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Cardiac Vagal Tone as an Index of Autonomic Nervous Function in Healthy Newborn and Premature Infants

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Purpose: Multiple studies have documented that high resting levels of cardiac vagal tone suggest higher levels of self-regulation. The aim of this study was to evaluate cardiac vagal tone as an indicator of autonomic nervous function in healthy newborn and premature infants. **Methods:** This study was conducted using a descriptive comparison design and a convenience sampling strategy. The participants were 72 healthy and 62 premature infants delivered in a university hospital. Continuous heart rate data recordings from the infant's ECG were analyzed and Mxedit software was used to calculate mean heart period and an index of cardiac vagal tone. **Results:** The healthy infants had significantly higher cardiac vagal tone than the premature infants, when the influence of gestational age was removed using analysis of covariance. However, there were no significant differences in heart rate and heart period between the two groups when the influence of gestational age was removed using analysis of covariance. **Conclusion:** The results of this study show that cardiac vagal tone may be used as an index for determining infant's autonomic nervous function. Nursing staff in pediatric departments can use cardiac vagal tone with ease, as this index can be calculated in a noninvasive method from the ECG.

Key words: Cardiac vagal tone, Healthy newborn infant, Premature infant

INTRODUCTION

During the last two decades the survival for premature infants has significantly increased due to advances in perinatal and neonatal treatment and improvement in the care of high-risk infants. Although the survival rates for premature infants have shown improvement, clinical assessment and management of premature infants are very important and essential for further improvement in the outcomes for premature infants (Doussard-Roosevelt, Porges, Scanlon, Alemi, & Scanlon, 1997).

The survival of premature infants is based on successful self-regulation of the physiological systems that support growth and restorative processes. The autonomic nervous system is the primary regulator of physiological homeostasis. Thus, assessment should be directed at evaluating the central nervous system structures and functions that promote physiological states fostering growth and restorative processes. Heart rate is a very useful and popular assessment to evaluate of physiological self-regulation. Therefore, a fuller understanding of central nervous control mechanisms of heart rate during the early stages of human development would be of great value to neonatal assessment and management (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Verklan & Padbye, 2004).

Heart rate is controlled by the sympathetic and parasympathetic components of the autonomic nervous system. These two components are mutually antagonistic in their actions, sympathetic stimulation leads to acceleration of the heart rate, whereas parasympathetic impulses through the vagus nerve system produce deceleration of the heart rate (Porges, 1983; Yasuma & Hayano, 2004). These two control systems have different time constants and the end result of their interactions is the R to R interval differences

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of the heart rate, or heart rate variability. More recently, it has been found that the specific type of heart rate variability related to the vagus nerve system is respiratory sinus arrhythmia, rather than overall heart rate variability. The output of the nucleus ambiguous branch of the vagus has a respiratory rhythm of increasing and decreasing tone to the sino-atrial node, because the nucleus ambiguous is an integral component of the medullary respiratory system. The functional consequence of this rhythmic modulation of nucleus ambiguous vagal tone to the sino-atrial node is to produce respiratory oscillations in the heart rate pattern known as respiratory sinus arrhythmia (Porges, 1996).

Porges (1983) developed a statistical method for accurately extracting the amplitude of respiratory sinus arrhythmia, labeled cardiac vagal tone to emphasize that it is an index of vagal tone. Porges (1983) suggested that the index of cardiac vagal tone might be used to infer the effects of the parasympathetic nervous system on the heart via the vagus, and serve as a predictor of neurophysiologic development and subsequent health outcomes among neonates.

Massin and von Bernuth (1997), Mehta et al. (2002), and Richards (1995) reported that the reliability of this index in infant is acceptable and may be utilized to examine the effects of underlying disease processes or therapeutic interventions on cardiac autonomic tone during infancy and childhood.

Cardiac vagal tone has been studied to evaluate the autonomic nervous system fluctuations in heart rate related to maturation in full term and premature infants. Porges (1988) reported that the means of the cardiac vagal tone were 3.8 for full term neonates (n=180) and 2.0 for high-risk neonates (n=180). DiPietro, Larson, and Porges (1987) and Fox and Porges (1985) reported that healthy full term infants showed higher cardiac vagal tone than premature infants, reflecting the immaturity of the autonomic nervous system in the premature infants.

Levels of cardiac vagal tone in infants are also influenced by levels of illness (Hanna et al., 2000), sleep state (Villa et al., 2000), stimulation (Brown, 2007; Lee, 2002), and a range of competent behaviors (Steward, Moser, & Ryan-Wenger, 2001). Results of studies on both full term and premature infants suggest that levels of cardiac vagal tone reflect the autonomic nervous development of the infants.

Although the findings of the studies support the use of cardiac vagal tone as a predictive index of neurophysiological reactivity in neonates, well-documented normal values of cardiac vagal tone to provide parameters of normal and abnormal autonomic nervous functioning are not available. The two main reasons are related to methodological differences among the researchers and the small number of neonates included in the studies (Longin, Schaible, Lenz, & König, 2005; Mehta et al., 2002). These variations in normal values of cardiac vagal tone in neonates indicate that there is a need to reassess the measures to establish normative data on cardiac vagal tone in neonates.

The aims of this study were to assess the reliability of cardiac vagal tone as an index of autonomic nervous function and to establish normal values for infants. So, this study compared cardiac vagal tone, heart rate, and heart period between healthy newborn and premature infants.

The results of this study should improve understanding of the autonomic control of the cardiac system in infants and lead to the development of new means for noninvasive assessment of autonomic nervous function.

METHODS

Design and sample

A descriptive comparison design and a convenience sampling strategy were used to answer the study question.

The participants were 76 healthy infants recruited from the newborn nursery and 62 premature infants from the neonatal intensive care unit at S University Hospital. The nursing department of S University Hospital approved the research protocol and permission of the ethics commission of the hospital was also obtained. Written informed consents were obtained from the parents of all research participants. Even the medical textbooks define that full-term infant is between 38 to 42 weeks gestational period, if baby's weight was more than 2,400 grams, Apgar score was good, and gestational period was between 36 and 42 weeks, the medical staffs of S University Hospital decided a baby put into the newborn nursery. So, the sample for healthy infants in this study included asymptomatic infants who were between 24 and 72 hr old, weighing more than 2,400 grams, and having a gestational period of between 36 and 42 weeks (Mehta et al., 2002).

Healthy infants were excluded from the study if they were: born to mothers who used any medications during pregnancy known to affect the cardiovascular system; born to mothers with acute or chronic diseases, such as hypertension, hepatitis, diabetes, or sepsis; symptomatic or requiring administration of oxygen for more than 5 min, ventilator support, or admission to the neonatal intensive care unit; or born with associated congenital anomalies.

The selection criteria for premature infants included all infants born between 27 weeks and 35 weeks gestational age with birth weight between 1,000 g and 2,399 g without any of the following conditions: major congenital anomalies; sepsis; surgery; medications with central nervous system effects; seizures; or persistent mechanical ventilation.

Demographic and medical characteristics at the time of each infant's birth were collected from a chart review.

Power calculation

Sample size calculations were using two group comparisons to detect the differences of cardiac vagal tone between healthy newborn and premature infants. The sample size of 64 per group needed with alpha=.05, power=.80, u=1, medium effect size (.25) (Lee, Im, & Park, 1998). Therefore, the original plan was to recruit more than 70 pairs of infants to allow potential attrition. Because the heart rate data of 12 infants were not good to detect the peak of the R wave, the final data of the sample infants were 134.

Measures

Data for healthy infants were obtained when they were between 24 and 72 hr old and for premature infants during the second day after enteral feeding was starting, because the initiation of enteral feeding means that the premature infant is physiologically stable (Lee, 1999). Data collection for both groups was always done 1 hr after a feeding in the afternoon. All data collection began with the infants in a sleep state and continued for 10 min of undisturbed time, because handling may affect the physiological status of the infant (Yasuma & Hayano, 2004).

After skin preparation, five ECG electrodes were placed on the chest and abdomen of the infant to conduct the electrocardiogram signal. A physician reviewed all of the ECG recordings to get confirm the ECG data were not wrong recording and to exclude a baby who had the exclusion criteria. Continuous heart rate data was recorded during 10 min while the infant was in a state of sleep. The recordings were made from the infant's AFO 400 ECG portable monitor (made in Korea) on a laptop computer through the Wavelet software program (redeveloped by Lee & Jang in 2000). The Wavelet software program collects continuous ECG analog data and outputs a digitized file, which detects the peak of the R wave for each beat and quantifies sequential times between heartbeats (i.e., heart period) in milliseconds (msec). These files were examined to eliminate artifact interference with the electrocardiogram signal before analysis and were analyzed to calculate mean heart period and an index of cardiac vagal tone using the Mxedit software developed by Porges (1983). This study attempted to get the reliability of cardiac vagal tone that was developed by Porges (1983). So, this study used the Porges method. The Porges method applies time series procedures to heart period data (msec). These steps included: 1) conversion of heart period into time-based data by sampling at 200 msec intervals; 2) detrending of periodicity in heart rate slower than respiratory sinus arrhythmia with a 21-point moving polynomial. The resulting trend is removed from the original time series yielding a residual series free of both linear (i.e., bad data) and higher order trends (i.e., bradycardia episodes); 3) band pass filtering to extract variance of heart period ($msec^2$) within the frequency band (0.3-1.3 Hz) of spontaneous breathing in the neonate; and 4) calculation of the natural logarithm of the band-passed variance, which serves as the estimate of cardiac vagal tone (In [$msec^2$]). To increase the stability of the estimate, means of these values were computed at 15-sec epochs.

Data analysis

Independent t-test and Chi-square analyses were conducted to assess equivalence between the two groups on demographic and perinatal entry variables. Because cardiac vagal tone is influenced by gestational weeks, ANCOVA analyses with gestational age as a covariance were used to compare heart rate, heart period, and cardiac vagal tone between the two groups (Doussard-Roosevelt et al., 1997; Rosenstock, Cassuto, & Zmora, 1999). Finally, Pearson correlation coefficient analysis was used to assess the relationships between perinatal measures (gestational age, weight at birth, height at birth, and Apgar scores) and heart rate, heart period, and cardiac vagal tone.

RESULTS

Table 1 presents frequency and means for differences in perinatal and demographic variables for the two groups. There were 72 healthy newborn infants and 62 premature infants. There was no statistical differences between the two groups for the infant' gender. However, significant differences were found between the two groups for the other variables, including gestational age, Apgar score, weight at birth, height at birth, and type of delivery.

Cardiac vagal tone, heart rate and heart period between the two groups

The mean cardiac vagal tone of the healthy newborn infants was approximately 3.0 with a standard deviation (SD) of approximately 1.0 (Table 2). In contrast, the mean cardiac vagal tone of the premature infants was 2.2 (SD=0.6). The result from independent t-test on cardiac vagal tone between the two groups, showed that the premature infants, as a group, have significantly lower cardiac vagal tone than the healthy newborn infants (t=5.4, *p*=.000). The gestational age was significantly longer for the healthy newborn infants than the premature infants (t=21.5, *p*=.001). Since the gestational age might influence cardiac vagal tone (Doussard-Roosevelt et al., 1997; Rosenstock et al., 1999), the researcher tried to separate the effects of maturation from time on cardiac vagal tone using statistical methods. Even when this significant influence of gestational age was removed with analysis of covariance, there was still a highly significant difference between the two groups in cardiac vagal tone (F=6.0, *p*=.02) (Table 2). However, there was no significant groups-by-gestational age interaction for cardiac vagal tone (F=0.1, *p*=.82).

There were also significant differences in heart rate (t=-8.0, *p*<.001) and heart period (t=7.7, *p*<.001) in t-test between the two groups. However, when the influence of gestational age was removed with analysis of covariance, there were no significant difference in heart rate (F=2.5, *p*=.12) or heart period (F=3.1, *p*=.08) in Table 2. There were significant groups-by-gestational age interactions for heart rate (F=6.4, *p*=.01) and heart period (F=5.5, *p*=.02).

Interrelationship of perinatal characteristics, cardiac vagal tone, heart rate, and heart period

Relationships between the perinatal characteristics (gestational age, weight at birth, height at birth, and Apgar scores) and the dependent measures (cardiac vagal tone, heart rate, and heart peri-

Table 1. Demographic and Perinatal Characteristics for the Two Groups

		Full term infant (n=72)	Premature infant (n=62)	χ^2 or t	*p*
Gender (male/female)	N	28 (44)	33 (29)	2.76	.097
Gestational age (at birth, in days)	M (SD)	273.7 (11.6)	228.6 (12.7)	21.5	.001
Apgar at 1 min	M (SD)	8.7 (0.7)	6.1 (2.1)	9.9	<.001**
Apgar at 5 min	M (SD)	9.8 (0.4)	7.5 (1.3)	14.4	<.001**
Weight at birth (grams)	M (SD)	3,231.3 (457.7)	1,665.3 (380.6)	21.3	<.001**
Height at birth (cm)	M (SD)	53.2 (2.9)	42.4 (2.5)	22.7	<.001**
Type of delivery (ND/C-Section)	M (SD)	36 (36)	11 (51)	15.22	<.001**

***p<.001.
ND/C-Section=Normal Delivery/Cesarean-Section.

Table 2. Differences in Heart Rate, Heart Period and Cardiac Vagal Tone between Groups by ANCOVA

	Full term infant (n=72) M (SD)	Premature infant (n=62) M (SD)	F		F	
			Groups x gestational age	*p*	Groups	*p*
Heart rate (min)	128.7 (10.1)	146.1 (14.9)	6.4	.01*	2.5	.12
Heart period (msec)	470.7 (38.8)	415.7 (43.9)	5.5	.02*	3.1	.08
Cardiac vagal tone	3.0 (1.0)	2.2 (0.6)	0.1	.82	6.0	.02*

Covariate: Gestational Age. *p<.05.

Table 3. Interrelationship of Perinatal Characteristics, Cardiac Vagal Tone, Heart Rate, and Heart Period (N=134)

	Heart rate	Heart period	Cardiac vagal tone
Gestation age	-.59**	.57**	.38**
Weight at birth	-.58**	.56**	.39**
Height at birth	-.52**	.50**	.36**
Apgar at 1 min	-.50**	.48**	.30**
Apgar at 5 min	-.55**	.53**	.32**

**p<.01.

od) were explored. The correlation coefficients are presented in Table 3, showing that cardiac vagal tone was significantly related to gestational age (r=.38, p<.01), weight at birth (r=.39, p< .01), height at birth (r=.36, p<.01), Apgar at 1 min (r=.30, p< .01), Apgar at 5 min (r=.32, p<.01). There were also significant relationships between heart rate and heart period and perinatal characteristics (gestational age, weight at birth, height at birth, and Apgar scores).

DISCUSSION

Heart rate variability has long been used as the index of central nervous system status (Verklan & Padbye, 2004). Cardiac vagal tone is one indicator of heart rate variability (Porges, 1983). This study compared cardiac vagal tone, heart rate, and heart period between healthy newborn and premature infants. There were significant findings concerning cardiac vagal tone that contribute to greater understanding of the neural control influencing cardiac function in infant and facilitate the application of this index in a variety of clinical settings.

Even when the average heart rate of healthy infants (128.7 beats per minute [bpm]) and premature infants (146.1 bpm) was in the normal range, there were significant differences in cardiac vagal tone, heart rate and heart period between healthy infants and premature infants. These results are consistent with several previous studies (Eiselt et al., 1993; Rosenstock et al., 1999). Eiselt et al. (1993) reported that differences of high-frequency heart rate variability were present between newborns (n=16) and premature infants (n=12) (p<.01). The report of Longin, Schaible, Demirakca, Lenz, and König (2006) showed that heart rate and high-frequency heart rate variability were highly significant differences (p<.001) between the two groups and Rosenstock et al. (1999) suggested that heart rate variability increased with gestational age and early postnatal age. Premature infants seem to have lower heart rate variability than term infants. These results suggest that heart rate, heart period and cardiac vagal tone are good indicators for the evaluation of physiological self-regulation in infants and can distinguish on the functional state of the autonomic nervous system in neonates.

The finding also showed that there were significant correlations between perinatal measures (gestational age, weight at birth, height at birth, and Apgar scores) and heart rate, heart period, and cardiac vagal tone. These results are consistent with those of Doussard-Roosevelt et al. (1997), and Harrison, Williams, Leeper, Stem, and Wang (2000). Doussard-Roosevelt et al. (1997) reported that gestational age, Apgar scores, and birth weight correlated positively with heart rate and cardiac vagal tone. These results of this study indicate that heart rate, heart period and cardiac vagal tone are validated as indicators of the self-regulation of the physiological systems in infants.

However, there were no significant differences in heart rate and heart period when gestational age was removed as a covariance. The only significant difference between the two groups when gestational age was controlled with covariance analysis was for cardiac vagal tone. Heart rate has been a popular measure, in part because the cardiovascular system is well developed, in full term infants as well as in preterm infants. Heart rate can be detected from approximately the 4th week after conception and both sympathetic and parasympathetic systems are operative by term. Also, the clear presence of cardiac vagal tone, heart rate variability due to the influence of the rate breathing, in the full term infant indicates definite cardiorespiratory coordination by well-known brain structures. This respiratory-heart rate coupling, mediated by the vagus, has also been clearly demonstrated in stable premature infants by 36-37 weeks gestational age and reflects a transition from sympathetic to parasympathetic dominance occurring during the postnatal period (Doussard-Roosevelt et al., 1997). Porges (1996) suggested that a sympathovagal imbalance appears in high risk premature infants. So, cardiac vagal tone would be a more sensitive indicator than heart rate and heart period for neurophysiologic development outcomes in these infants. The results of this study also support the use of cardiac vagal tone as a more useful and reasonable index for detection of individual difference of autonomic nervous functions in infants.

To establish the normal value of cardiac vagal tone in infants, the means for cardiac vagal tone in this study were compared with the means of other studies. However, there was little difference in the normal value of cardiac vagal tone according to the researchers. The mean cardiac vagal tone was 3.8 for the full term neonates (n=180) and 2.0 for the high-risk infants (n=180) in Porges' study (1988) and DiPietro et al. (1987) reported means for cardiac vagal tone ranging from 3.25 to 4.10 in sleep with 100 healthy newborns between 17 and 56 hr postpartum. In the study by Fox and Porges (1985) the means for cardiac vagal tone were reported as 4.72 in healthy preterm infants (n=10) and 5.75 in healthy term infants (n=16) at the midpoint between feedings. The means for cardiac vagal tone were 2.10 for healthy preterm infants (n=9) during active sleep (Hofheimer, Wood, Porges, Pearson, & Lawson, 1995), and 1.24 for healthy preterm infants (n=84) at 6 to 9 days of age who were between 27 and 33 weeks gestational age at birth (Harrison et al., 2000). In this study, the mean cardiac vagal tone was 3.0 for the healthy newborn and 2.2 for the premature infants. Even though the studies including this study used the same method to calculate cardiac vagal tone, they did not identify the same normal values for normal healthy newborn infants or for premature infants. These differences occurred as results of discrepancies in the number and condition of infants at the time of the research. These results only show that premature infants seem to have lower cardiac vagal tone than full term infants. The reason for lower cardiac vagal tone in premature infants as compared to full term infants is explained by Longin et al. (2006). The catecholamine levels are increased in premature infants due to the situation of severe stress. This rise in baseline heart rate and therefore impairment of heart rate variability and decrease of cardiac vagal tone may be a result of an abnormally high level of sympathetic activity. Griffin, Scollen, and Moorman (1994) and Landrot et al. (2007) suggested that impairment of heart rate variability might be induced by excessive sympathetic input or withdrawal of parasympathetic input. Maturation of the autonomic nervous system after birth in normal full term infants results in a decrease in heart rate and increases in cardiac vagal tone. Because the sympathetic component of the autonomic nervous system predominates during fetal life and at birth, the maturational changes after birth reflect increasing development of the parasympathetic component (MaCain, Fuller, & Gartside, 2005). According to the polyvagal theory (Porges, 1996), high levels of cardiac vagal tone at rest suggest higher levels of self-regulation. In this study, cardiac vagal tone of the healthy newborn infants was higher than that of the premature infants, indicating that healthy newborn infants have better function of central nervous system than premature infants. Decreased cardiac vagal tone indicates a disturbance of autonomic function or decreased ability of the sinus node to respond to environmental signals. Decreased cardiac vagal tone may be a marker of poor autonomic nervous function in infants.

CONCLUSION

The results of this study confirm that vagal tone is an indicator of the neural control influencing cardiac function and a sensitive indicator of autonomic nervous function in infants.

These data, by providing validation of cardiac vagal index for infants, may contribute to increased confidence in cardiac vagal tone as a marker for determining the likely outcome of neonatal disorders affecting neurophysiologic development and may be used in clinical settings and in many diverse study areas. Therefore, cardiac vagal tone may be a new and, important tool in clinical assessment for the early detection of autonomic neuropathy. Cardiac vagal index can be measured by noninvasive method through ECG. This means that nurses and other health care professionals can easily use cardiac vagal tone to monitor pediatric patients.

To achieve a standard value, further research is needed to examine a larger, more homogeneous sample of infants in terms of age. Also, patent ductus arteriosus and foramen ovale of baby might affect cardiac vagal tone, further work is necessary to identify which variables influence cardiac vagal tone.

REFERENCES

Brown, L. (2007). Heart rate variability in premature infants during feeding. *Biological Research for Nursing, 8,* 283-293.

DiPietro, J. A., Larson, S. K., & Porges, S. W. (1987). Behavioral and heart rate pattern differences between breast-fed and bottle-fed neonates. *Developmental Psychology, 23,* 467-474.

Doussard-Roosevelt, J. A., Porges, S. W., Scanlon, J. W., Alemi, B.,

& Scanlon, K. (1997). Vagal regulation of heart rate in the prediction of developmental outcome for very low birth weight preterm infants. *Child Development, 68,* 173-186.

Eiselt, M., Curzi-Dascalova, L., Clairambault, J., Kauffmann, F., Medigue, C., & Peirano, P. (1993). Heart rate variability in low-risk prematurely born infants is not reaching normal term. A comparison with full-term newborns. *Early Human Development, 32,* 183-195.

Fox, N. A., & Porges, S. W. (1985). The relationship between developmental outcome and neonatal heart period patterns. *Child Development, 56,* 28-37.

Griffin, M. P., Scollen, D. F., & Moorman, J. R., (1994). The dynamic range of neonatal heart rate variability. *Journal Cardiovascular Electrophysiology, 5,* 112-124.

Hanna, B. D., Nelson, M. N., White-Traut, R. C., Silvestri, J. M., Vasan, U., Rey, P. M., et al. (2000). Heart rate variability in preterm brain-injured and very-low-birth- weight infants. *Biology of the Neonate, 77,* 147-155.

Harrison, L. L., Williams, A. K., Leeper, J., Stem, J. T., & Wang, L. (2000). Factors associated with vagal tone responses in preterm infants. *Western Journal of Nursing Research, 22,* 776-795.

Hofheimer, J. A., Wood, B. R., Porges, S. W., Pearson, E., & Lawson, E. (1995). Respiratory sinus arrhythmia and social interaction patterns in preterm newborns. *Infant Behavior and Development, 18,* 233-245.

Landrot, I. D., Roche, F., Pichot, V., Teyssier, G., Gaspoz, J., Barthelemy, J., et al. (2007). Autonomic nervous system activity in premature and full-term infants from theoretical term to 7 years. *Autonomic Neuroscience: Basic and Clinical, 136,* 105-109.

Lee, E. O., Im, N. Y., & Park, H. A. (1998). *Nursing medical research and statistics analysis.* Seoul: Soo Mun Sa.

Lee, H. K. (2002). Effects of sponge bathing on vagal tone and behavioral responses in premature infants. *Journal of Clinical Nursing, 11,* 510-519.

Lee, K. J. (1999). Effects of a sensory stimulation on weight, stress hormone and behavioral state in premature infants. *Journal Korean Academy of Nursing, 2,* 445-455.

Longin, E., Schaible, T., Demirakca, S., Lenz, T., & König, S. (2006). Heart rate variability during extracorporeal membrane oxygenation and recovery in severe neonatal disease. *Early Human Development, 82,* 135-142.

Longin, E., Schaible, T., Lenz, T., & König, S. (2005). Short term heart rate variability in healthy neonates: Normative data and physiological observations. *Early Human Development, 81,* 663-671.

MaCain, G. C., Fuller E. O., & Gartside, P. S. (2005). Heart rate variability and feeding bradycardia in healthy preterm infants during transition from gavage to oral feeding. *Newborn and Infant Nursing Reviews, 5,* 124-132.

Massin, M., & von Bernuth, G. (1997). Normal range of heart rate variability during infancy and childhood. *Pediatric Cardiology, 18,* 297-302.

Mehta, S. K., Super, D. M., Connuck, D., Salvator, A., Singer, L., Fradley, L. G., et al. (2002). Heart rate variability in healthy newborn infants. *The American Journal of Cardiology, 89,* 50-53.

Porges, S. W. (1983). Heart rate patterns in neonates: A potential diagnostic window to the brain. In T. Field & A. Sostek (Eds.), *Infants born at risk: Physiological, perceptual, and cognitive processes* (pp. 3-22). New York, NY: Grune & Stratton.

Porges, S. W. (1988). Neonatal vagal tone: Diagnostic and prognostic implications. In P. N. Vietze & H. G. Vaughn (Eds.), *Early identification of infants with developmental disabilities* (pp. 147-159). New York, NY: Grune & Stratton.

Porges, S. W. (1996). Physiological regulation in high-risk infants: A model for assessment and potential intervention. *Development and Psychopathology, 8,* 43-58.

Richards, J. E. (1995), Reliability of respiratory sinus arrhythmia in r-r- intervals, in 14-, 20-, and 26-week-old infants. *Infant Behavior and Development, 18,* 155-161.

Rosenstock, E. G., Cassuto, Y., & Zmora, E. (1999). Heart rate variability in the neonate and infant: Analytical methods, physiological and clinical observations. *Acta Paediatrica, 88,* 477-482.

Steward, D. K., Moser, D. K., & Ryan-Wenger, N. A. (2001). Biobehavioral characteristics of infants with failure to thrive. *Journal of Pediatric Nursing, 16,* 162-171.

Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. (1996). Heart rate variability: Standards of measurement, physiological interpretation, and clinical use. *Circulation, 93,* 1043-1065.

Verklan, M. T., & Padbye, N. S. (2004). Spectral analysis of heart rate variability: An emerging tool for assessing stability during transition to extrauterine life. *Journal of Obstetrics, Gynecologic, & Neonatal Nursing, 33,* 256-265.

Villa, M. P., Calcagnini, G., Pagani, J., Paggi, B., Massa, F., & Ronchetti, R. (2000). Effects of sleep stage and age on short-term heart rate variability during sleep in healthy infants and children. *Chest, 117,* 460-466.

Yasuma, F., & Hayano, J. (2004). Respiratory sinus arrhythmia: Why does the heartbeat synchronize with respiratory rhythm? *Chest, 125,* 683-690.