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Original article

Relationship between frequency spectrum of heart rate variability and autonomic nervous activities during sleep in newborns

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Abstract

Introduction: We analyzed the frequency spectrum of two neonatal sleep stages, namely active sleep and quiet sleep, and the relationship between these sleep stages and autonomic nervous activity in 74 newborns and 16 adults as a comparison.

Method: Active and quiet sleep were differentiated by electroencephalogram (EEG) patterns, eye movements, and respiratory wave patterns; autonomic activity was analyzed using the RR interval of simultaneously recorded electrocardiogram (ECG) signals. Power values (LFa, absolute low frequency; HFa, absolute high frequency), LFa/HFa ratio, and the values of LFn (normalized low frequency) and HFn (normalized high frequency) were obtained. Synchronicity between the power value of HFa and the LFa/HFa ratio during active and quiet sleep was also examined by a new method of chronological demonstration of the power values of HFa and LFa/HFa.

Results: We found that LFa, HFa and the LFa/HFa ratio during active sleep were significantly higher than those during quiet sleep in newborns; in adults, on the other hand, the LFa/HFa ratio during rapid eye movement (REM) sleep, considered as active sleep, was significantly higher than that during non-REM sleep, considered as quiet sleep, and HFa values during REM sleep were significantly lower than those during non-REM sleep. LFn during quiet sleep in newborns was significantly lower than that during active sleep. Conversely, HFn during quiet sleep was significantly higher than that during active sleep. Analysis of the four classes of gestational age groups at birth indicated that autonomic nervous activity in a few preterm newborns did not reach the level seen in full-term newborns. Furthermore, the power value of HFa and the LFa/HFa ratio exhibited reverse synchronicity.

Conclusion: These results indicate that the autonomic patterns in active and quiet sleep of newborns are different from those in REM and non-REM sleep of adults and may be develop to the autonomic patterns in adults, and that parasympathetic activity is dominant during quiet sleep as compared to active sleep from the results of LFn and HFn in newborns. In addition, in some preterm infants, delayed development of the autonomic nervous system can be determined by classifying the autonomic nervous activity pattern of sleep stages.

Keywords: EEG; Autonomic nervous system; Neonatal sleep; Heart rate variability

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1. Introduction

Heart rate variability (HRV) is a cardiac phenomenon in which the RR interval varies between beats. HRV results from regulation by the sinoatrial node, which is the natural pacemaker of the heart, and the parasympathetic and sympathetic divisions of the autonomic nervous system. In adults, spectral analysis of HRV has been used in physiological analyses of autonomic nervous system function, and in analyses of the pathophysiology of psychosomatic disorders [1–3]. Nevertheless, there are only a few reports of use of spectral analysis of HRV to analyze physiological and clinical disorders in the fetus or newborn. Furthermore, there are no reference values available for neonatal autonomic nervous system parameters, such as LFa (absolute low frequency component), HFa (absolute high frequency component), and LFa/HFa ratio. One reason for the paucity of such data is the difference between newborns and adults in terms of cardiac output and lung tidal volume. In fact, the heart and respiratory rates in newborns are approximately twice those in adults. Therefore, reference values for autonomic parameters in adults are not applicable to newborns [4,5].

Newborn sleep is differentiated into two stages: active sleep and quiet sleep. The differentiation between these two sleep stages is based on electroencephalogram (EEG) characteristics, eye movements, respiratory wave patterns, general movements, heart rate and respiratory rhythm [6–9]. In newborns, HRV characteristics and irregular respiratory rhythms, indicating active sleep, are similar to those during rapid eye movement (REM) sleep in adults, whereas quiet sleep is similar to non-rapid eye movement (non-REM) sleep [10,11]. Based on the physiological characteristics of these two sleep stages, it appears that the autonomic nervous system also regulates newborn sleep cycles. However, there is little data on the relationship between neonatal sleep stages and autonomic activity. Thus, we investigated autonomic activity during active and quiet sleep in neonates using physiological characteristics and EEG patterns for the determination of sleep stages, and evaluated autonomic activity by performing Fourier analysis of the ECG-RR interval with the EEG recorded at the same time. We sought to determine whether the power values for the sympathetic nervous system parameter, LFa/HFa, and the parasympathetic nervous system parameter, HFa, and the synchronicity between HFa and LFa/HFa, could be analyzed by a new method of demonstrating the changes with time in the power values of HFa and LFa/HFa.

2. Subjects

Subjects were selected from 431 newborns admitted to the neonatal intensive care unit of Nara Medical University Hospital from January 2007 to January 2011. An EEG was performed for 266 of these newborns at the time of their discharge. From these 266 newborns, we selected those who met the following criteria for study: at least 5 min of EEG recordings were available during both active and quiet sleep stages, and absence of the following disorders: neonatal asphyxia (Apgar score < 7 points at 5 min), intracranial hemorrhage, severe infection, metabolic abnormalities, or congenital malformations. In total, 74 newborns were included in the study (42 males, 32 females). Gestational age was calculated as the number of weeks until birth from the mother's last menstrual period before pregnancy. The mean birth weight (BW, 1642.5 ± 629.1 g) and mean gestational age at birth (GA, 32 weeks $\pm$ 4 days) was calculated for all subjects; GA was corrected based on the date when the EEG was recorded (mean: 37 weeks 2 days; range: 35 weeks 0 days to 43 weeks 6 days). The neonates were categorized into the following four subgroups based on their GA at birth: $<$28 weeks ($n = 12$), 28 weeks to $<$34 weeks ($n = 38$), 34 weeks to $<$37 weeks ($n = 19$), and $\geq$37 weeks ($n = 5$). Sixteen healthy adults with no significant heart disease or neurological disorder (mean age 51.4 years; 10 males, 6 females) were also included in the study as an adult reference. This study was approved by the ethics committee of Nara Medical University as part of the study on environmental care of the newborn.

3. Methods

EEG recordings were performed in a central EEG examination room that was maintained at a constant temperature (24 °C), shielded from electromagnetic waves, and had consistent lighting conditions (0–5 Lx). The digital EEG was recorded with Neurofax EEG (model 1524, Nihon Kohden Co., Tokyo, Japan) using a time constant of 0.3 s, calibration wave of 50 μV/5 mm, 120-Hz high-cut filter, and a 200-Hz sampling frequency. EEGs were recorded with 11 derivation reference electrodes that were fixed to the scalp (10/20 method) with plate electrodes (Ag/AgCl) (Nihon Kohden, Tokyo, Japan), and were recorded simultaneously with right and left eyelid movement, mandibular electromyographic activity (EMG), respiratory waves (thermistor method), and electrocardiograms (ECG, limb lead I).

We recorded EEGs for the entire sleep cycle in the supine position. Active and quiet sleep were differentiated by their EEG patterns, eye movements, and respiratory wave patterns. Adult sleep consists of repeated cycles of non-REM and REM sleep.

Non-REM sleep consists of sleep stages I to IV. Adult REM sleep is readily identified by rapid eye movements. We performed spectral analysis of HRV using 5-min segments of digital ECG data (lead I) recorded in each sleep cycle. Spectral analyses were performed with MemCalc/win (GMS Co., Tokyo, Japan). The

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