The influence of stress reduction during pregnancy on infant outcome

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Our unique project is based on an ongoing European prenatal stress research focusing on the effect of prenatal stress on early sensory-cognitive development. We capitalize on the methodologically sound maternal and infant physiological measures...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON35275

Source
ToetsingOnline

Brief title
Pregnancy and Mindfulness

Condition

- Other condition
- Pregnancy, labour, delivery and postpartum conditions
- Cognitive and attention disorders and disturbances

Synonym
attention problemes, Stressregulationproblems

Health condition

Aangeboren kwetsbaarheid gerelateerd aan het stresssysteem (HPA-as en autonoom zenuwstelsel)

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit van Tilburg
Source(s) of monetary or material Support: March of Dimes (USA); aanvraag ingediend op 24 september 2011

Intervention

Keyword: Event related brain potential, Infant Cognition, Pregnancy, Stresssystem

Outcome measures

Primary outcome

1.Birth outcome:. Gestational length at birth and birth weight and length are important outcome measures (T4). 2.Psychological measures of mother. The State Trait Anxiety Inventory (STAI) and Perceived Stress Scale (PSS) are used to select women at recruitment and, together with the Pregnancy Anxiety Questionnaire (PRAQ-short) and the Five Factor Mindfulness Questionnaire (FFMQ), will also be completed to measure the effect of the MBSR and examine their association with the physiological stress measures. The STAI consists of 20 items measuring state anxiety (transient emotional condition) and trait anxiety (dispositional anxiety). The PSS, contains 10 items measuring the perception of stress. The FFMQ , has 39 items measuring five facets of mindfulness skills. The PRAQ-short measures anxieties related to pregnancy and contains 10 items. 3.Physiological measures and biochemical assays of the woman, fetus and infant 3.1. HPA-axis and ANS activity. Basal and stress-related activity is measured before, during, and after the standard TSST, which combines a mental arithmetic task with a free speech task in front of a critical audience and which has been shown to induce reliable physiological stress responses. Salivary cortisol is measured four times from

before to one hour after the stressor. ANS activity is recorded using the validated Vrije Universiteit Ambulatory Monitoring System (UV-AMS; http://www.psy.vu.nl/vu-ams/) throughout the laboratory session. This device measures heart rate, heart rate variability, skin temperature, skin conductance and respiration frequency. In addition, in order to assess acute responses to mindfulness exercises, HR(V) will be measured during 50% of the MBSR sessions, i.e. 2-weekly at T2. Finally, to assess the cortisol awakening response (CAR) and diurnal profile, on the day before the laboratory stress test (TSST), the mothers will provide 6 saliva samples: at awakening, 30, 45 and 60 minutes after awakening (to measure the CAR), and app. 4 hours later (noon) and app. 12 hours later (evening). We will use electronic monitoring devices to know the exact hour when the mothers took the saliva samples. Saliva samples will also be analyzed for alpha-amylase levels, an enzyme considered to reflect changes in the ANS during stress. In the infants, saliva samples will be taken two times before the ERP assessment (at arrival in the lab and 15* later), and 3 times after the assessment (at 0, 15 and 30 minutes). 3.2 Heart rate monitoring in the fetus and infant. We use a simple and powerful non-invasive methodology by using Monica Healthcare*s AN24 fetal monitor. This device placed on the maternal abdomen enables reliable detection of the fetal heart*s RR-intervals, thus providing a fetal ECG. It has been shown that prolonged fECG recordings of good quality can be obtained during the night, when the mother is asleep], between 20 and 30 weeks GA. We will perform fetal heart rate monitoring for 8 hours during the night (11 PM to 7 AM) at the pregnant woman*s home, synchronously with performing maternal heart rate. At 2 months after birth, the

infant*s heart rate and HRV is measured during the lab visit, with BIOSEMI equipment. The fetal and infant electric heart rate signals, like those of the mother, will be subjected to HRV analysis in the time and frequency domains .

3.3 HRV parameters. Maternal HRV parameters are standardized by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. In time domain the following measures will be calculated: the standard deviation of the 5 minute average of RR intervals (SDANN), the square root of the mean of the sum of the squares of differences between consecutive RR-intervals (rMSSD) and the percentage of intervals that vary more than 50 ms from the previous interval (pNN50). The latter two are strongly related to parasympathetic control [143-144]. In the frequency domain, low frequency power (LF: 0.04 - 0.15 Hz), high frequency power (HF: 0.16 - 0.40 Hz), total power (0.01 - 1.00 Hz), and the LF/

HF ratio will be calculated. Vagal activity is the major contributor to the HF

component, while the LF component may be seen as reflecting both sympathetic and vagal activities. In addition, various non-linear parameters of HRV will be evaluated to search for non-linear fluctuations in heart rate. 3.4 Auditory ERP in the infant. The auditory mismatch negativity (MMN) paradigm used in an ongoing study of ours and the infant equivalent mismatch response (MMR) were designed in collaboration with Istvan Winkler, an internationally recognized ERP expert (Hungarian Academy of Sciences, Budapest). These measures assess whether and how strongly infants react to novel and other deviant sounds. At two months after birth, ERPs will be recorded during a passive auditory oddball paradigm involving 4 types of sounds of 200ms duration at a uniform 300ms pre-stimulus interval: (1) 1050 frequent standard complex tones (500Hz); (2) 150 tones with 100ms pre stimulus (ds1); (3) 150 white noise segments (ds2); and (4) 150 various environmental sounds (ds3). MMR-related difference waves are calculated by subtracting responses elicited by the standard tones separately from those elicited by each of the deviants (ds1,ds2, ds3).

Secondary outcome

Relevant covariates. Maternal age, parity, gravidity, education, socio-economic status (SES), ethnicity, smoking, alcohol, glucocorticoid exposure, prescription drug use (i.e., antidepressant (SSRI), anti-hypertensive, anti-asthmatic, anti-epileptic, steroids) will be gathered from the medical files of the mothers and from questionnaires completed by the mother. These data will be used as covariates in analyses (T1 to T5) as appropriate.

Study description

Background summary

A large body of research provides empirical evidence for the hypothesis that the risk of a shorter length of gestation and of late preterm birth is increased when high levels of maternal anxiety or chronic stress are present during pregnancy. The interaction between the maternal stress system and the physiology of pregnancy and parturition is seen as one of the pathophysiological mechanism explaining preterm birth. There is also evidence for an association between high levels of maternal stress and anxiety during pregnancy and birth defects in the offspring, including cognitive functioning. Moreover it is hypothesized that antenatal exposure to maternal chronic stress may induce morphological and functional changes in the hippocampus, amygdala and prefrontal cortex by which a neurobiological vulnerability is acquired already prenatally. There still is, however, a lack of knowledge about the underlying mechanisms. On the one hand a better understanding of the biology of preterm parturition and of (subtle) birth defects and their underlying pathophysiological processes is necessary to set up preventive and curative treatment of women at enhanced risk for giving birth to babies with birth defects and/or for preterm parturition. On the other hand, by examining in pregnant women the effectiveness of a standardized stress reduction intervention program on maternal stress systems and also the infant stress system and cognitive functioning, hypotheses about the proposed underlying mechanisms will have a chance to be tested

Study objective

Our unique project is based on an ongoing European prenatal stress research focusing on the effect of prenatal stress on early sensory-cognitive development. We capitalize on the methodologically sound maternal and infant physiological measures that were finalized in this study. A first aim of the new project is to study the stress system of the pregnant woman (i.e. the hypothalamus-pituitary-adrenal cortex (HPA)-axis and autonomic nervous system (ANS)), with physiological measures, to identify those atypical responses in highly stressed pregnant women which increase the risk of negative outcomes for the fetus. A second aim is to examine, by means of a randomized controlled trial, the effects of a standardized mindfulness-based stress reduction (MBSR) intervention on HPA-axis and ANS of the mother and ANS of the fetus, as well as on length of gestation at birth, birth weight and HPA-axis, ANS and sensory-cognitive functioning at two months of age. We expect that effective interventions during pregnancy will facilitate optimal growth and development of the offspring. The primary hypotheses to be tested in our study concern the effects of the MBSR intervention. We will determine whether the MBSR intervention is associated with: a) a decrease in stress symptoms (anxiety,

depression and distress) of the pregnant woman reflecting a better coping with stress; b) favorable changes in HPA-axis activity in the pregnant mother (e.g, steeper diurnal cortisol profile and lower cortisol awakening response); c) favorable changes in ANS activity in the pregnant woman (e.g., higher heart rate variability); d) favorable changes in ANS activity in the fetus and infant (e.g., higher heart rate variability); e) favorable birth outcomes (e.g., increased gestational age at birth and increased birth weight); f) more optimal early sensory-cognitive development, reflecting optimal brain function.

Study design

General procedure and subjects Sample (n=140). After obtaining permission from a nationally recognized medical ethics committee, eligible women, aged 18-40, will be recruited at 10-12 weeks* gestation for longitudinal study with infant follow-up. Women will be approached for participation at the Obstetrical and Gynecological Board consultations of several hospitals in the cities of Tilburg and Eindhoven and at midwife consultation institutes. Inclusion criteria are: (a) scores at least higher than the 67th percentile on standardized stress and anxiety questionnaires, (b) no current substance abuse problems, (c) no severe psychiatric problems, (e.g., psychoticism, current suicidal ideation), and (d) no pregnancy-associated medical problems such as diabetes or hypertension. Assessment time points (T): TI to T5 (see Table 1) and time table of the study (see Table 2) T1: once between 11 and 14 weeks gestational age (GA): pre-testing of maternal HPA-axis and ANS, before MBSR intervention sessions. T2: 2-weekly between 15 and 23 weeks GA, assessment of maternal HPA-axis and ANS and fetal ANS during the period of MBSR intervention sessions; T3: once at 29 weeks GA: post-testing of maternal stress system and of infant ANS, 6 weeks after completion of the MBSR intervention sessions; T4: two days after birth, postnatal follow-up immediately after birth T5: two months after birth; long term postnatal follow-up of mother and infant.

Intervention

A stress reduction intervention is given to the experimental group, weekly between week 15 and 23 of gestation and each session lasts 150 minutes, We will examine the short-term and long-term effects of a MBSR intervention given to pregnant women, using a randomized controlled trial in which the IG (n=70) receives a MBSR intervention and the matched CG (n=70) receives standard prenatal care. We will follow both groups of women and their infants up until two months after birth. After having given informed consent, women will be randomly assigned to the MBSR IG or matched CG. Women of the CG will receive care as usual and will be given a chance to participate in an MBSR intervention after T5. At baseline, before the intervention (T1), all participants will complete psychological measurements (i.e., questionnaires) and physiological measurements. The latter will include basal HPA-axis and ANS measurements (i.e., salivary cortisol and alpha-amylase) on the day before the stress

assessment and HPA-axis (i.e., cortisol) and ANS-functioning (i.e., heart rate variability (HRV)) during the standardized laboratory stress protocol, i.e. the Trier Social Stress Test (TSST). After randomization, the IG starts a standardized MBSR training [101] adapted for pregnant women [116]. The training consists of eight weekly sessions (about 7 women per group) with a duration of 150 minutes from week 15 to 23 of gestation (T2). In addition, participants are instructed to practice daily for at least 40 min; a booklet is provided containing relevant information. Six weeks after the training, i.e. at 29 weeks of gestation (T3), questionnaires, physiological measures (and biochemical assays), including at least a version of a mental arithmetic task of the TSST. Some of these measurements are also taken at T4 (2 days after birth) and/or T5 (2 months after birth). Moreover, fetal heart rate will be monitored at 22 (T2) and 29 (T3) weeks GA for 8 hrs continuously during the night. Finally, infant-HPA-axis (cortisol), ANS (alpha-amylase and HRV) and sensory-cognitive functioning (using an auditory event related potential paradigm), are measured at two months after birth (T5).

Study burden and risks

Completing the questionnaires takes 15 to 30 minutes; taking the saliva samples takes a few minutes every time; to attach and detach the VU-ambulant monitoring system will take 10 minutes. The observations in the university lab (2 times during pregnancy) take about 60 minutes For the Mindfulness-training (to reduce stress) there are 8 sessions that last 150 minutes each The final observation in the lab (including the baby and the mother) takes 60 to 75 minutes and completion of the questionnaires takes 30 minutes.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Pregnant woman: -18 to 40 year old -score higher then Pc 67 on standardised stress and anxiety questionnaires -no substance abuse problems -no severe psychiatric problems -no pregnancy-related medical problems (e.g. diabetes, hypertension) or obstetrical problems

Exclusion criteria

Pregnant woman: -other medical or obstetrical complications during this pregnancy -18 to 45 year old -score lower then Pc 67 on standardised stress and anxiety questionnaires -substance abuse problems -severe psychiatric problems -pregnancy-related medical problems (e.g. diabetes, hypertension) or obstetrical problems

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	140
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	13-12-2011
Application type:	First submission
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL38557.008.11