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Anxious women do not show the expected decrease in cardiovascular stress responsiveness as pregnancy advances

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ABSTRACT

Altered stress responsiveness is a risk factor for mental and physical illness. In non-pregnant populations, it is well-known that anxiety can alter the physiological regulation of stress reactivity. Characterization of corresponding risks for pregnant women and their offspring requires greater understanding of how stress reactivity and recovery are influenced by pregnancy and women's anxiety feelings. In the current study, women were presented repeatedly with mental arithmetic stress tasks in the first and third pregnancy trimester and reported their trait anxiety using the state trait anxiety inventory. Cardiovascular stress reactivity in late pregnancy was lower than reactivity in the first pregnancy trimester (heart rate (HR): $t(197) = 4.98$, $p < .001$; high frequency heart rate variability (HF HRV): $t(196) = -2.09$, $p = .04$). Less attenuation of stress reactivity occurred in more anxious women (HR: $b = 0.15$, SE = 0.06, $p = .008$; HF HRV: $b = -10.97$, SE = 4.79, $p = .02$). The study design did not allow the influence of habituation to repeated stress task exposure to be assessed separately from the influence of pregnancy progression. Although this is a limitation, the clear differences between anxious and non-anxious pregnant women are important, regardless of the extent to which differing habituation between the groups is responsible. Less dampened stress reactivity through pregnancy may pose long-term risks for anxious women and their offspring. Follow-up studies are required to determine these risks.

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1. Introduction

Pregnant women undergo marked changes in maternal cardiovascular function during pregnancy, such as increased basal stroke volume (SV) and heart rate (HR) (Abbas, Lester, & Connolly, 2005; Silversides & Colman, 2007). The autonomic nervous system (ANS) plays a central role in these changes. Basal ANS activity is shifted towards higher sympathetic (e.g., shorter pre-ejection period (PEP) and increased skin conductance level (SCL)) and lower vagal modulation (e.g., reduced HR variability (HRV)) over the course of pregnancy (DiPietro, Costigan, & Gurewitsch, 2005; Ekholm & Erkkola, 1996; Kuo, Chen, Yang, Lo, & Tsai, 2000).

These changes go along with attenuated cardiovascular responses to stress, as HR and blood pressure (BP) reactivity are typically attenuated as pregnancy progresses (DiPietro, Costigan, & Gurewitsch, 2003; Entringer et al., 2010; Matthews & Rodin, 1992). Studies of ANS stress responsiveness during pregnancy are rare. Evidence of declining SCL stress reactivity between 24 and 36 weeks gestation is an important finding (DiPietro et al., 2003) and a report of decreased HRV responsiveness with advancing pregnancy is valuable but this finding had marginal statistical significance (Klinkenberg et al., 2009). No studies exist examining PEP reactivity to laboratory stressors during pregnancy. Moreover, studies of stress reactivity in pregnancy have generally examined the magni-

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tude of physiological change following an acute stressor and have generally not reported on how pregnant women recovered from stress (Christian, 2012; de Weerth & Buitelaar, 2005).

If stress reactivity attenuates during pregnancy, as suggested by these early studies, it raises the question of why this might occur. One possibility is that high stress reactivity in pregnancy could be detrimental to the mother, the child, or both. Therefore, a protective mechanism may be operating to limit stress-induced changes in the hormonal, cardiovascular and metabolic environments of the pregnancy that could be harmful. For example, previously it has been demonstrated that stress is associated with vasoconstriction, which can alter uteroplacental blood flow, reducing oxygen and nutrition delivery with potentially negative effects on fetal growth (Alder, Fink, Bitzer, Hösli, & Holzgreve, 2007; Copper et al., 1996; McCubbin et al., 1996) and nervous system development (Sjöström, Valentin, Thelin, & Marsál, 1997). However, more recent studies could not replicate the association between maternal anxiety and reduced uterine blood flow (Mendelson, DiPietro, Costigan, Chen, & Henderson, 2011; Monk et al., 2012).

In men and non-pregnant women, stress reactivity differs according to level of anxiety. High anxiety is associated with exaggerated cardiovascular (HR and BP) stress responses (Gramer & Saria, 2007; Pointer et al., 2012). There is some evidence that depression and anxiety affect stress responsiveness during pregnancy but this has not been studied extensively (Christian, 2012; de Weerth & Buitelaar, 2005). Findings have also been inconsistent, suggesting that anxious pregnant women may have lower (Monk et al., 2000; Saisto, Kaaja, Helske, Ylikorkala, & Halmesmäki, 2004) or unaltered (Monk, Myers, Sloan, Ellman, & Fifer, 2003) HR and BP reactivity to psychological stress. Our study was designed to address this lack of evidence and to assess both reactivity to and recovery from stress.

Our aims were: (a) to characterize typical *autonomic* stress responsiveness (i.e., reactivity and recovery) through different pregnancy trimesters and (b) to test the hypothesis that anxiety may alter stress responsiveness during pregnancy.

2. Methods

2.1. Participants

The prenatal early life stress (PELS) study is a longitudinal study and focuses on associations between prenatal stress risk factors, birth outcomes and altered pregnant women's physiology and child's psychophysiology and neurodevelopment. The national ethics committee and the ethics committee of the Sint Elisabeth hospital, Tilburg, The Netherlands both approved the study protocol. Pregnant women were recruited from a hospital and midwiferies around Tilburg. They filled out questionnaires about their emotions and their ECG was recorded during each pregnancy trimester. After birth, psychophysiological measurements of the children and mothers took place. All participants and their partners provided written informed consent. None of the participants smoked, drank alcohol, were under treatment for a current mental disorder, or used cardiovascular medications or antidepressants.

One hundred and seventy women completed stress tasks during the first (8–14th week of gestation, $N = 133$) and/or third pregnancy trimester (31–37th pregnancy week, $N = 138$) and 157 of these 170 participants filled out a standardized anxiety self-report questionnaire at 15–22 weeks of pregnancy.

2.2. Material

2.2.1. Relaxation and stress tasks

In the first and third pregnancy trimesters, each pregnant woman undertook a 25-min task consisting of five testing phases, lasting for 5 min each. Stress was induced in the second and fourth phase, with the remainder being relaxation phases. Participants viewed peaceful pictures and listened to restful music during the relaxation phases (Taelman, Vandeput, Vlemincx, Spaepen, & Van Huffel, 2011). During the stress phases, participants were asked to solve complex mental arithmetic problems, involving five mathematical operations on 2–3 digit numbers without verbalization (e.g., 361 + 17/24 × 2 + 13). They were asked to choose the correct answer from three possibilities presented by a computer. Feedback on the task was given after completion of the last phase (Vlemincx, Taelman, De Peuter, Van Diest, & Van den Bergh, 2011).

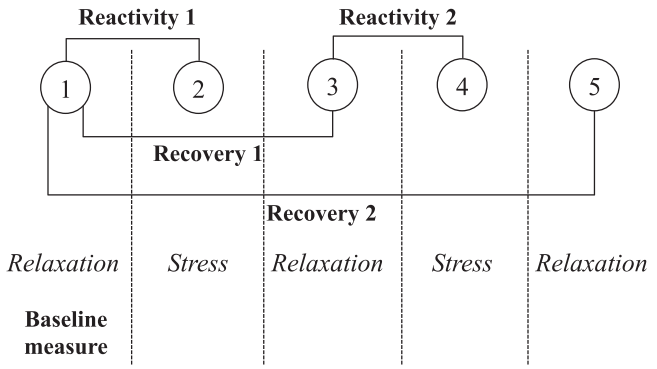

Fig. 1. Diagram showing how the reactivity and recovery measures were calculated from the HR/HRV data collected during the mental arithmetic stress task. As indicated in the figure, the measurement in the first phase was use as a baseline measure.

2.2.2. ECG and ICG recording

Maternal electrocardiography (ECG) and impedance cardiography (ICG) was recorded with the Vrije Universiteit Ambulatory Monitoring system (VU-AMS) during the stress task using seven Ag/AgCl electrodes placed according to the VU-AMS configuration guidelines (Goedhart, Sluis, Houtveen, Willemsen, & Geus, 2007). The skin was cleaned with alcohol to keep electrode resistance low. Cardiovascular measurements were determined for the three relaxation phases and two stress phases, each lasting 5 min. The first relaxation phase was used as baseline measure. Cardiovascular *reactivity* to the stress phase was calculated by subtracting the cardiovascular measurements of each of the stress phases with the level of the previous relaxation phase. Hence, we explicitly choose to work with two reactivity measures, one derived from the difference between phase 1 and 2 (i.e., reactivity to first stressor presentation), and one between phase 3 and 4 (i.e., reactivity to second stressor presentation). Cardiovascular *recovery* from a stressor presentation was derived from the subtraction between cardiovascular measurements in the relaxation phase that follows the stressor presentation and baseline cardiovascular measurements (i.e., in the first relaxation phase) (Stewart & France, 2001). Fig. 1 shows a graphical representation of the calculation of the reactivity and recovery measures.

2.2.3. The state trait anxiety inventory (STAI)

In the second pregnancy trimester the participants filled out the questions constituting the trait anxiety subscale of the Dutch, psychometrically validated version of the state trait anxiety inventory (STAI) (Van der Ploeg, Defares, & Spielberger, 1980). The trait subscale has been identified recently as the best instrument to assess general maternal anxiety during pregnancy (Nast, Bolten, Meinlschmidt, & Hellhammer, 2013). Trait anxiety refers to differences in anxiety proneness and is seen as a personality trait. This subscale contains 20 items scored from 1 to 4 and has a reliability coefficient (Cronbach's alpha) of 0.75 in our sample.

2.3. Data processing and analyses

ECG data were processed using custom software written in Matlab R2012b (Mathworks, Natick, USA) to obtain indices of parasympathetic and sympathetic ANS activity, according to published standards (Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology, 1996). These measures were HR, high frequency (0.15–0.4 Hz, HF) HRV, and the sympathetic measure pre-ejection period (PEP). ECG beat detection was carried out with the Hilbert transform algorithm (Benitez, Gaydecki, Zaidi, & Fitzpatrick, 2001). Potentially erroneous beat detections were identified and screened using a standard approach (Berntson, Quigley, Jang, & Boysen, 2007). The power spectral density (PSD) analysis used for the calculation of HF HRV was computed using the fast Fourier transform (FFT). Variables that were right-skewed were transformed to normality. Data of four women were excluded due to extreme HRV values; visual inspection of the ECGs suggested that these outliers were due to cardiac arrhythmias.

In the present study, RMSSD HRV, the square root of the mean squared differences of successive interbeat intervals, had similar relationships with outcome measures as those seen with HF HRV. Therefore, RMSSD HRV was not included as an additional measure of parasympathetic activity.

For the calculation of PEP the ICG dZ/dt signal (first derivative) was ensemble averaged from consecutive cardiac cycles and synchronized with the ECG signal. PEP, which is an indicator of sympathetic activity, was calculated from the ICG as the interval between ECG's R-wave onset and the ICG's B-point. The B-point, which represents the opening of the aortic valve, was determined as the 15% response point of the negative peak of the dZ/dt waveform (dZ/dt$_{min}$) from the baseline (Ono et al., 2004).

2.4. Statistical analysis

All analyses were conducted using Stata 12.1. Repeated measures ANOVA were conducted to validate that the mental arithmetic task evoked significant responses in HR, HRV and PEP. These ANOVA analyses were also used to determine HR, HRV and PEP differences between pregnancy trimesters. Differences in reactivity and recovery between the first and third pregnancy trimester were tested using paired samples t-tests.

Multilevel (i.e., pregnancy trimester and first/second stressor presentation) regression analyses were conducted to examine the potential association between trait anxiety and cardiovascular responsiveness during pregnancy. Both levels fit with the reactivity and recovery measures described in the material section and shown in Fig. 1. Two-way and three-way interaction effects were assessed to test whether reactivity and recovery in HR, HRV and PEP differ across levels of anxiety, pregnancy trimesters and first and second presentation of the stressor.

All regression models were adjusted for levels of HR, HRV or PEP in the first phase of the mental task (baseline), as well as for common confounders such as age and pre-pregnancy BMI (Vallejo, Márquez, Borja-Aburto, Cárdenas, & Hermosillo, 2005). Other potential covariates (i.e., gravidity, parity, educational level and the gestational age of the fetus at the time of measurements) were tested in repeated analyses but were not included in the final analyses, because they did not influence the results.

3. Results

Characteristics of the pregnant women are shown in Table 1. There were no significant associations between trait anxiety, gravidity, parity, marital status, educational level and any of the cardiovascular baseline levels. Pre-pregnancy BMI was positively correlated with baseline HR in third trimester ($r = 0.23$, $n = 133$, $p < 0.01$), and negatively correlated with baseline PEP in both trimesters (trimester 1: $r = -0.36$, $n = 122$, $p < 0.001$; trimester 3: $r = -0.26$, $n = 124$, $p < 0.01$). Age was negatively correlated with baseline HF HRV in both trimesters (trimester 1: $r = -0.19$, $n = 138$, $p = 0.02$; trimester 3: $r = -0.23$, $n = 133$, $p < 0.01$).

3.1. HR, HRV and PEP differences between task phases and between pregnancy trimesters

Repeated measures ANOVA (pregnancy trimester × task phase) were executed to validate that the mental arithmetic task evoked significant responses and indicated significant differences between the five phases of the mental arithmetic task for pregnant women's HR and HRV (HR: $F(4161) = 49.02$, $p < .001$; HF HFV: $F(4161) = 11.39$, $p < .001$) but not for PEP ($p > .1$). HR, HRV and PEP were significantly different between pregnancy trimesters (HR: $F(1161) = 581.87$, $p < .001$; HF HRV: $F(1161) = 362.44$, $p < .001$; PEP: $F(1157) = 219.53$, $p < .001$).

3.2. Comparison of reactivity and recovery measures between trimesters

Differences in reactivity and recovery between the first and third pregnancy trimester were tested using paired samples t-tests (see Table 1). HR and HRV reactivity, but not PEP reactivity, in late pregnancy were lower than in the first pregnancy trimester (HR: $t(193) = 5.01$, $p < .001$; HF HRV: $t(187) = -2.00$, $p < .05$). Furthermore, HR, HRV and PEP recovery were greater in the third pregnancy trimester compared to the first trimester (HR: $t(201) = 2.74$, $p = .01$; HF HRV: $t(187) = -2.24$, $p = .03$; PEP: $t(176) = -2.23$, $p = .03$), indicating that the difference between HR, HRV or PEP after a stressor presentation and baseline HR, HRV or PEP was smaller in the third pregnancy trimester compared to the first trimester.

3.3. Comparison of reactivity and recovery measures between first and second stressor presentation

The multilevel regression analyses showed that stress presentation was significantly related to HR reactivity, indicating that HR reactivity was significantly lower during the second stressor presentation ($b = -1.67$, SE = 0.28, $p < .001$). Analogously HF HRV decreases less during the second stressor presentation ($b = 94.27$, SE = 23.46, $p < .001$). Recovery from the second stressor presentation was significantly larger than recovery from the first stressor presentation (HR: $b = -1.27$, SE = 0.26, $p < .001$; HF HRV: $b = 43.61$, SE = 18.11, $p = .02$), indicating that the difference between HR or HRV after the stressor presentation and baseline HR or HRV was smaller after the second presentation compared to after the first presentation.

3.4. Relationship between anxiety and stress responsiveness during pregnancy

Multilevel regression analyses showed significant two-way interactions between trait anxiety and pregnancy trimester for HR and HF HRV reactivity, adjusted for baseline levels of HR and HF HRV (HR: $b = 0.15$, SE = 0.06, $p = .008$; HF HRV: $b = -10.97$, SE = 4.79, $p = .02$), indicating that in the third pregnancy trimester, compared to less anxious women, more anxious women have higher HR and HF HRV responses to stress, independent of the baseline level of HR or HF HRV (Table 2 and Fig. 2a and b). Given the significant decrease in HR and HRV reactivity between the first and third pregnancy trimester, this implies that compared to less anxious women, more anxious women have less dampened HR and HRV reactivity

Table 1
Descriptive statistics for variables related to pregnant women. Observed differences between the first and third pregnancy trimester were tested using paired samples *t*-tests.

Mothers	*M*	(SD)	%
Trait anxiety	36.67	5.29	
BMI before pregnancy (kg/m^2)	24.19	4.09	
Gravidity	1.08	1.29	
Parity	0.61	0.65	
Marital status			
Married or cohabiting			97.45
Single			2.55
Educational level			
Secondary school			32.48
Higher vocational education			39.49
University degree			28.02

	1st trimester			3rd trimester			
	n	*M*	(SD)	*n*	*M*	(SD)	*p* value
Age (years)	125	32.58	(4.26)	129	32.77	(4.33)	
Weeks pregnant during measurement	125	13.61	(1.28)	129	33.96	(1.80)	
Baseline HR (bpm)	125	80.25	(9.45)	129	89.29	(10.01)	<.001
Baseline HF (ln ms^2)	122	6.05	(1.07)	128	5.30	(1.21)	<.001
Baseline PEP (ms)	122	74.36	(20.51)	124	60.95	(20.64)	<.001
HR reactivity (bpm)	125	4.45	(5.28)	129	2.17	(4.38)	<.001
HF reactivity (ms^2)	122	−139.16	(456.10)	128	−52.17	(318.10)	<.05
PEP reactivity (ms)	122	0.78	(12.60)	124	−0.79	(10.64)	>.1
HR recovery (bpm)	125	.26	(4.29)	129	−.87	(4.27)	.01
HF recovery (ms^2)	124	74.94	(462.62)	128	37.80	(263.08)	.03
PEP recovery (ms)	122	−2.71	(15.30)	124	−1.92	(12.98)	.03

Table 2
Multilevel regression analyses between trait anxiety and reactivity of HR, HF HRV and PEP ($n = 157$).

	HR reactivity			HF HRV reactivity			PEP reactivity		
	Coef.	SE	*p*	Coef.	SE	*p*	Coef.	SE	*p*
Baseline level	−0.05	0.02	.04	−0.28	0.03	<.001	−0.07	0.03	<.001
Trait anxiety	−0.04	0.06	.51	3.04	4.14	.46	0.15	0.14	.30
Trimester (3rd vs. 1st)	−6.85	2.16	.008	397.78	178.75	.03	−0.48	7.55	.95
Trait anxiety × trimester	0.15	0.06	.01	−10.97	4.79	.02	−0.06	0.20	.79
Presentation of stressor (2nd vs. 1st)	−1.67	0.28	<.001	94.27	23.46	<.001	0.13	1.06	.90
Age	−0.03	0.06	.63	−0.40	4.27	.92	0.22	0.13	.09
BMI	−0.01	0.06	.84	0.61	4.36	.89	−0.01	0.13	.96
Constant	11.32	3.94	.004	−109.41	255.29	.67	−6.24	8.64	.47

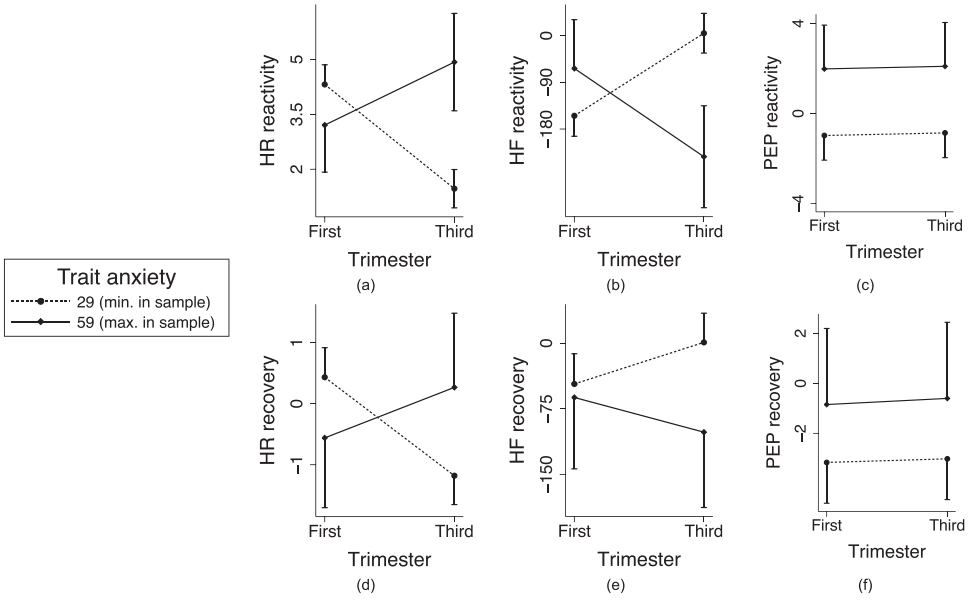

Fig. 2. The association between trait anxiety and cardiovascular reactivity (a–c) (significant interaction) and recovery (d–f). The lines in the plots are constructed by connecting the points displaying the estimated marginal mean of a reactivity/recovery measure (adjusted for the covariates) in each pregnancy trimester. The minimum and maximum scores for trait anxiety in our sample (29 and 59, respectively) were used to make separate lines.

Table 3
Multilevel regression analyses between trait anxiety and recovery of HR, HF HRV and PEP ($n = 157$).

	HR recovery			HF HRV recovery			PEP recovery		
	Coef.	SE	p	Coef.	SE	p	Coef.	SE	p
Baseline level	−0.17	0.02	<.001	−0.22	0.02	<.001	−0.19	0.04	<.001
Trait anxiety	−0.03	0.05	.51	−0.51	3.60	.89	0.23	0.19	.23
Trimester (3rd vs. 1st)	−2.47	2.03	.22	69.70	139.36	.62	9.33	7.79	.23
Trait anxiety × trimester	0.08	0.05	.13	−2.90	3.74	.44	−0.27	0.21	.19
Presentation of stressor (2nd vs. 1st)	−1.27	0.26	<.001	43.61	18.11	.02	0.19	1.02	.85
Age	−0.14	0.05	.01	−1.18	3.88	.76	0.31	0.20	.13
BMI	−0.06	0.06	.28	2.00	3.94	.61	−0.04	0.22	.85
Constant	21.42	3.55	<.001	73.08	225.08	.75	−6.88	12.78	.59

in the third trimester compared to the first trimester. There was no main effect of trait anxiety on HR, HRV or PEP reactivity ($p > .05$) (Table 2 and Fig. 2c), indicating that in the first trimester there were no significant differences in cardiovascular reactivity between high and low anxious women. There was no main effect of trait anxiety on HR, HRV or PEP recovery ($p > .05$), nor were there significant trait anxiety × pregnancy trimester interactions for HR, HRV or PEP recovery ($p > .05$) (see Table 3 and Fig. 2d–f).

The multilevel regression analyses showed that stressor presentation interactions with pregnancy trimester and/or trait anxiety were not significant for any reactivity or recovery measure. Nevertheless, separate single-level regression analyses showed that in the third pregnancy trimester reactivity to the second stressor presentation is higher in more anxious women (HR: $b = 0.14$, SE = 0.07, $p = .05$; HF HRV: $b = -11.79$, SE = 5.11, $p = .02$;) compared to less anxious women.

4. Discussion

To the best of our knowledge, this is the most detailed longitudinal study that gives insight into cardiovascular and autonomic reactivity in pregnancy. Previous studies either focused on only one pregnancy trimester (Klinkenberg et al., 2009), had significantly less participants (Klinkenberg et al., 2009; Matthews & Rodin, 1992), or did not include HR as well as measures of parasympathetic and sympathetic activity (DiPietro et al., 2003; Entringer et al., 2010; Matthews & Rodin, 1992). HR and HRV measures, but not PEP, differed over the various phases of the mental arithmetic task, in the first as well as in the third trimester. Stress reactivity was lower in the third pregnancy trimester, but the decrease in reactivity between early and late pregnancy was smaller in more anxious women compared to less anxious women.

Induced stress was associated with increased HR and decreased HRV in the mental arithmetic task. This is in line with previous research focusing only on the third pregnancy trimester (Klinkenberg et al., 2009). The stress task that we used did not lead to significant changes in PEP. This suggests that stress responses elicited with the mental arithmetic task are mainly reflected in a decreased parasympathetic nervous system activity but not in a significant change in the sympathetic nervous system activity as measured with PEP. Autonomic responses to stressful tasks vary according to the type and severity of the stressors and according to populations. Further study will be required to determine whether the lack of sympathetic responsiveness to this particular task was due to dampened sympathetic responsiveness due to pregnancy or to an insufficiently stimulating stressor. Importantly, PEP may be influenced by other circulatory parameters, such as cardiac preload (Nakamura, Wiegner, Gaasch, & Bing, 1983). In most cases, these other influences are unvarying and small and are, therefore, disregarded. However, there are substantial volume shifts occurring over the course of pregnancy that could theoretically influence PEP (Thornburg, Jacobson, Giraud, & Morton, 2000). Unfortunately, we were unable to account for such influences and, therefore, our PEP results should be interpreted cautiously. Additionally, future studies could consider assessing sympathetic activity by measuring skin conductance responses instead of PEP reactivity. Both measures are responsive to sympathetic activity, but PEP and skin conductance responses tend to be uncorrelated, suggesting that the heart and skin might reflect different aspects of SNS activity (Goedhart, Willemsen, Houtveen, Boomsma, & De Geus, 2008).

In women without a tendency for anxiety, HR and HRV reactivity to the stress phases were significantly reduced in the third pregnancy trimester, compared to the first trimester. Previous studies presented similar results for attenuated HR and BP reactivity in late pregnancy (DiPietro et al., 2003; Entringer et al., 2010). Importantly, the present study also found significantly reduced autonomic stress reactivity in the third pregnancy trimester, for which so far only marginal evidence existed (Klinkenberg et al., 2009). It must be noted that from the present study design it cannot be ruled out that the attenuated stress responses in the third pregnancy trimester are (partially) the result of a habituation process, as the same stress task was already presented in the first trimester. Therefore, future studies need to include a control group consisting of non-pregnant women to assure that the current findings are not driven by habituation to the stress task. Additionally, it is also recommended to compare two independent samples of women in their first pregnancy trimester and women in their third pregnancy trimester.

The results in the present study indicated significant interactions between pregnancy trimester and women's trait anxiety on HR and HRV reactivity. These interactions suggest that more anxious pregnant women have less dampened stress reactivity in late pregnancy. It is possible that reduced stress habituation in the more anxious women may explain this finding, as anxiety is known to negatively affect habituation to novel stimuli (Thayer, Friedman, Borkovec, Johnsen, & Molina, 2000). Our study design did not include a non-pregnant comparison group to test habituation over 9 months to repeated stimulation with the stressor. Thus, we cannot determine if reduced stress responsiveness in the non-anxious pregnant women was the result of normal habituation or of pregnancy. However, other studies have also shown that cardiovascular (DiPietro et al., 2003; Entringer et al., 2010), hormonal (Kammerer, Adams, von Castelberg, & Glover, 2002) and psychological stress reactivity (Glynn, Wadhwa, Dunkel-Schetter, Chicz-Demet, & Sandman, 2001) are attenuated in late pregnancy and habituation effects may merely operate over shorter timescales than 6 months. It is thought that the stress sensitivity is dampened as pregnancy advances to protect the growing fetus (Christian, 2012; Glynn & Sandman, 2011; Glynn, Schetter, Hobel, & Sandman, 2008). There is evidence that women who fail to show decreased stress reactivity are at increased risk of adverse outcomes such as preterm birth (Entringer et al., 2010; Glynn et al., 2008). Moreover, abnormal stress responsiveness in pregnant women is known to predict risk of adverse cardiovascular outcomes in pregnancy (Christian, 2012) or later in life (Chida & Steptoe, 2010; Schwartz et al., 2003; Steptoe & Kivimäki, 2013). Increased reactivity during pregnancy has also been linked to greater risks of chronic

hypertension, maternal cardiovascular morbidity and neonatal morbidity/mortality (Cuevas & Germain, 2011; Magnussen, Vatten, Smith, & Romundstad, 2009; Young, Levine, & Karumanchi, 2010).

We also found that in the third pregnancy trimester, more anxious women react more strongly to the second presentation of the stressor than less anxious women. Similar patterns of individual differences in cardiovascular response adaptation have been found in non-pregnant people with neuroticism (Hughes, Howard, James, & Higgins, 2011), which is fundamentally related to trait anxiety (Reiss, 1997). It is important to mention that our findings with respect to the second presentation of the stressor were based on single-level regression analyses. Future research needs to further address the role of anxiety during pregnancy in responses to repeated stressors.

Both HR and HRV reactivity differed significantly between pregnancy trimesters but only HR recovery and not HRV recovery was significantly different between trimesters. Furthermore, no significant interactions between trait anxiety and pregnancy trimester with HR or HRV recovery were found. The stress task used in the present study has five-minute relaxation phases for each participant. As individuals can vary greatly in the speed of physiological recovery from a stressor, five minutes might be not enough to truly measure physiological recovery (de Weerth & Buitelaar, 2005). A better approach may be to observe how long it takes to return to baseline HR and HRV levels after termination of a stressor. Such a recovery measure might reveal more inter-individual differences, which might have stronger relationships to anxiety. Further research is required to investigate if the present findings can be confirmed or opposed when recovery is measured in a different way.

As suggested in the task force paper on HRV (Task Force of the European Society of Cardiology the North American Society of Pacing Electrophysiology, 1996), we used power spectrum analysis with a fixed bandwidth based on typical adult respiratory rates to estimate the power of respiratory sinus arrhythmia (predominantly mediated by vagus nerve activity). This approach has been widely adopted but might be improved by the measurement of individual respiratory rates. However, these data were not available in our study.

Our study has a number of strengths: compared to previous studies, we studied a relatively large population of pregnant women, included data from the first pregnancy trimester, presented stressors more than once and used autonomic measures such as HRV and PEP. Finally, the present study measured anxiety using the STAI, which is generally acknowledged as the best instrument to assess maternal anxiety during pregnancy, and in particular the trait anxiety subscale (Nast et al., 2013).

In summary, this study provides insight into how autonomic control evolves throughout pregnancy. Moreover, it offers good evidence that trait anxiety is associated with less dampened cardiovascular reactivity in late pregnancy than typically occurs. Existing evidence suggests that high reactivity in late pregnancy is linked to worse outcomes for the pregnant women and their offspring. Therefore, further research should test whether anxiety-reducing interventions in anxiety-prone pregnant women reduce these risks.

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