Published in final edited form as:

J Dev Orig Health Dis. 2011 December ; 2(6): 365–374. doi:10.1017/S2040174411000596.

Associations Between Fetal Inflammation and Cognitive Functions in Middle Aged Adults

Pam Factor-Litvak¹, Nadine Straka¹, Sara Cherkerzian^{2,3}, Marcus Richards^{4,5}, Xinhua Liu⁶, Arnold Sher⁷, Greg Neils⁸, Stephen Buka⁹, Ezra Susser^{1,10}, and Jill Goldstein^{2,3,11}

¹ Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA

² Brigham & Women's Hospital Departments of Psychiatry and Medicine, Division of Women's Health, Connors Center for Women's Health & Gender Biology, Boston, MA, USA

³ Departments of Psychiatry and Medicine, Harvard Medical School, Boston, MA

⁴ Medical Research Council (MRC) Unit for Lifelong Health and Aging, London, UK

⁵ Department of Epidemiology and Public Health, University College London, London, UK

⁶ Department of Biostatistics, Mailman School of Public Health, Columbia University, New York, NY

⁷ ICSD USA, Millburn NJ, USA

⁸ Sergievsky Center, College of Physicians and Surgeons, Columbia University, New York, NY

⁹ Department of Community Health, Brown University, Providence, RI, USA

¹⁰ Department of Psychiatry, College of Physicians and Surgeons, Columbia University, New York, NY and New York State Psychiatric Institute

¹¹ Department of Psychiatry, Division of Psychiatric Neuroscience, Massachusetts General Hospital, Boston, MA

Abstract

Exposure to prenatal inflammation, measured using proxies such as preterm birth, low birth weight and maternal preeclampsia, has been associated with decrements in scores on tests of intelligence in children and adolescents. We examined whether these decrements persist into middle adulthood and expand into other domains of cognitive functioning. Using data from the Early Determinants of Adult Health project and from the ancillary project, Fetal Antecedents of Major Depression and Cardiovascular Disease, we selected term same sex sibling sets or singletons from these sets, from the New England Family Study (NEFS) and the Child Health and Development Studies (CHDS), discordant on either fetal growth or preeclampsia to test the hypotheses that prenatal exposure to inflammation was associated with decrements in attention, learning and executive function 40 years later. Exposure was defined as a continuous measure of percentile birth weight for gestational age, fetal growth restriction (< 20th percentile of birth weight for gestational age) or maternal preeclampsia. Given that the sample was comprised, in part, of sibling sets, the analyses were performed using mixed models to account for the inter-sibling correlations. Analyses were performed separately by study site (i.e. NEFS and CHDS). In

the NEFS we found a small association between fetal growth restriction and working memory for males, such that the working memory score declined by 1.5 points (95% CI -2.4, -0.27). This association was significantly different from the estimated association in females. We discuss the possible reasons for this association which include the possible mediating effects of the postnatal environment.

Keywords

Neurocognition; fetal programming; fetal inflammation

Introduction

Over the past 50 years, interest in the prenatal determinants of neuropsychological function has flourished. Indeed, a substantial literature links birth weight, as an indicator of the intrauterine environment, with deficits in overall cognition during childhood and in early adolescence. Reductions in birth weight are related to fetal growth restriction and to preeclampsia, both of which may be proxies for inflammatory processes. Collectively studies of low birth weight (LBW; < 2500 grams) children compared to those of normal birth weight find small decrements in overall cognition (measured using tests of intelligence, IQ). A summary of 10 studies concluded that at age 6-14, LBW children had lower mean IQ scores compared to normal birth weight children, after adjustment for demographic and socioeconomic variables¹. In an early analysis from the New England (NE) cohort of the National Collaborative Perinatal Project (NCP)², LBW was the strongest predictor, compared to other perinatal factors, of IQ at age 7. Reductions in cognitive scores are also found for children of preeclamptic mothers, although less consistently than for LBW children³⁻⁸. Thus, the sum of the evidence suggests that markers of fetal inflammation are associated with reductions in IQ, but little is known regarding other cognitive function.

While these data are compelling, several questions remain regarding the impact of fetal growth on cognitive abilities, other than IQ. First, are reductions in birth weight related only to IQ or to other cognitive tasks such as attention, vigilance and verbal fluency? Previous studies suggest that LBW is associated with equal decrements in verbal and performance IQ^{1,9,10}. Children with LBW scored lower on tests of language, spatial, fine motor, tactile, visual motor and dexterity abilities^{9,11-15}, suggesting that a wide range of abilities are influenced by LBW. However, few data are available on attention or verbal fluency tasks. Second, are associations between birth weight and cognitive abilities other than IQ confounded by variables in the social and familial environment? Matte, et al¹⁶ used a powerful same sex sibling design to evaluate the associations between birth weight and IQ; in boys, they found a 0.5 point reduction in IQ for each 100 gram decrement in birth weight and no association in girls. The same sex sibling design is used in the present study and substantially reduces confounding due to early socioeconomic and familial factors. Third, are associations between birth weight and cognitive abilities other than IQ only for children with LBW or do they persist across the range of birth weights (i.e. from 2500 to 4000 grams)? If the associations between fetal growth and cognitive abilities are mediated by subtle impairments in brain growth and development, then it is entirely plausible that

associations would persist across this range. Early analyses of the NCPP found monotonic increases in IQ over the birth weight range from 1500 to greater than 3500 grams¹⁷; however these analyses did not adjust for potential confounders. Other studies report differences in age 6 IQ of approximately 4 points comparing children with birth weights greater than 3300 grams to those 2201 – 3300 grams¹¹. Again, few data are available for cognitive tasks other than IQ. Fourth, do the associations between birth weight and measures of cognition persist into adulthood? A study of Danish conscripts¹⁸ found an increase in cognitive test scores with increasing birth weight (up to 4200 grams). Richards et al¹⁹ also found a positive gradient between birth weight and cognitive scores through age 26, suggesting persisting associations albeit at reduced magnitudes compared to analyses performed earlier in childhood. Indeed, associations were completely absent for cognitive scores at age 43. Finally, are these associations gender specific? A large literature suggests gender specific differences in cognitive function (reviewed in^{20,21}). In general, females perform better on tests of verbal fluency and perceptual speed and males perform better on tests of spatial perception and quantitative problem solving. Further, both animal and human studies suggest that the developing male brain may be more susceptible to insults²²⁻²⁶ possibly because the pace and asymmetries of brain development differ by hormonal status and gender. The earlier analysis of the NCPP data found stronger associations in boys compared to girls for within family variation in birth weight; however the between family variation in birth weight did not significantly differ between boys and girls^{16, 27}. Two other studies, however, found stronger associations between birth weight on verbal memory in girls^{28,29} suggesting the need for studies of specific cognitive functions other than IQ.

We have the opportunity to examine several of these open issues within the context of the Early Determinants of Adult Health project and its extension, Fetal Antecedents of Major Depression and Cardiovascular Disease. Design considerations from these studies address many of the open issues including measurement of a variety of cognitive tasks specifically chosen to address differences in gender specific cognitive functions, the powerful same-sex sibling design to control for early life and familial confounding and for those participants not in a sibship, careful measurement of a wide variety of socioeconomic and demographic factors in early life and in adulthood, a wide range of birth weights, and follow up until mid life.

Methods

Sample Ascertainment

Data for these analyses include participants in the Early Determinants of Adult Health (EDAH) project and in the Shared Fetal Antecedents of Major Depression and Cardiovascular Disease (MDCVD) project. Briefly, for the core EDAH sample (see Susser, et al this issue) from the New England Family Study (NEFS) and from the parallel Child Health and Development Study (CHDS) in Oakland, California, we identified all same-sex sibling pairs who met the following criteria. Eligible sibling sets included those where two or more members were discordant on birth weight, adjusted for gestational age. In New England, the low birth weight proband was below the lowest 20th percentile of the gender-specific birth weight for gestational age distribution and the higher birth weight sibling was

at or above the 20th percentile and at least 10 or more percentile points higher. These criteria applied to approximately half of the CHDS sibling sets; the remainder included sibling sets in which the two siblings differed by at least 10 percentile points on the birth weight for gestational age distribution, but where the lower birth weight sibling was not in the lowest quintile of the birth weight for gestational age distribution. Further, both siblings had to be between 38 and 43 completed weeks of gestation. Siblings were required to live within commuting distance of the clinics in Boston or Oakland.

In the NEFS for the MDCVD study, we extended the size of the cohort and included sibling pairs discordant on maternal preeclampsia (PE) (defined below). These sibling pairs were, as above, required to be between 38 and 43 completed weeks of gestation. Among the same-sex sibling sets discordant for PE, there were 425 subjects (Females, n = 188; Males, n = 237) identified from 196 families. All participants recruited from PE families underwent the same assessment as did those from the Early Determinants of Health Study. We excluded participants with a history of bipolar or other psychotic disorders (15 from the NE-NCPP and 4 from the CHDS).

We restricted the sample for this analysis to those who had data on any of the cognitive assessments and complete data on relevant covariates. Thus, a total of 474 participants were studied: 247 from the New England NCPP and 227 from the CHDS. There are 213 males; 108 of whom are in same sex sibling sets discordant for fetal growth and/or PE (54 sibling sets total). There are 261 females; 174 of whom are in same sex sibling sets discordant for fetal growth and/or PE (87 sets total). 20 participants were from mixed male-female sibling sets (10 sets total). The siblings of the remaining participants did not participate in this study.

Exposure Ascertainment

Exposure was defined in three ways. First, FGR was defined as birth weight below the sex-specific 20th percentile for gestational age based on the 2000-2001 US Natality Dataset³⁰. Second, exposure to preeclampsia was defined according to the National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy³¹. Mild preeclampsia was defined if after the 20th completed gestational week there was evidence of systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg, and proteinuria 1+ in a clean void on at least 2 occasions and in the absence of a urinary tract infection, or persistent edema of hands and face. Severe preeclampsia was defined if after the 20th completed gestational week there was evidence of systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg on at least 2 occasions, 6 hours apart at bed rest, and either proteinuria ≥ 5 grams in 24 hours in a clean void, oliguria (< 400 excreted urine in a 24 hour period), or cerebral or visual disturbances, retinopathy, headache, right upper quadrant or epigastric pain, pulmonary edema or cyanosis or laboratory abnormalities (increased liver enzymes or decreased platelets). Chronic hypertensive disease with superimposed preeclampsia after the 20th gestational week was defined as an elevation of at least 30 mmHg in systolic or 15 mmHg in diastolic blood pressure and the development of a significant degree of proteinuria. Mild preeclampsia, severe preeclampsia and preeclampsia superimposed on chronic hypertension were

collapsed for these analyses. Finally, we defined exposure to fetal inflammation as either FGR and/or preeclampsia.

Neurocognitive Tests

Our measures included attention, learning and executive function.

Working Memory/Vigilance—Working memory was assessed using the Seidman Continuous Performance Test (CPT)³². This test requires the subject of listen to a series of letters read aloud and to tap a pencil on the desk when certain criteria are met. In the vigilance section of the test, subjects tap after the letter “Q” when it follows from the letter “A”. In the working memory section of the test, subjects tap after hearing a “Q” that comes four letters after hearing an “A”. This latter section has an interference section imbedded as additional distracter; “Q”s are included in the letter string. As in previous work, we use the following scores based on omission errors from the Seidman CPT: vigilance (total number of omissions in two trials) and interference-working memory (total number of omissions).

Verbal Learning—Verbal learning was assessed using a modification of the California Verbal Learning Test (CVLT)³³. This test consists of a list of 16 words which are read to the subject at 1 second intervals. The subject is asked to recall as many of the words that he/she can. The major feature of the CVLT is that the words are drawn from semantic clusters, which may aid recall. Our modification repeated this procedure three times. The sum of correct recalled words over the three trials gives the total recall score. We also asked the subject to recall as many words as possible after a 10 minute delay (delayed recall).

Verbal Fluency—Verbal fluency was assessed using the FAS Test³⁴. In this task, the subject is asked to say as many words as he/she can in one minute that begin with a given letter. The test is repeated for each letter: F, A and S. Responses are recorded as the words in 15 second intervals. For this analysis, we sum the correct words over all intervals and letters.

Subtle Brain Dysfunction—We used the WAIS Digit Symbol Test³⁵ to identify subtle brain dysfunction. This test requires the participant to encode a series of letters with symbols, presented in a key on the top of the test form. The participant is given 90 seconds to complete this task, and must encode the numbers in the order on the page. The score is the number of correct encoded numbers in the given amount of time, and is converted to a standard score. Based on new findings from brain imaging, it is thought that the Digit Symbol Test is most sensitive to the processes of visual search, associative learning and working memory³⁶.

Measurement of Covariates

In both the NCPP and the CHDS, mothers were administered structured interviews at the time of study entry. At the adult follow up visit, participants were administered structured interviews by trained personnel. Data were obtained regarding demographic and socioeconomic variables, life style characteristics (smoking, alcohol use, sleep, physical activity), self rated health status, family health history, and major depressive disorder using the depression module of a structured psychiatric interview (the Structured Clinical

Interview for DSM Disorders³⁷). For the latter, all clinical interviewers were trained by expert psychometricians and quality was continually checked by the team supervised by JG. All diagnostic material and test scores were reviewed by JG and diagnoses assigned by consensus. For the few disagreements among the diagnostic team, a third clinician reviewed the material. A measure of socioeconomic status (SES) was developed using the methods outlined by Myrlandopoulos and French³⁸ to construct the SES index used in the NCPP, operationalized as the combination of scores for education, occupation and family income to derive a composite numerical index. Low SES is an important modifier of the impact of fetal risk factors on our outcomes of interest. We categorized low SES as the bottom tertile of the distribution.

Statistical Analysis

Summary statistics were calculated for sample characteristics. Chi-square tests were used to detect group differences for categorical variables.

The percentile birth weight for gestational age, FGR, preeclampsia and fetal inflammation were the main predictors of interest. To examine the associations between a predictor and the cognitive test scores, we used mixed linear models³⁹, which account for the within-sibling correlation in the outcome measures of test scores. Model parameters were estimated using the maximum likelihood method. All models were adjusted for age at the time of testing, race (white vs. other), a summary index of SES and smoking (never, former, current, unknown). Because most of the sample obtained either perfect or near-perfect (i.e. one incorrect) scores on the test of vigilance, we applied logistic regression models with repeated binary measures, perfect vs. less than perfect scores to examine the associations with exposures. Model parameters were estimated using generalized estimating equations which accounts for within-sibling correlations in outcome measures, and all models were adjusted for the same variables as above.

All analyses were stratified by study site (Boston, Oakland) and gender. We also conducted secondary, post hoc stratification by SES, classified in tertiles. The Wald statistic was employed to assess whether the parameter estimate for the exposure measures differed between men and women and between Boston and Oakland.

Results

Participants in the NEFS and the CHDS were different in terms of several sociodemographic variables (table 1). In the NEFS participants were more likely to be white, have lower educational attainment and be in the lowest tertile of SES compared to those in the CHDS. Additionally, NEFS participants were more likely to be current smokers and to have a diagnosis of major depressive disorder. These differences held for men and women separately (data not shown).

The distribution of birth weight percentile for gestational age differed in the total NEFS and CHDS samples. By design, participants in the NEFS tended to be of lower birth weight for gestational age and were more likely to exhibit fetal growth restriction compared to participants in the CHDS (table 2). These differences were more pronounced among the men

(data not shown); in the NEFS 49% of men were < 25th birth weight percentile for gestational age compared to 28% of men in the CHDS and 35% of men were fetal growth restricted compared to 22% in the CHDS. For women, in the NEFS, 48% were < 25th birth weight percentile for gestational age compared to 34% in the CHDS and 42% of women were fetal growth restricted compared to 33% in the CHDS. By design, the mothers of participants in the NEFS were more likely to have preeclampsia than those in the CHDS.

The overall mean scores on the neurocognitive battery were in the expected range (table 3). In both sites, women performed better than men on the test of verbal learning and on coding ($p < .01$ for all). Women in the NEFS performed better on delayed free recall ($p < .01$) compared to men while they did so only marginally in the CHDS ($p = .13$). Women in the CHDS performed better on the test of verbal fluency ($p = .06$) compared to men. Compared to men in the NEFS, those in the CHDS performed better on both tests of verbal learning (for immediate free recall $p = .02$, for delayed free recall $p = .01$). Both men and women in the CHDS performed better on the coding task compared to those in the NEFS ($p = .25$ and $p = .05$ respectively).

Overall mean scores on the neurocognitive battery increased with increasing adult socioeconomic status (table 4). This held for both men and women and in the NEFS and the CHDS. For example, in the NEFS men, immediate recall on the CVLT increased from 22.9 to 23.6 to 26.7 for tertiles 1,2, and 3 of adult SES. In CHDS men, immediate recall scores were 24.0, 24.6 and 30.4 for tertiles 1,2, and 3 respectively. A similar increasing trend was found for women: in the NEFS the scores were 25.5, 27.5, and 30.0 and in the CHDS scores were 26.8, 29.0 and 29.9 for tertiles 1,2, and 3, respectively.

Excepting working memory, the relationships between any marker of fetal inflammation in the NEFS and neurocognitive performance were not significant (table 5A). In the NEFS, a significant decrement in working memory score was found in male participants, such that for every 10-percentile increase in birth weight for gestational age, the score increased by .3 points (95% confidence interval (CI) .068, .54). No decrements were found in women, and the difference in the association between men and women was statistically significant (Wald statistic -2.14 , $p = .03$). Further, for males who were fetal growth restricted, the working memory score declined by 1.5 points (95% CI -2.4 , -0.27) compared to non fetal growth restricted men. No significant decrement in working memory score was found in women, and the differences between the associations in men and women seemed different (Wald statistic $= 1.83$, $p = .06$).

Few associations were found between markers of fetal inflammation in the CHDS and neurocognitive performance (table 5B). In women, we found significant increases in immediate recall related to fetal inflammation; the estimated regression coefficients were significantly different from those in men for birth weight percentiles and FGR (Wald statistics $= -2.12$ and 1.78 respectively and $p = .03$ and $.08$, respectively).

In secondary analyses, we found no associations between inflammatory markers and neurocognitive function for participants in the lowest SES tertile. In the higher two SES tertiles, we found small, but significant associations between markers of fetal growth and

verbal fluency. Women who experienced fetal growth restriction scored approximately 4 points lower on the test of verbal fluency (95% CI $-7.7, -0.20$). Consistent results were found for percentile birth weight for gestational age.

Discussion

In our study of midlife cognitive function in relation to markers of fetal inflammation, we found few associations that were significant at conventional levels. In male participants from the NEFS, we found significant associations between percentile birth weight for gestational age and fetal growth restriction, categorized as the lowest 20th percentile birth weight for gestational age and working memory. We note that percentile birth weight for gestational age is a particularly good measure of fetal growth in term or near term births⁴⁰. We also found associations between FGR and immediate recall in CHDS women such that FGR was associated with better functioning. In secondary analyses, we also found an association between fetal growth restriction and verbal fluency among women in the upper two SES tertiles. That we find only 4 statistically significant findings in 64 comparisons may be indicative of a type II error. However, there may be other explanations for the lack of findings.

First, the births in this study were term. Previous studies suggest that decrements in childhood and adolescent IQ were related to low birth weight (i.e. < 2500 grams), and that these decrements declined in magnitude with post natal experience¹⁹ and may disappear in middle age. A systematic review of the literature (Shenkin et al 2004) relating birth weight to cognitive ability in childhood suggests that small but consistent positive associations between birth weight and childhood IQ, not confined to births < 2500 grams. However, as depicted in figure 3 of Shenkin, et al, after adjustment for potentially confounding variables, the steepest declines in childhood IQ occurred below a threshold of 3000 grams and leveled off above 3500 grams.

Second, we only obtained a cross sectional depiction of brain functions at age 43. Much has been written concerning the ability of the brain to recover from early insults given an enriched post natal environment. In the 1958 British birth cohort⁴¹, for example, both weight at birth and social circumstances in the post natal environment contributed to cognitive test performance up through age 17 as well as to the highest qualifications achieved by age 33. Two studies from Norway^{42,43} find small associations between birth weight and a proxy measure of IQ in young adults; one of these studies used sibship controls. Birth weight, however, was not a significant predictor of cognitive function later in life⁴⁴ and social circumstances in childhood remained a strong predictor of cognitive function among a cohort of Finnish men after adjustment for adult social circumstances⁴⁵. We note that our use of sibship controls reduces the impact of confounding by early familial and genetic factors⁴⁶. Thus, it is not surprising that men in the NEFS performed worse than men in the CHDS on the test of working memory given the sociodemographic differences both in childhood and as adults. Offspring of CHDS mothers were more likely to be of higher SES in childhood, as the Kaiser Health Plan required at least one adult in the home to be employed (see Susser, et al, this issue), and thus were more likely to be from more enriching environments. Men in the NEFS, on the other hand, were less likely to graduate from

college, were more likely to be classified in the lowest tertile of SES and were more likely to smoke compared to those from the CHDS.

Third, the association in the data was specific to men. The incidence of a number of neurodevelopmental disorders is greater in men^{47,48}, including autism, schizophrenia, learning disabilities and mental retardation. Although the underlying reason for such a difference remains unknown, there is increasing evidence, including some from our team, that sex differences in the development of specific brain regions place the male and female offspring at differential risks for the expression of different disorders in adulthood^{23,49,50} (see also Goldstein, et al. this issue). In particular, there is a large literature suggesting that sex differences in the associations between birth weight and later cognitive and behavioral outcomes may be due to differential impact of sex steroid hormones^{24,51-54}. Studies in animal models, as well as humans, find associations between sex steroid hormones on the development of gray and white matter and on the pace and asymmetry of brain development, both of which vary by sex with the male brain lagging behind the female brain⁵⁵⁻⁵⁷. Indeed, a large literature in animal models and in humans suggests a greater vulnerability of males to fetal or early postnatal insults with males having greater deficits in general cognitive ability, language, memory and attention^{21,22,58-61}.

In secondary analyses, we found an association between fetal growth restriction and verbal fluency in women in the higher adult socioeconomic strata. Most literature finds that women outperform men in tests of verbal fluency⁶²⁻⁶⁴. As suggested by Singh-Manoux⁶⁵ and others, adult socioeconomic position is one of the proximal determinants of cognition, with socioeconomic position in earlier life, as well as educational attainment, having more distal, indirect effects. One might expect the most vulnerable subgroup to be men in the lower socioeconomic strata. However, it may be that men in the lower socioeconomic strata are already functioning at a nadir, and that associations are found in the group with the highest potential functional capacity⁴⁹.

This study had several strengths over previous research. First, we selected all subjects from two comprehensive birth cohorts with well defined exposure measures and comprehensive data on social circumstances at birth. Second, we selected sibling pairs and although not all members of a sibship agreed to participate, we were able to control for early environmental conditions. Third, we employed a comprehensive battery of neurocognitive tests which were designed to measure a wide range of functions. Finally, the adult assessment battery collected a rich set of variables to control for possible confounding. Unfortunately, we do not have data on social circumstances and educational attainment over the period from birth to approximately age 43 and cannot test whether such variables mitigate any possible effects of fetal growth restriction⁶⁶. Further subtle effects of fetal risk factors may be more evident at the level of the brain than at the level of cognitive performance.

In summary, only small effects in cognition were found 45 years after in utero exposure to markers of fetal inflammation. The effects were limited to the adult sons of NEFS participants, who were, in both childhood and adulthood, of lower socioeconomic circumstances compared to the adult sons of CHDS participants. These results suggest that, in term infants, cognitive performance in adulthood is only partly a result of fetal

circumstances and that the postnatal environment throughout the life course may mitigate any subtle brain abnormalities from minor fetal insults that do not lead to prematurity.

Acknowledgements

This work was supported by NIMH-NHLBI RO1 MH074679 (Goldstein, P.I.) and NIA P01 AG023028 (Susser, overall PI) and, in part, by ORWH-NIMH P50 MH082679 (Goldstein, P.I.). The authors would like to thank Harlin Aizley, Ed.M. for her clinical diagnostic interviewing expertise and collection of RRV data, Jo-Ann Donatelli, Ph.D. for her clinical expertise in training and quality control of psychiatric and cognitive data, Christiana Provencale, M.A. for her efforts in managing the recruitment team at Brown, Barbara Cohn, Ph.D. and Piera Cirillo M.P.H. for providing access to the CHDS archived data and for providing the sample from the CHDS, Howard Andrews, Ph.D. for his contribution to data management, Catherine Schaefer, Ph.D. for overseeing the original NIA work in California, and Kim Fader, M.A. for her administrative help in maintaining connections between multiple sites involved in this work.

References

1. Breslau N. Psychiatric sequelae of low birth weight. *Epidemiol Rev.* 1995; 17:96–106. [PubMed: 8521950]
2. Rieder RO, Broman SH, Rosenthal D. The offspring of schizophrenics: II. Perinatal factors and IQ. *Arch Gen Psychiatry.* 1977; 34:789–799. [PubMed: 879975]
3. Many A, Fattal A, Leitner Y, Kupfermine MJ, Harel S, Jaffa A. Neurodevelopmental and cognitive assessment of children born growth restricted to mothers with and without preeclampsia. *Hypertension in Pregnancy.* 2003; 22:25–29. [PubMed: 12648440]
4. Many A, Fattal-Valevski A, Leitner: Neurodevelopmental and cognitive assessment of 6-year old children born growth restricted. *Int J Gynecol Obstet.* 2005; 89:55–56.
5. Ehrenstein V, Rothman KJ, Pedersen L, Hatch EE, Sorensen HT. Pregnancy-associated hypertensive disorders and adult cognitive function among Danish conscripts. *Amer J Epidemiol.* 2009; 170:1025–1031. [PubMed: 19726495]
6. Ounsted MK, Moar VA, Good FJ, Redman CWG. Hypertension during pregnancy with and without specific treatment; the development of children at the age of four years. *Brit J Obstet Gynecol.* 1980; 87:19–24.
7. Ounsted M, Cockburn J, Moar VA, Redman CWG. Maternal hypertension with superimposed pre-eclampsia: effects on child development at 7 ½ years. *Brit J Obstet Gynecol.* 1983; 90:644–649.
8. Seidman DS, Laor A, Gale R, Stevenson DK, Mashiach S, Danon Y. Pre-eclampsia and offspring's blood pressure, cognitive ability and physical development at 17-years-of-age. *Brit J Obstet Gynecol.* 1991; 98:1009–1014.
9. Klein NK, Hack M, Breslau N. Children who were very low birth weight: development and academic achievement at nine years of age. *J Dev Behav Pediatr.* 1989; 10:32–37. [PubMed: 2925866]
10. Breslau N, Delrotto J, Brown GG, Kumar S, Ezhuthachan S, Hufnagle KG, Peterson EL. A gradient relationship between low birth weight and IQ at age 6 years. *Arch Pediatr Adolesc Med.* 1994; 148:377–383. [PubMed: 8148937]
11. Breslau N, Chilcoat H, DelDotto J, Andreski P, Brown G. Low birth weight and neurocognitive status at six years of age. *Biol Psychiatry.* 1996; 40:389–397. [PubMed: 8874840]
12. Petersen M, Greisen G, Kovacs R, Munck H, Friis-Hansen B. Status at four years of age in 280 children weighing 2300g or less at birth. *Dan Med Bull.* 1990; 37:546–552. [PubMed: 1705878]
13. Mutch L, Leyland A, McGee A. Patterns of neuropsychological function in a low-birthweight population. *Dev Med Child Neurol.* 1993; 35:943–956. [PubMed: 8224562]
14. Rikards AL, Kitchen WH, Doyle LW, Ford GW, Kelly EA, Callahan C. Cognition, school performance and behavior in very low birth weight and normal birth weight children at 8 years of age: a longitudinal study. *J Development Behavior and Pediatrics.* 1993; 14:363–368.
15. Roth SC, Baudin J, McCormick DC, Edwards AD, Townsend J, Stewart AL, Reynolds EO. Relation between ultrasound appearance of the brain of very preterm infants and

neurodevelopmental impairment at eight years. *Dev Med Child Neurol.* 1993; 35:755–768. [PubMed: 7689065]

16. Matte TD, Bresnahan M, Begg M, Susser E. Influence of variation in birth weight within normal range and within sibships on IQ at age 7 years: Cohort study. *Br Med J.* 2001; 323:310–314. [PubMed: 11498487]
17. Hardy, JB.; Mellits, ED.; Reed, DM. *The Epidemiology of Prematurity: Epidemiology Workshop, National Institute of Child Health and Development. Urban and Schwarzenberg; Baltimore: 1976. 1977. Relationship of low birth weight to maternal characteristics of age, parity, education and body size.*
18. Sorensen HT, Sabroe S, Olsen J, Rothman KJ, Gillman MW, Fisher P. Birth weight and cognitive function in young adult life: historical cohort study. *Br Med J.* 1997; 315:401–403. [PubMed: 9277604]
19. Richards M, Hardy R, Kuh D, Wadsworth ME. Birth weight and cognitive function in the British 1946 birth cohort: longitudinal population based study. *Br Med J.* 2001; 322:199–202. [PubMed: 11159613]
20. Collaer ML, Hines M. Human behavioral sex differences: a role for gonadal hormones during early development? *Psychol Bull.* 1995; 118:55–107. [PubMed: 7644606]
21. Goldstein JM, Seidman LJ, Goodman JM, Koren D, Lee H, Weintraub S, Tsuang MT. Are there sex differences in neuropsychological functions among patients with schizophrenia? *Amer J Psychiatry.* 1998; 155:1358–1364. [PubMed: 9766767]
22. Goldstein JM, Seidman LJ, Santangelo S, Knapp P, Tsuang MT. Are schizophrenic men at higher risk for developmental deficits than schizophrenic women? Implications for adult neuropsychological function. *J Psychiatric Res.* 1994; 28:483–489.
23. Goldstein, JM.; Walder, DJ.; Sharma, T.; Harvey, P. Oxford University Press; United Kingdom: 2006. Sex differences in schizophrenia: the case for developmental origins and etiological implications; *The Early Course of Schizophrenia*; p. 147-173.
24. Goldstein JM, Seidman LJ, Horton NJ, Makris M, Kennedy DN, Caviness VS, Faraone SV, Tsuang MT. Normal sexual dimorphism of the adult human brain assessed by in vivo magnetic resonance imaging. *Cerebral Cortex.* 2001; 11:490–497. [PubMed: 11375910]
25. Nunez JL, McCarthy MM. Sex differences and hormonal effects in a model of preterm infant brain injury. *Ann NY Acad Sci.* 2003; 1008:281–284. [PubMed: 14998896]
26. Lauterbach MD, Raz S, Sander CJ. Neonatal hypoxic risk in preterm birth infants: the influence of sex and severity of respiratory distress on cognitive recovery. *Neuropsychology.* Dec; 2001 1989 15103(6):411–420. 1287–95. [PubMed: 11499996]
27. Clark AS, Goldman-Rakic PS. Gonadal hormones influence the emergence of cortical function in nonhuman primates. 1989; 103:1287–1295.
28. Huppert, FA.; Whittington, JE.; Cox, BD.; Huppert, FA.; Whichelow, M. Dartmouth; Aldershot UK: 1993. Changes in cognitive function in a population sample; *The Health and Lifestyle Survey: Seven Years on a Longitudinal Study of a Nationwide Sample, Measuring Changes in Physical and Mental Health, Attitudes and Lifestyle*; p. 155-172.
29. Richards M, Stern Y, Marby R, Wadsworth M. Childhood IQ, education and midlife cognitive function in a national UK birth cohort. *Neuroepidemiology.* 1998; 17:213. abstract.
30. Oken E, Kleinman KP, Rich-Edwards J, Gillman MW. A nearly continuous measure of birth weight for gestational age using a United States national reference. *BMC Pediatrics.* 2003; 3:6. [PubMed: 12848901]
31. National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol.* 1990; 163:1691–1712. Part 1. [PubMed: 2104525]
32. Seidman LJ, Breiter HC, Goodman JM, Goldstein JM, Woodruff PW, O; Craven K, Savoy R, Tsuang MT, Rosen BR. A functional magnetic resonance imaging study of auditory vigilance with low and high information processing demands. *Neuropsychology.* 1998; 12:505–518. [PubMed: 9805320]
33. Delis, DC.; Kramer, JH.; Kaplan, E.; Ober, BA. Pearson; 2000. California Verbal Learning Test – Second Edition (CVLT-II).

34. Bolla KI, Lindgren KN, Bonaccorsy C, Bleecker ML. Predictors of verbal fluency (FAS) in the healthy elderly. *J Clin Psychol.* 1990; 45:623–628. [PubMed: 2246370]
35. Wechsler, D. Psychological Corporation; San Antonio, TX: 1997. Wechsler Adult Intelligence Scale—Third edition (WAIS-III).
36. Usui N, Haji T, Maruyama M, Katsuyama N, Uchida S, Hozawa A, Omori K, Tsuji I, Kawashima R, Taira M. Cortical areas related to performance of WAIS digit symbol test: a functional imaging study. *Neuroscience Letters.* 2009; 463:1–5. [PubMed: 19631255]
37. First, MB.; Gibbon, M.; Spitzer, RL.; Williams, JBW.; Benjamin, LS. American Psychiatric Press, Inc.; Washington, D.C.: 1997. Structured Clinical Interview for DSM-IV Axis II Personality Disorders, (SCID-II).
38. Myrionthopoulos NC, French KS. An application of the US bureau of the census socioeconomic index to a large diversified patient population. *Soc Sci Med.* 1968; 2:283–299. [PubMed: 5760819]
39. Gelman, A.; Hill, J. Cambridge University Press; New York: 2006. Data Analysis Using Regression and Multilevel/Hierarchical Models.
40. Hutcheon JA, Platt RW. The missing data problem in birth weight percentiles and thresholds for “small-for-gestational-age”. *Amer J Epidemiol.* 2008; 167:786–792. [PubMed: 18343882]
41. Jefferis BJ, Power C, Hertzman C. Birth weight, childhood socioeconomic environment and cognitive development in the 1958 British birth cohort study. *Br Med J.* 2002; 325:305–310. [PubMed: 12169505]
42. Eriksen W, Sundet JM, Tambs K. Birth weight standardized to gestational age and intelligence in young adulthood: a register-based birth cohort study of male siblings. *Amer J Epidemiol.* 2010; 172:530–536. [PubMed: 20631044]
43. Eide MG, Oyen N, Skjaerven R, Bjerkedal T. Associations of birth size, gestational age, and adult size with intellectual performance: evidence from a cohort of Norwegian men. *Pediatr Res.* 2007; 62:636–642. [PubMed: 17805203]
44. Martyn CN, Gale CR, Sayer AA, Fall C. Growth in utero and cognitive function in adult life: follow up study of people born between 1920 and 1943. *Br Med J.* 1996; 312:1393–1396. [PubMed: 8646096]
45. Kaplan GA, Turrell G, Lynch JW, Everson SA, Helkala EL, Salonen JT. Childhood socioeconomic position and cognitive function in adulthood. *Int J Epidemiol.* 2001; 30:256–263. [PubMed: 11369724]
46. Susser E, Eide MG, Begg M. Invited commentary: the use of sibship studies to detect familial confounding. *Amer J Epidemiol.* 2010; 172:530–536. [PubMed: 20631044]
47. Schendel D, Rice C, Cunliffe C. The contribution of rare diseases to understanding the epidemiology of neurodevelopmental disabilities. *Adv Exp Med Biol.* 2010; 686:433–53. [PubMed: 20824459]
48. Goldstein, JM.; Lewine, RRJ.; Castle, DJ.; McGrath; Kulkarni, J. Women and Schizophrenia. Cambridge University Press; Cambridge: 2000. Overview of sex differences in schizophrenia: where have we been and where do we go from here?; p. 111–143.
49. Goldstein JM, Seidman LJ, O’Brien L, Horton N, Kennedy DN, Makris N, Caviness VS, Faraone SV, Tsuang MT. Impact of normal sexual dimorphisms on sex differences in structural brain abnormalities in schizophrenia assessed by magnetic resonance imaging. *Arch Gen Psychiatry.* 2002; 59:154–164. [PubMed: 11825137]
50. Anastario M, Salafia CM, Fitzmaurice G, Goldstein JM. Impact of fetal versus perinatal hypoxia on sex differences in childhood outcomes: developmental timing matters. *Soc Psychiatry Psychiatr Epidemiol.* in press.
51. De Courten-Myers GM. The human cerebral cortex: gender differences in structure and function. *J Neuropath Exp Neurol.* 1999; 58:217–226. [PubMed: 10197813]
52. Resnick SM, Berenbaum SA, Gottesman II, Bouchard TJ Jr. Early hormonal influences on cognitive functioning in congenital adrenal hyperplasia. *Dev Psychol.* 1986; 22:191–198.
53. Murphy DGM, Allen G, Haxby JV, Largay KA, Daly E, White BJ, Powell CM, Schapiro MB. The effects of sex steroids, and the X chromosome on female brain function: a study of the

- neuropsychology of Turner syndrome. *Neuropsychologia*. 1994; 32:1309–1323. [PubMed: 7877742]
54. Schumacher M, Legros JJ, Balthazart J. Steroid hormones, behavior and sexual dimorphism in animals and men: the nature-nuture controversy. *Exp Clin Endocrinol*. 1987; 90:129–156. [PubMed: 3322849]
 55. Raz S, Lauterbach MD, Hopkins TL, Glogowski BK, Porter CL, Riggs WW, Sander CJ. A female advantage in cognitive recovery from early cerebral insult. *Dev Psychol*. 1995; 31:958–966.
 56. Bowers JM, Waddell J, McCarthy MM. A developmental sex difference in hippocampal neurogenesis is mediated by endogenous oestradiol. *Biol Sex Differ*. 2010; 22:8–21. [PubMed: 21208470]
 57. Zhang JM, Konkle AT, Zup SL, McCarthy MM. Impact of sex and hormones on new cells in the developing rat hippocampus: a novel source of sex dimorphism? *Eur J Neurosci*. 2008; 27:791–800. [PubMed: 18333959]
 58. Benes FM, Turtle M, Khan Y, Farol P. Myelination of a key relay zone in the hippocampal formation occurs in the human brain during childhood, adolescence, and adulthood. *Arch Gen Psychiatry*. 1994; 51:477–484. [PubMed: 8192550]
 59. Jernigan TL, Trauner DA, Hesselink JR, Tallal PA. Maturation of human cerebrum observed in vivo during adolescence. *Brain*. 1991; 114:2037–2049. [PubMed: 1933232]
 60. Giedd JN, Snell JW, Lange N, Rajapakse JC, Casey BJ, Kozuch PL, Vaituzis AC, Vauss YC, Hamburger SD, Kaysen D, Rapoport JL. Quantitative magnetic resonance imaging of human brain development: ages 4–18. *Cereb Cortex*. 1996; 6:551–560. [PubMed: 8670681]
 61. Witelson SF. Neural sexual mosaicism: sexual differentiation of the human temporo-parietal region for functional asymmetry. *Psychoneuroendocrinology*. 1991; 16:131–153. [PubMed: 1961836]
 62. Saykin AJ, Gur RC, Gur RE, Shtasel DL, Flannery KA, Mozley LH. Normative neuropsychological test performance: effects of age, education, gender and ethnicity. *Appl Neuropsychol*. 1995; 2:79–85. [PubMed: 16318528]
 63. Gur RC, Turetsky BI, Matsui M, Yan M, Bilker W, Hughett P, Gur RE. Sex differences in brain gray and white matter in healthy young adults: correlations with cognitive performance. *J Neurosci*. 1999; 19:4065–4072. [PubMed: 10234034]
 64. Harasty J, Double KL, Halliday GM, Kril JJ, McRitchie DA. Language-associated cortical regions are proportionally larger in the female brain. *Arch Neurol*. 1997; 54:171–176. [PubMed: 9041858]
 65. Singh-Manoux A, Richards M, Marmot M. Socioeconomic position across the lifecourse: how does it relate to cognitive function in mid-life? *Ann Epidemiol*. 2005; 15:572–578. [PubMed: 16118001]
 66. Factor-Litvak P, Sher A. Invited commentary: coming out of the box. *Amer J Epidemiol*. 2009; 169:1179–1181. [PubMed: 19357325]

Table 1

Demographic Characteristics of Participants in the EDAH-MDCVD Project

Characteristic	NEFS		CHDS	
	N	%	N	%
Total	247	100	227	100
Sex (Male)	106	42.9	107	47.1
Age at interview (mean, standard deviation)	44.2	2.5	43.4	2.0
Race (White)	226	91.9	122	53.7
Adult Socioeconomic Status (tertiles)				
1st: <=3.8	88	35.6	59	26.0
2nd: 3.9-6.3	76	30.8	75	33.0
3rd: >=6.4	78	31.6	76	33.5
Marital Status				
Married or living with partner	161	65.5	144	63.4
Divorced or separated	37	15.0	29	12.8
Single or widowed	48	19.5	54	23.8
Adult Educational Attainment				
< High school graduate or GED	139	56.7	125	55.3
Some college, trade school or associate's degree	85	34.7	73	32.3
College graduate or higher	21	8.6	28	12.4
Total				
Adult Smoking Behavior				
Never	30	13.4	56	24.9
Ever, but current status unknown	58	25.9	81	36.0
Past	85	38.0	60	26.7
Current	51	22.8	28	12.4
Total				
Adult Alcohol Consumption				
Never or Not in the Past Year	107	43.7	95	42.0
< Once Per Month	93	38.0	83	36.7
1-3 Times Per Month	32	13.1	38	16.8
At least once per week	12	5.0	10	4.4
Adult Diagnosis of Major Depressive Disorder	102	41.3	56	24.7

Table 2

Markers of Fetal Growth and Inflammation of Participants in the EDAH-MDCVD Sample

Characteristic	NEFS		CHDS	
	N	%	N	%
Total	247	100	227	100
Birth Weight Percentile for Gestational Age				
< 10	45	18.2	28	12.3
10-24.9	65	26.3	46	20.3
25-49.9	68	27.5	73	32.2
50-74.9	41	16.6	45	19.8
75	28	11.3	35	15.4
Total				
Fetal Growth Restriction	98	39.7	65	28.6
Preeclampsia	86	34.8	7	3.1
Fetal Inflammation	160	64.8	69	30.4

Table 3

Neuropsychological Outcomes of Participants in the EDAH-MDCVD Sample

Characteristic	NEFS			CHDS		
	N	%		N	%	
Total	247	100		227	100	
Men	106	42.9		107	47.1	
Women	141	57.1		120	52.9	
	N	Mean	SD	n	Mean	SD
Auditory CPT- Vigilance (# hits)						
Total	246	17.4	1.9	224	17.6	0.9
Men	106	17.3	2.5	107	17.6	1.2
Women	140	17.4	1.3	117	17.7	0.7
Working Memory with Interference (# hits)						
Total	245	9.1	2.9	224	9.7	3.3
Men	105	9.3	3.0	107	9.8	3.8
Women	140	9.1	2.8	117	9.6	2.9
Verbal Learning (California Verbal Learning Test)						
Immediate recall total correct (trials 1-3)						
Total	247	26.1	5.8	217	27.4	6.3
Men	106	24.2	4.8	105	26.1	7.0
Women	141	27.5	6.0	112	28.5	5.5
Delayed free recall						
Total	245	9.1	3.0	220	10.0	3.4
Men	105	8.0	2.6	105	9.6	3.4
Women	140	9.9	3.0	115	10.4	3.3
Verbal Fluency (total FAS words)						
Total	246	39.5	11.6	227	40.0	12.4
Men	106	38.5	11.7	107	38.4	11.6
Women	140	40.3	11.5	120	41.5	13.0
WAIS Digit Symbol/Coding						
Total	246	10.3	2.7	223	11.0	3.2
Men	106	9.3	2.6	106	10.2	3.2
Women	140	11.1	2.5	117	11.8	3.1

Table 4

Neurocognitive Test Results by Adult Socioeconomic Status by Sex and Site

Variable	Auditory CPT						Verbal Learning						Delayed Recognition			Verbal Fluency			Coding		
	Vigilance			Working Memory with Interference			Immediate recall			Delayed Free Recall			n			Mean			SD		
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
NEFS Men																					
SES tertiles (sites combined)																					
1st	38	17.2	2.9	37	8.5	2.9	38	22.9	4.2	38	7.4	2.7	38	14.1	2.3	38	34.2	10.6	38	7.9	2.7
2nd	36	17.6	1.0	36	9.5	3.0	36	23.6	4.5	35	7.9	2.3	35	14.5	1.4	36	38.0	11.8	36	9.7	2.6
3rd	29	17.8	0.5	29	9.8	3.0	29	26.7	5.4	29	8.9	2.7	29	15.1	1.0	29	44.6	11.0	29	10.4	1.7
NEFS Women																					
SES tertiles (combined)																					
1st	50	17.6	0.8	50	8.9	2.5	50	25.5	5.8	50	8.5	3.0	50	14.4	2.0	50	36.8	9.4	49	9.9	2.2
2nd	39	16.9	2.0	39	8.2	2.8	40	27.5	5.2	40	9.9	2.6	40	15.0	1.5	39	39.8	10.0	40	11.7	2.2
3rd	49	17.6	0.8	49	9.7	2.9	49	30.0	5.8	48	11.4	2.6	48	15.4	1.0	49	44.5	12.6	49	12.1	2.3
CHDS Men																					
SES tertiles (sites combined)																					
1st	30	17.3	1.8	30	8.8	3.0	30	24.0	7.1	30	8.3	2.8	30	14.2	1.9	30	36.5	11.1	30	8.6	2.3
2nd	38	17.7	0.8	38	9.4	3.8	36	24.6	6.9	36	8.7	3.4	37	14.9	1.8	38	37.4	11.2	37	9.8	2.8
3rd	33	17.9	0.4	33	11.8	3.7	33	30.4	5.2	33	12.1	2.5	33	15.5	0.9	33	42.7	11.8	33	12.5	3.0
CHDS Women																					
SES tertiles (sites combined)																					
1st	29	17.4	0.9	29	9.2	2.7	26	26.8	6.0	28	9.4	4.0	28	14.2	4.1	29	32.1	9.4	28	9.5	2.8
2nd	34	17.8	0.6	34	9.8	3.1	32	29.0	5.1	33	11.0	3.0	33	15.4	0.9	37	41.1	12.2	35	11.6	2.6
3rd	43	17.8	0.5	43	10.2	2.8	43	29.9	5.4	43	10.8	2.9	43	15.4	1.0	43	48.5	12.1	43	13.4	2.8

Table 5A

Markers of fetal inflammation as predictors of adult performance on neurocognitive tests stratified by sex in NEFS sample (controlled for age, race, tertiles of socioeconomic status, adult smoking behaviour, sibships)

Neurocognitive Test	Women				Men			
	n	b	SE	p-value	n	b	SE	p-value
Working Memory								
Birthweight Percentile	138	−0.002	0.009	0.82	102	0.030	0.012	0.03
Fetal Inflammation		−0.732	0.502	0.16		−0.473	0.658	0.49
Fetal Growth Restriction		−0.047	0.488	0.92		−1.517	0.637	0.04
Preeclampsia		−0.910	0.505	0.08		0.230	0.716	0.75
Immediate Recall								
Birthweight Percentile	139	−0.010	0.018	0.60	103	0.010	0.019	0.62
Fetal Inflammation		0.417	0.980	0.67		1.320	1.007	0.22
Fetal Growth Restriction		0.029	0.956	0.98		−0.094	1.008	0.93
Preeclampsia		0.405	1.004	0.69		1.086	1.091	0.34
Delayed Free Recall								
Birthweight Percentile	138	0.011	0.009	0.24	102	0.008	0.010	0.46
Fetal Inflammation		−0.370	0.470	0.44		0.717	0.543	0.21
Fetal Growth Restriction		−0.689	0.459	0.14		−0.059	0.541	0.92
Preeclampsia		0.404	0.489	0.42		0.507	0.587	0.41
Verbal Fluency								
Birthweight Percentile	138	−0.012	0.036	0.74	103	−0.100	0.044	0.04
Fetal Inflammation		1.418	1.949	0.47		1.125	2.360	0.64
Fetal Growth Restriction		1.322	1.896	0.49		1.013	2.365	0.68
Preeclampsia		0.304	2.007	0.88		−0.350	2.602	0.90

Table 5B

Markers of fetal inflammation as predictors of adult performance on neurocognitive tests stratified by sex in CHDS sample (controlled for age, race, tertiles of socioeconomic status, adult smoking behaviour, sibships)

Neurocognitive Test	Women				Men			
	n	b	SE	p-value	n	b	SE	p-value
Working Memory								
Birthweight Percentile	106	−0.017	0.011	0.12	101	0.001	0.014	0.96
Fetal Inflammation		0.646	0.624	0.31		0.476	0.790	0.55
Fetal Growth Restriction		0.860	0.645	0.19		0.461	0.807	0.58
Preeclampsia		−1.253	1.467	0.40		−1.074	2.534	0.68
Immediate Recall								
Birthweight Percentile	101	−0.048	0.020	0.02	99	0.019	0.024	0.44
Fetal Inflammation		2.029	1.159	0.09		−0.851	1.400	0.55
Fetal Growth Restriction		2.568	1.195	0.04		−0.743	1.427	0.61
Preeclampsia		0.187	2.792	0.95		−2.966	4.483	0.52
Delayed Free Recall								
Birthweight Percentile	104	−0.017	0.012	0.16	99	0.002	0.011	0.85
Fetal Inflammation		0.602	0.689	0.39		−0.650	0.644	0.33
Fetal Growth Restriction		0.967	0.708	0.18		−0.708	0.655	0.29
Preeclampsia		−0.543	1.779	0.76		−1.129	2.078	0.59
Verbal Fluency								
Birthweight Percentile	109	0.055	0.042	0.20	99	0.017	0.044	0.71
Fetal Inflammation		−3.445	2.345	0.15		−2.323	2.569	0.38
Fetal Growth Restriction		−2.631	2.414	0.28		−1.429	2.634	0.59
Preeclampsia		−9.388	5.647	0.11		−14.784	8.112	0.09