30 October 2023 Accepted: 26 September 2024
Published online: 28 October 2024

References

1. Buss C, Davis EP, Hobel CJ, Sandman CA. Maternal pregnancy-specific anxiety is associated with child executive function at 6–9 years age. Stress. 2011;14(6):665–76.

2. Power J, van IJzendoorn M, Lewis AJ, Chen W, Galbally M. Maternal perinatal depression and child executive function: A systematic review and meta-analysis. J Affect Disord. 2021;291:218–34.
3. Kim YH. Korean mothers' alcohol consumption trajectories from childbirth to 6 years postpartum and children's executive function difficulties at first grade. Soc Psychiatry Psychiatr Epidemiol. 2020;55(4):497–506.
4. Knopik VS, Micalizzi L, Marceau K, Loviska AM, Yu L, Bien A, et al. The roles of familial transmission and smoking during pregnancy on executive function skills: A sibling-comparison study. Dev Psychopathol. 2022;34(5):1803–15.
5. Rasmussen C. Executive Functioning and Working Memory in Fetal Alcohol Spectrum Disorder. Alcohol Clin Exp Res. 2005;29(8):1359–67.
6. Onah MN, Field S, van Heyningen T, Honikman S. Predictors of alcohol and other drug use among pregnant women in a peri-urban South African setting. Int J Ment Health Syst. 2016;4(10):38.
7. Shakeel N, Eberhard-Gran M, Sletner L, Slinning K, Martinsen EW, Holme I, et al. A prospective cohort study of depression in pregnancy, prevalence and risk factors in a multi-ethnic population. BMC Pregnancy Childbirth. 2015;15(1):5.
8. Noble KG, Norman MF, Farah MJ. Neurocognitive correlates of socioeconomic status in kindergarten children. Dev Sci. 2005;8(1):74–87.
9. Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. Cognit Psychol. 2000;41(1):49–100.
10. Miyake A, Friedman NP. The Nature and Organization of Individual Differences in Executive Functions: Four General Conclusions. Curr Dir Psychol Sci. 2012;21(1):8–14.
11. Best JR, Miller PH. A Developmental Perspective on Executive Function. Child Dev. 2010;81(6):1641–60.
12. Ferguson HJ, Brunsdon VEA, Bradford EEF. The developmental trajectories of executive function from adolescence to old age. Sci Rep. 2021;11(1):1382.
13. Er-Rafiqi M, Guerra A, Le Gall D, Roy A. Development of inhibition and working memory in school-age Moroccan children. Child Neuropsychol. 2022;28(7):938–61.
14. Mann TD, Hund AM, Hesson-McInnis MS, Roman ZJ. Pathways to School Readiness: Executive Functioning Predicts Academic and Social-Emotional Aspects of School Readiness. Mind Brain Educ. 2017;11(1):21–31.
15. Zysset AE, Kakebeeke TH, Messerli-Bürgy N, Meyer AH, Stülb K, Leeger-Aschmann CS, et al. Predictors of Executive Functions in Preschoolers: Findings From the SPLASHY Study. Front Psychol. 2018;29(9):2060.
16. Lawson GM, Hook CJ, Farah MJ. A meta-analysis of the relationship between socioeconomic status and executive function performance among children. Dev Sci. 2018;21(2):e12529.
17. Toor HK, Hanif R. Executive Function Touch battery: Translation and preliminary measure validation for Pakistani preschoolers. PLoS ONE. 2022;17(9):e0274431.
18. Diamond A. Chapter 19 - Executive functions. In: Gallagher A, Bulteau C, Cohen D, Michaud JL, editors. Handbook of Clinical Neurology. Elsevier; 2020 [cited 2024 Jun 18]. p. 225–40. (Neurocognitive Development: Normative Development; vol. 173). Available from: https://www.sciencedirect.com/science/article/pii/B9780444641502000204
19. O'Donnell KJ, Glover V, Barker ED, O'Connor TG. The persisting effect of maternal mood in pregnancy on childhood psychopathology. Dev Psychopathol. 2014;26(2):393–403.
20. Van den Bergh BRH, van den Heuvel MI, Lahti M, Braeken M, de Rooij SR, Entringer S, et al. Prenatal developmental origins of behavior and mental health: The influence of maternal stress in pregnancy. Neurosci Biobehav Rev. 2020;1(117):26–64.
21. Korja R, McMahon C. Maternal prenatal mood problems and lower maternal emotional availability associated with lower quality of child's emotional availability and higher negative affect during still-face procedure. Infancy. 2021;26(6):901–19.
22. Louw JG, van Heerden A, Olivier L, Lambrechts T, Broodryk M, Bunge L, et al. Executive Function After Prenatal Alcohol Exposure in Children in a South African Population: Cross-sectional Study. JMIR Form Res. 2021;5(7):e20658.
23. Vrantsidis DM, Clark CAC, Chevalier N, Espy KA, Wiebe SA. Socioeconomic status and executive function in early childhood: Exploring proximal mechanisms. Dev Sci. 2020;23(3):e12917.
24. Delagneau G, Twilhaar ES, Testa R, van Veen S, Anderson P. Association between prenatal maternal anxiety and/or stress and offspring's cognitive functioning: A meta-analysis. Child Dev. 2023;94(3):779–801.
25. Park M, Brain U, Grunau RE, Diamond A, Oberlander TF. Maternal depression trajectories from pregnancy to 3 years postpartum are associated with children's behavior and executive functions at 3 and 6 years. Arch Womens Ment Health. 2018;21(3):353–63.
26. Faleschini S, Rifas-Shiman SL, Tiemeier H, Oken E, Hivert MF. Associations of Prenatal and Postnatal Maternal Depressive Symptoms with Offspring Cognition and Behavior in Mid-Childhood: A Prospective Cohort Study. Int J Environ Res Public Health. 2019;16(6):1007.
27. Blaisdell CJ, Park C, Hanspal M, Roary M, Arteaga SS, Laessig S, et al. The NIH ECHO Program: investigating how early environmental influences affect child health. Pediatr Res. 2022;92(5):1215–6.
28. Gillman MW, Blaisdell CJ. Environmental influences on Child Health Outcomes, a Research Program of the National Institutes of Health. Curr Opin Pediatr. 2018;30(2):260–2.
29. Willoughby MT, Blair CB, Wirth RJ, Greenberg M. The measurement of executive function at age 5: psychometric properties and relationship to academic achievement. Psychol Assess. 2012;24(1):226–39.
30. Dukes KA, Burd L, Elliott AJ, Fifer WP, Folkerth RD, Hankins GDV, et al. The safe passage study: design, methods, recruitment, and follow-up approach. Paediatr Perinat Epidemiol. 2014;28(5):455–65.
31. Pini N, Myers MM, Elliott AJ, Shuffrey LC, Lucchini M, Sania A, et al. Cluster Analysis of Alcohol Consumption during Pregnancy in the Safe Passage Study. Annu Int Conf IEEE Eng Med Biol Soc IEEE Eng Med Biol Soc Annu Int Conf. 2019;2019:1338–41.
32. Sania A, Myers MM, Pini N, Lucchini M, Nugent JD, Shuffrey LC, et al. Prenatal smoking and drinking are associated with altered newborn autonomic functions. Pediatr Res. 2023;93(1):242–52.
33. Bergink V, Kooistra L, Lambregtse-van den Berg MP, Wijnen H, Bunevicius R, van Baar A, et al. Validation of the Edinburgh Depression Scale during pregnancy. J Psychosom Res. 2011 Apr;70(4):385–9.
34. Levis B, Negeri Z, Sun Y, Benedetti A, Thombs BD. Accuracy of the Edinburgh Postnatal Depression Scale (EPDS) for screening to detect major depression among pregnant and postpartum women: systematic review and meta-analysis of individual participant data. BMJ. 2020;11(371):m4022.
35. Sinesi A, Maxwell M, O'Carroll R, Cheyne H. Anxiety scales used in pregnancy: systematic review. BJPsych Open. 2019;5(1):e5.
36. Emons WH, Habibović M, Pedersen SS. Prevalence of anxiety in patients with an implantable cardioverter defibrillator: measurement equivalence of the HADS-A and the STAI-S. Qual Life Res. 2019;28(11):3107–16.
37. Meades R, Ayers S. Anxiety measures validated in perinatal populations: a systematic review. J Affect Disord. 2011;133(1–2):1–15.
38. Dukes K, Tripp T, Willinger M, Odendaal H, Elliott AJ, Kinney HC, et al. Drinking and Smoking Patterns during Pregnancy: Development of Group-based Trajectories in the Safe Passage Study. Alcohol Fayettev N. 2017;62:49–60.
39. Dukes KA, Tripp T, Petersen J, Robinson F, Odendaal H, Elliott A, et al. A modified Timeline Followback assessment to capture alcohol exposure in pregnant women: Application in the Safe Passage Study. Alcohol Fayettev N. 2017;62:17–27.
40. Sania A, Pini N, Nelson M, Myers MM, Shuffrey LC, Lucchini M, et al. The K Nearest Neighbor Algorithm for Imputation of Missing Longitudinal Prenatal Alcohol Data [Internet]. Rochester; 2022. [cited 2024 Oct 2]. Available from: https://papers.ssrn.com/abstract=4065215.
41. Willoughby MT, Blair C. Test-retest reliability of a new executive function battery for use in early childhood. Child Neuropsychol. 2011;17(6):564–79.
42. Model-Building Strategies and Methods for Logistic Regression. In: Applied Logistic Regression. John Wiley & Sons, Ltd; 2013 [cited 2024 Jul 1]. p. 89–151. Available from: https://onlinelibrary.wiley.com/doi/abs/https://doi.org/10.1002/9781118548387.ch4
43. Zelazo PD, Anderson JE, Richler J, Wallner-Allen K, Beaumont JL, Weintraub S. Ii. Nih Toolbox Cognition Battery (cb): Measuring Executive Function and Attention. Monogr Soc Res Child Dev. 2013;78(4):16–33.
44. Jacobsen GM, de Mello CM, Kochhann R, Fonseca RP. Executive Functions in School-age Children: Influence of Age, Gender, School Type and Parental Education. Appl Cogn Psychol. 2017;31(4):404–13.

45. Veraksa A, Gavrilova M, Lepola J. Learning motivation tendencies among preschoolers: Impact of executive functions and gender differences. Acta Psychol (Amst). 2022;1(228):103647.
46. Raver CC, Blair C, Willoughby M. Poverty as a Predictor of 4-Year-Olds' Executive Function: New Perspectives on Models of Differential Susceptibility. Dev Psychol. 2013;49(2):292–304.
47. Kuhn L, Camerota M, Willoughby MT, Blair C. A Comparison of Three Executive Function Batteries in a Preschool-Aged Sample. OSF; 2024 [cited 2024 Jun 26]. Available from: https://osf.io/xeqaj
48. Pearson RM, Bornstein MH, Cordero M, Scerif G, Mahedy L, Evans J, et al. Maternal perinatal mental health and offspring academic achievement at age 16: the mediating role of childhood executive function. J Child Psychol Psychiatry. 2016;57(4):491–501.
49. Plamondon A, Akbari E, Atkinson L, Steiner M, Meaney MJ, Fleming AS, et al. Spatial working memory and attention skills are predicted by maternal stress during pregnancy. Early Hum Dev. 2015;91(1):23–9.
50. Ross KM, Letourneau N, Climie E, Giesbrecht G, Dewey D. Perinatal Maternal Anxiety and Depressive Symptoms and Child Executive Function and Attention at Two-years of Age. Dev Neuropsychol. 2020;45(6):380–95.
51. Coplan RJ, O'Neil K, Arbeau KA. Maternal Anxiety During and After Pregnancy and Infant Temperament at Three Months of Age. J Prenat Perinat Psychol Health. 2005;19:199–215.
52. Frigerio A, Nazzari S. Antenatal maternal anxiety, maternal sensitivity and toddlers' behavioral problems: An investigation of possible pathways. Early Hum Dev. 2021;1(157):105364.
53. Vujovic M, Sovilj M, Plesinac S, Rakonjac M, Jelicic L, Adamovic T, et al. Effect of antenatal maternal anxiety on the reactivity of fetal cerebral circulation to auditory stimulation, and early child development. Srp Arh Celok Lek. 2019;147(5–6):327–34.
54. Choe DE, Deer LK, Hastings PD. Latent class analysis of maternal depression from pregnancy through early childhood: Differences in children's executive functions. Dev Psychol. 2023;59(8):1452.
55. Shuffrey LC, Fifer WP. Prenatal Risk Factors and Neurodevelopment. Encyclopedia of Infant and Early Childhood Development (Second Edition), Elsevier; 2020 [cited 2021 Oct 13]. 608–620 p. Available from: https://doi.org/10.1016/B978-0-12-809324-5.23054-X
56. Mattson SN, Bernes GA, Doyle LR. Fetal Alcohol Spectrum Disorders: A Review of the Neurobehavioral Deficits Associated With Prenatal Alcohol Exposure. Alcohol Clin Exp Res. 2019;43(6):1046–62.
57. McLachlan K, Zhou D, Little G, Rasmussen C, Pei J, Andrew G, et al. Current Socioeconomic Status Correlates With Brain Volumes in Healthy Children and Adolescents but Not in Children With Prenatal Alcohol Exposure. Front Hum Neurosci. 2020 [cited 2023 May 30];14. Available from: https://www.frontiersin.org/articles/https://doi.org/10.3389/fnhum.2020.00223
58. Cuevas K, Deater-Deckard K, Kim-Spoon J, Watson AJ, Morasch KC, Bell MA. What's Mom Got to Do with It? Contributions of Maternal Executive Function and Caregiving to the Development of Executive Function Across Early Childhood. Dev Sci. 2014;17(2):224–38.
59. Morales S, Bowers ME, Shuffrey L, Ziegler K, Troller-Renfree S, Hernandez A, et al. Maternal education prospectively predicts child neurocognitive function: An environmental influences on child health outcomes study. Dev Psychol. 2024;60(6):1028–40.
60. Andrews K, Atkinson L, Harris M, Gonzalez A. Examining the effects of household chaos on child executive functions: A meta-analysis. Psychol Bull. 2021;147:16–32.
61. Blair CB, Granger DA, Willoughby MT, Mills-Koonce R, Cox M, Greenberg MT, et al. Salivary Cortisol Mediates Effects of Poverty and Parenting on Executive Functions in Early Childhood. Child Dev. 2011;82(6):1970–84.
62. Helm AF, McCormick SA, Deater-Deckard K, Smith CL, Calkins SD, Bell MA. Parenting and Children's Executive Function Stability Across the Transition to School. Infant Child Dev. 2020;29(1):e2171.
63. Sosic-Vasic Z, Kröner J, Schneider S, Vasic N, Spitzer M, Streb J. The Association between Parenting Behavior and Executive Functioning in Children and Young Adolescents. Front Psychol. 2017;30(8):472.

Publisher's Note