Analyzing Fetal and Maternal Cardiorespiratory Interactions During Labor

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Abstract

There has been very little research focused on analyzing the directed interactions between fetal and maternal heart rate and respiration during labor or otherwise. In this work we focused on a measure of information flow between the mother and fetus as a prelude to identifying features correlated with outcome. We used the PhysioNet 'Abdominal and Direct Fetal Electrocardiogram Database' representing 5-minute multichannel ECG recordings from 5 pregnant women during labor. Each recording comprised four simultaneously acquired maternal abdomen ECG leads and a fetal scalp recording. Fetal and maternal beat to beat intervals were extracted to estimate heart rate and respiration from both mother and fetus. The interactions between fetal and maternal breathing and heart rates were assessed by Neural Network-based Granger Causality (NNGC) with non-uniform embedding. For all cases the causal influence was unidirectional from respiration to heart rate for mothers and fetuses. The strongest causal link was from fetal heart period and breathing movement to maternal heart period, indicating that the maternal heart rate is mainly influenced by the fetal cardiorespiratory activity during labor. This implies that a change in the fetal breathing movement and heart rate can invoke a maternal physiological response to satisfy the fetal oxygen demand during the course of labor. Future work will focus on a larger cohort and using the information flow as a parameter to identify fetal maturity, distress and complications during labor.

1. Introduction

Despite the advances in fetal and maternal healthcare, birth is still associated with a considerable risk, causing 2.6 million stillbirths, 2.8 million infant deaths and 287,000 maternal deaths globally each year [1]. Intrapartum Fetal Heart Rate (FHR) monitoring has been commonly used to detect early signs of fetal distress which has decreased neonatal mortality and morbidity [2]. While the obstetricians and midwives are trained to categorize the morphological appearances of decelerations, less attempt has been made to understand how the fetus reacts and adapts to oxygen deprivation. This has resulted in adverse outcomes, unnecessary interventions and expensive litigation [3]. Considering that both mothers and fetuses experience changes in hemodynamic and autonomic nervous system (ANS) activity during labor, simultaneous assessment of maternal heart rate (MHR) and FHR can improve detection of fetal acidemia and other fetal and maternal complications [4]. It can also facilitate investigation of the pathophysiological relationship between the mother and the fetus, as well as the interpretation of fetal reactions to adverse conditions during labor.

Previous studies have demonstrated the evidences of relationship between the fetal and maternal diurnal heart rate rhythms during pregnancy [5]. Short time coupling of FHR and MHR has been also found by Van Leeuwen et al., using phase synchronization analysis, as the phase locking of the rhythmic maternal and fetal heartbeats [6]. In our recent study we used Transfer Entropy (TE) and found directed interactions between maternal and fetal heart rates at various time delays, evolving with advancing gestation [7]. Analysis of TE showed an increase in transfer of information from mother to fetus with gestational age and a decrease on the other direction, alongside a decreased delay (faster fetal response) in information transfer with gestational progression [7].

Adult cardio-respiratory studies have shown that the cardiovascular and cardio-respiratory systems are complex physiological systems with direct and indirect interactions [8]. These interactions are mainly reflected in the Respiratory Sinus Arrhythmia (RSA), the rhythmic fluctuation of cardiac cycle intervals with respiration [8]. Considering this cardiorespiratory relationship, maternal respiration and fetal breathing movements can potentially contribute to fetal and maternal heart rate and their interactions. Fetal-maternal heart rate synchronization was previously analyzed while controlling maternal respiration and maternal aerobic exercise [9, 10], concluding that high maternal breathing rate may induce the synchronization [9]. A recent study investigated the effect of maternal

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RSA in the fetal hemodynamics regulation, in both normal conditions and Pre-eclampsia, which is one of the life-threatening complications of pregnancy [11]. It was found that maternal RSA affects the fetal umbilical venous blood flow and the fetal autonomic nervous regulation in healthy pregnancies. For the cases with pre-eclampsia, reduced effect of maternal RSA on the maternal hemodynamics was observed, and the control of fetal hemodynamics diminished with deterioration of cardiorespiratory synchronization [11]. In severe pre-eclampsia, fetal cardiovascular system was found to be completely separate from the mother [11], which suggests a potential application of assessing fetal-maternal cardio-respiratory relationship in detection and evaluation of pre-eclampsia. These studies show the importance of maternal breathing contribution to fetal and maternal heart rate and their interactions, which however requires more analysis to understand their "causal" relationship and also the effect of fetal breathing movements.

Although previous studies have uncovered the FHR and MHR relationship during pregnancy, further investigation is still required to analyze this relationship during labor. Furthermore the causal influence of maternal respiration and fetal breathing movements need to be considered in conjunction with FHR and MHR, as possible interacting factors. These research gaps have been addressed in the current study.

2. Methods

2.1. Database

A publicly available database was used from Physionet [12] containing abdominal and direct Fetal Electrocardiogram (FECG) recordings obtained from 5 different women in labor, between 38 and 41 weeks of gestation [13]. The recordings were acquired in the Department of Obstetrics at the Medical University of Silesia and each recording comprised four differential signals from maternal abdomen and one direct FEGC from the fetal scalp.

2.2. Estimation of fetal and maternal heart rates and respiratory sinus arrhythmia

Fetal ECG was extracted from abdominal recordings by a multi-step approach, comprised of pre-processing, Independent Component Analysis (ICA) for maternal ECG extraction, mother QRS detection and ECG canceling and second ICA to enhance the fetal ECG signal [14]. Fetal QRS locations were detected using a previously published peak energy detection method, described in [15], from both the extracted (indirect) FECG and the direct scalp FECG. Each FECG signal was subject to noise and transient signal loss, causing missing R-peaks or double R-peak detection which could be detected based on standard deviation of RR-intervals. Therefore, RR-intervals from both signals were analyzed in moving 10-second windows to select the best channel resulting in the lowest standard deviation. Maternal QRS locations were also detected using a previously published peak energy detection method, described in [15]. The best channel was then selected again by selecting the one with the lowest standard deviation of RR-intervals in a given 10-second window. Maternal and fetal RR-interval time series were further visually inspected for ectopic beats and artifacts.

The respiration was derived indirectly from the Respiratory Sinus Arrhythmia (RSA) effect, derived from the maternal and fetal RR-intervals [16]. Following [17], the RR-intervals were first resampled to 10 Hz, and then a band-pass filter was applied to isolated the frequency range associated with respiration activity, i.e. 0.1-0.45 Hz for maternal and 0.2-1 Hz for fetal breathing. The filtered time series were then standardized through dividing by the 75%-percentil of all local maxima and the peaks were detected by setting a threshold of 0.3, as described in [18]. Maternal and fetal breath to breath (MBB and FBB) intervals were detected from peak to peak intervals. All RR-intervals and breath-to-breath time series were then re-sampled to 5Hz. Fetal Heart Rate (FHR), Fetal Breathing Rate (FBR), Maternal Heart Rate (MHR) and Maternal Breathing Rate (MBR) were derived from RR-intervals and breath-to-breath intervals, and presented in beat-per-minute and breath-per-minute units.

2.3. Neural Network Granger Causality

In order to find directed dynamical interactions between fetal and maternal heart and respiration periods, the normalized time series (to zero mean and unit variance) were modeled using neural networks. The prediction errors were then used to evaluate the Granger Causality (GC). In recent work, Montalo *et al.* presented a Neural Network Granger Causality (NNGC) measure that was defined as

$$\mathrm{NNGC} = \varepsilon_r - \varepsilon_f \tag{1}$$

where ε is the difference between the prediction error obtained by the network with ε_r or without ε_f taking into account an entity's past states [19]. This model-free approach used Non-Uniform Embedding framework as a feature selection algorithm, to identify only the past states which significantly improved the prediction, reducing the chance of over-fitting. The model order (the number of past states considered for each series) was chosen to be 10 samples of fetal and maternal heart and breathing periods. The MuTE (Matlab Transfer Entropy) toolbox was used to measure the NNGC for fetal and maternal time series [20].

3. Results

The median and interquartile ranges for fetal and maternal heart rate and breathing rate are summarized in table 1. Figure 1 shows the directional links between fetal and maternal heart rates and breathing rates, which were associated with nonzero NNGC measures (color-coded, with hotter colors indicating higher relative information transfer, and arrows indicating direction). As the figure shows, for all cases the causal influence was unidirectional from respiration to heart rate. Therefore in the database studied in this work, both fetal and maternal respiration activities act only as a source affecting the fetal and maternal heart rates, while not being affected by them. However, the effect of respiration was generally weaker than the maternal-fetal heart rate interaction. While for three of the cases MHR was the main target (information sink), for cases 2 and 3 FHR was affected by MHR. We found that for these two cases the FHR was lower, and case 2 with the lowest FHR of all, was affected significantly by both maternal heart rate and respiration (the significance is confirmed through NUE process).

Table 1. The median and interquartile ranges for maternal and fetal heart rate (MHR and FHR) in beat-per-minute and breathing rate (MBR and FBR) in breath-per-minute.

Case ID	MHR	MBR	FHR	FBR
1	81.4	21.2	127.5	39.4
	[78.3,84.5]	[17.2,24.3]	[125.8,128.9]	[33.4,46.0]
2	85.7	20.7	125.3	38.9
	[78.0,93.3]	[16.5,23.9]	[122.7,128.3]	[31.9,45.2]
3	77.0	20.3	126.0	39.6
	[73.3,87.5]	[16.8,23.5]	[124.4,126.9]	[33.5,45.7]
4	81.4	19.2	128.9	39.9
	[74.4,87.2]	[16.1,22.8]	[126.4,132.1]	[31.0,46.2]
5	96.0,	20.9	131.6	38.1
	[89.3,98.6]	[17.3,23.5]	[127.6,134.5]	[31.7,43.3]

4. Discussion and Conclusion

In this preliminary study of five normal laboring mothers, fetal and maternal cardiorespiratory activity tends to have a directed causal flow. Specifically, fetal and maternal respiration were sources, affecting the fetal and maternal heart rates. This result is in agreement with the known fact that respiration modulates heart rate through the influence of breathing perturbations on the intrathoracic pressure transmitted to the cardiac output [21, 22]. We found more significant interaction between maternal and fetal heart rates, which was also observed during pregnancy in previous studies [7, 23]. It was previously hypothesized that the fetus responds to mechanical or auditory stimuli associated with the maternal rhythms, and FHR changes accordingly [23, 24]. Also a change in the fetal breathing movement and heart rate can invoke a maternal physiological response to satisfy the fetal oxygen demand during the course of labor. This effect of FHR and FBR on MHR was particularly marked for the cases with higher FHR.

This study provided a preliminary insight into the fetal and maternal cardiorespiratory interactions during labor. Further investigation using a direct measurement of maternal respiration, together with the use of ultrasound to detect fetal breathing movement, may be revealing. There is also a need to evaluate the information flow and the fetal responses under abnormal conditions such as pre-eclampsia, placental dysfunction, fetal hypoxia and acidosis in future studies. The information flow may also be utilized as a parameter to identify activity in utero (such as sleep), and to detect prematurity and fetal distress, since the information flow is likely to change in each of these states.

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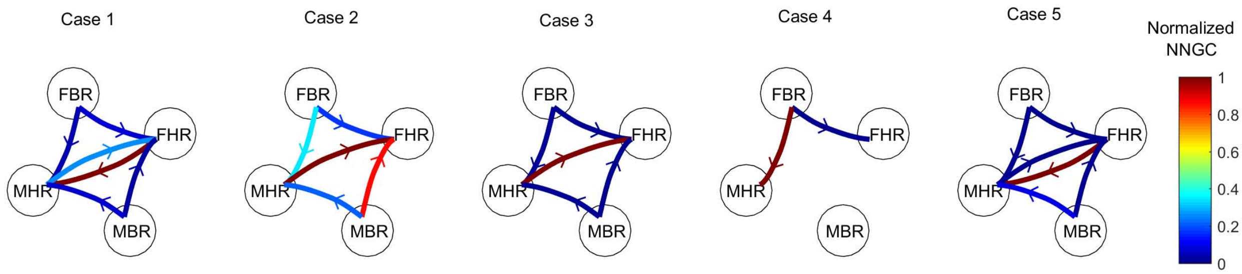

Figure 1. Fetal and maternal cardiorespiratory network is illustrated for each case. The nodes represent fetal and maternal heart and breathing rates. The causal links are color-coded based on the NNGC, with a hotter color indicating a higher relative information flow.

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