Cardiac Changes During Sleep in Sleep-deprived Infants

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Objective: To evaluate the influence of a brief period of sleep deprivation on cardiac autonomic controls during sleep in healthy infants.

Design: Twelve healthy infants with a median age of 8 weeks (range, 7 to 18 weeks) were recorded polygraphically during a morning and an afternoon nap in a sleep laboratory. They were sleep deprived for approximately 2 hours, either in the morning or in the afternoon, before being allowed to fall asleep. Six infants were sleep deprived before the morning nap, and 6 before the afternoon nap. During both naps, their sleep, breathing, and heart-rate characteristics were continuously recorded. Spectral analysis of heart rate was evaluated as a function of sleep stages. Two major peaks were recognizable: a low-frequency component related to sympathetic and parasympathetic activities and a high-frequency component reflecting parasympathetic tonus. The ratio of low-frequency to high-frequency powers was calculated as an index of sympathovagal interaction.

Results: When sleep deprived, the infants had an increase in basal heart rate during non-rapid eye movement sleep (P=.021). With sleep deprivation, the ratio of low-frequency to high-frequency powers increased in non-rapid eye movement sleep (P=.005). These findings were consistent with an increase in sympathetic tone.

Conclusion: Infants exposed to short-term sleep deprivation manifest changes in cardiac autonomic controls during sleep. These findings could be relevant to mechanisms associated with the sudden infant death syndrome.

Key Words: autonomic nervous system, infant, sleep deprivation, sudden infant death syndrome

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INTRODUCTION

SLEEP-DEPRIVATION STUDIES IN INFANTS, AS OPPOSED TO THOSE IN ADULTS OR ANIMALS, ARE SCARCE. The available studies for infants suggest an increase in sleep efficiency and quiet sleep density and an increased frequency of obstructive apnea, mainly during active sleep.1,2 In adults and animals, sleep deprivation blunts the ventilatory responses to hypoxia and hypercapnia,3 decreases the arousal responses to chemical stimulation,4 increases the frequency and duration of obstructive sleep apnea,5 decreases genioglossal electromyogram activity,6 increases the pressure to sleep, and elevates sympathetic tone.7

The potential to elevate sympathetic tone by sleep deprivation in adults has significant implications in the study of mechanisms involved in the sudden infant death syndrome (SIDS). A body of evidence suggests that a cardiovascular collapse occurs in at least some SIDS cases8; such collapse would be mediated primarily by the sympathetic arm of the autonomic nervous system.

The incidence of SIDS is enhanced by sleep deprivation.9,10 During the last 24 hours before death, SIDS victims slept significantly less than control infants.11 Recent changes in normal life routine occurred more frequently in SIDS than in control infants.12,13 Sleep deprivation can result from handling conditions as well as from sleep fragmentation14-17 due to respiratory or digestive infections,18-20 fever,21 or airway obstructions during sleep.22,23 Almost 70% of SIDS victims suffered from minor intestinal or respiratory infection during the last 24 hours prior to their death.18-20 Dysregulation of autonomic nervous system controls such as high sympathetic activity or low parasympathetic tone has been found in infants who become SIDS victims24-29 and in healthy infants exposed to environmental factors known to increase the risk for SIDS, such as prenatal exposure to cigarette smoke,30 prone sleeping,31,32 or high environmental temperature.33

For these reasons, we examined changes in autonomic balance, as reflected by assessment of heart rate (HR) variability, in healthy infants following a short duration of sleep deprivation.

METHOD

Patients

Healthy infants were prospectively recruited between September 2000 and December 2001 to evaluate the effects of sleep deprivation during sleep. The infants were eligible for the study if they met the following criteria: they were about 8 weeks old, in good health, were sleeping supine, had a regular sleep-wake schedule, were born to nonsmoking parents, had no family history of SIDS, and had parents who would actively contribute to the study. Indeed, great care was taken by parents to avoid any changes in sleep habit or sleep deprivation the night before the test. The infants were recorded polygraphically for 1 day in a pediatric sleep laboratory.

Monitoring Procedures

Monitoring was carried out in a quiet, dimly lit room at an ambient temperature ranging from 21° to 24°C. All patients slept supine, without restraints. They were observed continuously during recordings. Their behavior and nursing interventions were charted. Feeding was administered on demand. The infants wore their own pajamas and were covered with 2 layers of blankets. The clothing and bedding corresponded to 3° Tog insulation.34 The following variables were recorded simultaneously: 8 scalp electroencephalograms with central, temporal, and occipital leads; 2 electrooculograms; digastic electromyogram; and electrocardiogram (ECG). Respiratory movements were measured with the use of thoracic and abdominal strain gauges, and airflow was measured by oral and nasal thermistors. Oxygen saturation was recorded continuously by a pulse oximeter (Nellcor, USA). An actigraph was placed on 1 arm to measure body movements. The data were collected on computerized polygraph recorders (Morpheus System, Medatec, Belgium).
Sleep Deprivation

The morning of the study, the infants were admitted to the sleep laboratory at approximately 9:00 AM. They were allowed to fall asleep after feeding. Before either the morning or afternoon nap, they were sleep-deprived for approximately 2 hours before being allowed to fall asleep. Sleep deprivation was implemented by keeping the infant awake by playing, handling, and providing mild tactile and auditory stimulations. Six infants were sleep-deprived before the morning nap and 6 before the afternoon nap to avoid confounding effects due to differences in sleep tendency across the day. The sleep characteristics of each infant were compared between the non–sleep-deprived (normal) and the sleep-deprived condition.

Data Analysis

Sleep Stages

Every 30-second period of the recording was scored as non-rapid eye movement (NREM), rapid eye movement (REM), or indeterminate sleep; wakefulness; or movement time according to standard criteria. Sleep efficiency was defined as the time spent sleeping divided by the total recording time, multiplied by 100. During both normal and deprived sleep, the frequency of NREM, REM, and movement time was calculated by dividing their duration by the total duration of the period, multiplied by 100. Scoring was done visually by 2 independent scorers to ensure reliability. Evaluation of the recordings was performed without knowledge as to whether or not sleep was deprived. Interscorer agreement was 95%. Scoring discrepancies were discussed, and codes thus agreed upon were used for data analysis.

Cardiorespiratory and Oxygen Saturation

Sleep apneas were scored only if they lasted 3 seconds or more. Central apneas were scored when flat tracings were obtained from the thermistors. To avoid artifact scoring due to thermistor deflections were obtained from the strain gauges while a flat tracing of breathing movements. An obstructive apnea was scored when continuous deflections were obtained from the strain gauges while a flat tracing was recorded from the thermistors. To avoid artifact scoring due to thermistor displacement, obstructive apneas preceded by body movements, crying, or sighs were rejected. Mixed apneas were defined as central apneas followed directly by obstructive episodes and were scored together with obstructive apneas. Median values for oxygen saturation and respiratory rate were calculated on 1-minute stable sleep epochs at least 5 minutes after any change in body position, movement, sigh, or arousal. A drop in oxygen saturation referred to changes greater than 3% of basal values. Frequency of apnea and drops in oxygen saturation were calculated as an index by dividing the absolute number of events during the period by the total sleep time of the period.

Spectral Analysis of HR

The ECG channel was recorded at 300 Hz. The algorithm was based on an adaptive statistical analysis of the second derivative of the ECG signal. The QRS complexes were located within an error less than 4 milliseconds. Premature ventricular contractions and artifact RR intervals due to gross body movements, apneas, sighs, or arousals were eliminated by visual analysis of the HR data. Spectral analyses were restricted to artifact-free segments. Spectral analysis was performed following the method described by Akselrod. Recommendations of the task force on HR variability were respected. The signals were subjected to Hamming windowing and then to the Cooley and Tukey algorithm. Fast Fourier transforms were calculated for 4 epochs of 8-minute slices of data. Each epoch was selected during normal and deprived sleep, in both REM and NREM sleep. The resulting power spectral density was the squared absolute value of the Fourier transform of the preprocessed signal and was expressed in milliseconds squared. The relevant frequency range spanned from 0.04 Hz to 2 Hz. Mean HR values were calculated on these periods. Overall HR variability was defined as the standard deviation of RR values. Respiratory frequency during the selected period was measured visually after being printed on paper. For each period, the major component in the low-frequency (LF) band of the HR spectrum was related to the major component in the high-frequency (HF) band corresponding to the mean respiratory frequency as determined by analysis of breath-to-breath intervals. In HR power spectrum, 2 major peaks were recognizable: a LF component, defined by a center frequency of 0.1 Hz (0.04 Hz - 0.15 Hz) related to sympathetic and parasympathetic activities, and a HF component, defined by respiratory band reflecting parasympathetic tonus. Spectral components were represented as power (in milliseconds squared). Normalized power, expressed in percentage, was obtained by dividing the power of the period by the total power component. The ratio of LF to HF powers was calculated as an index of sympathovagal interaction. To determine if any observed differences in spectral-analysis results were related to the differences seen in HR, each spectral value was normalized for HR (spectral power was divided by the square of the mean HR value of the analyzed epoch).

Statistical Analysis

Statistical analysis was performed with the use of the Wilcoxon matched-pairs test, with a level of significance of P < .05. The Spearman test was used for correlation studies. Statistical analyses were done to compare normal and deprived sleep. The aim and methodology of the study were approved by the University Ethics Committee and were explained to the parents, who gave their informed consent.

RESULTS

The general characteristics of the subjects are shown in Table 1. The median duration of sleep deprivation was 120 minutes (range, 90 to 260 minutes). Most sleep characteristics were similar for the sleep-deprived and the normal conditions. These included sleep efficiency (median value of 94.7% in the sleep-deprived and 93.9%
in the normal sleep condition; range, 66.4% - 100%); time awake (median value of 4.8% in the sleep-deprived and 6.2% in the normal sleep condition; range, 0% - 50.6%); REM sleep (median value of 46.3% in the sleep-deprived and 39.6% in the normal sleep condition; range, 14.7% - 64.3%); and NREM sleep (median value of 46.6% in the sleep-deprived and 41.5% in the normal sleep condition; range, 25.2% - 80.8%). No differences were seen in the frequency of central apneas (median values of 2.1 apneas per hour in the sleep-deprived and 2.6 apneas per hour in the normal conditions; range, 0 - 8 per hour of sleep); the duration of central apneas (median values of 5 seconds in the sleep-deprived conditions and 4.7 seconds in the normal conditions; range, 3 - 7 seconds); the frequency of periodic breathing (median values of 0% in both conditions; range, 0% - 27.8%); or the duration of obstructive apneas (median value of 5.6 seconds in sleep-deprivation and 4 seconds in the normal sleep condition; range, 3 - 9 seconds).

As shown in Table 2, sleep deprivation was associated with a decrease in density of movements (P<0.019) and an increase in the frequency of obstructive apneas (P<0.018), especially in REM sleep (P<0.012). Following sleep deprivation, the infants had higher basal HR (P<0.021) and shorter RR intervals (P<0.012) during NREM sleep (Table 2). During REM sleep, RR variability was decreased in the sleep-deprived condition (P<0.017). No significant differences were seen in breathing rates between sleep-deprived and normal conditions in either REM or NREM sleep.

No differences were seen in the time of selected epochs for spectral analysis during either NREM or REM sleep. The median time of recording for NREM sleep was 3:43 PM in the sleep-deprived condition (range, 11:31 AM - 6:06 PM) and 4:04 PM in the normal condition (range, 11:17 AM - 7:39 PM). For REM sleep, the median time of recording was 4:12 PM in the sleep-deprived condition (range, 11:55 AM - 6:44 PM) and 4:36 PM in the normal condition (range, 11:50 AM - 7:09 PM).

The LF to HF power ratio was significantly lower in NREM than in REM sleep (P<0.012), but the significance of the finding tended to disappear when LF power values were normalized by HR (P<0.068). Following sleep deprivation, the ratio of LF to HF powers increased during NREM sleep (P<0.005) (Table 3). During both REM and NREM sleep, the sleep-deprived and the normal conditions could not be differentiated for either the total HF powers or HF normalized power values. No relationship was found between autonomic nervous tone and gestational age, birth weight, age and weight at study, gender, time or type of feeding, or order of sleep deprivation (morning or afternoon). No correlation was found between duration of sleep deprivation and cardiac autonomic parameters.

### DISCUSSION

Significant changes in cardiac autonomic controls were seen during the recovery sleep period that followed sleep deprivation, especially during NREM sleep. These included an increase in basal HR, LF power, and LF to HF power ratio. The observed changes in autonomic controls could not be ascribed to experimental conditions known to modify autonomic tone in infants, such as maternal smoking, changes in body position, or increases in ambient temperature.

We must admit several limitations. Firstly, the limited number of infants studied and the short durations of sleep deprivation could have prevented us from identifying a statistical significance for some of the changes observed following sleep deprivation. Secondly, we did not monitor the previous 24 hours at home before the test to ensure that the sleep conditions were normal. We selected infants with regular sleep/wake schedules. As it was very difficult to recruit infants for this study, most of the infants in this study were the children of doctors and nurses in our pediatric departments. Parents who agreed to participate in this study were aware of the methodology of the study and took care to avoid any changes in sleep habit or sleep deprivation before the test. Thirdly, the studies were carried out in a laboratory environment that could have disturbed the infants’ sleep or autonomic status. Such effects would, however, influence infants in both experimental conditions. Fourthly, no spectral analysis was performed on respiratory movements, and cross-spectral analysis of respiration and HR changes was not evaluated. Low-frequency breathing patterns, as are seen with irregular breathing or sleep apnea, could amplify the LF power per se without changing cardiac autonomic drive. We measured the respiratory frequency during the selected period. With this method, we previously found similar results to those of authors using cross-spectral analysis of respiration. The 2-month-old infants studied were in good health, with a low index of obstructive apneas. Even in sleep-deprived conditions, the frequency of apneas remained within the normal range for healthy 8-week-old infants. Even more, the autonomic tonus after sleep deprivation changed in NREM sleep, although the frequency of obstructive apnea did not increase in this stage. Finally, care must be exerted in interpreting the LF to HF ratio. Within the LF range, HR fluctuations depend on both sympathetic and parasympathetic controls.VASomotor or thermal influences may be seen under 0.09 Hz, and baroreceptor influences contribute to changes within the 0.1 to 0.15 Hz frequency band. Within the HF band, the respiratory peak has been shown to be mainly vagally mediated. Vagal efferent fibers could not originate from a common brainstem structure. The HF peak, which corresponds to respiratory sinus arrhythmia, would reflect only the part of the vagal efferent system from the nucleus ambiguus. Spectral HR techniques do not permit the evaluation of the influence of the other branch of the parasympathetic system issued from the dorsal motor nucleus. With these restrictions in mind, the ratio of the LF to HF powers is usually considered as an index of sympathovagal interaction.

In their study of adult subjects, Spiegel et al found changes in cardiac autonomic control following sleep deprivation similar to those found in the present study. Insufficient sleep has been associated with increases in sympathetic tone, expressed by increases in both LF to HF ratios and urinary catecholamine excretions, during the night and the following day, leading to increases in blood pressure. In their study, Kato and colleagues identified an increase in resting blood pressure following sleep deprivation that was associated with a decrease in muscle sympathetic activity. Pressor response to sleep deprivation would not mediate by muscle sympathetic vasoconstriction. These changes could be attributed either to the activation of the renin-angiotensin system together with enhanced production of vasoconstrictor endothelin or to changes

| Table 3: Results of Spectral Analysis of the Heart Rate of 12 Infants During NREM and REM Sleep in 2 Study Conditions* |
|-----------------|-----------------|-----------------|
| STUDY CONDITION | Sleep-deprived | Not Sleep-deprived |
| **NREM SLEEP** |
| Total power, ms² | 232.55 (44.70-652.70) | 103.85 (53.70-312.00) |
| LF power, ms² | 87.30 (26.30-322.20) | 39.35 (9.70-121.70) |
| LF normalized power, % | 51.40 (35.25-78.86) | 30.39 (14.76-63.11) |
| HF power, ms² | 14.73 (3.90-177.50) | 22.85 (4.90-177.10) |
| HF normalized power, % | 3.12 (1.82-11.12) | 1.57 (0.26-3.16) |
| LF/HF power ratio, % | NS | 0.005 |
| **REM SLEEP** |
| Total power, ms² | 292.5 (247.2-666.3) | 426.3 (147.8-1070.6) |
| LF power, ms² | 128.3 (89.4-201.6) | 151.5 (82.3-317.6) |
| LF normalized power, % | 37.57 (27.22-54.37) | 36.38 (29.67-57.37) |
| HF power, ms² | 30.8 (20.7-89.8) | 37.60 (20.10-126.6) |
| HF normalized power, % | 10.25 (7.89-13.52) | 9.85 (6.38-16.07) |
| LF/HF power ratio, % | 48.84 (22.6-620.9) | 3.53 (1.86-608) |
| REM/NREM SLEEP |
| HF normalized power, % | NS | NS |
| LF/HF power ratio, % | NS | 0.012 |

*Results are presented as medians and range. NREM indicates non-rapid eye movement; REM, rapid eye movement; ms, milliseconds; NS, not significant; LF, low frequency; HF, high frequency; LF/HF, low frequency/high frequency ratio.
in baroreflex sensitivity.51 Sleep deprivation could reset the sensitivity of the baroreflex to higher set points.52 As found in other studies,32 we were unsuccessful in this study in measuring blood pressure in infants by automated techniques, as inflation and deflations of the cuff often provoked arousals.

The clinical significance of the observed changes in autonomic cardiac controls remains unknown. These changes could reduce the electrical stability of the heart and precipitate ventricular fibrillation and sudden cardiac death.53,54 Increased sympathetic cardiac control could also favor a resetting of the baroreceptors55 and a blunting of the blood–pressure-related arousal reactions following external stimuli.56 Attenuated vagal or increased sympathetic activity could likewise reduce behavioral adaptation to environmental stresses.57,58

Despite the limitations of the study, it was shown that when sleep deprived, the infants showed a higher cardiac sympathetic tonus during recovery sleep. It remains to be determined whether these changes contribute to the increased risk of sudden death reported in sleep-deprived infants.5,10

REFERENCES


