

Pregnancy affects appraisal of negative life events

Laura M. Glynn^{a,*}, Christine Dunkel Schetter^b, Pathik D. Wadhwa^a, Curt A. Sandman^a

^aDepartment of Psychiatry and Human Behavior, University of California, Irvine, 2501 Harbor Boulevard, No. 7, Costa Mesa, CA 92626, USA

^bDepartment of Psychology, University of California, Los Angeles, CA, USA

Received 24 June 2002; accepted 6 May 2003

Abstract

Objective: It has been demonstrated that physiological responses to stress are diminished late in pregnancy. This study investigates whether emotional responding is diminished as well by measuring affective responses to specific life events during pregnancy. **Methods:** A total of 292 pregnant women reported the occurrence of and affective responses to a range of major life events during gestation. Two analyses were conducted (across events and within events) on these responses to determine whether life events occurring in the first trimester were rated as more

stressful than those that occurred in the third trimester. **Results:** Both within-event and across-events analyses of responses to life events demonstrated that events occurring early in pregnancy were perceived as more stressful than events occurring later in pregnancy. **Conclusion:** Responses to stress and affective state are progressively altered in pregnant women, suggesting that timing of stress exposure during gestation may be critical in determining its impact.

© 2004 Elsevier Inc. All rights reserved.

Keywords: Affect; Emotion; Life events; Pregnancy; Prenatal stress; Preterm birth

Introduction

Prenatal stress is associated with a range of adverse outcomes in humans [1–7], with the most compelling evidence supporting the link between stress and the adverse birth outcomes of low birth weight and preterm birth [8–11]. Preterm delivery (gestational length <37 weeks) and low birth weight (birth weight ≤ 2500 g) account for a sizeable percentage of live births in the US and are the most prevalent causes of perinatal, neonatal and infant morbidity and mortality in nonanomalous infants [12]. Despite advances in prenatal medical care, the incidence of premature births has not decreased in the US in recent years [13].

The relation between stress and the adverse outcomes of low birth weight and shortened gestational length exists both when stress is measured as the occurrence of negative events [14–16] and when measured in the form of stress appraisals (such as reports of perceived stress or negative emotion [9,17,18]). However, these studies reveal mixed results, some indicating that stress is a predictor of adverse

birth outcome, and others finding no association (for reviews, see Refs. [10,19,20]). These discrepancies may exist because the relation is weak and inconsistent or because the construct of stress is not being adequately measured. Animal research suggests that it may be premature to conclude the former, because large causal effects of prenatal stress on adverse outcomes have been repeatedly observed (for a review, see Ref. [21]).

In order to characterize more precisely the effects of stress on birth outcome, it is critical to ascertain the variables that affect the amount of stress a woman experiences during pregnancy and that affect the impact of stress on birth outcomes. An understanding of these variables may help explain inconsistencies among studies examining the effects of stress on birth outcomes. A number of such factors have been identified, and these include race/ethnicity [22,23], acculturation [24] marital status [25], body mass index [26], obstetric risk [27], smoking [28], social support [29] socioeconomic status [30,31] and personality traits [18,32].

One rarely studied factor that may affect stress responses and the impact of stress during pregnancy is the timing of stress during gestation. It is well established that the timing of stress is important because of critical periods of development in the fetus [33,34]. However, timing of

* Corresponding author. Tel.: +1-714-940-1925; fax: +1-714-940-1939.

E-mail address: lglynn@uci.edu (L.M. Glynn).

stress could also be important because maternal responses to stressful events may differ depending upon when the events occur during gestation. Physiological responses to stressor challenge decrease as pregnancy advances. Responding of both the hypothalamic–pituitary–adrenal and sympathetic–adrenal–medullary systems are progressively dampened during pregnancy [35–39]. Such changes in the physiological stress response may be associated with attenuated psychological responding. For example, Glynn et al. [14] found that appraisals of the emotional impact of a major earthquake were related to the time of gestation at which the earthquake occurred. Those who experienced the earthquake early in pregnancy rated it as more stressful than those who experienced it late in pregnancy.

The purpose of the present study was to characterize stress appraisals at different stages of pregnancy by examining affective responses to a diverse set of stressful life events. If dampened physiological reactivity found in other studies is associated with diminished affective responding, then we should find that life events experienced early in pregnancy are appraised as more stressful than those experienced later.

Method

Participants

A total of 292 women who were attending a prenatal clinic associated with the University of California, Irvine, participated. Participants were recruited into the study during the late second or early third trimester of pregnancy. Sixty-two percent of the women who were approached agreed to participate. Those consented had a mean age of 26.0 years, were 46.6% primiparous, 63.3% married, 44.5% Hispanic and 48.8% White non-Hispanic. Each woman had a singleton pregnancy. All participants gave written, informed consent and the study was approved by the Institutional Review Board of the University of California, Irvine.

Gestational age assessment

Because we were interested in the timing of stress during pregnancy, it was particularly important that our estimates of date of conception and gestational age be accurate. Gestational age was determined by the best obstetric estimate based on a combination of last menstrual period and early uterine size and was confirmed by ultrasonography at 20 weeks. For cases in which a discrepancy between last menstrual period, clinical examination and ultrasonography exceeded the margin of error for ultrasonographic biometry for gestational age, the estimate of gestational age was revised according to the results of the ultrasonography.

Life events assessment

Participants completed an interview concerning 24 major life events once during gestation and once postpartum. The life events instrument was adapted for pregnancy from one employed in a large epidemiological study of mental health [40]. At the first assessment (approximately 32 weeks of gestation), all life events from conception until that point in pregnancy were reported. At the second assessment (approximately 6 weeks postpartum), women reported all events that had occurred since the first interview at 32 weeks of gestation until birth. In addition to reporting whether or not any of the events had occurred, each woman also reported the date of the event and how upsetting or aversive she had found the event. This affective rating was made on a four-point scale with the endpoints “not at all” and “extremely.” Approximately one third ($n=93$) of the women were excluded from the life events analyses because they reported experiencing none of the life events included in the instrument during pregnancy. We conducted analyses comparing those who experienced life events to those who did not on several demographic and medical variables.

Of the 24 life events, 18 were included in the analyses (see Table 1 for a list of events). Five events were excluded because they occurred less than 10 times in the population and thus were not of sufficient number to include in the analyses (these events included: severe car accident, burglary, mugging or attack, sexual harassment or discrimination, and racial discrimination). Natural disasters were also excluded because data from this event were examined and reported elsewhere (see Ref. [14]). We conducted two different analyses on these life events, one across events and one within events. In the analysis across events, for each woman, we randomly selected one life event from among those that she had experienced (if she only had experienced one, we chose that one). This was necessary to avoid

Table 1
Mean affective rating of life events for the first and third trimesters

Event	First trimester	Third trimester
Change in living conditions	2.20 ($n=20$)	1.63 ($n=24$)
Extra responsibilities	2.55 ($n=20$)	2.00 ($n=20$)
Serious injury or illness	3.55 ($n=11$)	3.46 ($n=28$)
Financial problems	3.47 ($n=19$)	3.35 ($n=17$)
Problems in romantic relationship	3.74 ($n=19$)	3.08 ($n=13$)
Serious arguments	3.60 ($n=10$)	3.29 ($n=21$)
Job loss	2.89 ($n=19$)	3.13 ($n=16$)
Problems at work	3.43 ($n=14$)	3.60 ($n=10$)
Death of family or friend	4.00 ($n=6$)	3.87 ($n=16$)
Separation or divorce	3.00 ($n=10$)	2.82 ($n=11$)
Separated from romantic partner	3.42 ($n=12$)	2.86 ($n=7$)
Problems with alcohol or drugs	3.33 ($n=9$)	3.25 ($n=8$)
Someone important moves away	3.22 ($n=9$)	2.86 ($n=7$)
Emotional problems	3.33 ($n=9$)	3.25 ($n=8$)
Legal problems	3.50 ($n=6$)	3.10 ($n=10$)
Sexual problems	3.50 ($n=6$)	3.12 ($n=8$)
Loss of valuable possession	3.00 ($n=2$)	3.80 ($n=6$)
Threatened with physical harm	4.00 ($n=5$)	4.00 ($n=2$)

problems of nonindependence — assuring that each woman contributed a rating of only one life event. After identifying an event, the affective rating of that particular event was transformed to a z score based on the distribution of all responses for that same event (responses from every participant who had experienced that event). The transformation to a standardized score was necessary because the mean rating of each event differed widely. For example, the death of a family member or friend had an average rating of 3.83 while the burden of extra heavy responsibilities had an average rating of 2.56. By standardizing each rating based on the distribution of ratings for that particular life event, we were able to compare responses to different life events with a range of reported severity. We then conducted an analysis of variance (ANOVA) to determine whether the trimester in which an event occurred was associated with the affective response to the event (z score).

For the within-event analysis, the mean affective response of all women who experienced a life event in the first trimester was compared to the mean response of all women who experienced the same life event in the third trimester. For example, the mean rating of all participants who experienced legal trouble during the first trimester was compared to the mean rating of all participants who experienced legal trouble during the third trimester. After calculating the means for each event, we then tested whether the number of times the rating for the first trimester exceeded that of the third trimester was greater than would be expected by chance. This second analysis determines whether a change in the emotional impact of life events during pregnancy is due to a change in the perception of a few life events only, or whether life events in general are perceived as less stressful later in pregnancy.

Results

Comparison of women with life events to those with no life events

Comparisons were conducted to examine whether the subset of women who experienced life events during pregnancy ($n=199$) differed from those who had not experienced life events ($n=93$) on several demographic and medical factors. t Tests revealed that the two groups did not differ significantly in maternal age, parity or length of gestation (all t 's < 1.17 ; P 's $> .29$). Chi-square tests revealed no difference in the ethnic distribution or marital status between the study sample and the remainder of the sample (both χ^2 's < 2.67 ; P 's $> .45$).

Life events

The across-events analysis, which examined whether the standardized affective response scores to a range of life events differed depending on the timing of the event,

confirmed that women who experienced life events early in pregnancy rated them as more stressful than those who experienced them later in pregnancy (see Fig. 1). A one-way ANOVA with trimester of pregnancy as the between-subjects factor yielded a main effect of trimester with a first trimester mean z score of .14, a second trimester mean of .03 and a third trimester mean of $-.34$ [$F(2,196)=4.77$; $P<.01$]. Post hoc comparisons determined that the first trimester mean was significantly higher than the third trimester mean (Sheffé test; $P<.05$) while the second trimester mean did not differ statistically from the first trimester mean (Sheffé test; $P=.82$) and was marginally significantly higher than the third trimester mean (Sheffé test; $P=.07$).

The results of the second analysis within events are consistent with the results of the between-events analysis, suggesting that the emotional impact of specific life events declines as pregnancy progresses. Table 1 shows for each life event the mean affective response for the first and third trimesters. As expected, more often than predicted by chance, the first trimester rating exceeded the third trimester rating. In fact, for 14 out of the 18 life events, a specific stressor was reported to be less upsetting if it occurred during the third trimester than if it occurred during the first (binomial test; $P<.05$). This analysis demonstrates the wide range of events for which perception of stress differs depending on stage of pregnancy.

Assessment of sociodemographic variables

Because ethnicity, parity and socioeconomic status could potentially influence stress appraisals [22,23,30,31,41], we included these variables in an ANCOVA. We entered parity (primiparous vs. multiparous), ethnicity (White non-Hispanic vs. all other ethnicities) and annual household income (income was measured with an ordinal scale ranging from 1 = less than US\$10,000 to 10 = over US\$90,000) as covariates in the model with trimester of life event

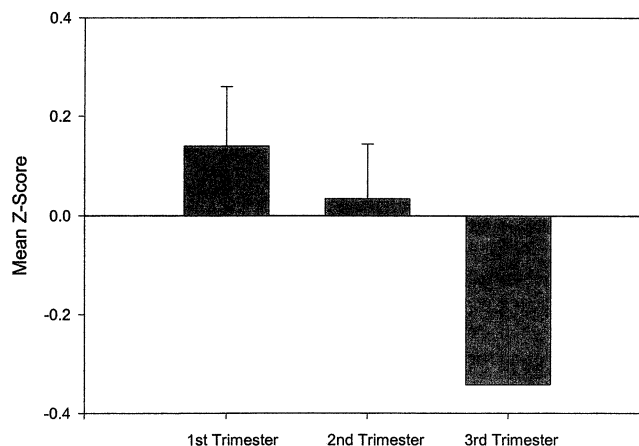


Fig. 1. Mean (and S.E.) stress appraisal during each trimester of pregnancy ($N=199$).

occurrence. With the addition of the three covariates, the main effect of trimester of occurrence remained unaltered [$F(2,189)=4.90$; $P<.01$]. First trimester stress appraisals were higher than third trimester appraisals. Parity was associated with stress appraisals ($P<.01$), with primiparous women exhibiting lower ratings on average than multiparous women. Neither ethnicity nor household income showed a statistically significant association with stress appraisals (both P 's $>.4$).

Do the different assessment periods account for the timing effects?

Because our life events appraisals were conducted both during pregnancy and during the postpartum period, and because mood (including depression and anxiety [42]) may differ systematically between these two periods, a final analysis was included to assure that emotional state at the time of assessment did not account for the differences in affective responses. An additional ANOVA was conducted including only those women who had provided the stress appraisals at the pregnancy interview (32 weeks of gestation). If systematic differences in mood between the assessment points did not account for the results, then the decline in stress appraisals should remain when the appraisals included in the analysis were limited to one assessment period. With the analysis of the 32-week subsample, the effect of timing on stress appraisals remained unchanged. Women who experienced the stressor in the first trimester rated it as more stressful than those who experienced it during the third trimester [$F(2,150)=4.26$; $P<.05$].

Discussion

Our data suggest that emotional responding does change as pregnancy advances. Life events that are experienced later in pregnancy are perceived as less stressful than those that occur earlier. These findings extend those from a previous study showing that responses to the acute stress of a major earthquake decreased as pregnancy advanced [14]. The present data show that emotional responses to eighteen separate life events are attenuated later in pregnancy as well.

It is possible that the results could be associated with some sort of recall bias due to the fact that the number of days between the life event and the recall of that event was not consistent (there was a longer distance between event and recall for those events that occurred early in pregnancy compared to late). We believe that a recall bias associated with this difference does not provide a plausible explanation for our results. In order for a recall bias explanation to account for our results, it would have to postulate that the larger the distance between the negative event and the recall, the more severe the report of the event. Empirically, this does not appear to be the case. At least one study [43] has

shown that the tendency to overestimate the intensity of emotions from the more distant past does not exist.

There are both peripheral and central physiological changes during pregnancy that could account for the altered emotional responding we have documented. Pregnancy is associated with progressive changes in the endocrine, immune and cardiovascular systems [44–47], and these peripheral changes affect responding to exogenous stressors [37,39,48]. For example, blood pressure, heart rate and catecholamine responses to stress are reduced during pregnancy [35–39]. It is possible that these peripheral changes have implications for central processes as well. Several experimental studies have demonstrated a role for hormones and cytokines in initiating changes in the major neurotransmitter systems [49–54]. In addition, there exist pregnancy-associated central changes that, in conjunction with or independently of the peripheral changes, could account for our findings. Recent nonhuman animal studies suggest that during pregnancy, changes in the neurotransmitter oxytocin may induce alterations in stress responses and anxiety-related behavior [55,56].

The notion of critical periods during pregnancy is not new. For some time, it has been recognized that during certain periods of fetal development, especially early in gestation, insults and teratogens have particularly devastating consequences [33,34]. Because of pregnancy-related changes in maternal affect and physiology, the strength of the relation between stress and length of gestation may also depend, in part, on the timing of stress. Our findings suggest that the timing of stress in human pregnancy is important in determining its impact on affective responses. In addition, preliminary evidence suggests that early stress is more likely to result in shorter gestation than is later stress [14]. A failure to account for when the stress happens may result in a misestimation of the relation between stress and pregnancy outcome.

Acknowledgments

This work was supported by USPS (NIH) grants HD-28413 and HD-40967.

References

- [1] Barker DJP. Mothers, babies and health in later life. 2nd ed. Edinburgh: Churchill Livingstone, 1998.
- [2] Carmichael SL, Shaw GM. Maternal life event stress and congenital anomalies. *Epidemiology* 2000;11:30–5.
- [3] Meijer A. Child psychiatric sequelae of maternal war stress. *Acta Psychiatr Scand* 1985;72:505–11.
- [4] Nimby GT, Lundberg L, Sverger T, McNeil TF. Maternal distress and congenital malformations: do mothers of malformed fetuses have more problems? *J Psychiatr Res* 1999;33:291–301.
- [5] Stott DH. Follow-up study from birth of the effects of prenatal stresses. *Dev Med Child Neurol* 1973;15:770–87.
- [6] van Os J, Selton JP. Prenatal exposure to maternal stress and

- subsequent schizophrenia: the May 1940 invasion of The Netherlands. *Br J Psychiatry* 1998;172:324–6.
- [7] O'Connor TG, Heron J, Golding J, Beveridge J, Glover V. Maternal antenatal anxiety and children's behavioral/emotional problems at 4 years: report from the Avon longitudinal study of parents and children. *Br J Psychiatry* 2002;180:502–8.
- [8] Copper RL, Goldenberg RL, Das A, Elder N, Swain M, Norman G, Ramsey R, Cotroneo P, Collins BA, Johnson F, Jones P, Meier AM. The preterm prediction study: maternal stress is associated with spontaneous preterm birth at less than thirty-five weeks' gestation. *Am J Obstet Gynecol* 1996;175:1286–92.
- [9] Hedegaard M, Henriksen TB, Secher NJ, Hatch M, Sabroe S. Do stressful life events affect duration of gestation and risk of preterm delivery? *Am J Epidemiol* 1996;7:339–45.
- [10] Paarlberg KM, Vingerhoets AJ, Passchier J, Dekker GA, Van Geijn HP. Psychosocial factors and pregnancy outcome: a review with emphasis on methodological issues. *J Psychosom Res* 1995;39:563–95.
- [11] Wadhwa PD, Sandman CA, Porto M, Dunkel-Schetter C, Garite TJ. The association between prenatal stress and infant birth weight and gestational age at birth: a prospective investigation. *Am J Obstet Gynecol* 1993;169:858–65.
- [12] Matthews TJ, Curtin SC, MacDorman MF. Infant mortality statistics from the 1998 period. Linked birth/infant death data set. National vital statistics reports. vol. 48. Hyattsville (MD): National Center for Health Statistics, 2000. pp. 1–28.
- [13] Ventura SJ, Martin JA, Curtin SC, Matthews TJ. Births: final data for 1997. In: National vital statistics reports, . Hyattsville (MD): National Center for Health Statistics, 1999;vol. 47. pp. 1–94.
- [14] Glynn LM, Wadhwa PD, Dunkel-Schetter C, Chicz-DeMet A, Sandman CA. When stress happens matters: effects of earthquake timing on stress responsivity in pregnancy. *Am J Obstet Gynecol* 2001;184:637–42.
- [15] Mutale T, Creed F, Maresh M, Hunt L. Life events and low birth-weight—analysis by infants preterm and small for gestational age. *Br J Obstet Gynaecol* 1991;98:166–72.
- [16] Newton RW, Hunt LP. Psychosocial stress in pregnancy and its relation to low birth weight. *Br Med J* 1984;288:1191–4.
- [17] Lobel M, Dunkel-Schetter C, Scrimshaw SC. Prenatal maternal stress and prematurity: a prospective study of socioeconomically disadvantaged women. *Health Psychol* 1992;11:32–40.
- [18] Rini CK, Dunkel-Schetter C, Wadhwa PD, Sandman CA. Psychological adaptation and birth outcomes: the role of personal resources, stress, and sociocultural context in pregnancy. *Health Psychol* 1999;18:333–45.
- [19] Hoffman S, Hatch MC. Stress, social support and pregnancy outcome: a reassessment based on recent research. *Paediatr Perinat Epidemiol* 1996;5:380–405.
- [20] Lobel M. Conceptualizations, measurement, and effects of prenatal maternal stress on birth outcomes. *J Behav Med* 1994;17:225–73.
- [21] Braastad BO. Effects of prenatal stress on behavior of offspring of laboratory and farmed mammals. *Appl Anim Behav Sci* 1998;61:159–80.
- [22] Zambrana RE, Dunkel-Schetter C, Collins NL, Scrimshaw SC. Mediators of ethnic-associated differences in infant birth weight. *J Urban Health* 1999;76:102–16.
- [23] Collins JW, Shay DK. Prevalence of low birth weight among Hispanic infants with United States-born and foreign-born mothers: the effect of urban poverty. *Am J Epidemiol* 1994;139:184–92.
- [24] Zambrana RE, Scrimshaw SCM, Collins N, Dunkel-Schetter C. Prenatal health behaviors and psychosocial risk factors in pregnant women of Mexican origin: the role of acculturation. *Am J Public Health* 1997;87:1022–6.
- [25] Tilden VP. The relation of selected psychosocial variables to single status of adult women during pregnancy. *Nurs Res* 1984;33:102–7.
- [26] Cliver SP, Goldenberg RL, Cutter GR, Hoffman HJ, Copper RL, Gotlieb SJ, Davis RO. The relationships among psychosocial profile, maternal size and smoking in predicting fetal growth retardation. *Obstet Gynecol* 1992;80:262–7.
- [27] Georgas J, Giakoumaki E, Georgoulas N, Koumandakis E, Kaskarelis D. Psychosocial stress and its relation to obstetrical complications. *Psychother Psychosom* 1984;41:200–6.
- [28] Paarlberg KM, Vingerhoets AJ, Passchier J, Heinen AGJJ. Smoking status in pregnancy is associated with daily stressors and low well-being. *Psychol Health* 1999;14:87–96.
- [29] Collins NL, Dunkel-Schetter C, Lobel M, Scrimshaw SC. Social support in pregnancy: psychosocial correlates of birth outcomes and postpartum depression. *J Pers Soc Psychol* 1993;65:1243–58.
- [30] Pagel MD, Smilkstein G, Regen H, Montano D. Psychosocial influences on new born outcomes: a controlled prospective study. *Soc Sci Med* 1990;30:597–604.
- [31] Seguin L, Potvin L, St. Denis M, Loiselle J. Chronic stressors, social support, and depression in pregnancy. *Obstet Gynecol* 1995;85:583–9.
- [32] Lobel M, DeVincent CJ, Kaminer A, Meyer BA. The impact of prenatal maternal stress and optimistic disposition on birth outcomes in medically high-risk women. *Health Psychol* 2000;19:544–53.
- [33] Beckman DA, Brent R. Basic principles of teratology. In: Reece AE, Hobbins JC, Mahoney M.J., Petrie R.H., editors. *Medicine of the fetus and mother*. Philadelphia (PA): J.B. Lippincott, 1992. pp. 293–9.
- [34] Grimm VE. Effect of teratogenic exposure on the developing brain: research strategies and possible mechanisms. *Dev Pharmacol Ther* 1987;10:328–45.
- [35] Barron WM, Mujais SK, Zinaman M, Bravo EL, Lindheimer MD. Plasma catecholamine responses to physiologic stimuli in normal human pregnancy. *Am J Obstet Gynecol* 1986;154:80–4.
- [36] Matthews KA, Rodin J. Pregnancy alters blood pressure responses to psychological and physical challenge. *Psychophysiology* 1992;29:232–40.
- [37] Nisell H, Hjendahl P, Linde B, Lunell NO. Sympatho-adrenal and cardiovascular reactivity in pregnancy-induced hypertension: I. Responses to isometric exercise and a cold pressor test. *Br J Obstet Gynaecol* 1985;92:554–60.
- [38] Nisell H, Hjendahl P, Linde B, Lunell NO. Sympathoadrenal and cardiovascular reactivity in pregnancy-induced hypertension: II. Responses to tilting. *Am J Obstet Gynecol* 1985;152:554–60.
- [39] Schulte HM, Weisner D, Allolio B. The corticotropin releasing hormone test in late pregnancy: lack of an adrenocorticotropin and cortisol response. *Clin Endocrinol* 1990;33:99–106.
- [40] Golding JM. Role occupancy and role-specific stress and social support as predictors of depression. *Basic Appl Soc Psychol* 1989;10:173–95.
- [41] Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis. *Bull World Health Organ* 1987;65:663–737.
- [42] Evans J, Heron J, Francomb H, Oke S, Golding J. Cohort study of depressed mood during pregnancy and after childbirth. *BMJ* 2001;323:257–60.
- [43] Levine LJ. Reconstructing memory for emotions. *J Exp Psychol Gen* 1997;126:165–77.
- [44] Monga M, Creasy RK. Cardiovascular and renal adaptation to pregnancy. In: Creasy RK, Resnick R, editors. *Maternal–fetal medicine: principles and practice*. Philadelphia (PA): Saunders, 1994. pp. 758–67.
- [45] Strelkauskas AJ, Davis IJ, Dray S. Longitudinal studies showing alternations in the levels and functional response of T and B lymphocytes in human pregnancy. *Clin Exp Immunol* 1972;32:531–9.
- [46] Szereday L, Varga P, Szekeres-Bartho J. Cytokine production by lymphocytes in pregnancy. *Am J Reprod Immunol* 1997;38:418–22.
- [47] Yen SC. Endocrinology of pregnancy. In: Creasy RK, Resnick R, editors. *Maternal–fetal medicine: principles and practice*. Philadelphia (PA): Saunders, 1994.
- [48] Chrousos GP, Torpy MB, Gold PW. Interactions between the

- hypothalamic–pituitary–adrenal axis and the female reproductive system: clinical implications. *Ann Intern Med* 1998;129:229–40.
- [49] Bianchi M, Sacerdote P, Panerai AE. Cytokines and cognitive function in mice. *Biol Signals Recept* 1998;7:45–54.
- [50] Brace M, McCauley E. Oestrogens and psychological well-being. *Ann Med* 1997;29:283–90.
- [51] Joels M, Karten Y, Heslen W, de Kloet ER. Corticosteroid effects on electrical properties of brain cells: temporal aspects and role of anti-glucocorticoids. *Psychoneuroendocrinology* 1997;22:S81–6.
- [52] Rubinow DR, Schmidt PJ, Roca CA. Estrogen–serotonin interactions: implications for affective regulation. *Biol Psychiatry* 1998;44:839–50.
- [53] Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocr Rev* 2000;21:55–89.
- [54] Wolf OT, Kirschbaum C. Actions of dehydroepiandrosterone and its sulfate in the central nervous system: effects on cognition and emotion in animals and humans. *Brain Res Brain Res Rev* 1999;30:264–88.
- [55] Neumann ID, Johnstone HA, Hatzinger M, Liebsch G, Shipston M, Russell JA, Landgraf R, Douglas AJ. Attenuated neuroendocrine responses to emotional and physical stressors in pregnant rats involve adenohipophysial changes. *J Physiol* 1998;508:289–300.
- [56] Neumann ID, Torner L, Wigger A. Brain oxytocin: differential inhibition of neuroendocrine stress responses and anxiety-related behavior in virgin, pregnant and lactating rats. *Neuroscience* 2000;95:567–75.