Neonatal magnetocardiography and Fourier spectral analysis

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Summary

Objective: In this study we investigated the relationship between heart rate variability (HRV) and respiration in healthy and probably asphyxiated infants using magnetocardiographic (MCG) recordings.

Methods: Ten healthy and eight infants from pregnancies complicated by preeclampsia with indications of mild perinatal asphyxia were included in the study. All were near term. Maternal age ranged from 16 to 39 years (mean = 29.05, SD = 6.13). Spectral analysis was used to find out any association between respiration and HRV.

Results: Respiratory sinus arrhythmia (RSA) was reduced in preeclamptic infants with indications of mild perinatal asphyxia. This difference was statistically significant ($p < 0.0002$, t-test), whereas the heart rate of the two groups was not statistically significant ($p = 0.1$, t-test).

Conclusion: The results suggest that infants with indications of mild preeclampsia differ from controls in respiratory activity and this difference is independent of basal heart rate. Thus, spectral analysis could be useful for the estimation of influence of mild perinatal asphyxia in the RSA rhythm of newborns.

Key words: Magnetocardiography; Infant; Power spectra analysis; Respiratory sinus arrhythmia; Mild asphyxia.

Introduction

Heart rate variability (HRV) is affected by many factors such as respiration, temperature, state of oxygenation, blood pressure and physiological parameters. Respiratory sinus arrhythmia (RSA) is the mechanism by which respiration modulates heart rate. A number of theories have been proposed to describe RSA: increased filling of the right atrium during inspiration as a cause of cardiac acceleration (1); central modulation of the baroreflex (2); interaction between respiration and baroreflex (3).

During the last decade there has been an increasing interest in HRV and its significance to neonatal well-being. Porges [4] used power spectral analysis in the heart rate of neonates and associated it with the respiratory frequency band as a measure of RSA amplitude. Kitney *et al.* [5] reported a common frequency in respiratory amplitude, breath duration recordings and HR spectra in a 6-week-old infant. Giddens and Kitney [6] and Dykes *et al.* [7] described an interaction between respiration and heart rate in which the HR spectra showed a frequency from the breath amplitude of full-term infants in addition to the RSA and called this phenomenon "breath amplitude sinus arrhythmia". Work in animals [8] suggests that spectra analysis gives information about their neurological development.

Diminution or absence of RSA and decreased beat-to-beat variability have been reported in asphyxiated infants, in severe cardiac disorders, in sudden infant death syndrome, in respiratory distress syndrome and in diabetic autonomic neuropathy [9-12]. It has also been reported that RSA regulates the short-term beat-to-beat variability [13].

An alternative technique for the detection of electrical events in the heart besides electrocardiography (ECG) is magnetocardiography (MCG). Recordings of MCG do not require any electrodes because the detector is not even in contact with the body. The ECG is a record of the potentials appearing at electrodes attached to the skin, thus DC potentials appear at the elctrode-skin interface. These potentials are usually highly variable from subject to subject and electrode site, they can depend strongly on skin preparation and the type of paste, and they often will drift in amplitude slowly with time. For these reasons, the very low-frequency components of ECG are normally filtered out and do not appear in the tracing [14-17].

Clinical studies support that the existence of normal HRV is based on a well-oxygenated central nervous system [28]. As asphyxia is often associated with perinatal brain damage an interaction between breathing and HRV could explain the appearance of reduced variability [9]. The aim of this study was to identify whether heart rate power spectra differs between infants born from preeclamptic pregnancies with signs of mild asphyxia in comparison to infants from normal uncomplicated pregnancies by applying Fourier analysis techniques in MCG recordings.

Materials and Methods

Ten healthy neonates from uncomplicated pregnancies (gestational age 37-41 weeks) and eight infants from pregnancies complicated by preeclampsia (gestational age 37-38 weeks) with indications of mild perinatal asphyxia (cord pH < 7.2, 1st

min Apgar score < 7, no neurological deficiency), probably due to decreased uteroplacental perfusion were included in this study. Maternal age ranged from 16 to 39 years (mean = 29.05, SD = 6.13). Inclusion criteria for the newborn infants were as follows: a) gestational age > 37 weeks b) normal delivery c) birth weight 2130 - 4100 kg d) no neurological defects on clinical examination. The criteria of diagnosing preeclampsia were those defined by the American College of Obstetricians and Gynecologists [19]: a blood pressure of 140/90 mmHg or higher on two separate measurements 24 hours apart, with proteinuria or edema or both, in the absence of any underlying chronic renal or vascular disease.

The rules of the Helsinki Declaration were followed: parents were fully informed and a written consent was obtained for each newborn. The local ethics committee was notified and approved the study. Throughout the entire period of measurement, a sleep state analysis was carried out, focusing on quiet sleep. Closed eyes, absence of body and eye movements and a prevailing muscle tone defined quiet sleep states. Biomagnetic recordings were obtained on the 2nd day after birth. All infants breathed spontaneously during the measurements. The measurements began at 11:00 am - 1 h after the last feeding.

The MCG was recorded digitally for 10 min by a single channel biomagentometer (DC-SQUID model 601, USA) [14, 16, 17]. The SQUID gradiometer operates at the low liquid helium temperature of 4° K on the basis of the Josephson effect of superconductivity [20]. In order to minimize the incidence of stray electromagnetic variations, recordings were taken in an electrically shielded room of low magnetic noise. We digitized the signals using a 12-bit precision analog to digital converter with a sampling frequency of 256 Hz. The MCG signals were band-pass filtered with cut-off frequencies of 0.1-100 Hz. The associated Nyquist frequency limit with the above-mentioned sampling frequency is 128 Hz, which is well above the constituent frequency components of interest in MCG recordings and avoids artifacts. The tip of the single channel biomagnetometer was placed 2-3 cm above the infants' hearts at the position where the QRS signal was found to be at its maximum.

The biomagnetometer allows on-line determination of the R-R intervals. After the R-R interval is determined, the segment of the digitally recorded MCG signal is compressed and stored together with the R-R interval for later off-line analysis; 1024 consecutive R-R intervals were obtained and used for further analysis. The individual R-R intervals that deviated from the time series mean by > 60% were removed and the segments from the beginning or end of the tracing where nonstationarity was existence, were cut out. These criteria were chosen so that the respiratory rate of the free-breathing infants would be as regular as possible.

In the time domain the R-R intervals of each time series were calculated. Fast Fourier transform was performed yielding the power spectra. Neonates exhibit HRV fluctuations in a wide range of frequencies. The very low frequency band (0-0.02 Hz) usually has contributions of slow trend artifacts and is avoided. The low frequency band (0.02-0.15 Hz) includes contributions from the thermoregulatory fluctuation tone (0.02-0.09 Hz) and the baroreceptor control fluctuations (0.09-0.15 Hz). It may also contain fluctuations due to breath amplitude modulation [7]. The high frequency band (0.2-2 Hz) contains primarily the reflection of the respiratory activity [6, 13]. We define the peak in the respiratory spectrum as the band in the range of 0.37 to 2 Hz (corresponding to respiratory rates between 22 and 120 breaths/min) with the greatest respiratory spectra power.

Results

In Table 1 the comparison of matching variables in the eight probably asphyxiated infants and ten controls is shown. Student's t-test revealed a statistical significance between the two groups in gestational age at birth (p < 0.0001) and in birth weights (p = 0.0032).

In Table 2 the heart rate and frequencies for the ten controls are listed with mean values 121.3±9.5 bpm and 0.75±0.10 Hz. The individual values for the heart rate and RSA frequencies in the eight probably-asphyxiated infants are listed in Table 3 with mean values 128.7±8.3 bpm and 0.86±0.11 Hz, respectively. The Student's t-test revealed that the heart rate of the two groups was not statistically significant (p = 0.1) whereas the frequencies between the groups were statistically significant (p = 0.041).

Individual values for RSA are represented also in Tables 2 and 3 with mean values 4.67±0.93 and 2.23±1.17 for the healthy and probably-asphyxiated infants, respectively. This difference was statistically significant (p < 0.0002, Student's t-test).

Table 1. — *Comparison of matching variables in eight probably-asphyxiated infants and ten controls.*

	Probably asphyxiated	Controls
Gestational age at birth (weeks)	37.25 ± 0.46	39.30 ± 0.94
Birth weight (g)	2879 ± 198	3345 ± 335
Apgar (1 min)	6 ± 1	8 ± 1
Apgar (5 min)	7 ± 0	9 ± 0
% Male, % Female	50/50	40/60

Table 2. — *Mean heart rate and frequencies from infants with signs of mild asphyxia.*

Patient	Heart rate (bpm)	Frequencies (Hz)	RSA
1	134	1.01	1.2
2	141	0.98	0.8
3	128	0.93	2.3
4	135	0.89	3.2
5	123	0.83	3.4
6	116	0.78	3.8
7	132	0.68	2.3
8	121	0.81	0.9
Mean ± SD	128.7 ± 8.3	0.86 ± 0.11	2.23 ± 1.17

Table 3. — *Mean heart rate and frequencies from control infants.*

Patient	Heart rate (bpm)	Frequencies (Hz)	RSA
1	125	0.56	3.2
2	132	0.67	4.3
3	127	0.68	5.2
4	110	0.75	5.8
5	114	0.78	6.1
6	105	0.83	4.2
7	132	0.88	3.8
8	129	0.91	4.5
9	123	0.68	5.5
10	116	0.76	4.1
Mean ± SD	121.3 ± 9.5	0.75 ± 0.10	4.67 ± 0.93

Discussion

Spectral analysis has recently become a useful tool in the study of heart rate variability. Several studies have investigated the use of spectral analysis for the assessment of autonomic development in the pediatric population [21-24]. In adults, this technique has been used to study patients with cardiac or autonomic disorders [25].

A decrease in HRV was identified in infants who were considered at increased risk for sudden infant death syndrome (SIDS). Kluge *et al.* [12] reported that the extent of RSA in the high frequency region of the power spectrum is decreased in infants 1-6 weeks old who later succumb to SIDS, which is in agreement with Schechtman *et al.* [26]. Veerappan *et al.* [27] demonstrated an elevated level of parasympathetic activity by significantly higher frequency power in premature infants at approximately 34 weeks' postconception suffering from bradycardia during feeding. Baldzer *et al.* [28] found that 11 out of 20 neonates < 60 hours old had a RSA power greater than 20% of the total power which is in agreement with Thomson *et al.* [29] and demonstrates that RSA is a significant contributor to neonates 2-5 days old with a power greater than 30%.

The efferent pathway producing the RSA rhythm is considered to be the vagus nerve innervating the heart [30]. Vagal activity decreases during the inspiratory phase of the respiratory cycle resulting in an acceleration of heart rate.

Some mechanisms have been proposed as the cause of the inhibition of vagal activity. The respiratory modulation of the baroreceptor reflex has been regarded as an important contributor [31]. A mechanism of vagal inhibition mediated by the lung stretch receptors is also apparent [32]. Heart rate changes are also reported to be associated with central respiratory rhythm even when the lungs are inflated independently at different rates and a generated inhibition of vagal activity must occur [33]. All of these inputs cause inhibitory effects to the vagal preganglionic cardiomotor neurons during inspiration and result in the release of vagal tone on the heart, which is the cardiac acceleration [34]. Eckberg *et al.* [35] and Porges [4] agree that RSA originates in the brain stem and consequently in the vagal efferent activity of the heart. Thus, RSA is associated with interactions between respiratory neurons, peripheral receptors and the autonomic control of the heart. The presence of RSA at this early stage of life explains the newborns' capacity to react to perturbations to the system and aids their adaptation to environmental change.

Several investigators have reported a high correlation between low Apgar scores and neurological abnormalities [36-38]. Their studies demonstrated that the brain stem persists a high degree of damage in neonates who sustained hypoxic ischemic injury. The results of this study suggest that RSA is lower in probably- asphyxiated infants, which means that the modulation of heart rate by respiration is significantly reduced.

Spectra analysis is a method to study the interaction between heart rate and respiration. It may be used to study rhythmic activity of beat-to-beat variability and respiration by decomposing both series into functions of different frequencies. It has been previously used to study RSA in neonates [6, 9, 12, 27-29]. The effects of asphyxia on RSA in human fetuses are still under investigation. Since asphyxia is often associated with perinatal brain damage an abnormal interaction between breathing and HRV reduces the beat-to-beat variability. Thus, the spectra analysis technique in heart rate variability in neonates from preeclamptic pregnancies with signs of mild asphyxia could be useful in the estimation of neonatal well-being.

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