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Heart rate variability during REM and non-REM sleep in preterm neonates with and without abnormal cardiorespiratory events

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ABSTRACT

Aim: Analyse heart rate variability (HRV) of preterm neonates undergoing a polysomnography in relation to the occurrence of abnormal cardiorespiratory events on one hand and the type of sleep states on the other hand.
Methods: To quantify nonlinear HRV, the numerical noise titration technique is used, adapted to neonatal heart rate data. HRV is calculated for 30 preterm neonates with mean post-conceptional age of 36.4 weeks, divided into three groups according to the occurrence of abnormal events during the polysomnographies and the eventual home monitoring.
Results: Periods of non-REM sleep have lower noise limit values and can be distinguished significantly from periods of REM sleep and from the total recording period. The presence of abnormal events does not influence this finding. Significant differences between groups are only found during non-REM segments by means of the noise limit value computed via numerical noise titration while the linear HRV parameters were not able to discriminate.
Conclusion: ECG measurement of a relatively short non-REM sleep period without specific abnormal events is sufficient to define a mature cardiorespiratory pattern in preterm infants.
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1. Introduction

Heart rate variability (HRV) represents a non-invasive marker of autonomic activity. Numerous studies confirmed the potential of HRV with respect to several diseases and clinical conditions, although the practical use of HRV is mainly oriented towards the assessment of diabetic neuropathy and the prognosis of risk after acute myocardial infarction in adults [1–3]. Throughout the last decades, a multitude of methods have been developed to quantify HRV. In 1996, an international Task Force proposed standards for the measurement and calculation of a set of time- and frequency-domain HRV parameters. These are currently referred to as 'standard' or 'conventional' HRV parameters [1]. Analysis methods derived from nonlinear system dynamics have opened a new approach for studying and understanding the characteristics of cardiovascular dynamics. Conventional spectral analysis of HRV can provide analytical features of its cyclic variation but fails to show the dynamic properties of fluctuations. Nonlinear methods are typically designed to assess the quality, scaling and correlation properties; rather than the magnitude of variability as with conventional HRV methods. During the last decade, studies using robust nonlinear detection techniques have provided some of the strongest support for the presence of chaos in HRV [4]. Specifically, the method of noise titration [5,6] provides a highly sensitive test for deterministic chaos and a relative measure for tracking chaos of a noise-contaminated signal in short data segments.

Polysomnography (PSG) is the continuous recording of physiological parameters such as heart rate (HR), respiration and peripheral oxygen saturation (SaO_2). An apparent life threatening event (ALTE) is defined as an episode that is frightening to the observer and is characterized by some combinations of apnea (central or occasionally obstructive), color change (usually cyanotic or pallid), marked change in muscle tone, choking or gagging [7]. In preterm neonates, usually with a heart rate between 120 and 160 beats per minute (bpm), and infants having experienced ALTE, more subsequent life threatening events are found when the polysomnography is abnormal [8,9]. Polysomnographies can thus be used to identify risk infants who need cardiorespiratory home monitoring (ECG, respiration and possibly

Abbreviations: HRV, heart rate variability; REM, rapid eye movement; PSG, polysomnography; SaO_2, oxygen saturation; ALTE, apparent life threatening event; ECG, electrocardiography; EOG, electro-oculography; EMG, electromyography; bpm, beats per minute; FU, follow-up; NL, noise limit; PCA, post-conceptional age; GA, gestational age; RRI, R–R interval; RSA, respiratory sinus arrhythmia; SDNN, standard deviation of normal-to-normal (NN) intervals; RMSSD, root mean squared differences of successive NN intervals; SDANN, standard deviation of the average NN intervals calculated over 5 min periods; TI, triangular index; LE, Lyapunov exponent; OSAS, obstructive sleep apnea syndrome; NLD, nonlinear detection; PVC, premature ventricular contraction.

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SaO_2). In the University Hospital of Leuven, the criteria for an abnormal polysomnography are threefold, central or obstructive apnea for more than 15 s combined with a bradycardia below 60 bpm or oxygen saturation below 80%, or a bradycardia below 50 bpm for at least 4 s. The home monitoring is also evaluated in cases of bradycardia below 50 bpm for at least 4 s as criterion for abnormal follow-up (FU) [8]. Children with an abnormal polysomnography were systematically followed up with a cardiorespiratory home monitor with memory, so that new events at home could be documented. According to the results of the polysomnographies and follow-up, infants can thus be divided into 3 groups: NN (normal PSG and normal FU), AN (abnormal PSG and normal FU) and AA (abnormal PSG and abnormal FU). For each infant, periods of non-REM sleep and REM sleep can be indicated.

We hypothesize here that the deficiencies in the autonomic nervous system that cause the abnormal cardiorespiratory events are reflected in the heart rate, not only in abnormal bradycardia but also in more subtle changes. Analogously, we expect different cardiovascular fluctuations in different sleep states of neonates. Fetal heart rate variability (HRV) was already studied in test animals and several relations were found with sleep and other biological rhythms [10]. HRV will differ during non-REM compared to REM [11], therefore these periods may be characterized by nonlinear HRV parameters. Thus an automatic distinction between non-REM sleep and REM sleep in neonates may be within reach.

The present study investigates whether REM sleep and non-REM sleep periods can be distinguished in general and in particular in the different aforementioned groups (NN, AN, AA) using the noise limit (NL) value of the numerical noise titration technique, calculated within periods free from abnormal bradycardia. This could well improve the rating of REM and non-REM sleep in the future.

2. Methods

2.1. Data acquisition

For the present study, polysomnographies of preterm neonates recorded in the University Hospital Gasthuisberg (Leuven) between 2000 and 2003 were available. An abnormal PSG was recorded in 39 preterm infants, 15 of whom experienced further abnormal events during the follow-up. Some were excluded because of too many artefacts, mainly due to movement. Moreover, maturation is an important determinant of heart rate requiring age-matched AN and AA groups. Therefore, 10 subjects were selected in each group. Also ten age-matched infants were retained from the NN group. The mean post-conceptional age (PCA) at the time of the PSG was 36.4 weeks for the NN preterms, 36.3 weeks for the AN preterms and 36.4 weeks for the AA preterms. The mean gestational age (GA) at birth was 32.3 weeks, 31.9 weeks and 32.3 weeks respectively for the NN, AN and AA preterms. Other anthropomorphic details about the study population are given in Table 1.

The physiological parameters measured during the polysomnographies included electrocardiogram (ECG), thoracic and abdominal respiratory movements, nasal flow (thermistor), SaO_2, chin electromyogram (EMG) and electro-oculogram (EOG).

As we were not interested in a detailed sleep scoring, but only in well defined periods of REM and non-REM sleep, EEG was not needed and a non-standard method could be used. Periods of REM sleep were defined by the irregular breathing pattern (irregular rapid respirations), movement, tonically inhibited muscle tone on the EMG and single rapid eye movements on the EOG. Non-REM sleep was defined by slow-wave activity on the EOG, slow and regular respirations and normal muscle tone on the EMG. To prevent contamination of the study results, heart rate (variability) was excluded as a criterion to categorize sleep periods. Only well defined periods of REM and non-REM were selected. All polysomnographies were rated independently by one single investigator (HD) who was not involved in the HRV analysis [12–14].

After sampling all signals at 100 Hz, the RR intervals (RRI) were derived from the ECG signal. The R peaks were detected by an automatic peak detection algorithm based on the second derivative of the digitized ECG signal. To avoid errors due to faulty peak detection, all RR interval series were inspected for false and missed peaks, and corrected if necessary. The mean duration of the ECG recordings was more than 8 h (504.35 ± 161.24 min), yielding on average 75,000 RRI per patient.

2.2. Standard HRV parameters

Four standard time-domain HRV parameters were calculated as recommended by the Task Force [1]: SDNN, RMSSD, TI and SDANN. SDNN is the standard deviation of normal-to-normal intervals and RMSSD gives the root mean squared differences of successive normal-to-normal intervals. TI means triangular index and is defined as the number of normal-to-normal intervals divided by the maximum of the density distribution of all normal-to-normal intervals. The fourth measure, SDANN, is the standard deviation of the average normal-to-normal intervals calculated over 5 min periods.

2.3. Numerical noise titration

A nonlinear data analysis technique is used in this study, called numerical noise titration. In fact, it is a better alternative for the Lyapunov exponent (LE), which is a measure of the exponential divergence of nearby states. LE fails to specifically distinguish chaos from noise and cannot detect chaos reliably unless the data series are inordinately lengthy and virtually free of noise, but those requirements are difficult – mostly even impossible – to fulfill for most empirical data [5,6]. In contrast, numerical noise titration is an analytical technique that provides a sufficient and robust numerical test of chaos and a relative measure of chaotic intensity, even in the presence of significant noise contamination.

Table 1
Anthropomorphic details of the study population with median and 95% confidence interval (CI) for all different parameters in each group.

	AA		AN		NN	
	Median	95% CI	Median	95% CI	Median	95% CI
Apgar 1 min	7.00	6.14–8.86	8.00	3.55–8.00	8.00	1.00–9.00
Apgar 5 min	8.00	7.14–9.00	8.00	3.55–8.86	9.00	7.48–9.00
Days of ventilation	0.00	0.00–1.00	0.00	0.00–4.31	0.00	0.00–0.00
Days of CPAP	0.00	0.00–10.00	1.00	0.00–11.03	0.00	0.00–4.63
Birth weight	2240.00	1373.82–2566.20	2100.00	1284.51–2330.68	2082.50	1462.12–2606.75
Age in postnatal days on moment of registration	21.00	14.00–61.86	28.00	20.69–48.90	29.50	9.28–63.63
Postmenstrual age at birth	34.00	28.55–34.86	32.00	30.00–34.00	33.00	29.95–35.00
Postmenstrual age at moment of registration	37.00	36.00–37.00	36.00	36.00–37.00	37.00	36.00–39.05

Statistical analysis by ANOVA test did not show any significant difference between the groups.

White, and therefore linearly correlated, noise of increasing standard deviation (σ) is added to the data until its nonlinearity can no longer be detected, within a prescribed level of statistical confidence, by a particular indicator at a limiting value σ = noise limit (NL) value. As indicator for the nonlinearity, the Volterra–Wiener nonlinear identification method is used. A detailed version of the numerical noise titration technique can be found in Appendix A.

NL>0 indicates chaos and the value of NL gives an estimate of its relative intensity. Conversely, if NL = 0, then it may be inferred that the series either is not chaotic or the chaotic component is already neutralized by the background noise in the data. Therefore, the condition NL>0 provides a simple sufficient test for chaos.

2.4. Data analysis

For each RR interval series, both short term and long term variabilities were assessed. For the short term HRV, all non-REM sleep and REM sleep periods were analysed separately. For the long term HRV, the complete recordings were analysed. The HRV measures calculated on the complete RR interval series are referred to as "global" HRV measures.

SDNN and RMSSD were calculated both globally and on the separate sleep states. TI and SDANN were only calculated for the complete RR interval series because they cannot be estimated accurately on short segments. Regarding the numerical noise titration algorithm, the technique was applied on the resampled (2 Hz) RR interval time series using a 300-second window and sliding the window every 30 s.

Resampling the RR interval time series to a fixed sampling frequency is important because the algorithm requires equidistant samples. A sampling frequency of 2 Hz is chosen because this corresponds well to the natural neonatal heart rhythm, usually between 120 and 160 bpm. Other resampling frequencies were tried out to study their influence, but a higher resampling frequency resulted in loss of information due to interpolation.

2.5. Statistical analysis

Statistical analysis was performed with Matlab R2006b. Differences between behavioural states as non-REM and REM sleep periods were analysed pairwise by the nonparametric Wilcoxon signed rank tests. Those tests are robust with respect to outliers, which are present in this study, because they deal with the order and not with the absolute values. Comparing the three groups to each other was done by the nonparametric Mann Whitney U test. $P<0.05$ was considered statistically significant.

3. Results

For the standard time-domain HRV parameters, the mean ± standard deviation values for each group of subjects are shown in Table 2. No differences between groups are observed, neither in the complete recording, nor in non-REM or REM segments.

A typical result of applying the numerical noise titration technique to a RR interval time series is shown in Fig. 1. On top, the 2 Hz resampled RR interval time series of a preterm infant is shown while the periods of non-REM and REM sleep are indicated in the middle frame by −1 and +1 respectively. The NL signal, containing one NL value for each window of 5 min, slid every 30 s, is plotted in the bottom frame. It also illustrates that NL values can strongly fluctuate in time, even within the same subject and the same conditions, e.g. sleep state. Therefore, we calculated the mean NL value for each subject. Other measures such as median NL and 3 proportionality measures, were calculated too, but since they all give similar results, those measures will not be outlined here.

The NL values (mean ± standard deviation) are given in Table 3 for all groups and each behavioural state. Differences between groups were only visible during the non-REM segments. In these quiet periods, both AN and AA subjects have significantly lower NL values compared to NN subjects.

Table 2
Standard time-domain HRV parameters, calculated on the complete RR interval series and on all non-REM sleep and REM sleep segments.

	NN	AN	AA
Complete RR series			
RR (ms)	405 ± 21	401 ± 22	396 ± 15
SDNN (ms)	41.4 ± 9.5	42.4 ± 9.9	43.6 ± 8.7
RMSSD (ms)	10.3 ± 2.4	10.1 ± 3.2	10.8 ± 3.9
TI	9.1 ± 2.6	8.7 ± 2.3	9.7 ± 2.2
SDANN (ms)	27.0 ± 8.2	26.0 ± 4.8	29.5 ± 6.8
Non-REM segments			
RR (ms)	432 ± 32	426 ± 44	431 ± 25
SDNN (ms)	12.2 ± 4.9	10.7 ± 5.4	9.9 ± 3.8
RMSSD (ms)	7.2 ± 2.6	5.9 ± 3.0	6.8 ± 3.9
REM segments			
RR (ms)	408 ± 25	407 ± 33	412 ± 18
SDNN (ms)	26.7 ± 5.8	27.1 ± 11.3	25.6 ± 9.5
RMSSD (ms)	8.0 ± 1.6	7.7 ± 2.4	8.3 ± 3.5

The mean values ± standard deviations for each group of subjects are shown. No significant differences between groups are found.

During periods of non-REM sleep, the NL values are in general much lower, as could already be observed in Fig. 1. The boxplots in Fig. 2 confirm this finding. In each group, non-REM seems to be different from REM and from the total recording period. The P-values in Table 4 show that these differences are statistically significant, independently whether PSG and follow-up were normal or abnormal. When looking to the complete population of 30 neonates, even REM periods could be discriminated from the complete recording period.

4. Discussion

Measuring heart rate variability is a useful method to understand the state of the autonomic nervous system (ANS). The normal variability is due to the autonomic neural regulation of the heart and the circulatory system. In premature infants the ANS is still immature and this is reflected in the higher incidence of severe bradycardias and acute life threatening events in this group are most probably a reflection of this immaturity [15].

A typical neonatal RR interval series was shown in Fig. 1. A closer look at the data reveals several *rhythmical fluctuations*. Respiratory sinus arrhythmia (RSA) is a periodic fluctuation in heart rate associated with respiration [16]. Since the respiration rate in neonates, typically between 40 and 80 breaths per minute, is sometimes larger than half the heart rate, usually between 120 and 160 bpm, RSA cannot always be observed in neonates as limited by the Nyquist theorem. Respiratory events such as sighs [17], respiratory pauses (apneas) [18] or periodic breathing also influence the heart rate. Furthermore, slower rhythmical fluctuations with a period around 30 heart beats (10 s) can be observed in most RR interval series, Although this 10 s-rhythm has been described in many other studies, its origin remains uncertain. It is believed to be related to the Mayer waves observed in blood pressure and is attributed to baroreceptor reflex [16]. Some other phenomena such as non-nutritive sucking cause similar rhythms in the RR interval series [19]. In addition to RSA and the 10 s-rhythm, in some RR interval time series slower rhythmical fluctuations due to thermoregulation [20] or body movements are observed.

Another specific heart rate pattern, which is also found in full-term neonates and sometimes even in adults, is the observation of spikes. There are two types of spikes: short HR decelerations and spikes due to cardiac arrhythmias such as premature beats which affect only one or two RR intervals. Faulty peak detection, e.g. missed RR peaks or false detections, causes similar effects as certain cardiac arrhythmias. However, such spikes are not present in our RR interval series, as all

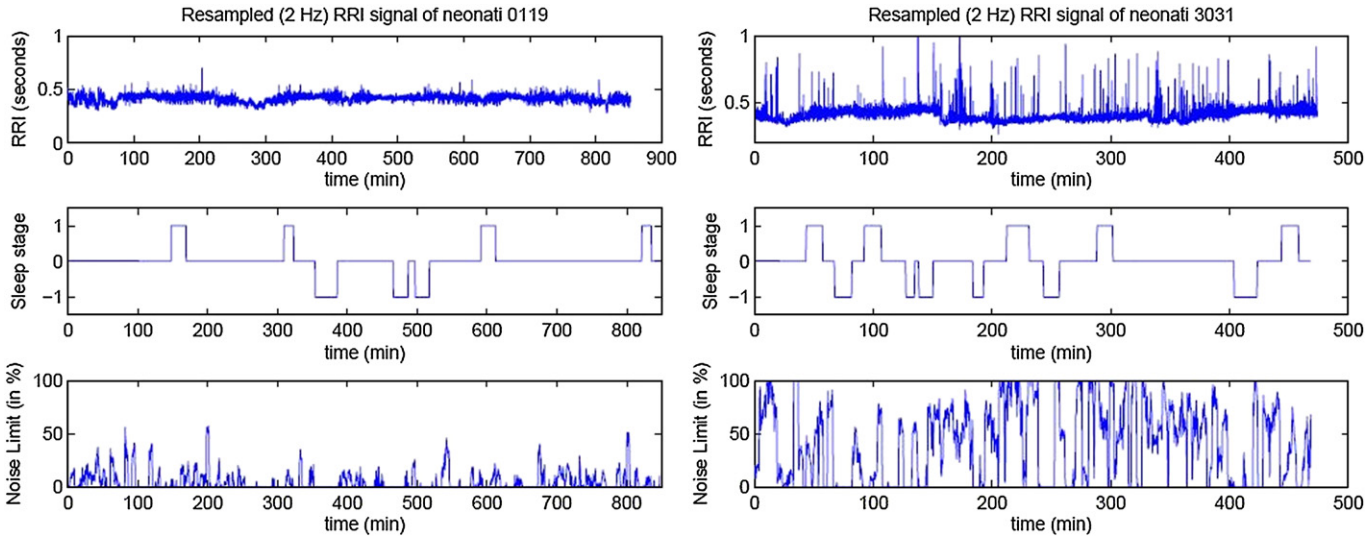

Fig. 1. Typical result of applying the numerical noise titration technique to a RR interval time series coming from a subject of (a) NN group and (b) AA group. On top, the 2 Hz resampled RR interval time series is given, while the periods of non-REM and REM sleep are indicated in the middle by respectively −1 and +1. The NL signal, containing one noise limit value for each window of 5 min, slid every 30 s, is plotted in the bottom frame, where the vertical lines indicate the boundaries of the non-REM periods.

faulty peak detections or premature ventricular contractions (PVC) were manually corrected based on the ECG recording.

The behavioural state has an important effect on heart rate. Heart rate is lower during non-REM sleep than during REM sleep or wakefulness [16,21]. The duration of the non-REM periods depends in general on age. For our recordings it was mostly between 10 and 30 min, which corresponds to approximately 2000 to 4000 RR intervals. In each ECG signal, multiple periods of non-REM and REM could be determined with a mean total duration of 53.74 ± 26.76 min and 62.08 ± 14.00 min respectively.

The present results support the idea that different sleep states have, already from birth on, different cardiovascular fluctuations. The mean heart rate and SDNN values in this study are comparable to the values reported in literature for healthy preterm infants with similar age (PCA, GA) [22–25]. Regarding the other standard time-domain HRV measures, to our knowledge, no comparable data is available in literature. Compared to normal full-term neonates with postnatal age of less than 72 h, all standard time-domain parameters are smaller [26]. This finding agrees with results from studies on the maturation of the cardiac control in neonates [22,23]. Heart rate, SDNN and RMSSD are significantly smaller in non-REM than in REM, a finding which was also observed in other studies [22,25,27,28].

The numerical noise titration technique showed that periods of non-REM sleep have lower noise limit values and can be distinguished significantly from periods of REM sleep and from the total recording period. The RR interval series during non-REM sleep is less chaotic and in many cases NL is 0, which means that that signal part can be modeled sufficiently well in a linear way. The presence of abnormal events does not influence this finding. Moreover, if we do not consider each group separately, but all subjects together, a stronger difference between the sleep states is found and even REM periods become statistically significant from the total recording.

Table 3
Results of numerical noise titration calculated on the complete RR interval series and on all non-REM sleep and REM sleep segments.

NL	NN	AN	AA
Complete RR series	16.62 ± 8.07	15.12 ± 5.87	17.40 ± 11.80
REM segments	12.84 ± 7.25	14.64 ± 8.12	14.17 ± 13.17
Non-REM segments	4.38 ± 2.77	1.67 ± 1.29[a]	1.39 ± 1.81[b]

The mean values ± standard deviations for each group of subjects are shown.
[a] $P<0.05$ by Mann Whitney U test compared to NN group.
[b] $P<0.01$ by Mann Whitney U test compared to NN group.

The use of a nonlinear HRV parameter is a new aspect in the domain of sleep study of preterm neonates. During the last years, a large dataset of 190 sleep scored infants is collected and analysed in the CHIME study with as main goal the development of a reliable decision system to determine sleep and wake based only on the electrocardiogram (ECG) of infants via HRV parameters [29,30]. Although HRV is investigated many times in different ways the last decades, the numerical noise titration technique is a very interesting and useful technique to distinguish sleep states from each other. Because the numerical noise titration technique only emerged recently, it has not yet been widely applied. In Zapanta et al. and Deng et al. [31], the technique has been applied for studying obstructive sleep apnea syndrome (OSAS) in children. Those studies concluded that it can be used to identify normal subjects from OSAS patients and that heart rate exhibits higher chaotic intensity in REM compared to non-REM sleep. However the latter was also investigated in this study, we have to emphasize that children and preterm neonates are two completely different population groups because their sleep patterns differ enormously [27,32–34].

Not only differences between sleep states were examined, but also a comparison between groups was done. While the standard time-domain measures could not discriminate between NN, AN and AA, neither in the complete recording, nor in non-REM or REM periods, the nonlinear NL parameter succeeded. It proves that nonlinear measures can give extra information because they reflect other aspects of heart rate variability [3,15]. Here, that other aspect reveals how chaotic the tachogram is. The more the signal is chaotic, the less predictable it is and different studies showed a loss of heart rate variability in pathologic situations such as central hypoventilation or sudden infant death syndrome [28] and sepsis or urinary tract infection [35]. For this reason, NL is significantly higher for NN subjects compared to AN or AA subjects, at least during non-REM segments. Therefore, this study suggests that analysing non-REM periods might be sufficient to indicate whether a polysomnography was normal or abnormal, just based on the tachogram and without need of a full PSG. However, this link between the level of maturity of the cardiorespiratory system and the lack of chaos during non-REM periods requires more data reflecting different gestational ages. NL is lower in the AA than the AN group, although not statistically significant, maybe due to the limited number of neonates in each group. From a practical point of

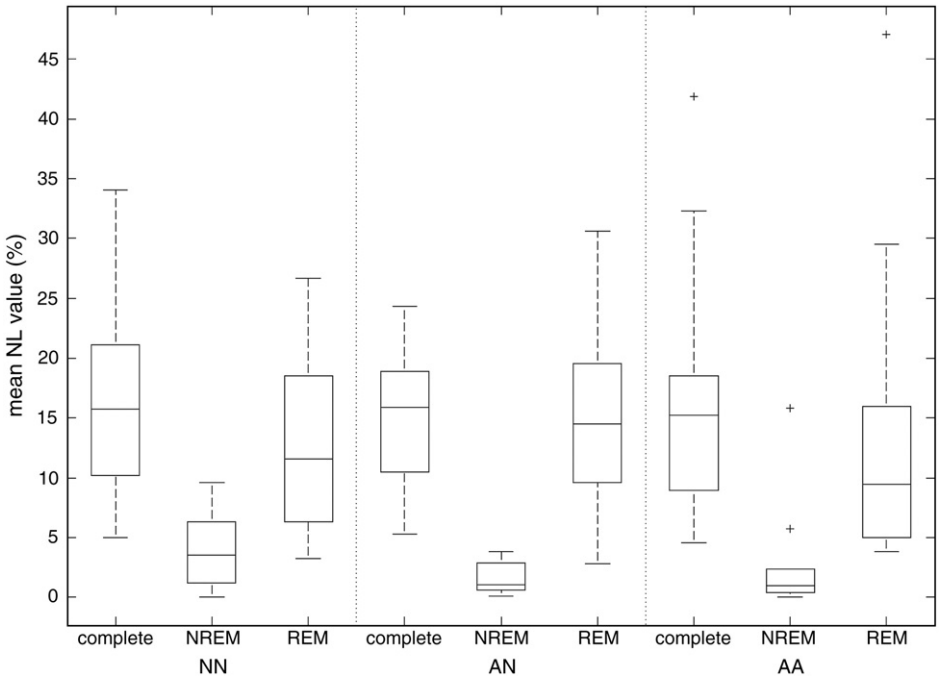

Fig. 2. Boxplots to compare pairwise in each group different behavioural states with the mean NL value as measure.

view, it should be very interesting if AN and AA neonates can be discriminated because this will help in deciding whether a baby needs a follow-up by home monitoring or not.

A similar study in preterm newborns was done by Morren [36] by making use of detrended fluctuation analysis (DFA). This well accepted classical technique computes nonlinear HRV parameters providing information about the scaling behaviour of the underlying system. That study did not show any significant difference between the groups when considering the complete night recording, nor in active sleep periods. Only the long term correlation coefficient α_2 in a quiet sleep period showed significantly higher values for the AA group compared to NN and AN. Therefore, DFA might be useful to discriminate between AN and AA as aimed in this study. A drawback of this study was the limitation that not all periods of active and quiet sleep in the PSG were analysed, but only the first ones so that the results cannot be generalized.

It is important to note that nonlinear HRV techniques will not replace linear analysis, but have to be considered as a complementary approach, yielding information about a specific aspect of scaling behaviour or complexity. Nonlinear techniques have the advantage over linear techniques in providing better repeatability and reliability across measurements (small random error). Therefore, nonlinear indices may be more suitable for diagnostic purposes, as well as for assessing individual treatment effects [37].

6. Conclusions

In this study, the heart rate variability (HRV) of preterm infants during polysomnography was analysed. In addition to standard time-domain HRV parameters, a nonlinear technique, called numerical noise titration, was used to quantify more dynamical aspects of the heart rate variability. The methodology for calculating these HRV parameters was adapted to deal with the specific characteristics of neonatal heart rate data and the relatively low ECG sampling rate (100 Hz). Regarding the numerical noise titration technique, periods of non-REM sleep have strongly significantly lower noise limit values, which means that the RR interval series is less chaotic during non-REM sleep. This provides further insights in the mechanisms causing periods of non-REM or REM sleep.

While the standard time-domain measures could not discriminate between NN, AN and AA, neither in the complete recording, nor in non-REM or REM periods, the nonlinear NL parameter succeeded.

Table 4
P-values of the differences in mean NL in the three different groups between behavioural states.

P-value	NN	AN	AA	All
Complete vs. non-REM	**0.002**	**0.002**	**0.002**	**1.73 E−6**
Complete vs. REM	0.131	0.695	**0.049**	**0.017**
Non-REM vs. REM	**0.006**	**0.002**	**0.002**	**2.35 E−6**

The Wilcoxon signed rank test for matched samples was used to assess the statistical significance. $P<0.05$ was considered statistically significant and is printed in bold.

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Appendix A. Numerical noise titration algorithm

Numerical noise titration is a nonlinear data analysis technique – used in this study – that is a better alternative for the Lyapunov exponent (LE), which is a measure of the exponential divergence of nearby states. LE fails to specifically distinguish chaos from noise and cannot detect chaos reliably unless the data series are inordinately lengthy and virtually free of noise, but those requirements are difficult – mostly even impossible – to fulfill for most empirical data. In contrast, numerical noise titration is an analytical technique that provides a sufficient and robust numerical test of chaos and a relative measure of chaotic intensity, even in the presence of significant noise contamination.

The different sections of the numerical noise titration algorithm are well described in [22].

A.1. Modeling

For any heartbeat RR time series y_n, $n=1, 2,\ldots, N$, a closed-loop version of the dynamics is proposed in which the output y_n feeds back as a delayed input. The univariate time series are analysed by using a discrete Volterra autoregressive series of degree d and memory κ as a model to calculate the predicted time series y_n^{calc}:

$$y_n^{\text{calc}} = a_0 + a_1 y_{n-1} + a_2 y_{n-2} + \ldots + a_\kappa y_{n-\kappa} + a_{\kappa+1} y_{n-1}^2 + a_{\kappa+2} y_{n-1} y_{n-2} + \ldots + a_M y_{n-\kappa}^d = \sum_{m=1}^{M-1} a_m z_m(n) \quad (1.1)$$

where $M=(\kappa+d)!/(\kappa!\,d!)$ is the total dimension. Thus, each model is parameterised by κ and d which correspond to the embedding dimension and the degree of the nonlinearity of the model (i.e. $d=1$ for linear and $d>1$ for nonlinear model). The coefficients a_m are recursively estimated from [1] by using the Korenberg algorithm.

A.2. Nonlinear detection (NLD)

The goodness of fit of a model (linear vs. nonlinear) is measured by the normalised residual sum of squared errors:

$$\varepsilon(\kappa,d)^2 = \frac{\sum_{n=1}^{N} (y_n^{\text{calc}}(\kappa,d) - y_n)^2}{\sum_{n=1}^{N} (y_n - \mu_y)^2} \quad (1.2)$$

with $\mu_y = \frac{1}{N}\sum_{n=1}^{N} y_n$ and $\varepsilon(\kappa,d)^2$ represents a normalised variance of the error residuals. The optimal model $\{\kappa_{\text{opt}}, d_{\text{opt}}\}$ is the model that minimizes the Akaike information criterion:

$$C(r) = \log \varepsilon(r) + \frac{r}{N} \quad (1.3)$$

where $r \in [1,M]$ is the number of polynomial terms of the truncated Volterra expansion from a certain pair (κ, d).

A.3. Numerical noise titration

The NLD is used to measure the chaotic dynamics inherent in the RR series by means of numerical noise titration as follows:

1. Given a time series y_n, apply the NLD to detect nonlinear determinism. If linear, then there is insufficient evidence for chaos.
2. If nonlinear, it may be chaotic or non-chaotic. To discriminate these possibilities, add a small (<1% of signal power) amount of random white noise to the data and then apply NLD again to the noise corrupted data. If linear, the noise limit (NL) of the data is zero and the signal is non-chaotic.
3. If nonlinearity is detected, increase the level of added noise and again apply NLD.
4. Repeat the above step until nonlinearity can no longer be detected when the noise is too high (low signal-to-noise ratio). The maximum noise level (i.e. NL) that can be added to the data just before nonlinearity can no longer be detected, is directly related to the Lyapunov exponent (LE).

A.4. Decision tool

Under this numerical titration scheme, NL>0 indicates the presence of chaos, and the value of NL gives an estimate of relative chaotic intensity. Conversely, if NL = 0, then the time series may be non-chaotic or the chaotic component is already neutralized by the background noise. Therefore, the condition NL>0 provides a simple sufficient test for chaos. Details of NLD and numerical noise titration are discussed in [5,6].

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