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EFFECT OF THE INCUBATOR ENVIRONMENT ON SLEEP ORGANIZATION IN PREMATURE INFANTS

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EFFECT OF THE INCUBATOR ENVIRONMENT ON SLEEP ORGANIZATION IN PREMATURE INFANTS

by

Meredith M. Platt

A dissertation submitted to the Graduate
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Abstract

EFFECT OF THE INCUBATOR ENVIRONMENT ON SLEEP ORGANIZATION IN PREMATURE INFANTS

by

Meredith M. Platt

Advisor: Professor Gerald Turkewitz

Many individuals who were prematurely born show psychological and physiological problems that are difficult to relate to earlier pre- or post-natal insults. One possible source of insult is the time the infant spends in the intensive care unit. The purpose of this study was to explore the influence of the environment of the intensive care unit on sleep organization in premature infants by examining responses to change in the incubator environment. A full sleep period was recorded under two conditions in 17 healthy premature infants at the time of weaning from incubator to crib: <u>On</u>, in which the motor of the incubator was on, and <u>Off</u>, in which the motor was turned off, portholes opened and infants loosely swaddled. That portion of the sleep record containing the EEG pattern known as <u>tracé</u> <u>alternant</u> was identified as evidence of a state of arousal similar to quiet sleep in the full-term infant. Only those epochs of the record were further analyzed. Components of sleep state and correlations of these components were assessed using Pearson product moment correlations and MANOVA. Degree of organization of quiet sleep state was assessed in each condition in terms of the correlations.

The results show that the first phase of the usual transition from incubator to crib has an impact on sleep organization. Respiration rate and variability were significantly lower in the *Off* condition than in the *On* condition with nearly all of the infants responding in a similar manner. The effect of the change in the incubator environment on other components of sleep were more dependent upon the infants' prior developmental and environmental history. For example, correlation between heart rate variability and respiration variability was positively related to estimated gestational age at birth and negatively related to the number of days in the incubator. Results show that the infant's environmental and developmental history influence the rate of occurrence of the individual sleep components, the organization of these components, and their response to environmental change.

Dedication

TO GORDON AND ALEXANDER PLATT

Acknowledgements

The prematurely born infants who participated in this study could not choose to do so themselves. I am deeply grateful to them and their parents for agreeing to take part with the hope that other infants might ultimately benefit.

I thank Dr. Gerald Turkewitz for believing in the project and in me. Without his patient listening, relentless optimism, good humor, professional values, and friendship in grim moments, I'm sure my doctoral world would have stopped turning long ago.

Dr. Bernard Karmel invited me to do the study at Mt. Sinai and agreed to be on my Committee. He provided me with his equipment and was always available with encouragement, technical assistance and statistical expertise. I'm very grateful to him. Dr. Peter Moller, my third Committee member, provided support throughout as well as meticulous and worthwhile criticisms of the manuscript. The very careful critiques and editing provided by Dr. Katharine Lawson and Dr. Michael Myers contributed substantially to the manuscript.

A great deal of support and good will were provided by Judith Garvey, R.N., the nursing staff, Dr. Edwin Brown and the medical personnel at Mt. Sinai neonatal intensive care unit during the year and a half the data were collected. I also thank Dr. John Dowd of Mt. Sinai for his wonderful sense of humor and for teaching me to survive equipment failures. Frequent discussions with Dr. Judith Gardner have been very helpful in understanding premature infant development. I also thank Mr. James C. Hansel for invaluable computer assistance.

A number of Hunter College students faithfully scored data for a year without complaining and without pay. I acknowledge their good and faithful work with gratitude: Diane Bodoni, Lisa Hjardemaal, Barbara Liberman, Olga Sacasa, Karen Schlichting, and Karlene Virgo. I especially thank Barbara Liberman for helping solve scoring problems and for contributing the most over the longest period of time.

The friendship of Dr. Molly Laird has been an anchor, a life raft, a parachute, and always a joy. I am happy that we began together and will be graduated together.

I thank my son, Alex, who once believed all mothers go to school all their lives, and who has put up with it just about enough. Last, and most, I thank my husband, Gordon, for his love and for saying "you can" every time I said "I can't."

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INTRODUCTION

Background:

The medical profession has been increasingly successful in recent years in saving the lives of smaller and sicker prematurely born infants (Lee, Paneth, Gartner, Pearlman, & Gruss, 1980; McCormick, 1985). However, many infants later show learning, motor or other types of psychological or physiological problems. It is extremely difficult, if not impossible, to connect these central nervous system problems with specific pre- or post-natal insults that occurred perhaps months or years before (Porges, 1983; Holmes, Reich, & Pasternak, 1984).

One possible source of insult or disruption in the developmental process is the time the infant spends in the intensive care unit. The effects of non-medical aspects of the neonatal intensive care unit on the development of these infants are not known. Current evidence suggests that there is a high density of environmental events to which the infants are exposed and this stimulation (light, sound, and handling, for example) influences the behavior of the premature infants, possibly negatively (Gottfried, Wallace-Lande, Sherman-Brown, King, Coen, & Hodgman, 1981; Lawson, Daum, & Turkewitz, 1977; Lawson, Turkewitz, Platt &

McCarton, 1985). There is already enough evidence available to strongly suggest that aspects of the environment are, in fact, contributing to later problems (Peabody & Lewis, 1985). We now need to know more specifically about central nervous system development as a function of aspects of the intensive care unit environment. Such knowledge would make intervention feasible.

In the present study, I chose to examine the possible influence of the incubator and, in particular, the sound of the incubator motor, because an infant spends anywhere from 4 days to 6 weeks or longer in it and the effects of the incubator environment on the central nervous system are not known. I chose to look at the effects of the incubator on the organization of the infant's sleeping pattern for two reasons: First, sleep state psychophysiology is one reflection of nervous system integrity in both adults and infants (Anders, 1978) and atypical sleep patterns, such as those found in the infants of drug-dependent mothers, are considered a sign of nervous system disturbance (Dinges, Davis, & Glass, 1980). By studying sleep, we obtain clues to the status of the nervous system. Second, the organization of sleep patterns in premature infants is known to be less developed than in full-term infants and to remain different in some respects even 8 months later (Dreyfus-Brisac, 1970, 1974, Parmelee, 1975). If differences in sleep pattern organization are seen under different environmental conditions, it might be possible to alter that environment to enhance sleep development.

The intrauterine environment:

To approach this problem, it was necessary to first consider the potential differences between the intra and extrauterine environments. The prematurely born infant has left an intrauterine environment in which thermal regulation is controlled by the mother's thermo-regulatory system. It is an environment which includes, in addition to maternal neurohormonal secretions and somesthetic stimulation from the fluids surrounding the body of the fetus, a variety of acoustic events such as the rhythmic sounds of blood flow in the maternal vessels and the sound of the mother's speech.

Intrauterine ambient sound levels have been difficult to determine because of the difference in airborne and fluid sound. Walker, Grimwade, and Wood (1971) found 85 dB of sound within the uterus and attributed the high level to turbulent blood flow and muscle movement. However, they used a microphone covered with a rubber sleeve and had to approximate the difference caused by an impedence mismatch between the intrauterine fluid and the air within the rubber sleeve-covered microphone. Although Henshall (1972) cited intensity levels found by himself and others ranging between 84 and 96 dB, he noted that if the fluid medium is allowed for, a 95 dB level in utero is equivalent to 57 dB of air-born sound. Bench (1968) found internal sound intensities 4 weeks after birth to be 54 dB. Those measured at 37 weeks gestation were 72 dB but he attributed this to pulsations of the uterine artery which was close to the location of the microphone.

Armitage, Baldwin, and Vince (1980) and Vince, Armitage, Baldwin, Toner, and Moore (1982) used a hydrophone inside the amniotic sac of pregnant ewes. The authors note that as a model for the human body in this context, the ewe has disadvantages, such as anatomical differences associated with ruminants and a cotyledenous placenta. They did not perceive sounds from the maternal cardiovascular system and they suspect this was because these sounds occur at very low frequency. Average sound levels were lower than those found by Walker, et al. (1971). Above 500 Hz signals from inside the ewe, when she was quiet, were about the noise level of the amplifier (40-50 dB). Sounds from within the mother, heard only intermittantly, were at low frequencies up to about 500 Hz and only rose to a high level (70-100 dB sound pressure level when the sound level is made equivalent to that in a 100 Hz band) at very low frequencies, below about 300 Hz. Heart rate sounds occurred only at certain times at extremely low frequencies (30-80 Hz). Attenuation of external sounds was rarely more than 30 dB. Attenuation was least below about 500 Hz and relatively constant between 500 and 2000 Hz. Their results suggested that low frequency sounds penetrate the body wall better than higher frequency sounds. If these sounds were above 65-70 dB they were available to be heard by the fetus. They concluded that sounds generated by or within the mother are varied and of rather low frequency. An important methodological difference between the work done with ewes and that with humans is that the ewes were recorded well before term, perhaps accounting for the lower background noise, while human studies were done at term, before or after rupture of the membranes.

Just what sound the fetus actually hears while in utero is not well understood. Rubel recently (1984) reviewed current work on the ontogeny of auditory system function. Structurally, the shape of the pinna and the size of the ear canal, which comprise the external ear, influence what sound reaches the tympanic membrane. The relatively small ear canal and pinna of the full-term newborn will tend to resonate at higher frequencies, where the newborn is less sensitive than adults. Because the immature ear canal is more compliant than in the adult, maximum gain due to resonance will be less in the neonate. This probably results in an overall loss of sensitivity in the upper half of the frequency range due to immaturity of the external ear. Middle ear structures provide a 35-40 dB pressure gain so at the youngest ages middle ear function is an important factor limiting hearing sensitivity. Rubel (1984) pointed out that,

> In order to understand the development of hearing we must document changes in the efficiency and spectral purity of information transfer from the acoustic environment to the inner ear...This gap in our knowledge is particularly apparent when we consider differences that must exist between animals which develop hearing prenatally (humans, most ungulates, and precocial birds) and those which begin hearing after birth (such as most rodents and carnivores). In animals that hear prenatally, the external and middle ear spaces are fluid-filled. Therefore, the role of the tympanic membrane and ossicular chain must be very different.

> Presumably the conduction of sound to the inner ear in an aquatic embryo will follow principles similar to bone conduction. Empirical studies of the transfer function under these conditions, however, are not available. (p. 215)

Rubel further points out that no single event triggers the onset of cochlear function but, rather, onset is the product of the simultaneous and synchronous maturation of many mechanical and neural properties.

Even in the final stages, maturation does not occur simultaneously throughout the length of the cochlea. Differentiation occurs first in the mid-basal region and spreads in both directions, with the apex maturing last. Most animals do not simultaneously begin hearing all frequencies that will be included in their adult range. Behavioral and physiological responses are first elicited by low or mid-low frequencies, and responsiveness to the highest frequencies develops last.

Attempts have been made to determine when the fetus begins responding to sound during development. Using a behavioral measure, Birnholz and Benacerraf (1983) played 110 dB of vibroacoustic stimulation with broad spectral peaks at about 250 and 850 Hz via a disk applied directly to the maternal abdomen overlying a fetal ear. The authors estimated that the 110 dB would be reduced to 95 dB by transmission through the abdominal and uterine walls. That figure generally agrees with Bench's (1968) finding that attenuation, which is frequency dependent, would be 19 dB at 200 Hz and 24 dB at 500 Hz. Birnholz and Benacerraf (1983) cited evidence suggesting background noise intensity within the uterus is 75 dB. It is not clear if this figure allows for the fluid medium. They found that eye-blink responses (observed with ultrasonic imaging) could be elicited between 24 and 25 weeks gestational age and were present consistently after 28 weeks. Increases in fetal heart rate responses to 80 dB of sound at about 2000 Hz have also been confirmed at 32 weeks gestation (Jensen, 1984). Grimwade, Walker, Bartlett, Gordon, and Wood (1971) elicited heart rate increase in fetuses 38-42 weeks gestation when pure-tone sounds of 500-1000 Hz were played at an estimated intrauterine sound pressure level of 80 dB.

There is also evidence that there are differences in response to sound stimulation when the fetus is in different states. Granier-Deferre, Lecanuet, Cohen, Sureau, and Busnel (1984) found that when a noise filtered below 800 Hz was played at 106 and 113 dB (estimated to be 86 and 93 dB in utero) to fetuses between 37 and 40 weeks gestation, habituation occurred only in a state equivalent to active sleep in the neonate. Habituation did not occur during quiet sleep.

Therefore, if the fetus can respond at 28 weeks to 250 and 850 Hz sounds at 95 dB, it is highly likely that hearing is even further developed during the 30 to 40-week period and responses to sound may be state dependent. Responsiveness at lower frequencies and intensities in utero has not been reported.

The extrauterine environment:

In the incubator, the infant lies unclothed (except perhaps for a diaper) on a mattress. This means that although there is some tactile stimulation from the mattress and from handling by the medical staff, such stimulation is qualitatively different from what would be experienced in utero.

Preterm infants are poorly insulated against heat loss and are at special risk for hypothermia (Holmes et al., 1984). They respond to cold when thermal receptors in the skin are stimulated. The more skin that is exposed, the more the potential for heat loss. The face is particularly sensitive so even if the rest of the infant's body is warm, a great deal of heat can be lost from the warm face to the cooler environment. Infants respond to heat loss with a rise in metabolic rate. If the environmental temperature remains below what the infant can generate to replace heat loss, he becomes hypermetabolic. The absolute amount of heat an infant can generate will be affected by gestational and postnatal age. The rate at which heat is lost varies depending on body size, tissue composition and thickness, skin blood flow, and vascular shunting (Perlstein, 1983).

In the NICU, thermal control is provided by warm air circulated throughout the incubator by a motor. This air creates a "breeze" across the infant's skin which adds a "wind" factor to the warming of the skin. Sensors placed on the infant's skin and in the incubator atmosphere assure what is called a "neutral" temperature environment. If the infant's skin temperature falls below a set level the air is warmed until the appropriate skin temperature level is reached. The motor that circulates the air produces a low but steady level of vibration in the incubator.

Sound levels in both the room environment and within the incubator appear to be higher than the infant experiences in utero. While sound levels recorded near the cervix at term may be generally similar to what has been recorded in the incubator, based on the work of Vince et al. (1982), it is likely that sounds in utero in earlier weeks of gestation are lower than what the infant experiences in the incubator. Lawson et al. (1977) recorded a mean characteristic sound pressure level of 68.8 dB in intermediate care or "grower rooms" and 83-88 dB in intensive care rooms. Since there was no basis for selection of a weighted scale appropriate to the premature infant, the authors used a linear scale to determine sound pressure level. An average sound level of 82 dB on the linear scale was recorded by Gottfried et al. (1981) in an intermediate care room and 85.8 in an intensive-care unit.

In a study by Douek, Bannister, Dodson, Ashcroft, & Humphries (1976), the peak sound level reached was 80 dB. (The weighting for this peak was not specified.) Abramovich, Gregory, Slemick, and Stewart (1979) recorded sound levels varying from 58 to 72 dB on all weightings of an octave band sound level meter.

Sound levels which I measured in incubators prior to the present study showed a mean unweighted sound level of 75 dB with peaks between 80-90 dB. These findings are very similar to those of Bess, Peek and Chapman (1985). Although Gottfried et al. (1981) did not find a significant difference between the levels they recorded outside an incubator and within it, Falk and Woods (1973) found differences of up to 20 dB. They recorded sound levels within the incubator with the motor running and with the motor turned off. Greatest differences were between 125 and 250 Hz.

The preliminary data gathered for the present study indicated that both unweighted overall sound levels and levels in the lower frequencies were at least 5 dB higher inside the incubator than outside it when the motor was turned on. Eighteen samples from incubators made by two manufacturers were collected at frequency bands from 31.5 to 31,500 Hz. Samples were taken from both inside and outside the incubator. There were no significant differences related to time of day. Figure 1 shows that between 31.5 Hz and 500 Hz the sound was approximately 5 dB louder inside the incubator than outside. Above 500 Hz, the sound was 5 to 8 dB louder outside compared with inside. Thus, the lower frequencies were dominant and it is possible that the sound of the human voice, which falls within the 1,000 to 4,000 Hz range, was partially attenuated within the incubator. When the incubator motor was turned off and the portholes were left open, there was less of a difference between levels inside and outside between 31.5 and 125 Hz. This is shown in Fig. 2. Between 125 Hz and 4000 Hz the sound was as much as 10 dB louder outside than inside the incubator. Again, it is possible that the incubator is attenuating the human voice.

Fig. 1. Comparison of sound levels inside the incubator with sound levels outside the incubator when the motor was _On_. Variability shown is the standard deviation.

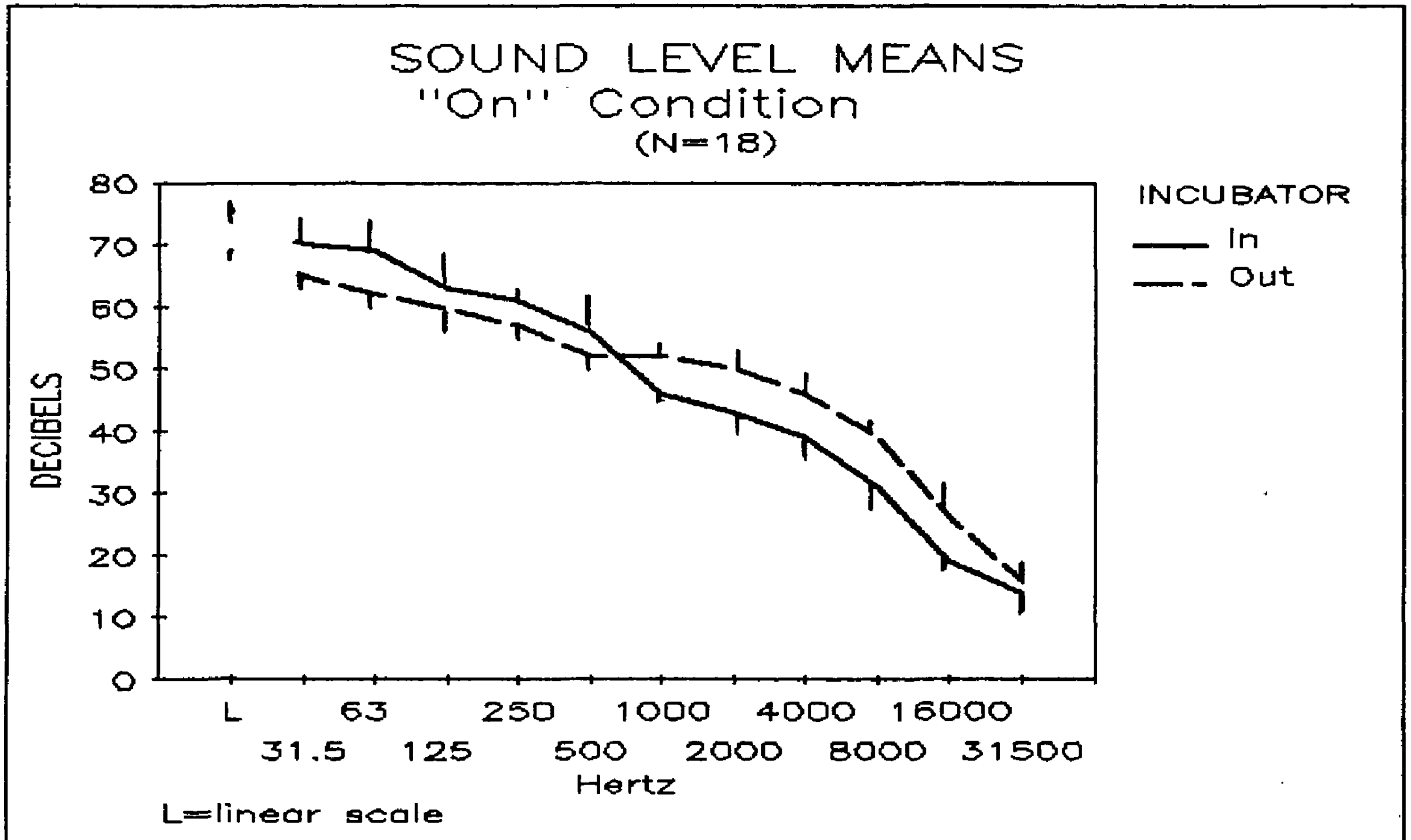

SOUND LEVEL MEANS
"On" Condition
(N=18)
DECIBELS
0
10
20
30
40
50
60
70
80
L
31.5
63
125
250
500
1000
2000
4000
8000
16000
31500
Hertz
L=linear scale
INCUBATOR
In
Out

Fig. 1

Fig. 2. Comparison of the sound levels inside the incubator with sound levels outside the incubator when the motor was _Off_. Variation shown is the standard deviation.

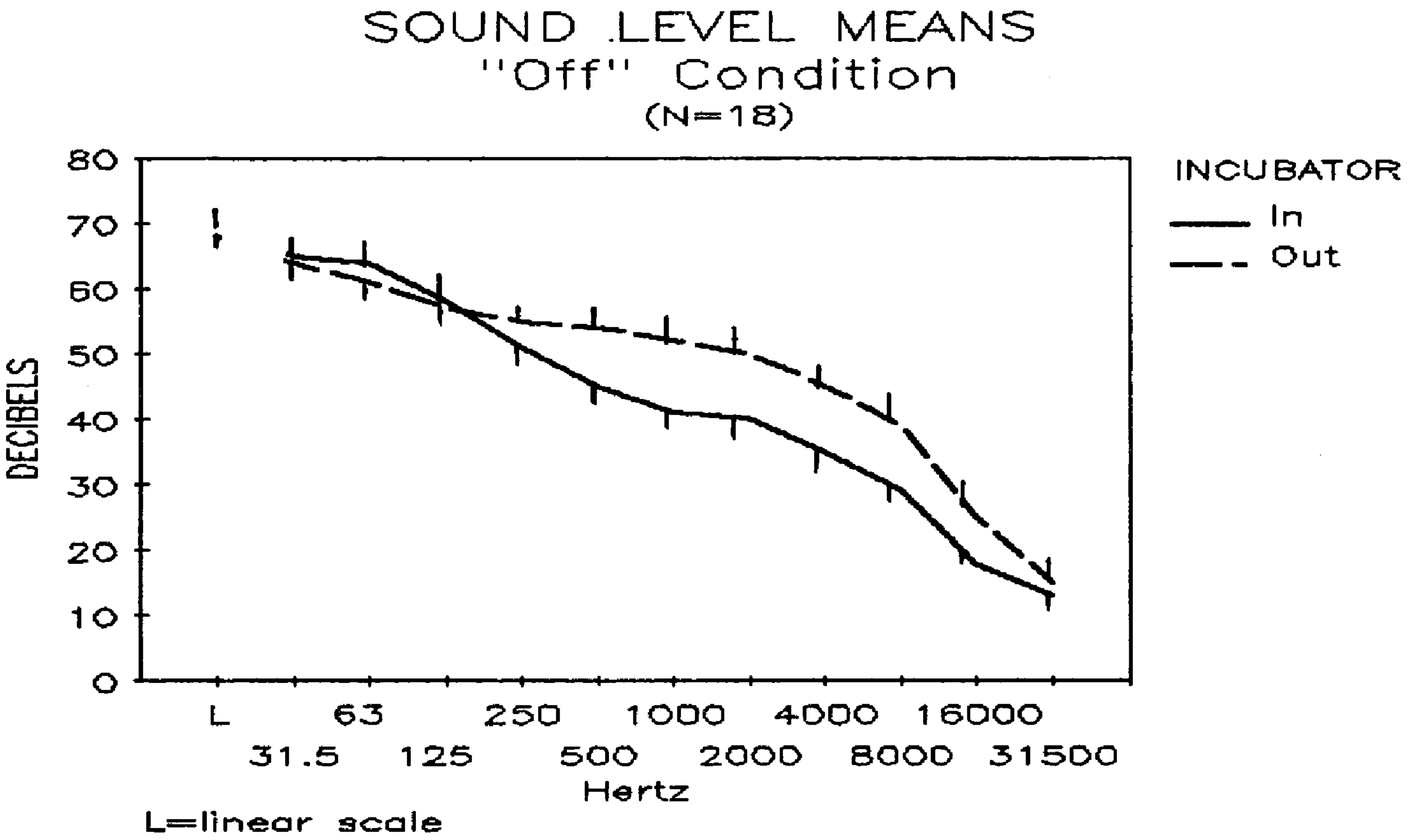

SOUND LEVEL MEANS
"Off" Condition
(N=18)
DECIBELS
0
10
20
30
40
50
60
70
80
INCUBATOR
In
Out
L
31.5
63
125
250
500
1000
2000
4000
8000
16000
31500
Hertz
L=linear scale

Fig. 2

Sounds from outside the incubator are somewhat muffled and speech sounds are, for the most part, not concordant with handling of the infant by the speaker. Within the incubator, the circulating air produces a steady "whooshing" sound with greatest energy primarily in the low frequencies that the infant hears 24 hours a day.

In adults, a continuous level of sound pressure above 90 dB is considered "unsafe" because it causes demonstrable damage to the cochlea. While a previous study (Abramovich et al., 1979; Stewart & Abramovich, 1979), failed to show a correlation between incubator sound levels and hearing loss, there could be differences between adults and infants in what level is "safe." Cochlear damage occurred in 2-week old guineapigs placed in incubators while no damage occurred to adult guineapigs (Douek et al., 1976). Gottfried et al. (1981) considered the sound levels they recorded to be excessively high at times and potentially hazardous. However, although premature infants most likely do hear incubator machinery and other noise in the room and although there is suggestive evidence that damage can occur, a direct connection of hearing loss to sound at these levels has not been made.

In addition to sound levels in general, tape recordings made from inside an incubator have indicated that speech sounds are clearly audible within the incubator (Lawson et al., 1977). However, it is not known if the higher sound levels in the lower frequencies and the infant's possibly greater sensitivity to the lower frequencies results in masking of the human voice when the incubator is operating.

The sound in the incubator is important for three reasons: First, the dominant frequency range found in the incubator sound was similar to that found in utero. That is, the greatest energy was in the very low frequencies. As Fig. 1 shows, infants were exposed to 70 Hz and below at 65 to 70 dB. Second, from what is known of the development of audition, sensitivity is likely to be greatest in the low frequencies during the early stages of development. Lower frequency sounds have been studied by Hutt, Hutt, Lenard, Bernuth, & Muntjewerff (1968) who found that full-term infants 3 to 8 days old were most sensitive to 70 Hz sound (producing a startle response) and could discriminate between 125 and 250 Hz. The authors suggested a possible adaptive value for this sensitivity and ability to discriminate among tones:

> The lower the frequency of a stimulus, the greater the length of basilar membrane which

> will be displaced by a travelling wave; hence the greater excitation elicited by the stimulus. Still greater excitation will be produced by a broad-band stimulus with a low frequency fundamental and high energy peaks at several different points in the frequency spectrum...the fact that this tone [70 Hz] was so frequently accompanied by startles suggests that excitation throughout the length of the basilar membrane may elicit defensive reflexes, perhaps accompanied by protective adjustments of the middle ear muscles....The most effective stimuli were those the fundamental frequencies of which were within the range of the fundamentals of the voice. Thus the structure of the human auditory apparatus at birth ensures both that there is a limit of basilar membrane excitation beyond which defensive reflexes are evoked, and that the voice at normal intensities is non-aversive and prepotent (p.890).

Rubel (1984) also pointed to this adaptive function in his description of auditory ontogeny: "It is perhaps not coincidental that low frequencies are present in the environment of young organisms, whether in a burrow, in an egg, or in utero. If the development of normal function is dependent on external stimulation, then the developmental pattern we have proposed will provide a mechanism to insure that each neuronal region receives adequate stimulation from the environment" (p. 219).

Third, the sound in the incubator is important because particular kinds of sound will have at least a temporary influence on the sleep of premature and full-term infants. The playing of a heartbeat sound, for example, influenced the duration of sleep states in prematures by decreasing the duration of the first active epoch and increasing the duration of the first quiet sleep epoch (Schmidt, Rose, & Bridger, 1980). Brackbill (1973) found that continuous white noise of 85 dB played to month-old term infants reduced arousal level both behaviorally and physiologically. Brackbill (1971) also found that this pacification effect is cumulative across modalities in full-term infants. If both visual and auditory stimulation were presented, for example, the quieting effect was greater than with single modality stimulation.

The effects of the premature shift from the uterine environment to the incubator on the developing fetus are not known. Another major environmental shift having unknown consequences occurs when the infant is moved from the incubator to a crib. The infant is first usually clothed in a shirt and diaper, swaddled, and remains for one sleeping period with the incubator turned off and the portholes opened to adjust to room air. The infant is then moved to a crib.

A number of studies have shown that swaddling can influence infant state. Two separate studies by Lipton, Steinschneider, and Richmond (1960, 1965) examined full-term infants. In the first study, responses of infants to a stream of oxygen when swaddled or unswaddled were examined. The results showed less variability in heart rate in the swaddled condition for 8 of the 10 infants tested; no crying and more sleeping when swaddled, and a slower respiratory rate by 7 of the 10 infants. No analysis of the prestimulus conditions was included.

In the second investigation, eight infants were studied in three conditions while completely clothed in long tight stockings pinned to their diapers and shirts with blind-ending sleeves which covered the hands and fingers. The three conditions were: (1) free, (2) partially swaddled with a diaper wrapped around the legs to hold them in extension and a light receiving blanket surrounding the infant up to but not including the arms, and (3) completely swaddled with both arms extended and tightly wrapped. The investigators recorded the cardiac response before a stimulus was presented and immediately following the stimulus. Respiration was recorded using a thermistor and sleep was behaviorally observed.

Data from the first study was statistically analyzed and included in the results of the second study. When the prestimulus heart rates among the different conditions were compared, both studies showed the individual infants had significantly more variability in heart rate when free. Seven of the eight infants in the second study had significantly higher heart rates when free. All 10 infants in the first study had greater mean heart rates when free (half were significant). The authors did not find significant differences in respiration rates. Only 3 of the total of 18 infants showed significant differences between swaddled and free conditions. These showed their longest (slowest) respiratory cycle in the free condition.

Regarding sleep, both groups slept more when swaddled than when free but these differences were significant only in the first study.

Infants in Lipton et al.'s study had been fed prior to testing and the importance of this can be seen in a study by Giacoman (1971). Also looking at full-term infants, she had two groups of infants, hungry and satiated, and each was observed in two conditions, swaddled and free. Videotape was used for behavioral analysis. In general, there was more sleep and drowsiness and less crying when swaddled than when free. However, the satiated infants were more drowsy and cried less when <u>free</u>. Swaddling affected the hungry babies, who cried less, were more drowsy and slept more when swaddled than when free. Swaddling appeared to have an arousal reducing effect in the hungry infants but not the satiated infants.

Unfortunately, not many studies have focused on premature infants and swaddling. Gardner (1979) and Gardner & Turkewitz (1982) looked at how heart rate differed as a function of arousal condition in premature infants. There were four conditions in the study: Hungry infants who were swaddled; hungry infants who were free; satiated infants who were swaddled, and satiated infants who were free. They found that heart rate was highest when the infant was unswaddled and hungry; lowest when swaddled and fed.

In addition to swaddling, when the preterm infant is moved from the incubator to the crib the sound of the incubator motor (as well as its vibration) is no longer present and room sounds, including human speech, may be clearly heard. The infant must now use its own thermal control and the temperature in the room is not likely to be as high as that in the incubator. While much of the skin area that would normally lose heat is now covered, the head and face are usually exposed. When the motor is turned off, the temperature in the incubator adjusts to approximately that in the room. This will be modified by several factors: First, the acrylic plastic walls of the incubator act as a "greenhouse," absorbing infrared energy from visible light and radiating heat which could mean it is still warmer inside the incubator than outside. On the other hand, if the incubator is located next to a window at night, the heat stored in the walls could be lost and cool the interior of the incubator. Second, if the blanket and clothing used for the infant have not been warmed, heat loss from the incubator can result (Perlstein, 1983).

It is important to learn more about the impact of these environmental shifts because it is possible that some aspects of the environment enhance neurobehavioral development while others disrupt it.

Development of sleep patterns:

One neurobehavioral system that is developing rapidly and can be monitored under different environmental conditions is the organization of sleep state. "State" has been defined as, "constellations of certain functional patterns of physiological variables which may be relatively stable and which seem to repeat themselves" (Prechtl, Akiyama, Zinkin, & Grant, 1983, p. 1). Sleep state is customarily described in terms of the way the simultaneous responses of particular physiological components (usually, heart rate, respiration, EEG, eye movements, and EMG) conform to previously identified patterns. It is the concordance of the individual components to these particular patterns that comprises what is called the sleep state. For example, sleep states in the healthy full-term infant develop from a two-stage pattern at birth to an adult-like four-stage pattern by one year. Stage 1 in the newborn is called active sleep and is characterized by the presence of rapid eye movements under closed lids (REM), irregular respiration, and facial and localized body movement. The EEG is of low voltage (14-35 microvolts) which may be superimposed on slow waves (1-5 Hz). In adults, stage 1 is characterized by low voltage, mixed frequency EEG without REM, suppression of muscle tone and irregular respiration and heart rate. In the newborn's stage 2, quiet sleep, there is no REM, respiration is regular, and muscle tonus is absent. EEG is usually a *tracé alternant* and may also be comprised of continuous slow waves of medium to high voltage

(50-150 microvolts, .5-4 Hz). Chin movements may be present. For adults, stage 2 EEGs include sleep spindles against a low voltage, mixed frequency background. Stages 3 and 4 in adults are characterized by moderate to large amounts of high amplitude, slow wave EEG activity. Stage REM includes relatively low voltage, mixed frequency EEG, REM, low amplitude muscle tone, and irregular respiration (Anders, Emde, & Parmelee, 1971; Anders, 1978; Dreyfus-Brisac, 1974; Rechtschaffen & Kales, 1968).

During development the component behaviors which define the various sleep states (heart rate, rapid eye movements, etc.) seem to develop at different rates. EEG patterns seem advanced in premature infants, for example, while respiration patterns seem delayed (Parmelee, Wenner, Akiyama, Schultz, & Stern, 1967). The degree of concordance among the components with what is seen in the patterns of the full-term infant will vary. For example, in the preterm infant one might find the EEG pattern typical of quiet sleep together with irregular respiration and the presence of eye movements. Such a pattern would be considered an instance of poor concordance of components for quiet sleep when compared with the full-term infant. It is in this sense that the preterm infant's sleep is said to be less organized than the full-term infant's (Anders et al., 1971; Anders, 1978; Dreyfus-Brisac, 1974). This lack of organization or unstable organization has been documented by Dreyfus-Brisac (1970) in the premature infant. Lack of organization of state in the fetus has been confirmed in utero using ultrasound (Nijhus, Prechtl, Martin, & Bots, 1982).

Even when he or she reaches normal term gestational age, the premature baby's sleep pattern is not the same as the term baby's and at least one difference (the lack of coordination of respiration with other parameters) is still present 8 months past term (Dreyfus-Brisac, 1974; Parmelee, 1975). The reasons for these differences are not well understood.

The study:

The major concern of this study was how the "normal" environment typically experienced in the incubator, particularly the sound of the motor, might be affecting the development of physiological processes, in this case, sleep. The sound of the incubator is a significant stimulus which could influence sleep either by itself or in concert with other stimulation in the unit. Removal of the incubator sound could represent a significant change in that stimulation.

The final weeks of gestation are a time of rapid development for the fetus, and it is possible that environmental stimulation has, as Lawson et al. (1977) have pointed out, a very different effect on the premature infant than it would on an adult or even a full-term baby. Environmental factors may enhance or impede the emergence of well-defined rhythms (see Sostek, Anders & Sostek, 1976). The possibility of entrainment of state to environmental events is important because it suggests that persisting lack of organization or a different pattern of organization of sleep in the preterm infant might be connected in some way to inappropriate environmental entrainment.

It is not possible to adequately and empirically compare responses while the infant is in the intrauterine environment with those while in the incubator. However, it was possible to examine differences in sleep patterns while the incubator motor was On and while it was Off. In doing so, the goal was to learn as much about the real-world experience of the infant as possible by interfering with the normal routine as little as possible.

Therefore, this study focused on the moment the shift from the incubator to the crib took place; that is, the day the infant was ready to come out of the incubator and was judged no longer in need of it. The usual procedure in the nursery is to turn off the incubator motor after the 11 a.m. feeding, open the portholes, dress and swaddle the infant, and leave him or her in the same incubator for the next sleeping period. This is referred to as weaning the infant from the incubator. In the current study, standard physiological measures of the infants' sleep were recorded both just prior to and during this weaning period. That is, recordings were made while the incubator motor was operating (the morning sleep period) and not operating (the afternoon sleep period) so differences in individual components of sleep and concordances among these components measures could be examined. These data were used to consider whether there was possible environmental control over the degree of organization in the premature infants' sleep, and whether there was a relationship between the infants' behavior under these conditions and certain infant characteristics, such as gestational age at birth. Information is available on the sleep patterns of full-term infants for comparison. Although it would be valuable to have data on the effect of incubator noise on the sleep pattern of full-term infants, no attempt to collect such data was made in the present study because of possible harmful effects of such exposure.

The study addressed a number of specific issues:

If the motor in the incubator is turned off, will there be effects on the individual components of sleep? For example, will the respiration rate be higher or lower? Will it be more regular or irregular? A second issue concerns the effect of turning off the motor on the way these measures co-occur. For example, are respiration and heart rate both regular with the motor _On_ but only respiration regular with the motor _Off_? Will there be significant changes in the degree of concordance among all the components of sleep with patterns seen in full-term infants? A third issue deals with the influences of other factors, such as the length of time an infant has been in the incubator on his or her responses to the motor being turned off. How do patterns seen compare with available information on full-term infants? And, finally, what might these differences suggest about environmental control of the degree of organization of the premature infant's sleep?

Because this was a naturalistic study, it was much more of a hypothesis-generating than hypothesis-testing investigation. However, it was believed that the incubator environment, especially the sound of the motor, was influencing the organiziation of sleep so that if the motor was turned off, changes in the pattern would be seen.

MATERIALS AND METHOD

Rationale:

Sleep studies are usually conducted in a laboratory because they are both complex and cumbersome. An array of a dozen electrodes or more is fixed to the subject's head and face. The electrodes are connected to polygraph equipment and recordings are made continuously for at least one full night of sleep. Polygraph records are later visually inspected in order to assign sleep state to particular time periods or epochs. A great deal of information is available from these recordings and the extent of the analysis depends on the nature of the study.

The traditional methodology was modified here in several ways:

First, the purpose of this study was to assess the state of the central nervous system as reflected in the organization of sleep as described in the Introduction. Since premature infant sleep is poorly organized, the focus of data scoring and analysis was on the degree of organization of state and not on the amount of time spent in each state. Second, since the study examined the effects of aspects of the environment on the organization of sleep, recordings had to be made in the natural setting of the intensive care unit. Third, since the subjects were premature infants, it was essential to keep the procedure as simple and unintrusive as possible. Modifications in the number of electrodes used, procedures, and recording equipment were required. Finally, it was intended that the method being developed should be one that can be replicated and used in similar contexts not only to validate the procedures but to build a body of data on central nervous system responses to aspects of the environment.

Subjects:

Seventeen preterm infants in stable condition were monitored in the premature neonatal unit of The Mt. Sinai Medical Center. Prematurity was defined according to the scale devised by Dubowitz and her associates (1970). While no attempt was made to closely circumscribe the characteristics of the 17 infants included, those under 1500 g at birth and those with complex physiological problems--for example, infants who were on a respirator for more than a week or who had respiratory distress syndrome or other known neurological impairments such as hydracephalus--were not included. Of the 17 infants, only one had been on a respirator. The aim was to include a moderately broad and reasonably healthy sample. Data were collected on the infants' prior history: initial and current diagnoses, birth process complications, maternal complications, analgesic given to the mother, the infant's past and current medication, time on a respirator and under phototherapy. Table 1 shows the birth and recording information. Mean birth weight for the group was 2196 g (range= 1780-2800 g); mean gestational age at birth was 35.0 weeks (range= 31.0-37.0 wks); mean gestational age at the time of recording was 37.0 weeks (range= 35.0-39.0 wks); mean number of days spent in the incubator was 15.0 (range= 4.0-30.0 days). Nine females and eight males were studied. All infants had passed the Crib-O-Gram test for hearing (Simmons, 1976; Simmons & Russ, 1974). For this test, a device placed under the infant's mattress detects movement response to white noise sounds at varying intensities. The Crib-O-Gram can reveal gross but not subtle degrees of hearing loss.

Procedure:

The progress of each infant being considered for the study was followed. The house staff advised when a baby was ready to be removed from the incubator. At that time, permission was obtained from a parent and a consent form was signed. The infants were monitored first for one sleep cycle with the incubator sound On and then one sleep cycle

Table 1. Characteristics of the 17 infants included in the study. Rec weight indicates the weight of the infant at the time of recording; PCA indicates the post-conceptional age of the infant at the time of recording.

Birth weight (grams)	Sex	EGA(wks)* at birth	Apgars 1 & 5min	Rec weight (grams)	PCA(wks) at rec	Days in Inc.
1780	F	34.0	9/10	1980	37.5	25
1840	M	31.0	8/9**	2300	36.0	29
1840	F	34.0	8/9	2040	37.0	21
1840	F	32.0	7/8	2250	36.0	30
1850	F	34.0	5/6***	2190	36.5	17
1930	F	34.0	8/9	1930	37.0	21
2110	F	35.0	7/9	2020	37.0	13
2130	M	34.5	9/9	2010	36.0	10
2180	F	35.0	8/9	2390	37.0	15
2250	F	37.0	8/9	2230	38.0	7
2260	M	37.0	9/9	2220	39.0	15
2280	M	33.5	7/9	2310	36.5	19
2380	F	35.0	7/8	2410	35.5	4
2520	M	35.0	9/9	2450	36.5	10
2570	M	37.0	8/9	2510	37.5	4
2780	M	36.0	9/9	2640	37.0	5
2800	M	35.0	7/8	2780	36.5	11
Mean: 2196		34.6		2275	36.8	15

*Estimated gestational age was assessed by use of the Dubowitz Test (Dubowitz, Dubowitz, and Goldberg, 1970). **Infant was on a respirator for one week. ***Infant showed no spontaneous responses immediately following caesarian birth but responded to oxygen and was crying within two minutes. The infant was not placed on a respirator.

with the incubator sound _Off_ and the portholes open to admit room air and sound. All observations were made while infants were in the incubator because the change to a new environment, the bassinette, would confound the data. All observations for a particular infant took place on the same day, as soon after the 8 a.m. feeding as practicable. Infants were fed approximately every 3 hours. Because hospital routines rarely entailed feeding at precisely 8 a.m., the actual start of recording time for each infant varied. The mean time of day for the start of recording with the incubator motor _On_ was 9:19 a.m. (range= 8:34-10:22 am). Mean time of day for the start of recording with the motor _Off_ was 12:25 p.m. (range= 11:45-1:04 p.m.) Recordings were terminated either for feeding or because the infant was awake and fussing.

Characteristic and peak sound pressure levels (Bruel & Kjaer Precision Sound Level Meter) were measured as well as a frequency analysis of the sound spectra (Bruel and Kjaer Octave Filter Set) under both conditions, inside and outside the incubator, for each infant. Sound levels were recorded outside the incubator while standing next to the incubator, facing the center of the room. Sound levels inside the incubator were noted prior to recording by placing the head of the sound meter through the porthole at the end of the incubator near the infant's head and closing the porthole around the meter. Light levels were also noted, using a Gossen Lunasix light meter. The observer stood next to the incubator and pointed the meter towards the center of the room.

Five measures of sleep were continuously recorded: Heart rate and respiration, which were recorded directly from Hewlett Packard ICU monitors, EEG, eye movement (EOG), and muscle tonus (EMG). These measures were selected because prior studies have shown them to occur in identifiable patterns in the sleep of healthy, term infants (Prechtl & Lenard, 1967). They have also been the measures used when recording sleep patterns of premature infants (Dreyfus-Brisac, 1970).

Heart rate and respiration were recorded from standard neonatal electrodes attached to Hewlett-Packard Model B neonatal monitors while EEG, EOG, and EMG were recorded using Beckman miniature electrodes attached to a Teca model physiological amplifier. Data were stored on FM-tape using an 8-channel FM tape recorder (Vetter, Model A). EEG was recorded on a single channel, using bipolar leads placed over the left position in the frontal (F3) and left position in the parietal (P3) area with a forehead lead as ground. A single channel of EOG was recorded from bipolar leads placed slightly lateral to the outer canthus of each eye. EMG was recorded from an electrode placed over the chin muscle and referenced to the region behind the ear. Electrodes were attached using Grass electrode paste at the beginning of each condition (On/Off) to avoid differences due solely to one initial application of electrodes. During the On condition, infants wore only a diaper. During the Off condition, infants also wore undershirts and were loosely swaddled.

To assure appropriate recording levels for each measure, prior to each session all channels of the tape recorder were calibrated with an oscilliscope and a function generator (EL Instruments, model FG-2). During recording, any one channel could be observed on the oscilloscope (Tektronix Type 502 dual beam) to monitor the ongoing bioelectrical activity and to detect artifactual signals which usually are related to altered positions of the electrodes. Tapes were played through a polygraph to provide a hard-copy record for later visual and quantitative analysis. Behavioral observations were verbally recorded using a microphone connected to an available channel in the tape recorder as an additional ongoing commentary to help interpret the record during later analysis.

Data scoring and analysis:

Rationale: Conventionally, the concordance of all the measures within an epoch to established sleep state criteria is assessed by visual inspection of the polygraph record and sleep state is assigned according to these criteria. Quantitatively, the method is crude but quite adequate for many sleep studies, especially with adults. However, Prechtl et al., (1983), pointed out that since the concept of state "stands or falls with the variables that are applied, as well as with their assessment, it is evident that only operational definitions are acceptable" (p.1). Their study made a strong case for operationalizing terms and providing computer analysis of polygraph records. Their methodology, however, required computer programs for newborn infant EEG that even now are not widely available. Moreover, the problem of writing programs to assess EEG in preterm infants is more formidable because the patterns can be more individual. Anders (1974) later devised a methodology that could be more readily shared by others than could computer analysis and permitted the exploration of many aspects of sleep. Included was a way of assessing the degree of organization of sleep state; that is, how well the pattern of the components met the criteria for each state. Each measure was coded discontinuously (e.g., respiration: regular, irregular, periodic) using the method described in the Infant Scoring Manual (Anders, et al., 1971), which is based on visual inspection. A way of scoring heart rate was not included in this analysis.

The method of assigning sleep state to each epoch has also been used with premature infants by adapting the criteria. However, because of the lack of organization of premature sleep, <u>states</u> of sleep comparable to the full-term baby are difficult to assign (Prechtl, Fargel, Weinmann, & Bakker, 1979; Stefanski, Schulze, Bateman, Kairam, Pedley, Masterson, & James, 1984). In particular, in the premature infant, the criteria for state include an overlapping in which a pattern assigned to one state can also be found in another.

In the present study it was assumed that assigning state would be inappropriate for preterm infants. If we are to assess changes in organization over time, under different environmental conditions, and among infants with different medical histories, a method specifically suited to this task was needed.

The goals of the methodology in the present study were to (1) assess the degree of organization within a sleep epoch as one barometer of central nervous system integrity; (2) operationalize the definitions used in sleep criteria to the extent possible by using quantitative, continuous data from the polygraph record (e.g., number of eye movements, heart rate, heart rate variability) instead of qualitative, discontinuous data (e.g., "regular" respiration, eye movements "present" or "absent"); develop an efficient system that would minimize the amount of analysis needed to provide the information sought about the centeral nervous system; use recording methods (FM-tape and polygraph hard copy) that can be analysed by hand and potentially by computer.

Scoring: Polygraph records were comprised of 20-sec pages (epochs) of all five measures (heart rate, respiration, EEG, EOG, EMG) simultaneously displayed. This record was first inspected visually. Epochs of EEG records which were identified by visual inspection and verbal record as containing artifact, excessive movement, or mechanical electrode or equipment failure were eliminated from further consideration.

A scoring method based on the EEG, was considered appropriate. This component has been used as a reference for state of arousal by Dreyfus-Brisac (1970). Even with this measure, most EEG patterns are not exclusive to a particular sleep state in infants. For example, a mixed pattern (predominantly continuous polymorphic activity of 4-7 Hz, averaging 50 microvolts in amplitude, intermingled with slower waves of slightly higher voltage) or immature rhythmic slowing (monomorphic high voltage, >100 microvolts, occurring often in sequences lasting longer than 10 sec) might be seen either when the baby is awake or in active sleep. However, one EEG pattern, the tracé alternant (TA), is present reliably only during quiet sleep in newborn full-term infants (Parmelee, 1975). It can be clearly identified in the preterm infant's polygraph record (Figure 3). It is also considered developmentally precocious relative to the other recorded measures (Monod & Garma, 1971).

Therefore, epochs where TA occurred were identified as likely to indicate a state of arousal which was most similar to that found during quiet sleep in the full-term infant.

Fig. 3. Polygraph record from one infant in the study showing _tracé alternant_ EEG pattern typical of quiet sleep in the full-term infant (center tracing). Also shown are tracings of heart rate (HR), respiration (RESP), eye movements (EOG), and muscle movement (EMG).

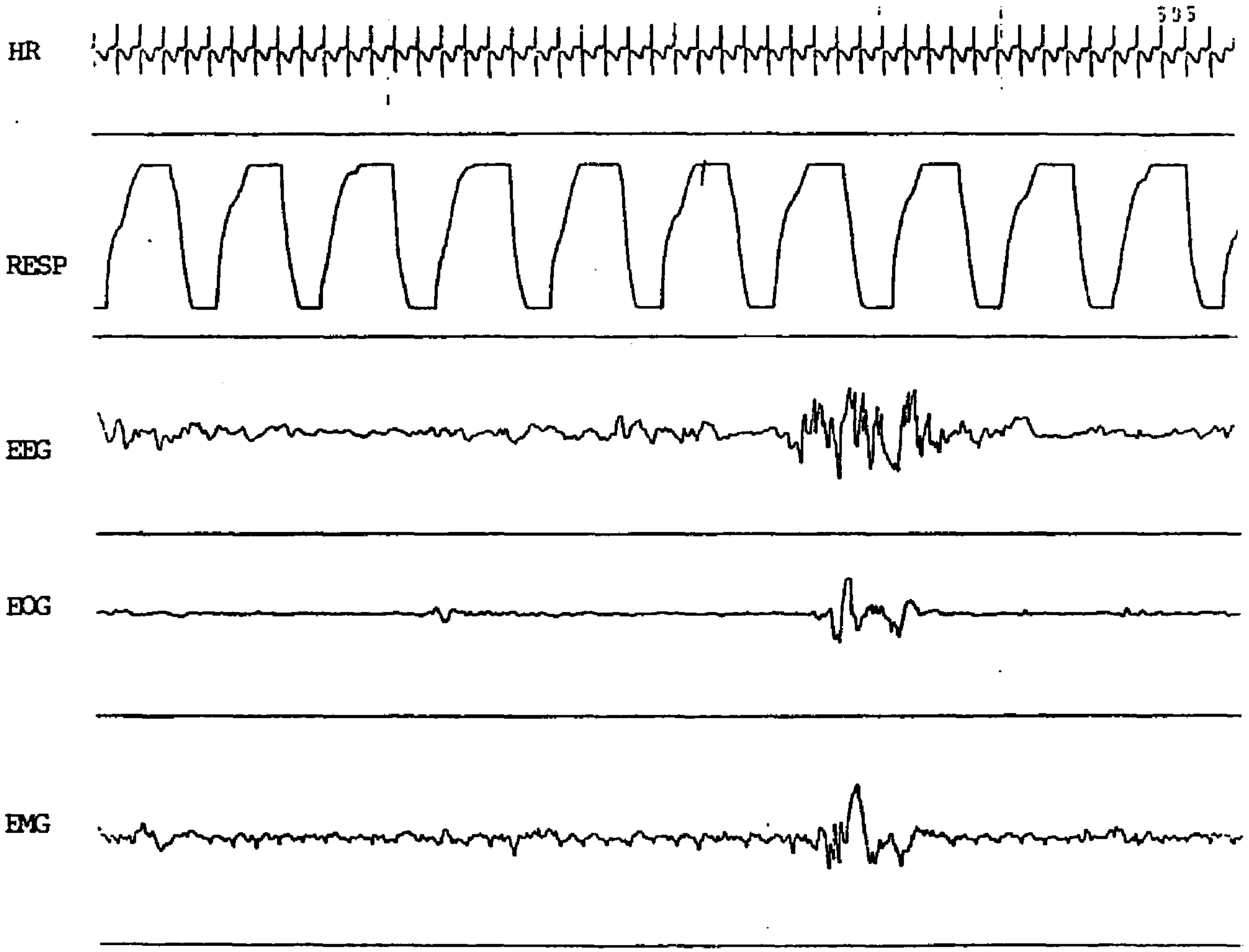


FIG. 3

Conventionally, the identified pattern of a particular measure does not necessarily have to appear in every consecutive epoch to be counted within a particular state. A predetermined, arbitrary, criterion is set for each measure. For example, if eye movements appear for a number of epochs but on the next epoch do not appear, REM sleep might still be scored for three one-minute epochs. If eye movements fail to appear after that time, state change is considered to have taken place and the subsequent portions of the record are scored as indicating a different state. Since state was not being scored in this present study, if the TA burst pattern (50-100 microvolts, 0.5-3 Hz separated by periods of attenuated activity, typically <5 microvolts, lasting 10-40 sec) appeared in one epoch but changed to a different pattern on the next, only the first epoch was scored TA.

Only those epochs scored TA received further analysis. This meant that epochs with other EEG patterns that might be scored quiet sleep state using other criteria were not included here. Since state was not scored, this study did not address the issue of how much quiet sleep occurred in each condition as a proportion of the total record.

By identifying the TA pattern, it was possible to relate the other measures to this one to assess the degree of organization. Comparisons between degrees of organization in _On_ and _Off_ sessions could then be made.

EEG was scored independently by two different scorers and any discrepencies were reconciled by a third. The polygraph record was covered during scoring except for a "window" opening which revealed the EEG measure. Agreement between the two scores averaged 90.3% (range= 86-95%).

The criteria for quiet sleep in a full-term infant require a regular heart rate and respiration rate, no eye movements, and little facial or chin movements. In scoring these measures in the premature infant, therefore, the rate and variability of heart rate and respiration, the rate of occurrence of eye movements, and the number of seconds of EMG were considered.

Heart rate was scored by measuring in millimeters seven interbeat intervals starting at the beginning of each page and seven intervals starting at the center of each page. This resulted in two samples for each 20-sec epoch. These data were entered on a Lotus spreadsheet. Each value was next converted to heart rate per minute. The following calculations, based on these heart rates, were made: heart rate mean per sample, mean per page, standard deviation per sample, standard deviation per page, coefficient of variation per page (standard deviation divided by the mean), and the difference between the two samples per epoch. The coefficient of variation was calculated as a measure of variability which allowed for differences in heart rate among the infants. Scoring was done by one person. As a check on reliability, a second person then scored 10% of the pages (randomly chosen) from each infant's record. Reliability was assessed in two ways: mean discrepancy between the mean heart rate scored for each page by the two people scoring (mean discrepancy= 0.32 beats per min, range= 0.02-1.59 bpm), and the mean discrepancy between the standard deviation for each page scored by each person (mean discrepancy= .74 beats per standard deviation).

Each epoch of respiration was scored by measuring the longest breathing cycle and the shortest breathing cycle within an epoch by using calipers to measure the time from the start of one inspiration to the start of the next. This time period was then translated into breaths per minute. Using a Lotus spreadsheet, the mean respiration rate and the variability (the difference between the high and low rate for each epoch and the ratio of the difference between the high and low to the mean) were calculated. The respiration ratio provided a measure of variability while allowing for the differences in breathing rate among the infants. Each record was scored by two observers and discrepancies reconciled by a third person. The mean rate of agreement between the first two scorers was 91.2%, range was 86-97%.

In previous studies, the term "regular" was usually defined by visual inspection only (e.g., Gabriel, Grote, & Jonas, 1981). If the breaths appeared to be generally of the same amplitude and frequency, the epoch was scored regular. This presents a problem when attempting to determine how "regular" premature infant breathing is relative to the full-term infant. Dreyfus-Brisac (1974) used a more objective definition of "regular" and so for comparison purposes, each 20-sec epoch in the present study was also scored for degree of regularity using her criteria: variation of breaths per minute less than 20 were scored as Regular breathing; variation in breaths per minute between 20 and 50 were scored Semi-regular; variation greater than 50 was scored Irregular breathing. More than 5 seconds of no breathing was scored Periodic. (While this is not the only possible definition of periodic breathing, it was used to remain consistent with the literature.) The percentage of epochs in the total sample scored for each category was calculated.

EMG for each epoch was scored by counting the number of seconds movement was present in each epoch. A rate of EMG per epoch was calculated for each infant by dividing the total duration of EMG in the sample by the total duration of the sample. Each infant's record was scored by two scorers. Discrepancies were rescored and reconciled by a third. Reliability was determined by the per cent epochs in agreement between the first and second scorers (mean= 94.9%, range= 89-100%).

For EOG, the number of eye movements present in each epoch was scored. A rate of eye movements per 20-sec epoch was calculated. For this measure, records of two infants had to be excluded because of a high rate of mechanical artifact. Records were scored by two separate raters and disagreements were reconciled by a third who rescored those epochs. Mean reliability between the first two raters was 89.3%, range was 87-96%, and the range across babies was 87-96%.

Analysis: Three major issues were addressed in the analysis of the data. The first issue concerned the behavior of the infants in the two conditions. Were there differences in the rate, variability or occurrence of the individual measures when the _On_ condition was compared with the _Off_ condition?

Were there differences between the _On_ and _Off_ condition in how well the components were correlated with each other? For example, when respiration variability was low or high, was heart rate variability also low or high? Analysis was between pairs of components and combinations of three and four components.

The second issue concerned the behavior of the premature infants when compared to full-term infants. In what ways did the rates, variabilities, etc. of the individual components differ from previous data on full-term infants? In what ways did the degree of correlation of components compare with that in full-term infants? The third issue concerned the relationship of various aspects of sleep to the infants' prior history. For example, was there a correlation between heart rate and gestational age at birth, birth weight, or the length of time the infant had been in the incubator?

To address all these questions, the calculations made from the raw data were entered into new Lotus spreadsheets. Each infant had a spreadsheet for each condition that included the following information for each epoch in the sample:

Heart rate: mean rate, standard deviation, ratio;

Respiration: mean rate, ratio;

EOG: number of eye movements present;

EMG: number of seconds of movement present;

First, to obtain an overall rate of occurrence for each measure, the mean of the On and Off values for each infant in each measure was calculated. Then, Wilcoxon signed-ranks tests were used to compare the behavior of the individual components in the On and Off conditions. The Wilcoxon test is considered a more powerful test than the Paired Samples t test at this sample size (N=17) (Blair & Higgins, 1985). The measures examined were: heart rate, heart rate standard deviation, respiration rate, respiration ratio, per cent epochs of respiration scored using the four categories (regular, semi-regular, irregular, periodic), EMG rate (seconds per epoch), and rate of eye movements per epoch. (Note: All analyses were also done using the heart rate ratio instead of heart rate standard deviation but no differences resulted and so only the results using heart rate standard deviation will be reported.)

Pearson Product Moment correlations were used to examine the association between pairs of measures, such as the correlation between heart rate variability and respiration variability. Product moment correlations provided the degree of correlation and the direction of that correlation (positive or negative). The measures examined in this phase of the analysis were: heart rate standard deviation, respiration ratio, seconds of EMG, number of eye movements. All possible combinations of these measures were examined.

To examine the overall difference between correlations in the _On_ and _Off_ conditions, the median of the Pearson product moment correlations was calculated for each of the six possible pair combinations. This resulted in a matrix for the _On_ and _Off_ conditions which is presented descriptively.

Multiple analysis of variance was used to examine more than two measures at a time. This provided an overall index of correlation but not the direction of the correlation. Measures examined were the same as for the Pearson correlations: heart rate standard deviation, respiration ratio, seconds of EMG, and number of eye movements. All combinations of two, three and four measures were examined in each condition for each infant.

In order to examine possible sources for differences among infants, data were correlated with factors reflecting differences in the infant's history. A principle components factor analysis was done which resulted in the identification of two factors. These were a Developmental Factor (predominately determined by weightings for estimated gestational age at birth and birthweight) and an Environmental Factor (predominately determined by number of days in the incubator at testing and post-natal age at testing). However, to provide a more fine-grained analysis, data were also correlated separately with estimated gestational age at birth, birthweight, days in the incubator at testing, and post-natal age at testing. These factors will be referred to as the Infant Factors.

Partial correlations of the Developmental Factor and the Environmental Factor were also done to determine if one element (such as post-natal age at testing) was significant when the effects of other elements were partialled out.

Some of the infant factors were highly correlated with each other:

Estimated gestational age at birth
and days in the incubator.........= -.80
Estimated gestational age at birth
and birthweight..................= .62
Estimated gestational age at birth
and postnatal age at testing......= -.77
Birthweight and postnatal age at
testing..........................= -.56
Postnatal age at testing and days
in the incubator.................= .79

Pearson Product Moment correlations were used to analyze the Developmental, Environmental, and Infant Factors. Data used for correlating the overall rate (mean of the On plus the Off conditions) with these Factors were: heart rate, heart rate standard deviation, respiration rate, eye movement rate, EMG rate. Data used to look at the difference between the On and Off conditions with the Factors were (a) for combinations of measures, the p-values obtained in the MANOVA (On condition minus Off condition): heart rate standard deviation, respiration ratio, eye movement rate, EMG rate, and (b) for individual measures, the difference in the mean rate (On minus Off): heart rate, heart rate standard deviation, respiration ratio, eye movement rate, EMG rate.

The goal of the analysis was to see how closely the basic rates of response of the individual components in the _On_ and _Off_ conditions matched previous data and then, how closely correlated the measures were in each epoch. Quiet sleep criteria in the full-term infant required that there simultaneously be low heart rate and heart rate variability (relative to other stages of sleep), low respiration rate and variability, and a low rate of occurrence of eye movements and facial movements. Thus, if the basic rates found in the preterm infant matched those accepted for quiet sleep criteria in the full-term infant and there was a positive correlation between or among components, concordance with the quiet sleep pattern was said to be present to the degree of the correlation.

CHAPTER 3

RESULTS

The sample:

Of the 489 min of total record examined for respiration, only 4.3 min (1.0%) were excluded because of mechanical artifact. Only one epoch (0.3 min) of the total heart rate scored had to be eliminated because of artifact. The eye movement records of two infants were eliminated from consideration due to artifact. Of the remaining 455 min, 34 (7.5%) were eliminated due to mechanical failure. Of the total 489 min of EMG recording examined, 4 min (0.8%) were eliminated due to artifact. There were no differences in light levels in the room between the On condition and the Off condition (On: x= 211 lux; Off: x= 210 lux). Sound levels were nearly identical to the preliminary recordings described in the Introduction.

It is important to remember that the data being examined were restricted to that portion of the record when the TA pattern of EEG was present. That is, during a time that would be called quiet sleep in a full-term infant. As noted, each 20-sec epoch was first scored for the presence of the TA EEG pattern. The resulting sample of epochs was scored for the other four measures. Table 2 shows the percentage of TA epochs found in the total record for each infant. There was a considerable range in the number of epochs on which TA occurred (0.4-27.3 min) as well as in the percentage of the infant's total record during which the infant exhibited TA (3.2-29.7%). Wilcoxon signed-rank tests showed no significant difference, however, between the _On_ and the _Off_ conditions for these values or percentages. Pearson product moment correlations did not reveal any systematic relationship between the amount of TA and the rate or variability of the individual measures in either condition. The starting time of TA epochs varied for both conditions. Signed-rank tests showed neither the mean nor range was different between conditions. When the motor was on, TA did not appear until a mean of 28.1 min had elapsed from the start of recording (range= 0 to 76 min) When the motor was off, the mean latency to the appearance of TA was 20.8 min (range= 0-77 min). Signed-rank tests did not reveal a difference between the two conditions.

Major findings:

There were two major results. First, there were significant differences in breathing rate and variability when the infants were in the _On_ and _Off_ conditions. This

Table 2. Total recording time and total time scored as trace alternant (TA) for each infant (N=17).

Infant Code	Rec Time (min)		Trace alternant (min)	
	On	Off	On (%of rec time)	Off (%)
F	109.3	125.0	16.6 (15.2)	25.6 (20.5)
G	107.3	93.6	13.6 (12.7)	5.6 (6.0)
H	119.0	122.3	13.6 (11.5)	18.0 (15.1)
I	126.3	86.3	4.0 (3.2)	4.3 (5.0)
J	112.7	136.3	19.3 (17.1)	14.0 (10.3)
K	92.0	92.3	25.3 (27.5)	21.0 (22.7)
M	101.0	109.0	20.6 (20.3)	9.3 (8.5)
N	97.6	62.3	23.0 (23.5)	3.3 (5.3)
O	114.0	90.6	16.0 (14.0)	4.7 (5.1)
P	92.0	93.3	27.3 (29.7)	30.3 (32.5)
Q	109.0	122.0	17.0 (15.6)	19.3 (15.8)
R	92.6	120.6	10.3 (11.1)	17.6 (14.6)
S	140.6	109.6	7.3 (5.2)	9.3 (8.5)
T	92.6	92.6	8.7 (9.3)	13.0 (14.0)
U	89.3	100.6	6.7 (7.5)	10.3 (10.3)
V	96.6	89.6	14.3 (14.8)	5.0 (5.6)
W	120.3	108.0	20.3 (16.9)	12.6 (11.7)

was the only instance in which nearly all the infants' responses were similar. Responses of the individual infants in the other measures varied. Second, some of the measures were significantly correlated with the Infant Factors. Primarily, the mean heart rate and the degree of correlation between heart rate variability and respiration variability varied as a function of both developmental and environmental factors.

Respiration:

Regarding respiration, there were substantial individual differences in mean breathing rate (range= 36-74 breaths per minute). The basis for this variability could not be determined as the overall rate (the mean of the On and Off conditions combined) for each infant was not significantly correlated with any Infant Factors.

However, there were highly consistent differences between respiratory behavior in the On and Off conditions. Wilcoxon signed-ranks tests showed that the Mean respiration rate for the infants, the Lowest rate scored in any epoch, and the Highest scored in any epoch were all significantly lower in the Off than in the On condition. High: N= 17, T= 12, $p<.01$; Low: N= 17, T= 12, $p<.01$; Mean: N= 17, T= 4, $p<.01$ (Table 3). These breathing changes were characteristic of nearly all the infants. For example, Fig. 4 shows that 16 (94%) of the 17 babies had a higher

Table 3. Comparison of mean respiration rates in the *On* condition and the *Off* condition (N=17).

Respiration	On	Off	Wilcoxon T
Mean	49.9	39.8	4 p<.01
Low	33.9	27.3	12 p<.01
High	64.6	51.2	12 p<.01
Range	30.6	23.9	26..p<.02

Fig. 4. Number of infants whose respiratory rate was higher in each condition (_On_ and _Off_).

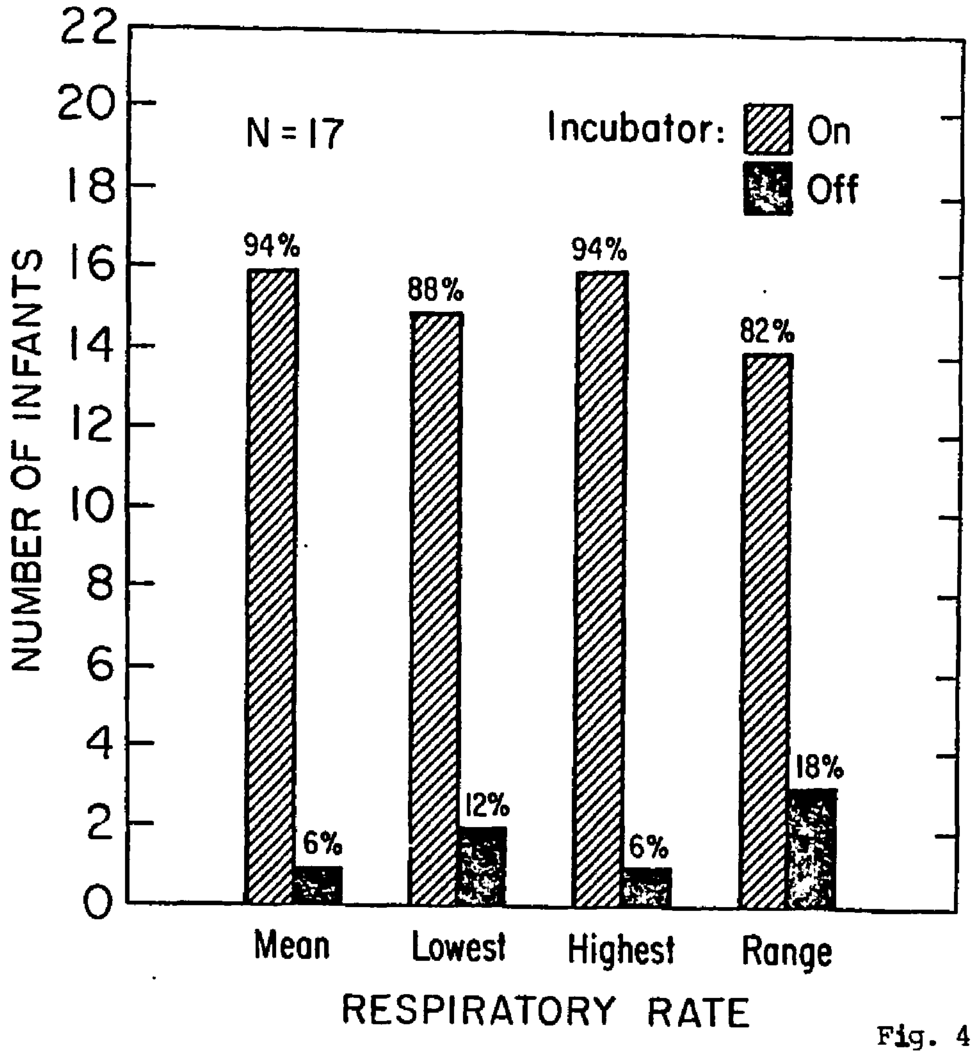

22
20
18
16
14
12
10
8
6
4
2
0
NUMBER OF INFANTS
N = 17
Incubator: ▨ On
▩ Off
94%
6%
88%
12%
94%
6%
82%
18%
Mean
Lowest
Highest
Range
RESPIRATORY RATE

Fig. 4

mean rate in the On condition than in the Off condition. Looking at the lowest breathing rate scored in any epoch for each infant, Fig. 4 shows that 15 infants (88%) had their lowest rate in the On condition.

The difference in breathing rate between the On and the Off conditions (breathing rate during the On condition minus the rate during the Off condition) was negatively correlated with the Developmental Factor ($r= .58$, $p<.02$). This correlation was largely attributable to EGA at birth ($r= -.50$, $p<.02$). (See Table 4.)

Perhaps a more important finding (shown in Table 3), was that breathing was less variable in the Off condition. That is, the range (the difference between the High and Low breathing rate) was significantly lower in the Off than in the On condition ($N= 17$, $T= 26$, $p<.02$). Inspection of Fig. 4 indicates that 14 infants (82%) had a range that was greater (indicating more variability) in the On condition than in the Off condition. Only 3 showed the reverse pattern.

Each epoch was also scored for type of breathing (Regular, Semi-regular, Irregular, Periodic) as described in the Materials and Methods section and the percentage of the total number of epochs during which the infants exhibited each type of breathing was calculated.

Table 4. Breathing rate in the On condition minus the breathing rate in the Off condition (On/Off Difference) in relation to gestational age at birth (EGA). N=17

EGA at birth (weeks)	On/Off Difference
31	16.1
32	15.6
34	28.5
34	13.9
34	11.6
34	8.4
34	4.5
35	14.9
35	15.9
35	7.1
35	5.9
35	- 4.2
35	17.6
36	9.1
37	3.1
37	2.0
37	1.0

Table 5 shows that a significantly higher percentage of epochs was scored Regular breathing in the _Off_ than in the _On_ condition (N= 17, T= 26, p<.02). Likewise, a significantly lower percentage of epochs was scored Semi-regular (N= 17, T= 23, p<.02) Four infants did not have any epochs of irregular breathing and there was no significant difference in the occurrence of this type of breathing between conditions. For periodic breathing, two infants had none in the _On_ condition and one had none in the _Off_ condition. One infant had no periodic breathing in either condition. There was no significant difference between conditions in the amount of periodic breathing. In order to facilitate comparisons with previously reported studies, the data were also analyzed in terms of the amount of regular respiration scored as a percentage of the _total_ recording time (not just TA). This is shown on Table 6. Previous investigations have shown that regular respiration, which characterizes quiet sleep in full-term neonates, is not prevalent in prematures. The reported percentage of regular respiration for full-term infants is about 30%. Dreyfus-Brisac (1970) reported means of 8 and 9% regular breathing in a total sleep period. In the present study, the mean per cent was similar and was slightly higher in the _Off_ condition (8%) than in the _On_ condition (6.4%). The difference was not significant.

Table 5. Comparison of percentage of epochs scored for each type of breathing.

Respiration	On	Off	Wilcoxon T	
Regular	37.0	55.7	26	p<.02
Semi-Regular	44.9	28.9	23	p<.02
Irregular	9.0	6.2	NS	
Periodic	9.1	6.2	NS	

Table 6. The percentage of the total recording time scored as regular respiration for each infant in both conditions (N=17).

TOTAL REC TIME (MIN)	ON CONDITION (%)	OFF CONDITION (%)
109.3	12.1	19.4
107.3	5.9	0.4
119.0	2.9	9.0
126.3	0.0	0.4
112.2	5.4	8.3
92.0	10.1	13.7
101.0	11.2	4.6
97.6	9.9	0.5
114.0	3.4	1.3
92.0	20.0	24.6
109.0	10.1	12.3
92.6	3.0	10.5
140.6	0.9	7.3
92.6	0.7	5.4
89.3	3.7	8.3
96.6	6.7	3.3
120.3	2.2	6.7
MEAN:	6.4	8.0

Looking again at the scoring for degree of regularity used by Dreyfus-Brisac (1974), Fig. 5 shows that during the Off condition breathing became more regular and less semi-regular for most of the infants. Only 3 babies (18%) had more epochs of Regular breathing in the On than in the Off condition and 14 (82%) had more epochs of Regular breathing in the Off than in the On condition. Fourteen infants (82%) had more epochs of Semi-regular breathing in the On condition.

Heart rate:

Regarding heart rate, there was also a considerable range in the mean heart rate for the group (118-163 bpm). In the full-term infant, baseline heart rate reaches a maximum of 132 bpm between 4 and 8 weeks after birth. Baseline heart rate for preterms reaches 148 bpm during the same time period. However, baseline heart rate is related to gestational age at birth, postnatal age, and state of sleep or wakefulness (Cabel, Siassi, & Hodgman, 1983). Heart rate is higher during wakefulness and lower in quiet sleep than in active sleep (DeHaan, Patrick, Chess, & Jaco, 1977). Looking specifically at regular heart rate, Prechtl et al. (1983), found the mean cardiac rate during quiet sleep was 115 bpm in 4- to 8-day-old full-term

Fig. 5. Number of infants having more epochs of each type of breathing in each condition (_On_ and _Off_).

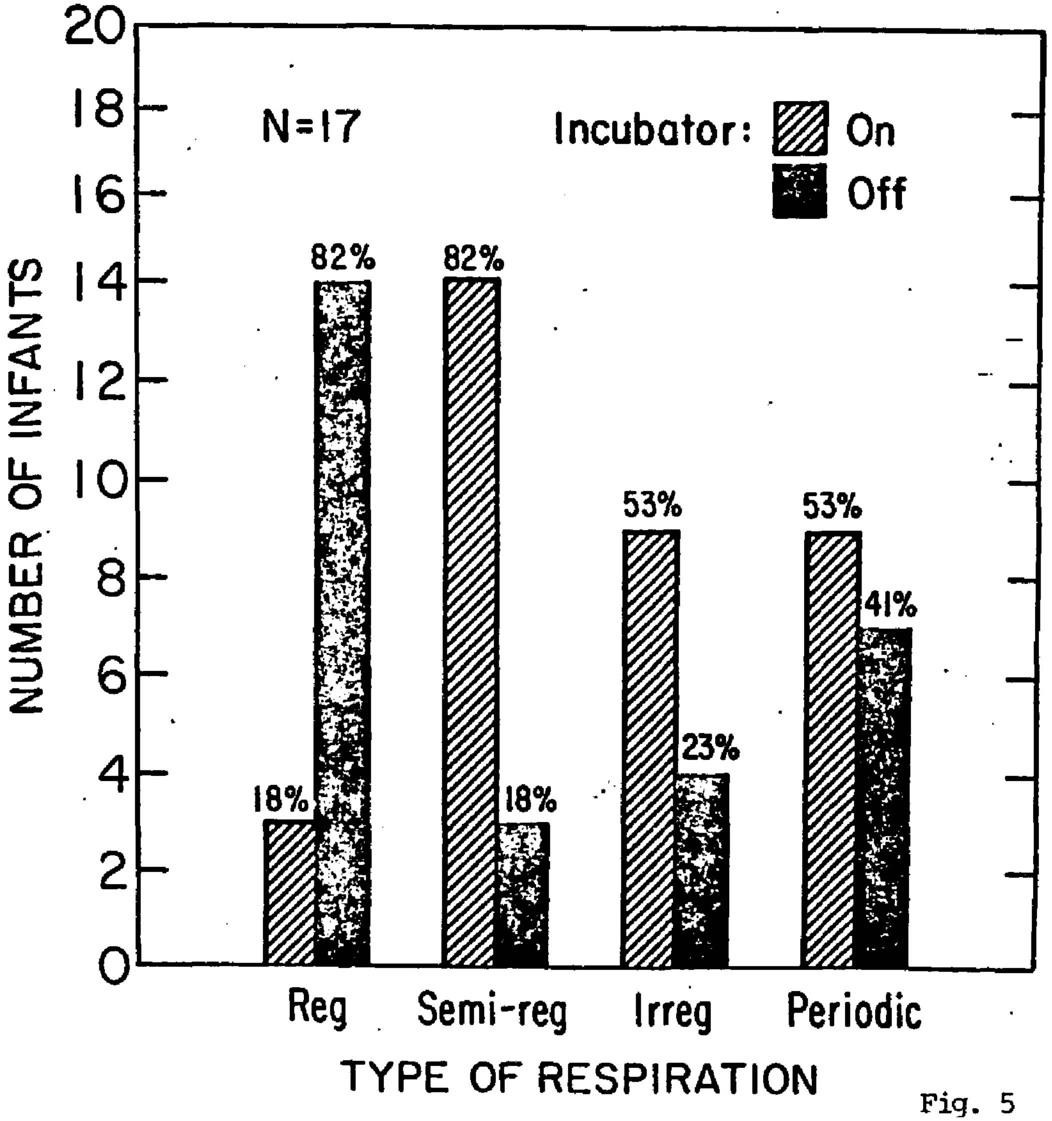

20
18
16
14
12
10
8
6
4
2
0
NUMBER OF INFANTS
N=17
Incubator: ▨ On
■ Off
18%
82%
82%
18%
53%
23%
53%
41%
Reg
Semi-reg
Irreg
Periodic
TYPE OF RESPIRATION

Fig. 5

infants.

In the present study, some of the variability could be accounted for by some of the Infant factors. Correlations of the overall heart rate with the Developmental Factor and Environmental Factor, were significant (Developmental Factor: $r= -.73$, $p<.001$; Environmental Factor: $r= .76$, $p<.001$). The overall heart rate was negatively correlated with estimated gestational age at birth ($r= -.74$, $p<.001$) and birthweight ($r= -.58$, $p<.02$). The more mature and heavier the infant at birth, the lower the heart rate. Overall heart rate values were _positively_ correlated with post-natal age ($r= .76$, $p<.001$) and the number of days the infant had been in the incubator ($r= .69$, $p<.01$). That is, the longer the time since birth and the longer the infant had been in the incubator, the higher the overall heart rate. Dreyfus-Brisac (1974) found regular cardiac rhythm under 130 bpm until 37 weeks gestation. (The mean rate was considered regular when it varied less than 10 bpm for 2 consecutive minutes.) After 38 weeks, it was significantly higher than 130 bpm.

Contrasting with the change seen in respiration, Wilcoxon signed-rank tests showed no significant difference in heart rate or in heart rate variability when the _On_ condition was compared with the _Off_ condition:

Mean On: 139.38 (Range= 124.27-164.06)
Mean Off: 138.36 (Range= 121.58-158.12)
SD On: 4.87 (Range= 3.90-6.11)
SD Off: 5.12 (Range= 3.65-6.85)

Figure 6 shows that while 10 infants had a higher mean heart rate in the *On* condition, 7 had a higher rate in the *Off* condition. Heart rate variability was not significantly correlated with any of the Infant Factors. The degree of difference between the heart rates in the two conditions was not significantly correlated with any Infant Factors but in the *Off* condition, mean heart rates of infants who had been in the incubator for longer periods were lower than in the *On* condition. As can be seen in Table 7, seven of the nine infants (78%) who had been in the incubator for more than 2 weeks showed lower heart rates in the *Off* condition. All six infants who were <35 wks and <2000 g at birth had lower heart rates in the *Off* condition than in the *On* condition. Only five of the eight infants who had been in the incubator for less than two weeks showed the opposite pattern.

With regard to the degree of difference between heart rate variability in the *On* and *Off* conditions, there was a significant negative correlation with the number of days the infants were in the incubator $(r= -.49, p<.02)$. The

Fig. 6. Number of infants having a higher mean heart rate (HR) and heart rate standard deviation (HRSD) in each condition.

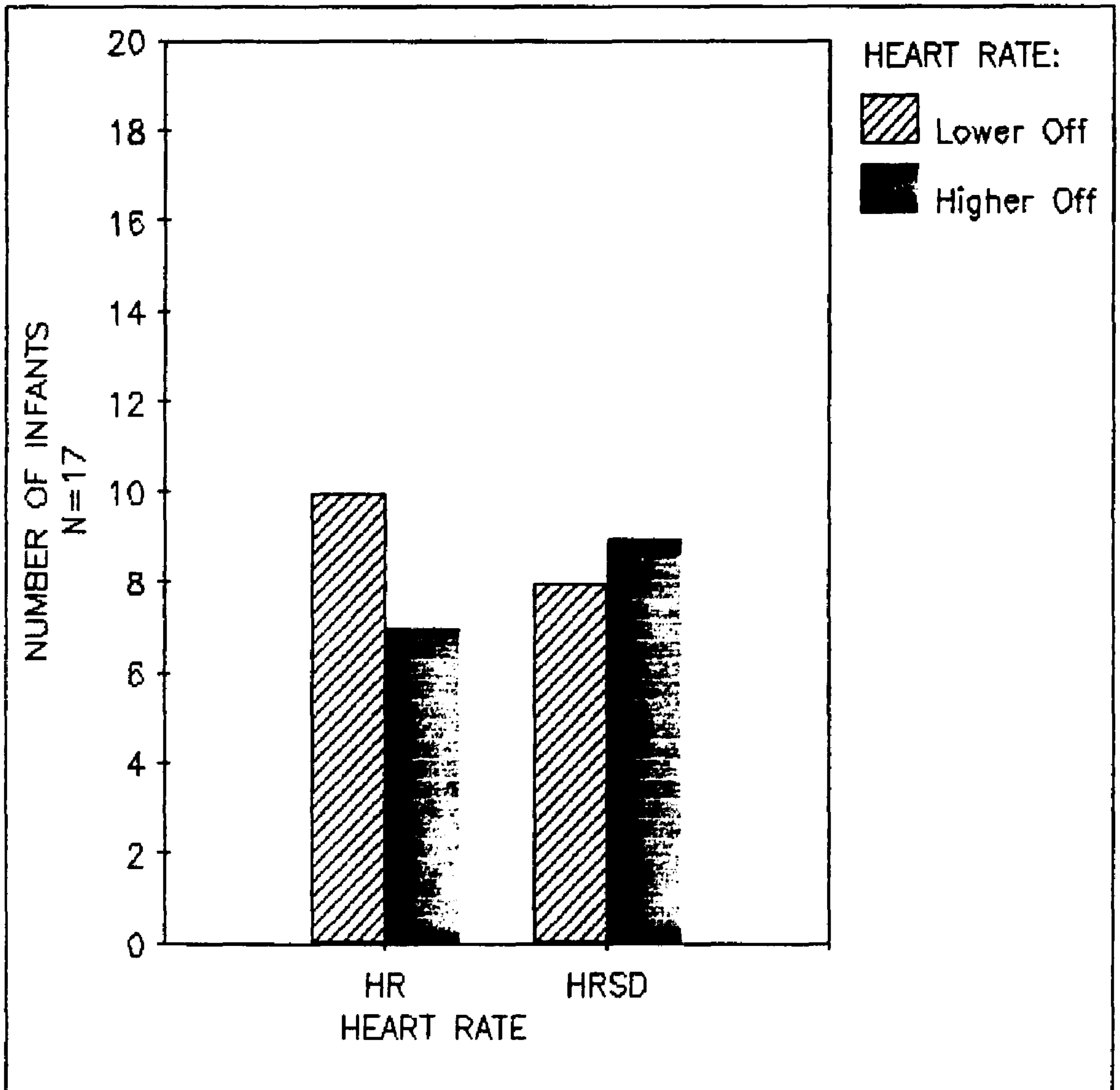

20
18
16
14
12
10
8
6
4
2
0
NUMBER OF INFANTS
N=17
HR
HRSD
HEART RATE
HEART RATE:
Lower Off
Higher Off

Fig. 6

Table 7. Differences between mean heart rate in the On condition and mean heart rate in the Off condition as a function of the number of days in the incubator at recording. (N=17)

Infant Code	Days in the Incubator	Difference (On minus Off)
M	4	- 1.8
I	4	3.4
R	5	-13.0
O	7	- 1.0
P	10	- 6.9
G	10	0.2
H	11	9.6
N	13	-11.8
Q	15	- 4.9
S	15	2.7
W*	17	8.4
K	19	- 3.5
J*	21	1.5
U*	21	25.8
V*	25	2.0
F*	29	2.1
T*	30	4.5

* indicates infants who were <35 wks and <2000 g at birth.

longer they had been in the incubator, the less of a difference in variability between conditions.

<u>Other state components</u>:

Correlations with Infant Factors were also seen in eye movements and EMG. The overall rate of eye movements and estimated gestational age at birth were significantly negatively correlated ($r= -.50$, $p< .05$). The older the infant at birth, the lower the eye movement rate. None of the other correlations with Infant Factors were significant. Comparison of the mean rates in the two conditions by means of Wilcoxon signed-rank tests showed no significant difference in eye movement rate between the <u>On</u> and <u>Off</u> conditions. Figure 7 shows that nine infants had a higher rate of eye movements with the machine off and six had a higher rate with it on.

The overall amount of EMG shown by the individual infants (On/Off conditions combined) was significantly correlated with the Environmental Factor ($r= .53$, $p<.05$). It was significantly negatively correlated with the number of days the infant had been in the incubator ($r= -.52$, $p<.05$) and positively correlated with estimated gestational age at birth ($r= .50$, $p<.05$). The less mature the infant at birth and the longer the time in the incubator, the lower the EMG rate. Partial correlations did not show postnatal age, Days in the incubator or estimated

Fig. 7. Rate of eye movements per epoch (N= 15) in the *On* condition and the *Off* condition.

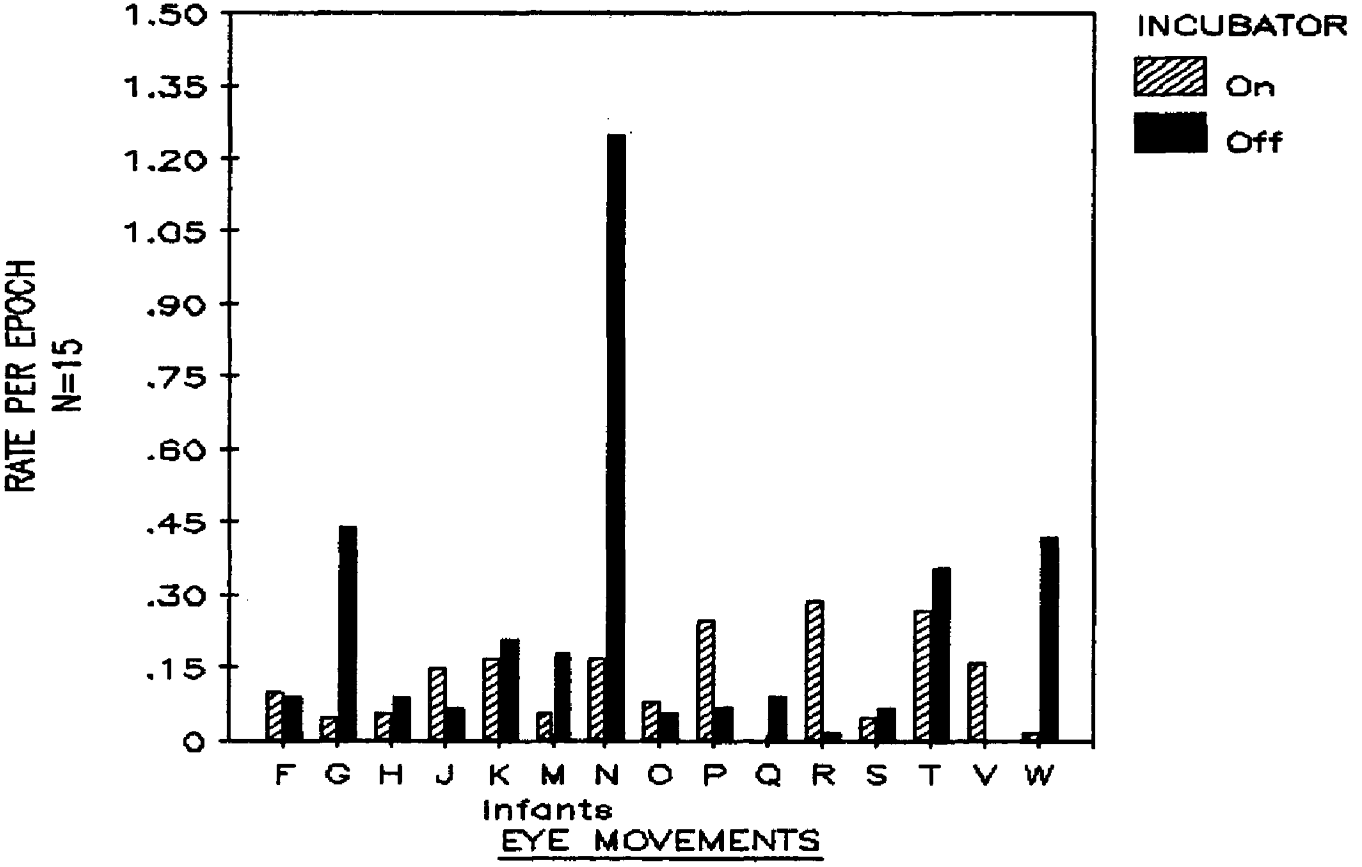

INCUBATOR
On
Off
RATE PER EPOCH
N=15
1.50
1.35
1.20
1.05
.90
.75
.60
.45
.30
.15
0
F
G
H
J
K
M
N
O
P
Q
R
S
T
V
W
Infants
EYE MOVEMENTS

Fig. 7

gestational age at birth to be significant when the effects of the other were partialed out. There was no significant difference between the rate of EMG in the On condition compared with the Off condition nor was there any correlation between this difference and the Infant Factors. As can be seen in Fig. 8, 10 infants had a higher rate of EMG with the motor off and 6 had a higher rate with it on.

Heart rate standard deviation/Respiration ratio:

Examination of the correlation of the overall heart rate variability with the respiration ratio (On and Off combined) showed great variability among the individual infants. Figure 9 shows that 6 infants had a significant positive correlation between heart rate variability and respiration variability, while 11 infants showed a low or negative correlation. There was one significant negative correlation.

The importance of differences in the characteristics and histories of the infants in determining the level of organization reflected in the correlation between measures is attested to by the fact that the degree of correlation (using r values) was significantly related to the

Fig. 8. Duration of movement (EMG) for each infant in the _On_ condition and the _Off_ condition.

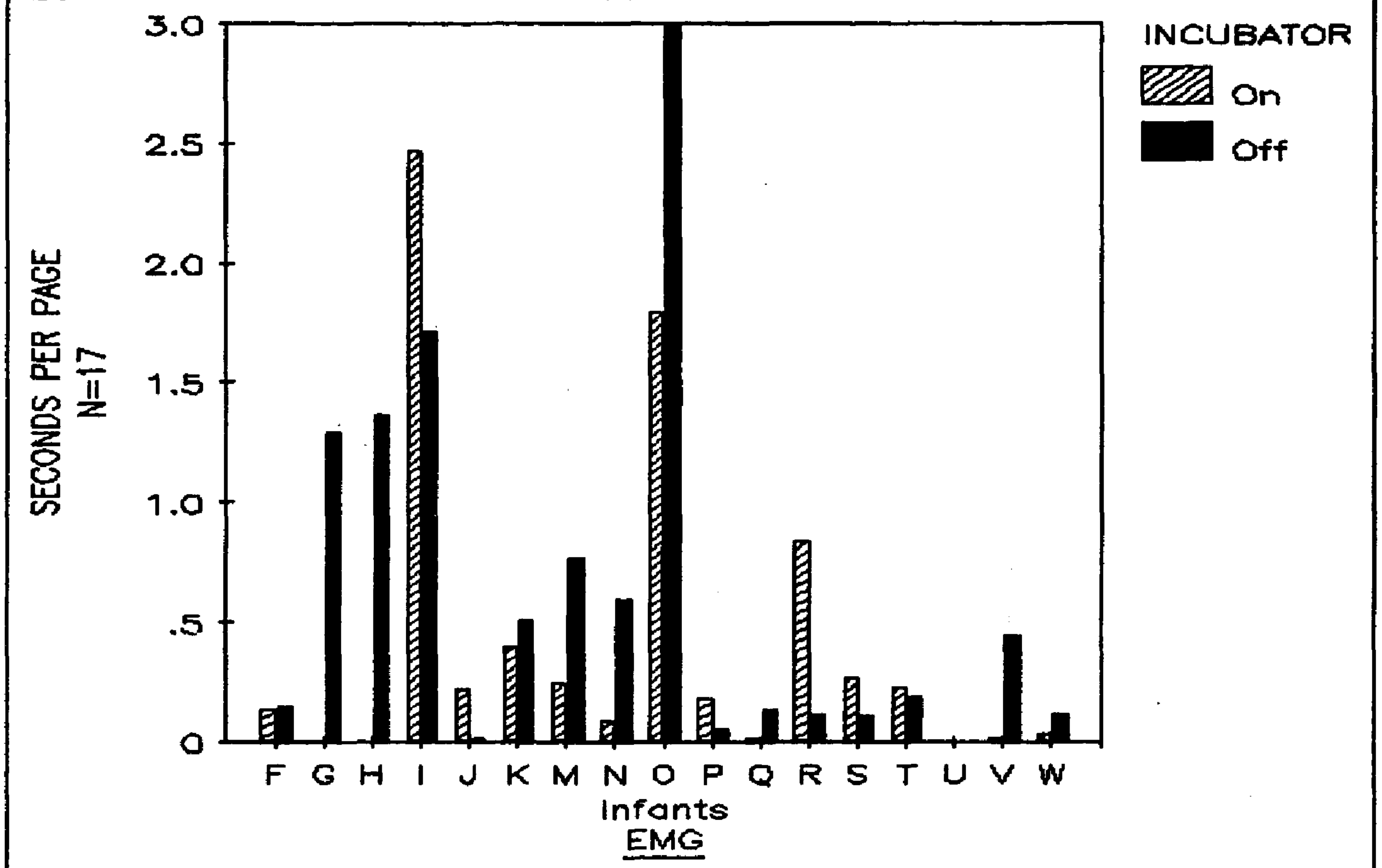
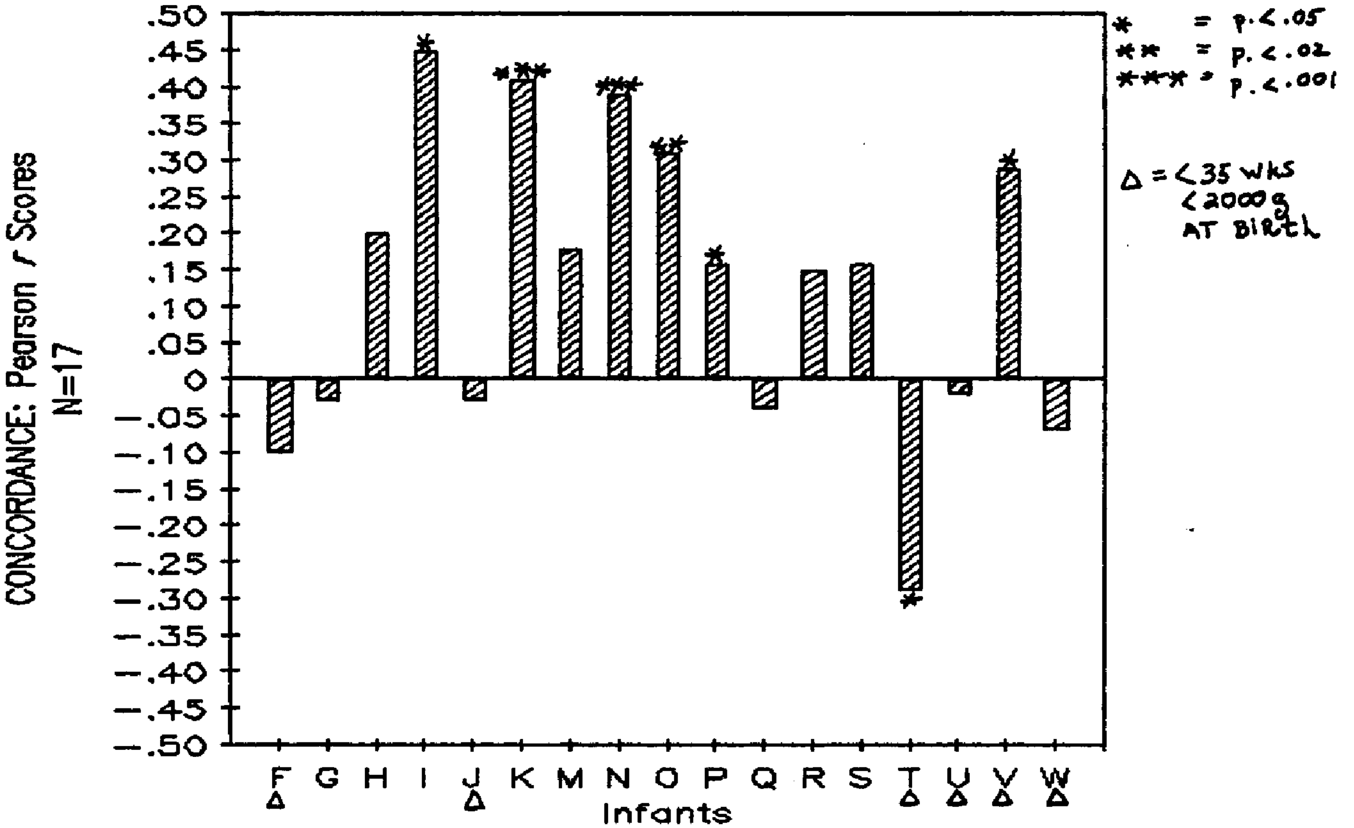

SECONDS PER PAGE
N=17
3.0
2.5
2.0
1.5
1.0
.5
0
F G H I J K M N O P Q R S T U V W
Infants
EMG
INCUBATOR
▨ On
■ Off

Fig. 8

Fig. 9. Degree of overall correlation between heart rate standard deviation and respiration ratio for each infant (N= 17). Overall correlation was obtained by product moment correlation of the *On* and *Off* conditions combined.



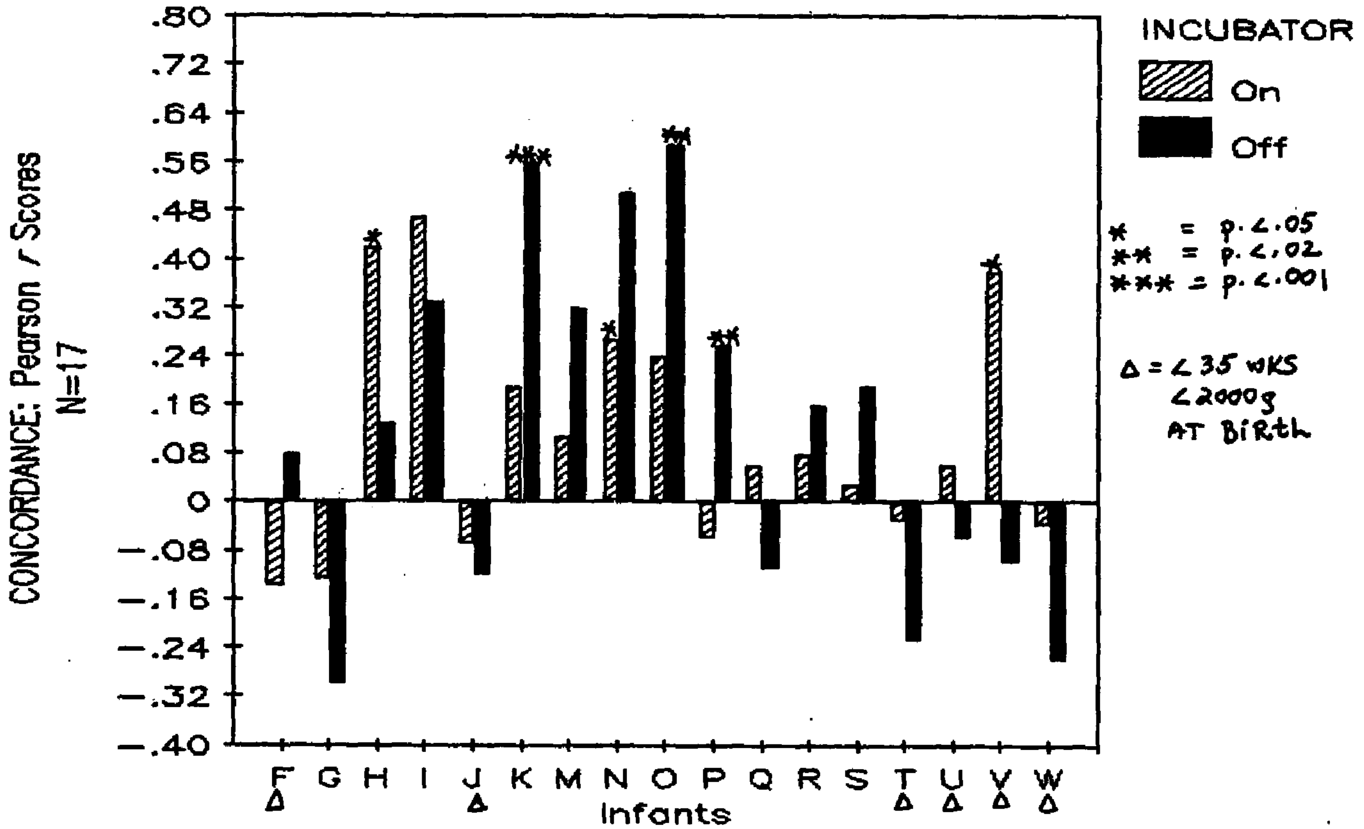
HEART RATE STANDARD DEVIATION/RESPIRATION RATIO

Fig. 9

Developmental Factor and Environmental Factor (r= .57, p<.05; r= -.65, p<.02, respectively). The degree of correlation between these two measures was positively related to estimated gestational age at birth (r= .63, p<.02). The older the infants were at birth, the higher the correlation. The correlation was negatively related to postnatal age (r= -.65, p<.001) and negatively related to days in the incubator (r= -.57, p<.02). That is, the greater the postnatal age and the longer the infant had been in the incubator, the lower the correlation between cardiac and respiration variability.

To see if there was greater correlation between heart rate variability and respiration variability in the _Off_ condition than in the _On_ condition, the correlation between these two components was examined in the two conditions separately. There was, again, considerable variability among the infants (see Fig. 10). There was no difference in the magnitude of association between the two conditions. However, it is worth noting that 5 of the 6 babies who were less than 35 weeks at birth and weighed under 2000 g at birth showed negative correlations of heart rate variability and respiration variability (Fig. 9), whereas only 2 of the remaining 11 were similarly negatively correlated. Five of these same 6 infants were also more negatively correlated in

Fig. 10. Degree of correlation (product moment correlation) between heart rate standard deviation and respiration ratio in the _On_ condition and the _Off_ condition for each infant (N= 17).



HEART RATE STANDARD DEVIATION/RESPIRATION RATIO

Fig. 10

the Off condition than in the On condition, whereas only 4 of the remaining 11 infants were less positively correlated in the Off condition. (Fig. 10). The suggestion is that the five infants who were younger and lighter at birth had less coordination of heart rate variability and respiration variability overall than the infants who were heavier and more mature at birth and this coordination was less in the Off than in the On condition.

Other results:

When correlations among other measures and among all measures were examined, variability among infants was similar to that found with heart rate variability and respiration ratio.

For example, 9 of the 15 infants showed significant overall correlations (the mean of the On plus Off conditions) between respiration variability and EMG rate (Pearson product moment correlation). Looking at the two conditions separately, 10 of the 15 infants who could be included in the analysis showed significant correlation: Three showed significant associations between respiratory variability and EMG rate in the On condition only, four in the Off condition only, and three in both conditions (Table 8). When the concordance between respiration variability and EMG was analyzed using MANOVA, 10 of the 15 infants

Table 8. Degree of overall correlation (Pearson r) between respiration ratio and EMG rate (N=17), and correlation in the On and Off conditions separately. *= p<.05, **= p<.01, ***= p<.001.

Infant Code	ON/OFF Mean	ON	OFF
F#	.44***	.25	.64*
H	.10	.15	-.06
I	.22	-.20	.23
J#	.32**	.40*	.24
K	.35***	.10	.60***
M	.32**	.32*	.31
N	.33	.44*	.22
O	.37**	.20	.55*
P	.29***	.24*	.35*
Q	.34***	.41*	.28*
R	.24*	.31	.17
S	.27	-.08	.46*
T#	.03	.01	.05
V#	.00	.00	-.01
W#	.50***	.42*	.58*

# indicates infants who were <35 wks and <2000 g at birth.

showed some concordance: four had significant concordance in both conditions, two were significant in the <u>On</u> condition, and four were significant in the <u>Off</u> condition.

When eye movements were added to the MANOVA analysis, the correlation among the respiration ratio, eye movements and EMG was similar to that for respiration and EMG: three infants showed significant concordance in both conditions (Table 9), three infants were significantly related in the <u>On</u> condition only and four in the <u>Off</u> condition only. Table 9 also shows a trend emerging. Those infants who had been in the incubator longer show significant correlation, especially in the <u>Off</u> condition. Five of the six infants who had been in the incubator for more than 2 weeks showed significant correlation in the <u>Off</u> condition while only two were significant in the <u>On</u> condition

When the correlation among all measures for each individual was examined, four infants showed significant correlation: One infant in both conditions, two in the <u>Off</u> condition only, and one in the <u>On</u> condition only. Three of the four were 35 weeks or older at birth and in the incubator less than 15 days.

Table 9. Degree of correlation among respiration ratio, eye movements, and EMG as a function of the number of days each infant had spent in the incubator (MANOVA p values, N= 12).

Days in Incubator	ON	OFF
4	*	-
5	*	-
7	-	***
10	**	***
11	-	-
13	***	-
15	-	*
17	***	***
19	-	***
21	***	***
29	-	***
30	-	-

*= p<.05, **= p<.02, ***= p<.01, -= NS.

In order to see if there was an overall difference for all the infants between the _On_ and _Off_ conditions in the various combinations of two components, a matrix was constructed using the median _r_ values for each combination (Table 9). There were no significant differences.

In summary, the results show that the basic rates of all the individual measures were similar to what has been found previously for premature infants in a similar state. However, there was a difference between the _On_ and _Off_ conditions in the respiration measures that was exhibited by nearly all the infants. The other measures were frequently related to developmental and environmental factors. How well coordinated the measures were with each other in each condition (and thus how well organized the sleep pattern in each condition) varied with the individual infant as well.

DISCUSSION

This study explored the influence of the environment of the intensive care unit on sleep organization by examining responses to change in the incubator environment. The results show that the first phase of the usual transition from incubator to crib has an impact on sleep organization. The nature of that impact points to possible CNS differences depending on gestational age at birth that result in different ways of responding to aspects of the environment.

The results can be examined on two levels: (1) the basic rates of occurrence of in the individual components and the degree of correlation among components, and (2) the impact of the change in environment; that is, the difference in measures between the On and Off conditions.

Basic rates and correlations:

Looking first at basic rates of occurrence, the literature suggests that base rates of such sleep measures as heart rate and respiration rate are a function of conceptional age at the time of recording, while data here show the importance of gestational age at birth. This could be seen, for example, in the correlation of overall heart rate, eye movement rate, and muscle movement rate with gestational age at birth. The more mature the infant at birth, the lower the heart rate and eye movement rate and the higher the muscle movement rate. The data suggest that the intervening days and weeks postnatally do not necessarily mean rates will "catch up" and be similar at 37 weeks conceptional age.

These data agree with Rose's finding (1983) of a strong correlation of basal heart rate levels with gestational age at birth but not with conceptional age at testing. She suggested that the high heart rate in infants more immature at birth may represent immaturity in the development of the parasympathetic nervous system resulting in low vagal tone, although neurophysiological evidence is lacking.

While high rates may, in fact, represent lack of maturity, we do not know why this lack of maturity persists. One reason may relate to the extrauterine environment. The data suggest that the effect of the postnatal environment is not innocuous. Heart rate and muscle movement rate were positively correlated with the Environmental Factor. Separately, heart rate was correlated positively with postnatal age and the number of days the infant had been in the incubator. The longer the time postnatally and the longer the time in the incubator, the higher the heart rate.

Although the components comprising the Environmental and Developmental Factors are correlated with each other, the Principal Components factor analysis did result in the two separate factors. Therefore, although the relationship of development and environment is complex, both were involved in these responses and were seen again in the correlations between components.

The degree of correlation among measures is one way of assessing the degree of organization of quiet sleep state in the preterm infant. Studies using this particular method of analysis have not been done with full-term infants so direct quantitative comparison cannot be made. However, quiet sleep state requires a positive correlation among the four measures: heart rate variability, respiration variability, eye movement rate, and muscle movement rate should all be low. A positive correlation between or among components suggests coordination of components and organization of sleep state while no correlation suggests lack of coordination and poor organization of sleep state and a negative correlation a possibly pathological or at least atypical organization. It was possible to make comparisons among infants to assess what factors might influence the degree of correlation of the components.

In this study, the degree of correlation between heart rate standard deviation and respiration ratio varied systematically among the infants and was significantly related to both the Environmental and Developmental factors. These data may reflect either a continuous range of correlation or two separate groups. Five of the seven infants showing a significant correlation were more than 35 weeks and more than 2000 g at birth. Five of the six infants less than 35 weeks and less than 2000 g at birth showed a negative correlation. Possibly due to some threshold effect which is not understood, the infants seemed to fall into two general categories, based on their age at birth and length of time in the incubator. In general, infants less than 35 weeks at birth who spent more than 2 weeks in the incubator showed low positive correlation or negative correlation. The reverse was true for those more than 35 weeks at birth who had been in the incubator for less than 2 weeks.

Impact of change in the environment:

Differences between the On and Off conditions suggested the impact the change in the environment had on the separate measures and the organization of the measures. In this study, the data showed that the responses to turning off the incubator and swaddling the infant were different for each measure. Respiration stood out as the only measure that was affected similarly in nearly all the infants. Both rate and variability of breathing were significantly lower in the Off condition than in the On condition. It has been suggested that the more immature the system, the more likely it is to either rely upon or be sensitive to environmental stimuli at particular periods. If it is sensitive to sound, for example, it will be likely to respond to changes in sound. The process is one in which the system is shifting from primarily endogenous control of responding to a combination of endogenous and exogenous sources of control. During the last 5 weeks in utero, for example, breathing movements (chest excursions) by the fetus are systematically related to maternal behavior. Patrick, Natale, & Richardson (1978) showed that breathing movements in fetuses of 34 and 35 weeks gestation were related to maternal meals and the time of day. There was a significant increase in fetal breathing activity during the second and third hours following maternal meals, when the mother's glucose levels peaked. There was also a significant increase in fetal breathing activity between 1 a.m. and 7 a.m. which was not related to increases in plasma glucose concentrations. It was the time of day when mothers were asleep. Because the pattern was not disturbed when the mothers changed position in bed or got up briefly, it is more likely that the apparent circadian pattern may be related to maternal hormones, although this has not been confirmed.

Breathing patterns are known to be poorly developed in premature infants and slow to reach levels similar to the full-term infant. It is possible that for infants in this study, who were not only denied the final weeks of maternal hormonal cycling but received other kinds of stimulation far different from what they would experience in utero, respiration remained particularly sensitive or vulnerable to certain aspects of the environment.

The importance of the infants' developmental and environmental history was also seen when comparing the two conditions of recording. The degree of difference between the On and Off conditions in respiration was significantly correlated with the Developmental Factor and the difference in heart rate with the Environmental Factor. In addition, although not significant, the correlation between heart rate standard deviation and respiration ratio for each infant in each condition was highly suggestive: Five of six infants less than 35 weeks and less than 2000 g at birth showed low or negative correlations in the _On_ condition. Five of these six had lower (less positive) or more negative correlations in the _Off_ condition than in the _On_ condition. Of the eight infants showing a more positive correlation in the _Off_ condition than in the _On_ condition, seven were more than 35 weeks and more than 2000 g at birth.

Correlation of all measures showed three of the four infants with significant correlations in either or both conditions were 35 weeks or older at birth and had been in the incubator less than 15 days.

All these data suggest that at about 37 weeks conceptional age, infants who were less than 35 weeks and less than 2000 g at birth have less mature heart rate and eye movement patterns, less integration of quiet sleep components than infants more mature at birth, and that this integration is reduced when the incubator environment is changed by turning off the motor and swaddling the infant. At 37 weeks conceptional age, infants more than 35 weeks and more than 2000 g at birth show the opposite pattern: more mature patterns of heart rate and eye movements and more concordance of quiet sleep components than the less mature infants, and even more integration in the _Off_ condition than in the _On_ condition.

These findings imply that to generalize about the development of sleep organization in groups of healthy preterm infants, environmental conditions at the time of recording must be taken into account.

Issues of CNS organization:

Several important questions about central nervous system organization are raised by these findings: (1) Does poorly organized quiet sleep persist because the needed mechanisms were poorly developed at birth and unable to continue developing at an appropriate rate under the conditions imposed by the extrauterine environment? Are some aspects of the uterine environment not found in the incubator environment necessary for certain phases of central nervous system development? (2) Because of the developmental stage of the infant at birth, does entrainment occur to elements of the environment, and (3) is there some aspect of the incubator environment that is contributing to a delay in development of sleep organizing mechanisms?

While the present study cannot adequately answer these questions, the data suggest an affirmative answer to either of the first two questions might be considered for the infants who were less mature at birth. Organization was low or negative at the conceptional age of 37 weeks and when the incubator environment was changed, it became lower or more negative. While it seems paradoxical that heart rate, respiration rate, and respiration ratio were lower for these infants in the _Off_ condition than in the _On_ condition, it merely suggests that the mechanisms involved in the development of the individual response measures may be different from the organizing mechanism. For the infants who were more mature at birth, an affirmative answer to the third question seems most appropriate. Some organization was present at the conceptional age of 37 weeks and when the incubator environment was changed, it became more positive.

The mechanisms underlying the organizing process of sleep are not known. Neurobehavioral development is dynamic and interactive. Turkewitz and Kenny (1982) have discussed how sensory systems often are finely tuned to compliment each other in their rate of development and their sensitivity to environmental stimulation. If events proceed on schedule, structural development and sensitivity arrive at particular points in development at appropriate times for organizaing mechanisms to function. A preterm birth, however, may compromise this schedule.

Although the degree of organization of the sleep measures was low in the _On_ condition for the infants who were less mature at birth, the fact that it was lower in the Off condition than in the On condition riases the possibility that sleep organiation might be sensitive to changes in the incubator environment. Such sensitivity is further suggested by recent evidence of entrainment of premature infant state to environmental events.

Little is known about entrainment to environmental events in human infants, but diurnal rhythms of different states in premature infants have been found to be associated with diurnal rhythms of different environmental events (Lawson et al., 1985). Lawson et al. (1985), examined the behavioral state of infants in relation to environmental events in two neonatal intensive care units. Categories of state, which were behaviorally observed, were (a) eyes closed, no activity except occasional startles (State Closed-Quiet), (b) eyes closed, activity (State Closed-Active), (c) eyes open, no gross motor activity (State Open-Quiet), (d) eyes open, activity (State Open-Active), and (e) eyes open or closed, crying and/or flailing (State Cry). Environmental events such as speech, nonspeech, handling and illumination level were recorded at the same time the infant was observed. Findings showed, for example, that in one intensive care unit infants showed reliable periodicity of State Open-Active which was correlated with both handling and light. The data indicated, however, that there was no one environmental event which serves as a principle determiner of all aspects of infant state. Instead, different aspects of state are associated with different environmental events.

When the correlation of the sleep components is higher in the *Off* condition than in the *On* condition, it is possible that the sound of the incubator has been disruptive to one or more components, affecting the organization of sleep. It is also possible that something in the *Off* condition, such as swaddling, could be having a positive effect.

The likelihood of these aspects of the environment--the sound of the incubator, swaddling, and temperature change-- influencing the components of sleep will be discussed in the next section.

Whether the differences in sleep organization between premature infants and full-term infants represent entrainment or disruption, the result is a possible dysfunction. Porges (1983) developed a hierarchial model of neurobehavioral organization to suggest possible points during ontogeny when a dysfunction might occur. Level I represents the organization of specific physiological systems, such as heart rate or respiration. On Level II, the nervous system attempts to coordinate these physiological systems by way of complex homeostatic mechanisms. The present study focused on this level. Porges pointed out that while the individual systems as viewed on Level I may show organizational qualities that appear appropriate, they may be disorganized in terms of coordination with each other. The patterns shown by heart rate variability and respiration variability in the present study are an example of this.

Because of the great sensitivity to environmental change seen in respiration, and because of the close functional relationship of heart rate and respiration, it would be useful to examine these two sleep components more closely.

Porges and his colleagues looked at the relationship between heart rate variability and respiratory variability as a way of empirically assessing the relationship between behavior and the central nervous system (Larsen & Porges, 1982; Porges, 1983; Porges, Bohrer, Cheung, Drasgow, McCabe, & Keren, 1980; Porges & Coles, 1982). They pointed out that in most research, it is assumed that the variability of the beat-to-beat heart rate is a function of centrally mediated influences manifested in the combined output of the sympathetic and parasympathetic nervous systems. However, some influences on heart rate variability are mediated by the nervous system and some are not. Other mediating variables are respiration, blood pressure, temperature regulation, blood gases, posture, movement, and psychological variables.

Studies have demonstrated that the respiratory influence on heart rate is mediated through the vagus nerve and Porges has developed a method of evaluating respiratory sinus arrhythmia. "Physiologically, respiratory sinus arrhythmia is a naturally occurring arrhythmia of the sinoatrial node that exhibits a periodicity similar to that of respiration. An increase in heart rate is observed during inspiration and during expiration heart rate decreases...breathing seems to turn the vagus 'on and off'" (Porges, 1983, p. 11). Using spectral analysis, Porges and his colleagues were able to partition from the total heart period variability a measure of respiratory sinus arrhythmia, which has been called $\hat{V}$. Using this index, which reflects central nervous system functioning, they were able to describe trends in the development of neural control of the heart. Their goal was to generate a more useful method for characterizing individual differences.

The measures used in my study, while examining interbeat intervals, did not measure vagal tone. However, the data suggest that examining vagal tone during quiet sleep in varying environmental conditions could provide important information about the developing central nervous system under different intensive care unit conditions. Based on Porges' data, it would not be surprising to find different levels of vagal tone at different conceptional ages but finding different levels at the same conceptional age, with the infant's state and environment controlled as in this study, could confirm fundamental nervous system differences which would not simply reflect intrinsic maturational differences.

Effects of sound, swaddling, and temperature:

Which aspects of the environment in the two conditions, the incubator motor, temperature, or swaddling, would be most likely to have produced the responses seen in this study?

The most interesting case can be made for the sound of the incubator. In general, we know the infant's hearing apparatus is developed sufficiently to hear the sound and that sounds have influenced quiet sleep. If, as Hutt et al. (1968) have suggested, sounds above and below adaptively optimal levels are stressful, then the removal of that sound could theoretically benefit individual components and overall correlation. This might apply to all infants whose overall correlation of components was higher in the Off condition than in the On condition. Likewise, the sound could play an entrainment role for those infants who were less mature at birth and showed less correlation of sleep components in the Off condition than in the On condition.

Infants in this study were in the incubator with the motor on virtually from birth until the day of recording. The number of days varied greatly among the infants (4-30 days). No previous experiment has examined the effects of continuous sound for a period even as long as one day and certainly not from birth. Comparing this "natural experiment" with previous studies must therefore be done with caution.

There have been many studies in the last two decades looking at the responses of full-term and preterm infants to different kinds of sound stimulation but few can be related directly to the present study. However, it is useful to examine some of these studies because they demonstrate that sound is a potent stimulus for both full-term and premature infants and raise a number of issues that must be considered when evaluating responses to sound. For example, different kinds of sounds have been shown to have different effects. For example, continuous sounds (up to about 2 hours) and rhythmic sounds have been shown to have a different effect than dysrhythmic sounds. Barnard and Bee (1983) found that when preterm infants less than 35 weeks gestational age at birth were exposed at a mean of 1 week of age (range= 3-15 days) to rhythmic rocking and heart beat sound (85 dB, <500 Hz) they showed decreased rates of activity while in the hospital, had fewer abnormal reflexes, and better orienting responses. There were three groups: for the first, rocking and heart beat sound occurred for 15 minutes of every hour; for the second, the stimulation appeared only if the infant was motorically inactive for 90 sec and stimulation could be retriggered by the infant with any subsequent 90-sec period of quiet; for the third group, stimulation was triggered by the infant but could not be retriggered for 45 min and thus this group received the same amount of stimulation as the first group but could initiate it themselves. A fourth (control) group received no stimulation. The results suggested that while contingency and temporal patterning both reduced motoric activity, the combination of the two (the self-activating group) reduced activity even more. It was not stated in the study but it is likely that the infants were in incubators at the time of recording. In general, continuous sounds have been reported to be more soothing than intermittant or dysrhythmic sounds (Brackbill, 1973; Birns, Blank, Bridger, & Escalona, 1965; Spiegler & Ourth, 1966).

However, the state of the infant will influence the response. For example, Birns et al. (1965) found that for highly aroused full-term infants a low, continuous (60 sec, 85 dB, 150 Hz) tone was more soothing than a higher continuous tone (60 sec, 90 dB, 500 Hz), a low, intermittant tone (4 sec on, 1 sec off, 150 Hz), or no tone at all. The authors used overall state ratings to determine level of arousal.

Schmidt et al. (1980), played a heartbeat sound to preterm infants during active and quiet sleep and measured their responses to tactile stimulation. They found that while heart rate went up in response to stimulation during active sleep, the sound had no effect on heart rate or spontaneous motility during quiet sleep. Infants were approximately 32 weeks gestation at birth, 37 weeks conceptional age at testing, and had been out of the incubator 24 hours when tested.

Their study also found that the heartbeat sound increased the length of the first quiet sleep epoch. They scored sleep by behavioral observation so it is possible that with the heartbeat sound On more regular respiration was seen, which would increase the amount of quiet sleep recorded. Respiration was not scored as a separate measure. This suggests that while the sound might not influence heart rate or motility during quiet sleep, it might influence respiration and the organization of sleep.

Responsivity in preterms may vary with the sensory modality, reflecting different levels of maturity in various sensory or response systems. Field, Dempsey, Hatch, Ting, and Clifton (1979) did two experiments comparing term and preterm infants' responses in two modalities (heart rate and limb movement) to auditory and tactile stimulation.

In the first experiment, two auditory stimuli (a rattle and a buzzer) were presented manually at 90 dB to term and preterm infants. Preterms had a mean gestational age at birth of 33 weeks and a conceptional age at the time of testing of 37 weeks. For the tactile stimulus, a plastic filament was presented to the lower left side of the the infant's abdomen. When the infant was in active sleep, three series of trials for the three stimuli were delivered in a habituation-dishabituation paradigm.

Both groups initially responded to all stimuli with increased movement and heart rate acceleration. but only the term infants responded to stimulus repetition by decreasing both cardiac and behavioral responses. Therefore, in a second experiment, the relation between cardiac and behavioral response systems was examined by measuring heart rate while preterm infants were actively sucking on a pacifier. It was thought that although limb movements might not be coordinated with cardiac reactivity another behavior might be. Results showed integration of autonomic and motor responsivity in preterms comparable to full-term infants. It was suggested that the stimulus discrimination and habituation demands of the first experiment may have overtaxed the preterm infants' ability to maintain response integration.

Monod and Garma (1971) did a longitudinal study of premature infants' responses to clicks and tone bursts and found that motor responses (startles, localized limb or facial movements) diminished with maturation (30-39 weeks) in quiet sleep but blinks and eye movements did not. Gestational age at birth ranged from 28-36 weeks. This suggests that motor responses in the conceptionally younger infant are more sensitive to intermittant sound stimulation during quiet sleep than they are in more mature infants, while eye movements are not. (In my study, the more mature the infant _at birth_, the lower the eye movement rate and higher the muscle movement rate.) It is worth noting that these stimuli were presented inside incubators where the ambiant noise level reported was 80 dB. Click bursts (3 msec) were presented at 103 dB, 600-900 Hz range, and tones (1.5 sec, 3.5 sec) were presented at 250, 700, 1000, and 2000 Hz at 85, 92, 90, and 91 dB, respectively.

All of these studies suggest that sound is a potent stimulus for both full-term and premature infants. Whether the infant's response is to increase, decrease, or keep unchanged its rate of behavior, or whether behavior becomes more or less organized, will depend on the particular response system, the excitatory or inhibitory nature of the stimulus, the infant's degree of sensitivity to the stimulus, and the state of arousal at the time of the stimulation. My study emphasizes that with preterm infants, gestational age at birth and the number of days in the incubator are also important factors to be considered. It is likely that the sound of the incubator is affecting sleep organization and the central nervous system for some infants. Further studies are needed to confirm in what way particular infants are affected.

While the possible effects of swaddling were not controlled in the present study, it was possible to anticipate the direction of change and look for a drop in heart rate and heart rate standard deviation (which might indicate a lowering of arousal), but not necessarily a drop in respiration rate (although this has not been looked at in premature infants). The question of whether the infant slept "more" was not addressed in this study. Any comparison with the literature was limited because the present study measured heart rate and respiration during a particular period of sleep.

The issue of swaddling is characterized by an absence of evidence that can be related to any previous investigations. In the present study, respiration rate dropped when the infant was swaddled but this did not occur in the Lipton et al. studies (1960, 1965) where the effects of swaddling were explicitly explored. Also, there was no significant drop in heart rate in the present study, which was the finding of both the Lipton, et al. (1960, 1965), and Gardner and Turkewitz (1982) studies. This may be because the infants in the present study were in a state of arousal approximating quiet sleep. One could argue that because quiet sleep was more organized for some infants in the <u>Off</u> condition than in the <u>On</u> condition, that swaddling had an effect. This effect would be comparable to the finding of "more" sleep in previous studies. This could be true for those infants but requires verification since previous studies have not looked at sleep organization and swaddling. In cases where results were related to the number of days the infant had been in the incubator, this would imply that the rate of response or degree of association among components was dependent upon how many days the infant had been <u>without</u> swaddling. In cases where a result was related to gestational age at birth, such as the lower correlation of heart rate standard deviation and respiration ratio in the <u>Off</u> condition than the <u>On</u> condition, this would suggest that swaddling had a disrupting effect for infant's who were younger at birth.

The final major element of the environment that should be considered as a possible influence on the infant's responses are the temperature in both conditions, which was not controlled. The major question is whether turning off the thermal control in the incubator and swaddling the infant produced internal temperature changes that forced the infant to adapt.

In the present study, the infants were dressed and swaddled in their own incubators while the motor was still on. Although clothing was not pre-warmed, the heat loss should not be great because of the warm mattress and continuing heat in the incubator. However, after the motor was turned off, the infant would have to adjust to the heat loss from the face and head (no infants in this study wore hats). How much heat is lost is not known. If the environmental temperature is close enough to the skin temperature that the heat loss is not greater than the rate of basal heat production, the infant will not become hypermetabolic.

To know the rate of metabolism would involve measuring oxygen consumption continuously which was not appropriate to this study. However, if metabolic rate rises, heart rate and respiration would be expected to rise. In fact, if body temperature became high, distress mechanisms would also increase metabolic rate and heart rate and respiration rates would rise. A rise in metabolism in the _Off_ condition, due to a temperature shift, does not seem likely since respiration was lower in the _Off_ condition than the _On_ condition for nearly all the infants.

Conclusion:

Despite sleep differences, generally healthy preterm infants grow and thrive within normal bounds. Many of these infants, however, may have developmental difficulties at a later age when their behavioral repertoire is more complex. If we are to intervene early to offset these difficulties, more must be learned about the process of central nervous system organization so these infants can be identified early. If the particular aspects of the environment and the manner in which they influence particular infants can be more closely identified, intervention is feasible. This study strongly suggests that we look at individual differences in behavior and development in preterm infants, accounting on some level for the influence of the postnatal environment on the organizing process of the central nervous system.

It will be important to record sleep patterns with a similar group of infants in swaddled and unswaddled conditions while the incubator is on to determine the relative effect of swaddling. It is equally important that infants be recorded at a later time, in the crib, to determine if the change in sleep organization is transitory or long-lasting. Finally, if vagal tone can be asssessed under these various conditions, we should have a much clearer view of the interaction between the central nervous system and environmental factors.

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