Parental psychopathology and the early developing child

The Generation R Study

Mijke Pietertje van den Berg

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The Generation R Study

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de ontwikkeling van het jonge kind

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Alle gelukkige gezinnen lijken op elkaar,
elk ongelukkig gezin is ongelukkig op zijn eigen wijze.

Openingszin Anna Karenina,
Lev N. Tolstoj (1828-1910)

Contents

Manuscripts based on this thesis

Chapter 2

- van den Berg MP, van der Ende J, Crijnen AAM, Hofman A, Jaddoe VWV, Mackenbach JP, Moll HA, Tiemeier H, Hengeveld MW, Verhulst FC. Maternal and paternal psychopathology during pregnancy in a multiethnic population-based study. The Generation R study.

Chapter 3

- van den Berg MP, van der Ende J, Crijnen AAM, Hofman A, Jaddoe VWV, Mackenbach JP, Moll HA, Tiemeier H, Hengeveld MW, Verhulst FC. Pathways from parental birth weight and parental psychopathology to child birth weight. The Generation R Study

Chapter 4

- van den Berg MP, van Lier PAC, van der Ende J, Hofman A, Jaddoe VWV, Moll HA, Tiemeier H, Hengeveld MW, Verhulst FC, Crijnen AAM. Empirical identification of early postpartum psychiatric symptom profiles. The Generation R Study.

Chapter 5

- van den Berg MP, van der Ende J, Crijnen AAM, Hofman A, Jaddoe VWV, Mackenbach JP, Moll HA, Tiemeier H, Hengeveld MW, Verhulst FC. Maternal and paternal depression during pregnancy and excessive infant crying. The Generation R Study.

Chapter 6

- van den Berg MP, van der Ende J, Crijnen AAM, Hofman A, Jaddoe VWV, Mackenbach JP, Moll HA, Tiemeier H, Hengeveld MW, Verhulst FC. Paternal depression during pregnancy and infant behaviour at 6 months. The Generation R Study.

Chapter 7

- van den Berg MP, van der Ende J, Crijnen AAM, Hofman A, Jaddoe VWV, Mackenbach JP, Moll HA, Tiemeier H, Hengeveld MW, Verhulst FC. Maternal depression during pregnancy and infant behaviour at 6 months. The Generation R Study.

1 Introduction

Introduction

Research on transgenerational aspects of common psychiatric disorders, such as anxiety and depression, has progressed significantly during the last decades. The first studies pertained to the association between maternal postpartum depression and child development. Maternal postpartum depression was found to affect social, behavioural, emotional and cognitive development of the child (Goodman and Gotlib, 1999; Grace et al., 2003; Murray and Cooper, 1997). Next, research shifted to the effect of maternal psychopathology during pregnancy on child outcomes at birth. Some studies showed that mothers who experienced more psychological distress during pregnancy had children with lower birth weight and an earlier gestational age (Chung et al., 2001; Glover and O'Connor, 2002; Hedegaard et al., 1993; Hoffman and Hatch, 2000). More recently, the effect of prepartum maternal psychopathology on long term child development has become an important focus of research. Controlled for postpartum maternal psychopathology, prenatal exposure to maternal anxiety proved to be adversely related to child development (Huizink et al., 2003; O'Connor et al., 2002).

Alongside the influence of maternal psychopathology, there is also growing evidence of the importance of the influence of paternal psychopathology on child development. Postpartum depression in fathers is not only correlated with postpartum maternal depression, it is also associated with adverse emotional and behavioural outcomes in children (Areias et al., 1996; Cox, 2005; Downey and Coyne, 1990; Goodman, 2004; Kane and Garber, 2004; Ramchandani et al., 2005).

Logically, a next step in research would be to focus on prenatal aspects of paternal psychopathology on child development. Although a direct effect of prenatal paternal psychopathology on intrauterine development of the child is unlikely, for several reasons it is important to focus on paternal psychopathology during pregnancy. Firstly, fathers contribute 50% of their children's genes. Since depression and anxiety are shown to have a highly heritability in infants (Boomsma et al., 2005), paternal psychopathology should be included in research on transgenerational aspects of psychopathology. Secondly, paternal psychopathology can be an important confounder in the associations between maternal psychopathology during pregnancy and the developing child, since paternal psychopathology is related to both maternal psychopathology and child development.

A prospective design, in which parental psychopathology is assessed before the child's birth, is needed to investigate and further our understanding of transgenerational aspects of psychopathology. Because in such a design a child-to-parent effect can be ruled out, it gives more insight in the direction and effect of both maternal and paternal psychopathology on the developing child.

Aims of the thesis

This thesis aims at extending existing knowledge on transgenerational aspects of common psychiatric disorders. Because information on the influence of paternal psychopathology during pregnancy on the early developing child is lacking, special focus is placed on the contribution of paternal psychopathology in the associations that were already found between maternal psychopathology and early child development. Therefore we will investigate the prevalence and influence of both maternal and paternal psychopathology during pregnancy on child birth weight and behaviour of 2 and 6-month-old infants.

The main aims of the present thesis are:

1. To assess the prevalence and correlation of common maternal and paternal psychopathology during pregnancy;
2. To examine the different pathways from parental birth weight and parental psychopathology during pregnancy (i.e. anxiety and depression) to child birth weight;
3. To examine the influence of both maternal and paternal depression during pregnancy on early infant behaviour.

The Generation R Study

The study presented in this thesis is embedded in the Generation R Study, a prospective population-based cohort study from fetal life until young adulthood. This study is designed to identify early environmental and genetic determinants of growth, development and health from fetal life until young adulthood. The background and specific research projects of the study have been described previously in detail (Hofman et al., 2004; Jaddoe et al., 2006).

Study area

The Generation R Study is conducted in Rotterdam, the second largest city in The Netherlands. The total population consists of almost 600,000 inhabitants of almost 150 different ethnicities. The study area is well defined by postal codes and covers the largest part of the city (almost 350,000 inhabitants). The number of children born in this study area is about 4,300 per year (2005). The largest ethnic groups in this population are the Dutch (56%), Surinamese (9%), Turkish (7%), Moroccan (6%), Dutch Antillean (3%) and Cape Verdian (3%) groups.

Inclusion

Eligible mothers were those who were resident in the study area at their delivery and had an (expected) delivery date from April 2002 until January 2006. Enrolment of mothers was aimed in early pregnancy (gestational age until 17 weeks), but was possible until birth of their child. Midwifes and obstetricians gave eligible mothers at their first prenatal visit in routine care verbal information about the study, handed out the information package and asked these mothers to make an appointment for the first ultrasound examination. The partners were not approached directly by the study staff but the mothers were informed about the importance of involvement of their partners in the study. There was no specific definition to identify the women's partners of being a partner or a biological father of the child. By matching the date of birth of the biological father reported by the mother and the self-reported date of birth of the participating partner, it is estimated that 99% of the participating partners is the biological father of the child. Because of this high percentage we considered the participating partners to be equal to the biological fathers in the studies described in this thesis.

Pilot phase

The Generation R Study entered its pilot phase in December 2001 with the recruitment of pregnant women. The main aim of this pilot phase was to test the logistics of the enrolment process. Data collection in pregnancy was complete in all enrolled mothers from the start of this pilot phase. Based on the results from this pilot phase, the defined study area was limited to postal codes covering the largest part of, but not the whole city. Full participant recruitment in the definite study area was established for mothers with an (expected) delivery date from January 2003. Mothers living outside the definite study area at their delivery date undergo a complete follow-up in pregnancy until birth of their child. The children of these mothers do not undergo a postnatal follow-up. Data collection and quality in these mothers are similar as in the other participants until the end of pregnancy. Therefore, these mothers are part of the total cohort for research projects studying outcomes in pregnancy. All enrolled mothers living in the defined study area and having an (expected) delivery date from April 2002 and January 2006 are included as participants in the cohort for both prenatal and postnatal follow-up.

Study cohort

A total of 9,778 mothers were enrolled in the study (figure 1). Of all mothers, 91% (n= 8,880) was enrolled in pregnancy. Only partners from mothers enrolled in pregnancy were invited to participate. In total, 71% (n= 6,347) of the partners were enrolled. The general characteristics of the mothers and their partners are presented in table 1. Of all participating mothers, enrolment was in early pregnancy in 69% (n= 6,748), in mid-pregnancy in 19% (n= 1,857), in late pregnancy in 3% (n= 275) and at birth of their child in 9% (n= 898).

Table 1. General characteristics of mothers and their partners

	Mothers (n = 9,778)	**Partners** (n = 6,347)
Gestational age at enrolment		
▪ Early pregnancy (< 18 weeks) (%)	69	-
▪ Mid-pregnancy (18 – 25 weeks) (%)	19	-
▪ Late pregnancy (≥ 25 weeks) (%)	3	-
▪ Birth	9	-
Pregnancy number in study		
▪ 1st pregnancy (%)	94	-
▪ 2nd pregnancy (%)	6	-
▪ 3rd pregnancy (%)	0.1	-
Age (years)*	29.7 (5.3)	32.7 (5.8)
Parity		
▪ 0 (%)	55	-
▪ 1 (%)	31	-
▪ ≥ 2 (%)	14	-
Ethnicity		
▪ Dutch, other-European (%)	58	70
▪ Surinamese (%)	9	6
▪ Moroccan (%)	7	4
▪ Turkish (%)	9	6
▪ Dutch Antillean (%)	4	3
▪ Cape verdian (%)	4	2
▪ Others (%)	9	9
Educational level		
▪ Primary education (%)	13	8
▪ Secondary education (%)	45	41
▪ Higher education (%)	42	51
Household income per month		
▪ <€ 800 (%)	9	-
▪ € 800-2200 (%)	36	-
▪ >€ 2200 (%)	55	-

Values are percentages

*Mean (standard deviation)

All subject characteristics, except gestational age at enrolment, are based on mothers enrolled in pregnancy

Of all mothers enrolled in pregnancy, 94% (n= 8,356), 6% (n= 516) and 0.1% (n= 8) were first, second and third pregnancies in the study, respectively. The mean age of pregnant women in our study was similar to the age of all pregnant women in the study area, which was 29.6 years in 2003 (www.cos.rotterdam.nl). Ethnicity of participating mothers and partners is defined according the classification of Statistics Netherlands (2004a). This means for one specific person that: This means for one specific person that: 1) if both parents are born in The Netherlands, the ethnicity is Dutch; 2) if one of the parents is born in another country than The Netherlands, that country counts; 3) if both parents are born in the same country other than The Netherlands, that country counts; 4) if the parents are born in the different countries other than The Netherlands, the country of mothers counts; and 5) if that person and both parents are born in different countries other than

The Netherlands, the country of birth of that specific person counts. As expected, the largest ethnic groups were the Dutch, Surinamese, Turkish and Moroccan groups. The ethnic distrubution differed only moderately from that of the population in the study area. Mean household income in Rotterdam is about € 1,600 and the percentage subjects with an educational level comparable to secondary or higher education level in Rotterdam is 56% (www.cbs.nl). The educational level of participating mothers and their partners is classified in groups according to the classification of Statistics Netherlands (2004b). Both household income and highest followed educational level in mothers and their partners in the study cohort suggest a selection towards a higher social economical status. However, differences between the population and cohort characteristics may be due to both a selected study population and to selective missing values of ethnicity and socio-economic status in the questionnaires. Additional efforts are currently made to complete the information on ethnicity, household income and educational level in the total cohort.

Children at birth

Characteristics of the live born children at birth are presented in table 2. Among these live births, 51% were male and 49% female. These percentages are similar to the population figures in The Netherlands and in Rotterdam (www.cbs.nl). Ethnicity of the children was defined using the strategy as described for the mothers and partners. The differences in ethnic distributions between all newborns in the study and the newborns participating in the study are similar to the differences found in the mothers.

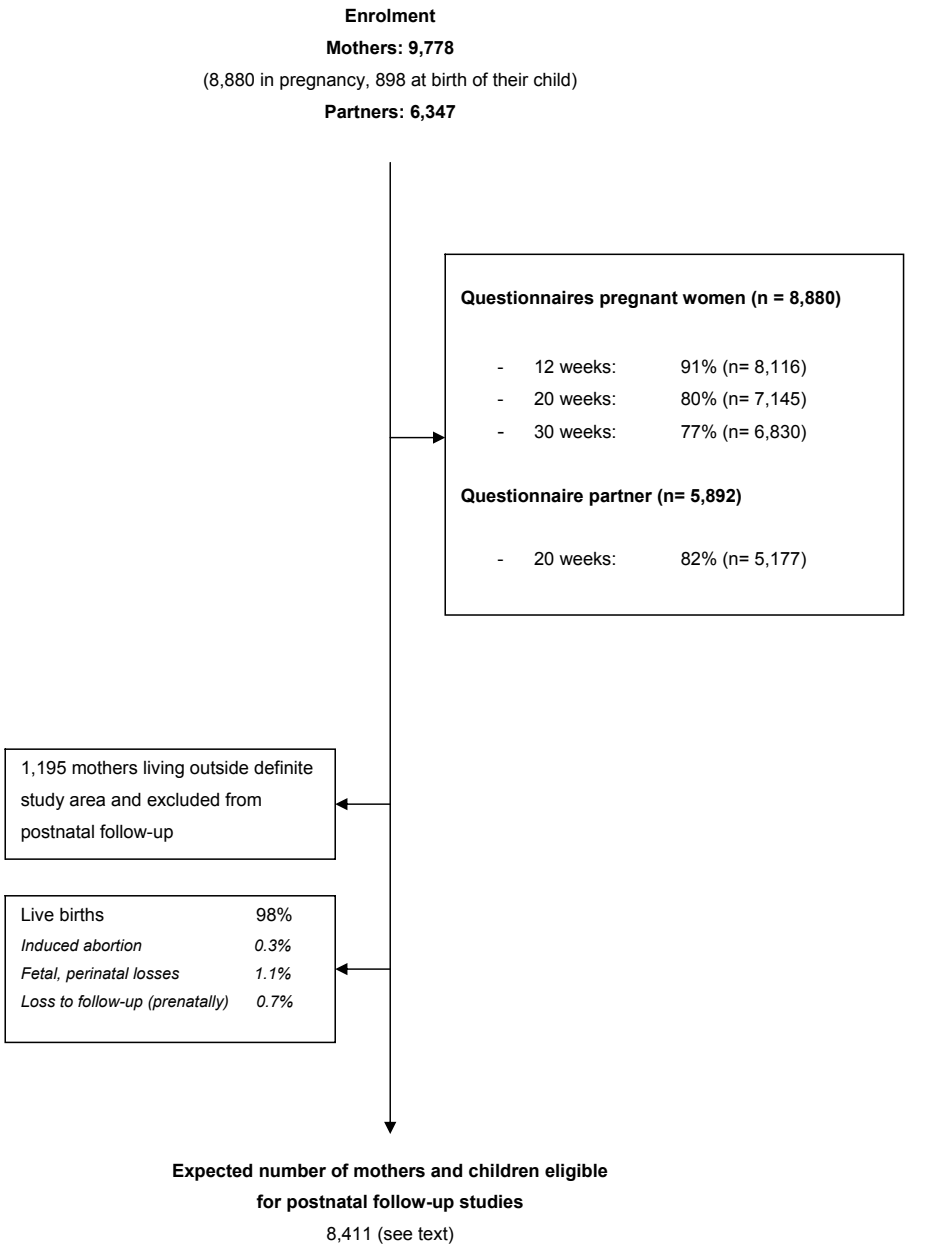
Overall response

Estimation of the precise number of eligible pregnant women in the study area in the whole period is difficult since there is no satisfactory registry. Therefore, it was not attempted to identify overall response rates in pregnancy. Since the children form a prenatally recruited birth-cohort, the overall response of the study is calculated at birth. Full participant recruitment in the definite study area was established for mothers with a delivery date from January 2003 until January 2006. The overall response in this period represents the number of children born from mothers living in the study area at their delivery date and participating in the study as percentage of the total number of children born with these criteria. Since data collection and cleaning is still ongoing, the response rate calculation was based on children born from January 2003 until January 2005. The number of live born children in the study area in this period is 8,494. A total of 5,189 mothers with living born children born in this period participated in the study, leading to a response rate of 61% at birth. Children born in 2002 do not contribute to this response rate since the recruitment process did not cover the whole definite study area. Data collection and cleaning for children born in 2005 is still ongoing but is not expected to materially change this response rate.

Postnatal follow-up

Of all 9,778 mothers, 1,195 mothers were living outside the definite study area at their delivery date and their children are not approached for postnatal follow-up studies. Of the remaining 8,583 mothers, it is expected that 98% (n = 8,411) have pregnancies re-

Figure 1. Participant enrolment and measurements in the first phase



sulting in living born children that could be approached for postnatal follow-up studies (figure 1). These mothers and their children are eligible for postnatal follow-up studies. Based on figures from 2003 and 2004, it is estimated that about 92% of these eligible mothers are willing to continue to participate in the postnatal phase with their children (i.e. give postnatal informed consent).

Assessments

Pregnant women received four questionnaires (of which we used three for this thesis) sent to their homes and their partner received one questionnaire sent to their home in the prenatal phase. In the postnatal phase up till 6 months, participants received four questionnaires, two for information on the mother and two for information on the child. Overall response rates for the prenatal questionnaires are presented in figure 1. Topics in these questionnaires that were used for this thesis included:

Mother (12 weeks pregnancy):

- Socio-economic, demographic factors and health related factors: age, country of birth, educational level, marital status number of living children, general perceived health, birth weight
- Substance use: alcohol use, smoking

Mother (20 weeks pregnancy):

- Psychopathology: Brief Symptom Inventory (de Beurs, 2004; Derogatis, 1993)
- Substance use: alcohol use, smoking

Partner (20 weeks pregnancy):

- Socio-economic, demographic factors and health related factors: age, country of birth, educational level, birth weight
- Substance use: alcohol use, smoking
- Psychopathology: Brief Symptom Inventory

Mother (30 weeks pregnancy):

- Household income

Mother (2 months after delivery):

- Psychopathology: Edinburgh Postnatal Depression Scale (Cox et al., 1987; Pop et al., 1992), 11 early postpartum psychiatric symptoms

Child (2 months after birth):

- Crying behaviour

Mother (6 months after delivery):

- Psychopathology: Depression scale of the Brief Symptom Inventory

Child (6 months after delivery):

- Child behaviour: activity level, distress to limitations, fear, duration of orienting, recovery from distress and sadness of an adapted version of the Infant Behaviour Questionnaire-Revised (Gartstein and Rothbart, 2003)

Overall response rates for the prenatal questionnaires varied from 77% to 91% (figure 1). For the postnatal questionnaires the estimated response rates were 80% at 2 months and 60% at 6 months. However, the response rates of specific questions may be lower due to missing values within questionnaires. Because of a variety of logistic reasons, some mothers did not receive one or more questionnaires. Additional efforts are currently made to complete the information on the time independent population descriptives (medical history, ethnicity, educational level, working conditions and household income).

Pregnancy outcomes

The obstetric records of all mothers are looked up in the hospitals and midwifery practices. Specialists in the relevant field code items in these records. The major pregnancy outcomes, including live births, induced abortion and fetal or perinatal loss, are known in 99% of all enrolled mothers. In all children known to be born alive, information about gender, birth weight and gestational age is available (table 2).

Table 2. Characteristics of newborns

Boys%	51
Birth weight (grams)*	3412 (561)
Gestational age (weeks)**	40 (35.4-42.1)
Ethnicity	
▪ Dutch, other-European (%)	62
▪ Surinamese (%)	8
▪ Moroccan (%)	7
▪ Turkish (%)	8
▪ Dutch Antilles (%)	4
▪ Cape Verdian (%)	3
▪ Other (%)	8

Values are percentages
*Mean (standard deviation)
**Median (95% range)
Figures are based on living born children

Data available for this thesis

Data cleaning and preparation for the whole Generation R cohort is still ongoing. In order to make full use of the data available, for the studies that are presented in this thesis various samples were used. For the studies that only focused on prenatal aspects of parental psychopathology and child development (chapter 2 and 3) we used all available data on children that were born until January 1st 2005, including the pilot phase that started in December 2001. Since postnatal recruitment was restricted to a study area not covering the whole city, for the studies that also focused on postnatal aspects of parental psychopathology and the developing infant (chapters 4, 5 and 6), we used all available data from children that were born until January 1st 2005 within the defined study area. As explained, this was established for mothers with an (expected) delivery date from January 2003 onwards. Additional information on sample selection and attrition is described in the method section of the individual studies.

Outline of the present thesis

In **Chapter 2**, the prevalence and correlation of maternal and paternal psychopathology during pregnancy are assessed, with special focus on the influence of ethnicity on psychopathology accounting for age and educational level. In this study we used the nine scales of the Brief Symptom Inventory, which cover: Somatization, Obsessive-Compulsivity, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism.

In **Chapter 3**, the different pathways from parental birth weight and parental psychopathology (i.e. anxiety and depression) to child birth weight are examined by means of path analyses.

In **Chapter 4**, different profiles of common early psychiatric postpartum symptoms in recently delivered women are identified through latent class analyses. Although this chapter is positioned beyond the strict scope of this thesis, the relevance of early identification of women at risk of postpartum depression was such that it warranted inclusion.

In **Chapter 5**, the association between paternal and maternal depression during pregnancy and two definitions of excessive infant crying is investigated, taking into account several confounders.

In **Chapter 6**, the influence of paternal depression during pregnancy on six scales of early infant behaviour (i.e. activity level, distress to limitations, fear, duration of orienting, recovery from distress and sadness) is investigated and adjusted for maternal depression during pregnancy and several other confounders.

In **Chapter 7**, the influence of maternal depression during pregnancy on six scales of early infant behaviour is investigated and adjusted for paternal depression during pregnancy, maternal depression postpartum and several other confounders.

Finally, in **Chapter 8**, the main findings and conclusions of this thesis are discussed. Implications and recommendations for clinical practise and future research are given.

2 Maternal and paternal psychopathology during pregnancy in a multiethnic population-based study

Abstract

Background

Research on psychopathology during pregnancy has traditionally focused on mothers, since maternal psychopathology is associated with adverse child outcomes. Until now little attention has been paid to paternal psychopathology during pregnancy. It is important to take paternal psychopathology during pregnancy into account as well, since paternal psychopathology is both related to maternal psychopathology and the social, behavioural, emotional and cognitive development of the child.

Objective

To assess the prevalence and correlation of maternal and paternal psychopathology during pregnancy in a large multiethnic population-based study.

Methods

At 20 weeks pregnancy 4,819 women and 3,656 partners from 12 different ethnic backgrounds completed the Brief Symptom Inventory (BSI), a questionnaire that covers nine psychiatric symptom scales. For the analyses we used a sub-sample consisting of ethnic homogenous groups.

Results

Mothers had much higher levels of overall psychopathology compared to fathers. The correlation between maternal and paternal psychopathology was .33 ($p < .001$). Ethnicity explained most of the variance on all symptom scales of the BSI. Participants with another ethnic background had higher psychopathology scores than native Dutch, even after adjustment for age and educational level.

Conclusion

Although maternal psychopathology during pregnancy is much higher than paternal psychopathology, they are significantly correlated. Of the investigated factors, ethnic background accounted for most of the explained variances in parental psychopathology during pregnancy. Therefore, it is recommended to further investigate the psychiatric risk factors associated with ethnicity.

Introduction

Research on common psychiatric disorders during pregnancy has traditionally focused on mothers. This is warranted since maternal psychopathology during pregnancy not only affects the mother but also negatively influences the child. It is known that maternal stress and anxiety during pregnancy are assiociated with preterm delivery and lower child birth weight for gestational age (Chung et al., 2001; Glover and O'Connor, 2002; Hedegaard et al., 1993). Also after child birth, maternal stress and anxiety during pregnancy are adversely related to child development (Huizink et al., 2003; Van den Bergh et al., 2005).

However, until now little attention has been paid to paternal psychopathology during pregnancy. Although a direct effect of prenatal paternal psychopathology on intrauterine development of the child is unlikely, it is important to focus on paternal psychopathology during pregnancy because it is suggested that paternal psychopathology may increase the effects of maternal depression on child outcomes through genetic or environmental influences (Goodman and Gotlib, 1999; Kane and Garber, 2004). Research on the influence of postpartum parental psychopathology on child development showed that if both parents are depressed, this might place children at even higher risk to develop emotional and behavioural problems than when only the mother is depressed (Dierker et al., 1999; Goodman, 2004; Weissman et al., 1984). Therefore, assessment of paternal psychopathology and the association with maternal psychopathology during pregnancy might be relevant for early identification of families at risk. We are only aware of one large population-based study that focused on paternal depression during pregnancy, which indeed found a significant correlation with maternal depression that was highly predictive for postpartum depression in both fathers and mothers (Deater-Deckard et al., 1998).

Another aspect that has not been addressed before in large population-based studies is the impact of ethnicity on common psychiatric disorders during pregnancy. From previous research it is known that there are ethnic differences in psychopathology in the general population (Weich et al., 2004), but whether those differences are important in a selective group of relatively healthy and young parents-to-be has not been studied before.

The aim of our study was to investigate the prevalence and correlation of both maternal and paternal common psychopathology during pregnancy in a large population-based study. Because our sample consisted of a multiethnic group of participants the second aim was to investigate the effect of ethnicity on parental psychopathology.

Methods

Design

This study was embedded in the Generation R Study, a prospective population-based cohort study from fetal life until young adulthood. The study is designed to identify early environmental and genetic determinants of growth, development and health from fetal life until young adulthood and has been described previously in detail (Hofman et al., 2004; Jaddoe et al., 2006). Briefly, the cohort includes 9,778 mothers (of whom 6,347 partners) and their children living in Rotterdam, one of the major cities of The Netherlands. Enrolment for mothers in the study was aimed in the first trimester of pregnancy but was possible until birth of their offspring from December 2001 until January 2006. Next to participating in physical examinations, fetal ultrasounds and biological samples, at 12, 20 and 30 weeks during pregnancy mothers completed questionnaires on social, developmental and health related topics. Fathers completed one questionnaire at 20 weeks pregnancy. Based on the annual birth rates in Rotterdam, the calcutated initial response was 61%.

The study cohort is a multi ethnic cohort with a large number of different ethnicities. Questionnaires were available in Dutch and translated in English, French, Portuguese and Turkish. When participants were not able to fill out the questionnaire in one of these languages (e.g. most Moroccans speak Berber, a non-written language) assistants who spoke the same language visited participants at home to help fill out the questionnaire.

The study has been approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. Written informed consent was obtained from all participants.

Population

Data cleaning and preparation for the whole Generation R cohort is still ongoing. For the current study we used all available data at 12 and 20 weeks pregnancy on parents of children that were born in 2002 and 2004. In this period 6,507 mothers and 4,764 fathers (73% of participating mothers) were included. Based on self-reported information, it is estimated that 99% of the participating partners is the biological father of the child. Of the included participants, 253 mothers and their partners dropped out of the study before 20 weeks pregnancy for the following reasons: induced abortion (n=22), intrauterine death (n=33), withdrawal from study (n=71) and lost to follow up (n= 127). Of the remaining participants on 4,819 (77%) mothers and 3,656 (81%) fathers we obtained valid information on psychopathology at 20 weeks pregnancy. For the aim of this study we chose to focus on the largest and homogeneous ethnic groups of our sample, i.e. Dutch, Surinamese, Turkish, Moroccan, Cape Verdian and Dutch Antillean. This led to our final number of 3,636 mothers and 3,127 fathers that were included for analyses.

Parental psychopathology

Parental psychopathology was assessed at 20 weeks pregnancy with the Brief Symptom Inventory (BSI), a validated self-report questionnaire with 53 items rated on a 5-point scale, ranging from "0= not at all" to "4= extremely" (de Beurs, 2004; Derogatis and Melisaratos, 1983; Derogatis, 1993). The BSI is a short version of the Symptom Checklist 90 (SCL-90) (Derogatis et al., 1976; Derogatis and Melisaratos, 1983). The items of the BSI define a broad spectrum of psychiatric symptoms in the preceding 7-days covering nine scales: Somatization, Obsessive-Compulsivity, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. Besides the scores on each subscale an overall score, the Global Severity Index (GSI) can be calculated, which is obtained by dividing the sum of the total item scores by the number of completed items.

Covariates

For mothers at 12 weeks pregnancy and for fathers at 20 weeks pregnancy information was obtained on age, country of birth and educational level.

Ethnicity of the parents was defined according the classification of Statistics Netherlands (2004a). A parent was considered Dutch if both their own and the country of birth of his or her parents is The Netherlands. A parent had another ethnicity if their own or at least one country of birth of his or her parents is other than The Netherlands. If a parent and his or her parents had different countries of birth other than The Netherlands, first the country of birth of the specific parent and second the country of birth of the mother of the parent was used to determine ethnicity. Education was divided in five categories: primary education (no education, primary education), secondary education 1st phase (lower vocational training, 3 years general secondary school), secondary education 2nd phase (intermediate vocational training, >3 years general secondary school, first year higher vocational training/university), higher education 1st phase (higher vocational training, university bachelor) and higher education 2nd phase (university, PhD).

Statistical analysis

SPSS for Windows (Version 12.0.1) was used for data analysis. For the effect of age, ethnicity and educational level on the nine scales of psychopathology and the GSI we used linear regression analyses, in which we analysed mothers and fathers separately. Because age, ethnicity and educational level were significantly related to all symptom scale scores, we present the full regression model for each scale. Effect sizes (R^2) for age, ethnicity and educational level were first calculated independently from the other variables and finally one effect size was calculated for all variables together. We applied Cohen's criteria to categorise effect sizes: effects accounting for 1-5.9% of the variance are considered small; effects of 5.9-13.8% are considered medium; and effects of more

than 13.8% are considered large (Cohen, 1988). Correlations of parental psychopathology were analysed using Pearson's correlation coefficients.

Results

Attrition

Analyses of missing data on maternal psychopathology at 20 weeks pregnancy showed that mothers with missing data were 1.5 (95% CI: 1.1–1.9) years younger, were significantly lower educated (2.7 versus 3.3; 95% CI: 0.4–0.6) and significantly more of non-Dutch origin (31% versus 15%; $\chi^2 = 168.96$; df = 1; $p < .001$). Analyses of missing data on paternal psychopathology at 20 weeks pregnancy showed that fathers with missing data were 0.7 (95% CI: 0.2–1.3) years younger, were significantly lower educated (2.9 versus 3.5; 95% CI: 0.3–0.9) and significantly more of non-Dutch origin (25% versus 12%; $\chi^2 = 100.76$; df= 1; $p< .001$).

General descriptives

Table 1 shows the distribution of age, ethnicity and educational level by gender of our sample; 71% of the participants were native Dutch, 9% Surinamese, 8% Turkish, 5% Moroccan, 4% Cape Verdian and 4% Dutch Antillean.

The distribution of age and educational level significantly differed among the ethnicities. Dutch participants were significantly older and more educated compared to the other ethnicities.

Table 1. General descriptives of parents with valid information on psychopathology at 20 weeks pregnancy

	Mothers (n= 3,636)	Fathers (n= 3,127)
Mean age, (SD)	29.8 (5.2)	32.8 (5.6)
Ethnicity, % (n)		
Dutch	65.9 (2,397)	75.2 (2,352)
Surinamese	10.4 (377)	7.1 (222)
Turkish	8.9 (322)	7.4 (232)
Moroccan	6.0 (219)	4.1 (127)
Cape Verdian	4.6 (169)	3.0 (94)
Dutch Antillean	4.2 (152)	3.2 (100)
Education, % (n)		
primary education	10.6 (379)	8.2 (249)
secondary education, 1st phase	17.0 (606)	15.0 (458)
secondary education, 2nd phase	29.6 (1,057)	27.7 (846)
higher education, 1st phase	20.1 (717)	18.1 (551)
higher education, 2nd phase	22.7 (809)	31.0 (946)

Internal consistency of the Brief Symptom Inventory and mean scores

The internal consistency for the GSI in this sample was α=.96 for mothers and α=.95 for fathers (table 2), which indicates high construct reliability. On most of the subscales, except for Hostility, Phobic Anxiety and Psychoticism in fathers, the Cronbach's α scores were higher than .70, which is satisfactory (Cronbach, 1951).

The overall mean scores of mothers were significantly higher than the mean scores of fathers in all scales.

Effect of age, ethnicity and educational level on psychopathology

The analyses on the effect of age, ethnicity and gender on the nine symptom scales and the GSI of the BSI, showed small to high effect sizes for mothers (table 3) and small to medium effect sizes for fathers (table 4).

The effect size of age in mothers varied from 1.9% (small) in Obsessive-Compulsivity to 7.2% (medium) in Somatization. In fathers the effect size of age varied from no effect (Somatization, Obsessive-Compulsivity, Interpersonal Sensitivity, Depression, Anxiety, Phobic Anxiety, and Psychoticism) to small effects (Hostility, Paranoid Ideation, Global Severity Index). In general there was a negative association between age and psychopathology in our sample.

The effect sizes of ethnicity varied from 4.1% (small) in Obsessive-Compulsivity to 16.3% (large) in Somatization among mothers. Mothers of Turkish, Moroccan and Cape Verdian ethnicity had highest scores on all symptom scales. Among fathers the effect size of ethnicity varied from no effect in anxiety to 6.7% (medium) in Paranoid Ideation.

Table 2. Internal consistency (Cronbach's α) and overall mean scores for women and men of nine symptom scales and the Global Severity Index (GSI) of the Brief Symptom Inventory

	Somatization	Obsessive-compulsive	Interpersonal Sensitivity	Depression	Anxiety	Hostility	Phobic Anxiety	Paranoid ideation	Psychoticism	GSI
Mothers										
Internal consistency	α= .76	α= .77	α= .76	α = .86	α= .82	α = .74	α= .78	α= .83	α= .71	α= .96
Mean score (SD)	.41 (.48)	.48 (.55)	.28 (.50)	.25 (.51)	.29 (.46)	.32 (.46)	.12 (.34)	.26 (.52)	.17 (.38)	.30 (.39)
Fathers										
Internal consistency	α= .75	α= .73	α= .70	α = .81	α= .73	α = .69	α= .69	α= .77	α= .63	α= .95
Mean score (SD)	.13 (.27)	.24 (.38)	.12 (.30)	.11 (.30)	.18 (.31)	.18 (.32)	.05 (.22)	.22 (.43)	.09 (.25)	.15 (.24)

Table 3. Effects of age, ethnicity and education on nine symptom scales and the Global Severity Index (GSI) of the Brief Symptom Inventory for mothers (n= 3,636)

	Somatization	Obsessive-Compulsive	Interpersonal Sensitivity	Depression	Anxiety	Hostility	Phobic Anxiety	Paranoid Ideation	Psychoticism	GSI
Constant	.60 (.06)*	.54 (.07)*	.55 (.06)*	.44 (.06)*	.37 (.06)*	.62 (.05)*	.23 (.04)*	.44 (.06)*	.32 (.05)*	.45 (.05)*
Age	-.011 (.002)*	-.007 (.002)*	-.013 (.002)*	-.011 (.002)*	-.007 (.002)*	-.014 (.002)*	-.006 (.001)*	-.011 (.002)*	-.008 (.001)*	-.009 (.001)*
Unadjusted R^2	7.2%	1.9%	4.6%	5.3%	3.3%	6.9%	3.4%	5.2%	4.4%	6.7%
Ethnicity										
Dutch (ref)	-	-	-	-	-	-	-	-	-	-
Surinamese	.15 (.03)*	.08 (.03)*	.07 (.03)*	.15 (.03)*	.03 (.03)	.09 (.03)*	.02 (.02)	.18 (.03)*	.07 (.02)*	.10 (.02)*
Turkish	.52 (.03)*	.29 (.04)*	.28 (.03)*	.33 (.03)*	.35 (.03)*	.23 (.03)*	.24 (.02)*	.33 (.03)*	.27 (.02)*	.33 (.02)*
Moroccan	.31 (.03)*	.16 (.04)*	.21 (.04)*	.26 (.04)*	.24 (.03)*	.16 (.03)*	.16 (.02)*	.20 (.04)*	.23 (.03)*	.23 (.03)*
Cape Verdian	.25 (.04)*	.19 (.05)*	.20 (.04)*	.32 (.04)*	.17 (.04)*	.22 (.04)*	.10 (.03)*	.29 (.04)*	.19 (.03)*	.23 (.03)*
Dutch Antillean	.10 (.04)*	-.04 (.05)	.04 (.04)	.17 (.04)*	.07 (.04)	.08 (.04)*	.07 (.03)*	.21 (.04)*	.11 (.03)*	.11 (.03)*
Unadjusted R^2	16.3%	4.1%	6.3%	9.6%	8.5%	7.8%	7.7%	9.4%	9.1%	13.0%
Education†										
I	.10 (.03)*	.04 (.04)	.07 (.03)*	.09 (.03)*	.12 (.03)*	.09 (.03)*	.09 (.02)*	.13 (.03)*	.04 (.03)	.09 (.03)*
II	.13 (.03)*	.13 (.03)*	.10 (.03)*	.11 (.03)*	.12 (.03)*	.12 (.03)*	.07 (.02)*	.11 (.03)*	.05 (.02)*	.11 (.02)*
III	.08 (.02)*	.12 (.03)*	.05 (.02)*	.06 (.02)*	.07 (.02)*	.07 (.02)*	.02 (.02)	.06 (.03)*	.02 (.02)	.07 (.02)*
IV	.03 (.02)	.10 (.03)*	.04 (.03)	.02 (.03)	.05 (.02)*	.01 (.09)	.04 (.02)*	.02 (.03)	.02 (.02)	.04 (.02)
V (ref)	-	-	-	-	-	-	-	-	-	-
Unadjusted R^2	7.2%	2.4%	3.4%	4.9%	4.1%	5.7%	3.8%	5.3%	3.4%	6.6%
R^2 model	18.9%	5.4%	8.5%	11.6%	10.0%	11.6%	9.4%	11.4%	10.4%	15.7%

Unstandardised regression coefficients with standard error between brackets

* p< .05

†Education: I= primary education, II= secondary education 1st phase, III= secondary education 2nd phase, IV= higher education 1st phase, V= higher education 2nd phase

Table 4. Effects of age, ethnicity and education on nine symptom scales and the Global Severity Index (GSI) of the Brief Symptom Inventory for fathers (n= 3,127)

	Somatization	Obsessive-Compulsive	Interpersonal Sensitivity	Depression	Anxiety	Hostility	Phobic Anxiety	Paranoid Ideation	Psychoticism	GSI
Constant	.12 (.03)*	.23 (.05)*	.11 (0.4)*	.11 (.04)*	.15 (.02)*	.32 (.04)*	-.009 (.03)	.19 (.05)*	.07 (.03)*	.16 (.03)*
Age	-.002 (.001)	-.002 (.001)	-.001 (.001)	-.002 (.001)	-.003 (.001)*	-.006 (.001)*	.001 (.001)	-.003 (.001)*	-.001 (.001)	-.002 (.001)*
R^2	.9%	.5%	.3%	.9%	.4%	3.1%	.1%	1.7%	.7%	1.6%
Ethnicity										
Dutch (ref)	-	-	-	-	-	-	-	-	-	-
Surinamese	.05 (.02)*	.10 (.03)*	.08 (.02)*	.11 (.02)*	.001 (.02)	.09 (.02)*	.05 (.02)*	.19 (.03)*	.09 (.01)*	.09 (.02)*
Turkish	.15 (.02)*	.11 (.03)*	.10 (.02)*	.15 (.02)*	.01 (.02)	.15 (.02)*	.09 (.02)*	.17 (.03)*	.14 (.02)*	.12 (.02)*
Moroccan	.14 (.03)*	.09 (.04)*	.09 (.03)*	.12 (.03)*	.08 (.03)*	.04 (.03)	.11 (.02)*	.11 (.04)*	.08 (.02)*	.11 (.02)*
Cape Verdian	.02 (.03)	.13 (.04)*	.03 (.03)	.08 (.03)*	-.01 (.04)	.09 (.04)*	.03 (.02)	.15 (.05)*	.04 (.03)	.06 (.02)*
Dutch Antillean	.04 (.03)	.07 (.04)	.07 (.03)*	.14 (.03)*	.03 (.03)	.15 (.03)*	.04 (.02)	.27 (.04)*	.11 (.03)*	.10 (.03)*
R^2	4.5%	2.2%	2.0%	4.6%	.6%	5.1%	3.1%	6.7%	4.6%	5.6%
Education										
I	.10 (.02)*	.11 (.03)*	.07 (.02)*	.10 (.02)*	.09 (.02)*	.13 (.02)*	.09 (.02)*	.21 (.03)*	.08 (.02)*	.11 (.02)*
II	.05 (.02)*	.05 (.02)*	.03 (.02)	.02 (.02)	.02 (.02)	.06 (.02)*	.02 (.01)	.15 (.02)*	.01 (.01)	.05 (.01)*
III	.05 (.01)*	.06 (.02)*	.02 (.02)	.03 (.01)*	.03 (.02)*	.06 (.02)*	.03 (.01)*	.12 (.02)*	.03 (.01)*	.05 (.01)*
IV	.04 (.01)*	.05 (.02)	.05 (.02)*	.03 (.02)*	.04 (.02)*	.03 (.02)	.02 (.01)	.06 (.02)*	.04 (.01)*	.04 (.01)*
V	-	-	-	-	-	-	-	-	-	-
R^2	2.6%	1.7%	1.1%	2.2%	.9%	.4%	2.3%	5.8%	2.1%	3.8%
R^2 model	5.6%	3.0%	2.4%	5.3%	1.4%	7.6%	4.2%	9.3%	5.5%	7.3%

Unstandardised regression coefficients with standard error between brackets

*p< .05

†Education: I= primary education, II= secondary education 1st phase, III= secondary education 2nd phase, IV= higher education 1st phase, V= higher education 2nd phase

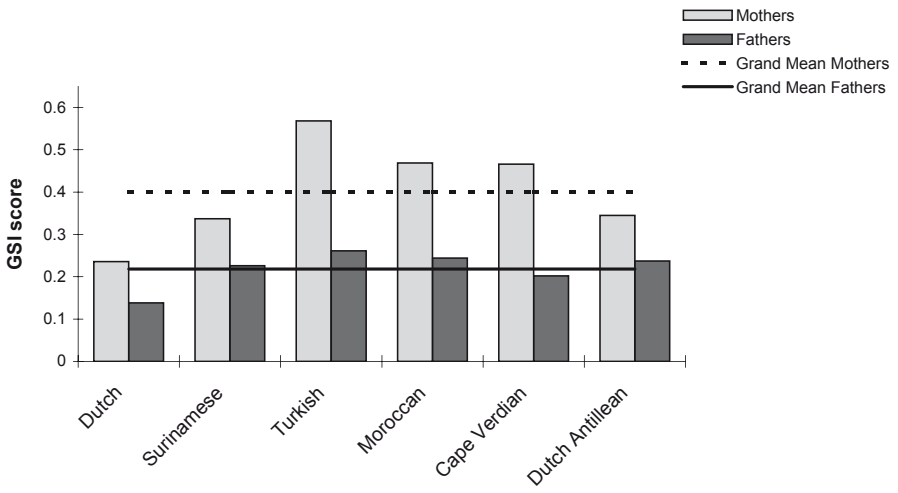


Figure 1. Mean GSI score by gender and ethnicity adjusted for age and educational level

Both in mothers and in fathers, ethnic background explained most of the variance compared to age and educational level.

The effect sizes of educational level among mothers varied from 2.4% (small) in Obsessive-Compulsivity to 7.2% (medium) in Somatization. Mothers from the second category of educational level (secondary education 1st phase) tended to have the highest scores on all symptom scales. In fathers the effect sizes of educational level varied from almost no effect in Anxiety and Hostility to 5.8% in Paranoid Ideation. Fathers with a lower educational level tended to have higher psychopathology scores compared to more educated fathers.

The means of the GSI, as a measure of overall psychopathology, corrected for age and educational level, are presented in figure 1. The grand estimated mean GSI score for mothers (.40) was significantly higher than for fathers (.22). Both Turkish and Moroccan mothers and fathers scored above the mean GSI score.

All mothers and fathers from other ethnicities had significantly higher GSI scores than the Dutch parents. Moroccan, Cape Verdian and Turkish mothers scored above the mean score for mothers. Turkish, Moroccan and Dutch Antillean fathers scored above the mean score for fathers. Among Cape Verdian and Dutch Antillean parents there were remarkable gender differences in BSI scores; Cape Verdian mothers scored above the mean, while Cape Verdian fathers scored below the mean, and Dutch Antillean mothers scored below the mean, while Dutch Antillean fathers scored above the mean.

Table 5. Correlation within couples of the Global Severity Index (GSI) of the Brief Symptom Inventory by ethnicity at 20 weeks pregnancy†

Ethnicity	Number of couples	Pearson's correlation	p value
Dutch	1,626	.29	< .001
Surinamese	112	.06	.51
Turkish	163	.48	< .001
Moroccan	78	.26	.02
Cape Verdian	46	.36	.02
Dutch Antillean	34	.56	.001
Total‡	**3,321**	**.33**	**< . 001**

† Only correlation coefficients of couples with the same ethnic background are calculated, therefore the summation of numbers is lower than the total

‡ All couples with both valid GSI-scores, regardless of ethnicity

Correlation of parental psychopathology

In table 5 the correlation between mothers and their partners is shown. From the 3,321 couples of whom we had both valid GSI scores, 2,266 (68%) had the same ethnic background. Significant correlations of parental psychopathology among different ethnicities varied from .23 (native Dutch) to .56 (Dutch Antillean). The overall correlation of psychopathology was .33.

Discussion

This population-based study focused on psychopathology during pregnancy of both mothers and fathers, which also accounted for ethnic background.

When we compare our mean scores on the nine symptom scales and the GSI of the BSI with Dutch (de Beurs, 2004), United States (Derogatis, 1993) and British community norms (Francis et al., 1990), the gender differences were about the same, meaning that women in general, irrespective of pregnancy have higher scores on psychopathology compared to men. However, fathers and mothers in our sample had lower scores on all scales, except for scores on the Somatization scale in women. Obviously, the higher mean scores on Somatization among mothers are influenced by the pregnancy, a period in which women naturally tend to have more physical complaints.

Our results suggests that parents-to-be, irrespective of ethnic differences, report lower levels of psychopathology compared to adults from the general population. This could either be due to selection bias toward more healthy participants or pregnancy related mechanisms. One explanation might be that pregnant women and their partners are healthier and live in better circumstances than people from the general population. Another explanation could be that pregnancy influences the way parents report on their

psychiatric problems. Pregnancy in general is considered a joyful event that could make people themselves more optimistic or it could be related to the positive reactions and special attention obtained from the environment.

Limitations

Our study is not without limitations. First, our initial response was 61% of all eligible (i.e. pregnant) participants. Non-response at baseline among the participants is not likely to be random. National and regional registries do not have subject characteristics in all children and their parents that enable detailed non-response analyses. However, the percentages of parents with another ethnic background and lower socio-economic status are lower among the participants than expected from the population figures in Rotterdam (2005). The largest ethnic groups in this population are the Dutch (56%), Surinamese (9%), Turkish (7%), Moroccan (6%), Dutch Antillean (3%) and Cape Verdian (3%) groups. Compared to the ethnic distribution of our sample, we had an overrepresentation of native Dutch participants. This selection would lead to bias in the found associations between parental psychopathology and ethnicity if non-response among non-Dutch participants is more strongly related to psychopathology than non-response in Dutch participants. This is not necessarily the case. Irrespective of ethnicity, it is likely that parents with more psychopathology are less willing to participate. This is indirectly supported by the relatively high number of missing data on the BSI among initially participating parents with lower age, a lower educational level and from other countries. Those are all factors related to higher levels of psychopathology. This selective non-response in psychopathology is likely to affect the frequency rates and, as a consequence, the statistical power and generalizability of the results. Therefore the prevalence rates should be carefully interpreted. However, in our sample it was still possible to find significant effects for age, ethnicity and educational level related to psychopathology. This suggests that our findings would probably have been even more significant when less selection occurred. Second, the BSI is not validated for parents with another ethnic background. However, the Cronbach's α of the subscales of the BSI were comparable among the different ethnic groups. Third, for this study we used educational level as the only indicator for socio-economic status. Parents from other countries had lower levels of education compared to the Dutch. We cannot rule out that other indicators of socio-economic status, like income and occupation, explained more of the variance than ethnic background. Finally, our results are based on self-report questionnaires which were mailed. Despite instruction, we cannot rule out that parents completed questionnaires dependently, which might have influenced the correlation coefficients.

Implications

Notwithstanding the aforementioned limitations, this study has some important clinical implications. First, up till now little attention has been paid to paternal psychopathology during pregnancy. Although the level of paternal psychopathology is much lower than maternal psychopathology on most symptom scales, the correlation between maternal and paternal psychopathology during pregnancy is .33 ($p < .001$) which is medium according to Cohen's criteria. This could either be due to 'assortative mating' (i.e. people with similar characteristics tend to attract each other), or to the possibility that living with a person with psychiatric problems can induce problems in the partner. It is difficult to disentangle the effects of the two mechanisms when people have lived together for some time, but it will be important to investigate whether children are at higher risk of developmental problems when both parents have high levels of psychopathology during pregnancy. Since evidence exists for an increased risk of emotional and behavioural problems in children when both parents are depressed in the postpartum period (Dierker et al., 1999; Goodman, 2004; Weissman et al., 1984), more research on this particular association during pregnancy is warranted since it could have major clinical implications. Also, if paternal psychopathology during pregnancy predicts child development over and above maternal psychopathology, this will have clinical implications.

Second, ethnic background was found to be an important factor in parental psychopathology. Not only in Rotterdam, but worldwide millions of people migrate, forcing people with different ethnic and cultural backgrounds to live together. Although the ethnic distribution varies in number and composition among different countries and cities, some aspects of ethnicity in relation to psychopathology are likely to be general. The strength of our study is that our sample consisted of young parents from both Dutch and other countries from different continents. Our results showed that all parents from other countries had higher levels of psychopathology compared to the native Dutch, even after adjustment for age and educational level. The fact that non-native Dutch parents in our sample had higher levels of psychopathology scores on the BSI could be related to true differences in the level of psychopathology across cultures or to cultural differences in perceiving and reporting psychopathology, or a combination of both.

In case of true differences in psychopathology this could be both related to genetic or biological factors and to the process of migration. If psychopathology is largely influenced by genetic or biological factors, one would expect that people with the same ethnic background, irrespective of whether they live in their mother country or whether they live in The Netherlands, in general have higher levels of psychopathology compared to the Dutch. On the other hand, if psychopathology is strongly related to migration, one should expect that migrated persons living in The Netherlands have higher levels of psychopathology than people with the same ethnic background living in their mother country. Whether this is the case should ideally be investigated using the same

instrument, in our case the BSI, in different countries. However, we are not aware of population-based studies performed with the BSI in the mother countries of the parents that participated in our study. Therefore we were not able to compare the cross-cultural differences in psychopathology between people living in their home country and people living in The Netherlands. Evidence for cross-cultural differences between countries is found in our previous reports on child behaviour problems in 12 different countries (Crijnen et al., 1997; 1999). In this study also higher prevalences of psychopathology scores were found in Non-Western (Jamaica, Puerto Rico) compared to Western (The Netherlands, Germany, Sweden, US, Australia) countries. However, it remains difficult to determine whether these differences reflect true differences (i.e. genetic or biological) in psychopathology or differences in reporting psychopathology, which we will discuss later. With respect to the effects of migration, there is certainly evidence that this plays a major role in psychopathology. Several studies using the BSI have focused on cross-cultural differences within one country, which generally show higher levels of psychopathology scores among immigrants independent of their country of origin (Coelho et al., 1998; Francis et al., 1990; Iwamasa and Kooreman, 1995; Lippincott and Mierzwa, 1995; Ponizovsky et al., 1998). In a recent review on cultural identity and migration a model is presented in which combinations of allocentric versus idiocentric individuals and collectivist versus egocentric societies are either protective or pathogenic with respect to migration and psychopathology (Bhugra, 2005). In the light of our study an explanation for the ethnic differences in psychopathology could be that allocentric individuals from a more collectivist society (like Turkey, Cape Verde or Morocco) move to an egocentric society with more idiocentric individuals (like The Netherlands) and are therefore at higher risk of developing psychiatric problems.

The ethnic differences in psychopathology could also be explained by differences in reporting psychiatric problems, independently from true levels of psychopathology. Firstly, there could be a difference in the perception of psychopathology due to different cultural norms. What is considered 'normal' in some cultures, could be considered pathologic in another culture (Draguns and Tanaka-Matsumi, 2003). Secondly, there can be a different threshold for reporting psychiatric problems. If one experiences psychiatric problems it is not always obvious to report these problems. In this respect shame and social desirability could also play a role in ethnic differences in psychopathology.

Our follow up study consisting of almost 10,000 children born in Rotterdam with parents from different ethnic backgrounds can contribute to the aforementioned question by investigating the cultural differences in psychopathology within the second generation. However, this study is not only relevant for the future outcomes in the children of our own study, it also hopes to encourage other investigators to use standardised instruments during pregnancy, like the BSI, and make cross-cultural comparisons possible to further our knowledge of different pathways of transgenerational psychiatry.

Conclusion

Although maternal psychopathology during pregnancy is much higher than paternal psychopathology, they are significantly correlated. If both parents have high levels of psychopathology during pregnancy, this could place children at higher risk of developmental problems. Also, if paternal psychopathology, over and above maternal psychopathology, has an effect on child development during pregnancy, it will have clinical implications. Physicians and health professionals, traditionally focusing on the well being and mental health of the pregnant woman, should pay attention to the mental well being of the partner as well. In this perspective one could think of the early identification and treatment of high risk couples instead of merely screening for maternal psychopathology.

Therefore, not only in research but also in clinical practice it is recommended to pay more attention to paternal psychopathology during pregnancy. It is possible that the presence of paternal psychopathology has a worse prognostic outcome in the treatment of maternal psychopathology when paternal psychopathology is not diagnosed and treated as well. Furthermore, of the investigated factors ethnic background explained most of the variance in parental psychopathology during pregnancy. Compared to the native Dutch, parents with another ethnic background scored much higher on all BSI scales. Therefore, it is important to invest in health programmes that especially target the detection and treatment of psychopathology in parents with another ethnic background.

3 Pathways from parental birth weight and parental psychopathology to child birth weight

Abstract

Background

From previous research it is known that associations exist between: parental birth weight and child birth weight; birth weight and adult psychopathology; and maternal psychopathology during pregnancy and birth weight of the child. This study is the first to combine these associations into one model.

Objective

To investigate the different direct and indirect effects from parental birth weight and parental psychopathology to child birth weight into one model.

Methods

Depression and anxiety scores of 6,507 mothers and 4,764 fathers at 20 weeks pregnancy and birth weights from 6,116 children were available. Path analyses with standardised regression coefficients (r) were used to evaluate the different effects.

Results

In the unadjusted path analyses direct effects existed between: maternal and paternal birth weight and child birth weight (respectively r= .17 and r= .13); maternal birth weight and maternal depression (r= -.05) and anxiety (r= -.06); maternal depression (r= -.06) and anxiety (r= -.06) and child birth weight. The indirect effect of paternal psychopathology via maternal psychopathology on child birth weight was larger than the indirect effect of maternal birth weight via maternal psychopathology on child birth weight. After adjustment for confounders, maternal (r= .10) and paternal (r= .08) birth weight and maternal depression (r= -.02) remained significantly associated with child birth weight. The indirect effect of paternal depression via maternal depression on child birth weight remained significant, where the indirect effect of maternal birth weight via maternal depression disappeared after adjustment.

Conclusion

After adjustment, parental birth weight and maternal depression – and not anxiety - were significantly associated with child birth weight. This suggests different underlying mechanisms in the relation between maternal depression and anxiety on child birth weight.

Introduction

The association between birth weight and psychopathology in adulthood and the association between maternal psychopathology during pregnancy and child birth weight have so far been studied separately. Low birth weight for gestational age seems to be associated with psychological distress and depression in adulthood (Cheung et al., 2002; Gale and Martyn, 2004; Thompson et al., 2001; Wiles et al., 2005). An association has also been found between maternal psychopathology (e.g. depression, anxiety, stress) and lower birth weight of the child (Mulder et al., 2002; Orr and Miller, 1995; Paarlberg et al., 1999; Rahman et al., 2004; Steer et al., 1992; Wadhwa et al., 1993; Zimmer-Gembeck and Helfand, 1996). This raises the question whether maternal psychopathology during pregnancy is an independent determinant of child birth weight or whether it is a mediator in the association between maternal birth weight and child birth weight. It is possible that maternal birth weight is an important confounder in the association between maternal psychopathology during pregnancy and child birth weight. This could be the case when mothers with lower birth weight give birth to children with lower birth weight through a genetic regulation of fetal growth and that low birth weight is an important determinant of psychopathology in adulthood. Evidence for a genetic regulation of fetal growth is found in prior studies that showed an independent influence of both maternal and paternal birth weight on child birth weight (Knight et al., 2005; Magnus et al., 2001).

For several reasons it is interesting to also investigate paternal factors in the associations between maternal birth weight, maternal psychopathology and child birth weight. First, paternal birth weight is associated with child birth weight through a genetic regulation of fetal growth (Knight et al., 2005; Magnus et al., 2001). Second, paternal birth weight is found to be related to paternal psychopathology during adulthood (Cheung et al., 2002; Thompson et al., 2001; Wiles et al., 2005). Finally, paternal psychopathology could indirectly influence the association between maternal psychopathology and child birth weight, since we found a moderate correlation (.33) between maternal and paternal psychopathology during pregnancy in a previous study (see Chapter 2).

Hence, if the association between maternal psychopathology during pregnancy and child birth weight is explained by a genetic regulation of fetal growth, rather than by the direct effect of maternal psychopathology, this has major implications in thinking about causal pathways. For example, the direction of causality could be that lower birth weight leads to psychopathology during adulthood, rather than that maternal psychopathology during pregnancy leads to lower child birth weight.

Therefore, the aim of this study is to disentangle direct and indirect effects of parental birth weight and parental psychopathology on child birth weight. This is the first study that combines three pathways that so far have only been studied separately. The first pathway is the direct relation between birth weight and psychopathology at

adult age. The second pathway is the direct effect of maternal psychopathology during pregnancy on child birth weight. The third pathway is the direct effect of parental birth weight on child birth weight. By combining these pathways in one path analytical model, it will also be possible to investigate indirect effects, for example the effect of paternal psychopathology via maternal psychopathology on child birth weight.

Methods

Design

This study was embedded in the Generation R Study, a prospective population-based cohort study from fetal life until young adulthood. The study is designed to identify early environmental and genetic determinants of growth, development and health from fetal life until young adulthood and has been described previously in detail (Hofman et al., 2004; Jaddoe et al., 2006). Briefly, the cohort includes 9,778 mothers (of whom 6,347 partners) and their children living in Rotterdam, one of the major cities of The Netherlands. Enrolment for mothers in the study was aimed in the first trimester of pregnancy but was possible until birth of their offspring from December 2001 until January 2005. Next to participating in physical examinations, fetal ultrasounds and biological samples, at 12, 20 and 30 weeks during pregnancy mothers completed questionnaires on social, developmental and health related topics. Fathers completed one questionnaire at 20 weeks pregnancy. The children were born between April 2002 and January 2006 and form a prenatally recruited birthcohort that is currently followed until young adulthood. Of all eligible children in the study area, 61% participate at birth in the study.

The study cohort is a multi ethnic cohort with a large number of different ethnicities. Questionnaires were available in Dutch and translated in English, French, Portuguese and Turkish. When participants were not able to fill out the questionnaire in one of these languages (e.g. most Moroccans speak Berber, a non-written language) assistants who spoke the same language visited participants at home to help fill out the questionnaire.

The study has been approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. Written informed consent was obtained from all participants.

Population

Data cleaning and preparation for the whole Generation R cohort is still ongoing. For the current study we used available data during 12 and 20 weeks pregnancy on parents and the birth outcomes of all children that were born until January 1st 2005. In this period 6,507 women and 4,764 partners (73% of participating women) were included. Based on self-reported information, it is estimated that 99% of the participating partners is

the biological father of the child. Of the included participants, 261 mothers and their partners dropped out of the study before 20 weeks pregnancy for the following reasons: induced abortion (n=22), intrauterine death (n=33), withdrawal from study (n=71) and lost to follow up (n= 127). Of the remaining parents on 4,811 (77%) women and 3,650 (81%) partners we obtained valid information on depression and anxiety at 20 weeks pregnancy and from 6,116 (94%) children we obtained birth outcomes.

Analyses of missing data on maternal psychopathology at 20 weeks pregnancy showed that mothers with missing data were 1.4 (95% CI: 1.1–1.9) years younger, were significantly lower educated (2.8 versus 3.3; 95% CI: 0.4–0.6), were significantly more of non-Dutch origin (28% versus 15%; $\chi^2 = 151.70$; df= 1; p< .001) and had children with 74 (95% CI: 40–108) grams lower birth weight. Analyses of missing data on paternal psychopathology at 20 weeks pregnancy showed that fathers with missing data were 0.9 (95% CI: 0.5–1.3) years younger, were significantly lower educated (2.9 versus 3.5; 95% CI: 0.3–0.9), significantly more of non-Dutch origin (23% versus 12%; $\chi^2 = 90.79$; df= 1; p< .001) and had children with 105 (95% CI: 63–143) grams lower birth weight.

Assessment

For this study we used information from questionnaires filled out at 12 and 20 weeks pregnancy. For mothers at 12 weeks and for their partners at 20 weeks pregnancy information was obtained on age, educational level, country of birth, parity (mothers), smoking and alcohol use during pregnancy (mothers), smoking and alcohol use 2 months before pregnancy (fathers) and birth weight. Birth weight was scored as: < 2000 g, 2000-2499 g, 2500–2999 g, 3000-3999 g and > 4000 g. Smoking was dichotomised in non-smoking and smoking. Alcohol use was dichotomised in non-alcohol and alcohol use. Ethnicity was defined according the classification of Statistics Netherlands (2004a). This means that a parent was Dutch if both the own and country of birth of his or her parents is The Netherlands. He or she has another ethnicity if their own or at least one parental country of birth is other than The Netherlands. Education was divided in five categories: primary education (no education, primary education), secondary education 1st phase (lower vocational training, 3 years general secondary school), secondary education 2nd phase (intermediate vocational training, >3 years general secondary school, first year higher vocational training/university), higher education 1st phase (higher vocational training, university bachelor) and higher education 2nd phase (university, PhD).

Parental psychopathology was assessed at 20 weeks pregnancy with the Brief Symptom Inventory (BSI), a validated self-report questionnaire with 53 items to be answered on a 5-point scale, ranging from "0= not at all" to "4= extremely" (de Beurs, 2004; Derogatis and Melisaratos, 1983; Derogatis, 1993). The BSI is a short version of the Symptom Checklist 90 (SCL-90) (Derogatis et al., 1976). The items of the BSI define a broad spectrum of psychiatric symptoms in the preceding 7-days covering nine scales:

Somatization, Obsessive-Compulsiveness, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. For this study we made use of the anxiety and depression scales. The internal consistencies in our sample were α= .83 for the Depression scale and α= .78 for the Anxiety scale, which is satisfactory (Cronbach, 1951).

Information on birth weight, gestational age and gender of the child was obtained from medical records completed by midwives and gynaecologists.

Statistical analysis

Path analysis with the MPlus program, version 3, was used (Muthén and Muthén, 2005). Path analysis is an extension of a regression model that can examine direct and indirect effects within a single model, instead of several separate regressions (Bollen, 1989). The data were modelled with full information maximum likelihood estimation to retain the total number of subjects for each analysis.

First, we used a simple path analysis to examine the direct and indirect effects of parental birth weight, parental depression and child birth weight. The same procedure was applied to parental anxiety. The directionality of the paths was constrained by their temporal relationships. The alpha level for statistical testing was set at $p < .05$.

Second, we introduced variables known from previous studies to confound the effect of parental psychopathology (i.e. depression and anxiety) and child birth weight. Those variables were: parental age, parental educational level, parental ethnicity, parental smoking, parental alcohol use and maternal nulliparity (Andersson et al., 2004). We started with a model in which the maternal and paternal birth weight and possible confounders were regressed on maternal and paternal depression and child birth weight. Again we applied the same procedure with maternal and paternal anxiety. Gestational age and gender of the child were only regressed on child birth weight, since they were not related to parental anxiety or depression. Variables not reaching significance were then removed from the model to improve the model. Because the models were not nested, a likelihood-ratio chi-square test for comparison of fit could not be used. Therefore we used the following goodness-of-fit indices: CFI (comparative fit index), TLI (Tucker Lewis Index) and RMSEA (root mean error of approximation). The following cut-off scores were used: CFI >.95, TLI > .95 and RMSEA <.06 indicating a good model fit (Hu and Bentler, 1999). Since unstandardised measurement units are difficult to interpret, we reported the standardised coefficients (r), which are similar to standardised beta weights in a regression analysis.

Results

Table 1 presents the characteristics of the child, paternal and maternal variables that were used in our path analyses. As expected maternal depression and anxiety levels were higher than paternal levels.

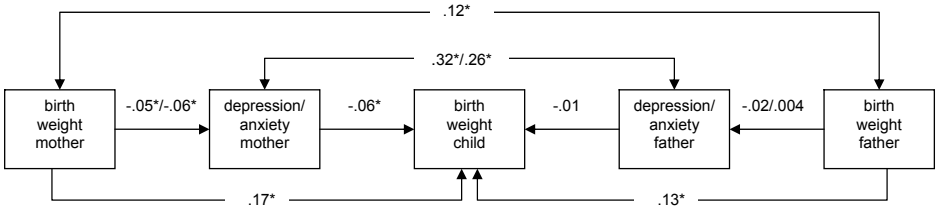
Figure 1 shows the combined results of separate path analyses with parental depression and anxiety in relation to parental and child birth weight. The results of this

Table 1. Child, maternal and paternal characteristics

	Child characteristics			
	Total (n)		**Mean (SD) / %**	
Birth weight	5,999		3,408 (567)	
Gender				
Girl	2,970		48.9	
Boy	3,102		51.1	
Gestational age	6,116		39.5 (2.6)	
	Maternal characteristics		**Paternal characteristics**	
	Total (n)	**Mean (SD) / %**	**Total (n)**	**Mean (SD) / %**
Age	6,506	29.6 (5.3)	5,746	32.6 (5.8)
Educational level				
Primary education	716	11.0	322	8.8
Secondary education 1st phase	876	16.0	520	14.2
Secondary education 2nd phase	1,649	30.2	1,021	27.9
Higher education 1st phase	1,008	18.4	662	18.1
Higher education 2nd phase	1,216	22.3	1,134	31.0
Dutch ethnicity				
No	2,777	49.7	2,467	46.2
Yes	2,805	50.3	2,873	53.8
Birth weight				
< 2000 g	90	2.6	29	1.2
2000-2499 g	257	7.3	98	4.1
2500-2999 g	737	20.9	338	14.2
3000-3999 g	2,108	59.9	1,501	63.0
> 4000 g	330	9.4	416	17.5
Smoking				
No	4,136	74.9	2,057	54.7
Yes	1,383	25.1	1,705	45.3
Alcohol use				
No	3,141	56.7	692	18.4
Yes	2,395	43.3	3,344	81.6
Primiparity				
No	2,356	42.9	-	-
Yes	3,141	57.1	-	-
Depression	4,811	.25 (.51)	3,650	.11 (.30)
Anxiety	4,815	.30 (.47)	3,658	.18 (.32)

Values are means (SD) in case of continuous variables and percentages in case of categorical variables

Figure 1. Path model of the effects of parental birth weight, parental depression/anxiety and child birth weight



The figure shows the combined results with standardised regression coefficients of separate path analyses with parental depression and anxiety. When regression coefficients differed, the first entry shows the results from the model with parental depression and after the slash, the second entry shows the model with parental anxiety.

* p< .05

Fit indices model with parental depression: χ^2= 14.60, df= 2, CFI= .97 TLI= .87, RMSEA= .03

R^2 birth weight child = .059; R^2 depression mother = .002; R^2 depression father= .001

Fit indices model with parental anxiety: χ^2= 6.01, df= 2, CFI= .99 TLI= .95, RMSEA= .02

R^2 birth weight child = .058; R^2 depression mother = .003; R^2 depression father= .000

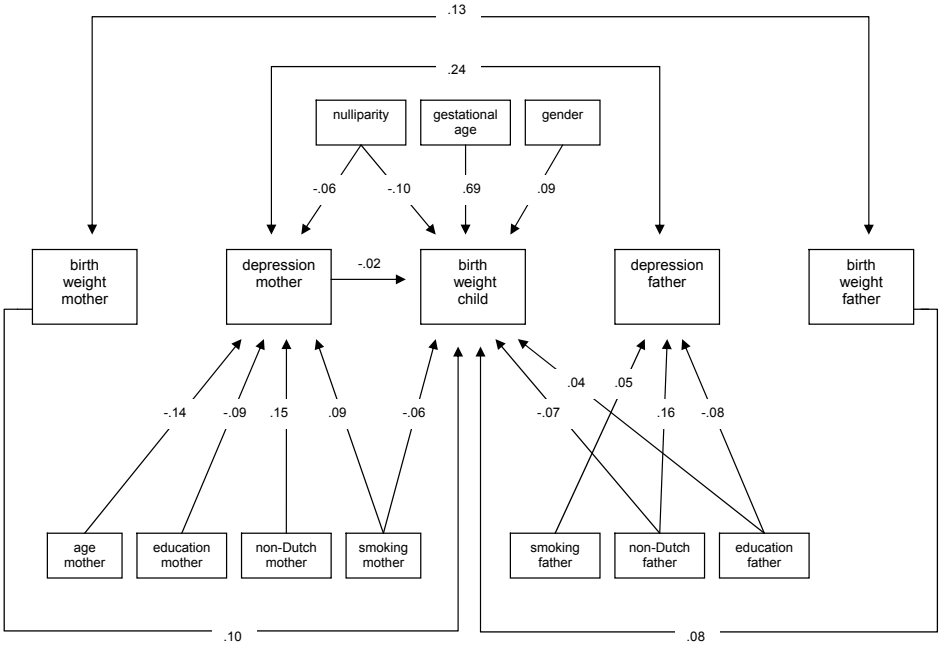
path analysis show a direct and an indirect significant effect of maternal birth weight on child birth weight. A total indirect effect can be obtained by multiplying the separate direct effects of a certain pathway. For example the total indirect effect of maternal birth weight via maternal depression on child birth weight was: -.05 (i.e. the effect of birth weight of the mother on depression during pregnancy) multiplied by -.06 (i.e. the effect of maternal depression on child birth weight), which is .003. This is much smaller than the direct effect of maternal birth weight on child birth weight (.17).

There was an indirect effect of paternal depression on child birth weight via maternal depression. This effect was larger (r= .32*-.06= -.02), than the indirect effect of maternal birth weight via maternal depression (.003). Paternal birth weight was only directly related to child birth weight (.13). The model yielded a good fit on the CFI and RMSEA indices, but a moderate fit on the TLI index.

The model with parental anxiety was comparable to the model with parental depression, except for the negligible larger effect of maternal birth weight on maternal anxiety (-.06) and the lower correlation between parental anxiety (.26). However, the model yielded a better fit on the CFI, TLI and RMSEA indices.

Next, we extended the simple path analysis with possible confounders in the relation between parental psychopathology and child birth weight. The full model with depression as a mediator between parental birth weight and child birth weight yielded the following fit indices: χ^2= 97.99; df= 16; CFI= .98; TLI= .95; RMSEA= .03, which is already a satisfactory fit. To improve the model we removed both maternal and paternal alcohol use and paternal age, because those variables did not have a significant effect on depression and child birth weight in the model. The final model is presented in figure 2, in which only significant effects are shown. The model fitted the data well and was slightly improved compared to the full model. After controlling for confounders the direct effect of maternal depression on child birth weight remained significant. The direct

Figure 2. Final path analysis model of the effects of parental birth weight, parental depression and child birth weight

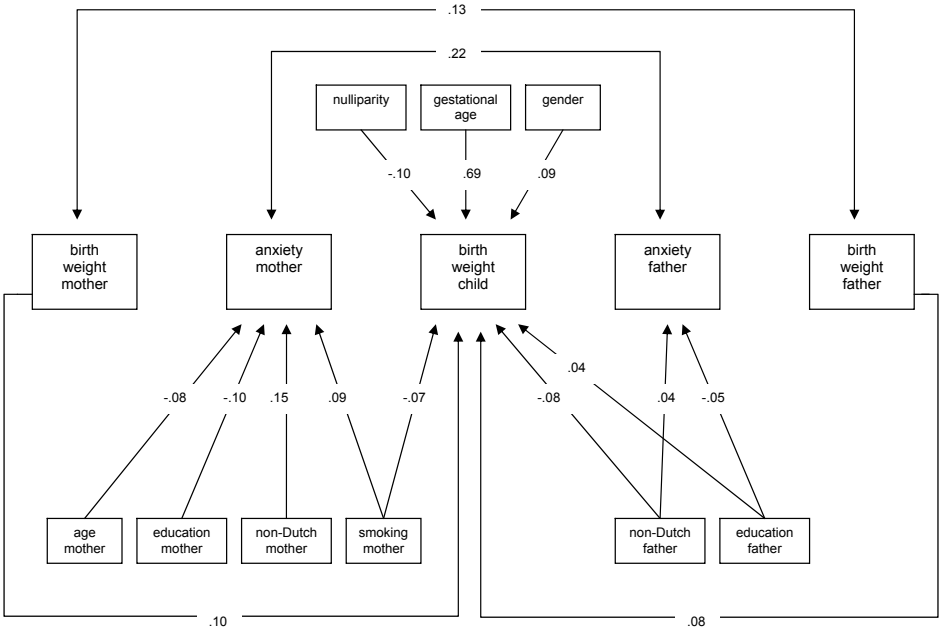


Model with significant (p<.05) standardised regression coefficients.
Model fit indices: χ^2= 88.26, df= 20, CFI= .98 TLI= .97, RMSEA= .02
R^2 birth weight child = .57; R^2 depression mother = .10; R^2 depression father= .04

effect from maternal birth weight to maternal depression disappeared and therefore also the indirect effect of maternal birth weight via maternal depression to child birth weight disappeared. The indirect, though very small (r= .24*.-02= -0.005) effect of paternal depression via maternal depression on child birth weight remained significant. The strongest effects child birth weight in the examined pathways were again maternal and paternal birth weight (.10 and .08 respectively).

The same procedure was applied to parental anxiety as a mediator. The full model with all confounders included yielded the following model fit: χ^2= 59.13; df= 16; CFI= .99; TLI= .97; RMSEA= .02. Again, both maternal and paternal alcohol use did not have a significant effect on anxiety and child birth weight in the model and were therefore removed. Paternal age and prenatal paternal smoking were also removed from the model, since they did not have a significant effect either. The final model is presented in figure 3, in which only significant effects are shown. The model fit indices were good and slightly improved compared to the full model. Besides the disappeared effect of maternal birth weight on maternal anxiety, like in the model with parental depression, in this model there was also no direct relation between maternal anxiety and child birth

Figure 3. Final path analysis model of the effects of parental birth weight, parental anxiety and child birth weight



Model with significant (p<.05) standardised regression coefficients.
Model fit indices: χ^2= 68.62, df= 19, CFI= .99 TLI= .97, RMSEA= .02
R^2 birth weight child = .57; R^2 anxiety mother = .07; R^2 anxiety father= .01

weight anymore. Only the direct effects of maternal and paternal birth weights on child birth weight remained significant (.10 and .08 respectively).

In tables 2 to 5 separate regression models are presented with the unadjusted and adjusted effects of parental depression and anxiety on child birth weight. Those models in general show the same significant associations.

Discussion

The aim of this study was to disentangle direct and indirect effects of parental birth weight and parental depression and anxiety during pregnancy on child birth weight. We investigated these pathways by means of path analysis, which has the advantage that both direct and indirect effects can be examined in the same model.

Effect of parental birth weight on child birth weight

In the simple, unadjusted, path analysis the strongest direct effect was between parental birth weight and child birth weight, respectively .17 for mothers and .13 for fathers. The correlation between maternal birth weight and child birth weight was significantly

Table 2. Maternal birth weight and maternal depression and anxiety during pregnancy

	β	SE	T	95% CI	Std β
Depression					
Model 0	-.04	.013	-3.01	-.07; -.01	-.07
Model 1	-.01	.013	-.93	-.04; .01	-.02
Anxiety					
Model 0	-.03	.012	-2.95	-.06; -.01	-.06
Model 1	-.01	.011	-1.07	-.04; .01	-.02

Model 0= unadjusted model
Model 1= adjusted for age, education, non-Dutch ethnicity, alcohol use, smoking
CI = confidence interval; Std β = standardised regression coefficient

Table 3. Paternal birth weight and paternal depression and anxiety during pregnancy

	β	SE	T	95% CI	Std β
Depression					
Model 0	-.01	.009	-1.13	-.03; .01	-.03
Anxiety					
Model 0	.002	.01	.19	-.02; .02	.004

Model 0 = unadjusted model
CI = confidence interval, Std β = standardised regression coefficient

higher than between paternal birth weight and child birth weight. This is similar to the studies of Magnus et al., 2001 who reported a mother-child correlation of .25 and a father-child correlation of .13 in birth weight and Knight et al., 2005 who found a mother-child correlation of .31 and a father-child correlation of .12. Both studies did not explain the difference in correlations between maternal and paternal birth weight and child birth weight, but they could possibly be explained by additional intrauterine effects like nutrition, or 'false paternity'. These differences in magnitude of the correlation between maternal and paternal birth weight and child birth weight therefore remain an interesting question for future research.

Effect of parental birth weight on parental psychopathology

In the unadjusted path analysis maternal birth weight was directly associated with maternal depression and anxiety during pregnancy. We did not find an effect of paternal birth weight on paternal depression and anxiety. This is consistent with a study (Gale and Martyn, 2004) in which also a significantly increased risk was found for women but not for men with lower birth weights to develop depression during adulthood. In this study an opposite effect at age 16, when lower birth weight in men and not in women was related to depression. Because at both ages the effects were adjusted for early child

Table 4. Maternal depression and anxiety during pregnancy and child birth weight

	β	SE	T	95% CI	Std β
Depression					
Model 0	-84.75	16.59	-5.07	-116.7; -51.7	-.08
Model 1	-34.18	13.58	-2.52	-60.7; -7.6	-.03
Model 2	-31.29	13.51	-2.32	-57.8; -4.8	-.02
Anxiety					
Model 0	-82.05	18.02	-4.55	-117.4; -46.7	-.07
Model 1	-27.94	14.52	-1.92	-56.4; .5	-.02

Model 0 = unadjusted model
Model 1 = adjusted for age, education, non-Dutch ethnicity, alcohol use, smoking, nulliparity, gender, gestational age
Model 2 = additionally adjusted for maternal birth weight
CI = confidence interval; Std β = standardised regression coefficient

Table 5. Paternal depression and anxiety during pregnancy and child birth weight

	β	SE	T	95% CI	Std β
Depression					
Model 0	-70.41	32.52	-2.17	-134.2; -6.7	-.04
Model 1	3.03	32.62	.09	-60.9; 67.0	.002
Anxiety					
Model 0	-11.29	31.12	-.36	-72.3; 49.7	-.001

Model 0 = unadjusted model
Model 1 = adjusted for age, education, non-Dutch ethnicity, alcohol use and smoking
CI = confidence interval; Std β = standardised regression coefficient

influences one could think of an age specific neurodevelopmental difference between men and women. However, this gender specific effect has not been replicated in a recent study (Wiles et al., 2005), which showed a significant risk of low birth weight both in men and women to develop psychological distress in adulthood.

After adjustment for confounders, the direct effect of maternal birth weight on maternal psychopathology disappeared. Our results suggest that parental psychopathology during pregnancy is mainly determined by other factors than birth weight, of which demographic and socio-economic variables we controlled for explained less than 10%.

Effect of parental psychopathology on child birth weight

In the simple path analysis we found a direct and negative effect of both maternal anxiety and depression during pregnancy on child birth weight. As expected we did not find a direct effect of paternal depression and anxiety on child birth weight. The direct effect of maternal anxiety disappeared after adjustment for confounders and the direct effect

of depression remained significant. As far as we know there are no studies that specifically focused on the different underlying mechanisms of the effect of maternal anxiety and depression on child birth weight. The biological and neuroendocrine mechanisms of anxiety and stress leading to adverse child birth outcomes are extensively studied, both in animals and in humans. These studies suggest that adverse child birth outcomes are influenced by the maternal-placental-fetal neuroendocrine axis with a specific role for placental corticotrophin-releasing hormone (pCRH) (Wadhwa, 2005). High levels of pCRH are both related to lower birth weight and lower gestational age of the child (Wadhwa et al., 2004). Because we adjusted for gestational age, it is not surprising that we did not find a significant relation between maternal anxiety and child birth weight, but this does not explain why the relation between maternal depression and child birth weight remained significant. The biological and neuroendocrine mechanism of depression leading to adverse child birth outcomes are less well understood, but from other studies it is known that raised CRH levels also play a crucial role in depression (Nemeroff, 1996). Because there is much overlap between depression and anxiety (in our study we found a correlation of .73 in mothers and .60 in fathers), the underlying mechanism of depression leading to adverse child birth outcome could partly be the same, i.e. influencing both child birth weight and gestational age. Therefore, the different impact of depression and anxiety on child birth weight should be explained by co-occurring intrauterine influences related to depression that do not – or less - occur in anxiety, of which inadequate nutrition and less optimal self-care could be important factors. There is evidence that malnutrition during pregnancy, especially in the second and third trimester is related to small for gestational age children (Stein et al., 2004), so this could be part of a possible interpretation for the difference between the impact of depression and anxiety on child birth weight.

Indirect effects

In the unadjusted model there was an indirect effect of paternal psychopathology (i.e. depression and anxiety) via maternal psychopathology (i.e. depression and anxiety) on child birth weight. This effect was small, but larger than the indirect effect of maternal birth weight via maternal depression and anxiety on child birth weight. In the adjusted models the indirect effects of maternal birth weight via maternal depression and anxiety disappeared and in the depression model the indirect effect of paternal depression via maternal depression on child birth weight remained significant.

This suggests that maternal psychopathology is not an important mediator between maternal birth weight and child birth weight and that the direct effects leading to child birth weight that we discussed before are more important.

Effect of confounders between parental psychopathology and child birth weight

In the final model, the influence of maternal confounders differed from the influence of paternal confounders. The influence of the confounders also differed between depression and anxiety. Of the maternal confounders only smoking directly influenced child birth weight. Of the paternal confounders, non-Dutch ethnicity and educational level directly influenced child birth weight. The influence of paternal non-Dutch ethnicity was relatively large. Considerable research has been focused on the effect of maternal ethnicity on child birth weight. This revealed two conclusions. The first is that non-white women tend to have a higher risk of giving birth to children with lower birth weight than white women. The second is that these differences are not only explained by genetic factors, but also by socio-economic status and social support (Collins et al., 2002; David and Collins, 1997; Drooger et al., 2005; Hessol et al., 1998). Our study additionally shows that maternal non-Dutch ethnicity is directly related to maternal psychopathology and that paternal non-Dutch ethnicity is directly related to child birth weight. Because our definition of non-Dutch ethnicity led to a very heterogeneous group (i.e. all parents that were born outside The Netherlands and irrespective of their race were pooled together), further research on the relation between parental ethnicity in combination with parental psychopathology and child birth is warranted.

Strengths and limitations

The major strength of this study is that it systematically investigated different pathways between birth weight and psychopathology in a large prospective population-based study.

This study is not without limitations. First, our initial response was 61% of all eligible (i.e. pregnant) participants. Non-response at baseline among the participants is not likely to be random. National and regional registries do not have subject characteristics in all children and their parents that enable detailed non-response analyses. However, the percentages of parents with another ethnic background and lower socio-economic status are lower among the participants than expected from the population figures in Rotterdam (2005). This selection would lead to bias in the found associations if non-response among parents with psychopathology is more strongly related to child birth weight than among participating parents with psychopathology. We do not expect that this is the case. The selection is likely to affect the frequency rates and, as a consequence, the statistical power in our study. However, we did find significant associations between maternal birth weight, maternal psychopathology and child birth weight, suggesting that these findings would probably have been even more significant when there was no selection bias. Second, we had to rely on anamnestic data considering parental birth weight, which might be related to substantial misclassification. Misclassification of parental birth weight would lead to bias when it is related to parental psychopathology.

This would be the case when parents with, for example, higher levels of psychopathology systematically under- or over report their birth weights. This seems not likely. In case of non-differential misclassification, which is more likely, the effects between parental birth weight and parental psychopathology and child birth weight are underestimated. However, from previous research it is known that the validity of self-reported birth weight in women is high (Allen et al., 2002; Sanderson et al., 1998; Troy et al., 1996), but for men this validity is not known. It is reassuring that the father-child correlations we found are similar to other studies which used paternal and child birth weights from medical birth registers (Knight et al., 2005; Magnus et al., 2001). Third, we cannot rule out 'false paternity' inflicting all effects related to paternal factors, since we had to rely on self-reported information about paternity. From a recent review it is estimated that 3.7% of the children is sired by another man than the father who believes he is the biological father (Bellis et al., 2005). If this is the case in our study, the found associations between paternal and child characteristics could be somewhat underestimated when genetic factors were of major importance.

Conclusion

The results of our study showed a direct effect of maternal depression - and not of anxiety - on child birth weight, even after adjusting for confounders and both maternal and paternal birth weight. This suggests different mechanisms between maternal depression and anxiety in influencing child birth weight. Since most studies focused on the influence of maternal anxiety or stress on child birth weight, it would be particularly interesting to examine the mechanisms of maternal depression in relation to child birth weight more extensively.

4 Empirical identification of early postpartum psychiatric symptom profiles

Abstract

Background

In the first weeks after delivery it is hard to distinguish mild psychiatric symptoms, often referred to as 'maternity blues', which do not need treatment, from serious psychiatric symptoms, like postpartum depression that should be recognised and treated as soon as possible.

Objective

The aim of this study was to empirically identify different profiles of common early psychiatric postpartum symptoms and their associated pre- and postpartum factors in a large population based study.

Method

Data were available from 2,594 women, followed from 12 weeks pregnancy until 2 months postpartum. Early postpartum symptom profiles were obtained by latent class analysis of 11 symptoms present in the first two weeks after delivery.

Results

Analysis revealed four symptom profiles. Low probability of occurrence on each symptom characterised the 'normative' group (39.1%). High probability of cognitive symptoms together with a longer duration of these symptoms characterised the 'cognitive problems' group (26.0%). Moderately elevated affective symptom probabilities with shorter duration characterised the 'mild affective problems' group (24.6%). High probabilities and longer duration characterised the 'serious problems' group (10.3%). The adjusted risks to develop serious problems that meet criteria for depression at 2 months postpartum were significant for the 'mild affective problems' group (OR 4.5) and the 'serious problems' group (OR 16.5). Different characteristics of the symptom profiles, like socio-economic factors and pregnancy and health related factors are discussed.

Conclusion

This study showed that postpartum psychiatric symptoms - instead of two distinct disorders - might be regarded as affective, cognitive and somatic problems that vary in co-occurrence, severity and duration.

Introduction

Affective, cognitive and somatic symptoms in recently delivered women are common and might or might not be serious. Frequently used terminology to describe the two most prevalent types of postpartum problems is 'maternity blues' (or synonyms like 'postpartum blues' and 'baby blues') and postpartum depression (Brockington, 1996b).

Maternity blues is a common but yet not-well described phenomenon that refers to a mild and transient pattern of symptoms during the first two weeks after delivery. It affects approximately half of the recently delivered mothers and does not need psychiatric treatment. Most characteristic of maternity blues is the sudden and incontrollable onset of crying spells that women themselves do not understand. Although crying is considered to be the core symptom of maternity blues, most women also suffer from other symptoms covering a broad spectrum of affective, cognitive and somatic symptoms (Brockington, 2004; Pitt, 1973; Yalom et al., 1968).

Postpartum depression is a well-known psychiatric disorder occurring in approximately 10-15% of recently delivered mothers (O'Hara and Swain, 1996). It is specified in the DSM-IV as a major depressive disorder, with an onset within four weeks postpartum. The symptoms of a postpartum depression are similar to those of maternity blues, but differ in duration (they should last at least two weeks) and severity (they should cause clinically significant distress or impairment of the woman's everyday functioning).

Although it is questionable whether maternity blues and postpartum depression are distinct entities, in previous research they are studied with different instruments and research designs. For studying maternity blues, no standardised assessment instruments are available and there is no consensus about the criteria for defining maternity blues, although descriptions are available of the day-to-day course of affective, cognitive and somatic symptoms in clinical samples in the first two weeks after delivery (Brockington, 1996b; Kennerley and Gath, 1989; Nagata et al., 2000; O'Hara et al., 1991; Pitt, 1973). In contrast, studies on postpartum depressive symptomatology are usually performed with well-known and validated instruments that assess depressive symptomatology using cut-off scores that are predictive of clinical depression, with the Edinburgh Postnatal Depression Scale (EPDS) (Cox et al., 1987) being the most widely used. This instrument focuses on affective symptoms and items which might confuse depression with physical reactions to childbirth (i.e. loss of energy, poor concentration, problems with sleeping) were omitted. Therefore the EPDS only partly overlaps with existing maternity blues scales that cover a broader range of symptomatology, including somatic and cognitive problems. Studies on postpartum depressive symptomatology usually cover a larger time span than maternity blues, varying from 1 week to several months postpartum.

However, as long as studies on maternity blues and postpartum depression are not combined, it is not possible to distinguish transient problems, referred to as maternity

blues, from problems reflecting the onset of a much longer lasting and more severe depression. For example, a study focusing only on postpartum depression showed high correlations between depression in the first week after delivery (i.e. before the DSM-IV A criterion of duration of 2 weeks could be fulfilled) and at 4 and 8 weeks follow-up (Dennis, 2004). The prevalence of major depression symptomatology assessed with the EPDS in this study was highest in the first week, 14.6%, compared to 9.2% and 8.0% after 4 and 8 weeks. This finding may suggest that a large part of recently delivered women had depressive symptoms that were transient and could have been labelled maternity blues symptoms. With respect to studies focusing exclusively on maternity blues the opposite can be possible: psychiatric symptoms that are initially attributed to maternity blues could persist in a postpartum depression.

For several reasons it is important to study variations in type, severity and duration of postpartum symptoms in the first weeks after delivery. Firstly, postpartum depression not only affects the mother, but also negatively influences the emotional and cognitive development of her child (Murray and Cooper, 1997; Righetti-Veltema et al., 2003). Early recognition and treatment of a postpartum depression benefits the mother and her child. Secondly, especially in the first two weeks after delivery the contact between health professionals and recently delivered mothers is frequent.

In conclusion, it is beneficial to identify women at risk of developing serious postpartum mood problems, based on observed or spontaneously reported early postpartum symptoms, next to existing assessment scales for maternity blues and depression.

The main objectives of this study will therefore be:

1. to identify groups of women who differ in type and severity of postpartum affective, cognitive and somatic symptoms;
2. to test differences between these groups in duration of symptoms;
3. to test differences between these groups in a number of socio-economic, health related and other factors;
4. to estimate the risk of developing symptoms, which fulfil criteria for postpartum depression at 2 months after delivery for each of these groups.

Methods

Design

This study was embedded in the Generation R Study, a prospective population-based cohort study from fetal life until young adulthood. The study is designed to identify early environmental and genetic determinants of growth, development and health from fetal life until young adulthood and has been described previously in detail (Hofman et al.,

2004; Jaddoe et al., 2006). Briefly, the cohort includes 9,778 mothers and their children living in Rotterdam, one of the major cities of The Netherlands. Enrolment for mothers in the study was aimed in the first trimester of pregnancy but was possible until birth of their offspring from December 2001 until January 2006. Next to participating in physical examinations at 12, 20 and 30 weeks during pregnancy and at regular times after pregnancy mothers completed questionnaires on social, developmental and health related topics. Based on the annual birth rates in Rotterdam, the calculated initial response was 61%.

The study cohort is a multi ethnic cohort with a large number of different ethnicities. Questionnaires were available in Dutch and translated in English, French, Portuguese and Turkish. When participants were not able to fill out the questionnaire in one of these languages (e.g. most Moroccans speak Berber, a non-written language) assistants who spoke the same language visited participants at home to help fill out the questionnaire.

The Medical Ethics Committee of Erasmus Medical Center has approved the study and written informed consent was obtained from all participants.

Population

Data cleaning and preparation for the whole Generation R cohort is still ongoing. For the current study we used available data on women of all children that were born between January 1st 2003 and January 1st 2005. In this period 4,606 women were included. Of the included participants, 132 women dropped out of the study before 20 weeks pregnancy for the following reasons: induced abortion (n= 17), intrauterine death (n= 22), withdrawal from study (n= 42) and lost to follow up (n= 51). Of the remaining women on 3,452 (75%) women we obtained valid information at 20 weeks pregnancy. Of these remaining women, another 28 women dropped out of the study before 2 months after delivery for the following reasons: intrauterine death (n= 3), neonatal death (n= 6), withdrawn from study (n= 4) and lost to follow up (n=15). Of the remaining women at 2 months after delivery we obtained valid information on 2,594 (56%) women.

Postpartum psychiatric symptomatology

Postpartum psychiatric symptomatology was assessed at 2 months after delivery in two ways: 1) by a questionnaire on early postpartum symptoms developed for this study that covered the whole period between delivery and 2 months postpartum; 2) by using the Edinburgh Postnatal Depression Scale (EPDS) at 2 months after delivery.

The selection of early postpartum symptoms that we used for our questionnaire was based on two criteria; they should cover frequently reported complaints on the affective, cognitive as well as somatic domains and the symptoms should be easy to understand and recognise, since our sample consisted of women with different ethnic

backgrounds. We selected symptoms (or their equivalents) that were present in at least two of five existing maternity blues scales developed by Handley (Handley et al., 1980), Kendell (Kendell et al., 1981), Kennerley (Kennerley and Gath, 1989), Pitt (Pitt, 1973) and Stein (Stein, 1980). Those symptoms were: anxiety, crying, forgetfulness, headache, irritability, lability, loss of energy, poor concentration, restlessness and sadness. We added negative feelings towards the baby, as a measure of severity for postpartum problems. Then we tested the usefulness of the symptoms by asking 50 women, who did not participate in the Generation R Study and who visited an infant welfare centre in Rotterdam, to interpret these symptoms/criteria. The items reflecting the symptoms lability and irritability were not understandable for about half the women without explanation and were thus omitted from the scale. One symptom, feeling insecure, was added because several women mentioned it as a symptom that they experienced shortly after delivery that was missing on our list. This led to our final list of 11 early postpartum symptoms: anxiety, crying, feeling insecure, forgetfulness, headache, loss of energy, negative feelings towards baby, nightmares, poor concentration, restlessness and sadness. In the questionnaire, mothers were requested to indicate for each symptom whether it was present or absent in the first two weeks after delivery, with the instruction that symptoms that were already present during pregnancy should not be scored. Next we asked on which day each newly developed symptom started and on which day it ended (or whether it was still present at the moment of assessment).

Postpartum depression was assessed with the Edinburgh Postnatal Depression Scale (EPDS), a widely used 10-item self-report scale that has been validated for the Dutch population (Cox et al., 1987; Pop et al., 1992). The EPDS asks for affective symptomatology in the previous week. Of the 11 early postpartum symptoms only the symptoms crying, anxiety and sadness were also on the EPDS. We used the validated cut-off score of more than 12 on the EPDS that has an optimal sensitivity of over 80% and a specificity of more than 95% for identifying mothers with a clinical depression in a community sample (Murray and Carothers, 1990).

Covariates

Information on demographic background, marital status, socio-economic factors, perceived health and substance use were collected from the 12 weeks pregnancy questionnaire. Two indicators of socio-economic status were included. Educational level was dichotomised into 'low education' indicating no education or primary education only versus more than primary education. Income was dichotomised into 'low income' indicating an income of less than 1200 euros net a month, which is at the social security level payment for a Dutch household, versus more than 1200 euros. Ethnicity is defined according the classification of Statistics Netherlands (2004a). This means that a women was considered Dutch if both her own and country of birth of her parents is

The Netherlands. The mother had another ethnicity if her own or at least one parental country of birth is other than The Netherlands. Our sample consisted of 51.5% native Dutch women, 9.0% Surinam, 8.7% Turkish, 6.3% Moroccan, 4.1% Cape Verdian, 2.6% Antillian/Aruban, 2.8% Indonesian, 1.9% African, 9.0% other Western countries and 4.1% other non-Western countries. Perceived general health was coded on a 5 point-scale, dichotomised in excellent, very good and good versus fair and poor. Maternal smoking was dichotomised in non-smoking and smoking. Alcohol use was dichotomised in non-alcohol and alcohol use.

At 20 weeks pregnancy, maternal depression and anxiety were assessed with the Brief Symptom Inventory (BSI), a validated self-report questionnaire with 53 items to be answered on a 5-point scale, ranging from "0= not at all" to "4= extremely" (de Beurs, 2004; Derogatis and Melisaratos, 1983). The BSI is a short version of the Symptom Checklist 90 (SCL-90) (Derogatis et al., 1976). The items of the BSI define a spectrum of psychiatric symptoms in the preceding 7-days covering nine scales. For this study we used the Anxiety and Depression scales. The internal consistencies in our sample were $\alpha = .83$ for the Depression scale and $\alpha = .78$ for the Anxiety scale. There is no established clinical cut-off score for this instrument; we therefore identified women with high levels of depression and anxiety based on a cut-off of 2 SD above the mean.

At 2 months after delivery, the mothers were asked whether their child was admitted to hospital during the first week after birth. This was used as an overall measurement of poor birth outcome of the child, which included premature birth, low birth weight, asphyxia, infections, jaundice and other severe problems occurring after birth.

Data analysis

Firstly, we applied latent class analysis (LCA) to empirically identify women with similar profiles of the 11 early postpartum symptoms. LCA is a statistical method that assumes that people from a heterogeneous population (e.g. recently delivered women) belong to a limited number of homogeneous groups or 'latent classes'. based on similar patterns of symptoms. An LCA provides two kinds of estimates: the probability of a woman to belong to each of the classes and the conditional probability of a woman in a particular class to have a specific symptom. The primary objective of an LCA is to find the smallest number of classes of women with similar profiles of postpartum symptoms that can provide a plausible interpretation. In the analyses, classes were added stepwise until the model fitted the data well according to the Bayes Information Criterion (BIC) (Kass and Raftery, 1993), with a lower BIC indicating a better model fit. Fifty random sets of starting values were used to control for model stability.

Secondly, we examined whether there were differences across the LCA classes. Differences in duration of symptoms and frequency of endorsement of covariates per class were tested with one-way ANOVAs and chi-square tests with posthoc Bonferroni tests.

Finally we used logistic regression to predict serious problems that meet criteria for depression at 2 months postpartum from class membership.

For the LCA we used the Mplus program, version 3.11(Muthén and Muthén, 2005) and for the ANOVAs, chi-square tests and logistic regression we used SPSS version 12.0.1.

Results

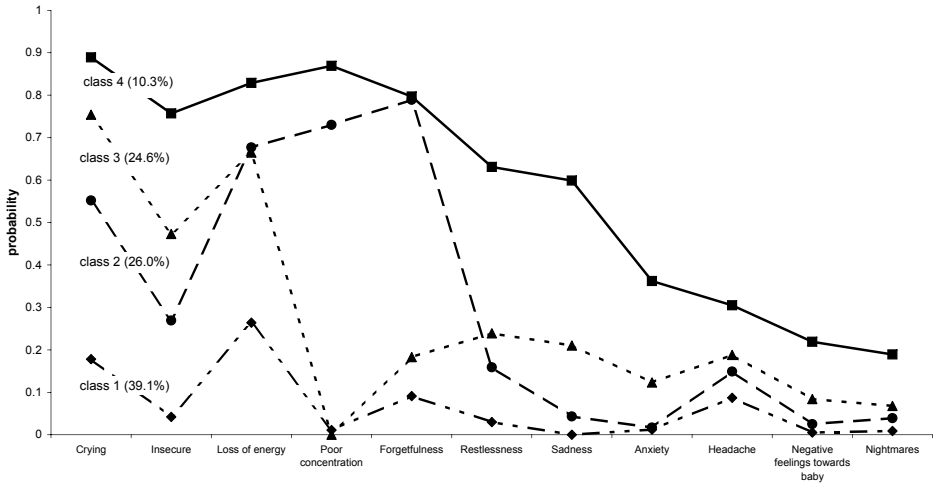
Attrition

Analyses of missing data on maternal postpartum symptoms and depression at 2 months after delivery showed that women with missing data were 2.2 (95% CI: 1.9–2.5) years younger, were significantly less educated (57% versus 33%; $\chi^2 = 141.02$; df= 1; p< .001), had significantly less income (50% versus 25%; $\chi^2 = 141.02$; df= 1; p< .001), were significantly more of non-Dutch ethnicity (53% versus 28%; $\chi^2 = 252.89$; df= 1; p< .001) and had .15 (95% CI: .11– .18) lower scores on depression and .14 (95% CI: .11– .17) lower scores on anxiety during pregnancy.

Latent class analyses

A stepwise addition of classes in the model revealed a decrease in the BIC from 26530.205 in a one-class solution, to 24022.737 in a four-class solution. With a five-class solution the BIC increased to 24047.119, suggesting that a four-class solution fitted the data best. The results of this solution are shown in Figure 1**.** Of the total sample, 1,015 (39.1%) were

Figure 1. Latent Class Analysis on early postpartum symptoms in a community based sample of 2,594 recently delivered women



members of class 1; 675 (26.0%) of class 2; 638 (24.6%) of class 3; and 266 (10.3%) of class 4. The first and largest class showed low overall symptom probabilities. We termed this class the 'normative' class. The second class was characterised by high probabilities of poor concentration (.73) and forgetfulness (.79) and low probabilities of the affective symptoms sadness (.04) and anxiety (.02). We termed class 2 'cognitive problems'. The third class showed higher probabilities of the affective symptoms sadness (.21) and anxiety (.12) than class 1 and 2, but contrary to class 2 no problems with concentration and relatively low probabilities of forgetfulness (.18). We therefore termed this 'mild affective problems'. The fourth class was characterised by overall high probabilities of symptoms, both on the affective and cognitive symptoms. We termed class 4 'serious problems'.

Table 1. Mean duration in days of early postpartum symptoms by class membership (n= 2,594)

	Mean Days (SD)					
	Class 1: Normative	**Class 2: Cognitive Problems**	**Class 3: Mild Affective Problems**	**Class 4: Serious Problems**	**F**	**P value**
Crying	6.4 (10.4)[a]	12.6 (18.5)[b]	12.8 (17.9)[b]	21.7 (22.0)[c]	22.30 (df= 3, 1183)	<.001
Feeling insecure	10.9 (18.2)[a]	19.1 (19.8)[a]	18.4 (19.8)[a]	30.4 (22.8)[b]	17.29 (df= 3, 672)	<.001
Loss of energy	22.6 (21.2)[a]	36.7 (22.1)[b]	28.7 (22.3)[a]	45.9 (19.1)[b]	47.66 (df= 3, 1221)	<.001
Poor concentration	-	37.7 (23.5)[a]	44.9 (22.0)	42.7 (21.4)[b]	3.50 (df= 2, 594)	.03
Forgetfulness	47.0 (19.8)	46.5 (21.3)	43.7 (21.0)	43.8 (20.7)	.91 (df= 3, 705)	.43
Restlessness	16.4 (15.4)[ac]	37.9 (21.4)[b]	28.3 (23.5)[c]	40.8 (21.1)[b]	14.01 (df= 3, 396)	<.001
Sadness	-	22.3 (19.5)	23.2 (23.0)[a]	32.3 (23.3)[b]	5.51 (df= 2, 269)	.01
Anxiety	25.0 (31.1)	42.9 (25.5)	30.8 (24.0)	34.7 (24.3)	.89 (df= 3, 168)	.45
Headache	11.4 (17.0)[a]	18.6 (21.8)	19.3 (22.3)	27.3 (23.9)[b]	6.68 (df= 3, 331)	<.001
Negative feelings towards baby	20.8 (21.4)	8.2 (7.6)[a]	21.7 (20.8)	27.5 (21.9)[b]	2.76 (df= 3, 105)	.05
Nightmares	27.1 (26.8)	23.2 (23.1)	27.3 (25.8)	28.6 (23.8)	.23 (df= 3, 108)	.88
Total	16.5 (19.5)[a]	28.9 (17.3)[b]	18.6 (15.3)[a]	29.9 (15.8)[b]	64.42 (df= 3, 1699)	<.001

Superscripts that differ represent significant (p< .05) differences between classes on that variable

Table 2. Frequency of endorsement of associated factors by class membership

	% (N)					
	Class 1: Normative	Class 2: Cognitive Problems	Class 3: Mild Affective Problems	Class 4: Serious Problems		
	(n= 1015)	(n= 675)	(n= 638)	(n= 266)	Statistic	P value
Mean age mother (SD)	30.7 (5.0)	31.4 (4.4)	30.4 (4.9)	30.6 (5.3)	4.83	.002
Living without a partner	11.0% (94)	8.0% (47)	10.0% (56)	11.9% (27)	4.56	.21
Low education	10.8% (95)	4.5% (27)	6.7% (39)	4.6% (11)	29.91	<.001
Low income	17.1% (143)	7.5% (45)	13.1% (72)	12.7% (30)	28.98	<.001
Other ethnicity	45.7% (407)	27.7% (167)	35.8% (209)	44.0% (106)	54.01	<.001
Unplanned pregnancy	22.7% (195)	16.9% (100)	20.7% (117)	27.4% (65)	13.35	.004
First child	18.4% (100)	24.2% (79)	39.0% (108)	42.2% (46)	55.32	<.001
Perceived poor health during pregnancy	5.7% (49)	3.7% (22)	4.0% (22)	12.3% (28)	26.88	<.001
Alcohol use during pregnancy	44.9% (393)	47.9% (346)	53.5% (305)	55.2% (132)	27.38	<.001
Smoking during pregnancy	19.8% (173)	20.5% (122)	26.5% (151)	23.9% (57)	10.37	.02
High level of depression during pregnancy	4.3% (37)	2.8% (17)	5.3% (30)	16.0% (38)	63.27	<.001
High level of anxiety during pregnancy	3.6% (31)	4.8% (29)	5.3% (30)	14.3% (34)	42.93	<.001
Child admitted to hospital	13.1% (130)	14.8% (96)	17.7% (110)	20.5% (53)	11.96	.01

Statistics are X^2 (df=3), except for mean age mother: F (df=3; 2,590)

Class characteristics

There were highly significant differences in the total number of symptoms across the four classes. Of class 1 only 7 (= 0.4%) women had more than two symptoms (mean .6; SD = .7) after delivery whereas in class 4 none of the women had less than four symptoms (mean 6.8; SD = 1.2). In class 2 and class 3 most of the women had between two and five symptoms, with a little but highly significant difference in a mean of 3.4 (SD = 1.1) symptoms in class 2 and 3.2 (SD = 1.2) symptoms in class 3.

Table 1 shows the mean duration in days of present symptoms across the classes. After a Bonferroni correction to account for multiple testing, only the duration of crying, feeling insecure, loss of energy, restlessness, headache and the total duration of symptoms significantly differed across the classes. The mean duration of the total of present symptoms was comparable between class 1 (16.5 days) and class 3 (18.6 days). The symptoms in these classes were significantly shorter in duration than in class 2 (28.9 days) and in class 4 (29.9 days), which showed similar symptom duration.

Table 2 summarizes the distribution of associated factors across the classes. Women in class 1 were lower educated, less often having their first child, drinking alcohol less often during pregnancy and their children were less often admitted to hospital in the

Table 3. Prevalence and risk of depression at 2 months postpartum by class membership

	Class 1: Normative	Class 2: Cognitive Problems	Class 3: Mild Affective Problems	Class 4: Serious Problems
	(n= 1,000)	(n= 666)	(n= 630)	(n= 262)
Prevalence depression* % (n)	2.7% (27)	3.5% (23)	7.1% (45)	27.1% (71)
Unadjusted Risk depression, OR (95%CI)	Reference	1.3 (0.7-2.3)	2.7 (1.7-4.5)	13.4 (8.4-21.4)
Adjusted Risk depression†, OR (95%CI)	Reference	2.5 (1.0-6.1)	4.5 (2.0-10.4)	16.5 (7.2-37.6)

* Total score of >12 on the Edinburgh Postnatal Depression Scale
† Adjusted for: age, low educated, low income, other ethnicity, poor health, alcohol use, high level of depression during pregnancy, high level of anxiety during pregnancy, admitted child

first week after delivery, compared to women in the other classes. Women in class 2 were older, less likely to be living without a partner, higher educated, having a higher income, more of Dutch origin, less likely to have an unplanned pregnancy and perceived to be in a better general health than women in other classes. Women in class 3 differed only significantly in smoking more often during pregnancy. Although these women had higher probabilities of affective symptoms after delivery than women from class 1 and class 2, the prevalences of high levels of anxiety and depression during pregnancy did not significantly differ from those classes. Women in class 4 were more often likely to be living without a partner, more often having an unplanned pregnancy, more often having their first child, having a poorer perceived health during pregnancy, having higher levels of anxiety and depression during pregnancy and their children were more often admitted to hospital after delivery.

In table 3 the prevalence and risk of serious problems that meet criteria for depression is estimated at 2 months after delivery across the classes. We adjusted for possible confounders i.e. variables that were significantly related to both class membership and depression at 2 months after delivery. All variables that were significantly related to class membership were also related to depression, except for having a first child not being significantly related to depression and this was therefore not included in the analyses. The overall prevalence of postpartum depression was 6.4%. The prevalence and risk of postpartum depression increased from class 1 to class 4 and was significant for women in class 3 (OR = 4.5) and 4 (OR = 16.5).

Discussion

Identification and characteristics of postpartum symptom profiles

We applied latent class analyses to empirically identify women with different postpartum symptom profiles. The LCA on 11 postpartum symptoms yielded four symptom profiles. If the symptom profiles would be in accordance with maternity blues and postpartum depression as distinct profiles, three classes would be expected: a 'normative', a 'maternity blues' and a 'depressive'. Therefore, finding four instead of three classes of postpartum symptom profiles, casts doubt on the fact that the two 'disorders', maternity blues and postpartum depression, are distinct entities. Instead, postpartum symptoms might better be regarded as affective, cognitive and somatic problems that vary in co-occurrence, severity and duration.

We classified the first and largest class (39.1%) as the normative group since the women of this class experience overall low probabilities of postpartum symptoms. Adding up the percentages of the three classes with women experiencing early postpartum problems (i.e. in the first two weeks), somewhat more than half of the women can be regarded as having postpartum problems. This is consistent with the findings in studies exclusively focusing on maternity blues (Pitt, 1973; Yalom et al., 1968).

Within the group of women experiencing early postpartum symptoms we classified a group (class 4) of 10.3% women with serious problems, reflected by high overall probabilities of symptoms. This group could also be distinguished from the other three groups by longer duration of symptoms and the highest risk of high scores on the EPDS scale, which indicates a high probability of meeting DSM-IV criteria for a clinical depression at 2 months after delivery. In this group the percentages of high levels of depression and anxiety during pregnancy were also significantly higher compared to the other groups. A recent review of studies on antenatal risk factors for postpartum depression showed that high levels of anxiety and depression during pregnancy are the strongest predictors of postpartum depression (Robertson et al., 2004). This finding and the high risk of meeting criteria for a depression at 2 months postpartum, support the identification of class 4 as women with serious problems indicating a high risk of developing a depression. Other determinants that are predictive of being assigned to class 4, such as life events (unplanned pregnancy, child admitted to hospital), lack of social support (living without a partner), low socio-economic status (low income) also support the validity of this class reflecting the presence of a group of women who have a high risk of developing a depression.

Based on the duration of symptoms, the occurrence of class 3 with a mean duration of 18.6 days, indicates that many women with mainly affective symptoms improve in the second week after delivery. The course of problems of women in class 3 therefore indicates a resemblance with the course followed by what is called maternity blues. As

discussed in the introduction, previous studies found an association between maternity blues and postpartum depression. Women in class 3 are at risk of having higher scores on the EPDS at 2 months after delivery indeed, but lower than the 'serious problems' group, therefore we identified class 3 as 'mild affective problems'. We found that women in class 3 were more likely to be younger, to live without a partner, to have their first child, to have less income and education and to have a child who is admitted to hospital compared to women in the other classes. The mild and mostly transient affective symptoms that women of class 3 develop after delivery might be explained by less support and less coping strategies to overcome external stressors like having their first child or having their child admitted to hospital.

Because of the mainly cognitive problems and the lower level of affective symptoms, we identified women in class 2 as 'cognitive problems' group. This group had a mean duration of problems of 28.9 days, which is much longer than the course that refers to what is called maternity blues. However, women in class 2 do not have a significantly increased risk of high scores on the EPDS scale at 2 months after delivery. This particular finding has not yet been described in previous studies. More general, a review of cognition and mood changes during pregnancy and post partum (Buckwalter et al., 2001) revealed that women might have cognitive changes during and after pregnancy. Subjective complaints rather than objective assessment of cognitive dysfunction mostly explained this finding. Women in class 2 were significantly older, had more education and a higher income, are more often likely to be living with a partner and are more often of Dutch origin than women in the other classes. Those are all characteristics of the higher socio-economic class within the Dutch population. A possible explanation for the high probabilities of cognitive problems in class 2 is that women from a higher socio-economic class are more self-demanding in their cognitive performances and therefore are more easily confronted with their cognitive impairment.

From our study, the most predictive factors for lower probabilities of postpartum problems are not having a first child and a child who was not admitted to hospital. Compared to the depressive group, women of this group also are in a perceived better health and had lower anxiety and depression levels during pregnancy. A plausible explanation for this group having the lowest probability of developing postpartum problems is that those women are more experienced in having a baby, are in better mental and somatic condition and are less exposed to external stressors.

Surprisingly, the symptom 'crying' which is considered to be the core symptom of maternity blues has increased probabilities in all classes, making it less useful as a clinical discriminator between serious and less serious postpartum problems. However, when a woman does not experience any crying spells during the first 2 weeks after delivery she is unlikely to develop serious problems that are long lasting and that meet criteria for postpartum depression, since 89% of women belonging to the 'serious problems' class

have bouts of crying. The somatic symptoms 'loss of energy' and 'headache' showed gradually increased probabilities among the 4 classes, making it not specific for characterisation of the classes. The probabilities of the symptoms 'negative feelings towards the baby' and 'nightmares' were only increased in the 'serious problems' class and could therefore be considered specific for this class.

Strengths and limitations

Strengths of this study are the large, multiethnic population-based sample and the follow-up design in which pre- and postpartum factors could also be taken into account. The empirical approach made it possible to identify distinct early postpartum symptom profiles that had plausible interpretations.

When considering the results, some limitations must also be discussed. First, the selection of early postpartum symptoms was mostly based on practical issues because a clear definition of what is commonly referred to as 'maternity blues' does not exist. The selection of other postpartum symptoms might have yielded different solutions. Second, we had to rely on women's memory about the presence and duration of specific symptoms that occurred within two weeks after delivery, which could have introduced recall bias. It is possible that women who are depressed at 2 months after delivery, more negatively evaluated the first weeks after delivery. It might also be that women who are not depressed at 2 months after delivery forgot that they had some complaints after delivery. Therefore, this study should be seen as an exploration to point out the focus of future research on early postpartum symptoms. Third, there was selective attrition. At 2 months after delivery we obtained valid information from 56.3% of women that were included at 12 weeks pregnancy, with more missing data from participants with lower socio-economic status and from non-Dutch origin. However, the aim of our study was to identify distinct postpartum symptom profiles, their associated factors and their relation to depression. Although the probabilities of belonging to a certain postpartum symptom profile could be influenced by selective attrition, it is not likely that the identification of the distinct postpartum symptom profiles and the factors that are related to class membership would be different. This would be the case when the association between psychopathology and the different covariates differs between women who remained in the study and women that dropped out. This seems unlikely in our study. In fact, the associations between the investigated factors and class membership would have been even more significant when there was no selective attrition, since lower socio-economic status, ethnic background and high levels of depression and anxiety are strongly related to class membership and depression.

Clinical implications

Population based studies that use an empirical method for identifying psychiatric symptom profiles, like the present study, can give more insight into patterns of commonly occurring postpartum problems. Although much effort is put into promoting routine use of postpartum screening instruments like the EPDS for the early detection of severe postpartum problems, in clinical practice this is not yet the case. Although it will certainly be worthwhile to invest more time and effort into the routine assessment of early postpartum symptoms and the follow-up of women with high scores on postpartum depression scales, this is not always feasible. More insight in different patterns and associated factors for early postpartum symptom profiles could therefore be of additional practical benefit for clinicians, midwives and maternity assistants. They frequently visit recently delivered women and are confronted with spontaneously observed or reported early postpartum symptoms. The results of our study contribute to early clinical recognition of more or less severe postpartum symptom profiles.

Although the main objective of this study was the identification of early postpartum symptom profiles, we also accounted for pre- and postpartum factors that were associated with the severity of postpartum problems. In general, we found that unplanned pregnancy, having a first child, perceived poor health during pregnancy, high levels of anxiety and depression during pregnancy and a child admitted to hospital were related to more serious psychiatric postpartum problems. Those findings are consistent with previous research and ideally should also be screened for by physicians and midwives as potential risk factors during pregnancy and shortly after delivery.

5 Maternal and paternal depression during pregnancy and excessive infant crying

Abstract

Background

Excessive infant crying, or infantile colic, is a common and often stress inducing problem that can ultimately result in child abuse. From previous research it is known that maternal depression during pregnancy is related to excessive crying, but so far little attention is paid to paternal depression.

Methods

In a prospective multiethnic population-based study we obtained information on both maternal and paternal depression at 20 weeks pregnancy by means of the Brief Symptom Inventory (BSI). Parental depression was related to excessive crying in 1,788 2-month-old infants. Two definitions of excessive crying were used: 1) perceived excessive crying and 2) the widely used Wessel's criteria for excessive crying (i.e. crying >3 hours >3 days in the past week).

Results

Maternal depression was significantly related to perceived excessive infant crying (adjusted odds ratio 1.51, 95% CI: 1.03–2.21) and paternal depression was significantly related to Wessel's criteria for excessive crying 2.26 (OR: 1.17–4.37).

Conclusion

Our findings indicate that paternal depression, next to maternal depression, during pregnancy might be a risk factor for excessive infant crying. This could be related to genetic transmission, direct interaction of the depressive father with the infant or indirectly through contextual stressors like familial or economic distress.

Introduction

Excessive infant crying, often called infantile colic, is a well-known and often stressful problem that usually starts in the first weeks after childbirth and ends by 4-5 months. There are different definitions of excessive infant crying (Reijneveld et al., 2001) and depending on this definition the prevalence rates vary from 5 to 28% (Lucassen et al., 2001). The aetiology remains unclear and although its name infantile colic refers to an abdominal cause, this is far from certain (Barr, 2002). Four main themes on the aetiology of excessive infant crying emerge from previous studies, i.e. excessive crying might be: the extreme end of normal crying, a result of painful gut contractions (e.g. due to allergy, lactose intolerance or excess gas), a less optimal parent-child interaction, or a collection of aetiologically different entities that are not easy to discern clinically (Lucassen et al., 1998).

A lot of effort has been devoted to treat excessive infant crying, but only a few interventions showed to be effective (Garrison and Christakis, 2000; Lucassen and Assendelft, 2001). Although excessive crying in most cases is a self-limiting condition, in some cases it is associated with child maltreatment with sometimes fatal abuse (Reijneveld et al., 2004). Early psychoeducation and support of the parents could be beneficial. Therefore, it will be important to identify parents at risk during pregnancy. In this respect maternal psychopathology (i.e. distress, anxiety and depression) seems to be a predictor of excessive infant crying (Canivet et al., 2004; Canivet et al., 2005; Miller et al., 1993; Rautava et al., 1993; Sondergaard et al., 2003; Zuckerman et al., 1990). Surprisingly, little is known about paternal factors during pregnancy that are associated with excessive infant crying. This gap in knowledge is of concern since paternal psychopathology is a known risk factor for child maltreatment (Sidebotham and Golding, 2001; Walsh et al., 2002), which could possibly be increased by excessive infant crying.

Our aim was to investigate the association between both maternal and paternal depression during pregnancy with excessive infant crying in a population-based cohort study. We used two definitions to determine excessive crying because varying definitions are shown to include different groups of infants with different risk factors (Reijneveld et al., 2002): 1) parent perceived excessive crying, because parental distress is the main impetus for seeking professional care (Barr, 2002); 2) a definition based on widely used criteria of Wessel (Wessel et al., 1954).

Methods

Design

This study is part of the Generation R Study, a prospective multiethnic population-based cohort study on growth, development and health of children followed from early fetal life. This study is designed to identify early environmental and genetic determinants of growth, development and health from fetal life until young adulthood and has been described previously in detail (Hofman et al., 2004; Jaddoe et al., 2006). Enrolment for mothers in the study was aimed in the first trimester of pregnancy but was possible until birth of their offspring from December 2001 until January 2006. Assessments in pregnant women included physical examinations, fetal ultrasounds, biological samples and questionnaires and were planned at the gestational age of 12, 20 and 30 weeks. The partners of participating women completed one questionnaire at 20 weeks pregnancy. The cohort includes 9,778 mothers and their children living in Rotterdam, The Netherlands. Based on the annual birth rates in Rotterdam, the estimated initial response was 61%.

The Medical Ethics Committee of Erasmus Medical Center has approved the study and written informed consent was obtained from all participants.

Population

Data cleaning and preparation for the whole Generation R cohort is still ongoing. For the present analyses we used all available data on participating women (n= 4,606), their partners (n= 3,376) and their children born between January 1, 2003 and December 31, 2004. Based on self-reported information, it is estimated that 99% of the participating partners is the biological father of the child. We obtained valid depression scores at 20 weeks pregnancy on 3,451 (75%) women and 2,606 (77%) men. From 2,747 (60%) children we obtained valid information on infant crying behaviour. We used the 1,788 cases for which we had valid information on both parental depression scores and infant crying. Analyses of missing data on infant crying showed .15 (95% CI: .12–.18) higher depression scores in mothers and .05 (95% CI: .03–.08) higher depression scores in fathers.

Parental depression

Parental depression was assessed at 20 weeks pregnancy with the Brief Symptom Inventory (BSI). The BSI is a well validated self-report questionnaire with 53 items to be answered on a 5-point scale, ranging from "0= not at all" to "4= extremely" (de Beurs, 2004; Derogatis, 1993). The items of the BSI cover nine scales of psychiatric symptoms occurring in the preceding 7 days. The score for each symptom scale is calculated by first summing the values (i.e. 0-4) for the items in each symptom scale. The sum is then divided by the number of endorsed items in that scale. For this study we used the Depression scale,

existing of 6 questions which address: "Thoughts of ending life", "feeling lonely", "feeling blue", "feeling no interest in things", "feeling hopeless about the future" and "feelings of worthlessness". The internal consistency for the Depression scale in our sample was α= .83, which is good (Cronbach, 1951).

Excessive infant crying

At 2 months after delivery we assessed crying behaviour of the infant. We based excessive crying on two criteria. The first was a general question whether parents themselves judged their infants' crying as excessive: "Do you think your baby cries a lot?" The second was based on the definition of Wessel: crying more than three hours per day on more than three days (i.e. at least 4 days) in the preceding week (Reijneveld et al., 2001; Wessel et al., 1954).

Covariates

Information on demographic background, marital status, socio-economic factors, perceived health and substance use was collected from the 12 weeks pregnancy questionnaire. Information on maternal smoking, alcohol use and paternal age, ethnicity, educational level, smoking and alcohol use was obtained from the 20 weeks questionnaire. Educational level was dichotomised into 'low education' indicating no education or primary education only versus more than primary education. Income was dichotomised into 'low income' indicating an income of less than 1200 euros net a month, which is at the social security level payment for a Dutch household, versus more than 1200 euros. Ethnicity was defined according the classification of Statistics Netherlands (2004a). This means that a parent is Dutch if both their own and country of birth of his or her parents is The Netherlands. He or she has another ethnicity if their own or at least one parental country of birth is other than The Netherlands. If a parent and his or her parents have different countries of birth other than The Netherlands, first the country of birth of the specific parent and second the country of birth of the mother of the parent is taken into account. Parental smoking was dichotomised in 'smoking' versus non-smoking. Parental alcohol use was dichotomised in 'alcohol use' versus no alcohol use.

Child birth weight was obtained from medical records.

Data analysis

To check for possible confounders in the relation between parental depression and excessive infant crying, we performed analysis of variance and chi-square tests. For these analyses the two definitions of excessive crying were examined separately because they could consist of different groups of infants with different risk factors.

To examine the association between parental depression and infant crying we performed logistic regression analyses. Because there is no established clinical cut-off score

for BSI symptom scores, we used the continuous scores. Analyses with dichotomised psychopathology scores based on a cut-off score of two standard deviations above the mean revealed similar associations (not shown).

Results

Infant crying behaviour was mostly reported by the mother (94%). There were no significant differences between both definitions of excessive infant crying rated by mothers or by fathers. Also maternal and paternal depression were not significantly associated with the informant of excessive infant crying.

Excessive infant crying according to Wessel's criteria occurred in 2.5% of the 2-months-old children, while 7.4% of the mothers perceived their infant as excessive crying (table 1 and 2). From the perceived excessive crying infants 30.3% fulfilled the Wessel's criteria and 88.9% of the excessive crying infants according to Wessel's criteria

Table 1. Maternal, paternal and child characteristics of perceived excessive infant crying

	No excessive crying	Perceived excessive crying	Test characteristics*	
	92.6% (n= 1,656)	7.4% (n= 132)	X^2/F	P value
Mean age				
Mother (SD)	31.1 (4.4)	30.9 (4.7)	.24	.62
Father (SD)	33.5 (5.2)	33.6 (6.4)	.003	.96
Child birth weight (SD)	3,492 (543)	3,480 (482)	.06	.81
First child	38.0%	39.8%	.15	.70
Low income	7.9%	9.4%	.51	.48
Low education				
Mother	4.2%	6.3%	1.14	.29
Father	5.5%	3.8%	.74	.39
Other ethnicity				
Mother	35.7%	41.7%	1.85	.17
Father	29.7%	30.3%	.02	.89
Smoking				
Mother	10.9%	19.1%	7.96	.01
Father	42.7%	40.2%	.32	.57
Alcohol use				
Mother	53.1%	48.9%	.87	.35
Father	87.5%	76.5%	12.84	<.001
Depression				
Mother (SD)	.15 (.35)	.25 (.45)	10.81	.001
Father (SD)	.09 (.25)	.14 (.40)	5.04	.03

* Statistics are F (df=1; 1,786) in case of continuous variables and X^2 (df= 1) in case of categorical variables

were perceived as excessive crying by the mothers. The correlation between the two definitions of excessive crying was .50 (p< .001).

Perceived excessive infant crying and excessive infant crying according to Wessel's criteria were not related to maternal age, child birth weight, having a first child, having a low household income, being born outside The Netherlands and low educational level. When country of birth was subdivided in specific countries (i.e. Dutch, Suriname, Turkish, Moroccan, Antillean, Cape Verdian and other industrialised and non-industrialised countries), it was also not significantly related to either of the two definitions of excessive crying. Mothers' perceived excessive crying was significantly related to maternal smoking and paternal alcohol use (table 1). There was a significant association between paternal age and paternal alcohol use and excessive crying according to Wessel's criteria (table 2). In the perceived excessive infant crying group the mean depression scores were higher in mothers compared to fathers, while in the excessive crying group according to Wessel's criteria the depression scores were about the same. Additional analyses showed that parental depression was significantly correlated (Pearson correlation .17, p<.001).

Table 2. Maternal, paternal and child characteristics of excessive infant crying according to Wessel's criteria†

	No excessive crying	**Wessel's excessive crying**	**Test characteristics***	
	97.5% (n= 1,743)	**2.5% (n= 45)**	**X^2/F**	**P value**
Mean age				
Mother (SD)	31.1 (4.4)	30.4 (4.9)	1.28	.26
Father (SD)	33.6 (5.3)	32.0 (6.0)	3.98	.05
Child birth weight (SD)	3,489 (539)	3,567 (515)	.89	.35
First child	38.3%	30.6%	.90	.34
Low income	7.6%	11.1%	.60	.44
Low education				
Mother	4.3%	7.0%	.70	.40
Father	5.5%	2.3%	.85	.36
Other ethnicity				
Mother	36.1%	40.0%	.29	.59
Father	29.6%	35.6%	.74	.39
Smoking				
Mother	11.4%	15.6%	.74	.39
Father	42.8%	28.9%	3.49	.06
Alcohol use				
Mother	53.1%	40.0%	3.03	.08
Father	87.5%	73.3%	7.16	.01
Depression				
Mother (SD)	.15 (.36)	.22 (.44)	1.69	.19
Father (SD)	.09 (.25)	.21 (.56)	8.96	.003

†crying more than three hours per day on more than three days in the preceding week

* Statistics are F (df=1; 1,786) in case of continuous variables and X^2 (df= 1) in case of categorical variables

Table 3. Association between maternal and paternal depression and the two definitions of excessive infant crying

	Excessive crying (perceived)		Excessive crying (>3 hours >3 days past week)	
Maternal depression				
Crude OR (95%CI)	1.78	(1.25 – 2.56)	1.50	(.81 – 2.78)
Adjusted OR (95%CI)	1.51	(1.03 – 2.21)*	1.14	(.58 – 2.24)†
Paternal depression				
Crude OR (95%CI)	1.76	(1.06 – 2.91)	2.47	(1.31 – 4.67)
Adjusted OR (95%CI)	1.49	(.88 – 2.53)*	2.31	(1.19– 4.48)†

* Adjusted for depression in other parent, maternal smoking and paternal alcohol use
†Adjusted for depression in other parent, paternal age and paternal alcohol use

Table 3 shows the association between maternal and paternal depression and excessive infant crying according to the two different definitions. Maternal and paternal depression during pregnancy were significantly associated with perceived excessive crying. After adjustment for maternal smoking and paternal alcohol use, only the association between maternal depression and perceived excessive crying remained significant. The OR for this association was 1.51 (95% CI: 1.03–2.21). Paternal depression during pregnancy was significantly associated with excessive crying according to Wessel's criteria. After adjustment the OR for this association was 2.26 (95% CI: 1.17–4.37).

Discussion

This prospective population-based cohort study showed that, depending on the definition of excessive infant crying, both maternal and paternal depression during pregnancy are associated with excessive infant crying at 2 months. Maternal depression was associated with perceived excessive crying, while paternal depression was associated with Wessel's criteria for excessive crying. This finding is in line with previous research, which showed that these two definitions of excessively crying infants partly pertain to different infants and also have different risk factors (Reijneveld et al., 2001; 2002).

The positive association between maternal smoking and infant crying is consistent with other studies (Reijneveld et al., 2005; Sondergaard et al., 2001). We also found significant associations between paternal age and alcohol use and excessive crying of the infant. These associations have not been found in previous studies and warrant further investigation, since they are beyond the scope of this study.

Strengths and limitations

Our study has several strengths. We used prospectively collected data in a large multiethnic population-based cohort. Prospective studies on infantile excessive crying are sparse, especially in relation to parental psychopathology. The prospective design makes it possible to rule out a child-to-parent effect in which the excessive crying of the child could lead to parental depression. Therefore, the associations we found provide evidence for a parent-to-child direction in the association between parental depression and excessive infant crying. Furthermore, our study is the first to focus on paternal depression and other paternal factors, and relate them to infant crying behaviour. Since most information on infant crying behaviour was provided by the mothers, the risk of rater bias as a potential confounding factor in the association between father-reported paternal depression and mostly mother-reported excessive infant crying is strongly reduced. Finally, we checked and controlled for several confounders, both maternal and paternal.

However, this study is not without limitations. It is likely that selection bias occurred. Our prevalence rates of excessive infant crying were lower compared to a representative Dutch study (Reijneveld et al., 2001). This could be explained by selection at inclusion or selective attrition, or a combination of both. The selective attrition is indirectly supported by significantly higher levels of parental depression among missing data on infant crying. Since parental depression was associated with excessive infant crying it is plausible that the non-response among parents with excessively crying infants was higher. Second, missing data on infant crying behaviour was related to higher maternal depression scores than to paternal depression scores. This suggests that especially the association between maternal depression and excessive infant crying may be underestimated. The association between paternal depression and excessive crying remained significant, which suggests that the association would probably have been more significant when no selection had occurred. Finally, we cannot rule out 'false paternity', since we had to rely on self-report information in this respect. From a recent review it is estimated that 3.7% of the children is sired by another man than the father who believes he is the biological father (Bellis et al., 2005). If this is the case in our study, the found associations between paternal and child characteristics could be somewhat underestimated when genetic factors were of major importance.

Implications

The use of different definitions (perceived versus Wessel's criteria) for excessive crying showed different associations for fathers and mothers, which need to be discussed. The finding that depression in mothers is associated with perceived excessive infant crying and not with excessive crying according to Wessel's criteria could be related to rater bias or selection bias, or a combination of both. From previous studies it is known that

depressed mothers tend to report more excessive crying due to their depression and irrespective of child characteristics (Beebe et al., 1993; Milgrom et al., 1995). The rather subjective question whether mothers themselves judged their infant's crying as excessive could therefore be more related to the coping of a mother to the crying behaviour of her infant than to the frequency and duration of crying. In this respect the criteria according to Wessel are less subjective, since they ask for duration and frequency of crying instead of perception of excessive crying. Although information bias related to depression in mothers could also have occurred in the registration of frequency and duration of crying, the finding that 12.1% of the infants that fulfilled Wessel's criteria for excessive crying were not perceived as excessive crying by their mothers, suggests that this group is less related to primary coping problems of the mother. Another explanation could be related to selective attrition of depressive mothers resulting in a lack of power to detect the association between maternal depression and excessive crying according to Wessel's criteria. An indication for this is that missing data on infant crying behaviour was related to higher maternal depression scores than to paternal depression scores. As we already mentioned, rater bias between paternal depression and excessive infant crying is strongly reduced because the information is obtained from different informants. Therefore it is not surprising that the association between paternal depression and the more objective excessive infant crying is more prominent.

We found an association between paternal depression and excessive infant crying. There are some possible mechanisms to explain this association. The first mechanism might be related to fathers' direct interacting with their child, with child abuse at the extreme end (Reijneveld et al., 2004). In our study we did not collect paternal data at 2 months after pregnancy, but it is likely that a considerable part of the fathers that was depressed during pregnancy is depressed after childbirth as well (Deater-Deckard et al., 1998). Second, paternal depression may have an indirect effect through contextual stressors. Familial distress (Papousek and von Hofacker, 1998) and mother-father interaction (Raiha et al., 2002) seem to be related to excessive infant crying. Also other contextual stressors like economic or societal stressors are related to paternal depression and child behaviour (Connell and Goodman, 2002). The third mechanism might be a genetic transmission. One could hypothesise that excessive infant crying is somehow related to depression as a manifestation of general distress and irritability. If this is the case, both maternal and paternal depression should be associated with early infant crying and there should be a relation between infant crying and later emotional problems or depression. Our results partly support the first assumption. Longitudinal studies on the long-term effects of excessive infant crying are inconclusive and mostly limited to the first year (Clifford et al., 2002; Lehtonen et al., 1994; Papousek and von Hofacker, 1998; White et al., 2000).

Although our findings are subject to some limitations and need to be replicated, they emphasise the importance of also taking paternal factors into account when studying early infant behaviour like excessive crying. If paternal depression during pregnancy is related to excessive crying indeed, it will be important to actively focus on early recognition and treatment of paternal depression as well. Since this is not yet common practice, this study hopes to encourage further initiatives in this respect.

6 Paternal depression during pregnancy and infant behaviour at 6 months

Abstract

Background

There is evidence that depression in fathers is associated with behavioural problems in children. However, little is known about the direction of the effect. Since most studies on the effect of paternal depression on child behaviour were performed in postpartum cross-sectional samples, a child-to-father effect could not be ruled out.

Objective

To investigate the association between paternal depression during pregnancy and six domains of behaviour in 6-month-old infants: activity level, distress to limitations, fear, duration of orienting, recovery from distress and sadness.

Methods

In a prospective multiethnic population-based study we obtained complete data from 1,571 fathers on depression at 20 weeks pregnancy assessed with the Brief Symptom Inventory (BSI) and infant behaviour at 6 months assessed with an adapted version of the Infant Behavior Questionnaire - Revised (IBQ-R). We performed regression analyses adjusted for maternal depression and several other confounders.

Results

In the unadjusted analyses paternal depression during pregnancy was associated with fear, recovery from distress and distress to limitations in boys. After adjustment, paternal depression was significantly associated with fear in 6-month-old boys. Paternal depression was not associated with behaviour of 6-month-old girls.

Conclusion

Our results suggest that paternal depression during pregnancy might be related to infant behaviour, particularly to fear in boys. This finding provides evidence for a father-to-child direction of paternal depression to early infant behaviour and could be explained by genetic transmission, direct interaction of the depressive father with the infant, or indirectly through contextual stressors like marital or economic distress.

Introduction

To further our understanding on transgenerational aspects of psychopathology it is necessary to focus on paternal psychopathology as well as on maternal psychopathology. Fathers not only contribute 50% of the genes of their children, they also play an increasing role in child-rearing (Pleck and Masciadrelli, 2004). Fortunately, research on paternal depression and its effect on child behaviour is emerging. Two recent reviews showed that paternal depression is significantly associated with both internalising and externalising behaviour problems in offspring, with a larger effect on internalising behaviour problems (Connell and Goodman, 2002; Kane and Garber, 2004).

However, important insights are lacking. For example, little is known about the direction of the association between paternal psychopathology and child behaviour problems. Because all research to date has been performed in samples after childbirth on with children of three years and older, child-to-parent effect of behavioural problems leading to paternal depression cannot be ruled out. Some evidence for a father-to-child direction has recently been found in a prospective population-based study that revealed an independent association between paternal depression 8 weeks after child birth and behavioural problems in 3,5 year old children (Ramchandani et al., 2005). In this study, however, a child-to-father direction cannot been totally ruled out since having a 2-month-old infant with difficult behaviour could already negatively influence paternal mood.

Therefore, the main aim of our study was to investigate the association between paternal depression during pregnancy and infant behaviour at 6 months after child birth. Because there is evidence that boys are more vulnerable to the effects of paternal depression (Ramchandani et al., 2005), we examined the influence of paternal depression during pregnancy on girls and boys separately.

Methods

Design

This study was embedded in the Generation R Study, a prospective population-based cohort study from fetal life until young adulthood. The study is designed to identify early environmental and genetic determinants of growth, development and health from fetal life until young adulthood and has been described previously in detail (Hofman et al., 2004; Jaddoe et al., 2006). Briefly, the cohort includes 9,778 mothers (of whom 6,347 partners) and their children living in Rotterdam, one of the major cities of The Netherlands. Enrolment for mothers in the study was aimed in the first trimester of pregnancy but was possible until birth of their offspring from December 2001 until January 2006.

Assessments in pregnant women included physical examinations, fetal ultrasounds, biological samples and questionnaires. Fathers completed one questionnaire at 20 weeks pregnancy. The children were born between April 2002 and January 2006 and form a prenatally recruited birth-cohort that is currently followed until young adulthood. Of all eligible children in the study area, 61% participate at birth in the study.

The study cohort is a multi-ethnic cohort with a large number of different ethnicities. Questionnaires were available in Dutch and translated in English, French, Portuguese and Turkish. When participants were not able to fill out the questionnaire in one of these languages (e.g. most Moroccans speak Berber, a non-written language) assistants who spoke the same language visited participants at home to help fill out the questionnaire.

The study has been approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. Written informed consent was obtained from all participants.

Population

Data cleaning and preparation for the whole Generation R cohort is still ongoing. For the present analyses we used all available data on children born between January 1, 2003 and December 31, 2004 and their parents. In this period 4,606 pregnant women and 3,376 of their partners were included. Based on self-reported information, it is estimated that 99% of the participating partners is the biological father of the child. We obtained valid depression scores at 20 weeks pregnancy on 2,606 (77%) fathers. From 2,104 (46%) infants we obtained valid information on their behaviour at 6 months.

Assessment of parental depressive symptomatology

Parental depression and anxiety was assessed at 20 weeks pregnancy with the Brief Symptom Inventory (BSI). The BSI is a well validated self-report questionnaire with 53 items to be answered on a 5-point scale, ranging from "0= not at all" to "4= extremely" (de Beurs, 2004; Derogatis, 1993). The items of the BSI cover nine scales of psychiatric symptoms occurring in the preceding seven days. For this study we used the Depression scale, existing of 6 questions which address: "Thoughts of ending life", "feeling lonely", "feeling blue", "feeling no interest in things", "feeling hopeless about the future" and "feelings of worthlessness". The total score for the depression scale was calculated by first summing the values (i.e. 0-4) for the items and then dividing by the number of endorsed items of the scale. The internal consistency for the Depression scale in our sample was $\alpha = .83$, which is very satisfactory (Cronbach, 1951).

Assessment of infant behaviour

At 6 months after delivery child behaviour was assessed using an adapted version of six scales of the Infant Behavior Questionnaire – Revised (IBQ-R) (Gartstein and Rothbart,

2003): activity level (i.e. movement of arms and legs, squirming and locomotor activity); distress to limitations (i.e. fussing, crying or showing distress while a) in a confining place or position; b) involved in caretaking activities; c) unable to perform a desired action); fear (i.e. startle or distress to sudden changes in stimulation, novel physical objects or social stimuli; inhibited approach to novelty); duration of orienting (i.e. attention to and/or interaction with a single object for extended periods of time); falling reactivity/rate of recovery from distress (i.e. rate of recovery from peak distress, excitement, or general arousal; ease of falling asleep); sadness (i.e. general low mood; lowered mood and activity specifically related to personal suffering, physical state, object loss, or inability to perform a desired action). The items on the IBQ-R ask parents to rate the frequency of specific behaviours observed over the past week. We adapted the original 7-point scale (ranging from "1= never present" to "7= always present"), to a 3-point scale ("0= never present", "1= sometimes present" and "2= often present") to enhance discriminative validity, because respondents seldom use the extreme positions of scales with a large amount of categories and reducing the number of levels to three will not result in significant loss of information (Streiner and Norman, 1998). Again, the score for each scale was calculated by first summing the values (i.e. 0-2) for the items in each scale and then dividing by the number of endorsed items in that scale. The internal consistencies for the IBQ-R in our sample ranged from $\alpha = .72$ for activity level and duration of orienting to $\alpha = .86$ for fear, which is satisfactory (Cronbach, 1951) and comparable to the internal consistencies of the original IBQ-R (Gartstein and Rothbart, 2003).

Covariates

For fathers all the information was obtained through a questionnaire filled out at 20 weeks pregnancy. For mothers at inclusion information was obtained about age, educational level, country of birth and number of living children. The occurrence of maternal smoking and alcohol use was asked for at 20 weeks pregnancy. Household income was obtained from the 30 weeks questionnaire and dichotomised in 'low income', indicating an income of less than 1200 euros net a month, which is at the social security level payment for a Dutch household, versus more than 1200 euro. Education was divided in five categories: primary education (no education, primary education), secondary education 1st phase (lower vocational training, 3 years general secondary school), secondary education 2nd phase (intermediate vocational training, >3 years general secondary school, first year higher vocational training/university), higher education 1st phase (higher vocational training, university bachelor) and higher education 2nd phase (university, PhD). Ethnicity of the child was based on the country of birth of the parents. If one parent was born outside The Netherlands, this country defined the ethnicity. If both parents were born in different countries outside The Netherlands, the country of birth of the mother defined the ethnic background. Smoking was dichotomised in 'smoking' and

'non-smoking' and alcohol use was dichotomised in 'alcohol use' and 'no alcohol use'. Child birth weight was obtained from medical records completed by midwives and gynaecologists.

Statistical analysis

SPSS for Windows (version 12.0.1) was used for data analysis. To examine the association between paternal depressive symptomatology and child behaviour we performed linear regression analyses. We adjusted for maternal depression because maternal psychopathology is an important known confounder in the association between paternal depression and infant behaviour. To check for other possible confounders in the relation between paternal depression and child behaviour, we performed Pearson correlation analyses with parental age, parental educational level, level of household income, parental smoking and alcohol use, being a first child and child birth weight. We performed an ANOVA to check for child ethnicity as a possible confounder. We considered variables that were both related to paternal depression and at least to four of the six IBQ-R scales as potential confounders in the association between paternal depression and infant behaviour.

Results

Sample characteristics and confounders

For 1,571 fathers we had complete data on depression and infant behaviour. Analyses of missing data showed significantly higher levels of depression in fathers with missing data on infant behaviour compared to fathers with non-missing data on infant behaviour. Analyses of missing data showed a .03 (95%CI: .01–.06) higher depression score in fathers with missing data on infant behaviour (.13 vs .09; df= 1; 2,604; F= 8.25; p< .004). Of all fathers with valid depression scores we obtained valid depression scores from 92.8% of the mothers. Information on infant behaviour was mostly reported by the mother (93%). There were no significant differences between infant behaviour scores rated by mothers or fathers. The general descriptives of the fathers, mothers and children we used for the analyses are shown in table 1 and 2. The number of available data varies per variable due to missing data.

Maternal age, paternal age, maternal educational level, maternal alcohol use, low income and child ethnicity were related to both paternal depression and at least to four of the six scales of the IBQ-R and therefore were considered potential confounders. Paternal educational level, parental smoking, child birth weight and being a first child were not significantly related to most of the IBQ-R scales.

Table 1. Paternal and maternal characteristics (n= 1,571)

	Father		Mother	
	n	Mean (SD)/%	n	Mean (SD)/%
Age (SD)	1,571	33.6 (5.1)	1,571	31.3 (4.4)
Educational level (%)				
Primary education	73	4.7	65	4.6
Secondary education 1st phase	159	10.3	114	8.0
Secondary education 2nd phase	409	26.6	354	24.8
Higher education 1st phase	316	20.5	371	26.0
Higher education 2nd phase	583	37.9	522	36.6
Smoking (%)				
No	915	58.5	1365	89.5
Yes	649	41.5	160	10.5
Alcohol use (%)				
No	194	12.5	719	47.1
Yes	1,360	87.5	807	52.9
Low household income (%)				
No	1,331	93.3	idem	idem
Yes	95	6.7		
Depression score (SD)	1,571	.09 (.27)	1,458	.15 (.37)

Table 2. Characteristics of 6-month-old infants (n= 1,571)

	Total (n)	Mean (SD)/%
Gender (%)		
Girl	769	49.2
Boy	795	50.8
Birth weight (SD)	1,564	3,494 (541)
First child (%)		
No	860	63.4
Yes	497	36.6
Ethnicity (%)		
Dutch	1,126	71.8
Turkish	60	4.1
Surinamese	64	3.8
Moroccan	31	2.0
Antillean	24	1.5
Cape Verdian	19	1.2
Other Western countries	162	10.3
Other non-Western countries	82	5.2

Effect of paternal depression on infant behaviour

None of the behaviour scales in girls were significantly related to paternal depression during pregnancy. In the unadjusted analyses fear, recovery from distress and sadness in boys were significantly related to paternal depression. After adjustment for maternal depression and other possible confounders fear in boys remained significant (table 3).

Table 3. Unadjusted and adjusted effects of paternal depression during pregnancy on six scales of the infant behaviour questionnaire-revised for 6-month-old girls and boys

	Unadjusted β (95% CI)	P value	Adjusted* β (95% CI)	P value
Girls				
Activity level	.06 (-.03; .16)	.21	-.04 (-.14; .06)	.39
Distress to limitations	.09 (-.001; .18)	.05	.01 (-.08; .11)	.81
Fear	.07 (-.02; .16)	.11	-.01 (-.10; .08)	.82
Duration of orienting	-.001 (-.11; .10)	.98	-.05 (-.17; .06)	.35
Recovery from distress	-.07 (-.14; .01)	.10	.01 (-.08; .09)	.88
Sadness	.04 (-.04; .12)	.33	.004 (-.08; .09)	.93
Boys				
Activity level	.07 (-.01; .15)	.09	-.01 (-.14; .12)	.91
Distress to limitations	.08 (-.01; .16)	.06	-.03 (-.16; .10)	.66
Fear	**.13 (.07; .20)**	**<.001**	**.13 (.03; .24)**	**.01**
Duration of orienting	-.03 (-.12; .06)	.50	.10 (-.04; .25)	.16
Recovery from distress	**-.08 (-.15; -.01)**	**.03**	-.02 (-.13; .10)	.79
Sadness	**.07 (.003; .15)**	**.04**	.02 (-.10; .14)	.74

Betas are unstandardised regression coefficients
*Adjusted for maternal depression, paternal age, maternal age, maternal educational level, maternal alcohol use, low household income, child ethnicity
Estimates significant at p<.05 are represented in bold

Discussion

This prospective multiethnic population-based study showed that paternal depression during pregnancy might be related to early infant behaviour. In the unadjusted analyses paternal depression during pregnancy was associated with fear, recovery from distress and distress to limitations in 6-month-old boys. After adjustment paternal depression was significantly associated with fear in boys. This finding provides evidence for a father-to-child direction of paternal depression to early infant behaviour. Obviously, paternal depression during pregnancy cannot directly interact with the intrauterine developing child. Therefore it could either be genetically related to fear in infant boys or when prepartum depression is strongly linked to postpartum depression in fathers, it could be of direct or indirect effect on the child, which we will discuss later.

Strengths and Limitations

This study is the first population-based study that focused on paternal depression during pregnancy and its influence on behaviour of the early developing child. By assessing paternal depression during pregnancy we ruled out a child-to-father effect in

which behavioural problems of the child could lead to paternal depression. Therefore, the association we found provides strong evidence for a father-to-child direction in the association between paternal depression and child behaviour, particularly fear in boys. Furthermore, the risk of rater bias in the associations between father-reported paternal depression and mostly mother-reported child behaviour is strongly reduced, since this information is provided by different informants. Also in contrast to most other studies, we checked and controlled for several confounders, both maternal and paternal.

The main limitation of our study was the selective attrition of fathers with higher depression scores. This would lead to bias in our study if the associations between paternal psychopathology and infant behaviour differ between those fathers who remained in the study and those who dropped out. We do not expect that this is the case. However, the selection is likely to affect the frequency rates and, as a consequence, the statistical power in our study. Therefore, the associations would probably have been more significant when no selection occurred. Also, we cannot rule out 'false paternity', since we had to rely on self-report information in this respect. From a recent review it is estimated that 3.7% of the children is sired by another man than the father who believes he is the biological father (Bellis et al., 2005). If this is the case in our study, the found associations between paternal and child characteristics could be somewhat underestimated when genetic factors were of major importance.

Implications

Because our study is the first to relate paternal depression during pregnancy to early infant behaviour we cannot compare our results to previous findings. Therefore, our results should be interpreted with caution and need to be replicated. Nevertheless, our finding that paternal depression has an effect on boys is in line with a study that focused on paternal postpartum depression and child development (Ramchandani et al., 2005).

There are several possible explanations for the association we found between paternal depression and fear in 6-month-old boys. First, genetic factors could explain part of this association. Since fathers contribute 50% of their genes to their children it is likely that children of depressed fathers may inherit a direct vulnerability for emotional problems. Although to our knowledge no genetic studies have been performed with the IBQ, a recent review on behaviour genetics in infants provided strong evidence of genetic influences on temperament including emotionality, activity, shyness, sociability, attention/persistence, approach, adaptability, distress, positive affect, and negative affect (Saudino, 2005). Depending on the samples, about 20 to 60% of the differences among infant behaviour were explained by genetic factors. Because the heritability estimates did not significantly differ across the different behaviours and also no gender differences were found, the specific vulnerability for boys that we found in our study could obviously not be explained by genetic factors alone.

Second, direct effects of paternal depression might influence child behaviour after birth. Although we do not have postpartum data on paternal depression, the correlation between prepartum maternal depression and postpartum maternal depression in our sample was .50. Also from other studies it is known that the stability from prepartum to postpartum psychopathology in both mothers and fathers is substantial (Deater-Deckard et al., 1998; Heron et al., 2004; Matthey et al., 2000). If prepartum paternal depression is correlated with postpartum depression, it might also predict the way fathers will interact with their infants. Although mothers in majority still are the primary caretakers in early infancy, fathers are also of influence in the direct interaction with their child. Evidence exists that quality of fathers' involvement is more closely associated with child outcome than the amount of time that fathers invest in their children (Pleck and Masciadrelli, 2004). In this respect the association between paternal psychopathology and child abuse is noteworthy (Sidebotham and Golding, 2001; Walsh et al., 2002), since one can imagine that hostile behaviour towards infants will be mainly expressed in fear. However this is a speculative assumption that needs to be further investigated. Furthermore, there is substantial evidence that depression in both parents has a negative effect on child behaviour through their maladaptive affect, behaviour, and cognitions (Connell and Goodman, 2002; Downey and Coyne, 1990; Grace et al., 2003; Zaslow et al., 1985).

Finally, the transmission of paternal depression could be related to contextual stressors like increased marital or economic distress, which negatively influence child development (Erel and Burman, 1995; Goodman, 2004; Kane and Garber, 2004). Although other contextual stressors are clearly associated with psychopathology, little is known about the relative strengths of such associations in men and women and their influence on child behaviour (Connell and Goodman, 2002).

Conclusion

Our results suggest that paternal depression during pregnancy is related to infant behaviour, independently from maternal depression and other possible confounders. This finding could be related to genetic transmission, direct interaction of the depressive father with the infant or indirectly through contextual stressors including marital or economic distress. Because up till now, both in research and in clinical practise, most attention is focused on maternal depression during pregnancy, we recommend that paternal depression during pregnancy should be actively considered and studied as well. Further research is warranted on the magnitude of the different mechanisms of paternal depression influencing infant behaviour and on its possible specific effect on the behavioural development of infant boys.

7

Maternal depression during pregnancy and infant behaviour at 6 months

Abstract

Background

From previous studies it is known that maternal stress and anxiety during pregnancy negatively influence cognitive, behavioural and emotional development of the child. However, the effect of maternal depression during pregnancy on infant behaviour has received little attention.

Objective

To investigate the association between maternal depression during pregnancy and six domains of behaviour in 6-month-old infants: activity level, distress to limitations, fear, duration of orienting, recovery from distress and sadness.

Methods

In a prospective multiethnic population-based study we obtained complete data on 1,453 mothers, fathers and 6-month-old infants. Parental depression was assessed at 20 weeks pregnancy with the Brief Symptom Inventory (BSI) and infant behaviour at 6 months was assessed with an adapted version of the Infant Behavior Questionnaire - Revised (IBQ-R).

Results

Maternal depression during pregnancy was associated with behaviour of 6-month-old infants, even after adjustment for postpartum maternal depression, paternal depression and other confounders. We found a significant effect of maternal depression during pregnancy on recovery from distress and sadness in girls, and on distress to limitations in boys.

Conclusion

Our results suggest that maternal depression during pregnancy is associated with infant behaviour of 6-month-old infants. These effects differed for girls and boys, suggesting a gender specific effect of maternal depression which warrants further investigation.

Introduction

Stress and anxiety during pregnancy are associated with cognitive, behavioural and emotional problems of the child (Huizink et al., 2004; O'Connor et al., 2003; Van den Bergh et al., 2005). This association remains significant after adjustment for postpartum maternal mood and other confounders in the pre- and postpartum period, like socio-economic status and substance abuse of the mother (Van den Bergh et al., 2005). However, up to now less attention is paid to the possible intrauterine effect of maternal depression on early infant behaviour. We are aware of only a few studies that focused on maternal depression during pregnancy and child development (Field, 1995; Luoma et al., 2001; Luoma et al., 2004). This is of concern, since an abundant amount of research has shown that postpartum maternal depression negatively influences the cognitive, behavioural and emotional development of the child (Goodman and Gotlib, 1999; Grace et al., 2003), which might partly be explained by prenatal influences.

Another topic that warrants further investigation is the influence of paternal factors in the association between maternal psychopathology during pregnancy and the developing infant. Since previous studies found a substantial correlation between maternal and paternal psychopathology during pregnancy (Deater-Deckard et al., 1998; Goodman, 2004) (see also Chapter 2) and also an association between paternal postpartum psychopathology and infant behaviour (Connell and Goodman, 2002; Kane and Garber, 2004; Ramchandani et al., 2005), paternal depression could be an important confounder in the association between maternal depression and child development. The relevance of accounting for paternal psychopathology during pregnancy is supported by a previous report (chapter 6), in which we found evidence for an independent effect of paternal depression on fear in boys.

Therefore, the first aim of our study was to investigate whether maternal depression during pregnancy is associated with early child behaviour after adjustment for postpartum maternal depression and several other confounders. The second aim was to investigate whether the effect of maternal depression on early infant behaviour is influenced by paternal depression during pregnancy. Because some studies found evidence for a specific vulnerability of boys for maternal depression, while others did not, we examined the influence of maternal depression during pregnancy in girls and boys separately (Connell and Goodman, 2002; Grace et al., 2003; Luoma et al., 2001; Murray et al., 1999; Ramchandani et al., 2005; Sinclair and Murray, 1998).

Methods

Design

This study was embedded in the Generation R Study, a prospective population-based cohort study from fetal life until young adulthood. The study is designed to identify early environmental and genetic determinants of growth, development and health from fetal life until young adulthood and has been described previously in detail (Hofman et al., 2004; Jaddoe et al., 2006). Briefly, the cohort includes 9,778 mothers (of whom 6,347 partners) and their children living in Rotterdam, one of the major cities of The Netherlands. Enrolment for mothers in the study was aimed in the first trimester of pregnancy but was possible until birth of their offspring from December 2001 until January 2006. Assessments in pregnant women included physical examinations, fetal ultrasounds, biological samples and questionnaires. Fathers completed one questionnaire at 20 weeks pregnancy. The children were born between April 2002 and January 2006 and form a prenatally recruited birth-cohort that is currently followed until young adulthood. Of all eligible children in the study area, 61% participate at birth in the study.

The study cohort is a multi-ethnic cohort with a large number of different ethnicities. Questionnaires were available in Dutch and translated in English, French, Portuguese and Turkish. When participants were not able to fill out the questionnaire in one of these languages (e.g. most Moroccans speak Berber, a non-written language) assistants who spoke the same language visited participants at home to help fill out the questionnaire.

The study has been approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. Written informed consent was obtained from all participants.

Population

Data cleaning and preparation for the whole Generation R cohort is still ongoing. For the present analyses we used all available data on children born between January 1, 2003 and December 31, 2004 and their parents. In this period 4,606 pregnant women and 3,376 of their partners were included. Based on self-reported information, it is estimated that 99% of the participating partners is the biological father of the child. We obtained valid depression scores at 20 weeks pregnancy on 3,451 (75%) women and on 2,606 (77%) partners. From 2,104 (46%) infants we obtained valid information on their behaviour at 6 months. Women without valid depression scores on their partner and on the behaviour of their child were excluded from the analyses (n= 1,998).

Assessment of parental depressive symptomatology

Parental depressive symptomatology was assessed at 20 weeks pregnancy with the Brief Symptom Inventory (BSI). The BSI is a well validated self-report questionnaire with 53

items to be answered on a 5-point scale, ranging from "0= not at all" to "4= extremely" (de Beurs, 2004; Derogatis, 1993). The items of the BSI cover nine scales of psychiatric symptoms occurring in the preceding seven days. For this study we used the depression scale, existing of 6 questions which address: "Thoughts of ending life", "feeling lonely", "feeling blue", "feeling no interest in things", "feeling hopeless about the future" and "feelings of worthlessness". The total score for depression was calculated by first summing the values (i.e. 0-4) for the items and then dividing by the number of endorsed items in the depression scale. The internal consistency for the depression scale in our sample was α= .83, which is very satisfactory (Cronbach, 1951).

Assessment of infant behaviour

At 6 months after delivery child behaviour was assessed using an adapted version of 6 scales of the Infant Behavior Questionnaire – Revised (IBQ) (Gartstein and Rothbart, 2003): activity level (i.e. movement of arms and legs, squirming and locomotor activity); distress to limitations (i.e. fussing, crying or showing distress while a) in a confining place or position; b) involved in caretaking activities; c) unable to perform a desired action); fear (i.e. startle or distress to sudden changes in stimulation, novel physical objects or social stimuli; inhibited approach to novelty); duration of orienting (i.e. attention to and/or interaction with a single object for extended periods of time); falling reactivity/rate of recovery from distress (i.e. rate of recovery from peak distress, excitement, or general arousal; ease of falling asleep); sadness (i.e. general low mood; lowered mood and activity specifically related to personal suffering, physical state, object loss, or inability to perform a desired action). The items on the IBQ ask parents to rate the frequency of specific behaviours observed over the past week. We adapted the original 7-point scale (ranging from "1= never present" to "7= always present"), to a 3-point scale ("0= never present", "1= sometimes present" and "2= often present") to enhance discriminative validity, because respondents seldom use the extreme positions of scales with a large amount of categories and reducing the number of levels to three will not result in significant loss of information (Streiner and Norman, 1998). Again, the score for each scale was calculated by first summing the values (i.e. 0-2) for the items in each scale and then dividing by the number of endorsed items in that scale. The internal consistencies for the IBQ-R in our sample ranged from α= .72 for activity level and duration of orienting to α= .86 for fear, which is satisfactory (Cronbach, 1951) and comparable to the internal consistencies of the original IBQ-R (Gartstein and Rothbart, 2003).

Covariates

For mothers at inclusion information was obtained about age, educational level, country of birth and number of living children. The occurrence of maternal smoking and alcohol use was asked for at 20 weeks pregnancy. For fathers all the information was obtained

through a questionnaire filled out at 20 weeks pregnancy. Household income was obtained from the 30 weeks questionnaire and dichotomised in 'low income', indicating an income of less than 1200 euros net a month, which is at the social security level payment for a Dutch household, versus more than 1200 euros. Education was divided in five categories: primary education (no education, primary education), secondary education 1st phase (lower vocational training, 3 years general secondary school), secondary education 2nd phase (intermediate vocational training, >3 years general secondary school, first year higher vocational training/university), higher education 1st phase (higher vocational training, university bachelor) and higher education 2nd phase (university, PhD). Ethnicity of the child was based on the country of birth of the parents. If one parent was born outside The Netherlands, this country defined the ethnicity. If both parents were born in different countries outside The Netherlands, the country of birth of the mother defined the ethnic background. Smoking was dichotomised in 'smoking' and 'non-smoking' and alcohol use was dichotomised in 'alcohol use' and 'no alcohol use'. Child birth weight was obtained from medical records completed by midwives and gynaecologists.

Statistical analysis

SPSS for Windows (version 12.0.1) was used for data analysis. To check for possible confounders in the relation between maternal depression and child behaviour, we performed Pearson correlation analyses with parental age, parental educational level, level of household income, parental smoking and alcohol use, being a first child and child birth weight. We performed an ANOVA to check for child ethnicity as a possible confounder. We considered variables that were both related to maternal depression and at least to four of the six IBQ-R scales as potential confounders. Firstly, we performed linear regression analyses to examine the association between maternal depression and the six scales of child behaviour. Secondly, we adjusted for possible confounders related to maternal alcohol use, demographic and socio-economic factors. Thirdly, to examine whether the effect of maternal depression during pregnancy had a direct intrauterine effect, we did an additional adjustment for maternal postpartum depression at 6 months. Finally, we adjusted for paternal depression and other possible paternal confounders.

Results

General descriptives

For 1,453 mothers we had complete data on both maternal and paternal depression and infant behaviour. Analyses of missing data showed .13 (95%CI: .09–.16) higher depression scores in mothers with missing data on infant behaviour. The same applied to paternal depression scores and missing data on infant behaviour, which showed higher depres-

Table 1. Maternal and paternal characteristics (n= 1,453)

	Mother		Father	
	n	Mean (SD)/%	n	Mean (SD)/%
Age (SD)	1,453	31.3 (4.3)	1,453	33.6 (5.2)
Educational level (%)				
Primary education	61	4.6	67	4.7
Secondary education 1st phase	105	7.9	144	10.1
Secondary education 2nd phase	333	25.1	379	26.6
Higher education 1st phase	351	26.5	297	20.8
Higher education 2nd phase	477	35.9	539	37.8
Smoking (%)				
No	1,095	81.0	850	58.8
Yes	249	19.0	596	41.2
Alcohol use (%)				
No	580	44.3	183	12.4
Yes	724	55.7	1,297	87.6
Low household income (%)				
No	2,235	93.6	idem	idem
Yes	85	6.4		
Depression score 20 weeks pregnancy (SD)	1,453	.15 (.37)	1,453	.09 (.26)
Depression score 6 months postpartum (SD)	1,423	.21 (.44)	-	-

sion scores for fathers on missing infant behaviour .13 (95%CI: .09–.16). At 6 months postpartum we obtained valid depression scores from 1,423 (98%) mothers. Information on infant behaviour was mostly reported by the mother (93%). There were no significant differences between infant behaviour scores rated by mothers or fathers. The general descriptives of the mothers, fathers and children we used for the analyses are shown in table 1 and 2. The number of available data varies per variable due to missing data.

Confounders

Maternal age, paternal age, maternal educational level, maternal alcohol use, low household income and ethnicity of the child, were considered possible confounders because they were both related to maternal depression and to at least four of the six scales of the IBQ-R. Paternal educational level, paternal alcohol use, parental smoking, being a first child and child birth weight were not related to most scales of the IBQ-R and were therefore not considered potential confounders. As expected, paternal depression was both related to maternal depression ($r= .18$; $p< .001$) and to all of the scales of the IBQ-R, except for duration of orienting.

Table 2. Characteristics of 6-month-old infants (n= 1,453)

	Total (n)	Mean (SD)/%
Gender (%)		
Girl	726	50.0
Boy	727	50.0
Birth weight (SD)	1,452	3,499 (543)
First child (%)		
No	805	63.6
Yes	416	36.4
Ethnicity (%)		
Dutch	1,050	72.4
Surinamese	53	3.7
Turkish	53	3.7
Moroccan	29	2.0
Antillean	23	1.6
Cape Verdian	18	1.2
Other Western countries	150	10.3
Other non-Western countries	75	5.2

Effect of maternal depression on infant behaviour of girls

In the unadjusted analyses maternal depression during pregnancy was significantly related to all IBQ-R scales in girls. After the first adjustment only recovery from distress and sadness in girls remained significant, with a diminished effect of maternal depression on all scales. Recovery from distress and sadness in girls remained significant after additional adjustment for postpartum maternal depression, showing again a diminished effect of maternal depression during pregnancy on those scales. After the final adjustment for paternal depression and paternal age these scales remained significant, while the effect of maternal depression on recovery from distress and sadness in girls did not change (table 3).

Effect of maternal depression on infant behaviour of boys

In the unadjusted analyses maternal depression during pregnancy was significantly related to all IBQ-R scales in boys, except for duration of orienting. After the first adjustment the same scales remained significant, though the effect of maternal depression during pregnancy was diminished on all scales except for sadness. After additional adjustment for postpartum maternal depression, maternal depression during pregnancy was still significantly associated with distress to limitations, fear and sadness in boys, though with a diminished effect on all scales. After the final adjustment for paternal depression and paternal age, only distress to limitations remained significantly associated with maternal depression. The effect of maternal depression during pregnancy on distress to limitations in boys was not altered after adjustment for paternal depression and age (table 3).

Table 3. Unadjusted and adjusted effects of maternal depression during pregnancy on six scales of the Infant Behavior Questionnaire-Revised for 6- months-old girls (n= 726) and boys (n= 727)

	Model 0 β (95% CI)	P value	Model 1 β (95% CI)	P value	Model 2 β (95% CI)	P value	Model 3 β (95% CI)	P value
Girls								
Activity level	**.12 (.05; .19)**	**.001**	.05 (-03.12)	.21	.03 (-.05; .12)	.43	.04 (-.05; .12)	.42
Distress to limitations	**.10 (.04; .17)**	**.002**	.06 (-.01; .15)	.08	.03 (-.05; .11)	.47	.02 (-.05; .11)	.48
Fear	**.11 (.04; .17)**	**.001**	.03 (-.04; .10)	.33	-.01 (-.09; .07)	.76	-.01 (-.09; .07)	.76
Duration of orienting	**.10 (.02; .17)**	**.02**	.09 (-.001; .17)	.05	.06 (-.04; .16)	.23	.06 (-.04; .16)	.22
Recovery from distress	**-.15 (-.21; -.09)**	**<.001**	**-.11 (-.17; -.05)**	**.001**	**-.08 (-.15; -.01)**	**.03**	**-.08 (-.15; -.01)**	**.03**
Sadness	**.12 (.07; .17)**	**<.001**	**.10 (.04; .17)**	**.002**	**.07 (.001; .15)**	**.05**	**.07 (.001; .15)**	**.05**
Boys								
Activity level	**.14 (.07; .20)**	**<.001**	**.09 (.02; .16)**	**.01**	.06 (-.01; .13)	.11	.06 (-.01; .14)	.09
Distress to limitations	**.13 (.07; .20)**	**<.001**	**.12 (.05; .19)**	**.001**	**.10 (.02; .17)**	**.01**	**.10 (.02; .18)**	**.01**
Fear	**.14 (.08; .19)**	**<.001**	**.09 (.03; .14)**	**.002**	**.07 (.002; .12)**	**.04**	.05 (-.01; .11)	.08
Duration of orienting	-.02 (-.09; .05)	.64	-.06 (-.13; .02)	.13	-.04 (-.12; .04)	.32	-.04 (-.12; .04)	.32
Recovery from distress	**-.09 (-.15; -.03)**	**.003**	**-.07 (-.13, -.01)**	**.03**	-.06 (-.12; .01)	.10	-.05 (-.12; .02)	.14
Sadness	**.10 (.04; .15)**	**.001**	**.10 (.04; .16)**	**.002**	**.07 (.02; .13)**	**.04**	.07 (-.001; .13)	.05

Betas are unstandardised regression coefficients

Model 0: unadjusted model

Model 1: adjusted for maternal age, maternal educational level, maternal alcohol use, low household income and child ethnicity

Model 2: as in model 1 but additionally adjusted for maternal depression at 6 months postpartum

Model 3: as in model 2 but additionally adjusted for paternal depression and paternal age

Estimates significant at p< .05 are represented in bold

Discussion

This prospective multiethnic population-based study showed that maternal depression during pregnancy was associated with behaviour of 6-month-old infants, even after adjustment for postpartum maternal depression, paternal depression and maternal and paternal confounders. Before adjustment, maternal depression during pregnancy was significantly associated with all behaviour scales in girls and boys, except for duration of orienting in boys.

The magnitude of the effect of maternal depression on behaviour in boys was less influenced after the first adjustment for maternal age, maternal educational level,

maternal alcohol use, low household income and ethnicity of the child, compared to behaviour in girls.

After additional adjustment for postpartum maternal depression, the association between maternal depression during pregnancy and recovery from distress and sadness in girls, and distress to limitations, fear and sadness in boys remained significant. This may suggest that maternal depression during pregnancy has a partially direct prenatal (i.e. intrauterine) effect on behaviour of their 6-month-old infants, since this effect cannot be attributed to the actual level of depression when mothers rated their infant's behaviour.

After the final adjustment for paternal depression and age, the effect of maternal depression during pregnancy on infant behaviour was different for girls versus boys. For girls the magnitude of the effect of maternal depression on recovery from distress and sadness was not influenced by paternal depression. This may suggest that paternal depression and age are not important confounders in the relation between maternal depression during pregnancy and infant behaviour in girls. For boys only distress to limitations remained significantly associated with maternal depression and the magnitude of the effect was not altered. The association between maternal depression on fear and sadness in boys disappeared. If we would not have adjusted for paternal factors, like in other studies on prenatal effects of maternal psychopathology on child behaviour, those effects would have been wrongly attributed to maternal depression during pregnancy.

Strengths and Limitations

Strengths of this study are the prospective population-based design and the adjustment for several confounders including paternal depression. By assessing parental depression during pregnancy one can rule out a child-to-parent effect in which behavioural problems of the child could induce parental psychopathology. Therefore, the associations we found provide evidence for a mother-to-child direction in the association between maternal depression and child behaviour. We were also able to examine the direct effects of maternal depression during pregnancy on the intrauterine developing child, since we were able to correct for postpartum maternal depression.

The main limitation of our study was the selective attrition of mothers with higher depression scores. This would lead to bias in our study if the associations between maternal psychopathology and infant behaviour differ between those mothers who remained in the study and those who dropped out. We do not expect that this is the case. However, the selection is likely to affect the frequency rates and, as a consequence, the statistical power in our study. Therefore, the associations would probably have been more significant when no selection occurred. Another limitation is that almost all information on child behaviour was provided by the mother; therefore rater bias could have occurred in the association between maternal depression and infant behaviour.

Although a review on the possible distortion of depressed mothers in reporting on their children's behaviour did not report evidence for this (Richters, 1992), it cannot be ruled out that in our study depressed mothers judged their infant's behaviour different than non-depressed mothers. Nevertheless, rater bias could not explain the persisting significant association between maternal depression during pregnancy and infant behaviour, since the postpartum depression scores that we used for adjustment were provided by the same mothers.

Conclusion and implications

The first aim of our study was to investigate whether maternal depression during pregnancy was associated with early child behaviour. We found evidence for an association between maternal depression during pregnancy and early infant behaviour, even after adjustment for postpartum maternal depression and confounders. As already discussed, this may suggest a direct effect of maternal depression on the intrauterine developing child. There is growing support for a fetal programming hypothesis which assumes that the HPA-axis, the limbic system and the prefrontal cortex of the child are affected by raised cortisol levels as a result of maternal stress during pregnancy (O'Connor et al., 2003; Van den Bergh et al., 2005). So far, this hypothesis is mostly tested in studies focusing on intrauterine effects of maternal anxiety or stress. In addition, our study might provide evidence for a direct intrauterine effect of maternal depression on infant behaviour. As we hypothesised, this finding could be explained by the high correlation between depression and anxiety – in our sample the correlation at 20 weeks pregnancy was .72 ($p < .001$) – suggesting that those scales partly measure the same underlying construct. However, this hypothesis should be tested in future research, since in our previous study (chapter 3) we found evidence for different effects of maternal anxiety and depression during pregnancy on child birth weight that could also influence the postnatal behavioural development of the child.

It is possible that genetic effects also partly explain the association between depression during pregnancy and early infant behaviour. In that case maternal depression during pregnancy should be more determined by genetic factors than postpartum depression, which should in turn be related to early infant behaviour through a combination of genetic and environmental factors. However, this hypothesis is not confirmed by previous research and warrants further investigation.

The second aim of our study was to investigate whether the effect of maternal depression during pregnancy on early infant behaviour was influenced by paternal depression during pregnancy. If paternal depression during pregnancy would have an effect on early infant behaviour, for which we found evidence in our previous report (chapter 6), we would expect that the effect of maternal depression during pregnancy decreases after adjustment for paternal depression. Strikingly, our results showed that paternal

depression did not influence the association between maternal depression during pregnancy and girls' behaviour, while it did influence the effect of maternal depression on some behaviour scales in boys.

Finally, we aimed at gender differences in the effect of maternal depression on early infant behaviour. Indeed we found different effects of maternal depression during pregnancy on boys' and girls' behaviour. In previous studies it is postulated that parents are more likely to identify with children of the same sex (Connell and Goodman, 2002), making it possible that depressed mothers rate their girls' behaviour different from their sons'. However, it is unlikely that depression of the mother prenatally determines how she will rate her girl's or boy's behaviour. Therefore, it is more likely that gender specific vulnerabilities for maternal and paternal depression exist. For girls, this specific vulnerability might be related more to maternal alcohol use and to socio-economic and demographic factors, because the effect of maternal depression on behaviour in girls decreased more strongly compared to boys after adjustment for these factors. For boys, this specific vulnerability might be more related to a combination of intrauterine, genetic and adverse effects of parent-child interactions associated with parental depression. Obviously, these findings need to be further investigated and replicated in future research.

8 General discussion

General discussion

In this thesis several aspects of parental psychopathology and the early developing child have been addressed. In contrast to most studies, special focus was placed on paternal psychopathology.

The studies described in this thesis were embedded in the Generation R Study, a prospective multiethnic population-based study on growth, development and health of children followed from early fetal life (Hofman et al., 2004; Jaddoe et al., 2006). Data cleaning and preparation for the whole Generation R cohort is still ongoing. For the present analyses we used all available data on children born until January 1st 2005; and their parents.

Parental psychopathology during pregnancy

Since research on common psychiatric disorders during pregnancy has traditionally focused on mothers, the first aim of the thesis was to assess the prevalence and correlation of common psychiatric problems in both mothers and fathers during pregnancy. Additional focus was placed on ethnic differences.

In the study presented in Chapter 2 we assessed the prevalence of maternal and paternal psychopathology during pregnancy using the nine scales of the Brief Symptom Inventory, which cover: Somatization, Obsessive-Compulsivity, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. The mothers and fathers in our sample had lower scores on all scales of the BSI compared with Dutch (de Beurs, 2004), United States (Derogatis, 1993) and British community norms (Francis et al., 1990), except for higher scores on Somatization in mothers, which probably reflects pregnancy related problems. This finding suggests that parents-to-be in our sample, irrespective of ethnic differences, have lower levels of psychopathology compared to adults in the general population. This could either be related to selection bias or to pregnancy related factors. On most symptom scales mothers had much higher psychopathology scores than fathers. This finding is consistent with other population-based studies among pregnant (Deater-Deckard et al., 1998) and non-pregnant participants (de Beurs, 2004; Derogatis, 1993; Francis et al., 1990).

Next we investigated the influence of ethnicity on the level of psychopathology. Compared to age and educational level, ethnicity explained most of the variance in all symptom scales of the BSI. Parents with ethnic backgrounds other than Dutch had higher psychopathology scores than native Dutch, even after adjustment for age and educational level. Among the parents with other ethnic backgrounds, the Turkish scored highest and more than two times higher than the Dutch parents. These ethnic differ-

ences in BSI scores could be related to true differences in the level of psychopathology across cultures or to cultural differences in perceiving and reporting psychopathology. These two influences could not be disentangled in the present study.

Because ethnicity is associated with parental psychopathology, child birth weight (Drooger et al., 2005) and childhood behaviour, ethnicity should be taken into account in studies on the influence of parental psychopathology on child birth outcomes and on the social, cognitive, emotional and behavioural development of the child (as we did in Chapter 3 to 7).

Finally, we investigated the correlation between maternal and paternal psychopathology. Research on the influence of postpartum parental psychopathology on child development showed that if both parents are depressed this places children at even higher risk to develop emotional and behavioural problems than when only the mother is depressed (Dierker et al., 1999; Goodman, 2004; Weissman et al., 1984). It would be likely that this association already exists during pregnancy, since it is known that psychopathology through pregnancy and postpartum period is rather stable (Deater-Deckard et al., 1998; Heron et al., 2004; Matthey et al., 2000), but this has never been confirmed.

Although the level of paternal psychopathology in our study was much lower than the level of maternal psychopathology on most symptom scales, the correlation between maternal and paternal psychopathology during pregnancy was .33 ($p < .001$) which is medium according to Cohen's criteria. This correlation warrants further investigation on the influence of paternal psychopathology during pregnancy on early infant behaviour, next to maternal psychopathology. Before focusing on the effect of interaction of parental psychopathology on child development (which we will do in future research), it will be necessary to investigate whether paternal psychopathology during pregnancy, over and above maternal psychopathology has an effect on child behaviour. On the other hand, the substantial correlation we found supports the relevance of investigating the influence of paternal psychopathology during pregnancy as a possible confounder in associations between maternal psychopathology during pregnancy and child development (as we did in Chapter 5, 6 and 7).

Psychopathology and birth weight

In previous research, associations have been found between parental birth weight and child birth weight (Knight et al., 2005; Magnus et al., 2001), birth weight and adult psychopathology (Cheung et al., 2002; Gale and Martyn, 2004; Thompson et al., 2001; Wiles et al., 2005) and maternal psychopathology during pregnancy and birth weight of the child (Chung et al., 2001; Glover and O'Connor, 2002; Hedegaard et al., 1993; Hoffman and Hatch, 2000). However, these associations were never combined into one model

before to test direct and indirect associations. It was relevant to combine the different associations that exist into one model to examine whether maternal psychopathology during pregnancy is an independent determinant of child birth weight or whether it is a mediator in the association between maternal birth weight and child birth weight. If the association between maternal psychopathology during pregnancy and child birth weight is explained by a genetic, or other biological, regulation of fetal growth, rather than by the direct effect of maternal psychopathology, this has major implications in thinking about causal pathways. For example, the direction of causality could be that lower birth weight leads to psychopathology during adulthood, rather than that maternal psychopathology leads to lower child birth weight. We also investigated paternal factors in the associations between maternal birth weight, maternal psychopathology and child birth weight because paternal birth weight is associated with child birth weight through a genetic regulation of fetal growth (Knight et al., 2005; Magnus et al., 2001) and paternal birth weight is found to be related to paternal psychopathology during adulthood (Cheung et al., 2002; Thompson et al., 2001; Wiles et al., 2005). Finally, paternal psychopathology could indirectly influence the association between maternal psychopathology and child birth weight, since we found a moderate correlation (.33) between maternal and paternal psychopathology during pregnancy in a previous study (see Chapter 2).

Since the Generation R Study provided information on parental birth weigh, parental psychopathology during pregnancy and child birth weight, we were able to examine the various associations into one model (see Chapter 3). In contrast with other studies, we did not find a direct effect of parental birth weight on psychopathology in adult life. However, we did find a relation between maternal depression - and not of anxiety - on child birth weight, even after adjusting for confounders and both maternal and paternal birth weight. This finding suggests that parental birth weight is not an important confounder in the associations between maternal psychopathology during pregnancy and child birth weight. Although the effect of maternal depression on child birth weight was significant, it was a small effect.

Identification of early postpartum psychiatric symptoms

Affective, cognitive and somatic symptoms in recently delivered women are common and might or might not be serious. Frequently used terminology to describe the two most prevalent types of postpartum problems is 'maternity blues' (or synonyms like 'postpartum blues' and 'baby blues') and postpartum depression (Brockington, 1996a). In Chapter 4 we argued that in stead of regarding maternity blues and postpartum depression as distinct entities, postpartum psychiatric symptoms might better be re-

garded as affective, cognitive and somatic problems that vary in co-occurrence, severity and duration. Therefore, we applied Latent Class Analyses (LCA) to empirically identify women with different postpartum symptom profiles. The LCA on 11 common reported postpartum symptoms (anxiety, crying, feeling insecure, forgetfulness, headache, loss of energy, negative feelings towards baby, nightmares, poor concentration, restlessness and sadness) yielded four symptom profiles. Low probability of occurrence on each symptom characterised the 'normative' group (39.1%). High probability of cognitive symptoms together with a longer duration of these symptoms characterised the 'cognitive problems' group (26.0%). Moderately elevated affective symptom probabilities with shorter duration characterised the 'mild affective problems' group (24.6%). High probabilities and longer duration characterised the 'serious problems' group (10.3%). The adjusted risks of clinically relevant high scores on the Edinburgh Postnatal Depression Scale (Cox et al., 1987) at 2 months postpartum were significant for the 'mild affective problems' group (OR 4.5) and the 'serious problems' group (OR 16.5).

Although the main objective of this study was the identification of early postpartum symptom profiles, we also accounted for pre- and postpartum factors that were associated with the severity of postpartum problems. In general, we found that unplanned pregnancy, having a first child, perceived poor health during pregnancy, high levels of anxiety and depression during pregnancy and having a child admitted to hospital were related to more serious psychiatric postpartum problems. Those findings are consistent with previous research and ideally should be screened for by physicians and midwives as potential risk factors during pregnancy and shortly after delivery.

With this study we showed that population-based studies that use an empirical method for identifying psychiatric symptom profiles can give more insight into patterns of commonly occurring postpartum problems. More insight in different patterns and associated factors for early postpartum symptom profiles could be of additional practical benefit for clinicians, midwives and maternity assistants, next to existing maternity blues and postpartum depression scales. The results of our study contribute to early clinical recognition of more or less severe postpartum symptom profiles.

Parental psychopathology during pregnancy and early infant behaviour

For several reasons it is important to focus on paternal psychopathology as well as on maternal psychopathology during pregnancy in understanding the transgenerational aspects of common psychiatric disorders, like anxiety and depression. First, both mothers and fathers contribute 50% of their genes to their offspring. Second, paternal psychopathology can be an important confounder in associations between maternal psychopathology during pregnancy and the emotional and behavioural development

of the infant, since it is both related to maternal psychopathology (as shown in Chapter 2) and behaviour problems in infants (Connell and Goodman, 2002; Kane and Garber, 2004). And finally, if paternal psychopathology during pregnancy has an independent effect on child development, this implies that the traditional focus on mothers' mental health during pregnancy should be reassessed and that a shift to the mental well-being of the father might additionally benefit the well-being of the future child.

With respect to the heritability of behaviour in infants, a recent review showed that about 20 to 60% of the differences among infant behaviour can be explained by genetic factors (Saudino, 2005). Furthermore, a recent twin study among 3-year-old children showed that the heritability of internalising (i.e. anxiety and depression) problems is high (76%) and decreases when children grow older (Boomsma et al., 2005). This means that at a younger age, genetic factors account for the majority of the variation in internalising problems and that with increasing age environmental influences become more important. Although our design was not genetically sensitive to estimate heritability, we were able to investigate the relative contribution of maternal and paternal psychopathology to behaviour in very young infants. For two reasons the design that we used in our study was suitable to test this contribution. First, we assessed both maternal and paternal psychopathology during pregnancy, thus before the child was born. By doing so, we ruled out a child-to-parent effect, in which behavioural problems of the child could contribute to parental psychopathology. Second, in the association between parental psychopathology and infant behaviour we adjusted for psychopathology in the other parent. This enabled us to assess the independent effects of both maternal and paternal psychopathology on infant behaviour.

In Chapter 5 we showed that both maternal and paternal depression were independently associated with excessive crying in 2-month-old infants, though in different ways. Maternal depression was associated with perceived excessive crying, for which in a rather subjective way was asked: "Do you think your baby cries a lot?" Paternal depression turned out to be associated with the more objective criteria of Wessel (i.e. crying more than three hours per day on more than three days in the preceding week). Although some caution should be exercised, we found that both maternal and paternal depression during pregnancy were independently and nearly equally related to excessive infant crying, depending on the definition used. This finding is in line with previous research, which showed that these two definitions of excessive crying partly apply to different infants and also have different risk factors (Reijneveld et al., 2001; 2002). The finding that both maternal and paternal depression is related to excessive infant crying is of particular clinical relevance. Because of the few effective somatic interventions, its stressfulness and the previously found association between parental psychopathology and abuse of excessive crying infants (Reijneveld et al., 2004), early psycho education

and support of both parents could prevent a mutual confirmation of negative parent-child interaction.

In Chapter 6 and 7, the influence of paternal and maternal depression during pregnancy on six scales of infant behaviour (i.e. activity level, distress to limitations, fear, duration of orienting, recovery from distress and sadness) was separately investigated in 6-month-old infants and adjusted for depression in the other parent. Because evidence exists for a specific vulnerability in boys to the effects of parental depression, we examined the influence of parental psychopathology in girls and boys separately (Connell and Goodman, 2002; Grace et al., 2003; Luoma et al., 2001; Murray et al., 1999; Ramchandani et al., 2005; Sinclair and Murray, 1998).

After adjustment for maternal depression during pregnancy and other confounders, we found that paternal depression was only associated with fear in boys. Paternal depression was not associated with behaviour in girls. The association between paternal depression during pregnancy and fear in boys provides evidence for an independent father-to-child direction of paternal depression to early infant behaviour. Our study is the first that found an association between paternal depression during pregnancy and infant behaviour, therefore we cannot compare our results to other studies. Because we do not have postpartum information on paternal psychopathology, we do not know whether our finding is independent of paternal depression in the postpartum period. If this would be the case, this association would provide evidence for a genetic effect. On the other hand, if prepartum depression is strongly linked to postpartum depression this could be related to the direct and negative effect of depressed father on child behaviour through their maladaptive affect, behaviour, and cognitions (Connell and Goodman, 2002; Downey and Coyne, 1990; Grace et al., 2003; Zaslow et al., 1985), or to contextual stressors, like marital or economic distress (Connell and Goodman, 2002; Erel and Burman, 1995; Kane and Garber, 2004). Therefore, further research is warranted on the different mechanisms of paternal psychopathology during pregnancy and its influence on infant behaviour and on its possible specific effect on the behavioural development of boys.

The investigation and interpretation of the association between maternal depression during pregnancy and infant behaviour was more complex, since also direct (i.e. intrauterine) effects could be of influence. Therefore we first adjusted for confounders, next for postpartum maternal depression and finally for paternal depression. This stepwise adjustment showed different effects of maternal depression. In the unadjusted analyses, maternal depression was related to all scales of infant behaviour, except for duration of orienting in boys. The first adjustment for confounders revealed that the effect of maternal depression decreased for behaviour in girls, while it did less influence the association with behaviour in boys. Additional adjustment for postpartum maternal depression and paternal depression did not strongly influence the association between

maternal depression during pregnancy and behaviour in girls, i.e. recovery from distress and sadness. However, after additional adjustment for postpartum depression, the association between maternal depression during pregnancy and behaviour in boys decreased. Also, after final adjustment for paternal depression the association between maternal depression during pregnancy and behaviour in boys further decreased, remaining a significant effect on distress to limitations only.

These findings showed that also maternal depression during pregnancy has a different effect on early infant behaviour in boys and girls, with different underlying mechanisms. Girls might be more vulnerable for contextual factors related to maternal depression, while boys might be more vulnerable for the combination of intrauterine, genetic and adverse effects of parent-child interactions associated with parental depression.

The independent effect (i.e. adjusted for postpartum depression and paternal depression) of maternal depression during pregnancy on distress to limitations in boys and recovery from distress and sadness in girls can have several explanations. Firstly, it could be a direct intrauterine effect. There is growing support for a fetal programming hypothesis which assumes that the HPA-axis, the limbic system and the prefrontal cortex of the child are affected by raised cortisol levels as a result of maternal stress during pregnancy (O'Connor et al., 2003; Van den Bergh et al., 2005). So far, this hypothesis is mostly tested in studies focusing on intrauterine effects of maternal anxiety or stress. In addition, our study might provide evidence for a direct intrauterine effect of maternal depression on infant behaviour as well. It is possible that genetic effects also partly explain the association between depression during pregnancy and early infant behaviour. In that case maternal depression during pregnancy should be more determined by genetic factors than postpartum depression, which should in turn be related to early infant behaviour through a combination of genetic and environmental factors. However, this hypothesis is not confirmed by previous research and warrants further investigation.

Strengths and limitations of the study

Strengths of this study are the prospective population-based design and the adjustment for several confounders including psychopathology in the other parent. The study cohort is rather unique since it consists of contemporary urban children including about 50% from ethnic minorities. Our study is the first that, next to maternal psychopathology, also investigated the influence of paternal psychopathology during pregnancy and other paternal factors on the early developing child. By assessing parental psychopathology during pregnancy one can rule out a child-to-parent effect in which behavioural problems of the child could induce parental psychopathology. Therefore, the associa-

tions we found provide evidence for a parent-to-child direction in the association between parental psychopathology and child behaviour.

However, some limitations must also be discussed. Of all eligible children at birth, about 61% participate in the study. It is likely that women and their partners with more psychopathology were less willing to participate. This is indirectly supported by the relatively high number of missing data on the Brief Symptom Inventory among initially participating parents with lower age, a lower educational level and from other ethnicities. Those are all factors related to higher levels of psychopathology. Also, the missing data on child behaviour were related to higher levels of both maternal and paternal psychopathology. This selective non-response and selective attrition would lead to bias in our studies if the selection mechanisms are related to both parental psychopathology and child outcomes. We do not expect that this is generally the case. However, the selection towards a more affluent and healthy study population is likely to influence the frequency rates and, as a consequence, the statistical power in our studies. Therefore, the associations would probably have been more significant when no selective attrition had occurred. Another limitation is that most of the infant behaviour was reported by the mothers. Prior studies have shown that different informants make different contributions to the prediction of psychopathology in children (Derks et al., 2004; Verhulst et al., 1997), therefore rater bias could have occurred in the reporting of child behaviour in our study as well. However, in the associations between father-rated paternal depression and mostly mother-rated infant behaviour, rater bias is strongly reduced, because the information was obtained from different informants. Finally, we could not rule out 'false paternity', since we had to rely on self-report data in this respect. From a recent review it is estimated that 3.7% of the children is sired by another man than the father who believes he is the biological father (Bellis et al., 2005). If this is the case in our study, the found associations between paternal and child characteristics could be somewhat underestimated when genetic factors were of major importance.

Clinical and research implications

Our study provides several clinical and research implications:

1. This thesis showed that both maternal and paternal psychopathology during pregnancy are significantly associated with several developmental outcomes in the child (i.e. birth weight, excessive infant crying and early infant behaviour). Therefore, it is important that midwives and gynaecologists are well-informed about the possible consequences of parental psychopathology during pregnancy on the developing infant. Ideally, parents-to-be should be routinely screened for psychiatric problems by means of validated psychiatric instruments like the Brief Symptom Inventory or

Edinburgh Postnatal Depression Scale, using cut-off scores that are indicative for serious psychiatric problems. Screen positive parents should then be referred for psychiatric assessment. In case the psychiatric problems underlie a psychiatric disorder, psychotherapeutic or pharmacotherapeutic treatment is indicated.

2. Although maternal psychopathology during pregnancy is much higher than paternal psychopathology, they are significantly correlated. Therefore, both in research and in clinical practice it is recommended to pay more attention to paternal psychopathology, during pregnancy already. It is possible that the presence of paternal psychopathology hampers the treatment of maternal psychopathology.
3. Of the investigated factors, ethnic background accounted for most of the explained variances in parental psychopathology during pregnancy. Compared to the native Dutch, parents with another ethnic background had much higher psychopathology scores. Therefore, it is important to invest in the identification of psychiatric risk factors, detection and treatment of psychopathology in parents with other ethnic backgrounds.
4. Our study suggests that maternal depression - and not anxiety - during pregnancy is significantly associated with lower birth weight of the child, also after adjusting for parental birth weight and other confounders. Although the clinical relevance of this finding might not be strong, it suggests different mechanisms between maternal depression and anxiety in influencing child birth weight that can further our understanding of underlying mechanisms leading to adverse child outcomes.
5. In the first two weeks after delivery it is hard to distinguish mild and transient postpartum psychiatric symptoms from serious psychiatric symptoms in recently delivered women. Therefore, it might be better to consider them as affective, cognitive and somatic problems that vary in co-occurrence, severity and duration, rather than to try and force these symptoms into diagnostic categories such as maternity blues or postpartum depression. We found that the co-occurrence of both affective, cognitive and somatic problems present in the first 2 weeks after delivery was most predictive of serious psychiatric problems at 2 months postpartum.
6. Excessive infant crying is associated with both maternal and paternal depression during pregnancy. Because of the few effective somatic interventions and its stressfulness, early psychoeducation, support and, if necessary, psychiatric treatment of parents at risk could be of benefit. Additionally, workers in infant welfare centers and clinicians should not hesitate to make use of the aforementioned validated psychiatric assessment instruments and refer for further psychiatric assessment when parents turn out to screen positive for serious psychiatric problems.

Suggestions for future research

Although this thesis revealed several findings on both maternal and paternal psychopathology and their association with different aspects of early infant development, our findings might generate future studies.

1. We studied the effect of parental depression during pregnancy in very young children. It is likely that some of the effects are transient, while others persist in long-term behavioural problems. Therefore, it would be interesting to investigate whether and to which extent these stabilities and changes over time are also influenced by maternal and paternal psychopathology.
2. The different effects of parental psychopathology on girls and boys, in which boys seem to be more vulnerable for both paternal and maternal psychopathology, deserve further exploration.
3. Instead of only maternal reports on early infant behaviour, multiple informants (i.e. fathers and other caretakers), clinically administered diagnoses on parental psychopathology and observations of infant behaviour are important to confirm the associations.
4. The different pathways of parental psychopathology leading to adverse child development should be further explored. These pathways include genetic and other biological factors (e.g. genetic polymorphisms, cortisol levels, psychophysiological measures, ethnicity), parent-child interaction (including father-child interaction) and contextual stressors (e.g. familial discord, economic pressure, cultural aspects).
5. It would be of particular clinical relevance to screen obstetric patients for high levels of psychopathology (like anxiety and depression) and randomise them for different treatments, for example the use of medication versus psychotherapy, to examine the effect of these treatments on the cognitive, emotional and behavioural development of the child. Possibly because growing evidence exists on the negative influence of maternal psychopathology during pregnancy on the intrauterine developing child, clinicians are nowadays less reluctant to prescribe or continue psychiatric medication during pregnancy. Especially the selective serotonine reuptake inhibitors (SSRI's) are advocated to be relatively safe during pregnancy, because so far research has not shown an elevated risk of malformations in the newborn child. However, little is known about the possible adverse effects of psychiatric medication during pregnancy on the long term cognitive, emotional and behavioural development of the child.

Final conclusion

This thesis aimed at extending the existing knowledge on transgenerational aspects of common psychiatric disorders. The main findings were:

1. During pregnancy mothers had much higher levels of psychopathology on most of the scales of the BSI compared to fathers. Maternal and paternal psychopathology were significantly correlated (.33). Ethnicity explained most of the variance of the investigated factors on all symptom scales of the BSI. Participants with other ethnic backgrounds had higher psychopathology scores than native Dutch, even after adjustment for age and educational level.
2. Maternal depression – and not anxiety – seems to be associated with lower birth weight of the child, even after adjustment for parental birth weight and other confounders.
3. Maternal and paternal depression during pregnancy did influence their children's behaviour in different ways. Both maternal and paternal depression during pregnancy were independently, though differently, related to excessive infant crying at 2 months. Maternal depression during pregnancy was independently associated with recovery from distress and sadness in 6-month-old girls, and to distress to limitations in 6-month-old boys. Paternal depression during pregnancy was not associated with behaviour of 6-month-old girls, while it was independently associated with fear in 6-month-old boys.

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Summary

Summary

The objective of this thesis was to further our knowledge on transgenerational aspects of common psychiatric disorders. In **Chapter 1**, the background and the main aims of the present study were presented. Up to now research tradition particularly focused on the influence of maternal psychopathology on the early developing infant. Although there is growing evidence of the importance of the influence of postpartum paternal psychopathology on child development, little is known about this influence during pregnancy. There are two main reasons to focus on paternal psychopathology during pregnancy. Firstly, fathers contribute 50% of their children's genes and depression and anxiety are highly heritable in infants. Secondly, paternal psychopathology can be an important confounder in associations between maternal psychopathology during pregnancy and the developing infant. A prospective design, in which parental psychopathology is assessed before the child's birth, is needed because then a child-to-parent effect can be ruled out. It also gives insight in the direction and effect of the influence of both maternal and paternal psychopathology on child development. This study was embedded in the Generation R Study, a prospective multiethnic population-based study on growth, development and health of children followed from early fetal life. The main aims of the present thesis were: 1) to assess the prevalence and correlation of common maternal and paternal psychopathology during pregnancy; 2) to examine the different pathways from parental birth weight and parental psychopathology during pregnancy (i.e. anxiety and depression) to child birth weight; and 3) to examine the influence of both maternal and paternal depression during pregnancy on early infant behaviour.

In **Chapter 2**, the prevalence and correlation of maternal and paternal psychopathology at 20 weeks pregnancy were assessed by means of the Brief Symptom Inventory (BSI). This is an instrument that covers nine symptom scales: Somatization, Obsessive-Compulsivity, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism. Mothers had much higher levels of overall psychopathology compared to fathers. The correlation between maternal and paternal psychopathology was medium. Ethnicity explained most of the variance of the examined factors on all symptom scales of the BSI. Participants with other ethnic backgrounds had higher psychopathology scores than native Dutch, even after adjustment for age and educational level.

In **Chapter 3**, the different pathways from parental birth weight and parental psychopathology (i.e. anxiety and depression) during pregnancy to child birth weight were examined. In the unadjusted analyses direct effects existed between: 1) maternal and paternal birth weight and child birth weight; 2) maternal birth weight and maternal depression and anxiety; and 3) maternal depression and anxiety and child birth weight. The indirect effect of paternal psychopathology via maternal psychopathology on child

birth weight was larger than the indirect effect of maternal birth weight via maternal psychopathology on child birth weight. After adjustment for confounders parental birth weight and maternal depression – and not anxiety - were associated with child birth weight. This suggests different underlying mechanisms in the relation between maternal depression and anxiety during pregnancy and child birth weight.

In **Chapter 4**, in an empirical way four different profiles of 11 common early psychiatric postpartum symptoms in recently delivered women were identified. Four symptom profiles were found. Low probability of occurrence on each symptom characterised the 'normative' group. High probability of cognitive symptoms together with a longer duration of these symptoms characterised the 'cognitive problems' group. Moderately elevated affective symptom probabilities with shorter duration characterised the 'mild affective problems' group. High probabilities and longer duration of all symptoms characterised the 'serious problems' group. The adjusted risks to develop serious problems that meet criteria for depression at 2 months postpartum were significant for the 'mild affective problems' group and the 'serious problems' group. Different characteristics of the symptom profiles, like socio-economic status and pregnancy and health related factors were discussed.

In **Chapter 5**, the association between paternal and maternal depression during pregnancy and two definitions of excessive infant crying was investigated. The two definitions of excessive crying were: 1) perceived excessive crying and 2) widely used Wessel's criteria for excessive crying (i.e. crying more than three hours per day on more than three days in the preceding week). The two definitions yielded partly different groups of infants which were differently associated with parental depression. Maternal depression during pregnancy was related to perceived excessive infant crying and paternal depression during pregnancy was related to Wessel's criteria for excessive crying. This study showed that paternal depression, next to maternal depression, during pregnancy might be a risk factor for excessive infant crying.

In **Chapter 6**, the influence of paternal depression during pregnancy on six scales of infant behaviour (i.e. activity level, distress to limitations, fear, duration of orienting, recovery from distress and sadness) was investigated in 6-month-old infants. After adjustment for maternal depression during pregnancy and several other confounders, paternal depression was associated with fear in boys. Paternal depression was not associated with behaviour in girls. The association between paternal depression during pregnancy and fear in boys provides evidence for a father-to-child direction of paternal depression to early infant behaviour.

In **Chapter 7**, the influence of maternal depression during pregnancy on six scales of infant behaviour in 6-month-old infants was investigated and adjusted for paternal depression during pregnancy, maternal depression postpartum and several other confounders. We found an effect of maternal depression during pregnancy on recovery

from distress and sadness in girls, and on distress to limitations in boys. These findings suggest a gender specific effect of maternal depression during pregnancy and early infant behaviour.

In **Chapter 8**, the main findings and conclusions of this thesis were summarised and discussed. The present study showed that, although mothers have much higher levels of psychopathology during pregnancy, there was a considerable correlation with paternal psychopathology. Moreover, parents with other ethnic backgrounds than Dutch had much higher levels of psychopathology. Parental psychopathology during pregnancy was related to several aspects of early infant behaviour at different ages. Although the influence of maternal psychopathology during pregnancy on early child behaviour was more distinct, paternal psychopathology was also independently associated with early child behaviour. Especially boys seemed to be more vulnerable to the effects of both maternal and paternal psychopathology during pregnancy.

Considering our results it is important to focus on paternal psychopathology during pregnancy as well as on maternal psychopathology, since both, though in different ways, are associated with behaviour in early developing infants.

Samenvatting

Samenvatting

Het doel van dit proefschrift was om meer kennis te vergaren over de transgenerationele aspecten van veel voorkomende psychiatrische stoornissen.

In **hoofdstuk 1** werden de achtergronden en de belangrijkste doelen van het onderzoek geschetst. Tot nog toe heeft de onderzoekstraditie zich vooral gericht op de invloed van psychiatrische problemen van de moeder op de vroege ontwikkeling van het kind. Hoewel er groeiend bewijs is voor het belang van de invloed van psychopathologie van de vader op de ontwikkeling van het kind na de geboorte, is er weinig bekend over deze invloed tijdens de zwangerschap. Er zijn twee belangrijke redenen om de psychopathologie van de vader al tijdens de zwangerschap te onderzoeken. Ten eerste dragen vaders voor 50% bij aan de genen van hun kind en zijn angst en depressie in sterke mate erfelijk. Ten tweede kan psychopathologie van de vader een belangrijke verstorende variabele (confounder) zijn in de associatie tussen psychopathologie van de moeder en de ontwikkeling van het kind. Om het effect van het kind op de psychopathologie van de ouders uit te sluiten is het nodig om prospectief onderzoek te verrichten waarin psychopathologie van de ouders wordt onderzocht voordat het kind geboren is. Dit geeft ook meer inzicht in de richting en de sterkte van de invloed van psychopathologie van zowel de moeder als de vader op de ontwikkeling van het kind. Deze studie was onderdeel van de Generation R Studie, een prospectief multi-etnisch onderzoek naar groei, ontwikkeling en gezondheid van kinderen gevolgd vanaf de vroege zwangerschap. De belangrijkste doelen van dit proefschrift waren: 1) het vaststellen van de prevalentie en de correlatie van veel voorkomende psychiatrische stoornissen bij moeders en vaders tijdens de zwangerschap; 2) het onderzoeken van de verschillende paden die leiden van het ouderlijke geboortegewicht via ouderlijke psychopathologie (d.w.z. angst en depressie) naar het geboortegewicht van het kind; en 3) het onderzoeken van de invloed van zowel maternale als paternale psychopathologie tijdens de zwangerschap op de ontwikkeling van het jonge kind.

In **hoofdstuk 2** werden de prevalenties en correlatie van maternale en paternale psychopathologie bij 20 weken zwangerschap vastgesteld met behulp van de 'Brief Symptom Inventory' (BSI). Dit is een instrument dat negen symptoom schalen bevat: Somatisatie, Obsessief-Compulsiviteit, Interpersoonlijke Sensitiviteit, Depressie, Angst, Vijandigheid, Fobische Angst, Paranoïde Ideaties en Psychoticiteit. Moeders hadden veel hogere psychopathologie scores dan vaders. De correlatie tussen maternale en paternale psychopathologie was middelmatig. Etniciteit verklaarde de meeste variantie van de onderzochte factoren binnen alle schalen van de BSI. Deelnemers met een andere etnische achtergrond dan de Nederlandse hadden hogere psychopathologie scores, zelfs na correctie voor leeftijd en opleidingsniveau.

In **hoofdstuk 3** werden de verschillende paden van ouderlijk geboortegewicht en ouderlijke psychopathologie (d.w.z. angst en depressie) tijdens de zwangerschap die leiden naar het geboortegewicht van het kind onderzocht. In de ongecorrigeerde analyses bestonden directe effecten tussen: 1) ouderlijk geboortegewicht en geboortegewicht van het kind; 2) geboortegewicht van de moeder en maternale depressie en angst; en 3) maternale depressie en angst en geboortegewicht van het kind. Het indirecte effect van paternale psychopathologie via maternale psychopathologie was groter dan het indirecte effect van het geboortegewicht van de moeder via maternale psychopathologie op het geboortegewicht van het kind. Na correctie voor confounders bleven geboortegewicht van de ouders en maternale depressie – en niet angst – significant gerelateerd aan geboortegewicht van het kind. Dit suggereert dat er verschillende onderliggende mechanismen zijn in de relatie tussen maternale depressie en angst tijdens de zwangerschap en geboortegewicht van het kind.

In **hoofdstuk 4** werden op een empirische manier vier verschillende profielen van 11 veel voorkomende psychiatrische symptomen in het kraambed geïdentificeerd. Een kleine kans op het optreden van elk symptoom karakteriseerde de 'normatieve' groep. Een grote kans op cognitieve symptomen en een langere duur van deze symptomen karakteriseerde de groep 'cognitieve problemen'. Een matig verhoogde kans op affectieve symptomen met een kortere duur van alle symptomen karakteriseerde de groep 'lichte affectieve problemen'. Hoge kansen en een langere duur karakteriseerden de groep 'ernstige problemen'. De gecorrigeerde risico's voor het voldoen aan de criteria om twee maanden na de bevalling een depressie te krijgen waren significant verhoogd voor de groepen 'lichte affectieve problemen' en 'ernstige problemen'. De verschillende kenmerken van de symptoomprofielen, waaronder socio-economische status en zwangerschaps- en gezondheidsgerelateerde factoren, werden besproken.

In **hoofdstuk 5** werd het verband tussen paternale en maternale depressie tijdens de zwangerschap en twee definities van excessief huilen in baby's onderzocht. Deze twee definities waren: 1) perceptie van excessief huilen en 2) de veelgebruikte criteria van Wessel voor excessief huilen (meer dan drie uur huilen per dag op meer dan drie dagen in de afgelopen week). De twee definities leverden gedeeltelijk andere groepen op die verschillend gerelateerd waren aan ouderlijke depressie. Maternale depressie tijdens de zwangerschap was gerelateerd aan de perceptie van excessief huilen en paternale depressie tijdens de zwangerschap was gerelateerd aan Wessels criteria voor excessief huilen. Deze studie liet zien dat paternale depressie, naast maternale depressie, al tijdens de zwangerschap een risicofactor kan zijn voor excessief huilen van baby's.

In **hoofdstuk 6** werd de invloed van paternale depressie tijdens de zwangerschap op zes baby-gedragsschalen (niveau van activiteit, van streek raken bij beperkingen, angst, aandachtsspanne, herstel na van streek raken en verdriet) in 6 maanden oude baby's onderzocht. Na correctie voor maternale depressie tijdens de zwangerschap en

andere ouderlijke confounders, bleek paternale depressie tijdens de zwangerschap gerelateerd aan angst bij jongetjes. Paternale depressie was niet gerelateerd aan gedrag van meisjes. Het verband tussen paternale depressie tijdens de zwangerschap en angst in jongetjes levert bewijs voor een vader-op-kind richting tussen paternale depressie en gedrag in baby's.

In **hoofdstuk 7** werd de invloed van maternale depressie tijdens de zwangerschap op zes baby-gedragsschalen in 6 maanden oude baby's onderzocht en gecorrigeerd voor paternale depressie tijdens de zwangerschap, maternale depressie na de bevalling en enkele andere confounders. We vonden een effect van maternale depressie tijdens de zwangerschap op 'herstel na van streek raken' en 'verdriet' in meisjes, en op 'van streek raken bij beperkingen' in jongetjes. Deze bevindingen suggereren een geslachtsspecifiek effect van maternale depressie tijdens de zwangerschap en gedrag in baby's.

In **hoofdstuk 8** werden de belangrijkste bevindingen en conclusies van dit proefschrift samengevat en besproken. Het huidige onderzoek toonde aan dat, hoewel moeders veel hogere psychopathologie scores hadden, er een significante correlatie was met paternale psychopathologie. Bovendien hadden ouders met een andere etnische achtergrond dan Nederlands hogere psychopathologie scores. Ouderlijke psychopathologie tijdens de zwangerschap was gerelateerd aan verschillende ontwikkelingsaspecten van baby's op verschillende leeftijden. Hoewel de invloed van maternale psychopathologie op het gedrag van het jonge kind meer uitgesproken was, was ook paternale psychopathologie op een onafhankelijke manier gerelateerd aan het gedrag van het jonge kind. Vooral jongetjes leken kwetsbaar voor psychopathologie van zowel de moeder als van de vader tijdens de zwangerschap.

Onze bevindingen onderstrepen het belang van paternale, naast maternale, psychopathologie tijdens de zwangerschap op de ontwikkeling van het jonge kind omdat zij, weliswaar op verschillende wijze, beide geassocieerd zijn met het gedrag van jonge kinderen.

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Curriculum Vitae

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Curriculum Vitae

Mijke Pietertje van den Berg werd op 12 november 1969 te Winterswijk geboren. In 1988 behaalde zij het gymnasiumdiploma aan het Vossius Gymnasium te Amsterdam. Omdat zij twee keer werd uitgeloot voor de studie Geneeskunde begon zij in 1988 aan de studie Slavische- taal en letterkunde en in 1989 aan de studie Scheikunde, beide aan de Universiteit van Amsterdam. In 1990 behaalde zij de propedeuse Scheikunde en in hetzelfde jaar ving zij aan met de studie Geneeskunde aan dezelfde universiteit. Tijdens haar studie deed zij in 1991 een verpleeghulpstage in een kinderziekenhuis in Moskou, in 1995 een epidemiologische onderzoekstage naar maternale sterfte in Tsjaad en in 1996 een keuze-coschap Kinder Intensive Care in Tasjkent, Oezbekistan. Naast de studie Geneeskunde behaalde zij in 1995 het doctoraal Russische Letterkunde en werd zij in 1997 beëdigd als tolk/vertaler Russisch. In de wachttijd voor de aanvang van de co-schappen schreef zij in opdracht van de ANWB de reisgids: 'Actief en Anders; Baltische Staten (Estland, Letland, Litouwen)'. In 1997 behaalde zij haar artsexamen.

Na haar artsexamen werkte zij van mei tot en met december 1997 als arts-assistent psychiatrie niet in opleiding (AGNIO) in het Reinier de Graafgasthuis te Delft, van januari tot en met maart 1998 als AGNIO neurologie in het Sint Lucas Andreas Ziekenhuis te Amsterdam en van april tot en met juni 1998 als AGNIO psychiatrie voor het Ministerie van Justitie, Districtspsychiatrische Dienst, arrondissement Den Haag. Van juli 1998 tot en met maart 1999 werd zij aangesteld als AGNIO psychiatrie met uitzicht op een opleidingsplaats in het Academisch Ziekenhuis Dijkzigt te Rotterdam. Voor aanvang van de opleiding tot psychiater werkte zij van april tot en met december 1999 als AGNIO neurologie in het Albert Schweitzer Ziekenhuis te Dordrecht.

In januari 2000 begon zij aan de opleiding tot psychiater in het Erasmus MC te Rotterdam (opleider: prof.dr. M.W. Hengeveld). Mede dankzij een GeestKracht OOG (Opleiding Onderzoeker GGZ) subsidie van ZonMw was het mogelijk haar opleiding tot psychiater vanaf 2002 te combineren met de in dit proefschrift beschreven studie. Dit deed zij vanuit de afdeling Kinder- en Jeugdpsychiatrie van het Erasmus MC – Sophia te Rotterdam (hoofd: prof.dr. F.C. Verhulst). Haar stage sociale psychiatrie volgde zij van april tot en met september 2004 bij RIAGG Rijnmond Noord-West (opleider: dr. M.J.A.M. Coopmans). In 2005 rondde zij de opleiding tot Master of Genetic Epidemiology af aan het Netherlands Institute for Health Sciences te Rotterdam.

Sinds haar registratie als psychiater in oktober 2004 combineert zij haar onderzoek met een aanstelling voor twee dagen in de week als staflid psychiatrie in het Erasmus MC te Rotterdam met als aandachtsgebied de zwangerschapsgerelateerde psychiatrie. In september 2005 ving zij tevens voor drie dagen in de week aan met de opleiding tot kinder- en jeugdpsychiater in het Erasmus MC – Sophia te Rotterdam (opleider: prof.dr. F.C. Verhulst).

Algemeen Dagblad 12 november 2005 (afgedrukt met toestemming van 'Djanko')