Stress during Pregnancy: Is the Autonomic Nervous System Influenced by Anxiety?

Joachim Taelman[1], Steven Vandeput[1], Devy Widjaja[1], Marijke AKA Braeken[2], Renée A Otte[2], Bea RH Van den Bergh[2], Sabine Van Huffel[1]

[1]Department of Electrical Engineering, ESAT-SCD, Katholieke Universiteit Leuven, Belgium
[2]Department of Developmental Psychology, Universiteit van Tilburg, The Netherlands

Abstract

The goal of this study was to investigate whether anxiety during pregnancy can be linked with the autonomic nervous system (ANS) via different heart rate variability (HRV) parameters. More than 100 pregnant women were included and underwent 24h ECG monitoring including a stress test and the state trait anxiety inventory (STAI) questionnaire, dividing them in a low, medium or high anxiety group. Standard time and frequency domain and nonlinear HRV parameters were calculated to describe self-similarity, complexity and chaotic signatures. Almost all HRV parameters were negatively correlated with the anxiety level, though not statistically significant, except the chaos level. Positive correlations were found for detrended fluctuation analysis and sympathetic activity parameters. Most of the significant between-group differences were found between the low and medium anxiety groups. To conclude, the ANS modulation is slightly influenced by the anxiety level, but not as strongly as hypothesized before.

1. Introduction

Stress and anxiety during pregnancy can influence the development of the fetus. A low birth weight [1] and prematurity [2] of the child are possible consequences resulting in long term problems [3]. Several studies reveal that cognitive, emotional and behavioral disorders occur more often when fetuses are more exposed to prenatal stress and anxiety [4]. The perceived stress level of the pregnant mothers are derived from traditional questionnaires such as STAI [5] and EDS [6].

Recently, there seems to be more and more interest in studying all kinds of emotions by means of physiological signals. It is known that stress influences the cardiac system, which is regulated by the autonomic nervous system (ANS). The sympathetic and parasympathetic modulation on the cardiac system can be quantified using heart rate variability (HRV) [7]. Mental stress in laboratory experiments (cognitive demands, mental arithmetic) has been associated with decreased HRV, indicating a disturbed ANS [8].

The goal of this study was to investigate whether anxiety during pregnancy, as indicated by the questionnaires, can be linked with differences in the autonomic heart rate modulation via HRV parameters during both a 24h recording of the ECG and a test where a mental load is induced. We hypothesized that perceived stress will be reflected in the differences in HRV parameters so that we would be able to distinguish between a low and a high anxiety group using these HRV parameters.

2. Methods

2.1. Data

140 women, aged from 18 to 40, were recruited from 10 to 12 weeks gestation onwards. Inclusion criteria were: no current substance abuse problems, no severe psychiatric problems and no pregnancy-associated medical problems such as diabetes or hypertension. The participants underwent a 24h ECG recording at 1000 Hz using the Vrije Universiteit - Ambulatory Monitory System (VU-AMS [9]) during daily activity. At the end of the 24h recording, the participants underwent a stress test of 25 minutes. The stress test consists of 5 periods of 5 minutes, in which alternating periods of rest and mental stress occurred (phases are numbered 1 to 5 in order of appearance; 1,3,5 = rest and 2,4 = mental task). The mental stress was induced by solving complex continuous mental calculations of five operations with a two or three digit number. This period was considered to be stressful as task difficulty was high. During rest, relaxing pictures were shown and music was played, exposing the participants to neutral stimuli reducing boredom during this phase.

The women were also requested to fill out the State Trait Anxiety Inventory (STAI) to determine the amount of anxiety present. The STAI consists of a state and a trait subscale; state anxiety is conceptualized as a transient emotional condition, while trait anxiety reflects a dispositional anxiety proneness. This study only considered the state anxiety. Based on the STAI score, subjects belonged to a low (STAI $\leq$ 28), medium (28 $<$ STAI $<$ 40) or high (STAI $\geq$ 40) anxiety group.

2.2. Heart Rate Variability analysis

A tachogram is derived from the raw ECG signals using the Pan-Tompkins algorithm. The Pan-Tompkins algorithm has a good performance in general. Nevertheless, errors will be introduced via wrong peak detections and missed peaks. Therefore, the tachogram is preprocessed as described by Widjaja et al [10].

Linear HRV parameters were obtained in agreement with the standards of measurement, proposed by the Task Force committee [7]. Mean and standard deviation (SD) of the tachogram, the square root of the mean squared differences between consecutive RR intervals (rMSSD), the percentage of intervals that vary more than 50 ms from the previous interval (pNN50) and the mean of the standard deviations within 5 minute segments (SDNN$_{index}$) were calculated in the time domain. The geometric measure we used is TINN, which is the width of the histogram. After resampling the tachogram at 2 Hz, the power spectral density (PSD) was computed by using the Welch method. In the frequency domain, low frequency power (LF: 0.04–0.15 Hz), high frequency power (HF: 0.15–0.40 Hz) and total power (0.01–0.40 Hz), as well as the ratio of low over high frequency power (LF/HF), were calculated. In addition, the power can be expressed in absolute values (ms^2) or in normalized units (n.u.).

Nonlinear parameters do not describe the amount of modulation as such, but are able to describe the scaling, complexity and chaotic properties of the signal. Often used parameters which study the scaling of the system are 1/f slope [11], fractal dimension (FD) [12] and detrended fluctuation analysis (DFA α_1 & α_2) [13] while the complexity is addressed via sample entropy (SampEn) [14]. Also a chaotic signature is calculated by means of the recently developed numerical noise titration technique (NLmean and NLdr) [15].

2.3. Statistical analysis

In order to quantify the relationship between the questionnaires and the HRV parameters, the Kruskal-Wallis test was used to differentiate between the three groups and the Spearman correlation coefficient ρ was used to calculate the correlation coefficient.

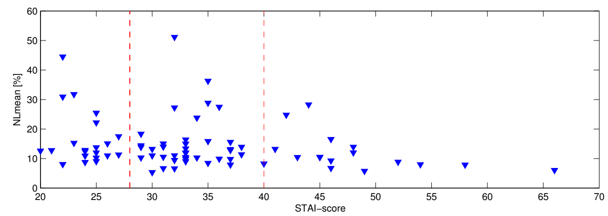

Figure 1. NLmean for the 6h-day measurements in function of the STAI score.

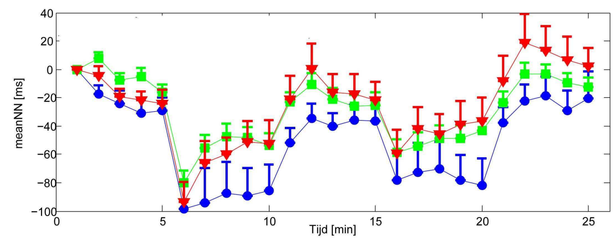

Figure 2. the standardized meanRR intervals during the test for the three anxiety groups. (◯ = high; □ = middle; ▽ = low).

3. Results

The activity during day and night are different. Therefore, 6 successive hours during day and night were selected manually and the HRV parameters were analyzed. Table 1 gives the most important results of the comparisons between the three anxiety groups. The Kruskal-Wallis test revealed several statistically significant differences, but the post hoc-test shows that these differences were mainly between the middle and low anxiety group and not between the high and the low anxiety group. A more general approach to look for a relationship between the STAI score and the HRV-parameters is calculating the correlation between the two variables. For the day-night comparisons, only a significant correlation coefficient is found for the NLmean parameter as shown in Figure 1 (ρ = -0.26, p = 0.021), but the figure does not reveal a convincing result. This negative correlation was more expressed during day than night time. Positive correlations were only found for parameters related to sympathetic activity (LF [n.u.] and LF/HF) and for the detrended fluctuation analysis (DFA) parameters. In contrast, the positive correlations were stronger at night compared to day time.

Figure 2 shows the normalized meanRR intervals during the stress test for the three anxiety groups. For the three groups, the different phases can be distinguished. We were more interested in the difference in reaction between the three different groups. Therefore, we deducted between-group analyses of the different HRV parameters for the different phases and for differences in phases. Table 2 gives an overview of the most important results. Some statisti-

Table 1. Comparison of HRV parameters of day and night between the different groups, based on their STAI score.

	time	High	Middle	Low	p_{H-L}	p_{K-W}
SDNN_{index}	d	57,71 ± 16,95	51,13 ± 15,24	59,22 ± 16,15	0,557	**0,036**
TINN	d	399,53 ± 152,69	341,33 ± 165,88	425,52 ± 158,62	0,403	**0,049**
DFA α_2	n	1,10 ± 0,11	1,01 ± 0,12	1,05 ± 0,10	0,094	**0,013**
NLmean	d	11,82 ± 6,07	14,91 ± 8,75	16,59 ± 9,11	**0,024**	**0,049**

d: day, n: night, p_{H-L}: p-value or comparison between high and low anxious, p_{K-W}: p-value for Kruskal-Wallis

Table 2. Most significant results for the different HRV parameters during the stress test between the three anxiety groups based on the STAI scores.

	Phase	High	Middle	Low	p_{H-L}	p_{K-W}
meanNN	5	773,04 ± 109,30	739,45 ± 67,90	791,90 ± 74,49	0,547	**0,049**
RMSSD	2 - 4	-1,76 ± 8,59	1,67 ± 6,64	-3,03 ± 5,71	0,326	**0,027**
SDSD	2 - 4	-1,55 ± 8,35	1,44 ± 5,87	-2,62 ± 5,49	0,241	**0,018**
HF	2 - 4	-66,50 ± 161,38	150,86 ± 580,34	-83,07 ± 236,64	0,727	**0,026**
LF/HF	2 - 4	0,91 ± 1,73	-0,34 ± 2,23	-0,13 ± 0,96	**0,049**	**0,049**

p_{H-L}: p-value or comparison between high and low anxious, p_{K-W}: p-value for Kruskal-Wallis

Table 3. Significant correlation coefficients during the stress test between HRV parameters and the STAI scores.

	Phase	ρ	p
SDNN	4	-0,233	0,040
pNN50	4	-0,225	0,048
	2 - 4	0,240	0,034
LF	3	-0,239	0,035
	4	-0,253	0,026
HF	2	-0,260	0,022
	3	-0,237	0,037
	3 - 4	-0,255	0,024
LF/HF	2 - 4	0,238	0,036

cally significant differences were present, but not to differentiate between the high and low anxiety group as hypothesized. This difference was statistically significantly present for LF/HF.

Table 3 shows the statistically significant correlation coefficients between the HRV parameters and the STAI scores. Several correlations are present, but ρ shows that these correlations are not persuasive. A general trend when analyzing the correlation coefficients is that the HRV parameters of the individual phases are negatively correlated with the STAI scores and are more present during phases with the mental load during the stress test.

4. Discussion and conclusions

The goal of this study was to investigate whether anxiety during pregnancy, as indicated with a self-rating score (the STAI score), can be linked with the functioning of the autonomic nervous system via different HRV parameters. Therefore, the cardiac system of several pregnant women was investigated for its sleep-wake rhythms and during a stress test. The ANS, characterized via different HRV parameters, showed little influence of anxiety, indicated by the STAI score. This revealed that a strong correlation between a psychological self-rating score and the physiological response of the subjects is absent [16].

A statistically significant indication of anxiety could be found in the chaos of the RR intervals: more anxiety leads to less chaos. This difference was only statistically significant during day, where the daily activity was not standardized and is therefore not a very strong evidence. Most other HRV parameters showed slightly negative correlations with the STAI score, indicating a reduced HRV for women with high anxiety that is in agreement with a reduced HRV for several pathologies. Two measures (LF [n.u.] and LF/HF), both related to the sympathovagal balance, showed positive correlations during day. These positive correlations were more present during night. In general terms, we can state that anxiety results in a higher sympathovagal balance while sleeping and in a global reduction of HRV during day, although these correlations were not statistically significantly different.

Anxiety, reflected from the STAI scores, revealed hardly any influence on the cardiac reaction during the stress test. All time domain measures indicated a negative correlation with the STAI score during the different phases of the stress test. This confirms the hypothesis that anxiety reduces the variability of the heart rate. HF, a marker of the parasympathetic modulation on the heart rate, revealed a statistically significant negative correlation coefficient during the different phases indicating a reduced parasympathetic influence in women with high anxiety. This was more apparent during the periods with mental load.

The statistically significant differences, described in this paper, were only marginal compared to the numerous analysis we performed during this study. The conclusions we could made were only from trends in the data. A limitation of the study was that the state anxiety of the STAI was used. The state anxiety is depending on the situation and can vary during day time. A better approach would be to use the trait anxiety of the STAI. Another limitation during the stress test could be the task we used to induce stress. These woman are pregnant and their main concern is to have a healthy baby. This concern is mainly responsible for the anxiety level. The mental arithmatic test could induce a different type of stress that is not linked with the concerns of the pregnant women. Solving these limitations could lead to better correlations between the psychological score and the physiological responses of the cardiac system.

This study is a small part of a bigger project with a follow up of the pregnant women and their babies. In future analysis, we will look whether the physiological scores via HRV for anxiety are a better predictor for the development of the fetus and its problems than the psychologic questionnaires.

Acknowledgements

Research supported by

• Research Council KUL: GOA Ambiorics, GOA MaNet, CoE EF/05/006 Optimization in Engineering (OPTEC), IDO 05/010 EEG-fMRI, IDO 08/013 Autism, IOF-KP06/11 FunCopt, several PhD/postdoc & fellow grants;

• Flemish Government: FWO: PhD/postdoc grants, projects: FWO G.0302.07 (SVM), G.0341.07 (Data fusion), G.0427.10N (Integrated EEG-fMRI) research communities (ICCoS, ANMMM); IWT: TBM070713-Accelero, TBM070706-IOTA3, TBM080658-MRI (EEG-fMRI), PhD Grants; Belgian Federal Science Policy Office: IUAP P6/04 (DYSCO, 'Dynamical systems, control and optimization', 2007-2011);ESA PRODEX No 90348 (sleep homeostasis)

• EU: FAST (FP6-MC-RTN-035801), Neuromath (COST-BM0601)

References

[1] Pagel M, Smilkstein G, Regen H, Montano D. Psychosocial influences on new born outcomes: a controlled prospective study. Soc Sci Med 1990;30(5):597–604.

[2] Mulder E, Robles de Medina P, Huizink A, Van den Bergh B, Buitelaar J, Visser G. Prenatal maternal stress: effects on pregnancy and the (unborn) child. Early Hum Dev 2002; 70(1-2):3–14.

[3] Santos A, Duret M, Mancini J, Gire C, Deruelle C. Preterm birth affects dorsal-stream functioning even after age 6. Brain Cogn 2009;69(3):490–494.

[4] Van den Bergh B, Mulder E, Mennes M, Glover V. Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. Neurosci Biobehav Rev 2005;29(2):237–258.

[5] Defares P, van der Ploeg H, Spielberg C. Een nederlandstalige bewerking van spielberger state-trait anxiety inventory: de zelf-beoordelingsvragenlijst. De psycholoog 1980; 15:460–467.

[6] Cox J, Holden J, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 1987;150(6):782.

[7] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability standards of measurement, physiological interpretation and clinical use. Circulation 1996; 71:1043–1065.

[8] Mezzacappa E, Kelsey R, Katkin E, Sloan R. Vagal rebound and recovery from psychological stress. Psychosom Med 2001;63:650–657.

[9] Vrijkotte T, van Doornen L, de Geus E. Effects of work stress on ambulatory blood pressure, heart rate, and heart rate variability. Hypertension 2000;35:880.

[10] Widjaja D, Vandeput S, Taelman J, Braeken M, Otte R, Van den Bergh B, Van Huffel S. Accurate R Peak Detection and Advanced Preprocessing of Normal ECG for Heart Rate Variability Analysis. In Proc of Computing in Cardiology 2010. September 2010; .

[11] Kobayashi M, Musha T. 1/f fluctuations of heart beat period. IEEE Trans Biomed Eng 1982;29:456–457.

[12] Katz M. Fractals and the analysis of waveforms. Comput Biol Med 88;18:145–156.

[13] Peng C, Havlin S, Hausdorff J, Mietus J, Stanley H, Goldberger A. Fractal mechanisms and heart rate dynamics. J Electrocardiol 1996;28:59–64.

[14] Richman J, Moorman R. Physiological time-series analysis using approximate entropy and sample entropy. Am J Physiol Heart Circ Physiol 2000;278:2039–2049.

[15] Poon C, Barahoma M. Titration of chaos with added noise. PNAS 2001;98:7107–7112.

[16] Morrow GR, Labrum AH. The relationship between psychological and physiological measures of anxiety. Psychol Med 1978;8(1):95–101.

Address for correspondence:

Joachim Taelman
ESAT-Sista
Kasteelpark Arenberg 10 bus 2446
3001 Leuven
Belgium
joachim.taelman@esat.kuleuven.be