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Trajectories of Parasympathetic Nervous System Function before, during, and after Feeding in Infants with Transposition of the Great Arteries

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Abstract

Background—Compromised parasympathetic response to stressors may underlie feeding difficulties in infants with complex congenital heart defects, but little is known about the temporal pattern of parasympathetic response across phases of feeding.

Objectives—To describe initial data exploration of trajectories of parasympathetic response to feeding in 15 infants with surgically corrected transposition of the great arteries and to explore effects of feeding method, feeding skill, and maternal sensitivity on trajectories.

Method—In this descriptive, exploratory study, parasympathetic function was measured using high frequency heart rate variability (HF HRV), feeding skill was measured using the Early Feeding Skills assessment, and maternal sensitivity was measured using the Parent-Child Early Relational Assessment. Data were collected before, during, and after feeding at 2 weeks and 2 months of age. Trajectories of parasympathetic function and relationships with possible contributing factors were examined graphically.

Results—Marked between-infant variability in HF HRV across phases of feeding was apparent at both ages, although attenuated at 2 months. Four patterns of HF HRV trajectories across phases of feeding were identified and associated with feeding method, feeding skill, and maternal sensitivity. Developmental increases in HF HRV were apparent in most breastfed, but not bottle-fed, infants.

Discussion—This exploratory data analysis provided critical information in preparation for a larger study in which varying trajectories and potential contributing factors can be modeled in relationship to infant outcomes. Findings support inclusion of feeding method, feeding skill, and maternal sensitivity in modeling parasympathetic function across feeding.

Keywords

congenital heart defects; heart rate variability; infant feeding

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Trajectories of Parasympathetic Nervous System Function before, during, and after Feeding in Infants with Transposition of the Great Arteries

Infants with complex congenital heart defects, such as transposition of the great arteries (TGA), require palliative or corrective surgery within the first days or weeks of life. These infants have difficulty regulating physiological processes such as feeding (Majnemer et al., 2009). The etiology of this disordered physiologic regulation is uncertain but may be associated with altered cardiorespiratory functioning (Jadcherla, Vijayapal, & Leuthner, 2009), stressors of surgery (du Plessis, 1999), or pre-existing neurologic dysfunction (Majnemer et al., 2009). The ability to regulate these autonomically controlled physiological processes adaptively is critical for later social, emotional, and behavioral regulation (Doussard-Roosevelt, McClenny, & Porges, 2001) and physical growth (Pillo-Blocka, Adatia, Sharieff, McCrindle, & Zlotkin, 2004).

Providing effective support to these infants requires sound knowledge of developmental trajectories of regulation of physiological processes. Support for such developing adaptive processes is a key goal of nursing care provided to infants with heart defects before corrective or palliative surgery and across the recovery period. Described here is the initial data exploration using graphical depictions of trajectories of autonomic nervous system function (ANS) as measured by high frequency heart rate variability during the physiological challenge of feeding in 15 infants with TGA.

Homeostasis and Stress

The ANS regulates physiologic processes through the parasympathetic and sympathetic nervous systems. Through precise regulation of physiologic states, the organism is maintained in a state optimal for growth and development (i.e., homeostasis, largely controlled by parasympathetic function) and for responding to challenges to homeostasis (i.e., stress reactivity, largely controlled by sympathetic function). During infancy, feeding is a challenge to the homeostatic state (Doussard-Roosevelt & Porges, 1999). In healthy term (Lappi et al., 2007) and preterm (Brown, 2007) infants, parasympathetic function is reduced during ingestion of milk to allow sympathetic effects to predominate to meet the metabolic demands needed to coordinate sucking, swallowing, and breathing. When the feeding is complete, parasympathetic activity again becomes more prominent to support digestive processes (Porges, 1996). Thus, by monitoring patterns of change in parasympathetic activity, an individual's capacity for responding to stress or challenge can be assessed (Porges, 1996).

The ANS function can be measured indirectly by examining patterns and frequency of variability in heart rate over time (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996). Heart rate variability refers to the minute changes in intervals between heart beats, reflecting a constant and precise interaction between the parasympathetic and sympathetic nervous systems. Different processes operate at different frequencies that can be identified and quantified (Task Force, 1996). High frequency heart rate variability (HF HRV) is widely accepted as an index of parasympathetic activity (Task Force, 1996) and is the focus of this presentation. In general, relatively higher levels of HF HRV during states of homeostasis (baseline) followed by reductions in response to stress and increases after the stress is resolved are considered healthy and adaptive (Porges, 1996). Children experience an increase in HF HRV between infancy and childhood (Massin & von Bernuth, 1997). Thus, baseline HF HRV increases with maturation, but the pattern of adaptive response to a stressor and subsequent recovery from a stressor retains a characteristic U-shaped pattern over time (Whited, Wheat, &

Larkin, 2010) that can be modeled as a quadratic curve (Henly, Wyman, & Findorff, in this supplement).

Congenital Heart Defects

Complex congenital heart defects are those that require palliative or corrective surgery within the first days or weeks of life and include cyanotic defects (e.g., TGA, tetralogy of Fallot, or hypoplastic left heart syndrome) and acyanotic defects (e.g., aortic stenosis, coarctation of the aorta, or atrioventricular canal defect). Diagnosis is made prenatally in more than half of the cases (Levey et al., 2010). Timing of surgery varies with the type of defect. For example, infants with TGA are typically repaired within the first week of life (Mussatto & Wernovsky, 2005) whereas infants with tetralogy of Fallot may not be repaired until they are between 3 and 6 months of age (Karl, 2008). Infants with TGA were chosen as the focus of this study because it is one of the most common defects and timing of corrective surgery is fairly uniform (Mussatto & Wernovsky, 2005). Additionally, limiting the study to one defect reduced the confounding effects of the unique functional and physiologic characteristics of different types of defects.

Mothers report that feeding is one of the most difficult and time-consuming aspects of caring for an infant with a congenital heart defect (Svavarsdottir & McCubbin, 1996). Infants with heart defects demonstrate more vomiting, more breathlessness, and reduced growth when compared to healthy infants (Clemente, Barnes, Shienbourne, & Stein, 2001). Practices related to feeding infants with complex congenital heart defects are changing. At the time of this study, infants with heart defects dependent on a patent ductus arteriosus who were receiving prostaglandins were not offered oral feedings preoperatively (Willis et al., 2008). Postoperative enteral feedings are usually initiated with nasogastric tube feedings when the chest incision is closed, the infant has been extubated, and cardiorespiratory stability is demonstrated. After continuous and then bolus nasogastric feedings are tolerated, oral feedings are initiated. Infants with TGA generally begin oral feedings 2 to 3 days after surgery.

Consistent with developmental changes in HF HRV in healthy infants, infants with different types of complex congenital heart defects have demonstrated consistent increases in HF HRV between the preoperative time point and 3–6 months after surgical correction or palliation (Kaltman et al., 2006). However, infants with heart defects also demonstrate lower baseline HF HRV in comparison with healthy infants of the same age (Heragu & Scott, 1999; Polson et al., 2006). The HF HRV was examined during feeding in a small sample of 10 infants with a variety of congenital heart defects after surgical correction or palliation (Winters et al., 2006). The rate was lower in infants with more severe defects, and expected reductions during feeding were not observed. Except for the Winters et al. (2006) study, the effect of feeding on ANS function has received little attention. These findings of lower baseline parasympathetic function and lack of parasympathetic response to the feeding challenge suggest that infants with complex congenital heart defects have less flexible, less responsive autonomic function, and this may impact their ability to maintain homeostasis as well as to mobilize resources needed to respond to stressors. Knowledge of infant physiologic response to stress is important for nurses to identify infants needing additional caregiver support during challenges such as feeding.

Contributing Factors

Many factors can affect ANS function during feeding. Feeding method, feeding skill, and maternal interaction with her infant during feeding are particularly pertinent to infants recovering from major heart surgery. Healthy breastfed infants have higher parasympathetic function at rest when compared with bottle-fed infants (Jacob, Byrne, & Keenan, 2009).

Although relationships between feeding skill and ANS have not been studied, feeding skill could impact ANS function during the challenge of feeding. Infant health status may affect feeding skill (Pridham, Steward, Thoyre, Brown, & Brown, 2007), and infants with complex congenital heart disease often experience delayed development of oromotor feeding skill (Jadcherla et al., 2009; Kogon et al., 2007). Theoretically, the effort to coordinate sucking, swallowing, and breathing would be particularly stressful and likely result in enhanced sympathetic activity and concurrent reductions in parasympathetic activity that may persist after the feeding is complete due to enhanced energy expenditure (Owens & Musa, 2009).

Maternal behavior in interaction with her infant affects the infant's ability to regulate physiologic processes (Feldman, Singer, & Zagoory, 2010). Schore's theory of the development of self-regulation in young children posits that the mother's ability to be attentive and responsive to the infant's internal state by correctly interpreting behavioral cues supports the infant's immediate and developing regulatory abilities (Schore, 1996). In the context of infant feeding, Schore's theory suggests that the mother's ability to respond sensitively will support the infant in successfully organizing and coordinating sucking, swallowing, and breathing. For example, a sensitive mother may structure and mediate the environment by positioning the infant's body in a cradled or fully supported semireclining position facing the mother, demonstrate less rigidity and more flexibility by pausing or ending the feeding when the infant becomes distressed or loses interest, and refrain from intrusive behavior such as jiggling the nipple in the infant's mouth.

Premature infants whose mothers demonstrate sensitivity to infant cues tend to be more able to regulate the physiological challenge of feeding (McCain, Fuller, & Gartside, 2005; Thoyre & Brown, 2004). The effect of maternal behavior on physiologic regulation in infants with complex congenital heart disease is not known. However, maternal interactions with four to six month old infants with complex congenital heart disease were shown to be qualitatively different than interactions between age-matched healthy infants and their mothers in ways that may be associated with less sensitivity, including less touching, less eye contact, and less expression of positive affect (Gardner, Freeman, Black, & Angelini, 1996; Lobo, 1992). In a more recent study, maternal sensitivity in interaction with their infants with TGA in the first few days after surgical correction was higher than that of mothers of age-matched healthy infants (Harrison, 2009). More information is needed about maternal-infant interactions and effects on infant physiology in the population of infants with congenital heart defects.

Issues and Purpose

Feeding poses a challenge to infants with complex congenital heart defects and their mothers. Compromised parasympathetic response to stressors may underlie feeding difficulties, but little information about the temporal pattern of parasympathetic response across phases of feeding is available. Individual differences in infant and maternal characteristics may be associated with variation in parasympathetic response trajectories among infants with the same heart defect. Longitudinal growth modeling offers a method of analyzing changes in biobehavioral responses to challenge over time. However, accurate models must be based on both theoretical and data-driven information. Before models can be constructed, the data must be examined for patterns of change and potential contributing factors. Visualizing data in an interactive graphical program is a powerful method of exploring data in preparation for generating and testing hypotheses (Theus & Urbanek, 2009).

The purpose of this paper is to describe the first steps in developing a longitudinal growth model for analyzing patterns of ANS response to the challenge of feeding infants with surgically corrected TGA at two points in time and to explore potential contributing factors.

The general approach to initial exploratory analysis suggested by Singer and Willett (2003) was used.

The research questions addressed were:

1. What patterns of HF HRV trajectories in infants with surgically corrected TGA can be detected graphically before, during, and after feeding at 2 weeks and 2 months of age?
2. What potential relationships can be visualized between individual HF HRV trajectories across phases of feeding and feeding method, infant feeding skill, and maternal sensitivity?
3. Is a quadratic curve the appropriate functional form for the trajectory of HF HRV across phases of feeding?

Method

Data described in this paper were collected for a study examining physiologic and arousal regulation in healthy infants and infants with TGA. This paper is focused exclusively on the data from all 15 infants with TGA and their mothers.

Setting and Sample

Fifteen infants with TGA and their mothers were recruited from three similarly sized nonprofit metropolitan children's hospitals in the Midwest. Inclusion criteria for the mother-infant dyads were: (a) full-term infants diagnosed with TGA either prenatally or after birth, with no comorbidities; and (b) English-speaking mothers at least 18 years of age or who were legally emancipated, and who would be the primary caregiver. Mother-infant dyads were excluded if the infant had been discharged home prior to readmission for surgery.

Variables and Measures

Parasympathetic function—The HF HRV was used as an index of parasympathetic function. Continuous electrocardiogram (ECG) recordings were collected with a three-channel ambulatory Holter recorder (Marquette Electronics, Inc., Milwaukee, WI). The ECG data were digitized at 128 Hz using a MARS 5000® Ambulatory ECG Analysis and Editing System (General Electric, Inc., Fairfield, CT). Each ECG complex was identified and morphology characterized by the computer software and edited for proper identification by the primary investigator. Final calculations were based solely on normal sinoatrial node initiated complexes, and HRV was calculated using frequency domain measures, determined by power spectral analysis. Using fast Fourier transformation of continuous ECG data segments, power in the high frequency domain was calculated separately for each infant based on average respiratory rate. The HRV data were log-transformed to account for skewed distributions (Kleiger, Stein, & Bigger, 2005) and expressed in milliseconds squared [HF ln (ms^2)]. Continuous ECG data were divided into three phases of feeding: 30 minutes before feeding to obtain a baseline measure prior to challenge, during feeding, and 60 minutes after feeding to monitor trajectory of recovery to baseline values. In a previous study, it was demonstrated that 30 minutes was not sufficient to capture recovery following feeding (Winters et al., 2006). The HF HRV was calculated in continuous 5-minute epochs across the three phases of feeding. Five-minute epochs are recommended for short-term HRV recordings (Task Force, 1996) and, as used in this study, reduced the effect of brief alterations in infant state and behavior (e.g., burping, defecating, brief crying, or brief arousal) on HF HRV values.

Two types of analyses were used. First, phase average HF HRV was calculated by averaging the 5-minute epochs over the duration of each phase. Second, trajectories of 5-minute epochs across the entire feeding were constructed to provide an accurate picture of within-phase variability. Figure 1 depicts the two types of trajectories for one infant. In the figure, the infant's phase averages demonstrate a clear reduction during feeding followed by a return to prefeeding values after the feeding is complete. However, visualization of the 5-minute epochs within each phase demonstrates wide variability within phases. Information about the variability within phases may be important for understanding overall infant response to the feeding challenge and suggests a need for identifying factors that may contribute to this variability.

Feeding method—Type of feeding was recorded as breastfed, bottle-fed, nasogastric tube-fed, and combinations thereof.

Feeding skill—The Early Infant Feeding Skills Assessment (EFS; Thoyre, Shaker, & Pridham, 2005) was used to measure feeding skill. The EFS is an observational checklist for assessing infant readiness for and tolerance of feeding and for profiling the developmental stage of specific feeding skills. It is appropriate for use in either preterm or full-term infants through 54 weeks postconceptual age (personal communication, S. Thoyre, July 24, 2006). The measure was scored in real time by the investigator during the 2-week and 2-month observations. Four subscales containing a total of 24 items from the Oral Feeding Skill section were used to measure behavioral indicators of infant feeding skill (optimal state and muscle tone, patterns of sucking, coordination of swallowing and breathing, and maintenance of physiologic stability). Three items were scored on a scale of 0 to 3; 20 items were scored on a scale of 0 to 2; one item was scored on a scale of 0 to 1. Higher scores indicated more feeding skill. A total score was obtained by summing then averaging the items, resulting in a possible high score of 2.1. A median split was used to classify infants as having less or more feeding skill. Internal consistency reliability for the TGA group was 0.9 at 2 weeks and 0.8 at 2 months. Detailed information about use of the EFS in the study is available in Harrison (2008).

Maternal sensitivity—The Maternal Support, Attunement, and Warmth (MSAW) subscale of the Parent-Child Early Relational Assessment was used to measure the quality of the mother's affect and behavior during infant feeding (Clark, 1999). This subscale was derived theoretically from items particularly pertinent to the feeding task: sensitivity and responsivity, flexibility, structuring and mediating the environment, lack of intrusiveness, consistency and predictability, positive affect, lack of depression or withdrawn mood, visual contact, warm and kind tone of voice, and amount of verbalization. Scores were based on observations from the first 5-minute section of videotaped feedings to capture the mother's approach to initiating the feeding. Each item was rated on the basis of duration, intensity, and frequency of the behavior or affect observed and scored on a scale of 1 to 5 with 1 = *negative affect or behavior* and 5 = *regulated, adaptive behavior*. The average was obtained for use in analysis. Using standard interpretation, scores of 4 or more reflected strength, whereas those less than 4 were regarded as of clinical concern. Internal consistency reliability was 0.9 at 2 weeks and at 2 months. Additional information about coding, training, and interrater reliability is available in Harrison (2008).

Procedure and Temporal Design

This protocol was approved by the Health Sciences Institutional Review Boards at the participating institutions. Mothers provided written consent. As shown in Figure 2, data were collected at two points in time. The first time point occurred after surgical correction when feedings had been initiated (at approximately 2 weeks of age) and the second time

point occurred 6 weeks later when the infants were approximately 2 months old and early recovery was complete. At each age, a Holter recorder was attached to the infant's chest using seven neonatal electrodes, and ECG recordings were made for 30 minutes prior to the feeding, during the feeding, and for 60 minutes after the feeding was completed. The duration of the feeding varied. Feedings were videotaped.

Data Analysis

Data were analyzed using SPSS version 17.0 and Mondrian (<http://Mondrian.theusRus.de>), an interactive data visualization program in which a number of data plots are constructed and then linked. A case or group of cases is selected (e.g., breastfed infants) and the values for that case or cases are highlighted in all plots displayed (e.g., scatterplots, bar charts, parallel coordinate plots), allowing visualization of relationships and interactions among variables.

Intra-individual change and interindividual differences in individual change reflected in infant trajectories of parasympathetic function across feeding were examined using graphs of HF HRV phase averages. Next, interindividual differences in HF HRV trajectories were depicted and explored using graphs showing relationships between contributing factors (feeding method, feeding skill, maternal sensitivity) and phase averages of HF HRV. Finally, intra-individual change and interindividual differences in HF HRV trajectories were examined by feeding method. Based on the theoretical expectation of reductions in HF HRV during feeding followed by increases in HF HRV postfeeding (a U-shaped curve), the trajectory of HF HRV values in 5-minute epochs across three phases of feeding were fit with a quadratic function for each infant at 2 weeks and 2 months. Time was treated as a continuous variable. Although the phase averages provided a realistic summary of overall parasympathetic activity during each phase, examination of 5-minute epochs produced more data points for each case, adding precision to the model for change as well as offering an accurate picture of variability for the duration of each phase.

Results

Sample

Infant and maternal data, including infant feeding skill and maternal sensitivity scores, are summarized in Table 1. The mothers were primarily non-Hispanic, White women in their late twenties who were married or partnered. The majority of infants were male and bottle-fed. Six infants were diagnosed prenatally. Surgery was completed when the infants were about 7 days old, and they were discharged approximately 2 weeks later. Four breastfed infants were exclusively breastfeeding; one breastfed infant was also receiving bottle feedings at 2 weeks, but was exclusively breastfed at 2 months. Five bottle-fed infants at 2 weeks and one at 2 months were also receiving nasogastric feedings. Mean minutes for each feeding phase were: prefeeding 23.1 ($SD = 7.7$); during feeding 18.4 ($SD = 8.2$); and postfeeding 57.0 ($SD = 5.9$).

Trajectories by Phase Averages at 2 Weeks and 2 Months

Trajectories of HF HRV using prefeeding, during feeding, and postfeeding phase averages at 2 weeks and 2 months are shown in Figure 3. The marked between-infant variability in both height and shape demonstrated in patterns of individual trajectories at 2 weeks appears to be attenuated at 2 months. Magnitude of HF HRV values is higher at 2 months. Six infants demonstrated adaptive response to the feeding challenge (U-shaped curves showing reductions from baseline during feeding and increases post-feeding), even with overall lower pre- and postfeeding values. To illustrate intra-individual change, HF HRV trajectories are

identified in Figure 3 for Infant 12, showing an adaptive response to feeding at 2 weeks, but strikingly lower HF HRV at 2 months with less response physiologically.

Trajectories and Contributing Factors

Feeding skill—Phase average trajectories at 2 weeks with trajectories highlighted for infants with less feeding skill (defined as scores below the median) are shown in Figure 4A. Infants with less feeding skill had HF HRV values distributed from low to high and exhibited trajectories of four different patterns: reductions during feeding, elevations during feeding, increases across feeding, and decreases across feeding. Visualized in this way, feeding skill did not appear to be related to patterns of HF HRV.

Trajectories for infants with lower feeding skill are again highlighted in Figure 4B at 2 months of age. As seen at 2 weeks, trajectories of infants with less feeding skill at 2 months were distributed from low to high values and exhibited patterns similar to those at 2 weeks. Again, feeding skill did not appear to be related to patterns of HF HRV.

Maternal sensitivity—Highlighted phase average trajectories at 2 weeks of age for infants whose mothers had lower sensitivity scores (defined as a score less than 4) are shown in Figure 4C. These infants demonstrated three patterns of trajectories: reductions during feeding, elevations during feeding, and decreases across feeding. Although one infant had high HF HRV values across feeding, the remaining four infants had HF HRV values in the mid- to lower range relative to the group.

Trajectories of infants with maternal low sensitivity scores are again highlighted in Figure 4D at 2 months of age. At this age, HF HRV values were distributed from low to high and exhibited similar trajectory patterns.

Feeding method—Relationships among feeding method, feeding skill, and maternal sensitivity at 2 weeks of age are illustrated in Figure 5A. All five breastfed infants had a higher feeding skill (scores above the median) and their mothers all scored high in sensitivity during the feeding. Figure 5B highlights HF HRV values across feeding in breastfed infants and shows that three of these breastfeeding infants had lower (less responsive) HF HRV values across phases of feeding relative to the group.

Among bottle-fed infants, seven of nine (78%) had feeding skill scores lower than the group median at 2 weeks (one infant receiving exclusive nasogastric feedings is not included). Maternal sensitivity scores were distributed more widely than with the breastfeeding mothers, and six (67%) scored in the area of clinical concern (scores less than 4). Patterns of HF HRV across feeding for these bottle-fed infants were distributed fairly evenly relative to the group. The infant with the lowest score in feeding skill (1.1) whose mother had *high* sensitivity scores (4.9) demonstrated relatively high HF HRV with a linear increase across phases of feeding (Figure 5). This pattern could be a variant of adaptive regulation demonstrating enhanced parasympathetic function postfeeding. Two infants had lower feeding skill (1.4, 1.5) and mothers with *low* sensitivity scores (3.4, 3.7). Both of these infants demonstrated a possibly maladaptive trajectory of lower prefeeding HF HRV, increases during feeding, and declining HF HRV postfeeding.

Relationships among feeding method, feeding skill, and maternal sensitivity at 2 months of age are shown in Figure 6A. Breastfeeding infants continued to have high feeding skill, and their mothers had high scores in sensitivity. Patterns of HF HRV across feeding in breastfeeding infants were shown in Figure 6B to be distributed more evenly relative to the group when compared with 2 weeks.

Six of ten (60%) of bottle-fed infants at 2 months of age had feeding scores below the group median, and maternal sensitivity scores continued to be widely distributed. The same infant with less feeding skill and high maternal sensitivity scores at 2 weeks of age (shown in Figure 6A with a square) again demonstrated a possibly adaptive HF HRV trajectory of increases across phases of feeding. The infant with less feeding skill (1.8) and lower maternal sensitivity (2.9) scores at 2 months (shown in Figure 6A with a circle) had an extremely low (less responsive) HF HRV that varied little across the feeding phases.

Exploration of Quadratic Curves

Based on the theoretical expectation of reductions in HF HRV during feeding followed by increases in HF HRV postfeeding (a U-shaped curve), data resulting from HF HRV values in 5-minute epochs were fit with a quadratic function for each infant at 2 weeks and 2 months. The mean of available time points for analysis was 19.9 ($SD = 2.2$). Quadratic regression lines are depicted for breastfeeding infants in Figure 7 and bottle feeding infants in Figure 8. Each infant's trajectory is shown at 2 weeks and 2 months of age and the during-feeding phase is shaded. The quadratic curves were both positive (U-shaped) and negative (inverted U-shaped) and several infants had considerable scatter around the regression line.

Breastfed infants—Four of the five breastfeeding infants showed clear increases in overall HF HRV values between 2 weeks and 2 months of age (Infants 1, 3, 5, and 8). At 2 weeks of age, two infants demonstrated the theorized U-shaped curve (Infants 3 and 5) and three infants demonstrated an inverted U-shaped curve (Infants 1, 8, and 9). By 2 months, all of the breastfed infants demonstrated some level of expected reductions across the feeding as a whole. However, clear reductions in the during-feeding phase followed by increases after feeding were not seen except for Infants 3 and 8 at 2 months. Data from one infant fit the regression line fairly well (Infant 5 at 2 weeks); the rest showed a fair amount of scatter around the regression line, (especially Infants 1 and 8 at 2 weeks and Infants 1, 3, 5, and 8 at 2 months).

Bottle-fed infants—Four of the eight bottle-fed infants showed increases in HF HRV between 2 weeks and 2 months (Infants 2, 4, 13, and 14), and two infants showed reductions (Infants 12 and 15). At 2 weeks, three infants had shallow U-shaped curves (Infants 2, 4, and 10) and two had more linear slopes (Infants 12 and 15). Four infants changed type of trajectory between 2 weeks and 2 months: three from U-shaped to inverted U-shaped (Infants 2, 4, and 10) and one from inverted U-shaped to U-shaped (Infant 11). Clear reductions in the during-feeding phase were seen in Infant 2 at 2 weeks and Infant 4 at 2 months. Data from four infants fit the regression line fairly well (Infants 4, 14, and 15 at 2 weeks; Infant 12 at 2 months); the rest showed a fair amount of scatter around the regression line.

Discussion

Although infants with complex congenital heart defects commonly experience difficulties with the challenge of feeding (Clemente et al., 2001), autonomic response to feeding in this population has not been well-studied. Knowledge of how these infants handle the challenge of feeding is important to identify possible interventions in support of adaptive autonomic function and development. The trajectory of autonomic response to feeding in healthy full-term infants has been examined in one study (Lappi et al., 2007); HF HRV decreased during feeding and increased immediately after feeding. Similar reductions in HF HRV during feeding and increases postfeeding have been demonstrated in healthy premature infants (Brown, 2007). This paper provided a description of an exploratory graphical analysis of HF

HRV across the challenge of feeding in a small sample of infants with TGA, with the expectation that similar reductions in parasympathetic function during feeding and increases postfeeding would be indicative of an adaptive response to this challenge to homeostasis.

Visual examination of trajectories of HF HRV across feeding in this sample of 15 infants with TGA revealed two important features. First, the magnitude of HF HRV values varied markedly among infants at both points in time. Significant individual variability in the magnitude of HF HRV values is recognized (Grossman & Taylor, 2007) and may suggest the need to focus primarily on the pattern of trajectory rather than relative magnitude of HF HRV value. Second, four primary patterns of trajectories relative to baseline were observed: (a) decreasing during feeding and increasing toward baseline postfeeding, (b) maintaining or slightly increasing during feeding and continuing to increase postfeeding, (c) decreasing during feeding and continuing to decrease postfeeding, and (d) increasing during feeding and decreasing toward baseline postfeeding. Significance of the four types of observed trajectories is not known, but will serve as the basis for future study.

The first pattern of decreased HF HRV during feeding followed by increases postfeeding was expected theoretically and was similar to that of healthy term and preterm infants. The second pattern of increasing HF HRV across feeding demonstrated that infants maintained or slightly increased parasympathetic function during feeding and increased parasympathetic function after the feeding was complete. This may be an alternative type of adaptive response to the feeding challenge. For some infants, maintaining or even increasing parasympathetic function during feeding may be important to avoid being overwhelmed by enhanced sympathetic activity. The subsequent postfeeding increase in HF HRV suggests an adaptive ability to support growth through enhanced parasympathetic function.

The third pattern depicting declining parasympathetic function across the duration of the feeding might be an indication of an inability to respond to or recover from the challenge of feeding. The fourth pattern of increases rather than decreases in HF HRV during feeding and reductions rather than increases postfeeding is opposite of the theoretically expected pattern. Higher parasympathetic activity has been associated with an increase in randomness of heart rate (Stein, Domitrovich, Huikuri, & Kleiger, 2005). A trajectory of increasing parasympathetic activity associated with the challenge of coordinating sucking, swallowing, and breathing may reflect more erratic cardiac rhythms as a result of high sympathetic activation from the effort of meeting the feeding challenge in these high-risk infants. Additional nonlinear analyses would be useful in further elucidating these processes (Stein et al., 2005). For example, Poincare plots provide graphical visualization of relationships between successive interbeat intervals. The shape and dispersion of the resulting ellipse provides evidence of the level of randomness of the heart rate associated with abnormalities in cardiac function (Stein et al., 2005). These trajectory patterns provide important information for selecting criteria for fitting nonlinear models. Based on the four types of trajectories observed, both positive and negative quadratic and linear functions need to be modeled in subsequent studies.

Developmental effects on HF HRV were demonstrated by increases in HF HRV between 2 weeks and 2 months of age in 80% of the breastfeeding infants and in 50% of the bottle-fed infants. These increases in magnitude over time are consistent with developmental changes in HF HRV that have been observed in healthy infants between birth and 6 years of age (Massin & von Bernuth, 1997). Lack of developmental change in many of the bottle-fed infants is concerning and deserves further investigation in subsequent larger longitudinal studies of a longer duration to determine how these trajectories change or remain stable over time.

Factors potentially influencing parasympathetic function in these infants included feeding method, feeding skill, and maternal sensitivity. Results from this initial analysis support inclusion of each of these variables in future statistical models.

Feeding skill and maternal sensitivity

Graphical depictions in this small sample did not suggest relationships between HF HRV patterns and either feeding skill or maternal sensitivity. However, HF HRV trajectories of individual infants illustrated potential concerns. The infant with the lowest feeding skill score whose mother had high sensitivity scores demonstrated steady increases in HF HRV across feeding at 2 weeks and at 2 months, suggesting the ability to maintain a physiological state supportive of homeostasis with the feeding challenge. In contrast, infants with feeding skill below the median whose mothers were less able to support their infants with sensitivity during feeding demonstrated unexpected increases during feeding (at 2 weeks of age), and very low HF HRV with little change across feeding (at 2 months of age), suggesting problems with these infants' abilities to recover adaptively. Perhaps maternal sensitivity during feeding is particularly important for autonomic function in infants with relatively less feeding skill. Inclusion of measures of maternal sensitivity as well as feeding skill in future statistical models will advance understanding of these relationships.

Feeding method

Magnitude of HF HRV and patterns of trajectories over time appeared to differ based on feeding method. Breastfed infants exhibited change toward a theoretically more adaptive ANS response over time as well as increases in magnitude of HF HRV over time. In contrast, the majority of bottle-fed infants did not develop anticipated U-shaped curves and many did not exhibit clear increases in magnitude. Inclusion of feeding method in future statistical models and combining measures of HF HRV with nonlinear measures of variability may enhance understanding in future research.

This study was designed to depict changes in HF HRV across feeding. First, phase averages were calculated from 5-minute segments within each phase. This provided a realistic summary of overall parasympathetic activity during each phase and suggested a need for both quadratic and linear regression lines. Second, trajectories of 5-minute epochs across phases of feeding were illustrated. This offered more precision in constructing a model of change over feeding phases and an accurate picture of variability within each phase. Although the quadratic curves constructed using 5-minute HF HRV epochs across feeding phases seemed appropriate for most infants, many were negative curves rather than the expected positive curve, and most infants demonstrated considerable scatter of HF HRV values around the regression lines. The significance of negative quadratic terms and change from positive to negative curves or vice versa between two weeks and two months is not known. Likewise, the significance of the widely scattered HF HRV values as compared to values more closely fitting a regression line is not known. Potential factors (external or internal) contributing to these intra-individual and interindividual differences will need to be identified and included in statistical models. An analysis of infant state measured every 30 to 60 seconds over the duration of the ECG recording would be valuable to assess effects of various infant states and behavior on HRV in this population.

Limitations—One limitation of the design is that the length of pre-feeding ECG data collection varied among infants. Despite scheduling data collection based on times when mothers anticipated a feeding, timing of feedings was not entirely predictable in these young infants. When the infant was ready to eat, the mother was allowed to feed. As a result, the number of prefeeding epochs averaged for phase HRV values were not equal among infants. This difference in prefeeding epochs also made comparisons of trajectories more difficult.

Summary—This exploratory data analysis provided critical information in preparation for a larger study in which varying trajectories and potential contributing factors can be modeled in relationship to infant outcomes. Examination of heart rate variability trajectories in future studies need to include both phase averages and 5-minute epochs, positive and negative quadratic and linear functions, and frequency domain and nonlinear HRV analyses. Findings from this initial analysis support inclusion of feeding method, feeding skill, and maternal sensitivity in statistical models constructed to examine autonomic nervous system function across feeding in infants with complex congenital heart defects.

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Figure 1.

Example of high frequency heart rate variability (HF HRV) measure in one infant across three phases of feeding by 5-minute epoch (solid line) and phase average (dashed line). During-feeding phase is shaded.

Figure 2. Data collection protocol. High frequency heart rate variability (HF HRV) measured pre-, during, and postfeeding. Maternal sensitivity, attunement, and warmth (MSAW) measured using one videotaped feeding at each age. Feeding skill measured in real time during feeding.

Figure 3. Individual trajectories of high frequency heart rate variability (HF HRV) by phase averages at 2 weeks and 2 months of age. Arrows identify Infant 12 trajectories at 2 weeks and 2 months, illustrating one infant's change over time.

Figure 4.

High frequency heart rate variability (HF HRV) by phase averages. Infants with feeding skill less than the group median are depicted in dashed lines at 2 weeks (A) and 2 months (B). Infants whose mothers' maternal sensitivity, attunement, and warmth (MSAW) scores were less than 4 are depicted in dashed lines at 2 weeks (C) and 2 months (D).

Figure 5. Relationships among feeding method; feeding skill; maternal sensitivity, attunement, and warmth (MSAW); and high frequency heart rate variability (HF HRV) at 2 weeks of age. One infant receiving exclusive nasogastric feedings at this age is not shown. (A) depicts feeding skill by maternal sensitivity for each infant. Breastfed infants are identified with triangles; bottle-fed infants with dots. Area of graph encompassing feeding skill below the median and maternal sensitivity, attunement, and warmth (MSAW) scores less than 4 is enclosed with dotted lines. Squared dot identifies one infant with less feeding skill and high MSAW scores. Circled dots identify two infants with less feeding skill and low MSAW scores. Arrows are drawn to these infants' high frequency heart rate variability trajectories in (B). (B) depicts high frequency heart rate variability by feeding phase. Breastfed infants are identified with dashed lines; bottle-fed infants with solid lines.

Figure 6.

Relationships among feeding method; feeding skill; maternal sensitivity, attunement, and warmth (MSAW); and high frequency heart rate variability (HF HRV) at 2 months of age. (A) depicts feeding skill by maternal sensitivity for each infant. Breastfed infants are identified with triangles; bottle fed infants with dots. Area of graph encompassing feeding skill below the median and maternal sensitivity, attunement, and warmth (MSAW) scores less than 4 is enclosed with dotted lines. Squared dot identifies one infant with less feeding skill and high MSAW score. Circled dot identifies one infant with less feeding skill and low MSAW score. Arrows are drawn to these infants' high frequency heart rate variability trajectories in (B). (B) depicts high frequency heart rate variability by feeding phase. Breastfed infants are identified with dashed lines; bottle-fed infants with solid lines.

Figure 7. Quadratic regression lines fit to 5-minute epochs of high frequency heart rate variability (HF HRV) across feeding in breastfed infants at 2 weeks and 2 months of age. During-feeding phase is shaded.

Figure 8.

Quadratic regression lines fit to five minute epochs of high frequency heart rate variability (HF HRV) across feeding in bottle fed infants at 2 weeks and 2 months of age. During-feeding phase is shaded. Two bottle-fed infants are not depicted: one was exclusively nasogastric tube fed at 2 weeks and one was missing during feeding data at 2 months due to equipment failure.

Table 1

Infant and Maternal Data

Variable	n	%	Mean	SD	Range
Infant male gender	9	60.0			
Feeding type					
Breast	5	33.3			
Bottle	10	66.7			
Prenatal diagnosis	6	40.0			
Infant weight (grams)			3484.1	482.5	2551–4252
Infant age (days)					
Surgery			6.8	2.9	2–11
2-week data collection			17.1	3.9	11–25
2-month data collection			59.1	4.4	52–67
Infant Early Feeding Skills score					
2 weeks (<i>median</i>)			1.7	0.3	1.1–2.1
2 months (<i>median</i>)			2.0	0.1	1.6–2.0
Maternal age (years)			28.7	5.0	21–37
Married/partnered mothers	15	100.0			
Maternal education					
Less than bachelor's degree	8	53.4			
Bachelor's degree or higher	7	46.6			
Race and ethnicity					
Black or African American	1	6.7			
Non-Hispanic, White	14	93.3			
Hispanic, White	0	0			
Maternal sensitivity scores					
2 weeks			4.1	0.6	3.0–4.9
2 months			3.9	0.7	2.8–4.7