

PSYCHOPATHOLOGY AND ITS TREATMENT: IMPLICATIONS FOR THE FETUS AND INFANT.

Principal Organizer –proposer- (Nine Glangeaud-Freudenthal, Ph.D., President-Elect, Marcé Society, INSERM, Villejuif, France)

Co-organizers –if any- (Michael O’Hara, University of Iowa, Katherine Wisner, University of Pittsburgh, Vivette Glover and Martin Kammerer, Imperial College, London)

Description and justification of the symposium:

Maternal depression and anxiety during and after pregnancy and its treatment have profound implications for the welfare of both mother and baby (and fetus). The purpose of this symposium is to explore a number of related issues including (1) the nature of depression during pregnancy and the postpartum period and the extent to which symptomatically and biologically it is distinct from depression occurring at other times and (2) the impact of depression, anxiety, stress, and the use of psychotropic medications on child birth outcomes (e.g., gestational age, birth weight) and child cognitive and emotional development. These problems are long-standing ones for the field and their exploration will be of significant interest to participants in the congress. Dr. Glangeaud-Freudenthal will chair the session and introduce the speakers. Dr. Kammerer will set the stage for the symposium with his exploration of the diagnostic and biological characteristics of depression in pregnancy and the postpartum period. This talk will be followed by Dr. Wisner describe the risks to mothers and offspring of exposure to depression and antidepressant medication during pregnancy. Drs. Glover and O’Hara will end the session with two coordinated talks that address issues of stress and psychopathology and their impact on the fetus and child up to two years of age. As a result of attending this symposium, participants will: 1) understand the unique symptomatic and biologic characteristics of perinatal depression, 2) be able to describe the consequences to the mother and child of maternal use of antidepressant medication during pregnancy, and 3) appreciate the impact of stress and psychopathology during pregnancy on the developing child.

Speakers

1. Nine Glangeaud-Freudenthal, PhD, President-Elect, Marcé Society, INSERM, Villejuif, France) (*Symposium Chair*)
2. Martin Kammerer, MD, PhD, Imperial College, London
Diagnostic and biological characteristics of depression in pregnancy and postpartum
3. Katherine Wisner, MD, MS, University of Pittsburgh, Pittsburgh
Impact of SSRI antidepressants and major depression on pregnancy and infant outcomes
4. Vivette Glover, PhD, Imperial College London
The effects of prenatal stress and anxiety on fetal and child neurodevelopment: possible mechanisms
5. Michael O’Hara, PhD, University of Iowa, Iowa City
Maternal psychopathology and stress: fetal, infant, and toddler outcomes

Full information of the proposal contact person

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Other considerations

This symposium is being submitted by the Marcé Society. Nine Glangeaud-Freudenthal, the symposium chair, is President-Elect and will be President at the time of the March meeting.

Katherine Wisner is currently President. Vivette Glover is currently Treasurer. Michael O'Hara is a Past-President. Martin Kammerer is a Member.

Diagnostic and biological characteristics of depression in pregnancy and postpartum

Martin Kammerer, MD PhD, Alyx Taylor PhD, Vivette Glover MA PhD DSc, & Maureen Marks DPhil

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Background: The physiological changes in peripartum may affect symptoms of depression and impact diagnostic judgments in the peripartum and influence which symptoms discriminate depressed and non-depressed women. Second, the sharp fall in cortisol and CRH after childbirth suggests that the HPA axis characteristics of postpartum depression are different from melancholic depression the latter being characterized by high cortisol levels.

Methods: A modified version of the SCID was used to assess symptoms of depression and melancholic and atypical subtypes in pregnancy and the postpartum period. In a second study we investigated the diurnal output of saliva cortisol in women with symptoms of depression postnatally in 21 depressed and 30 non-depressed women at 7.5 weeks postpartum, and 21 non perinatal controls, collected saliva at waking, 30 minutes, and three and twelve hours post waking.

Results: The antenatal symptom pattern (n=892 women) was different from the postnatal. The sensitivity of the symptoms ranged from 0.7% to 51.6%, and specificity from 61.3% to 99.1%. The best discriminating symptoms were motor retardation/agitation and concentration antenatally, and motor retardation/agitation, concentration and fatigue postnatally.

In a subgroup of this sample (n=449) 17% of the cohort met SCID criteria for a depression at least once in pregnancy, melancholic depression (2.4%), atypical depression (4.4%), and non specified depression (10.2%). Mood reactivity, distinct quality of mood and sleep pattern discriminated between the two groups. Also, there was a significant difference in diurnal pattern of cortisol between postnatally depressed and non-depressed women, due to differences at waking and +30 minutes.

Discussion: These findings suggest that perinatal depression has different associated symptoms from depression at other times. The cortisol pattern in the postnatally depressed women is similar to that reported for PTSD and atypical depression, and may reflect a response in vulnerable women to the marked cortisol withdrawal that occurs after delivery.

Keywords: Perinatal depression, diagnosis, classification, HPA axis

References

Kammerer, M., M. N. Marks, et al. (2009). "Symptoms associated with the DSM IV diagnosis of depression in pregnancy and post partum." Arch Womens Ment Health **12**(3): 135-41.

Kammerer, M., A. Taylor, et al. (2006). "The HPA axis and perinatal depression: a hypothesis." Arch Womens Ment Health **9**(4): 187-96.

Taylor, A., V. Glover, et al. (2009). "Diurnal pattern of cortisol output in postnatal depression." Psychoneuroendocrinology **34**(8): 1184-8.

Impact of SSRI antidepressants and major depression on pregnancy and infant outcomes

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Background. Prenatal SSRI exposure is associated with a small absolute risk (if any) for major defects. Research interest has shifted beyond first-trimester SSRI treatment and malformations to later exposure and other reproductive outcomes. However, little is known about offspring development following prenatal exposure to SSRI beyond the neonatal period. Exposure to major depression is also associated with adverse pregnancy outcomes that overlap with those of antidepressants.

Methods: This observational study included 238 infant-mother dyads with SSRI and major depression (without SSRI) exposures and controls with neither exposure. Maternal depression and SSRI exposure assessments were completed at 20, 30, and 36 prenatal weeks and 3, 6.5, and 12 months postpartum. Infant Bayley Scales of Infant Development (BSID) evaluations (motor, cognitive, and behavioral) were completed at two postpartum time points.

Results: Maternal gestational weight gain was not significantly lower in SSRI treated women with or without adjustment for preconception body mass index (BMI). Women with unmedicated depression tended to have a pattern of higher mean preconception BMI, coupled with lower mean weight gain, than women treated with SSRIs or controls. The mean infant birth weight, length and head circumference measures were similar across groups. Neonatal signs did not differ across groups. Women who were treated with SSRI continuously or who had major depression continuously throughout pregnancy had a greater than 20% risk of preterm birth compared to 6% in the control group. The distribution of early (<34 weeks) and late preterm (>37 weeks) births were similar in SSRI exposed compared to depression exposed infants. In the 175 mother-infant pairs with BSID examinations, neither prenatal SSRI nor depression exposures were significant predictors of cognitive scores in infants across one year. Infants with SSRI exposure and preterm birth had significantly lower motor scores (which parallels findings from two recent studies) compared to control infants.

Discussion: The preterm birth rate in gravidas with continuous SSRI or continuous depression exposures was threefold higher than in controls, which is a converging finding in the literature. Although statistically significant, the magnitude of the effect of SSRI exposure on infant motor development was small and scores remained well within the normal range; however, the impact was measurable beyond the immediate neonatal period. Prenatal maternal depression did not impact infant development.

References: Wisner KL, Sit DK, Hanusa BH, Moses-Kolko EL, Bogen DL, Hunker DF, Perel JM, Jones-Ivey S, Bodnar L, Singer L. Major depression and antidepressant treatment: Impact on pregnancy and neonatal outcomes. *Am J Psych* 166(5):557-66, 2009.

The effects of prenatal stress and anxiety on fetal and child neurodevelopment: possible mechanisms

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There is good evidence from several prospective studies that prenatal maternal stress, anxiety or depression can have long term consequences for the development of the fetus and the child. We have shown a range of effects on neurodevelopment, and both behavioural and cognitive outcomes can be altered. Such fetal programming is independent of the postnatal environment, although the nature of maternal care can have a modifying influence.

In animal models there is good evidence for the mediating effects of the HPA axis in both mother and fetus. In humans the evidence is less clear. We have found an inverse association between amniotic fluid cortisol and child cognitive ability at 17 months, but only in insecurely attached infants. We have also found a strong correlation between maternal and fetal cortisol levels, which is greater in more anxious mothers. Prenatal anxiety may affect the function of the placenta in a way that allows the fetus to be exposed to higher levels of cortisol, and this may in turn alter fetal neurodevelopment. Our most recent research shows an inverse relationship between maternal anxiety and placental weight.

The effects of prenatal stress or anxiety on the child are clinically significant. It is important to detect emotional and relationship problems of women early in pregnancy and intervene appropriately for each woman, both for her benefit and that of her child.

References

Glover V, Bergman K, Sarkar P, O'Connor TG.(2009) Association between maternal and amniotic fluid cortisol is moderated by maternal anxiety. *Psychoneuroendocrinology*. 34(3) 430-5

K O'Donnell K, O'Connor TG, Glover V (2009) Prenatal stress and neurodevelopment of the child: focus on the HPA axis and the role of the placenta. *Dev Neurosci*,;31, 285-92.

Bergman K, Sarkar P, Glover V, O'Connor TG. (2010) Maternal Prenatal Cortisol and Infant Cognitive Development: Moderation by Infant-Mother Attachment. *Biol Psychiatry*. [Epub ahead of print]

Maternal psychopathology and stress: fetal, infant, and toddler outcomes

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Background: Maternal psychopathology and stress during the perinatal period are often associated with suboptimal birth outcomes and infant development. However, stress is often measured inadequately and infant outcomes are often limited. In two studies maternal psychopathology was measured during pregnancy and/or during the first 16-42 months postpartum. Hypotheses were tested regarding the association between maternal measures of stress and psychopathology and infant outcomes (including birth weight, gestational age, infant temperament, and measures of infant behavior reflecting behavioral self-control).

Methods: In study 1, 270 pregnant women were recruited early in pregnancy and followed to 16-months postpartum. Psychopathology and stress were assessed at three time points in pregnancy and after delivery. Infant outcomes were assessed at birth and at 16 months of age. In study 2, 180 women and their 24-42 month-old infants were observed in several scenarios. Psychopathology was assessed using the LIFE Interview covering the period from conception to the present.

Results: Preliminary analyses reveal several interesting findings. Maternal depression during pregnancy was associated with lower birth weight, gestational age, and Apgar scores. Maternal depression and anxiety are associated with difficult child temperament. Data analysis is just beginning for study 2; however, relatively high rates of depressive and anxiety disorders are present. Data analysis for both projects will be complete in October.

Discussion: Maternal psychopathology during pregnancy and the postpartum period is common and has negative consequences for the offspring. Finding from these two studies again are highlighting the risks to offspring of mothers suffering from depression and anxiety.

References: Forman, D, O'Hara, M. W., Stuart, S., Gorman, L., Larsen, K. & Coy, K. C. (2007). Effective treatment for postpartum depression is not sufficient to improve the developing mother-child relationship. *Development and Psychopathology*, 19, 585-602.

Keywords: maternal psychopathology, perinatal, infant