Spontaneous Arousability in Prone and Supine Position in Healthy Infants

Ineko Kato, MD, PhD 1; Sonia Scaillet, MD 2; Jose Grosossier, MD 3; Enza Montemitro, MD, PhD 4; Hajime Togari, MD, PhD 5; Jian-Sheng Lin, MD, PhD 6; Andre Kahn, MD, PhD 6; Patricia Franco, MD, PhD 7

1 Department of Pediatrics, Nagoya City University Medical School, Nagoya, Japan; 2 Pediatric Sleep Unit, Free University of Brussels, Brussels, Belgium; 3 INSERM U628, Claude Bernard University Lyon 1, Lyon, France; 4 Pediatric Sleep Laboratory, University of Roma, Roma, Italy

Study Objective: Compared with control infants, those who will be future victims of sudden infant death syndrome (SIDS) show a decreased arousability during sleep, with fewer cortical arousals and more-frequent subcortical activations. These findings suggest an incomplete arousal process in victims of SIDS. Prone sleep position, a major risk factor for SIDS, has been reported to reduce arousal responses during sleep. The present study was undertaken to evaluate whether the prone sleep position impairs the arousal process in healthy infants.

Methods: Twenty-four healthy infants were studied polygraphically during 1 night: 12 infants regularly slept supine and 12 infants regularly slept prone. Infants were matched for sex, gestational age, and age at recording. Arousals were differentiated into subcortical activations or cortical arousals, according to the presence of autonomic and/or electroencephalographic changes. Frequencies of subcortical activations and cortical arousals were compared in the prone- and the supine-sleeping infants.

Results: Compared with supine sleepers, prone sleepers had significantly fewer cortical arousals during rapid eye movement (REM) sleep (p < .043). There were no significant differences in cortical arousals between the 2 groups during non-REM sleep. No significant differences were seen in the frequencies of subcortical activations during both REM and non-REM sleep between supine and prone sleepers. The ratio of cortical arousal to subcortical activation showed no significant differences between the prone and the supine sleepers.

Conclusions: Prone sleep position decreased the frequency of cortical arousals but did not change the frequency of subcortical activations, as has been previously found in SIDS victims. These results suggest specific pathways for impairment of the arousal process in SIDS victims.

Keywords: Sleep, arousal, infant, SIDS, position

Citation: Kato I; Scaillet S; Grosossier J; et al. Spontaneous arousability in prone and supine position in healthy infants. SLEEP 2006;29(6):785-790.

INTRODUCTION

FAILURE TO AROUSE FROM SLEEP MAY PLAY A ROLE IN SUDDEN INFANT DEATH SYNDROME (SIDS). 1-2 AN INSUFFICIENT PROSPENITY TO AROUSE COULD LOWER the chance of infants surviving when they are exposed to noxious conditions during sleep. 3 Compared with matched control infants, infants who eventually died of SIDS have been shown to have fewer body movements and awakenings from sleep, especially by the end of the night when most deaths occur. 4-5

Arousals reflect a progressive activation of various structures, from subcortical to cortical areas. 4-5 Autonomic and brainstem arousals can occur without changes in cortical activity. 6-10 We have previously showed that future SIDS victims have more subcortical activations and fewer cortical arousals than control infants, suggesting an incomplete arousal process in infants who eventually die of SIDS. 11

The prone sleeping position has been identified in worldwide epidemiologic studies as a major risk factor for SIDS. 12-14 Public awareness campaigns throughout the Western world have led to an over 50% reduction in postneonatal mortality and the frequency of SIDS. 15 This reduction in mortality has been mainly attributed to the avoidance of the prone sleep position. Various mechanisms have been postulated to explain the association of prone sleeping and SIDS. These include accidental suffocation, 16 oropharyngeal obstruction due to nasal obstruction, 17 posterior displacement of the mandible, 18 increased upper airway resistance, 19 inhibitory inputs from atrial stretch receptors, 20 compromise of cerebral blood flow during cervical hyperextension, 21 suffocation due to rebreathing expired air, 22,23 overheating, 24 development of nasal bacterial toxins, 25 and impairment of autonomic function. 26 A defective arousal response from sleep has also been postulated as a likely mechanism to explain why sleeping prone increases the risk of SIDS. 27 Compared with sleeping in the supine position, sleeping in the prone position is associated in healthy infants with a significant decrease in the frequency and duration of spontaneous arousals during both rapid eye movement (REM) and non-REM (NREM) sleep. 27-29 Sleeping prone has also been demonstrated to be associated with reduced responsiveness to a variety of internal or external arousal stimuli. 27-29,31

The present study was undertaken to evaluate whether prone sleep position in healthy infants impairs arousal process, as has been previously seen in SIDS infants.

METHOD

Patients

From April 1999 to April 2004, 24 infants were studied polygraphically during 1 night: 12 infants regularly sleeping supine and 12 infants regularly sleeping prone. They were matched for sex, gestational age, and age at the exam. All infants were admitted to join a sleep research program on sleep-related behavior. They had no family or personal history of SIDS. At the time of the study, all infants were healthy, not sleep deprived, and receiving no medication. The aim and the methodology of the study...
were approved by the University Ethical Committee and were explained to the parents, who gave their informed assent.

Polygraphic Studies

The infants were admitted to the sleep laboratory for a 9-hour, nighttime, monitoring session. The following variables were recorded simultaneously: 2 scalp electroencephalogram (F3T3, F4T4), 2 electrooculogram, and 1 electrocardiogram trace. Thoracic and abdominal movements were recorded by inductance plethysmography and airflow by nasal thermistors. Oxygen saturation was recorded continuously from a transcutaneous sensor (Nelcor, Hayward, CA). Gross body movements were measured with an actigraph placed on 1 arm. The data were collected with a computerized infant sleep recorder (Alice Recording System III, Healthdyne, Marietta, GA).

Body Positions

The infants were laid on a hard mattress covered by a single-layer sheet, without any pillow, and allowed to fall asleep in their usual supine or face-to-the-side prone position. Care was taken to avoid possible recording artifacts and prone sleeping face down.

Data Analysis

Sleep states were analyzed according to the recommended criteria. The methods for the analysis of sleep apnea are reported in our previous publications. Cortical Arousal and Subcortical Activation

Arousals were subdivided into subcortical activation or cortical arousal, according to the consensus on arousal scoring in healthy infants under 6 months of age. A subcortical activation was scored if no change in the electroencephalogram was seen, while at least 2 of the following changes occurred: a gross body movement detected by movement sensors or seen as an artifact movement in the somatic channels; changes in heart rate (at least 10% of baseline values); or changes in breathing pattern (frequency and/or amplitude) (Figure 1). A cortical arousal was scored using the above criteria, with the addition of the occurrence of an abrupt change in electroencephalogram background frequency of at least 1 Hz, for a minimum of 3 seconds (Figure 2). Total arousal corresponded to the sum of cortical arousal and subcortical activation. To evaluate the arousal process through the night, recordings were divided into 3-hour periods: 9:00 PM to midnight, 00:01 AM to 3:00 AM, and 3:01 AM to 6:00 AM.

Scoring of records was performed without knowledge of infant sleep position and study hypothesis. Two independent scorers analyzed the sleep recordings. Scoring discrepancies were discussed, and codes thus agreed on were used in the data analysis.

Statistical Analysis

Statistical assessments were made with the Mann-Whitney test, with a level of significance of p < .05. Values were expressed as median and range.

RESULTS

In each group, there were 12 infants (7 boys/5 girls) with a median postnatal age of 11 weeks (range: 10-19 weeks). In each group, one infant was born from a smoking mother. One of these two infants was born small for gestational age (supine sleeper). Six out of 12 infants in the prone group and 7 out of 12 infants in the supine group had received immunizations. The median delay of intervention, was respectively, 2.4 weeks (1.2-3.7 weeks) in the prone group and 2.6 weeks (2.4-8.8 weeks) in the supine group (NS). There were at least 7 days between immunization and sleep recording. The general characteristics of the infants are shown in Table...
There were no significant differences in the frequency of subcortical activations between REM and NREM sleep in both prone and supine sleepers. During REM sleep, there were more-frequent cortical arousals than subcortical activations in both supine and prone sleepers (respectively *p* = .014 and *p* = .011). No differences were found in NREM sleep (Table 2).

As seen in Table 2, compared with the supine sleepers, prone-sleeping infants had significantly fewer total arousals and cortical arousals during REM sleep (respectively *p* = .049 and *p* = .043) (Figure 3). There were no significant differences during NREM sleep.

No significant differences were seen in the frequencies of subcortical activations during REM sleep and NREM sleep between both supine and prone sleepers (Figure 3). The ratio of cortical arousal to subcortical activation showed no significant differences between the prone and supine sleepers in both REM and NREM sleep.

The analysis of time distribution of the arousals across the night showed that the frequency of cortical arousals was significantly lower in prone, compared with supine, sleepers in the first part of the night between 9:00 pm and midnight during REM sleep (median 13.6 per hour of sleep for prone sleepers, range 4.1-16.1 per hour of sleep; median 16.2 per hour of sleep for supine sleepers, range 11.7-40 per hour of sleep) (*p* = .049) (Figure 4). Comparing the 2 groups, no difference was seen in spontaneous cortical arousals in total sleep, REM sleep, or NREM sleep. The frequencies of arousal that followed either central or obstructive apneas were similar in prone sleepers and supine sleepers in all sleep stages. No relation was found between arousal characteristics and gestational age, birth weight, age and weight at study, sex, or time or type of feeding.

**DISCUSSION**

Compared with the supine position, prone sleep position decreased the frequency of cortical arousals in REM sleep. The frequency of subcortical activations and the ratio of cortical arousal to subcortical activation showed no significant differences between the prone and supine positions.

Because all infants were recorded in similar controlled conditions, the observed differences between the 2 groups could not be related to variance in experimental factors that modify arousal thresholds in infants, such as previous sleep deprivation, exposure to sedative drugs, type of feeding, pacifier use during the night, sleeping with the face covered, or sleeping in high environmental temperatures.

Several limitations should be described. First, the limited number of infants studied may prevent reaching significance in some analyses. The data depended on the limited number of polysomnographic studies prospectively collected in infants sleeping in the prone position because the prevalence of prone sleeping position has decreased drastically after the prevention campaign. All the infants sleeping in the prone position in our study were born at term and were in good health. The parents reported that their infants slept prone because they didn’t want to sleep in the supine position. Sleep position has been changed from supine to prone during the first 10 days of life.

1. Because of the study design, there were no differences in sex, gestational age, or postnatal age.

Comparing the 2 groups, no difference was seen in total sleep time, sleep efficiency, time spent in REM sleep, time spent in NREM sleep, time awake, or frequency and duration of central and obstructive apneas (Table 1). In both prone and supine sleepers, total arousals and cortical arousals were more frequent in REM than in NREM sleep (*p* < .001, in both groups) (Table 2). There were no significant differences in the frequency of subcortical activations between REM and NREM sleep in both prone and supine sleepers.

During REM sleep, there were more-frequent cortical arousals than subcortical activations in both supine and prone sleepers (respectively *p* = .014 and *p* = .011). No differences were found in NREM sleep (Table 2).

As seen in Table 2, compared with the supine sleepers, prone-sleeping infants had significantly fewer total arousals and cortical arousals during REM sleep (respectively *p* = .049 and *p* = .043) (Figure 3). There were no significant differences during NREM sleep.

No significant differences were seen in the frequencies of subcortical activations during REM sleep and NREM sleep between both supine and prone sleepers (Figure 3). The ratio of cortical arousal to subcortical activation showed no significant differences between the prone and supine sleepers in both REM and NREM sleep.

The analysis of time distribution of the arousals across the night showed that the frequency of cortical arousals was significantly lower in prone, compared with supine, sleepers in the first part of the night between 9:00 pm and midnight during REM sleep (median 13.6 per hour of sleep for prone sleepers, range 4.1-16.1 per hour of sleep; median 16.2 per hour of sleep for supine sleepers, range 11.7-40 per hour of sleep) (*p* = .049) (Figure 4). Comparing the 2 groups, no difference was seen in spontaneous cortical arousals in total sleep, REM sleep, or NREM sleep. The frequencies of arousal that followed either central or obstructive apneas were similar in prone sleepers and supine sleepers in all sleep stages. No relation was found between arousal characteristics and gestational age, birth weight, age and weight at study, sex, or time or type of feeding.

**DISCUSSION**

Compared with the supine position, prone sleep position decreased the frequency of cortical arousals in REM sleep. The frequency of subcortical activations and the ratio of cortical arousal to subcortical activation showed no significant differences between the prone and supine positions.

Because all infants were recorded in similar controlled conditions, the observed differences between the 2 groups could not be related to variance in experimental factors that modify arousal thresholds in infants, such as previous sleep deprivation, exposure to sedative drugs, type of feeding, pacifier use during the night, sleeping with the face covered, or sleeping in high environmental temperatures.

Several limitations should be described. First, the limited number of infants studied may prevent reaching significance in some analyses. The data depended on the limited number of polysomnographic studies prospectively collected in infants sleeping in the prone position because the prevalence of prone sleeping position has decreased drastically after the prevention campaign. All the infants sleeping in the prone position in our study were born at term and were in good health. The parents reported that their infants slept prone because they didn’t want to sleep in the supine position. Sleep position has been changed from supine to prone during the first 10 days of life.

1. Because of the study design, there were no differences in sex, gestational age, or postnatal age.

Comparing the 2 groups, no difference was seen in total sleep time, sleep efficiency, time spent in REM sleep, time spent in NREM sleep, time awake, or frequency and duration of central and obstructive apneas (Table 1). In both prone and supine sleepers, total arousals and cortical arousals were more frequent in REM than in NREM sleep (*p* < .001, in both groups) (Table 2). There were no significant differences in the frequency of subcortical activations between REM and NREM sleep in both prone and supine sleepers.

During REM sleep, there were more-frequent cortical arousals than subcortical activations in both supine and prone sleepers (respectively *p* = .014 and *p* = .011). No differences were found in NREM sleep (Table 2).

As seen in Table 2, compared with the supine sleepers, prone-sleeping infants had significantly fewer total arousals and cortical arousals during REM sleep (respectively *p* = .049 and *p* = .043) (Figure 3). There were no significant differences during NREM sleep.

No significant differences were seen in the frequencies of subcortical activations during REM sleep and NREM sleep between both supine and prone sleepers (Figure 3). The ratio of cortical arousal to subcortical activation showed no significant differences between the prone and supine sleepers in both REM and NREM sleep.

The analysis of time distribution of the arousals across the night showed that the frequency of cortical arousals was significantly lower in prone, compared with supine, sleepers in the first part of the night between 9:00 pm and midnight during REM sleep (median 13.6 per hour of sleep for prone sleepers, range 4.1-16.1 per hour of sleep; median 16.2 per hour of sleep for supine sleepers, range 11.7-40 per hour of sleep) (*p* = .049) (Figure 4). Comparing the 2 groups, no difference was seen in spontaneous cortical arousals in total sleep, REM sleep, or NREM sleep. The frequencies of arousal that followed either central or obstructive apneas were similar in prone sleepers and supine sleepers in all sleep stages. No relation was found between arousal characteristics and gestational age, birth weight, age and weight at study, sex, or time or type of feeding.

**DISCUSSION**

Compared with the supine position, prone sleep position decreased the frequency of cortical arousals in REM sleep. The frequency of subcortical activations and the ratio of cortical arousal to subcortical activation showed no significant differences between the prone and supine positions.

Because all infants were recorded in similar controlled conditions, the observed differences between the 2 groups could not be related to variance in experimental factors that modify arousal thresholds in infants, such as previous sleep deprivation, exposure to sedative drugs, type of feeding, pacifier use during the night, sleeping with the face covered, or sleeping in high environmental temperatures.

Several limitations should be described. First, the limited number of infants studied may prevent reaching significance in some analyses. The data depended on the limited number of polysomnographic studies prospectively collected in infants sleeping in the prone position because the prevalence of prone sleeping position has decreased drastically after the prevention campaign. All the infants sleeping in the prone position in our study were born at term and were in good health. The parents reported that their infants slept prone because they didn’t want to sleep in the supine position. Sleep position has been changed from supine to prone during the first 10 days of life.
Second, the scoring of cortical arousal and subcortical activation depended on the combination of autonomic and electroencephalographic changes. Scoring was based on the evidence that arousal is a continuous process that includes subcortical structure-induced autonomic changes and cortical activation. The visual scoring of cortical arousal corresponded to complete arousals, which included both autonomic and cortical activation. Arousal reactions that only included autonomic but no cortical changes were scored as subcortical activation. Because scoring was done visually, it cannot be excluded that spectral or other automatic techniques might have led to a different outcome. Third, because of the limited number of subjects available for analysis, this report was limited to the description of arousal characteristics. No multiple analyses were done on various infant characteristics that could lead to an identification of determinant factors in the arousal processes.

Sleeping in the prone position may have been associated in healthy infants with a significant decrease in the frequency of spontaneous arousals during both REM and NREM sleep. The mechanisms responsible for the depressed arousability in the prone position are not known. As occurs with swaddling, prone sleep limits arm movement, which is involved in startles, and favors a better sleep maintenance. This motor restriction could reduce the proprioceptive stimulations to the reticular activating system and, hence, the frequency of spontaneous behavioral arousals. Because basal parasympathetic tonus reflects the individual’s capacity to react, an increase in blood pressure and heart rate during spontaneous arousals are correlated with the intensity of arousals. The decreased frequency of spontaneous cortical arousals in the prone position could also be due to the changes in autonomic cardiac control, as has been demonstrated by position-related heart-rate changes, such as higher basal heart rate, lower heart-rate variability, and lower parasympathetic tonus. These autonomic changes could influence the other control mechanisms, including the functional resetting of baroreceptor sensitivity, and changes in blood pressure-related arousal stimuli. The mechanisms responsible for the position-dependent changes in autonomic controls could not be evaluated in our study. The changes in blood pressure were not measured in the sleeping infants because of methodologic constraints.

In healthy subjects, arousability increases across the night as a function of accumulated sleep time. Mobility increases linearly through the night, with the last interval containing more movements than the previous one. The transient increase in somatic activity toward the morning, primarily in active sleep, has been thought of as an extra mechanism to ensure awakening. In our study, the frequency of cortical arousals was lower in prone compared with supine sleepers across the night, but the statistical significance was reached during only the first part of the night. We cannot explain why this arousal depression is higher at the beginning of the night in the prone position. These results could be associated with changes in the control of autonomic cardiac function that has been reported to occur in the prone position. An explanation could be that the effect of position on baroreceptor gain would be more important at the start of the positional change. Otherwise, circadian influence on heart rates appears during the first 2 months of life. When the night is divided into 3 parts, heart rate during the first and last intervals of the night is elevated, in comparison with the middle of the night. This quadratic trend of sympathetic tone occurs in active sleep in infants who are 2 months of age and could contribute to the early night and nearly significant results in the late part of the night in the prone position. It remains to explain why these circadian fluctuations were not seen in the supine position, although the quadratic trend of heart-rate changes have also been found in this position.

As has been reported previously, we found that the probability of arousals from sleep was significantly higher in REM sleep than in NREM sleep for both sleeping positions. Arousal mechanisms are different in REM and NREM sleep. The level of cortical activity during REM sleep is more closely related to activity in wakefulness than to activity during NREM sleep. The excitatory processes that elicit the brainstem and cortical responses during sleep are possibly enhanced during REM sleep. In NREM sleep, the inhibitory influence that prevents the spread of arousal activity along the pathways from the brainstem to the cortex is more prominent than in REM sleep.

Compared with the supine position, the prone sleep position decreased the frequency of cortical arousals in REM sleep but did not significantly modify the frequency of subcortical activations and the ratio of cortical arousal to subcortical activation. Compared with control infants, future SIDS victims showed more-frequent subcortical activations and fewer cortical arousals. The ratio of cortical arousal to subcortical activation was significantly smaller in the infants who died of SIDS than in matched control infants during REM sleep. These results suggest that specific
pathways are involved in the impairment of the arousal process in SIDS victims and support the idea that structural or maturational dysfunction rather than functional changes could be implicated within the infants' arousal system in future SIDS victims. Present knowledge from the whole mammal to the cellular level suggests that cortical arousal and its maintenance require the convergent and divergent activity of an ascending network within a large reticular core extending from the medulla to the forebrain and involving several neurotransmitters or neuromodulators, such as brain monoamines and neuropeptides. The arousal process is also under the control of both cortical and cerebellar structures.

The underlying mechanisms in SIDS remain to be elucidated. Pathologic and immunohistochemical studies in SIDS infants have demonstrated diffuse lesions within different nuclei of the central nervous system, essentially at the brainstem level. Pathologic changes described in SIDS victims include brainstem gliosis and apoptosis, as well as hypoplasia of the arcuate nucleus. Delayed central nervous system myelination has also been described in SIDS victims and could be implicated in the reduced propagation of subcortical to cortical arousals. Functional changes could involve specific synaptogenesis or synaptic activities within cardiorespiratory and arousal systems, such as the noradrenergic, serotonergic, dopaminergic, cholinergic, somatostatin, histaminergic, or orexin binding sites. In SIDS victims, abnormalities of serotonergic neurons have been shown in the arcuate nucleus and also in the nuclei derived from the rhombic limb in ventral medulla. These structures are associated with respiratory, cardiovascular, and arousal controls. These developmental abnormalities could be secondary to metabolic, nutritional, or toxic insults or to genetic susceptibility. The arcuate nucleus has classically been thought to project to the cerebellum and could modulate vestibulo-cerebellar-fastigial nucleus-mediated compensatory responses to hypotension. A reduced serotonergic receptor binding in the arcuate nucleus could result in a critical reduction in the ability to respond to challenges that provoke hypotension. Proximal prone position could exacerbate this condition because systolic blood pressure has been reported to be lower in infants sleeping in the prone position, as compared with supine, position due to a reduction in vasomotor tone. Cerebellar structures are also involved in chemoreception, cardiopulmonary coupling, and arousal responses.

In conclusion, the prone sleep position decreased the frequency of cortical arousals but did not change the frequency of subcortical activations, as has been previously seen in SIDS victims. These results could contribute to our understanding of the mechanisms implicated in the death of some infants.

REFERENCES


52. Nogues B, Vecchieri-Blineau MF, Louvet S, Desfontaines O. Heart rate changes during sleep in normal two-month-old infants.