

OBSTETRICS

Maternal hypertensive disorders in pregnancy and self-reported cognitive impairment of the offspring 70 years later: the Helsinki Birth Cohort Study

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OBJECTIVE: We tested whether maternal hypertensive disorders during pregnancy predict self-reported cognitive impairment, which is one of the earliest behavioral markers of dementia, of the offspring 70 years later.

STUDY DESIGN: We included 876 participants of the Helsinki Birth Cohort Study 1934-44 who were born after normotensive, preeclamptic, or hypertensive pregnancies that were defined by the use of the mother's blood pressure and urinary protein measurements at maternity clinics and birth hospitals. The participants completed a psychological questionnaire that included questions on cognitive failures and dysexecutive functioning at an average age of 69.3 ± 3.1 (SD) years.

RESULTS: In comparison with the offspring who were born after normotensive pregnancies, the offspring who were born after preeclamptic

pregnancies reported more frequent complaints of cognitive failures, distractibility, and false triggering. Further, among women we found maternal hypertension without proteinuria that was associated with more frequent complaints of cognitive failures, forgetfulness, and false triggering.

CONCLUSION: Hypertensive disorders during pregnancy are associated with more frequent subjective complaints of cognitive failures of the offspring in old age.

Key words: adulthood, cognitive impairment, hypertensive disorders in pregnancy, offspring

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Empiric evidence suggests that a suboptimal prenatal environment, which is reflected in prematurity and smaller body size at birth, is associated with lower cognitive and executive function in childhood, adolescence, and adulthood¹⁻¹¹ and with cognitive decline up to old age.¹² Hypertensive disorders

(which include chronic hypertension, gestational hypertension, and [preeclampsia]) complicate approximately 10% of all pregnancies.¹³ These disorders threaten the health and well-being of both the mother and the fetus and are among the key underlying causes of prematurity and intrauterine growth restric-

tion. Thus, by affecting the fetal developmental milieu, hypertensive disorders may point to the mechanisms by which prenatal adversity associates with cognitive function in subsequent life.

The literature that reports associations between maternal hypertensive disorders in pregnancy and cognitive ability of the offspring is, however, scanty. The existing evidence shows that maternal hypertensive disorders are associated with poorer cognitive ability of the offspring in childhood and young adulthood.¹⁴⁻²³

Although some studies have reported null associations²⁴⁻²⁷ and even that maternal hypertensive disorders are associated with better cognitive ability of the offspring,²⁸ the findings tip in the direction of a negative association. Yet, it remains uncertain whether maternal hypertensive disorders continue to affect cognitive function in old age. We recently demonstrated that men who had been born after pregnancies that were complicated by a hypertensive disorder, in comparison with men who had been born after normotensive pregnancies,

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had lower cognitive ability at an average age of 68 years and displayed a greater decline in cognitive ability after age 20 years.²⁹ Here our primary aim was to extend these analyses by testing whether maternal hypertensive disorders during pregnancy are associated with self-reported cognitive impairment, namely subjective complaints of cognitive failures and dysexecutive functioning, which are among the earliest behavioral markers of dementia,^{30,31} in elderly men and women who participated in the Helsinki Birth Cohort study.

Our secondary aim was to test whether any potential associations between hypertensive disorders in pregnancy and self-reported cognitive impairment differ according to sex, childhood socioeconomic status, length of gestation, and parity. The rationale for testing modulation by these factors was motivated by studies that point to sex differences in cognitive aging.³² Further, the occurrence of hypertensive disorders in pregnancy may vary according to social class^{33,34} and hypertensive disorders, especially preeclampsia, that occur in preterm pregnancy are on average more severe and may be different in cause from disorders that occur at term.^{35,36} Finally, hypertensive disorders appear to occur more frequently and may be qualitatively different in primi- than in multiparous pregnancies.^{36,37}

METHODS

Participants

The Helsinki Birth Cohort Study comprises 13,345 men and women who were born as singletons between 1934 and 1944 in 1 of the 2 maternity hospitals in Helsinki, Finland. These men and women attended child welfare clinics during childhood and were still living in Finland in 1971, by which time a unique personal identification number had been assigned to each resident of the country. The study population has been described in detail previously.^{38,39}

From 2009–2010, a psychologic questionnaire that included questions on cognitive failures and executive function was administered to (1) a randomly selected subsample of women and men

($n = 2003$) who had from 2001–2004 participated in a detailed clinical examination⁴⁰ and (2) a subsample of men only ($n = 2786$; 642 of whom belonged also to the randomly selected clinical subsample) who participated in a testing of cognitive ability during their compulsory military service from 1952–1972.⁶ Altogether these subsamples comprised 3072 men and 1075 women. From 2009–2010, 1981 men and 954 women were still traceable: 709 had died; 312 had declined participation in subsequent follow-up evaluation; and 193 lived abroad or had an unknown address. Of the traceable subjects, 1095 men and 798 women (64.5%) returned the questionnaire. Of these, data on maternal blood pressure and protein tests during pregnancy to diagnose hypertensive pregnancy disorders were available on 511 men and 387 women; 499 men and 377 women had adequate data on gestational age based on last menstrual period⁴¹ and were included in this study sample. Our previous publications have addressed representativeness of the randomly selected subsample, the subset of military conscripts, and the subpopulation with data available on maternal hypertension and proteinuria in relation to the entire Helsinki Birth Cohort study cohort.^{6,23,40,42} The current study sample did not differ in maternal age, weight, height, parity, and birthweight from those who were still traceable from 2009–2010 but who did not return the questionnaire. The included participants more often were born to lower social classes (69%, 21%, and 10% of the included participants were born to manual working, junior clerical and senior clerical fathers, respectively, vs 63%, 23%, and 14% of the participants who did not return the questionnaire; $P = .002$).

The Ethics Committee of the Helsinki and Uusimaa Hospital District approved the study, and all participants signed written informed consent.

Measures

Hypertensive disorders

To identify pregnancy-related hypertensive disorders, we used the mother's blood pressure and urinary protein mea-

surements that were recorded at antenatal clinics or at birth hospital. These data and definitions of hypertensive pregnancy disorders have been described in detail.⁴² Briefly, all pregnant women were encouraged to attend the antenatal clinics, which were introduced in Helsinki in 1928.⁴³ Of the 13,345 participants in the original cohort, maternal antenatal clinics data were available for 6410 participants (48.0%) and included, on average, 2.0 blood pressure and 2.5 urinary protein measurements in each pregnancy. Based on this information, we defined 3 groups of mothers: (1) mothers with severe and nonsevere preeclampsia, with proteinuria (approximately, 1 mg/mL of albumin)⁴³ and a systolic blood pressure of ≥ 140 mm Hg or a diastolic pressure of ≥ 90 mm Hg; (2) mothers with gestational and chronic hypertension, with hypertension as in (1) but no proteinuria and with any systolic blood pressure ≥ 140 mm Hg or any diastolic blood pressure ≥ 90 mm Hg at <20 weeks gestation; and (3) normotensive mothers with neither systolic pressure of 140 mm Hg nor diastolic pressure of 90 mm Hg during pregnancy. These definitions are consistent with the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy 2000 criteria,^{42,44} with 2 exceptions: first, we considered 1 high blood pressure measurement to be sufficient for diagnosis because our data did not allow us to require 2 separate measurements according to the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy criteria; second, our data included only a qualitative measurement of proteinuria.^{43,44}

Other neonatal, maternal and adult characteristics

Data on offspring date of birth, weight (grams) and head circumference (centimeters) at birth; mother's height (centimeters), weight (kilograms), and age at delivery; parity, and date of last menstrual period were extracted from birth records. Birth, child welfare clinic, and school health care records included data on fathers' occupations, a marker of the family's socioeconomic status, which

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