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Anxiety during pregnancy and autonomic nervous system activity: A longitudinal observational and cross-sectional study

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ABSTRACT

Objectives: To assess the longitudinal change in autonomic nervous system (ANS) activity during pregnancy and the association between anxiety during pregnancy and ANS activity.

Methods: Pregnant Japanese women with a singleton fetus and normal pregnancy were recruited ($n = 65$). ANS activity and anxiety were measured using a self-rating questionnaire at approximately 20, 30, and 36 weeks of gestation. Very low (VLF) and high (HF) frequency bands of heart rate variability spectrums were used. Anxiety was assessed using the Japanese version of the State-Trait Anxiety Inventory. A score of 45 or more on trait-anxiety and the other represent the trait-anxiety group and the non- trait-anxiety group, respectively. The state-anxiety group and the non-state-anxiety group were defined in the same manner.

Results: Longitudinal observation of individual pregnant women indicated the significant increasing trend ($p = 0.002$) of VLF power and the significant decreasing trend ($p < 0.001$) of HF power during 20 to 36 gestation weeks. Compared with the non-trait-anxiety group, the trait-anxiety group had significantly lower VLF values at 20 gestational weeks ($p = 0.033$) and had significantly lower HF values at 30 and 36 gestational weeks ($p = 0.015$ and $p = 0.044$, respectively). The increasing rate of VLF from 20 to 36 gestational weeks was higher among the trait-anxiety group. The same associations were observed between the state-anxiety and non-state-anxiety groups at 20 gestational weeks.

Conclusions: Anxiety during pregnancy decreased heart rate variability. Anxiety in second trimester pregnancy promoted a subsequent increase in sympathetic activity.

1. Introduction

1.1. Background

Because of biological, psychosocial, and environmental factors, psychological disorders such as maternity blues and postpartum depression readily occur during the postpartum period [1]. Such disorders may cause dysfunctions in not only child-rearing but also mother-child interactions and have also been associated with long-term negative impacts on a child's emotional and behavioral development [2,3]. It has been suggested that a mother's problems can negatively impact the physical and psychological development of her infant [4]. In recent years, suicide rates have been high due to postpartum depression and other psychiatric factors [5–7]; therefore, prevention of severe and prolonged postpartum depression is of urgent importance.

It is becoming clear that depression and anxiety occur even more frequently during pregnancy than during the postpartum period [8,9]. According to an epidemiological survey performed in Japan, the prevalence rate of major depressive disorder during pregnancy is 5.6% and that of generalized anxiety disorder is 2.8%; both of these rates are higher than those during the postpartum period, when the occurrence of major depressive disorder is 5.0% and that of generalized anxiety disorder is 0.7% [10]. Surveys using the Edinburgh Postnatal Depression Scale show that the rates of depressive tendencies during pregnancy only, during pregnancy and the postpartum period, and during the postpartum period only were 11.1%, 6.6%, and 10.4%, respectively, indicating that 1 in 6 pregnant women have experienced depressive tendencies [11].

It has been suggested that depression and anxiety in pregnant women are related to premature birth, reduced birthweight, emotional and behavioral development disorders in the infant, gestational hypertension, preeclampsia, and other abnormalities during the

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gestational phase [12–14]. Regarding the underlying neuroendocrine system mechanisms, it is thought that hyperactivation of the sympathetic-adrenal-medullary axis and of the hypothalamic-pituitary-adrenal axis have an impact on growth and development during pregnancy until delivery and after the child is born [12–15]. Prior researches have reported reduced heart rate variability (HRV), decreased parasympathetic activity, and an overall shift of autonomic balance toward sympathetic predominance in individuals with depression and anxiety disorders [16–20]. There is limited research on the relationship between psychological disorders and autonomic nervous activity based on HRV during pregnancy [21–23].

Regarding autonomic nervous system activity in pregnant women, it has been reported that, compared with the non-pregnant phase, there is a decrease in sympathetic activity and increased parasympathetic activity during the first trimester; as the number of pregnancy weeks increases to the third trimester, this changes to increased sympathetic activity and decreased parasympathetic activity [24–35]. It has also been suggested that the increased sympathetic activity and decreased parasympathetic activity that characterize autonomic nervous system activity before delivery return to pre-pregnancy levels 3 months after delivery [36,37]. Gestational hypertension and preeclampsia have been reported to be due to sympathetic hyperactivity [27,38,39]. The autonomic nervous system is greatly involved in the physiological changes that occur in the female body as pregnancy progresses.

1.2. Objectives

The first aim of the present study was to perform longitudinal observation of individual pregnant women to clarify autonomic nervous system trends. The second aim was to clarify relationships between anxiety and autonomic nervous system activity according to gestational week. Our research results provide fundamental information for the creation of indices that are sorely needed for objective evaluations of physiological changes induced by anxiety during pregnancy to provide more effective support.

2. Subjects and methods

2.1. Participants

Study subjects were pregnant Japanese women aged 20 years or older at 16–19 weeks of gestation during enrollment. All had undergone prenatal examinations between October 2013 and July 2015 at the obstetrics and gynecology department of one general hospital in Aichi prefecture, Japan. All pregnant subjects had a singleton fetus. Exclusion criteria were as follows: chronic physiological or psychological disorders; alcohol consumption; smoking; obstetric or medical complications, including pregnancy-induced hypertension, placenta previa, and others; and pregnancy contemporaneous with treatment for a psychological disorder that affected the subject physiologically or psychologically. A total of 81 pregnant women participated in this study.

Written informed consent was obtained for each participant after explanation of the study aims and procedures. This study was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) and the study protocol was approved by the Ethics Review Committee of Nagoya University School of Medicine (Approval No. 11-174).

2.2. Study design and measures

Data collection was performed at approximately 20 weeks of gestation, approximately 30 weeks of gestation, and approximately 36 weeks of gestation. Whenever collecting data, we measured autonomic nervous system activity and anxiety using a self-rating questionnaire. Additionally, demographic and obstetric data were collected from the medical records. Data included age, parity, body height, and body weight during the non-pregnant condition at the three aforementioned gestational week data collection periods and at delivery.

2.2.1. Autonomic nervous system activity

HRV was measured to specifically examine the autonomic nervous system activity of pregnant women. The subjects assumed recumbent positions, either semi-Fowler's position or left/right lateral decubitus, to avoid supine hypotensive syndrome. After 10 min of rest in each position, R-R intervals were recorded for 5 min using a program for heartbeat fluctuation during real-time analysis (MemCalc/Bonaly Light; GMS Co., Ltd., Tokyo, Japan) and a small monitor attached to two electrodes (Wireless living body sensor RF-ECG; GMS Co., Ltd.). All pregnant women were measured at the same time of day (9:00–13:00, > 90 min after a meal) to avoid effects of circadian rhythms on heart rate variability.

R-R intervals were calculated using power spectral analysis with fast Fourier transformation. The range of 0.15–0.4 Hz was considered high-frequency (HF) power and the range of 0.003–0.04 Hz was considered very-low-frequency (VLF) power. HF power is related to respiratory sinus arrhythmia and is reflective of cardiac vagal function, whereas VLF power is not well defined in term of physiological mechanisms [40–44]. VLF power has been associated with thermoregulation and the renin-angiotensin system [45] and used as an indicator of slow temporal processes regulated by sympathetic nervous system [44].

2.2.2. Anxiety

Anxiety was assessed using the Japanese version of the State-Trait Anxiety Inventory [46] in which 20 items assess the trait-anxiety measure, reflecting a more stable personality characteristic over time. The other 20 items assess the state-anxiety measure, reflecting transient characteristics of anxiety. Each item is scored on a 4-point Likert scale (from 1 to 4), with the minimum and maximum total scores being 20 and 80, respectively.

During this study, trait-anxiety was evaluated at one time point (approximately 20 or 30 weeks of gestation; 22.3 ± 3.0 weeks) and state-anxiety was evaluated at three different time points (approximately 20, 30, and 36 weeks of gestation; 21.4 ± 1.2 weeks, 31.0 ± 0.9 weeks, 36.1 ± 0.6 weeks, respectively). A score of 45 or more on trait-anxiety and that of < 45 represent the trait-anxiety group and the non-trait-anxiety group, respectively. Similarly, a score of 45 or more on state-anxiety and that of < 45 at each of three different time points represent the state-anxiety group and the non-state-anxiety group, respectively.

2.3. Data analysis

First, HF and VLF were transformed using Log10 to obtain a normal distribution, because they were skewed. We examined the change in HRV and heart rate from 20 to 36 gestational weeks among those subjects whose variables were available at three time points. A repeated-measures analysis of variance was used for comparisons among the three gestational week time points. A paired *t*-test with Bonferroni correction was used for multiple comparisons. Geometric mean and mean ± standard deviation were calculated and converted to the original scale of measurement. Second, the frequency domain values were compared between the trait-anxiety group and the non-trait-anxiety group using Mann–Whitney *U* test. Similar analyses were performed for the state-anxiety group and the non-state-anxiety group according to gestational week. We used a significance level of 5% and a borderline significance level of 10% (i.e., $0.05 \leq p < 0.1$). SPSS 23.0J version for Windows software (IBM, Armonk, NY, USA) was used for the analysis.