



Parental psychological distress during pregnancy and childhood cardiovascular development. The Generation R Study

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ABSTRACT

Background: Maternal psychological distress during pregnancy might lead to higher fetal cortisol exposure, which subsequently leads to fetal cardiovascular developmental adaptations and cardiovascular dysfunction in later life.

Aims: We examined whether maternal and paternal psychological distress was associated with the cardiovascular outcome measurements in school age children.

Study design and subjects: In a population-based prospective cohort study among 4831 children, we assessed maternal and paternal psychological distress during pregnancy by questionnaire, using the Brief Symptom Inventory (see Fig. 1).

Outcome measures: At the child age of six years, we performed blood pressure and carotid–femoral pulse wave velocity measurements, and M-mode measurements of left cardiac structures and fractional shortening.

Results: We did not observe associations of high maternal and paternal psychological symptom scores with childhood blood pressure and carotid–femoral pulse wave velocity after adjustment for potential confounders. Maternal overall psychological symptoms were associated with a lower childhood left ventricular mass (difference -1.10 g (95% confidence interval -2.13 to -0.07) between mothers with high scores and normal scores), but not with other cardiac structures and fractional shortening. Paternal overall psychological symptoms showed a similar association with childhood left ventricular mass (difference -1.34 grams (95% confidence interval -3.69 to 1.02) between fathers with high scores and normal scores).

Conclusions: Our results do not support the hypothesis that maternal psychological distress affects cardiovascular development in early life. Similar associations of maternal and paternal psychological distress with left ventricular mass suggest that these associations could be due to unmeasured social and environmental factors, rather than direct intra-uterine effects.

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1. Introduction

Adverse fetal exposures may lead to permanent developmental adaptations in the structure and function of the cardiovascular system and other organ systems [1]. These adaptations may be beneficial on short-term, but increase the susceptibility of cardiovascular disease and metabolic diseases in later life [1]. This hypothesis is largely based on studies showing associations of low birth weight with high blood pressure, cardiovascular disease and its risk factors [2–4]. Maternal psychological distress during pregnancy might be one of the adverse fetal

exposures leading to fetal developmental adaptations [5], possibly by dysregulation of the maternal hypothalamic–pituitary–adrenal (HPA) axis [6], and higher fetal cortisol exposure [6]. Previous animal and human studies have shown that excessive exposure to exogenous glucocorticoids is associated with higher blood pressure in the offspring [7–10]. Mild endogenous elevations in cortisol levels, e.g. due to maternal psychological distress during pregnancy, might also lead to developmental adaptations [11], such as hyperactivity of the offspring's HPA-axis [12], and affect cardiovascular function in the offspring, but the number of studies is limited [13]. Recently, van Dijk et al showed that the presence of multiple psychosocial stressors during pregnancy was associated with higher blood pressure in children aged 5–7 years, although the authors acknowledged that after correction for multiple testing, all associations were not significant [14]. If associations are present at a young age, they may be less confounded by other variables

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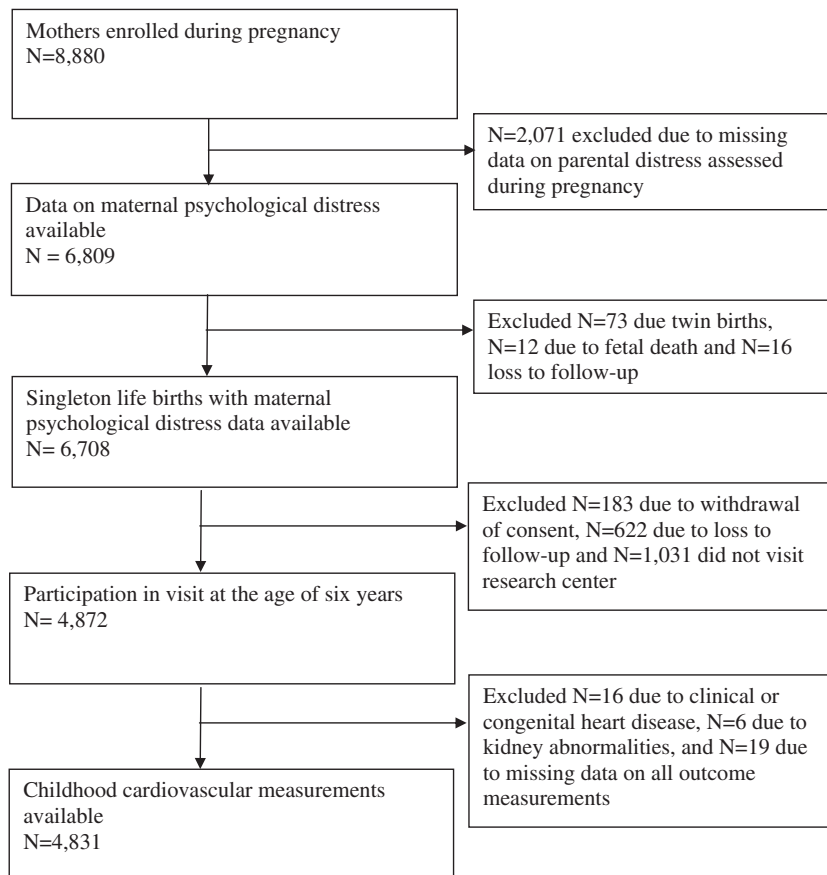


Fig. 1. Flowchart of the study population: the Generation R Study Cohort, Rotterdam, The Netherlands.

during the life course, than at older ages. Also, cardiovascular adaptations in childhood may track into adulthood. However, any association of maternal psychological distress with childhood blood pressure could be explained by direct intra-uterine mechanisms of high fetal cortisol levels, or by other environmental factors. Similar effect sizes for maternal and paternal psychological distress on childhood outcomes would indicate that associations are due to unmeasured shared social and environmental factors [15].

Therefore, we assessed in a large population-based prospective cohort study among 4831 children, the associations of maternal and paternal psychological distress with blood pressure, carotid–femoral pulse wave velocity and left cardiac structures and function in children at the age of six years.

2. Methods

2.1. Study design and population

The study was embedded in the Generation R Study, a population-based, prospective cohort study from fetal life onwards in Rotterdam, The Netherlands [16]. Enrolment in the study was aimed at early pregnancy, but was possible until birth of the child. Information about maternal psychological distress during pregnancy was collected in the second trimester of pregnancy. Between March 2008 and January 2012, all participating children and their mothers were invited to a dedicated research center, to participate in detailed follow-up measurements at the median age of 6 years (95% range 5.6 to 7.4 years). The study has been approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. Written informed consent was obtained from all parents of participants.

In total, 8880 mothers were enrolled in the study during pregnancy, of whom 6809 (75.5%) provided information about psychological symptoms during pregnancy. For the present study, only singleton live births were included ($n = 6708$), of whom 4872 (72.5%) children attended the follow-up visit between January 2009 and January 2012. Children with clinical or echocardiographic evidence of congenital heart disease or kidney abnormalities were excluded from the study ($n = 22$). Blood pressure, carotid–femoral pulse wave velocity or cardiac ultrasound measurements were successfully performed in 4831 children.

2.2. Parental psychological distress

Information on maternal and paternal psychological distress was obtained by postal questionnaires that were returned at around 20 weeks of gestation using the Brief Symptom Inventory and the subscale General Functioning of the Family Assessment Device [17]. Mother and father each completed the questionnaires. The Brief Symptom Inventory is a validated self-report questionnaire with 53 items [17]. These items define a broad spectrum of psychological symptoms in the preceding 7 days. A global index (Global Severity Index) and 3 symptom scales (Depression, Anxiety, and Hostility) were defined [17]. The Global Severity Index is a measure of current level or depth of the symptoms, and denotes overall psychological symptoms. Each item was rated on five-point uni-dimensional scales ranging from '0' (not at all) to '4' (extremely). A score is provided for each symptom scale by summing the item scores of each scale and dividing the results by the number of endorsed symptoms. This resulted in a range of scores from 0 to 4. Higher scores on these scales represented an increased occurrence of overall psychological symptoms, symptoms of depression, anxiety, or hostility. According to previous

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