Open access • Journal Article • DOI:10.1515/JPME.1983.11.1.32

Microprocessor-based long term cardiorespirography. II. Status evaluation in term and premature newborns. — Source link

H. Hörnchen, R. Betz, F. Kotlarek, P. Roebruck

Published on: 01 Jan 1983 - Journal of Perinatal Medicine (J Perinat Med)

Topics: Heart rate variability, Heart rate and Oxygen tension

J. Perinat. Med.
11 (1983) 32

Microprocessor-based long term cardiorespirography
II. Status evaluation in term and premature newborns*

H. Hörnchen, R. Betz, F. Kotlarek, P. Roebruck

Departments of Pediatrics (Director: Professor Dr. H. Schönenberg) and Medical Statistics and Documentation (Director: Professor Dr. med., Dipl. Math. R. Repges), Medical Faculty, RWTH Aachen

URBACH et al. [39] and RUDOLPH et al. [35] described as early as 1965 a loss of heart rate variability in severely ill newborns. Similar observations were made by EKERT and KÖHLER [6] and HON and coworkers [15]. Maturity [21, 36] and age [41] evidently influence heart rate variability as well. The present study aimed to investigate the role of machine processed parameters of heart rate variability for the evaluation of the status of premature and term newborns.

1 Methods and patients

All studies were made with the apparatus described in part I. "Routine" printouts were obtained every 5 minutes and indicated:

1. Actual heart rate (bpm); respiratory rate (derived from the formula (α), see part I) immediately prior to the printout.
2. HAMMACHER criteria [10] (Fig. 1):
   A. Oscillation amplitude: saltatory (SALT), undulatory (UD), limited undulatory (LIM. UD = EG. UD) or silent (SIL). By comparing the highest with the lowest heart rate within one minute the oscillation amplitude is calculated. After 5 minutes the most frequently occurring oscillation amplitude will be printed out.
   B. Oscillation Rate: A, B, C. The number of transients through the zero line is calculated once each minute, and the arithmetic mean is printed out after five minutes.
3. Long time variability (LTV as bpm).
   This value is derived similar to the ocsillation amplitude. After five minutes the arithmetic mean of all five differential values is obtained.

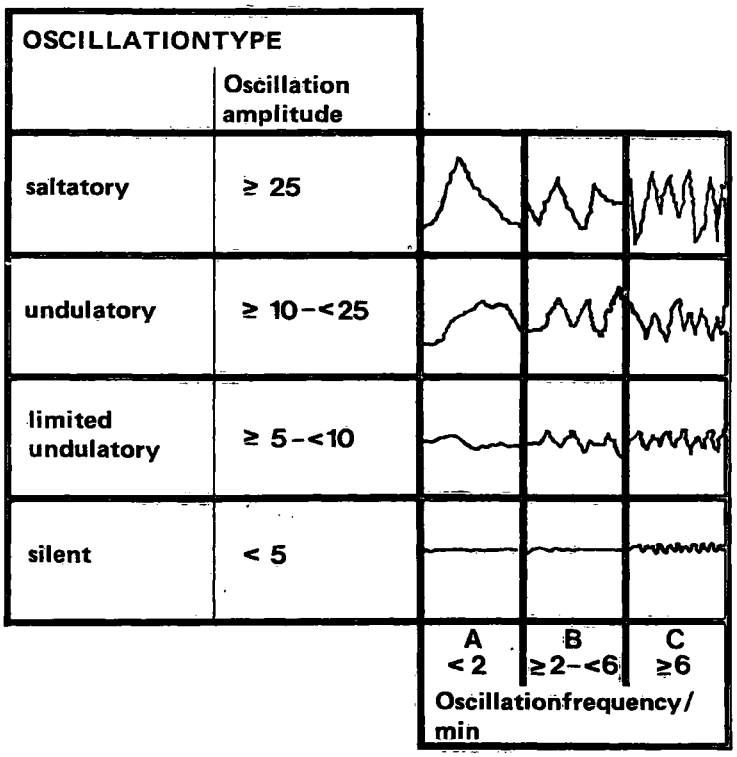

Fig. 1. Classification of oscillation amplitudes (numerical values indicate bpm) and oscillation rates according to HAMMACHER et al. [10].

* Presented in part at the second Tübingen Symposium on Computer Supported Intensive Care, March 25–28, 1981 [13]

0300-5577/83/0011-0032$02.00

4. Short time variability (STV in msec).
   Time differences between two subsequent RR intervals are added up for five minutes and divided by the number of occurring RR intervals. The derived values are indicated in milliseconds.
5. P-Value (P in bpm).
   The P value is defined as the largest difference in amplitude between two subsequent R peaks within five minutes.

A sinusoidal type of oscillations was not separately identified because it was observed only extremely rarely in preliminary studies. In addition, its recognition would have been associated with considerable technical problems.

The values from the printouts every 5 minutes were averaged separately for each patient after the conclusion of the runs. The frequency for oscillation amplitudes and rates was determined. "Alarm" printouts (see part I) and "routine" printouts immediately following alarm events were not included. Printouts from periods with gross body movements and from care-associated handling of the infant (physical therapy, suctioning, etc.) were not included in the evaluation because of the amplitude variations visible in the respirogram. Hence, the infants were in states 1, 2, and 3, occasionally in state 6, according to the scheme of PRECHTL and BEINTEMA [34]. Because of the long duration of the records it was not practical to correlate data to the separate states nor to attempt differentiation into phases of active sleep or quiet sleep.

About 65% of the routine printouts were usable. The usual length of recording was 12 hours for 75 infants (51 prematures and 24 term newborns). In 29 patients several 12 hour periods were recorded either consecutively or on various days. According to the severity of the infant's illness, the following groups were differentiated:

Group I – controls. Premature and term neonates with unremarkable CNS, cardiac, and pulmonary findings.

Group II – "sick" prematures and newborns not on mechanical ventilation. Diagnoses: Perinatal asphyxia, reccurring apneic attacks, aspiration syndromes.

Tab. I. Classification of patients according to the severity of their illness and gestational age in weeks. Number of patients: 75; number of records: 117.

Group	28–33	34–36	37–41	Number of Recordings
I				
n = 13	–	5	8	16
II				
n = 25	9	8	8	41
III				
n = 15	7	4	4	27
IV				
n = 9	5	2	2	13
V				
n = 13	9	2	2	20

Group III – Premature and term newborns on mechanical ventilators without neurological findings and without suspected intracranial hemorrhage. Diagnoses: pneumonia, amniotic fluid aspiration, respiratory distress syndrome.

Group IV – Mechanically ventilated premature and term newborns with subependymal and intraventricular hemorrhage (IVH) of Grade I and II [30], according to computer tomography.

Group V – Mechanically ventilated infants with intraventricular hemorrhage of Grade III and IV, according to CT scans or autopsy.

A classification of the patients according to these groups and gestational age (determination after 5), is given in Tab. I

2 Results and discussion

The evaluation of the "routine" printouts of 75 infants yielded noticable differences in the various groups. **With increasing severity of the illness the group mean values of the long time variability, short time variability, and P-value decreased considerably.** Long time variability and the newly introduced P-value largely coincided in their course. Silent and limited undulatory tracings became relatively more common while saltatory and undulatory patterns occcurred less often.

While in the controls the Type B of oscillation frequency [10] predominated (Group C was never observed), in Group II the oscillation fre-

Tab. II. Parameter of heart rate variability and patient data ([1]) = mean value)

Group	Birth Weight [1]) (g)	Gestational age[1]) (wks)	Age at Recording[1]) (days)	LTV $\bar{x}$ SD	STV $\bar{x}$ SD	P-value $\bar{x}$ SD	% SALT $\bar{x}$ SD	% UD $\bar{x}$ SD	% LIM. UD $\bar{x}$ SD	% SIL $\bar{x}$ SD	% A $\bar{x}$ SD	% B $\bar{x}$ SD	Number of Recordings
I Control Group n = 13	2615	37,1	4,2	27,1 (5,2)	7,8 (3,2)	15,0 (5,4)	56,7 (23,2)	41,6 (25,2)	1,2 (2,8)	0,5 (2,0)	29,1 (26,6)	70,9 (26,6)	16
II "Sick" n = 25	1763	34,4	4,1	14,5 (6,1)	3,6 (4,4)	10,3 (4,0)	8,5 (14,8)	58,4 (25,8)	24,7 (21,9)	8,4 (17,4)	75,3 (26,3)	24,7 (26,3)	41
III Ventilated Infants (pulm. disease) n = 15	1917	34,8	7,3	8,5 (6,9)	2,3 (1,9)	6,5 (4,7)	4,8 (5,9)	29,3 (31,7)	22,9 (21,5)	43 (42,4)	90,4 (16,3)	9,6 (16,3)	27
IV IVH (Grade I & II) (ventilated) n = 9	1648	33,3	5,6	4,3 (2,3)	1,3 (0,7)	3,9 (1,2)	0,1 (0,2)	6,5 (13,0)	24,2 (26,8)	69,2 (31,2)	99,4 (1,5)	0,6 (1,5)	13
V IVH (Grade III & IV) (ventilated) n = 13	1661	32,7	7,2	1,0 (0,8)	0,4 (0,5)	2,0 (0,6)	0 (0)	0 (0)	0,4 (1,8)	99,6 (1,8)	100 (0)	0 (0)	20

quency type A was more common. The differences between the mean values of the various groups was fairly distinct for most parameters. However, the standard deviations were at times quite large. We deliberately did not apply tests of statistical significance because even significant group differences say nothing or almost nothing about the diagnostic value of a particular parameter.

In addition the utilization of tests requires independent observations in the groups; this would have required a random elimination of some multiple recordings in the same child.

Of the examined parameters the long time variability, short time variability, and P-value were found to be best suitable for a rapid evaluation because these values were present in numerical form in each routine printout. The proportions of the various oscillation amplitudes and frequencies required further calculations because the routine printouts yielded only the type which occurred more frequently within the respective 5 minutes.

In severe intracranial hemorrhages the heart rate variability was decreased most (Tab. II) and thus allowed us to suspect this diagnosis. Otherwise heart rate analysis allowed only a global statement about the severity of the illness and was not able to aid in diagnosis because of disease-specific changes.

Decreases of heart rate variability were also noticed in infants with acute renal failure – presumably because of the cerebral edema, – following muscle relaxants after lengthy anesthesias, and after repeated high doses of sedatives.

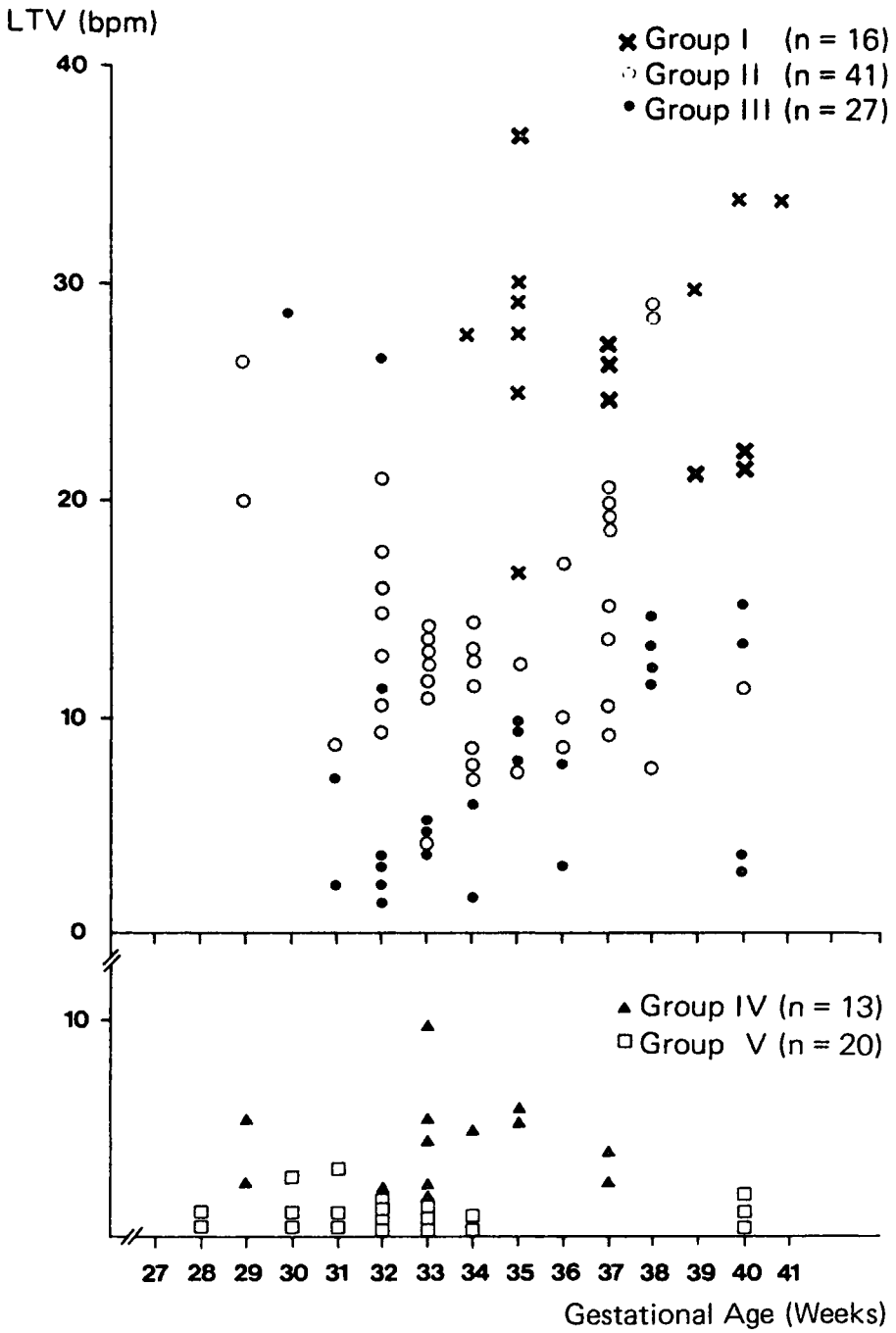

Fig. 2. Long time variability (LTV) and gestational age. Plots represent the mean value from one 12 hour recording (117 recordings in 75 patients). The lower plot indicates infants with intracranial hemorrhage.

VÄLIMÄKI et al. [41] described a correlation between heart rate variability and age; we noticed this as well (Group III in Fig. 3). Similarily it appears to be influenced by the gestational age [21, 26]. In Fig. 2 the mean value of the long time variability as calculated from routine printouts was plotted against the gestational age for each of the 117 recordings. In Fig. 3 the long time variability is correlated with the age at the time of the recording. In patients without intracranial hemorrhage long time variability appears to be greater with more advanced gestational and postnatal age (see also Fig. 4). In contrast the infants with intraventricular hemorrhage show only a low degree of long time variability which was not dependent on gestational or postnatal age. Similar results were found for all other parameters of heart rate variability.

In Fig. 4 the mean values of long time variability for the separate recordings for Groups I to III

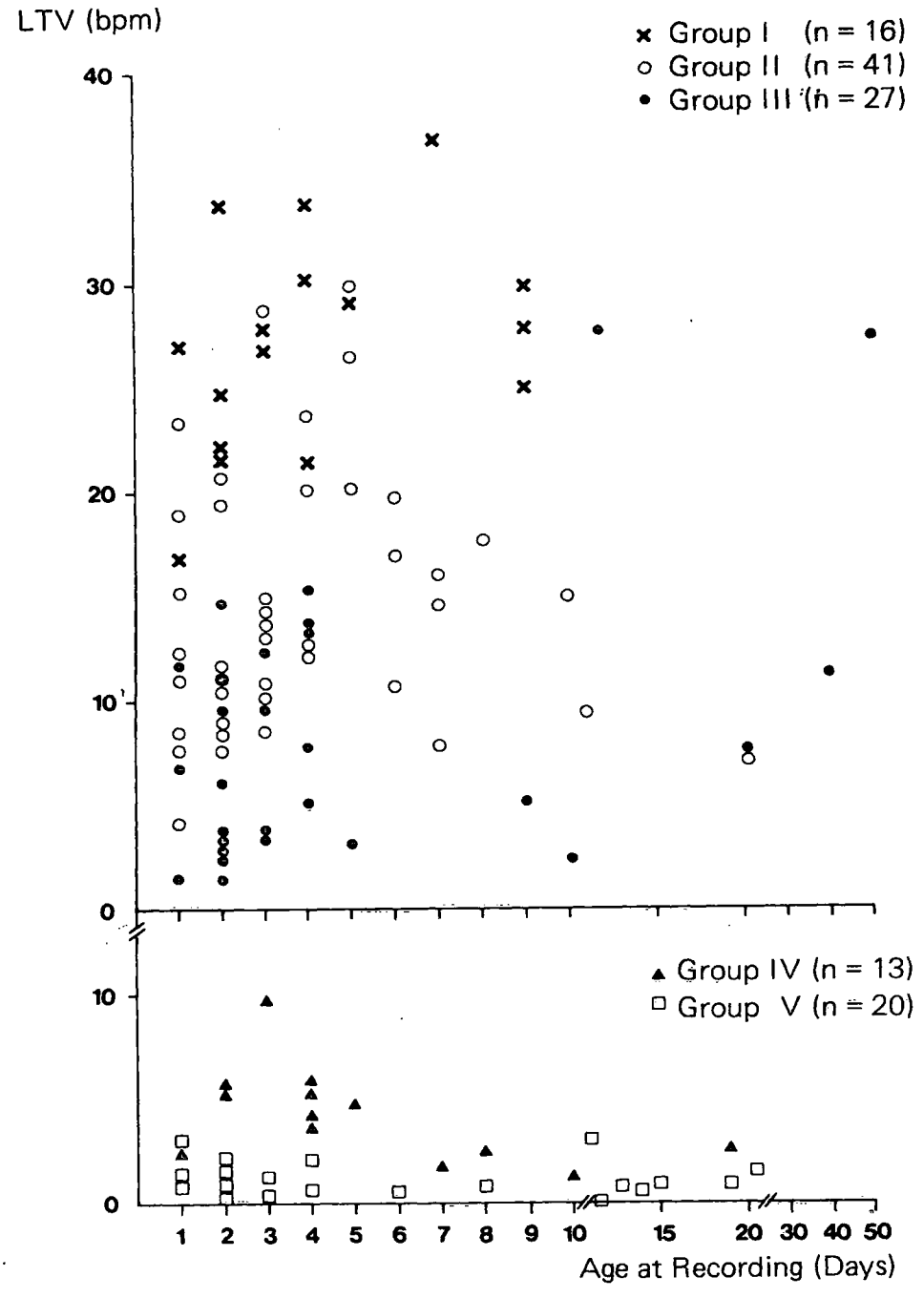

Fig. 3. Long time variability and age at the time of recording.

(without IVH) as well as IV and V (with IVH) were combined and mean group values and standard deviations were calculated. Marked difference between the groups without intracranial hemorrhages and those with hemorrhages were found also for long time variability, P-value, and silent oscillation amplitude. Short time variability, oscillation frequency A, and undulatory or limited undulatory oscillation types showed less differences.

Consecutive recordings in individual patients demonstrated also differences between those with and those without intracranial hemorrhages. Twenty infants without IVH and 9 with IVH were examined over two 12 hour periods. In the first group the heart rate variability was generally greater in the second (later) examination than in the first recording (Fig. 5). Infants with IVH on the other hand generally demonstrated a decrease of the variability. In several cases there was a

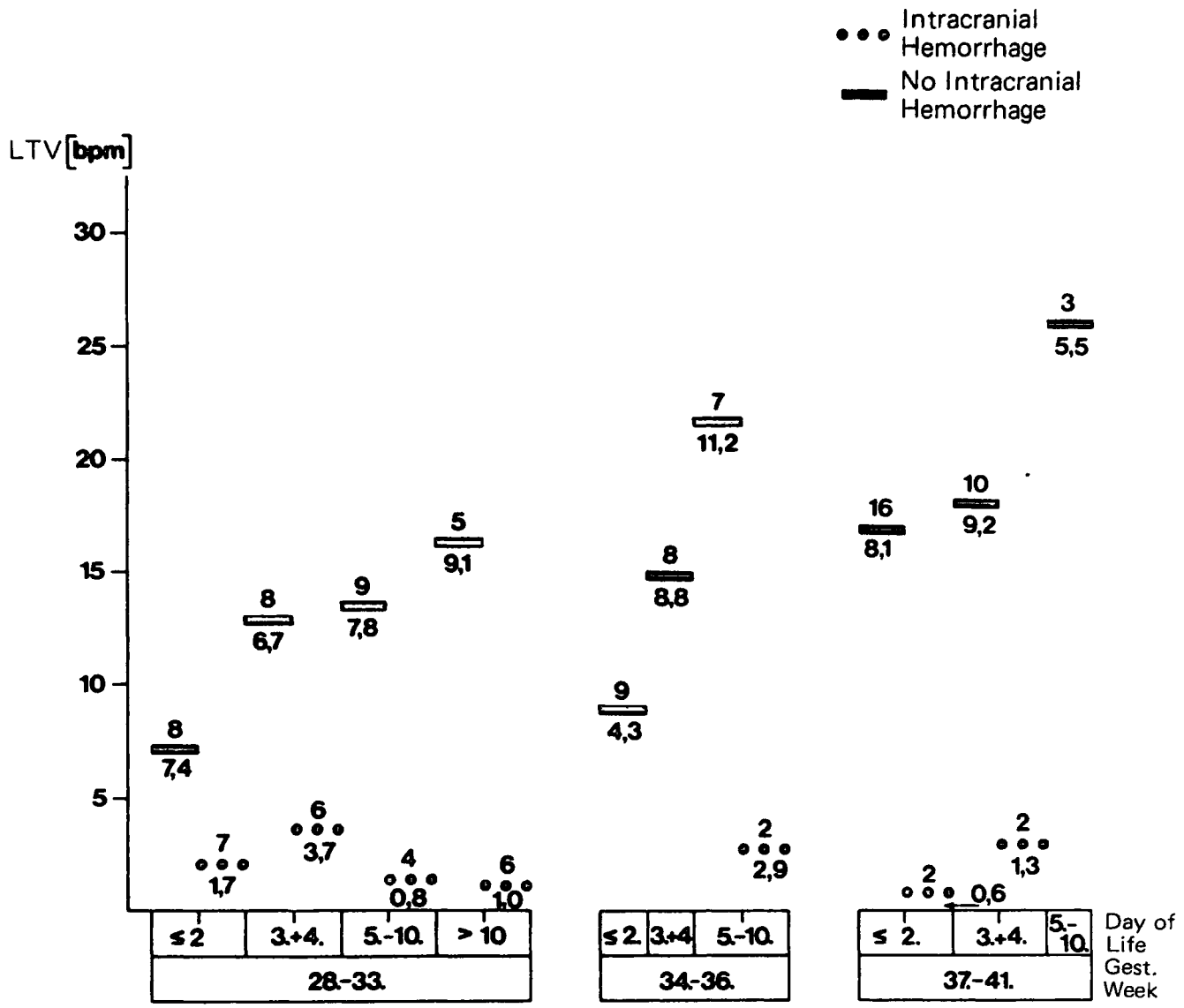

Fig. 4. Long time variability (LTV). The values from Fig. 2 or Fig. 3 have been combined where at least two recording periods were available, and plotted in two groups (intracranial hemorrhage, no intracranial hemorrhage). Indicated are mean values. Above the dots or bars the number of the recordings is indicated, below the standard deviation. Patients without intracranial hemorrhage show a more pronounced LTV with higher gestational age and higher age.

minimal increase. This positive and negative trend respectively was most clearly expressed for long time variability and P-value. There was no definite trend recognizable for short time variability. Oscillation amplitudes and frequency rates were less suitable for this analysis.

By means of the statistical method of linear discriminatory analysis we tested the usefulness of the recorded mean values of the following parameters: long term variability, short term variability, P-value, silent, limited undulatory and undulatory oscillation type as well as oscillation frequency A (which in turn determines saltatory oscillation amplitude and oscillation frequency B) for the diagnosis of intracranial hemorrhage. We amended the original planned correlation according to age at the time of recording and gestational age. The failure to obtain always correct correlations is insignificant because of small case numbers. The results of linear discriminatory analysis (Tab. III) were unsatisfactory because of the frequent false negative classifications. By using the available recordings "univariant reference areas" were determined which allowed the best possible separation of groups with and without intracranial hemorrhage. By using a combination of such reference areas marked reduction of false negative results from the linear discriminatory analysis was

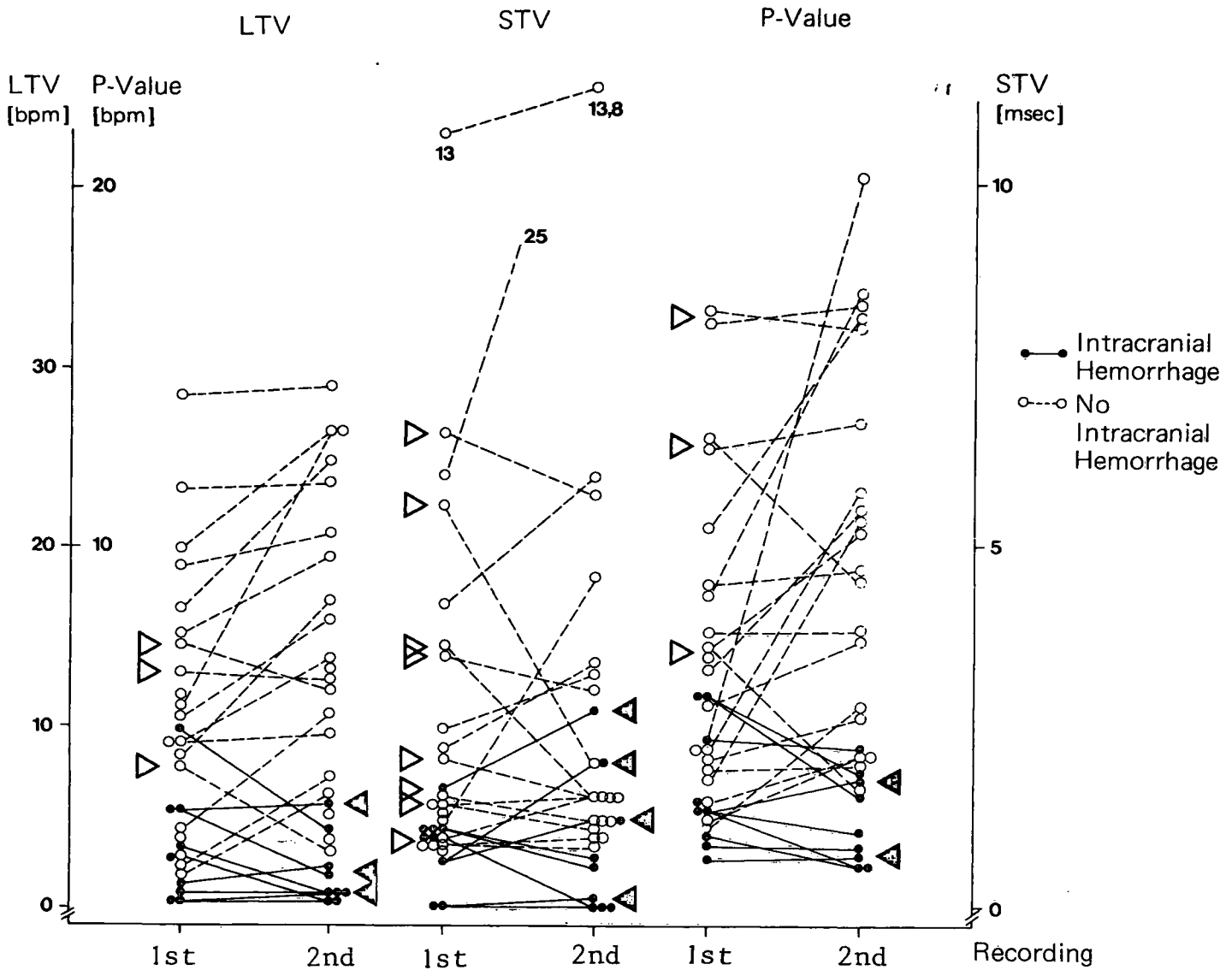

Fig. 5. Heart rate variability from repeated recordings of single patients (n = 29). Long time variability (LTV) and P-value are either larger or unchanged during the second examination against the fist examination in the absence of intracranial hemorrhage. For infants with intracranial hemorrhage, LTV and P-values are lower. Exceptions are marked with arrows (◁ = intracranial hemorrhage, ▷ = no intracranial hemorrhage). Short time variability (STV) does not have a similar positive or negative trend.

obtained while retaining the same rate of false positive correlations. Tab. III demonstrates the best results which could be obtained with linear discriminatory analysis and a combination of univariant reference areas (CUR). The method of reclassification yields the indicated rates of false classifications. The "leaving one out" method, which generally yields somewhat more accurate estimates was not applicable with CUR because the determination of the reference areas did not follow any rule which could be automated. From Tab. III long time variability and silence emerge as the most important diagnostic parameters. The use of more than two parameters did not add significant incremental information. These descriptive statistical methods may be criticizied for using several recording periods from the same children for analysis. However, we wanted to keep the case number as large as possible and we also came to the conclusion on the basis of observations (Fig. 5) that the random choice of one recording period per child would not have changed the results from those indicated in Tab. III.

It is not yet known why the parameters of heart rate variability are expressed variably depending on age, maturity, and severity of illness. A decrease of the heart rate variability in prematures and term newborns might be explained by a lower

of baseline autonomous activity with lower gestational age [42], a depression or injury of the regulatory center of the cardiovascular system in the medulla oblongata [1, 35], and a constantly overshooting sympathic stimulation [4]. The heart rate variability may be considered a measure of the autonomous system integrity of the organism [26]. A decrease of heart rate variations parallel to an increasing severity of the illness in our study supports this hypothesis.

Remarkable is the extreme limitation of the variability pattern in newborns with intracranial hemorrhage, evidently correlating with the severity of the hemorrhage. From case studies [7, 15] it has been known for some time that in intracerebral hemorrhage silent patterns dominate. POKORNY and coworkers [33] described from visual evaluations of cardiorespirograms in 9 infants with intracerebral hemorrhages in addition to silent patterns, the oscillation frequency A as typical. NISHIDA et al. [29] also reported on the loss of variability in cerebral damage. On the other hand KARCH [20] did not find a good correlation between heart rate variability and cerebral damage. However, this work was based on the analysis of polygraph records and computer tomograms were not done.

The loss of heart rate variability very likely could be caused by a damage of the vasomotor areas in the medulla oblongata from the increased intracranial pressure in severe cerebral hemorrhage (Group V). In germinal matrix hemorrhage and minor ventricular hemorrhage (Group IV) the neurophysiological knowledge about the supramedullary regulation of the heart rate might serve as an explanation [2, 23, 24, 25, 28]. According to these studies in addition to the classical circulatory center in the lower brainstem various areas of the palaeocortex and neocortex act on heart and circulatory activity. An intracranial hemorrhage of lesser dimensions might damage these areas and cause a depression of heart rate variability.

In summary, microprocessor-based cardiorespirography has proven to be useful in the evaluation of the status of premature and term newborns.

Tab. III. Various correlation methods for the recognition of intracranial hemorrhage LD = linear discriminatory analysis; UR = Univariate reference area; CUR = Combination of urinvariate reference areas; SIL = silent oscillation amplitude; BW = birth weight; OF.A = oscillation frequency (A).

Method Correlation	Used Parameters	False Classifications in % and Absolute Numbers (parenthesis), Total Number of Recordings from Children	
		Without IVH	With IVH
LD	SIL	16.7 (14) 84	12.1 (4) 33
LD	SIL, SIL/LTV	14.3 (12) 84	15.6 (5) 32
LD	SIL, SIL/LTV, LTV	13.1 (11) 84	15.6 (5) 32
LD	SIL, SIL/LTV, LTV, BW, age at rec.	14.3 (12) 84	15.6 (5) 32
UR	SIL	21.4 (18) 84	3.0 (1) 33
UR	LTV	15.5 (13) 84	6.1 (2) 33
UR	OF.A	34.5 (29) 84	0.0 (0) 33
UR	P-value	22.6 (19) 84	9.1 (3) 33
CUR	SIL, LTV	14.3 (12) 84	6.1 (2) 33
CUR	SIL, OF.A	17.9 (15) 84	3.0 (1) 33
CUR	SIL, P-value	16.7 (14) 84	9.1 (3) 33
UR	SIL, LTV	19.0 (16) 84	6.3 (2) 32
CUR	LTV, SIL/LTV	14.3 (12) 84	6.3 (2) 32
CUR	LTV, STV	14.3 (12) 84	6.1 (2) 33
CUR	STV, SIL/LTV	17.9 (15) 84	6.3 (2) 32
CUR	LTV, OF.A	15.5 (13) 84	6.1 (2) 33
CUR	STV, LTV, SIL/LTV	13.1 (11) 84	6.3 (2) 32
CUR	OF.A, LTV, SIL/LTV	14.3 (12) 84	6.3 (2) 32
CUR	STV, LTV, OF.A	14.3 (12) 84	6.1 (2) 33
CUR	OF.A, LTV, SIL	14.3 (12) 84	6.1 (2) 33
CUR	OF.A, STV, LTV, SIL, P-value	13.1 (11) 84	3.1 (1) 32

Machine computation facilitates and enhances the evaluation of cardiorespirograms considerably. Even though the number of evaluated patients is still relatively low, we consider it justified to use the method as a screening method for intracranial hemorrhage. Further confirmation of the diagnosis obviously is reserved for specific methods such as cranial computed tomography or sonography.

The transcutaneous determination of oxygen tension should be included as an additional parameter and included in computer process.

Summary

In 1965 URBACH et al. and RUDOLPH et al. [35, 39] described a loss of heart rate variability in severely ill neonates. In this study we investigated the correlation between instantaneous heart rate patterns and status diagnosis. We used a microprocessor-based cardiorespirography system. Seventy five newborn infants (51 prematures and 24 term neonates) were studied for about 12 hours each. Twenty nine patients had a second record after the first investigation. **Parameters were: Type of frequency and oscillation, long time variability (LTV), short time variability (STV) and the newly introduced P-value** (maximal difference between two successive R-peaks in five minutes). We found clear differences between the study groups. **With increasing severity of illness mean values ("group mean values") of long time variability, short time variability and P-value decreased. Fixed heart rate became predominant. The most pronounced loss of heart rate variability was seen in infants with severe intracranial bleeding,** thus offering a tentative diganosis. For statistical analysis long time variability and the silent oscillation type have been proved as best parameters for this diagnosis. Severely decreased heart rate variations also have been seen in infants with acute renal failure – possibly because of brain edema –, after application of muscle relaxants, repeated doses of sedatives, and after prolonged anesthesia.

Otherwise, the heart rate variability was probably dependent on age and gestational age in prematures and newborn infants without intracranial bleeding.

It is possible to use microprocessor-based long time cardiorespirography as a simple screening method for the diagnosis of neonatal intracerebral bleeding. In future experiences transcutaneous measurements of oxygen tension should be included.

Keywords: Cardiorespirography, status diagnosis, heart rate variability, long time variability, microprocessor system, neonatal intracranial bleeding, short time variability.

Zusammenfassung

Mikroprozessorgestützte Langzeitcardiorespirographie II. Zustandsberurteilung bei Früh- und Neugeborenen

URBACH und Mitarb. sowie RUDOLPH und Mitarb. [35, 39] beschrieben bereits 1965 einen Verlust der Herzfrequenzvariabilität bei schwerkranken Neugeborenen. In der vorliegenden Studie sollte untersucht werden, welche Bedeutung die mit Hilfe der mikroprozessorgestützten Langzeitcardiorespirographie ermittelten Parameter der Herzfrequenzvariabilität für die Zustandsbeurteilung bei Früh- und Neugeborenen haben. 75 Kinder (51 Frühgeborene und 24 reife Neugeborene) wurden im allgemeinen über 12 Stunden untersucht. Bei 29 Patienten wurden zur Verlaufsbeobachtung mehrere 12-stündige Perioden nacheinander oder an verschiedenen Lebenstagen aufgezeichnet. **Ermittelt wurden die Oszillationsamplituden und -frequenzen, die Langzeitvariabilität (LTV), die Kurzzeitvariabilität (STV) und der neu eingeführte P-Wert** (größte auftretende Differenz zwischen zwei aufeinanderfolgenden R-Zacken in fünf Minuten).

Bei der Auswertung ergaben sich deutliche Unterschiede in den einzelnen Erkrankungsgruppen. **Mit zunehmender Schwere der Erkrankung fielen die Mittelwerte („Gruppenmittelwerte") der Langzeitvariabilität, der Kurzzeitvariabilität und des P-Wertes erheblich ab.** Silente und eingeschränkt undulatorische Kurvenverläufe wurden relativ häufiger, saltatorische und undulatorische Muster seltener. **Bei schweren Hirnblutungen war die Herzfrequenzvariabilität am stärksten deprimiert,** dadurch eine Verdachtsdiagnose möglich. Bei der statistischen Überprüfung erwiesen sich Langzeitvariabilität und Silenz als beste Diagnose-Parameter.

Erhebliche Einschränkungen der Herzfrequenzvariabilität wurden auch bei Kindern mit akutem Nierenversagen – vermutlich durch ein Hirnödem –, nach Muskelrelaxation, nach langdauernden Narkosen, sowie nach mehrfach wiederholten Gaben hoher Dosen von Sedativa gesehen. Darüber hinaus war die Herzfrequenzvariabilität bei Früh- und Neugeborenen ohne Hirnblutung offensichtlich vom Lebensalter und vom Gestationsalter abhängig.

Die mikroprozessorgestützte Langzeitcardiorespirographie kann erfolgreich als einfache Screening-Methode zur Diagnose von neonatalen Hirnblutungen eingesetzt werden. Bei zukünftigen Untersuchungen sollte die transkutane Bestimmung des Sauerstoffpartialdruckes in das Programm einbezogen werden.

Schlüsselwörter: Cardiorespirographie, Herzfrequenzvariabilität, Kurzzeitvariabilität, Langzeitvariabilität, Mikrorechner, neonatale Hirnblutung, Zustandsbeurteilung.

Résumé

Méthode de cardiorespirographie à longue terme basée sur des microprocesseurs.
II. Jugement de l'état des prématurés et nouveau – nés
En 1965, URBACH et Coll. et RUDOLF et Coll. [35,39] décrivaient une perte de variabilité de fréquence cardiaque chez des nouveau-nés sévèrement malade. Dans cette étude nous avons recherché à l'aide de la cardiorespirographie à longue terme basée sur des microprocesseurs, l'importance de la variabilité de la fréquence cardiaque des prématurés et nouveau-nés. 75 nouveau-nés (51 prématurés et 24 à terme) furent étudiés, en général pendant une période de 12 heures. 29 patients furent soumis à un deuxième enrégistrement après la première investigation. **Les paramètres furent: type de fréquence et oscillation, variabilité à court terme (STV) et la valeur P nouvellement introduite** (différence maximale entre deux P's successifs en 5 minutes). Nous avons constaté une différence évidente entre les groupes étudiés. **Avec l'acroissement de la sévérité de la maladie, on constate une décroissance de la variabilité à longue terme, de la variabilité à courte terme et de la valeur P.** La fréquence cardiaque fixe devenait prédominante. **Une perte totale de la variabilite de la fréquence était visible chez les enfants souffrants d'hémorrhagie intracérébrale** de sorte qu'une tentative de diagnose était possible. En analyse statistique la variabilité à longue terme et le type d'oscillation silencieuse semblent être les meilleurs paramètres diagnostiques de même une diminution sévère de fréquence cardiaque a été observée chez des enfants, atteint d'insuffisance rénale aigue (probablement causée par un oedème cérébral), après relaxation musculaire, après des narcoses prolongées et après de doses répétitives de sédatifs. En outre des variations des rhythmes cardiaques dépendent probablement de l'âge et de l'âge gestationel chez des prématurés et nouveau-nés sans hémorrhagie intracérébrale. **Il est possible d'utiliser la cardiorespirographie à longue terme basée sur des microprocesseurs comme une simple méthode de détection de diagnose des hémorrhagies intracérébrales néonatale.** Dans des expériences futures il faudra introduire le tc PO_2.

Mots-clés.: Cardiorespirographie, hémorrhagie intracérébrale néonatale, jugement de l'état, microprocesseur, variabilité à courte terme, variabilité à longue terme, variabilité de fréquence cardiaque.

Bibliography

[1] BUCKINGHAM, S., S. C. SOMMERS, R. P. SHERWIN: Lesions of dorsal vagal nucleus in the respiratory distress syndrome. Am. J. Clin. Pathol. 48 (1967) 269

[2] CALARESU, F. R., A. A. FAIERS, G. J. MOGENSON: Central neural regulation of heart and blood vessels in mammals. Prog. Neurobiol. 5 (1975) 1

[3] CALDEYRO-BARCIA, R., C. CASACUBERTA, R. BUSTOS, G. GIUSSI, L. GULIN, L. ESCARCENA, C. MENDEZ-BAUER: Correlation of intrapartum changes in fetal heart rate with fetal blood oxygen and acidbase state. In: ADAMSONS, K. (ed.): Diagnosis and treatment of the fetal disorders. Springer, Berlin 1968

[4] CHEEK, D. B., M. MALINEH, J. M. FRAILLON: Plasma adrenaline and noradrenaline in the neonatal period, and infants with respiratory distress syndrome and placental insufficiency. Pediatrics 31 (1963) 374

[5] DUBOWITZ, L. M. S., V. DUBOWITZ, C. GOLDBERG: Clinical assessment of gestational age in the newborn infant. J. Pediat. 77 (1970) 1

[6] EKERT, W.-D., B. KÖHLER: Cardiorespirographische Untersuchungen bei cerebralen Erkrankungen. Monatsschr. Kinderheilk. 122 (1974) 643

[7] EKERT, W.-D., H. W. SCHENK: Cardiorespirographische Befunde bei Früh- und Neugeborenen. In: DUDENHAUSEN, J. W., E. SCHMIDT (eds.): Perinatale Medizin. Bd. VI. Thieme, Stuttgart 1975

[8] GRAUEL, E. L., P. KERO, I. VÄLIMÄKI, T. PELTONEN: Einfluß unterschiedlicher transkutan gemessener pO_2-Werte auf die Herzfrequenzvariabilität bei Neugeborenen. Kinderaerztl. Prax. 47 (1979) 315

[9] HAMMACHER, K., K. A. HÜTER, J. BOKELMANN, P. H. WERNERS: Foetal heart frequency and perinatal condition of the foetus and newborn. Gynaecologia 166 (1968) 349

[10] HAMMACHER, K., R. BRUN DEL RE, R. GAUDENZ, P. DE GRANDI, R. RICHTER: Kardiotokographischer Nachweis einer fetalen Gefährdung mit einem CTG-Score. Gynaekol. Rundsch. 14, Suppl. 1 (1974) 61

[11] HÖRNCHEN, H.: Die maschinelle Beatmung vitalgestörter Früh- und Neugeborener. Problematik und Komplikationen. Habilitationsschrift, Aachen 1981

[12] HÖRNCHEN, H., R. BETZ, F. KOTLAREK: Langzeitkardiorespirographie bei Früh- und Neugeborenen. In: VON LOEWENICH, V. (ed.): Pädiatrische Intensivmedizin III, Intensivmedizin, Notfallmedizin und Anästhesiologie Bd. 36 (in print)

[13] HÖRNCHEN, H., K. J. ESSER, R. BETZ, P. ROEBRUCK: Die Bedeutung der Herzfrequenzvariabilität für die Zustandsbeurteilung kranker Früh- und Neugeborener. Mikroprozessorgestützte Langzeitcardiorespirographie. Intensivmedizin, Notfallmedizin und Anästhesiologie (in print)

[14] HON, E. H.: The classification of fetal heart rate. I. A working classification. Obst. Gynec. 22 (1963) 137

[15] HON, E. H., B. ZANINI, L. A. CABAL: Neonatal heart rate monitoring. Ohne Verlagsangabe, Los Angeles 1975

[16] HUCH, R., D. W. LÜBBERS, A. HUCH: Reliability of transcutaneous monitoring of arterial pO_2 in newborn infants. Arch. Dis. Child. 49 (1974) 213

[17] HUCH, R., A. HUCH, H. U. BUCHER: Experience with the oxygen-cardiorespirogram in newborn

infants. In: ROOTH, G., L. E. BRATTEBY (eds.): Perinatal Medicine. Almquist & Wiksell, Stockholm 1976

[18] HUCH, R., A. HUCH: Zustandsdiagnostik beim Neugeborenen unmittelbar post partum durch das Sauerstoff-Kardiorespirogramm (SCR). In: EMMRICH, P. (ed.): Pädiatrische Intensivmedizin. Thieme, Stuttgart 1977

[19] JENKINS, J. G., M. MCC. REID, B. G. MCCLURE: Study of heart rate variability in sick newborn infants. Acta Paediatr. Scand. 69 (1980) 393

[20] KARCH, H.-D.: Erfassung zentralnervöser Funktionsstörungen bei Früh- und Neugeborenen unter Intensivtherapie. Die diagnostische Bedeutung polygraphischer Untersuchungen. Habilitationsschrift, Düsseldorf 1978

[21] KERO, P.: Heart rate variations in infants with the respiratory distress syndrome. Acta Paediatr. Scand. Suppl. 240 (1974)

[22] KLÖCK, F. K., H. P. CLOSS, R. AUSTERMANN, G. LAMBERTI, W. SCHWENZEL: Das Kardio-Respirogramm. Eine Erweiterung der postpartalen Zustandsdiagnostik des Neugeborenen. Z. Geburtsh. Perinat. 176 (1972) 266

[23] KOEPCHEN, H. P., P. H. WAGNER, H. D. LUX: Über die Zusammenhänge zwischen zentraler Erregbarkeit, reflektorischem Tonus und Atemrhythmus bei der nervösen Steuerung der Herzfrequenz. Pflügers Arch. Ges. Physiol. 273 (1961) 443

[24] KOEPCHEN, H. P.: Kreislaufregulation. In: GAUER, O. H., K. KRAMER, R. JUNG (eds.): Physiologie des Menschen, Bd. 3, Herz und Kreislauf. Urban & Schwarzenberg, München-Berlin-Wien 1972

[25] KORNER, P. I.: Central nervous control of automatic cardiovascular function. In: BERNE, R. M., N. SPERELAKIS, S. R. GEIGER (eds.): Handbook of Physiology, Sect. 2, Vol. 1. Waverly Press, Baltimore 1979

[26] LEISTNER, H. L., G. G. HADDAD, R. A. EPSTEIN, T. Z. LAI, M. A. F. EPSTEIN, R. B. MELLINS: Heart rate and heart rate variability during sleep in aborted sudden infant death syndrom. J. Pediatr. 97 (1980) 51

[27] VON LOEWENICH, V.: Apparative Überwachung des Neugeborenen. Gynäkologe 2 (1969) 99

[28] MANNING, J. W.: Cardiovascular reflexes following lesions in medullary reticular formation. Am. J. Physiol. 208 (1965) 283

[29] NISHIDA, H., K. OGUCHI, R. HAKU, T. MIHARA, S. HIRAISHI, K. YASHIRO: Clinical application of neonatal instantaneous heart rate monitoring (Part two: Asphyxia and variability of instantaneous heart rate). J. Perinat. Med. 9, Suppl. 1 (1981) 160

[30] PAPILE, L.-A., J. BURSTEIN, R. BURSTEIN, H. KOFFLER: Incidence and evolution of subependymal and intraventricular hemorrhage: A study of infants with birth weights less than 1500 gm. J. Pediatr. 92 (1978) 529

[31] PEABODY, J. L., G. A. GREGORY, M. M. WILLIS, A. G. S. PHILIP, J. F. LUCEY: Failure of conventional monitoring to detect apnea resulting in hypoxemia. Birth Defects 15 (1979) 275

[32] PÖRKSEN, C., H. LARSEN, P. HÜRTER: Evaluation of $tcpO_2$, beat-to-beat heart rate and respiration in neonates with episodes of cyanosis, bradycardia, or apnea. Birth Defects 15 (1979) 447

[33] POKORNY, A., J. MELKOVA, M. BROSHEOVA, B. SRP, Z. MALY: Die Kardiorespirographie bei physiologischen und pathologischen frühgeborenen Kindern. Zbl. Gynäkol. 100 (1978) 1491

[34] PRECHTL, H. F. R., D. J. BEINTEMA: Die neurologische Untersuchung des reifen Neugeborenen. 2. Aufl. Thieme, Stuttgart 1976

[35] RUDOLPH, A. J., C. VALLBONA, M. M. DESMOND: Cardiodynamic studies in the newborn. III. Heart rate patterns in infants with the respiratory distress syndrome. Pediatrics 36 (1965) 551

[36] SIASSI, B., J. E. HODGMAN, L. CABAL, E. H. HON: Cardiac and respiratory activity in relation to gestation and sleep states in newborn infants. Pediat. Res. 13 (1979) 1163

[37] STEMMANN, E. A., H. ALBRECHT, P. LEMBURG, U. ICKS, J. MORGENSTERN: Anwendung der Herzfrequenzanalyse in der Intensivpflege. In: BUTENANDT, I., K. MANTEL, J. G. SCHÖBER (eds.): Pädiatrische Intensivpflege. Enke Stuttgart 1973

[38] STEMMANN, E. A., F. KOSCHE, U. ICKS, H. ALBRECHT, P. LEMBURG, E. SCHMIDT: Registrierung der momentanen Herzfrequenz, eine neue Methode zur Überwachung gefährdeter Kinder. Monatsschr. Kinderheilk. 122 (1974) 596

[39] URBACH, J. R., B. PHUVICHIT, H. ZWEIZIG, E. MILLICAN, E. R. CARRINGTON, M. LOVELAND, J. M. WILLIAMS, R. L. LAMBERT, A. M. DUNCAN, S. L. FARRELL, P. O. SIMONS, I. L. SPURGEON: Instantaneous heart rate patterns in newborn infants. Amer. J. Obstet. Gynec. 93 (1965) 965

[40] VÄLIMÄKI, I.: Heart rate variation in full-term newborn infants. I. Use of a small, special purpose computer. Biol. Neonate 18 (1971) 129

[41] VÄLIMÄKI, I. A., P. M. RAUTAHARJU, S. B. ROY, K. E. SCOTT: Heart rate patterns in healthy term and premature infants and in respiratory distress syndrome. Eur. J. Cardiol. 1 (1974) 411

[42] VAPAAVUORI, E. K., E. A. SHINEBOURNE, R. L. WILLIAMS, M. A. HEYMANN, A. M. RUDOLPH: Development of cardiovascular responses to automatic blockade in intact fetal and neonatal lambs. Biol. Neonate 22 (1973) 177

[43] VERSMOLD, H. T., C. DÖHLEMANN, D. ONKEN, K. MESSOW, J. JÜCKSTOCK, K. J. RIEGEL: Hypoxie-Antwort der Herzfrequenz der Neugeborenen bei silentem Kardiogramm. In: EMMRICH, P. (ed.): Pädiatrische Intensivmedizin. Thieme, Stuttgart 1977

[44] WILLARD, D., J. MESSER, M. BENOIT: Simultaneous cardiorespirogram and continuous pO_2 monitoring of the newborn child. Paediatrician 5 (1976) 370

Received June 29, 1982. Accepted October 21, 1982.

Priv.-Doz. Dr. med. H. Hörnchen
Abt. Kinderheilkunde der
Medizinischen Fakultät an der
RWTH Aachen
Goethestrasse 27/29
D-5100 Aachen/FRG