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A comparison of heart rate variability in women at the third trimester of pregnancy and during low-risk labour

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HIGHLIGHTS

- A novel characterization of human heartbeat dynamics during labour.
- Vagal influence increased in labour in comparison to the third trimester of gestation.
- A cholinergic anti-inflammatory activity seems to be manifested in labour.
- Maternal heartbeat dynamics could indicate the physiological onset of labour.

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ABSTRACT

Heart rate variability (HRV) has been recognised as a non-invasive method for assessing cardiac autonomic regulation. Aiming to characterize HRV changes at labour in women, we studied 10 minute ECG recordings from young mothers ($n = 30$) at the third trimester of pregnancy (P) or during augmentation of labour (L) ($n = 30$). Data of the L group were collected when no-contractions (L-NC) or the contractile activity (L-C) was manifested. Accordingly, the inter-beat interval (IBI) time series were processed to estimate relevant parameters of HRV such as the mean IBI ($\overline{IBI}$), the mean heart rate ($\overline{HR}$), the root mean square of successive differences (*RMSSD*) in IBIs, the natural logarithm of high-frequency component (*LnHF*), the short-term scaling parameters from detrended fluctuation and magnitude and sign analyses such as (α_1, $\alpha_{1(MAG)}$, $\alpha_{1(SIGN)}$), and the sample entropy (*SampEn*). We found statistical differences ($p < 0.05$) for *RMSSD* among P and L-NC/L-C groups (25 ± 13 vs. $36 \pm 14/34 \pm 16$ ms) and for *LnHF* between P and L-NC (5.37 ± 1.15 vs. 6.05 ± 0.86 ms^2). Likewise, we identified statistical differences ($p < 0.05$) for $\alpha_{1(SIGN)}$ among P and L-NC/L-C groups (0.19 ± 0.20 vs. $0.32 \pm 0.17/0.39 \pm 0.13$). By contrast, L-NC and L-C groups showed statistical differences ($p < 0.05$) in $\alpha_{1(MAG)}$ (0.67 ± 0.12 vs. 0.79 ± 0.12), and *SampEn* (1.62 ± 0.26 vs. 1.20 ± 0.44). These results suggest that during labour, despite preserving a concomitant non-linear influence, the maternal short-term cardiac autonomic regulation becomes weakly anticorrelated (as indicated by $\alpha_{1(SIGN)}$); furthermore, an increased vagally mediated activity is observed (as indicated by *RMSSD* and *LnHF*), which may reflect a cholinergic pathway activation owing to the use of oxytocin or the anti-inflammatory cholinergic response triggered during labour.

1. Introduction

Contractions during labour are generally associated with an increased maternal heart rate and mean arterial pressure as well as the subsequent increase in cardiac output resulting from increments in both stroke volume and heart rate [1–5]. The details of how these haemodynamic changes are driven by autonomic adaptations and, moreover, the actual role of the autonomic nervous system (ANS) during

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pregnancy remain to be fully elucidated [6]. In this regard, several findings prompt to consider labour as an inflammatory event that is not only initiated by hormonal factors [7]. In consequence, it can be assumed that labour may also introduce an anti-inflammatory response carried out by the autonomic activity [8].

Insights about the ANS activity of pregnant women have been studied by analysing the variation between the successive cardiac inter-beat intervals (IBIs), also referred to as heart rate variability (HRV) [9–11], which is a non-invasive approach to quantify the autonomous cardiac response to adrenergic and cholinergic influences [12]. In general, time-domain and spectral analysis, but also scaling methods (i.e. detrended fluctuation analysis: DFA) are applied to obtain measures that are used to estimate the autonomic response.

Although some authors have assumed that during pregnancy maternal autonomic conditions mainly reflect a sympathetic involvement [9–11] to the aortocaval compression of late gestation [13], the dynamic patterns of maternal heartbeat fluctuations have not been thoroughly explored, in particular during labour. In this regard, previous studies have mainly focused on changes of the mean maternal heart rate in relation to uterine contractions [2,4,5]. Recently, Suzuki et al. assessed maternal HRV during labour using a power spectral analysis to describe beat-to-beat changes associated with the particular presence of uterine contractions. Despite that no differences in high-frequency (HF) components between uterine contraction and non-contraction periods were found, the low-frequency (LF) and very-low-frequency (VLF) components during uterine contractions were significantly stronger during contraction periods. Authors concluded that the maternal sympathetic activity was apparently increased during uterine contraction periods [14].

In this study, we evaluate the use of linear and non-linear parameters to analyse heartbeat fluctuations during labour. In particular, we aimed to compare short-term IBI fluctuations registered from low-risk women during augmentation of labour with data collected during the third trimester of pregnancy to identify dynamic HRV changes.

We hypothesised that the autonomic adaptations during labour, either to facilitate haemodynamic requirements or even to restrain or counteract inflammation, are manifested on heartbeat fluctuations.

2. Methods

2.1. Subjects and data collection

Electrocardiogram (ECG) recordings were collected from 30 women, who developed term pregnancy (39.6 ± 1.2 weeks) and underwent low-risk labour. All recordings and procedures took place at Maternal and Childhood Research Center (CIMIGen) having obtained consent from each patient on a voluntary basis. For data collection we used an ECG portable device (Monica AN24 monitor, Monica Healthcare, Nottingham, UK), with a sampling frequency of 900 Hz. During recordings, subjects were free to choose their preferred posture due to the portability of the system, yet ECG segments to be analysed were only selected when women maintained a semi-Fowler's position. The general characteristics and the pregnancy outcome of this group are presented in Table 1; no major complications occurred in newborns as indicated by weights and Apgar scores.

Table 1
Mean (±SD) of the general characteristics of the study population during labour (L) and at the third trimester of pregnancy (P).

	L $n = 30$	P $n = 30$
Age (years)	26 ± 5	23 ± 6
Weight (kg)	64 ± 13	73 ± 11
Height (cm)	156 ± 6	156 ± 5
Gestational age (weeks)	39.6 ± 1.2	34.8 ± 1.6
Newborn's birth weight (g)[a]	3175 ± 297	3186 ± 251
Newborn's 5-minute Apgar (points)[a]	8.9 ± 0.6	9.0 ± 0.0

[a] $n = 15$ (for P group).

Table 2
Mean (±SD) of labour characteristics of the study population ($n = 30$) during periods with contractions (L-C) and without contractions (L-NC).

	L-NC	L-C
Dilatation (cm)	4.2 ± 2.9	4.1 ± 2.6
Effacement (%)	53 ± 31	54 ± 28
Number of contractions (per 10 min)	1.7 ± 1.3*	3.7 ± 0.3

* $p < 10^{-6}$ between L-C and L-NC.

The first and second stages of labour were identified by the presence of regular uterine contractions and cervix effacement and dilatation [15] (see values at Table 2). The ECG recordings during labour were classified into two distinct classes: the labour-contraction (L-C) included 10 min segments where the uterine activity was observable (with three or more contractions), and the other class, labour-no contraction (L-NC), included 10 min segments involving fewer uterine activity or no contractions at all. All studied women received intravenous oxytocin to improve contractility according to the Mexican guidelines for augmentation of labour [16]. For comparison, we also recorded 10 min segments of data collected during the last trimester of gestation (37–39 weeks) of other 30 women at the semi-Fowler's position not showing any clinical manifestation of the initiation of labour (P) (Table 1).

ECG recordings were visually analysed by using the software of the device, which displays values of maternal heart rate in conjunction with an ECG-derived uterine activity signal (Fig. 1). To ensure the proper selection of L-C segments accompanied by uterine contractions, we also identified unequivocal increments of the displayed maternal heart rate because during well-established frequent contractions the haemodynamic adjustments should generally involve a compensation of cardiac output by an increased heat rate [4,5,17]. L-C and L-NC segments were only selected if these segments involve none or few maternal gross movements.

2.2. Data analysis

Raw maternal ECG recordings were then processed using previous validated algorithms to generate IBI series which corresponded to episodes of contraction (L-C), no contraction (L-NC) or pregnancy (P) segments [18]. All series (L-C = 30, L-NC = 30 and P = 30) consisted of 600 IBIs for each subject (7 ± 1 minute duration), were reconditioned by a filtering approach and tested in line with previous studies [19] to exclude for ectopic beats and artefacts.

The mean value of IBIs and HR, $\overline{IBI}$ and $\overline{HR}$ respectively, as well as the root mean square of successive differences (*RMSSD*) in IBIs and the natural logarithm of high-frequency (*LnHF*, 0.15–0.4 Hz) parameters, which quantify vagally-mediated high frequency fluctuations [12], were calculated for all series. The scaling parameters of all series were evaluated by applying detrended fluctuation analysis (DFA) and the magnitude and sign analyses (MSA). Accordingly, the DFA provided the scaling exponent, α_1, as follows [20].

The maternal IBI fluctuation series were integrated by:

$$Y(k) = \sum_{i=1}^{k}\left[IBI(i) - \overline{IBI}\right] \quad (1)$$

where $Y(k)$ represents the k-th value of the resulting integration ($k = 1,2\ldots L$), $IBI(i)$ is the i-th RR interval, and $\overline{IBI}$ is the mean RR value of the IBI series (Eq. (1)).

Next, the integrated series were divided into boxes having equal numbers of n samples. The local trends Y_n were obtained for all boxes