Development of Fetal Heart Rate Dynamics before and after 30 and 35 Weeks of Gestation

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Abstract

In this study, we have investigated how the dynamics of fetal beat-to-beat heart rate variability (fHRV) changes during development prior to 35 weeks and after 30 weeks of gestation. Noninvasive fetal electrocardiogram (ECG) signals from 45 pregnant women at the gestational age from16 to 41 weeks with normal single pregnancies were analysed. A nonlinear parameter called complex correlation measure (CCM) which measures the variability in the temporal structure of Poincaré plot was used to understand the dynamics of fHRV. Dependency of Results indicate that variability in fetal heart rates as captured by SD1 and SD2 markedly changes after 35 weeks of gestation whereas dynamics in fetal heart rates as captured by CCM substantially changes after 30 weeks of gestation. It might be due to significant amount of maturation of the autonomic nervous system might be done after 30 weeks and before 35 weeks and could potentially help identify the pathological autonomic nervous system development.

1. Introduction

Early in gestation the fetal heart rate is predominately under the control of the sympathetic nervous system and arterial chemoreceptors [1]. As the fetus develops its heart rate decreases in response to parasympathetic (vagal stimulation) nervous system maturation and variability becomes more pronounced [2]. In the normal fetus, there is an interplay between the sympathetic (acceleration) and parasympathetic (deceleration) nervous sytems in the control of heart rate. These systems exert their control via the cerebral cortex, the medulla oblongata, the sympathetic ganglia and the vagus nerve. The interaction between these systems results in a difference in the beat-to-beat intervals resulting in variability of the fetal heart rate tracing. In the term fetus, moderate variability is considered normal as it indicates a normally functioning central nervous system. Beat-to-beat or short-term variability is the oscillation of the FHR around the baseline in amplitude of 5 to 10 bpm. Long-term variability is a somewhat slower oscillation in heart rate and has a frequency of three to 10 cycles per minute and an amplitude of 10 to 25 bpm. Clinically, loss of beat-to-beat variability is more significant than loss of long-term variability [3]. Gestational age is an important factors that require consideration when assessing the fetal heart rate variability. The completion of the 35 gestational week marks a developmental milestone that is associated with a dramatically decreasing risk for the neonate in the case of a preterm delivery. About 90% of babies born this week can survive. Lungs are almost fully developed.

Fetal autonomic nervous system (ANS) function and its development in the course of pregnancy can be examined by the investigation of fetal heart rate variability (FHRV) analysis. However, the usual approach of determining HRV in a heart rate recording of defined length might not be able to reflect the dynamics of increasingly integrative autonomic heart rate regulation. Quantitative Poincaré plot analysis was used to assess the changes in CCM of HRV signals during parasympathetic blockade was discussed in our previous study [4]. The lowest value of CCM has also been found during atropine infusion which reduced the parasympathetic activity and reduces instantaneous changes in HRV signal. On the other hand, it was also found to be increased with increase in parasympa thetic activity during administration of low-dose scopolamine. Variability (increasing or decreasing) in the temporal structure.

The aim of this study was to describe the prenatal development of integrative ANS function prior to and after 35 weeks of gestation, exploring a new analyzing technique based on complex correlation measures (CCM).

2. Methods

2.1. Data

Recording of the abdominal ECG signals from 45 pregnant women at the gestational age of 16~41 weeks with normal single pregnancies were collected from Tohoku University Hospital. Out of them 27 cases were before 35 weeks and 18 were after 35 weeks of gestational age. A regrouping was done with 26 cases before 30 weeks and 17 were after 30 weeks. All recordings (each of 1 minute's length) were sampled at 1000 Hz with 16-bit resolution. The study protocol was approved by Tohoku University Institutional Review Board and written informed consent was obtained from all subjects.

FECG traces were extracted using a method that combines cancellation of the mother's ECG signal and the blind source separation with reference (BSSR) as described in our earlier study [5].

2.2. Complex correlation measure

Any heart beat within a series of beats has an influence on successive heart beats downstream necessitating a means of exploring this influence. The Poincaré plot allows determining linear and nonlinear components of the inter-beat variability and provides a quantitative measure of the temporal dynamics of the HRV signal [6-9]. An extension of the Poincaré plot is the complex correlation method (CCM). CCM extends the Poincaré plot analysis by providing temporal, dynamic information about the relationship of successive beat-to-beat variation over a varying number of beats. The CCM measures the point-to-point variation of the signal rather than gross description of the Poincaré plot. It is computed in a windowed manner which embeds the temporal information of the signal. A moving window of three consecutive points from the Poincaré plot are considered and the temporal variation of the points are measured. If three points are aligned on a line then the value of the variation is zero, which represents the linear alignment of the points. Moreover, since the individual measure involves three points of the two dimensional Poincaré plot, it is comprised of at least four different points of the time series for lag m = 1 and at most six points in case of lag m ≥ 3. Hence the measure conveys information about four different lag correlations of the signal. If the Poincaré plot is composed of N points then the temporal variation of the plot, termed as CCM, is composed of all overlapping three point windows and can be calculated as:

$$CCM(m) = \frac{1}{C_n(N-2)} \sum_{i=1}^{N-2} \|A(i)\|$$

where m represents lag of Poincaré plot, $A(i)$ represents area of the i-th triangle and C_n was considered to be 1 in this study. The length of major and minor axis of the ellipse are 2SD1, 2SD2, where SD1, SD2 are the dispersion perpendicular to the line of identity (minor axis) and along the line of identity (major axis) respectively. The detail mathematical formulation of CCM is reported in our previous study. The detail mathematical formulation of CCM is reported in our previous study [10].

3. Results

Table 1 shows that only CCM values are significantly different between the two groups of fetuses below rand above 30 weeks. On the other hand, Table 2 shows only SD1 and SD2 are significantly different between the two groups of fetuses below and above 35 weeks. Figure 1 shows that significantly positive correlations were found for SD1 and CCM values with gestational ages.

Results indicate that variability in fetal heart rates as captured by SD1 and SD2 markedly changes after 35 weeks of gestation whereas dynamics in fetal heart rates as captured by CCM substantially changes after 30 weeks of gestation. Significant positive correlations of CCM and SD1 with gestational ages might mean that short term variability and temporal dynamics of fetal heart rate variability increase over the development of fetal cardiac function.

Table 1: Mean ± SD values of SD1, SD2 and CCM parameters of two gestational age groups (below and above 30 weeks). * means p<0.05.

	Group1 (<=30 wks)	Group2 (>30 wks)
	Mean ± SD	Mean ± SD
SD1 (ms)	3.21 ± 3.56	8.27 ± 11.62
SD2 (ms)	12.86 ± 8.88	18.84 ± 11.40
CCM (ms^2)	103.46 ± 283.42*	489.56 ± 1074.45

Table2: Mean ± SD values of SD1, SD2 and CCM parameters of two gestational age groups (below and above 35 weeks). * means p<0.05.

	Group1 (<=35 wks)	Group2 (>35 wks)
	Mean ± SD	Mean ± SD
SD1 (ms)	3.09 ± 3.27*	12.09 ± 13.94
SD2 (ms)	13.17 ± 9.04*	21.66 ± 11.66
CCM (ms^2)	96.10 ± 257.83	774.75±1337.73

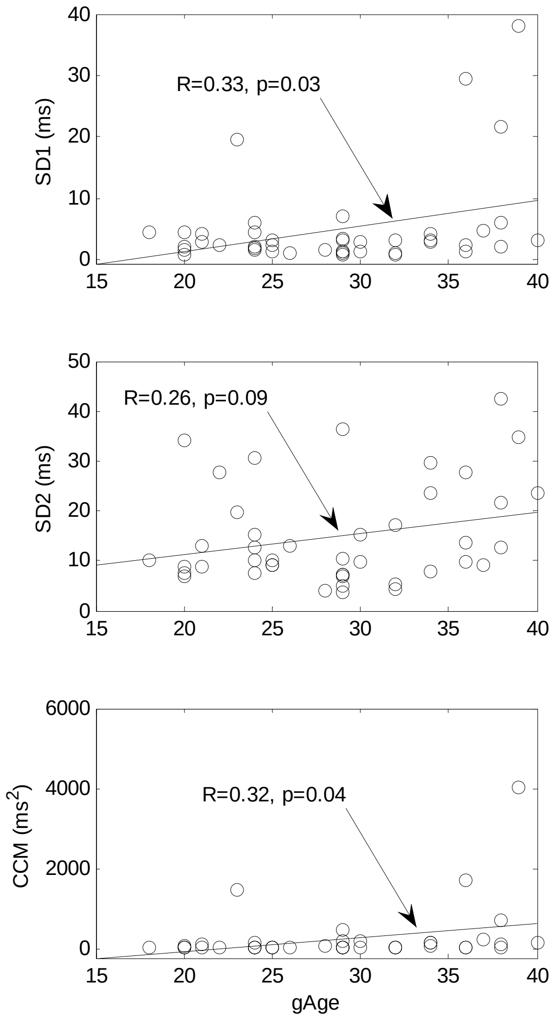

Figure1. Correlation of SD1, SD2 and CCM with gestational age.

4. Discussion

The goal of this study was to contribute to the assessment of the effectiveness of fHRV measures in further understanding the prenatal development of integrative ANS function prior to and after 35 weeks of gestation, employing Poincare plot based analysis techniques of heart rate variability and temporal dynamics of heart rates. Poincare plot technique can be applied on short term data to explore the variability and dynamics in time domain as previously applied in other studies [4, 11]. In this study, the length of the fetal ECG signals was 1 minute. Therefore, Poincare plot was considered. Fetal electrocardiography (ECG) which provides superior measurement of beat-to-beat intervals was used in this study.

The overall increase in SD1 and SD2 is associated with fetal growth in general and with the increase in neural development. The delivery time approaches closely after 35 weeks. SD1 and SD2 significantly increase after 35 weeks which might be caused by increase in fetal behavioral activities before delivery. On the other hand, significant change in CCM values after 30 but not after 35 weeks might indicate that dynamics in heart rate variability significantly develops between 30 to 35 weeks of gestation.

Autonomic nervous system activity (ANS) can be considered as a landmark of brain function, reflecting the overall fetal central nervous system (CNS) regulatory ability [12]. Investigation of ANS activity by using Poincare plot based fetal heart rate variability and dynamics during fetal gestational development may be one of the only available techniques for understanding fetal brain maturation.

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