FEEDING OUTCOMES IN VERY PRETERM INFANTS: PRELIMINARY EFFECTS OF POSITIONING

Jinhee Park

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Approved by:

Suzanne M. Thoyre, Ph.D., RN.

Susan Brunssen, Ph.D., RN.

Barbara Waag Carlson, Ph.D., RN.

Eric Hodges, Ph.D., FNP-BC.

Diane Hudson-Barr, Ph.D., RN.

George Knafl, Ph.D.

ABSTRACT

JINHEE PARK: Feeding Outcomes in Very Preterm Infants:
Preliminary Effects of Positioning
(Under the direction of Dr. Suzanne Thoyre)

Background/Significance: Oral feeding emerges during a dynamic process of the organization of inputs from subsystems within the infant and the environment. Very preterm infants (VP, ≤ 30 weeks gestational age) are at risk for impaired lung function, which significantly limits their organizational capacity and contributes to feeding difficulties. A head-elevated side-lying (HEL) position has recently been proposed as a strategy that may improve oral feeding in VP infants by supporting breathing during feeding.

Purpose: The primary purpose of this study is to test the preliminary effects of the HEL position on the physiologic stability and feeding performance of VP infants when bottle-fed, compared to the head-elevated supine (HES) position. In addition, methods for measuring changes in physiologic stability across the feeding period are examined.

Methods: Using a within-subject cross-over design, six VP infants were bottle-fed twice on one day, in both the HEL and HES positions. The following variables were measured before and/or during feeding: physiological stability (heart rate [HR], oxygen saturation [SpO_2], respiratory characteristics) and feeding performance (overall milk transfer, proficiency, efficiency, and duration of feeding). Three methods were used to examine changes in physiologic stability across the feeding period.

Results: Compared to the HES position, VP infants fed in the HEL position show significantly less variation in HR, less severe and fewer decreases in HR, shorter and more regular intervals between breaths, breathing frequency that is closer to the pre-feeding state, and more variation in breath duration. VP infants also demonstrate a more stable HR over time, especially during the early minutes of feeding, and improved regulated breathing over time by demonstrating shorter and more regular intervals between breaths and more variation in breath duration across the feeding period. In addition, the method using the first 6 minutes of bottle-in period is suggested as the most effective for examining significant changes in physiologic stability over time. No significant findings for SpO_2 and feeding performance are found.

Conclusions: The findings indicate that the HEL position may be a feeding strategy to support better regulation of breathing during feeding that allows VP infants to better maintain physiologic stability throughout the feeding.

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BPD	Bronchopulmonary dysplasia
CV	Coefficient of variance
CS	Continuous sucking
D-EFS	Dynamic-early feeding skills
ECG	Electrocardiogram
GA	Gestational age
HEL	Head-elevated side-lying
HES	Head-elevated supine
HR	Heart rate
IS	Intermittent sucking
LMM	Linear mixed modeling
NBRS	Neurobiological risk score
NCCC	Newborn Critical Care Center
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care unit
PMA	Postmenstrual age
RESCs	Respiratory characteristics
SD	Standard deviation
SpO_2	Oxygen saturation
VP	Very preterm

CHAPTER I

INTRODUCTION

In the United States, over 80,000 babies are born *very preterm* (VP $\leq$ 30 weeks gestational age) every year (Hamilton, Martin, & Ventura, 2010). These infants are at high risk for impaired lung function due to early exposure of the immature lungs to extrauterine conditions and their need for supplemental oxygen or airflow for prolonged periods (Ehrenkranz et al., 2005; Jobe & Bancalari, 2001). The impaired lung function, combined with prematurity, significantly interferes with these infants' ability to eat, which contributes to frequent feeding difficulties.

Oral feeding behavior emerges from nonlinear and dynamic interactions of multiple systems that are involved in oral feeding (Goldfield, 2007). These systems include the oral-motor, neurologic, cardio-respiratory, and gastrointestinal systems, which continuously self-organize both within and between the systems to establish stability in response to the internal inputs from the infant and external inputs from the environment. This self-organization process creates a functional feeding synergy, i.e., sucking, swallowing, and breathing, in which the infant sucks sufficiently to meet his or her nutritional needs for growth, swallows swiftly to minimize the disruption of breathing, and breathes with adequate depth and frequency to maintain physiologic stability.

However, for VP infants, impaired lung function limits their ability to self-organize, thus generating inefficient feeding synergies that contribute to feeding difficulties. VP infants are not able to integrate a sufficient number and depth of breaths into sucking and swallowing rhythms consistently; therefore, breathing is disrupted, interrupted, abbreviated, and for brief periods completely absent during feeding (Craig, Lee, Freer, & Laing, 1999; Gewolb & Vice, 2006; Lau, Smith, & Schanler, 2003). Thus, sucking strength and frequency is limited for VP infants, which in turn decreases their milk intake, and thus limits the amount of swallowing that is required and minimizes the interruption of breathing that swallowing creates (Gewolb, Bosma, Taciak, & Vice, 2001; Mizuno et al., 2007). Although this adaptation may increase a VP infant's physiologic stability, it is at the expense of sufficient intake. Further, when immaturity limits the ability of the infant to increase breathing by decreasing his or her sucking frequency or strength, insufficient breathing may result in physiologic distress, fatigue, and early cessation of feeding.

These inefficient or dysfunctional feeding synergies contribute to feeding difficulties in VP infants, as evidenced by increased physiological instability (Craig et al., 1999; Gewolb & Vice, 2006; Mizuno et al., 2007; Thoyre & Carlson, 2003), poor sucking patterns (Gewolb, Bosma, et al., 2001; Medoff-Cooper, McGrath, & Shults, 2002; Mizuno et al., 2007; Mizuno & Ueda, 2003), poor coordinated rhythms of swallowing and breathing (Gewolb & Vice, 2006; Lau et al., 2003; Mizuno & Ueda, 2003), poor intake (Lau et al., 2003; Mizuno et al., 2007), and a prolonged length of time before becoming a full oral feeder (Pickler, Mauck, & Geldmaker, 1997; Pridham et al., 1998). If left unresolved, feeding difficulties may persist for years after discharge from the hospital (Hawdon, Beauregard, Slattery, & Kennedy, 2000; Thoyre, 2007) and contribute to chronic growth failure and altered eating patterns (Kurzner et al., 1988; Wood et al., 2003). Thus, for VP infants, feeding strategies need to focus on supporting breathing in order to maintain physiological stability throughout feeding and to enable them to continue to feed long enough to obtain adequate nutritional intake for growth.

The correct positioning of the infant during feeding is a potential strategy for improving breathing during feeding (L. Clark, Kennedy, Pring, & Hird, 2007; McFarland, Lund, & Gagner, 1994; Mizuno et al., 2007). A head-elevated supine (HES) position is commonly used in the neonatal intensive care unit (NICU) when preterm infants are bottle-fed. This position reduces the work of breathing by facilitating an infant's lung expansion through a 45-60 degree angle of head elevation (Dellagrammaticas, Kapetanakis, Papadimitriou, & Kourakis, 1991; Jenni et al., 1997). It also enhances the caregiver's ability to provide support of the head-neck alignment in a neutral position and provides better visual access for nurses and parents to observe the infant's responses to feeding. However, the HES position may interfere with maintaining adequate patency of the upper airway by allowing the soft palate and tongue to fall back due to gravity, thus contributing to inefficient breathing. Also, gravity increases the transit time of the milk to the back of the oral cavity, so the infant may have less time to control the bolus of milk that creates the conditions for dysfunctional swallowing, thus increasing the potential for breathing interruptions and aspiration during feeding.

A head-elevated side-lying (HEL) position recently has been proposed as a potential strategy that may avoid some of the disadvantages of the HES position (L. Clark et al., 2007). The HEL position is a common position for an infant feeding naturally at the breast. Better coordination of breathing with swallowing (Goldfield, Richardson, Lee, & Margetts, 2006) and less disruption of breathing (Blaymore Bier et al., 1997; Dowling, 1999; P. P. Meier, 2001) have been reported in breastfeeding compared to bottle feeding. Because the HEL position may better mimic breast-feeding when an infant is bottle-fed, as compared to the HES position, infants who feed in the HEL position may be able to assume some of the advantages of breastfeeding to improve their breathing during feeding. The HEL position may also facilitate safe and efficient swallowing by creating conditions for better fluid management during feeding (Lau & Schanler, 2000; Mathew, 1991a). In the HEL position, the lowered angle of the bottle slows the gravitational milk flow by decreasing the hydrostatic pressure generated by the volume of milk in the inverted bottle. The milk flows into the infant's cheeks first and has a slower transit time to the back of the oral cavity. Thus, the slower flow of milk may allow the infant to have more time to form a bolus and control the movement of that bolus. This ability allows the infant to swallow more safely and efficiently, thereby preventing aspiration and prolonged breathing interruption. The HEL position also reduces the work of breathing by facilitating upper body antigravity control (Vanderghem, Beardsmore, & Silverman, 1983) and promoting better patency of the upper airway that may be a result of reduced gravitational effects on the anatomical tissues (e.g., tongue and soft palate) surrounded by the upper airway (Litman et al., 2005).

Despite the potential benefits of the HEL position, very limited evidence of the effects of this feeding position on feeding outcomes has been published. Thus, studies to test the preliminary effects of the HEL position as a feeding intervention are needed.

To examine the short-term effects of feeding interventions, a number of variables have been used. These variables are primarily cardio-respiratory variables that include heart rate (HR), respiratory rate, and/or percentage of hemoglobin saturated with oxygen, which is commonly referred to as oxygen saturation (SpO_2) (L. Clark et al., 2007; Dowling, 1999; Hill, Kurkowski, & Garcia, 2000; Mathew, 1991a; McCain, 1995; Mizuno, Inoue, &

Takeuchi, 2000; Pickler, Frankel, Walsh, & Thompson, 1996; Shiao, Youngblut, Anderson, DiFiore, & Martin, 1995), sucking performance (Mizuno et al., 2000; Pickler & Reyna, 2004; Scheel, Schanler, & Lau, 2005), and actual oral feeding performance, including overall milk transfer, proficiency, and/or efficiency (Dowling, 1999; Lau & Schanler, 2000; Pickler & Reyna, 2004). Most studies use the averaged values of each variable during the entire feeding time. Some studies analyze only subsections of feedings, e.g., continuous versus intermittent sucking periods (Shiao et al., 1995), or the first and last three minutes of feeding (Hill et al., 2000). However, because infants' oral feeding behaviors are emergent as the subsystems continuously interact, and thus can change across the feeding period, an averaged outcome based on the entire feeding or based on data extracted from subsections of the feeding cannot take into account feeding dynamics and the non-stationary state of infants' feeding responses.

For example, even if two infants have a similar number of physiologic distress events or the same mean SpO_2 level during feeding, the patterns of physiologic responses to feeding can be different from each other. One infant may exhibit more physiologic instability during the early period of feeding, but may gradually adapt and become more physiologically stable across time. In contrast, another infant may maintain physiologic stability during the early period of feeding, but may become fatigued and less physiologically stable as the feeding progresses. That is, these different patterns of physiologic stability can reflect different infant adaptive capacities. If the aim is to customize feeding interventions to the individual infant's needs, these two infants would require different feeding interventions. Thus, a more precise method of measuring physiologic stability across time may enhance the understanding of infants' feeding difficulties and bring more precision to the application of feeding interventions.

Therefore, the primary purpose of this study is to test the preliminary effects of the HEL position compared to the HES position on the physiologic stability and feeding performance of VP infants when bottle-fed. In addition, this research examines methods for measuring changes in physiologic stability across the feeding period.

RESEARCH QUESTIONS AND HYPOTHESES

It is hypothesized that, when compared to VP infants fed in the HES position, VP infants fed in the HEL position will demonstrate:

H1: greater physiologic stability (i.e., less variation in HR and SpO_2, less severe and fewer changes in HR and SpO_2, a higher respiratory rate that is closer to that of the pre-feeding state, and less variation in breath-to-breath intervals and in the duration and amplitude of breaths) and better feeding performance (i.e., overall milk transfer, proficiency, efficiency, and duration of feeding) over the entire feeding period; and

H2: fewer changes in physiologic stability from the pre-feeding period across the feeding period. Three methods are chosen to examine the changes in physiologic stability across the feeding period in order to explore this hypothesis.

If the HEL position is found to produce better responses than the HES position, this information will provide a foundation for developing a randomized controlled trial to investigate the effects of the HEL position more definitively using physiologic measures that are sensitive to the changing dynamics of VP infant feeding. This new feeding strategy has the potential to promote the development of oral feeding skills and support adequate growth and development in VP infants and serve as a feeding strategy that can readily be applied to neonatal care.

CHAPTER II

This chapter presents the theoretical framework and literature review. As the purpose of this study is to examine the preliminary effects of feeding position and methods for measuring changes in physiologic stability across feeding, the literature review discusses oral feeding during infancy, the development of oral feeding skills in preterm infants and VP infants, and feeding problems in VP infants and how feeding position may improve these problems.

The foundation for understanding the mechanisms of infant oral feeding is provided in discussion of the three major components of oral feeding, i.e., sucking, swallowing, and breathing, and their interrelationships during feeding. The next section discusses the challenges of preterm infants and VP infants for developing competent oral feeding skills. The section regarding feeding problems in VP infants summarizes the current literature on this topic and examines measures and variables that have been used to evaluate feeding problems in this population. Next, feeding positions that have been used when feeding infants, advantages and disadvantages of each feeding position as they apply to VP infants, and reasons that the HEL position is a potential strategy to improve feeding problems in VP infants are discussed. Finally, a brief discussion of nursing implications is provided in terms of ways that the HEL position is applicable to clinical settings as a feeding strategy as well as ways that methods used to determine changes in physiologic stability across the feeding are applicable to feeding research.

THEORETICAL FRAMEWORK

Dynamic systems theory guides the understanding of the complexities of feeding dynamics in infants and positioning as a feeding intervention (Goldfield, 2007; Thelen & Spencer, 1998; Thelen & Ulrich, 1991). Infant oral feeding is a highly complex and dynamic process in nature that requires interactions of multiple subsystems, including the oral-motor, neurological, cardio-respiratory, and gastrointestinal systems. These systems continuously interact both within and between the systems to establish stability in response to the internal inputs from the infant and external inputs from the environment during feeding. This continuous process of interactions among subsystems toward stability is called *self-organization* (J. E. Clark, 1995; Thelen & Ulrich, 1991). Through self-organization, the infant generates a functional feeding synergy, i.e., sucking, swallowing, and breathing, in which oral feeding behavior emerges as a consequence.

During feeding, the goals of breathing and feeding appear to compete with each other for the limited anatomical resources of the pharyngeal anatomy (Rogers & Arvedson, 2005). That is, for breathing, the airway opens to transfer air to the lungs, and for swallowing, the airway needs to be closed to move fluid and food directly into the esophagus. Thus, in the process of self-organization, these subsystems must find the most effective relationships amongst sucking, swallowing, and breathing that lead to conditions where the demands of breathing and feeding are balanced adequately. When the most ideal feeding synergies are created through self-organization, the demands of breathing and feeding are balanced adequately, and the infant sucks with efficiency and endurance to obtain adequate nutritional needs for growth, swallows safely and rapidly to minimize the interruption of breathing, and breathes with an adequate number and depth of breaths. However, when inefficient and dysfunctional feeding synergies are created for any reason, this balance of breathing and feeding is destabilized, and breathing may be suppressed excessively during sucking and swallowing, resulting in physiologic distress, fatigue, and early cessation of feeding. In this way, oral feeding behavior emerges from the ongoing interactions of constituent subsystems, rather than being fixed by maturational events in the nervous system (Thelen & Ulrich, 1991). Therefore, the feeding behaviors that have emerged through the self-organization process can be used to examine and understand infants' feeding difficulties.

Each subsystem involved in oral feeding also has the capacity for shaping and guiding the dynamics of the oral feeding system. That is, if any one of the subsystems is limited in its ability to self-organize, the self-organization of the entire feeding system and, therefore, the feeding synergy will be compromised. Thus, the functionality of each subsystem sets boundaries, thereby either facilitating or constraining the entire feeding system's ability to self-organize (J. E. Clark, 1995; Handford, Davids, Bennett, & Button, 1997; Humphry, 2002).

The functionality of each subsystem also can be affected by internal and external factors. Internal factors are the infant's inherent characteristics that impact oral feeding skills and may include, but are not limited to, the infant's level of maturity, health condition, and feeding experience. For example, immaturely developed oral-motor, neurological, cardio-respiratory, and/or gastrointestinal systems can interfere with any one or more of the functions of sucking, swallowing, and breathing, thus generating inefficient and dysfunctional feeding synergies that could contribute to feeding difficulties. However, these immature infant feeding skills improve and develop as the subsystems mature with an increase in postmenstrual age (PMA) (Amaizu, Shulman, Schanler, & Lau, 2008; Lau, Alagugurusamy, Schanler, Smith, & Shulman, 2000; Mizuno & Ueda, 2003). In addition, preterm infants who are born at a young gestational age (GA), especially less than 30 weeks, often have complications due to prematurity, most notably, necrotizing enterocolitis (NEC), neuro-developmental impairments, and bronchopulmonary dysplasia (BPD). These complications, combined with prematurity, can significantly interfere with any one or more of the functions of the subsystems that are involved in the feeding process. Therefore, such complications can limit the infant's ability to self-organize the entire feeding system, which could result in even more severe and frequent feeding difficulties as well as further interfere with the expected normal development of oral feeding skills (Gewolb, Bosma, et al., 2001; Gewolb & Vice, 2006). Many studies have documented the co-morbidities of preterm infants as a significant contributor to increased feeding problems and delayed development of competent oral feeding skills (Jadcherla, Wang, Vijayapal, & Leuthner, 2010; Pickler et al., 1997; Pickler & Reyna, 2003; Pridham et al., 1998).

Moreover, the feeding experience is one of the critical internal factors that impacts infant oral feeding skills. As infants explore the most effective feeding synergies through self-organization, they learn to reduce the competition between the goals of breathing and feeding by changing the characteristics of the sucking, swallowing, and breathing rhythms. Thus, the feeding synergies that emerge become more cooperative rather than competitive through experience with oral feeding. Clinical evidence supports this idea by showing a more rapid transition to full oral feedings and a shorter length of stay in the NICU when preterm infants have more oral feeding experience per day, regardless of the infant's health condition (Pickler, Best, & Crosson, 2009).

Because each subsystem is open to environmental factors, the functionality of these subsystems also can be affected by external factors. External factors are contextual factors that surround the infant during feeding and impact the oral feeding process. These environments include the distal environment (e.g., the NICU environment, especially lights and noise) and the proximal environment (e.g., flow of milk, the positioning of the infant, and the caregiver's feeding strategies). Successful and safe oral feeding requires that the infant can self-organize the feeding system in response to external and internal challenges well enough to maintain physiologic stability throughout the feeding. However, because preterm infants have increased internal challenges due to immature or impaired functionality of those subsystems (i.e., the oral-motor, neurological, cardio-respiratory, and gastrointestinal systems), the energy expenditure required to modulate these internal challenges is already high, and additional energy may be less available for external challenges. Thus, for preterm infants, especially those with increased internal challenges, external challenges from the environment become even more critical for the self-organization process.

Because external factors can be modified, they can be targeted to facilitate the self-organization of the feeding system. One external factor is NICU environment. Excessive noise and light in NICU have been documented as environmental stresses that create adverse changes in physiological responses (Peng et al., 2009; Wachman & Lahav, 2010) and to which the infant must adjust during feeding. Therefore, if the noise and light are controlled or minimized during feeding, the additional effort needed to deal with these demands could be avoided, thereby allowing the infant to focus on the oral feeding process.

Moreover, fast milk flow from the bottle can increase the bolus size of each suck and swallowing frequency, which can contribute to more interrupted breathing due to swallowing, thereby increasing breathing difficulties (Al-Sayed, Schrank, & Thach, 1994; Mathew, 1991a). In contrast, slow milk flow may allow infants to have more time to form a bolus and control its movement, thus contributing to safe and efficient swallowing that minimizes breathing interruptions and consequently improves feeding performance (Lau, Sheena, Shulman, & Schanler, 1997). Similarly, when the infant is fed in the side-lying or prone position, the upper airway may be less constrained by anatomical tissues (i.e., the tongue and soft palate) due to gravity than in the supine position, thereby promoting better patency of the upper airway (Litman et al., 2005). Thus, the flow of milk and feeding position are two of the external factors that may either impose more demands or reduce the challenge of feeding.

Finally, the caregiver co-regulates the feeding process. When the infant is fed by a supportive caregiver who recognizes and responds promptly to the infant's cues (e.g., holding the nipple still when the infant pauses to reorganize his/her breathing after sucking bursts, rather than jiggling it to stimulate sucking), the infant's ability to self-organize the feeding process may be improved (Thoyre & Brown, 2004).

In accordance with the extant subsystems that interact within the infant and environment, infants must take multiple paths to create the stability that emerges from the self-organization process (Goldfield, 1995; Thelen & Ulrich, 1991). Thus, identifying and examining changes in the feeding synergies that have emerged through the continuous self-organization process can contribute to a better understanding of infants' feeding difficulties. For example, most physiologically stable infants (e.g., healthy full-term and preterm infants) are able to adjust their breathing patterns along with sucking and swallowing to maintain physiologic stability over the course of the feeding, even if this adjustment is more efficient in full-term infants than preterm infants (Mathew, Clark, Pronske, Luna-Solarzano, & Peterson, 1985; Shivpuri, Martin, Carlo, & Fanaroff, 1983). Thus, the feeding systems of these physiologically stable infants may be better able to balance the demands of breathing and feeding (than those of VP infants who have more internal constraints), thereby decreasing any instability in their physiologic responses throughout the feeding and contributing to adequate nutritional intake for growth.

However, for VP infants (≤ 30 weeks of GA), the ability to self-organize system components is often compromised by their inherent impaired lung functioning and prematurity (Gewolb, Bosnia, Reynolds, & Vice, 2003; Gewolb & Vice, 2006; Mizuno et al., 2007). VP infants are not able to integrate a sufficient number and depth of breaths into sucking and swallowing rhythms consistently; breathing is disrupted, interrupted, abbreviated and, for brief periods, completely absent during feeding. VP infants may limit sucking in order to limit the amount of swallowing that is required to minimize the interruption of breathing that occurs during swallowing (Gewolb, Bosma, et al., 2001; Mizuno et al., 2007). This adaptation may increase their physiologic stability, but this strategy is at the expense of sufficient milk intake. Further, when immaturity limits the ability of the infant to increase breathing by decreasing his or her sucking frequency or strength, insufficient breathing may ensue, leading to physiologic distress, fatigue, and early cessation of feeding. Thus, the feeding system of VP infants may be less able to balance the demands of breathing and feeding than that of healthy term or preterm infants, thereby increasing the instability of the

VP infant's physiologic responses throughout the feeding and contributing to inadequate nutritional intake for growth.

Because infant feeding behaviors emerge from the interaction of multiple subsystems, these behaviors can be modified by changing the system components. All of the subsystems are not stationary, nor do they change in a synchronous manner, so some will restrict the infant's oral feeding performance more than others. The most compromised subsystem can be a *rate-limiter*, which holds back the infant's feeding performance (Thelen & Ulrich, 1991). For example, for preterm infants, the most immature function at the time of feeding can operate as a rate-limiter for feeding performance. For infants who were just introduced to oral feeding, their lack of feeding experience may act as a rate-limiter. Thus, manipulating the rate-limiter(s) can facilitate significant changes in the overall dynamics of the oral feeding system (Thelen & Spencer, 1998; Thelen & Ulrich, 1991).

Considering the high prevalence of lung disease in VP infants, impaired lung function in VP infants can operate as a primary rate-limiter for the efficient self-organization of the oral feeding process. For VP infants, feeding interventions that support breathing may create conditions for improved self-organization, thus leading to more efficient feeding synergies. Based on several potential benefits, the positioning of the infant during feeding is considered in this study to be a strategy that may support adequate breathing during feeding. Two feeding positions are compared: the HEL and HES positions.

In conclusion, during feeding, the oral-motor, neurologic, cardio-respiratory, and gastrointestinal systems self-organize both within and between systems to create stability (i.e., they balance the demands of feeding and breathing) in response to internal inputs from the infant and external inputs from the environment. For VP infants, impaired lung function operates as a rate-limiter for this self-organization process. Thus, VP infants are often challenged to develop efficient feeding synergies (i.e., coordination of sucking, swallowing, and breathing), and the ensuing instability of their physiologic responses throughout the feeding contributes to inadequate nutritional intake for growth. Thus, feeding interventions that support breathing may create conditions for improved self-organization, thereby leading to more efficient feeding synergies. The feeding position is one of the external factors that supports breathing and can facilitate self-organization of the feeding system in VP infants (Table 2.1).

Table 2.1. Dynamic Systems Theory Concepts, Feeding Concepts, and Variables

Concepts	Concept Used in Feeding	Variable
Stability vs. Instability	Coordination vs. competition amongst sucking, swallowing, and breathing	Physiological stability and feeding performance
Self-organization	Process of interactions amongst sucking, swallowing, and breathing toward the conditions where the demands of feeding and breathing are adequately balanced	Changes in physiological stability over the course of the feeding
Patterns	Relationship amongst sucking, swallowing, and breathing	Coordinated rhythms of sucking, swallowing, and breathing (in further work)
Rate-limiters	Factors that interfere most with oral feeding skills	Severity of lung disease
Internal Factors	Infant's inherent characteristics that affect oral feeding skills	Level of maturity Health condition Feeding experience
External Factors	Proximal and distal environments around the infant during feeding	NICU environment Flow of milk Positioning of the infant Caregiver's strategies for feeding
Intervention	Manipulation of the rate-limiter	HEL feeding position to support breathing

LITERATURE REVIEW

Oral Feeding During Infancy

An infant's task during oral feeding is to suck and swallow within an ongoing life-supporting respiratory cycle (Goldfield, 2007). Thus, infant oral feeding skills are reflected in the infant's ability to coordinate sucking and swallowing with breathing in order to maintain an adequate level of ventilation for physiological stability while engaging in feeding long enough to obtain an adequate nutritional intake for growth (Thoyre, Shaker, & Pridham, 2005). The precise and proper coordination of a suck-swallow-breath triad allows the infant to feed efficiently without undue effort; however, inadequate coordination may put the infant at risk for feeding difficulties. How well the infant achieves the proper coordination of sucking, swallowing, and breathing during feeding depends on the basic functioning of the oral-motor, neurological, and cardio-respiratory systems. Any one or more dysfunctions of any of these systems may operate as a physiologic constraint on the infant's ability to eat and may interfere with proper feeding coordination, thus leading to feeding problems.

Sucking

There are two types of sucking: nutritive sucking and non-nutritive sucking. Nutritive sucking is the process of obtaining nutrition, and non-nutritive sucking refers to sucking in the absence of nutrient flow. In the context of oral feeding, the term *sucking* refers to nutritive sucking. Sucking is an integrated movement of the lips, cheeks, tongue, jaw, and palate for the formation of a bolus and its propulsion to the back of the oral cavity for swallowing (Delaney & Arvedson, 2008; Rogers & Arvedson, 2005). A mature sucking pattern consists of the rhythmic alternation of suction and expression (Glass & Wolf, 1994; Lau et al., 2000). Here, *suction* is defined as the negative intraoral pressure that draws milk into the oral cavity, and *expression* is defined as the compression and stripping of the nipple between the tongue and the hard palate (Lau et al., 2000). The efficient rhythmic alternation of these two components of sucking allows infants to achieve adequate nutrients for growth.

Efficient sucking results from the involvement of intact and mature oral structures and neurological functions in order to develop the integrated oral-motor movements necessary for sucking. Full-term infants are born with well-developed oral structures and neurological function, so they have many advantages for developing efficient sucking (Glass & Wolf, 1994; Shaker, 1990). That is, well-developed buccal sucking pads located in the cheeks lateral to the mouth facilitate the ability to compress the nipple from the sides as the pads move inward during sucking. A well-defined rooting and sucking reflex helps the infant find the nipple and initiate sucking. Moreover, the innate physiological flexor tone, which keeps an infant's arms close in to the body, hips and knees flexed, and head and neck flexed forward, provides a stable base for oral-motor movements (Shaker, 1990).

For preterm infants, poorly developed oral-motor structures and neurological function can make efficient sucking difficult. For example, depending on the level of maturity, preterm infants may have small or absent sucking pads. This deficiency creates a wide-open space in the mouth that can interfere with efficiently creating negative pressure suction (Shaker, 1990). Also, preterm infants typically have weak muscle tone around the mouth and less tongue strength than full-term infants. These problems make it difficult for them to suck with an adequate amount of contraction, thereby contributing to reduced sucking strength and endurance (Lau et al., 2003; Medoff-Cooper, Warren, & Kaplan, 2001; Mizuno & Ueda, 2003). Further, their poorly developed neurological systems interfere with rhythmic and integrated oral-motor movement (Glass & Wolf, 1994; Shaker, 1990). The lack of physiological flexor tone, combined with the adverse effect of gravity in this case, also contributes to extended posture, which leads to poor neck, trunk, and shoulder stability. Such problems may place these infants at a disadvantage for efficient oral-motor movements. All of these disadvantages of preterm infants contribute to immature sucking patterns related primarily to expression, and these problems can lead to a decrease in the overall sucking efficiency and, thus, consumption of formula (Lau et al., 2000).

Swallowing

The normal process of swallowing is described traditionally in terms of three phases: oral, pharyngeal, and esophageal (Rogers & Arvedson, 2005). The oral phase is the preparatory stage of swallowing. During this oral phase, the infant sucks milk from the bottle or breast into the mouth, forms a bolus, and transports the bolus to the back of the oral cavity to generate the swallowing reflex by the integrated movement of his/her tongue, jaw, palate, and cheeks. The pharyngeal phase begins with swallowing. When swallowing is triggered, the muscles of the soft palate contract to seal off the nasal cavity from the milk, and the epiglottis effectively closes the airway by the upward movement of the laryngo-hyoid complex. During the esophageal phase, the upper and lower esophageal sphincters open to transport the bolus into the stomach (Rogers & Arvedson, 2005).

Safe and efficient swallowing, like efficient sucking, requires intact and mature oropharyngeal structures and neurological functions. Full-term infants are able to develop the integrated and properly timed oral-motor movements necessary for swallowing based on their well-developed oral-motor structures and neurological functions. However, for preterm infants, their immature neurological and oral-motor functions may interfere with any one or more functions of the sequential swallowing process, thereby contributing to aspiration or prolonged breathing interruption (Hanlon et al., 1997; Lau et al., 2003; Mizuno & Ueda, 2003). For example, the weak oropharyngeal muscle tone of preterm infants interferes with developing appropriate pharyngeal pressure gradients to propel the bolus through the pharynx, so the bolus may not be cleared efficiently from the pharynx by one swallow, which may create conditions for fluid threats to the airway and/or continued stimulation of the swallowing reflex, thereby leading to multiple swallows that obstruct the airway for a prolonged period (Hanlon et al., 1997). Moreover, immature neurologic control in response to sensory receptors can contribute to a persistent swallowing reflex even after the bolus is cleared, also leading to increased breathing interruption during swallowing (Hanlon et al., 1997). Immature neurologic control also interferes with the ability to swallow during the safest time when no airflow is present (i.e., at the beginning and end of inspiration or expiration) to minimize the risk of aspiration (Lau et al., 2003; Mizuno & Ueda, 2003). Therefore, all of these abnormal swallowing patterns in preterm infants can interrupt the feeding process and contribute to feeding difficulties.

Breathing

Oral feeding is a physiologically expensive work for the infant, requiring some respiratory adjustments to maintain adequate physiologic stability during feeding. Several clinical studies have documented decreases in respiratory frequency, minute ventilation, and tidal volume during oral feeding (Al-Sayed et al., 1994; Bamford, Taciak, & Gewolb, 1992; Koenig, Davies, & Thach, 1990; Mathew et al., 1985). However, most healthy full-term and preterm infants, who are physiologically stable, are able to adjust their breathing patterns in response to changing physiologic demands of feeding over time; i.e., they can integrate a sufficient number and depth of breaths for adequate ventilation into sucking and swallowing rhythms. However, for preterm infants with lung disease, their lung function is not suitably stable and flexible enough to adjust their breathing patterns to sucking and swallowing (Craig et al., 1999; Gewolb & Vice, 2006). Breathing is disrupted, interrupted, abbreviated, and at times completely absent, thus contributing to physiological distress (Craig et al., 1999; Gewolb & Vice, 2006; Lau et al., 2003; Mizuno & Ueda, 2003).

Relationship of Sucking and Breathing

Two distinct phases of nutritive sucking, namely the continuous sucking (CS) and intermittent sucking (IS) phases, have been identified in infant feeding and are thought to be important in the regulation of breathing during feeding (Mathew, 1991b; Mathew et al., 1985). Initially, the infant demonstrates vigorous and continuous sucking patterns with long sucking bursts and few or brief sucking pauses, often for periods lasting at least 30 seconds, in order to stimulate the milk to ‘let down’ from the breast (considered the CS phase). After this pattern is observed, the infant gradually shifts to more intermittent sucking patterns with shorter sucking bursts and longer sucking pauses than in the CS phase (considered the IS phase). During the CS phase, more formula is consumed, but breathing is reduced markedly by sucking and swallowing (Shiao, 1997). During the IS phase, most physiologically stable infants (e.g., healthy full-term and preterm infants) are able to stabilize their respiration to the approximate previous level, even if the recovery is more gradual in preterm infants than full-term infants (Mathew et al., 1985; Shivpuri et al., 1983).

However, preterm infants with respiratory problems may not be able to recover their respiration to the approximate level for maintaining physiologic stability. The changes in ventilation during the CS phase may be too great to recover, and the challenges associated with increasing ventilation to recover often result in physiologic distress (Craig et al., 1999;

Gewolb & Vice, 2006; Mizuno et al., 2007), thus interfering with the ability to continue to suck over the course of the feeding (Gewolb, Bosma, et al., 2001; Mizuno et al., 2007). Moreover, preterm infants, especially those with respiratory problems, are not able to intersperse breaths into sucking and swallowing rhythms properly, so that they often present only a suck/swallow dyad during the sucking bursts with breathing that follow in an alternating fashion (Palmer, 1993). Therefore, in these infants, the length of the sucking burst has a more direct effect on breathing during feeding than it does for physiologically stable infants.

Relationship of Swallowing and Breathing

The most notable characteristic of swallowing in relation to breathing regulation during feeding is that the pharyngeal anatomy is shared for both the swallowing and breathing functions; however, the two activities are mutually exclusive (Rogers & Arvedson, 2005). Thus, breathing is inhibited briefly during swallowing, a phenomenon referred to as *obligatory deglutition apnea* (Hanlon et al., 1997), such that swallowing can significantly affect breathing during feeding. Safe and efficient swallowing relies on well-timed and continuous reconfigurations of the pharynx to prevent aspiration and to reduce the duration of breathing interruptions caused by swallowing. The development of rhythm in temporally integrated motor functions is an inherent part of neurological functioning. Healthy infants with intact and mature neurological functions are able to fit the timing of the swallow so that it occurs at the safest time when there is no airflow, i.e., at the beginning or end of inspiration or expiration, and to close and reopen the airway in a fast repetitive fashion either for feeding or breathing (Lau et al., 2003; Mizuno & Ueda, 2003). However, for preterm infants, immature neurological functions often interfere with this integrated action, resulting in a prolonged duration of swallowing and inadequate timing of swallowing within the respiratory cycle, which can contribute to an increase in the breathing interruptions required for swallowing and risk of aspiration (Hanlon et al., 1997; Lau et al., 2003; Mizuno & Ueda, 2003). Thus, inefficient swallowing in preterm infants is a significant factor that causes breathing difficulties during feeding.

Relationship of Sucking and Swallowing

During oral feeding, sucking is generally followed by swallowing, but swallowing is delayed until an appropriate volume is accumulated within the infant's mouth in order to stimulate the swallow reflex (Rogers & Arvedson, 2005). That is, the ratio of sucking to swallowing depends on the sucking volume. Koenig et al. (Koenig et al., 1990) compare the relationship between sucking and swallowing during the CS phase with that during the IS phase when healthy full-term and preterm infants are being bottle-fed. During the CS phase, most sucks are paired with swallows, whereas during the IS phase, about one-third of the sucks are followed immediately by swallows. This pattern was found to be similar for full-term and preterm infants. Increased swallowing during the CS phase is thought to be a consequence of an increase in the volume of milk with each suck.

In summary, oral feeding skills involve sucking, swallowing, and breathing, and these components are related to each other for efficient and successful feeding. Dysfunction in any one of these three functions may have a profound effect on the other functions, thus interfering with proper coordination. The stable functioning of the oral-motor, neurological, and cardio-respiratory systems underlies the proper function of each individual component involved in oral feeding as well as the coordination amongst these functions. However, for preterm infants, these immaturely developed systems can alter any one or more of the functions of sucking, swallowing, and breathing and interfere with proper feeding coordination, thus leading to feeding problems.

Development of Oral Feeding Skills in Preterm Infants

Since 1980, the rate of preterm births (< 37 weeks of GA) has climbed steadily from 9.5% to 12.8% for all live births in the United States (Hamilton et al., 2010). Although improvements in the treatment of preterm infants in NICUs have greatly enhanced these infants' chances of survival, many common care issues still remain areas of concern. Prominent among these concerns is early feeding problems. Once medical stability has been attained for these infants, successful oral feeding, either from the bottle or breast, is often the final competency that preterm infants need to attain before being discharged home.

However, successful progression to full oral feeding is often a difficult and time-consuming task for preterm infants due to their complex medical and developmental issues. The inadequate feeding capabilities of preterm infants often delay discharge, thus increasing the length of hospital stay, which has been correlated with increased medical costs and an iatrogenic risk of complications (Kirkby, Greenspan, Kornhauser, & Schneiderman, 2007). More importantly, persistent feeding difficulties lead to poor nutritional status and growth failure that have consequences regarding the subsequent stages of growth and neuro-developmental milestones after discharge (Thoyre, 2007; Wood et al., 2003). Therefore, assisting preterm infants to develop competence in oral feeding is a primary responsibility of nurses and families during the final weeks of neonatal care.

Breastfeeding is the preferred feeding method for preterm infants because it is less physiologically stressful than bottle feeding (Dowling, 1999; Goldfield et al., 2006; P. P.

Meier, 2001). Despite this benefit, breastfeeding preterm infants presents unique challenges, including establishing and maintaining the mother's milk supply and providing adequate caloric and nutritional intake (Callen & Pinelli, 2005). Immediately after birth, younger preterm infants do not have the capability to breastfeed with sufficient endurance and frequency to stimulate maternal milk production due to their immaturity and health issues. Thus, mothers of preterm infants must begin to establish their milk supply by pumping, and they are often required to pump their milk for months until their infant is physiologically stable enough to attempt nutritive sucking at the breast. Therefore, mothers of preterm infants often have difficulty establishing and maintaining a sufficient milk supply.

In addition, even after breastfeeding has been initiated, extra milk must be provided from the bottle because the mother is not always able to be present during feeding times or because intake from the breast is not consistently adequate. Also, especially for younger preterm infants, human milk may not be sufficient as the sole source of nutrients. Human milk fortifier often needs to be added to the breast milk to increase the caloric intake and provide additional nutrients for adequate growth and development. Consequently, breastfeeding preterm infants is not always possible in the NICU, and most preterm infants are at least partially bottle-fed either formula or expressed breast milk.

For preterm infants, feeding milestones include the first bottle feeding and the achievement of independent bottle feedings, i.e., sufficient intake so as not to require supplemental gavage feeding. Oral feeding requires the integration of multiple systems, both within and outside the infant. However, preterm infants are born before the maturation of these systems, especially the oral-motor, neurological, cardio-respiratory, and gastrointestinal systems. Currently, no universally agreed upon criteria are available for determining when to initiate and how to best maintain oral feeding in preterm infants. However, many clinicians typically rely on empirical criteria based on the infant's PMA (i.e., 34 weeks of PMA or greater) and developmental and maturational characteristics (e.g., nutritive sucking and gag reflex) (Kinneer & Beachy, 1994). That is, preterm infants must begin oral feeding when they are also in the process of developing motor and sensory neuro-pathways and becoming competent at physiologic and behavioral regulation (Thoyre, 2007). Thus, preterm infants often experience feeding difficulties due to their immature systems. Feeding difficulties are especially common during the transition period when infants are seeking ways to accomplish oral feeding using a trial and error approach. Further, repeated feeding difficulties may provide negative neurological stimulation that alters or delays the development of oral feeding skills, which can be associated with long-term feeding problems (Hawdon et al., 2000; Thoyre, 2007). Therefore, understanding feeding behaviors in preterm infants and developing early interventions during this transition period may facilitate the process of developing oral feeding skills and, consequently, prevent feeding problems over the long term.

Although feeding problems in preterm infants arise from the infants' own immaturity, it is believed that immaturity is transient and problems associated with it are likely to be resolved as an infant matures (Lau et al., 2003; Mizuno & Ueda, 2003). However, when complications due to prematurity are present (e.g., NEC, neurologic impairments, and BPD), these complications, combined with prematurity, increase feeding problems (Pickler et al., 1997) and often interfere with the anticipated maturation patterns of oral feeding skills (Gewolb, Vice, Schwietzer-Kenney, Taciak, & Bosma, 2001), thus placing these infants at risk for persistent feeding problems for years after hospital discharge (Thoyre, 2007).

Persistent feeding problems have the potential for serious health consequences, including malnutrition and impaired intellectual growth (Ernst, Radmacher, Rafail, & Adamkin, 2003; Johnson, Cheney, & Monsen, 1998; Wood et al., 2003).

The most common complication of prematurity is impaired pulmonary function. All preterm infants have obvious or subtle altered pulmonary function due to early exposure of their immature lungs to air, the act of breathing, or to factors that interfere with the normal genetic schedule of lung development in late gestation (Friedrich et al., 2007; Friedrich, Stein, Pitrez, Corso, & Jones, 2006; Hjalmarson & Sandberg, 2002). Compared to infants born at term, even those preterm infants without lung disease have abnormal lung function, including increased airway resistance, less lung compliance, lower functional residual capacity, and impaired gas mixing capacity (Friedrich et al., 2006; Hjalmarson & Sandberg, 2002; Hoo, Dezateux, Henschen, Costeloe, & Stocks, 2002). When immature lungs interact with exposure to supplemental oxygen and/or positive pressure ventilation, more severe impairments are seen. BPD, the most severe pulmonary disease of infancy, is viewed as a continuum of disturbed pulmonary development (Hjalmarson & Sandberg, 2005) and is classified as mild, moderate, or severe, depending on the duration and degree of supplemental oxygen that is required (Jobe & Bancalari, 2001).

VP infants, who comprise approximately 2% of live births in the United States, are at high risk for developing severe lung disease because they often need respiratory support, such as supplemental oxygen or air flow, for prolonged periods to support their immaturely developed lungs (Ehrenkranz et al., 2005; Jobe & Bancalari, 2001). Many factors may contribute to feeding difficulties in VP infants; however, impaired lung function is thought to be the foremost contributor that significantly interferes with the normal development of oral feeding skills (Gewolb, Bosma, et al., 2001; Gewolb et al., 2003; Gewolb & Vice, 2006; Mizuno et al., 2007). For VP infants, impaired lung function interferes with the ability to integrate a sufficient number and depth of breaths into adequate sucking and swallowing rhythms (Craig et al., 1999; Gewolb & Vice, 2006). Inadequate breathing causes a persistent reduction in the amount of air that remains in the lungs after expiration (functional residual capacity) throughout feeding, resulting in decreased blood oxygenation (Mizuno et al., 2007; Thoyre & Carlson, 2003). The infant becomes fatigued easily and may not have the energy to continue the efficient coordination of sucking, swallowing, and breathing, thus leading to feeding difficulties, including an increased risk of aspiration, physiological distress and poor intake. Further, repeated feeding difficulties may provide negative feedback that alters or delays the development of adequate oral feeding skills and may lead to persistent feeding difficulties for years after discharge (Hawdon et al., 2000; Thoyre, 2007), thus contributing to chronic growth failure (Bott et al., 2006; Johnson et al., 1998).

Therefore, for VP infants, feeding interventions need to focus on supporting adequate ventilation in order to maintain physiological stability throughout feeding, which will enable the infant to continue to feed with the least amount of expended energy.

Feeding Problems in Very Preterm Infants

Feeding difficulties for VP infants in NICU during early oral feeding have been well-documented by examining short-term feeding outcomes (e.g., physiologic stability and feeding performance) and long-term feeding outcomes (e.g., the length of the transition period to full oral feeding).

Physiologic Stability

Physiologic stability during feeding has been evaluated using cardio-respiratory variables that include respiration, e.g., respiratory rate, intervals between breaths, duration and depth of breaths, and the relationship of breathing with swallowing, and/or SpO_2, as well as HR.

Respiration. Mizuno et al. (2007) reported some respiratory characteristics and SpO_2 levels for VP infants when these infants were able to fully oral feed (average 40 weeks of PMA) in terms of the severity of lung disease: no BPD, moderate BPD, and severe BPD. The respiratory variables used in the study include respiratory rate and the duration of deglutition apnea during feeding (calculated as the duration of apnea associated with each swallow). Infants with either moderate or severe BPD demonstrated a higher mean respiratory rate and longer deglutition apnea time during feeding than infants without BPD, and more severe apnea was seen in infants with severe BPD. Also, the partial pressure of carbon dioxide (PCO_2) level and SpO2 level were examined. A higher PCO_2 level, longer periods of oxygen desaturation, and a decreased mean SpO_2 during feeding were noted in infants with BPD compared to those without BPD. More severe desaturation was seen in infants with severe BPD. In sum, the Mizuno et al. study shows that infants with BPD have difficulty maintaining physiologic stability during feeding, and these difficulties depend on the severity of BPD.

Craig et al. (1999) examined respiratory patterns by examining respiratory rate and variation in duration and depth of breaths during sucking periods and non-sucking pause periods with six preterm infants (23 to 29 weeks of GA) with BPD, and compared these infants to their full-term counterparts (n = 12). The preterm infants were studied once a week for four weeks shortly after being available for oral feeding (35 to 40 weeks of PMA at the first test session). The full-term infants demonstrated more irregular duration and depth of breaths during the sucking periods than the pause periods; however, during the pause periods, their breathing patterns became more orderly and consistent. Preterm infants with BPD failed to show any uniformity in breathing patterns, even during the pause periods, compared to sucking periods across all test sessions. These erratic breathing patterns were more significant when the infant had severe BPD. The Craig et al. study demonstrates that breathing during the sucking period is interrupted constantly by the need to protect the airway when swallowing the milk during the sucking periods. This occurrence causes significantly more irregular breathing patterns both in full-term and preterm infants, but full-term infants are able to reorganize their breathing patterns during the pause period to meet their respiratory needs. However, preterm infants with BPD are not able to adapt their breathing patterns in response to the demands of feeding.

Gewolb and Vice (2006) also studied some respiratory characteristics by examining the variability of the intervals between breaths during swallow runs (i.e., three swallows with inter-swallow intervals of ≤ 2 seconds) and apneic swallows (i.e., swallows in runs of three swallows not associated with breathing movements) in preterm infants with BPD (n = 14) compared to those without BPD (n = 20). The GA ranged from 26 to 33 weeks, and all infants were studied between 32.1 to 39.7 weeks of PMA. To control potential bias by the variability in PMA across groups, each group was stratified at ≤ 35 and > 35 to 40 weeks of PMA. The variability of intervals between breaths was quantified using the coefficient of variation (CV), which was significantly higher for infants with BPD than for infants without BPD at both ≤ 35 and > 35 weeks of PMA. The percentage of apneic swallows was higher for infants with BPD than for infants without BPD at both ≤ 35 and > 35 weeks of PMA, but a significant difference was seen only at > 35 weeks of PMA. These results indicate that infants' feeding skills may improve with maturation and/or experience in the group of infants without BPD, but for infants with BPD, BPD remains a significant factor that interferes with the development of infant oral feeding skills. This Gewolb and Vice (2006) study indicates that the integration of respiration during feeding is compromised in infants with BPD, and even after infants have matured, BPD can still be a significant factor that interferes with the normal expected development of oral feeding skills.

Two studies found in the literature examine physiologic stability using preterm infants, including VP infants, but not in relation to BPD. First, Mizuno and Ueda (2003) studied SpO_2 and respiratory rates during weekly bottle feedings from 32 to 36 weeks of PMA with 24 preterm infants (< 32 weeks of GA). These infants were free of apnea or supplemental oxygen for at least 48 hours before the time of the study. A bottle with a controlled flow of milk (i.e., slower flow than with standard bottle nipples) was used in this study. At 32 and 33 weeks of PMA, more than half of these infants exhibited brief apnea, coughing, and oxygen desaturation below 85% during feeding; however, after 34 weeks of PMA, all infants were able to finish the feeding without apnea and oxygen desaturation below 85 percent. Moreover, the respiratory rate decreased significantly from the pre-feeding level during both the CS and IS phases for all weeks of PMA, but the reduction during the IS period after 34 weeks of PMA was smaller than that at 32 or 33 weeks of PMA. Thus, the Mizuno and Ueda (2003) study indicates that when preterm infants do not have respiratory complications, feeding difficulties are likely to be resolved as infants mature.

The second study that examines physiologic stability using preterm infants, including VP infants, but not in relation to BPD, is that of Thoyre and Carlson (2003). They examined the occurrence, severity, and pattern of oxygen desaturation with 22 preterm infants (average 28 weeks of GA) when they were bottle-fed near the time of discharge from the NICU (range 33.5 to 40 weeks of PMA). These infants averaged 10.82 separate desaturation events during feeding, which is defined as any decrease in SpO2 below 90% for ≥ 1 second and spent, on average, 20% of their feeding time with desaturation events. A total of 140 desaturation events (59%) were classified as mild (SpO_2 85-89), 47 events (20%) were classified as moderate (SpO_2 81-84), and 51 events (21%) were classified as severe ($SpO_2 \leq 80$). Moreover, the desaturation events were distributed fairly evenly, with slightly more events during the final third when the feeding time was divided into three equal periods. This Thoyre and Carlson (2003) study demonstrates that VP infants remain vulnerable to hypoxemic events during feeding near the time of discharge, which is not consistent with the results from the Mizuno and Ueda study (2003). However, at the time of their study, Thoyre and Carlson (2003) did not control for respiratory problems and used the standard flow bottle nipples that are commonly used to feed most infants. These factors may have contributed to increased oxygen desaturation during feeding.

Given that the safest period for swallowing is when there is no airflow (i.e., at the beginning and end of inspiration or expiration), three studies of VP infants (Gewolb & Vice, 2006; Lau et al., 2003; Mizuno & Ueda, 2003) examined respiration in relation to swallowing. Gewolb and Vice (Gewolb & Vice, 2006) classified the relationship between breathing and swallowing based on nine possible pairs of swallowing (S) with inspiration (I), expiration (E), and apnea (A, i.e., no airflow detected for more than two seconds), as follows:

(1) I-S-I, i.e., interrupted inspiration, (2) A-S-I, i.e., apnea followed by a swallow, then inspiration, (3) E-S-I, i.e., end of expiration, (4) I-S-A, inspiration preceding a swallow followed by apnea, (5) A-S-A, i.e., a run of apneic swallows, (6) E-S-A, i.e., expiration preceding a swallow followed by apnea, (7) I-S-E, i.e., end of inspiration, (8) A-S-E, i.e., apnea followed by a swallow then expiration, and (9) E-S-E, i.e., interrupted expiration. Infants with BPD are more likely to have a greater percentage of swallows directly related to apnea (A-S-A, A-S-E, A-S-I, E-S-A, I-S-A) than non-BPD infants (Gewolb & Vice, 2006).

These results are consistent with those reported in the Mizuno and Ueda study (2003) in which the phases of swallowing were examined weekly from 32 to 36 weeks of PMA for 24 preterm infants who were born less than 32 weeks of GA. The A-S-A pattern was noted as the most dominant pattern in younger preterm infants at 32 and 34 weeks of PMA; with maturation, the most dominant pattern was I-S-E (Mizuno & Ueda, 2003).

The study by Lau et al. (2003) also supports these findings. Preterm infants (26 to 29 weeks of GA) were studied during one to two oral feedings per day and when they reached independent oral feeding. Full-term infants were studied during their first two weeks and between two to four weeks of age. For preterm infants, the swallows occurred most commonly during apneic swallow runs. However, with experience, preterm infants shifted to swallowing more during the inspiration phase, even if swallowing related to apnea was more frequent. Full-term infants were likely to swallow at the start and/or end of inspiration and at the start and/or end of expiration, suggesting that full-term infants exhibit safe swallowing to minimize the risk of aspiration and/or the path of least resistance to conserve energy (Lau et al., 2003).

Heart rate. In addition to respiration, HR is used as a cardio-respiratory variable during feeding. During activities such as feeding, cardiac output increases to provide the necessary blood, oxygen, and nutrients to tissues in response to increased respiratory efforts. Adults are able to increase the contractility of the heart to increase cardiac output, but the immature hearts of infants rely more on HR rather than stroke volume to increase their cardiac output (Blackburn, 2007). Thus, HR can be an indicator of the physiologic work of infants to maintain stability. However, compared to other cardio-respiratory variables, HR has not been examined extensively as an indicator of physiologic stability during the feeding of VP infants.

Several studies have included HR as a variable of physiologic stability for testing feeding strategies with VP infants (Hill et al., 2000; Shiao, Brooker, & DiFiore, 1996). Hill et al. (2000) examined the effect of oral supports, i.e., cheek and jaw supports, to provide the stability of oral-motor movements for sucking during feeding. Although no significant difference in HR was found between groups with and without oral supports, HR tended to increase in infants without oral supports compared to infants with oral supports. This finding may indicate that the provision of oral supports decreases the physiologic work of feeding.

Shiao et al. (1996) examined physiologic stability with and without a nasogastric tube present during feeding. Increased oxygen desaturation events were reported when infants did not have a nasogastric tube. Desaturation events were related significantly to a low HR and instability in HR before and after desaturation. These findings may demonstrate that a low HR and an increase in the instability of HR are indicators of physiologic distress when infants fail to maintain physiologic stability. Thus, a change in HR can represent physiologic stability, and further studies are needed to understand this variable during feeding in VP infants.

All of these studies, both respiratory- and HR-related, contribute to the understanding of feeding difficulties in VP infants; however, they all have some limitations. Some studies use the averaged values of each variable during the entire feeding (Mizuno et al., 2007; Thoyre & Carlson, 2003), and some studies analyze only subsections of feedings, e.g., the CS and IS phases (Mizuno & Ueda, 2003; Shiao et al., 1996), two sucking bursts from the first and last two minutes of feeding (Lau et al., 2003), swallow runs (Gewolb & Vice, 2006), sucking and pause periods (Craig et al., 1999), or the first and final three minutes of feeding (Hill et al., 2000). However, because infant feeding behaviors are emergent as the infant's subsystems interact and, thus, can change across the feeding period, an averaged outcome obtained from the entire feeding period or from data extracted from subsections of the feeding cannot take into account feeding dynamics and the non-stationary state of infants' feeding responses. Thus, a more precise method of measuring physiologic stability across time may enhance the understanding of infants' feeding difficulties and bring more precision and effectiveness to the application of feeding interventions.

Feeding Performance

Feeding performance has been examined along with sucking performance and variables that are based on the actual amount of milk transferred to the infant. These feeding performance measures include proficiency (the percentage of milk taken during the first five minutes of the feeding), efficiency (the amount of milk consumed in milliliters divided by total feeding time, i.e., ml/min), and overall milk transfer (the percentage of milk taken during the entire feeding) (Lau et al., 2000; Lau et al., 1997; Mizuno & Ueda, 2003).

Feeding performance has been studied extensively because it is the most observable indicator of the development of preterm infants’ oral feeding skills. Mizuno and Ueda (2003) studied sucking pressure, duration, and amplitude weekly from 32 to 36 weeks of PMA with 24 healthy preterm infants (< 32 weeks of GA). Sucking pressure, frequency, and duration increased with age, especially between 33 and 36 weeks of PMA, and efficiency (ml/min) was enhanced with an increase in PMA.

Similarly, Lau et al. (1997) examined the presence of two components of sucking (i.e., suction and expression) and actual oral feeding performance (i.e., proficiency, efficiency, and overall milk transfer) with healthy preterm infants (26 to 29 weeks of GA) when infants were introduced to oral feeding (34.3 ± 1.6 weeks of GA) and reached full oral feedings (37.2 ± 2.0 weeks of GA). Over time, the sucking patterns switched from premature sucking patterns that primarily use the expression component to a more mature pattern that consists of both suction and expression. Proficiency, efficiency, and overall milk transfer also improved significantly over time; however, no correlation was found between the oral feeding performance measures and the predominant sucking pattern used by the infant. Thus, actual oral feeding performance may be enhanced by other factors, such as increased strength and endurance and decreased fatigue throughout the feeding, rather than solely from maturation of sucking patterns.

In another study by Lau et al. (2000), the development of sucking patterns is evaluated using a systematic scale with five primary stages based on the presence/absence of suction and the rhythm of the two components of sucking (suction and expression). Seventy-two healthy preterm infants (26 to 29 weeks of GA) were assessed three times when these infants were taking 1-2, 3-5, and 6-8 oral feedings per day. These infants were around 34 weeks of PMA at the first feeding observation. Similar to the results of the previous Mizuno and Ueda (2003) and Lau et al. (1997) studies, the sucking patterns matured with an increase in PMA and the number of oral feedings per day. Overall milk transfer and efficiency also were enhanced when infants reached the more mature stages of sucking. Thus, these three studies (i.e., Mizuno and Ueda 2003, and Lau et al. 1997 and 2000) demonstrate that an infant's sucking ability and feeding performance may be compromised by immaturity; however, this situation can improve with maturation.

Medoff-Cooper, Bilker, and Kaplan (2001) conducted a cross-sectional study to examine changes in sucking performance as a function of GA with 186 healthy preterm infants (33 to 40 weeks of GA) who were capable of oral feeding soon after birth. These infants were grouped by GA (33, 34, 35, 36, 37, and term age). Each sucking parameter was assessed for a five-minute session of feeding during the first week of oral feeding. Overall, sucking performance improved with an increase in GA as evidenced by an increased number of sucks, increased and stabilized sucking pressure, longer sucking bursts, a decreased number of sucking bursts, and stabilized 'intersuck' intervals within bursts.

A more recent study by Medoff-Cooper et al. (2002) also examined the sucking abilities of 213 infants when they reached 40 weeks of PMA according to GA. These infants were divided into three groups: (1) 75 infants born at 24-29 weeks, (2) 68 infants born at 30-32 weeks, and (3) 70 term infants. Nine sucking parameters were assessed: the number of sucks, number of bursts, intersuck intervals, sucks per burst, interburst width, suck width, intersuck width, mean maximum pressure, and intersuck width/interburst width. VP infants in Group 1 showed significantly fewer sucks, an increased suck width, and a lower ratio of sucks to bursts compared to the other two groups. However, the most competent group of infants at the time of data collection was the group of more mature preterm infants (Group 2). This outcome may have been the result from the benefits attained from the increased feeding experience compared to that of Group 3 as well as greater maturity at birth and fewer medical complications compared with Group 1. Therefore, these two studies also support that sucking performance improves with maturation of the feeding system. However, the level of maturity alone is not sufficient for predicting sucking skills. Infants' health conditions and feeding experience during the postnatal period also can be significant factors for the development of oral feeding skills.

Two studies are found that examine sucking performance in relation to BPD. Gewolb et al. (2001) examined the sucking ability of preterm infants (26 to 32 weeks of GA) according to level of maturation in relation to BPD. Fourteen preterm infants with BPD were studied weekly from 32.1 to 39.7 weeks of PMA and compared with a PMA-matched control group without BPD ($n = 20$). To control potential bias by the variability in PMA across groups, each group was stratified at ≤ 35 and > 35 to 40 weeks of PMA. Infants with BPD showed decreased sucking frequency and duration and increased variability of peak-to-peak intervals for sucking compared to infants without BPD, but a significant difference was evident only in the group of infants at > 35 weeks of PMA. Also, for infants with BPD, no improvement in sucking ability was found with an increase in PMA. That is, BPD appears to be a significant factor that contributes to a decrease in sucking ability even after 35 weeks of PMA.

Mizuno et al. (2007) examined the differences in sucking ability among 20 preterm infants who were born less than 31 weeks of GA, according to the severity of lung disease: no BPD, moderate BPD, and severe BPD. The study was conducted when the infants were able to take full oral feedings (average 40 weeks of PMA). Three sucking parameters were measured: sucking frequency, pressure, and duration of each suck and burst. Not surprisingly, for infants with severe BPD, all of the sucking parameters lagged behind their non-BPD counterparts, and only sucking frequency and pressure significantly decreased in comparison to infants with moderate BPD. This result may have two possible explanations. The weak sucking effort in infants with severe BPD may be compensatory strategy to avoid the respiratory compromise associated with sucking and swallowing and, therefore, may be advantageous in maintaining breathing. Otherwise, because infants with severe BPD demonstrate higher PCO_2 levels and decreased SpO2 levels compared to other groups, this increased physiological distress may have a disadvantageous effect on sucking performance. The results from the two studies support that respiratory problems significantly interfere with efficient sucking performance as well as the normal development of sucking.

In summary, feeding performance is compromised by the immature feeding system of preterm infants, but can be improved with maturation and/or experience with oral feedings. However, when infants have medical complications, such as BPD, oral feeding skills are compromised more significantly and may not follow a normal expected developmental process.

Long-Term Outcomes

From a broad perspective, feeding problems also have been reported in terms of the time required for initiating oral feeding and achieving full oral feeding. VP infants, especially those with medical complications, require a longer time to initiate oral feeding and to become full oral feeders than preterm infants without complications (Pickler et al., 1997; Pridham et al., 1998).

Significance/Gap

Oral feeding is a physiologically demanding task that requires the efficient coordination of sucking, swallowing, and breathing in order to maintain an adequate level of ventilation for physiological stability while engaging in feeding long enough to obtain adequate nutritional intake for growth (Thoyre et al., 2005). For VP infants who have impaired pulmonary functionality, the effort required to feed, combined with challenges associated with respiration, often results in feeding difficulties, evidenced by physiological distress (Craig et al., 1999; Gewolb & Vice, 2006; Mizuno et al., 2007; Thoyre & Carlson, 2003), poor sucking patterns (Gewolb, Bosma, et al., 2001; Medoff-Cooper et al., 2002; Mizuno et al., 2007; Mizuno & Ueda, 2003), poor coordinated rhythms of swallowing and breathing (Gewolb & Vice, 2006; Lau et al., 2003; Mizuno & Ueda, 2003), poor intake (Lau et al., 2003; Mizuno et al., 2007), and a prolonged length of time to become a full oral feeder (Pickler et al., 1997; Pridham et al., 1998). Up to 80% of VP infants are reported to have feeding difficulties after hospital discharge (Thoyre, 2007), which can lead to chronic growth failure (Kurzner et al., 1988; Wood et al., 2003). Thus, for VP infants, feeding strategies need to focus on supporting adequate breathing in order to maintain physiological stability throughout feeding, thus enabling the infant to continue to feed.

The positioning of the infant during feeding is a potential factor for supporting breathing during feeding (L. Clark et al., 2007; McFarland et al., 1994; Mizuno et al., 2007). However, limited experimental evidence regarding positioning is available. Therefore, studies and tests of the effects of feeding position on the feeding outcomes of VP infants during feeding are needed.

Feeding Position in Very Preterm Infants

Several positions have been used for infant feeding. A traditional position for infant feeding is a cradle position in which the infant is placed in a semi-reclining position with the support of one of the caregiver's arms. The cradle position is frequently chosen by parents when feeding their infant, both at the breast and bottle, because this position can provide closeness to their infant, which helps promote infant-parent bonding. However, this position may not be adequate for breathing for preterm infants, because these infants have less head control and rely on the caregiver to maintain their head and neck in neutral alignment. It is common for a cradled position to result in an excessively flexed neck (that is, the head bent too far forward). Especially for VP infants who often experience breathing difficulties during feeding, the cradle position may provide additional respiratory challenges, thereby increasing feeding difficulties.

The HES position is commonly used in the NICU when VP infants are bottle-fed. In this position, the infant sits in a reclining position at a 45-60 degree angle to the buttocks on the caregiver's lap. The caregiver supports the infant's head, neck and trunk with one hand while holding the bottle with the other hand. The HES position aims for head elevation to reduce the work of breathing by facilitating the infant's lung expansion (Dellagrammaticas et al., 1991; Jenni et al., 1997) and provides good support of the head-neck alignment in the neutral position. The HES position also can provide good visual access for nurses and parents to observe infants' responses to feeding. However, the HES position has some disadvantages.

In the supine position, gravity may cause the soft palate and tongue to fall back and push the infants' head backward without careful support by the caregiver, thereby narrowing the upper airway (Carlo, Beoglos, Siner, & Martin, 1989; Litman et al., 2005). This occurrence increases resistance to airflow, which interferes with efficient breathing during feeding. In addition, gravity makes the milk move quickly to the back of the oral cavity, so that the infant may have less time to form a bolus and control its movement.

The HEL position has been recognized recently as a more useful strategy for feeding VP infants, especially those who have breathing difficulties during feeding, and it may compensate for some of the disadvantages of the HES position. In the HEL position, the infant is placed in a side-lying position on the caregiver's lap with a head elevation at about a 45 degree angle. The infant's head and trunk are in a natural straight alignment, and the infant's head and neck are supported by the caregiver's hand in a neutral flexion.

This position is natural for when infants are fed at the breast. Clinical observations have shown that there is better coordination of breathing with swallowing (Goldfield et al., 2006) and less disruption of breathing during breastfeeding compared to bottle feeding (Blaymore Bier et al., 1997; Dowling, 1999; P. P. Meier, 2001), and positioning may be a contributing factor to these differences. The HEL position may also facilitate improved fluid management during feeding, which reduces the duration of breathing interruptions caused by swallowing (Lau & Schanler, 2000; Mathew, 1991a). In the HEL position, the lowered angle of the bottle may slow the gravitational milk flow by decreasing the hydrostatic pressure generated by the volume of milk in the inverted bottle. Further, milk may flow to the cheek first and have a slower transit time to the back of the oral cavity, thus giving the infant more time to form a bolus and control its movement. The HEL position may also reduce the work of breathing by facilitating upper body antigravity control (Vanderghem et al., 1983) and promoting better patency of the upper airway (Litman et al., 2005). In the HEL position, gravity allows the infant to achieve a flexed-toward-midline body position more easily, which may ensure smooth and well-modulated oral-motor movements (Wolf & Robin, 1992, pp. 85-157). The HEL position may also require less effort from the caregiver to provide the head-neck support that promotes patency of the upper airway (Carlo et al., 1989). Because the infant's body is well-supported by a pillow and/or the caregiver's lap in the HEL position, the caregiver can focus on the position of the head and neck. Moreover, when the infant is able to experience both breast and bottle feedings, the infant can be fed in a consistent position for both feeding conditions, which may reduce the infant's efforts to adjust to changes in position and facilitate the infant's learning how to eat.

Although numerous potential benefits of the HEL position have been noted, experimental evidence is very limited. Only two studies have been conducted in the area of infant feeding position (L. Clark et al., 2007; Mizuno et al., 2000). Mizuno et al. (2000) examined the effects of a prone position – as compared to a supine position – on SpO_2, sucking performance, and ventilation volume during bottle-feeding with 14 sick infants (12 full-term and 2 preterm) who often experienced feeding difficulties. One of the two positions was randomly selected and applied for one hour before and during feeding. The other position was evaluated at the next feeding with the same infant in the same manner. Milk flow was standardized at a consistent flow rate in both positions. Higher SpO_2 levels, a lower percentage of feeding time when the SpO_2 was less than 90%, and greater tidal volume were observed in the prone position compared to the supine position. Also, the infant showed greater sucking pressure, shorter durations for each suck, more frequent sucks and higher sucking efficiency (ml/min) in the prone position than in the supine position. No significant difference was seen in respiration rate between the positions. Even if feeding performance and physiological distress during feeding improved significantly in the prone position compared to the supine position, the prone position may not be as easily accepted as the other positions (e.g., supine or side-lying position). Furthermore, because the direction of the bottle is required to be opposite to that in the other positions (e.g., supine or side-lying position), a special bottle system is needed to generate milk flow. Also, the results obtained from sick infants cannot be applied to those for VP infants. However, this study does demonstrate that the position of the infant during feeding makes a difference in feeding outcomes.

The second study is a pilot study that uses a cross-over design with six VP infants fed three times for three to five days both in the HES and HEL positions (total feeding observations = 36) and examines the effects of feeding position on the physiological variables of HR and SpO_2 during bottle feeding (L. Clark et al., 2007). Mean variation of HR and mean SpO_2 levels were calculated for the baseline and the first and middle three minutes of feeding. The variability of HR increased and the SpO_2 decreased from the baseline in the early three minutes of feeding in both positions. However, as the feeding progressed, this change recovered toward the baseline in the HEL position, whereas the SpO_2 declined further, and the variability of HR did not recover at the baseline in the HES position. However, statistically significant difference was found only for SpO_2. Even though this study has a small sample size, the trends shown in the study support further examination of the HEL position as a feeding strategy to gain physiological stability during feeding for VP infants.

These two experimental studies demonstrate the potential of position as a strategy during feeding that can impact an infant’s oral feeding outcomes. However, because Mizuno et al. (2000) examined the effects of only the prone position mainly with term infants who were ill, the study cannot provide experimental evidence for the HEL position for VP infants.

The L. Clark et al. (2007) pilot study supports further examination of the effect of the HEL position during bottle feeding of VP infants.

The primary purpose of this study is to test the preliminary effects of the HEL position (compared to the HES position) on the physiologic stability and feeding performance of VP infants when bottle-fed. In addition, methods for measuring changes in physiologic stability across the feeding period are examined.

Nursing Implications

Feeding position is a feeding strategy that can be readily applied to neonatal care. However, because of limited experimental evidence about feeding positions, no precise and consistent feeding position is currently recommended for health care professionals to follow. Therefore, a small-sized study to examine the preliminary effects of the HEL position on VP infants during feeding may provide a foundation for developing a randomized controlled trial in a larger group to investigate the effects of the HEL position more definitively than has been undertaken previously. Understanding the effects of positioning on the feeding outcomes of VP infants will add to the knowledge base aimed to promote the development of oral feeding skills and support adequate growth and development in these infants. In addition, the method of measuring physiologic stability across the feeding time can enhance the understanding of VP infants' feeding difficulties and bring more precision and effectiveness to the application of this feeding intervention.

CHAPTER III

METHODS

This study compares the preliminary effects of the HEL position and the HES position on the physiologic stability and feeding performance of VP infants when bottle-fed. In addition, methods for measuring changes in physiologic stability across the feeding time are examined. To examine the preliminary effects of the HEL position, two hypotheses are tested. When compared to infants bottle-fed in the HES position, VP infants bottle-fed in the HEL position will demonstrate (1) greater physiological stability (less variation in HR and SpO_2, less severe and fewer changes in HR and SpO_2, a higher respiratory rate that is closer to that of the pre-feeding state, and less variation in breath-to-breath intervals, duration and amplitude of breath) and better feeding performance (overall milk transfer, proficiency, efficiency, and duration of feeding), and (2) fewer physiological changes from the pre-feeding period across the feeding period.

To measure changes in physiologic stability across the feeding time, three methods that create intervals of feeding time were tested in this study. Simulations for each method were conducted to determine the most useful method, as determined by the one that requires the smallest number of infants to detect a position effect with 80% power.

In order to evaluate the feasibility and acceptability of possible data collection and analysis plans, a pilot trial with one infant was conducted. Based on this feasibility study, modifications were made to the data collection and analysis plans and are now incorporated into the methods for the dissertation study. (See Appendix A for the complete feasibility study.)

Research Design

A within-subject cross-over design, in which each participant was fed in both the HEL and HES positions, is used for this study. To control for differential carry-over effects, counterbalancing strategies were used in which each participant was randomly assigned to one of two possible sequences: HES position first and then HEL position, or HEL position first and then HES position (Brink & Wood, 1998). To control for infant maturation and attrition, the two study feedings were completed in a single day. This study design was chosen to control for various subject characteristics (e.g., level of maturity, health condition, and feeding experience prior to the study) that could affect infant oral feeding skills (Howe, Sheu, Hinojosa, Lin, & Holzman, 2007; Pickler, Best, Reyna, Wetzel, & Gutcher, 2005; Pickler et al., 1997; Pridham et al., 1998) and ensure the equivalence of the groups being compared.

Setting

The Newborn Critical Care Center (NCCC) at North Carolina Children's Hospital in Chapel Hill, North Carolina was chosen as the study site. A single site was selected to reduce possible sources of extraneous variation (such as different hospital policies) on preterm infant feeding. The NCCC is a leading level three nursery in the Southeast for neonatal care and consists of seven rooms and 60 beds. Three of the rooms are devoted to intermediate care with separate nursing staffs, where the study was conducted. Approximately 750 infants are admitted each year from more than 50 counties throughout North Carolina.

Sample

Six VP infants who met the inclusion criteria were selected for this study, regardless of gender, race, or ethnicity. Inclusion criteria for this study include: (1) the infant must be born at or less than 30 weeks of GA, (2) the infant must be able to feed orally, and (3) the infant's mother must be willing to allow the infant to bottle-feed for two feedings on the study day. Infants were enrolled in the study when they began oral feeding. Once infants were able to consume by mouth at least 50% of their prescribed milk for three consecutive days, the study commenced. Infants were excluded if they had congenital conditions or had acquired medical conditions that may be associated with feeding difficulties beyond the scope of this intervention. Such conditions may include a congenital anomaly that interferes with oral feeding (e.g., cleft palate or paralysis of facial muscles), grade IV intraventricular hemorrhage, high risk for neurological impairments (≥ 8 on neurobiologic risk score [NBRS]), ventilator-dependence beyond 60 days of life, and/or inability to begin oral feeding prior to 40 weeks of PMA. Infants also were excluded if neither the mother nor father understood or read English.

The expected sample demographics were based on the population of the NCCC nursery in 2009: 137 infants were admitted who were less than 30 weeks of GA, and 111 of these infants survived to discharge; 49.5% of the infants were male and 50.5% were female; and the breakdown for race was 42% White, 43% Black, 2% Asian, 10% Hispanic, and 3% Other. Given these data, it was anticipated that recruitment for the study could be completed in less than two months. It was expected that about half the infants would be male and half female. Many Hispanic infants were expected to have parents who did not speak or read English; however, it was anticipated that approximately 20% of Hispanic parents who were eligible for this study (10% of the VP nursery population) would speak or read English based on the nursery population in 2009. Therefore, taking into consideration the percentage of Hispanic infants with parents who are able to speak or read English, the demographic breakdown of infants enrolled in the proposed study was expected to be 48% Black, 45% White, 2% Hispanic, and 5% Asian and Others.

Data collection was completed between June 1 and September 30, 2011. The study sample includes 67% female and 33% male; and the breakdown for race is 50% White, 33% Hispanic, and 17% Black. The distribution of the sample by gender or race is slightly different from that of the VP nursery population in 2009 because only the subgroup of VP infants who met the inclusion and exclusion criteria for this study during a certain period of a year is included in this study.

Recruitment and Retention

Once approval from both the Institutional Review Board at the University of North Carolina at Chapel Hill and the Nursing Research Council at the UNC Health Care System had been obtained, recruitment began. To identify eligible infants for the study, the principal investigator (PI) visited the NCCC every day for about an hour. Once a potential candidate was identified through monitoring the unit census data and through chart review, the PI followed the infant's progress until the infant met the criteria for recruitment. When the infant began oral feeding, the PI asked the nurse (for that day and for that infant) to inform the infant's mother that her child was eligible for the feeding study and to ask if the mother would be interested in learning more about the feeding study. If the mother was interested, the PI met with the mother in the nursery at a time convenient for the mother to explain the study and obtain consent (Appendix B). The PI closely followed the feeding progress of the enrolled infants through regular visits to the nursery. Once an infant was able to eat by mouth at least 50% of his or her prescribed milk for three consecutive days, the study feeding was scheduled with the NCCC staff and mother. At the conclusion of the study, each mother was given a photograph of her infant taken during the study in appreciation of her infant's participation.

All eligible infants, regardless of gender or race, were approached for recruitment. Sixteen infants were identified as potential candidates for the study. However, mothers for two infants did not want their infants to participate in the study; two infants were under contact precautions when the study needed to be conducted; one infant was transferred before the study was scheduled; one infant became a full oral feeder before the study was scheduled; and one infant began to use a special nipple and bottle system for managing her feeding problems, which was contrary to study protocol. After excluding these seven infants, the study was conducted with nine infants. However, three of the nine infants also had to be excluded later from the analysis because of problems with synchronization between the physiological and behavioral data, inaccurate calibration of measurements, and clinical events that affected the infant's physiologic responses to feeding during one of the feeding observations. The final study sample was six VP infants.

Intervention

Each infant was bottle-fed in the two feeding positions, HES and HEL (Figure 3.1). To control for variation in the interactions between the infant and caregiver during feeding across feeding positions, one neonatal nurse in the NCCC performed both of the bottle feedings per infant. Also, the nurse who fed each infant was asked to follow a standardized feeding protocol to the extent possible (Appendix C). In the HEL position, the infant was placed in a side-lying position on the caregiver's lap with one ear facing the ceiling and the head and trunk elevated to approximately a 45-60 degree angle. The infant's head and trunk were in a neutral straight alignment, and the infant's head and neck were supported by the caregiver's hand in neutral flexion, i.e., chin tilted down slightly, without the neck being extended and without excessive flexion. In the HES position, the infant was placed in a reclining position at approximately a 45-60 degree angle to the buttocks on the caregiver's lap, also with the infant's head, neck, and trunk in neutral straight alignment. In both feeding positions, the infant was swaddled with a blanket, providing a flexed body position.

HES position

HEL position

Figure 3.1. Feeding Positions used in the Study. HES = head-elevated supine; HEL = head-elevated side-lying.

Variables and Measures

Four types of variables were measured prior to and/or during feeding: a) physiologic stability, b) feeding performance, c) infant characteristics, and d) intervention fidelity. The timeline, specific variables, and measures are described in Table 3.1.

Table 3.1. Variables and Measures

Concept	Variable	Measure	Pre-feed	Feed
Physiologic stability	Heart rate (HR)	HR: Mean, Standard Deviation (SD), Coefficient of Variance (CV), % of feeding time > 10%, > 15%, and > 20% above pre-feeding period, % of feeding time < 10%, < 15%, and < 20% below pre-feeding period, % of feeding time <100bpm	X	X
	Oxygen saturation (SpO_2)	SpO_2: Mean, SD, CV, % of feeding time < 5% pre-feeding period (classified as mild [5-10%], moderate [10-15%], or severe [>15%]), % of feeding time <85%	X	X
	Respiratory characteristics (RESCs)	RESCs: Mean, SD, CV of intervals between breaths, duration and amplitude of breaths, respiratory rate, breathing pause < 3 seconds	X	X
Feeding Performance	Overall milk transfer	Percentage of prescribed milk consumed		X
	Proficiency	Percentage of prescribed milk taken during the first 5 minutes of the feeding		X
	Efficiency	Total volume/total feeding time (ml/min)		X
	Duration of Feeding	Total feeding time minus non-feeding and burping periods (min)		X
Infant Characteristics - Level of maturity	Gestational age (GA), Postmenstrual age (PMA)	History of Hospitalization Form Feeding Data Collection Form	X	
- Health condition	Neuro-biological risk score (NBRS), severity of lung disease[a]		X	

- Feeding experience	Number of cumulative nipple feedings prior to the study		X	
- Additional descriptors	Gender, birth weight, weight on the day of study, APGAR score, types and lengths of supplemental oxygen or air flow		X	
Intervention Fidelity -Caregiver feeding actions	Proportion of onset of feeding based on caregiver's preparation of infant for feeding and infant readiness	Dynamic-Early Feeding Skills (D-EFS) coding scheme		X
	Number of rest periods provided by the caregiver, stimulating infant sucking, and limiting milk flow events			X
-Infant position	Proportion of feeding time that the infant is held in a semi-upright position for the condition of the HES position and in a side-lying position for the condition of the HEL position			X

Note. [a] The severity of lung disease was identified when the infant reached 36 weeks of PMA, according to definitions of lung disease (Jobe & Bancalari, 2001).

Physiologic Stability

The physiological variables used in this study are HR, SpO_2, and RESCs, and these variables were measured continuously 30 minutes prior to the feeding until the feeding was completed. *Pre-feeding period* is defined as a 2-minute period prior to the feeding when the infant is calm and quiet in the bed and no demands are placed on him or her; this period is used to calculate a pre-feeding level for each feeding. *Feeding period* is defined as the period of time from the first time the bottle is placed in the infant's mouth until the last time it is removed. The feeding period is used to calculate the overall physiologic stability during the entire feeding. *Bottle-in period* is defined as the amount of time that the bottle is placed in the infant's mouth; it is calculated by subtracting the non-feeding and burp periods from the feeding period. The feeding period and bottle-in period vary from infant to infant in terms of length of feeding time, because some infants feed longer than others. The bottle-in periods are used to measure overall physiologic stability without potentially confounding data (i.e., non-feeding and burp periods) and to measure changes in physiologic stability over time.

Heart rate. HR was measured using the BioNex Bio-Potential Amplifier (MindWare Technology, Gahanna, OH), which is a commercially available instrument that is used to monitor electrocardiograms (ECGs), sampling at 1,000 samples per second. The ECG signals were simultaneously digitized by the amplifier and stored as an analog waveform on the computer using BioLab Data Acquisition Software (MindWare Technology, Gahanna, OH). HR in beats per minute (bpm) were extracted from the RR interval on the ECG signals for every one second as a digitized text file using AcqKnowledge software (BIOPAC Systems Inc., Goleta, CA), and this text file was used for analysis. Under resting conditions, the newborn's heart rate ranges from 120 to 160 bpm, with significant state-related variations, such as infant's age and health condition (Blackburn, 2007).

During the pre-feeding, feeding, and bottle-in periods, the mean, standard deviation (SD), coefficient of variance (CV, i.e., the ratio of the SD divided by the mean for the assigned period) for HR were calculated for each infant by feeding position. The SD and CV were used to index the function stability for HR. Additionally, the percentages of time with increases and decreases in HR were calculated during the bottle-in periods. Increases in HR are defined as changes in HR that are at least 10% (mild), 15% (moderate), and 20% (severe) above the HR of the pre-feeding period, and decreases in HR are defined as changes in HR that are at least 10% (mild), 15% (moderate), and 20% (severe) below the HR of the pre-feeding period, and below 100 bpm.

Oxygen saturation. Percentage of hemoglobin saturated with oxygen, which is commonly referred as SpO_2, was measured using the Radical-7 Pulse Co-Oximeter (Masimo Corporation, Irvine, CA) with the averaging set at two seconds, sampling at 1,000 samples per second. The Radical-7 Pulse Co-Oximeter measures a more accurate level of arterial oxygen saturation in the blood than a traditional pulse oximeter, because the Radical-7 Pulse Co-Oximeter extracts the best possible signal, especially under challenging clinical conditions (e.g., movement and low perfusion), by transmitting four wavelengths of light through the tissue of the infant's foot to better distinguish all four types of hemoglobin: oxyhemoglobin (oxygenated blood), deoxyhemoglobin (non-oxygenated blood), carboxyhemoglobin (blood with carbon monoxide content), and methemoglobin (blood with iron in the ferric state) (Goldman, Petterson, Kopotic, & Barker, 2000; Jubran, 1999). The accuracy of the SpO_2 level as determined by this co-oximeter, as reported by the manufacturer, is ±3 % above 70%, regardless of movement and low perfusion. The SpO_2 signals also were simultaneously digitized by the amplifier and stored as an analog waveform on the computer using BioLab Data Acquisition Software (MindWare Technology, Gahanna, OH). The SpO_2 trends for every one second were simultaneously extracted as a digitized text file using the BioLab software, and this text file was used for analysis. The optimal range of SpO_2 in preterm infants has not fully defined, however, in practice, between 85 to 95% is commonly considered as an acceptable range limit to detect acute hypoxemia as well as to avoid hyperoxemia.

During the pre-feeding, feeding, and bottle-in periods, the mean, SD, and CV of SpO_2 were calculated for each infant by feeding position. The SD and CV were used to index the function stability of SpO_2. Additionally, the percentages of time with changes in SpO_2 were calculated during the bottle-in periods. Changes in SpO_2 are defined as decreases in SpO_2 at least 5% below the SpO_2 of the pre-feeding period and below the value of 85%. The percentages of feeding time when SpO_2 decreases at least 5% below the pre-feeding period are further classified as mild (5-10%), moderate (10-15%), or severe (>15%) desaturation.

Respiratory characteristics. RESCs were measured using the respiratory effort monitoring system (Ambu Sleepmate, Glen Burnie, MD), sampling at 1,000 samples per second. This respiratory effort monitoring system measures the chest expansion that is associated with respiratory effort by a movement detection sensor that has elastic strips and bands on both sides and that is placed around the infant's chest. A flat small microphone attached to the infant's neck also measures breathing and swallowing sounds, and these amplified sounds are used to validate breathing. Respiratory signals were digitized by the amplifier and stored as an analog waveform on the computer. The peaks and troughs were marked on the respiratory waveform using the AcqKnowledge software (BIOPAC Systems Inc., Goleta, CA), and these peaks and troughs were used to calculate the intervals between breaths and the duration, amplitude of breaths, and respiratory rate per minute. Under resting conditions, the newborn's respiratory rate ranges from 30 to 60 breaths per minute, with significant state-related variations, such as infant's age and health condition (Blackburn, 2007).

Interval between breaths corresponds to the distance between peaks, *breath duration* corresponds to the distance between troughs, and *breath amplitude* corresponds to the distance between a depth of trough and the depth of the next peak (Figure 3.2). Respiratory rates were computed from the peaks for a breath. During the pre-feeding and the first six minutes of a bottle-in period, the mean, SD, and CV of each of these measures and respiratory rates were calculated. The SD and CV were used to index the functional stability of the interval between breaths, breath duration and amplitude. During the first six minutes of the bottle-in period, the percentages of time with breathing pauses of more than three seconds also were calculated. Because respiration is measured by the chest movement associated with respiratory effort, this signal can be highly confounded by the infant's movements during non-feeding and burping periods. Therefore, to remove potentially confounding data, only the bottle-in periods were used for respiratory analysis (i.e., the break periods were eliminated from the feeding period). In addition, the first six minutes of the bottle-in period were chosen for the respiratory analysis because this analytic procedure is new and the initial minutes of the feeding period have been found to be the most vulnerable period for physiological changes (Thoyre & Carlson, 2003).

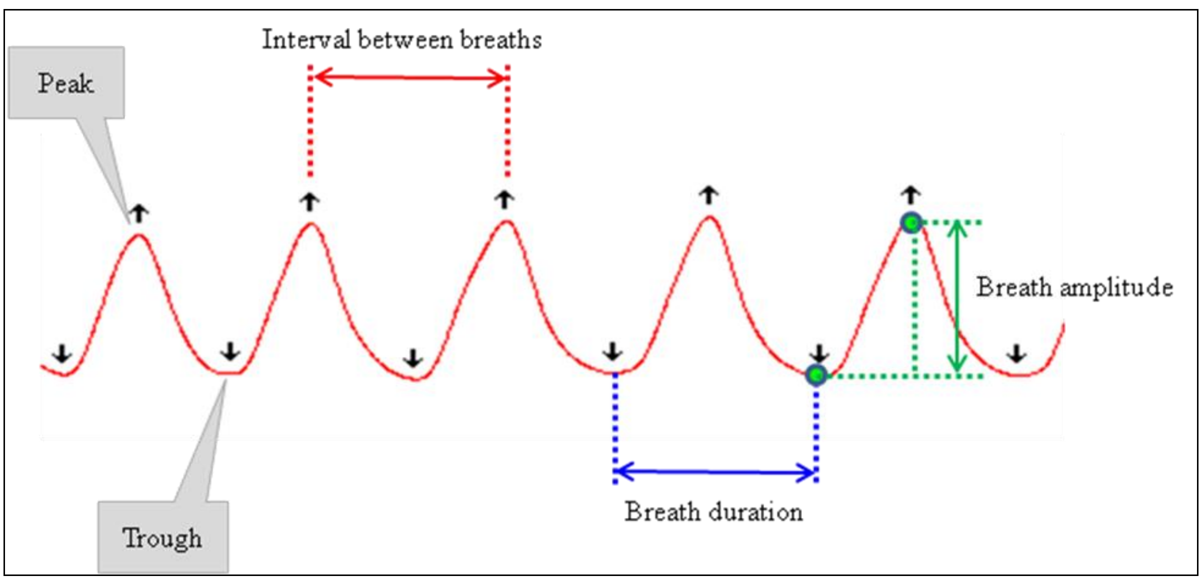

Figure 3.2. Definitions of Respiratory Characteristics

Feeding Performance

Feeding performance measures include overall milk transfer, proficiency, efficiency (Lau et al., 1997; Pickler et al., 2005; Pickler, Chiaranai, & Reyna, 2006), and duration of feeding. *Overall milk transfer* refers to the percentage of milk taken from the prescribed amount of milk during the entire feeding and is an index that incorporates the infant's oral motor skills and overall level of endurance. *Proficiency* refers to the percentage of milk taken from the prescribed amount of milk during the first five minutes of feeding. Proficiency is an index of the infant's oral motor skills because its measurement is taken at the beginning of a feeding when fatigue is expected to be minimal. *Efficiency* refers to the amount of milk consumed in milliliters divided by total feeding time (ml/min) and is an index of the infant's oral motor skills as well as fatigue (Lau et al., 1997; Pickler et al., 2005). *Duration of feeding* is defined as the feeding time in minutes that does not include non-feeding and burping periods. Lau et al. (1997) have reported an indicator of successful oral feedings using feeding performance measures with 82 VP infants at their first oral feeding. Ninety-six percent of the infants were successful at oral feeding (i.e., overall milk transfer $\geq$ 80%) when they demonstrated an efficiency of $\geq$ 1.5 ml/min and proficiency $\geq$ 30 percent. These infants also became full oral feeders at an earlier PMA than their counterparts who did not meet both criteria (Lau et al., 1997).

To calculate overall milk transfer and efficiency, the amount of prescribed milk (ml) was recorded prior to the feeding, and the amount of prescribed milk taken (ml) was recorded at the end of the feeding. The total length of feeding time in minutes, including non-feeding and burping periods, was calculated retrospectively from the mark on the physiologic data stream when the bottle was first inserted and last removed. To determine proficiency, the feeding was stopped briefly at five minutes using a stopwatch, and the amount of milk remaining in the bottle (ml) was recorded. In order to minimize interruption of the natural flow of sucking, if the infant was sucking at the 5-minute stopping point, then the recording of the remaining milk waited until the end of this sucking burst. Fluid lost during feeding was measured by the difference in bib weight of a bib weighed between pre-and post-feedings, and this weight was subtracted from the amount of milk consumed. To calculate the duration of feeding time in minutes, the duration of the non-feeding and burping periods also was calculated retrospectively from the mark on the physiologic data stream when the bottle was inserted and removed. Duration of feeding was calculated by subtracting the non-feeding and burping periods from the total length of feeding time.

Infant Characteristics

Infant characteristics, as incorporated in this study, include level of maturity, health condition, feeding experience, and additional descriptors obtained from the infant's medical records using the History of Hospitalization Form (Appendix F) and Feeding Data Collection Form (Appendix G). For this study, *level of maturity* is assessed by both GA, as determined by maternal dates and physical examination, and PMA, a calculation of GA plus postnatal age. *Health condition* is assessed in terms of neurological and respiratory status. Neurological status is identified using NBRS (range of 0-28) to identify the degree of neurological risk of the infant (Brazy, Eckerman, Oehler, Goldstein, & O'Rand, 1991; Brazy, Goldstein, Oehler, Gustafson, & Thompson, 1993). The NBRS (Appendix D) has seven items that indicate possible medical conditions that are associated with neurologic problems. They were scored for severity on a 4-point Likert scale based on a medical chart review. A high NBRS indicates a high risk of neurologic problems. A significant correlation of the

NBRS with the Bayley mental and psychomotor developmental scores (r = -.37 to -61) and with abnormal neurologic examination scores (r = .59 to .73) at 6, 15, and 24 months corrected age have been reported with a total of 257 infants ≤ 1500 g birth weight (Brazy et al., 1991; Brazy et al., 1993). The inter-rater reliability between scores was 97% using ten chart reviews (Brazy et al., 1991). Respiratory status is identified using diagnostic criteria for BPD (none, mild, moderate, or severe), depending on the duration and degree of supplemental oxygen required at 36 weeks of PMA (Jobe & Bancalari, 2001) (Appendix E). To collect these data, the PI revisited the nursery for chart reviews when the infant reached 36 weeks of PMA. *Feeding experience* is measured by the number of cumulative oral feedings either from the bottle or breast prior to the study (Pickler et al., 2005; Pickler & Reyna, 2003). *Additional descriptors* include gender, race, birth weight and weight at the time of study, APGAR score, and types and durations of supplemental oxygen or air flow.

Intervention Fidelity

Fidelity is assessed by determining whether the assigned position was delivered properly, and whether the caregiver's feeding strategies were carried out consistently within and across the infants according to the specified feeding protocol (Appendix C). To assess intervention fidelity, the behaviors of both the infants and caregivers were recorded using a Panasonic digital video camera HDC-TM700 with a close-up angle of the infant's face and upper body. The entire feeding period recorded on the videotapes was coded continuously using the Noldus Observer XT (Noldus Information Technology Inc., Asheville, NC), an observational coding program.

To assess whether the assigned position was delivered properly, two infant position variables were evaluated using the 'infant position' subscale of the dynamic-early feeding skills (D-EFS) observational coding scheme: (1) the proportion of feeding time that the infant is held in a semi-upright position for the condition of the HES position (*supine*), and (2) the proportion of feeding time that the infant is held in a side-lying position for the condition of the HEL position (*side-lying*). To assess the feeding strategies implemented by the caregiver, the 'caregiver feeding action' and the 'infant engagement' subscales of the D-EFS observational coding scheme were revised based on the feeding protocol. Five caregivers' feeding behaviors were evaluated using the revised coding scheme: (1) whether the caregiver prepared the infant for the feeding by rooting and inviting the infant to participate (*prep*), (2) whether the feeding began with the infant in a state of readiness (*ready*), (3) the number of rest periods provided with the bottle out of the mouth (*numb rest periods*), (4) the number of times the infant received stimulation that could cause an increase in sucking and potentially cause more milk to be expelled into his or her mouth (*stim suck*), and (5) the number of times the flow of milk was limited to allow time for the infant to swallow and resume a pattern of breathing (*limit flow*).

Duration was calculated for the codes of the 'infant position' subscale and divided by the duration of the bottle-in periods (i.e., non-feeding and burping periods removed) to calculate the proportion of feeding time when the infant is held in a semi-upright position for the condition of the HES position (*supine*) and in a side-lying position for the condition of the HEL position (*side-lying*). Frequency was calculated for the codes to assess the caregivers' feeding behaviors. The frequencies of the two codes used to assess the caregivers' feeding behaviors were further divided by the total number of bottle-in episodes to calculate the proportion of onsets of the feeding that is contingent upon the caregiver's behavior to prepare the infant (*prep*) and the infant's readiness (*ready*). Specific descriptions of each code are provided on the revised D-EFS list (Appendix H).

Kappa coefficients have been reported for the caregiver feeding actions (81 to 93%), infant engagement (54%), and infant position (77%) from 75 feeding observations from 20 preterm infants born at less than 32 weeks of GA (Thoyre, 2009). However, the revised codes have not been used prior to this study; therefore, they were assessed and refined, as needed, prior to the coding data for this study based on discussion with the mentor and using videotapes from the feasibility study and past studies of the mentor.

The PI coded all of the data. The mentor created a gold standard by coding three videotapes of past studies conducted by the mentor using the coding scheme that is used in this study. Before data coding commenced, the PI was trained with the gold standard until the Kappa coefficient reached 85% or greater. The PI also re-coded the three videotapes after finishing half of the data coding for this study to assess a drift in reliability as well as intra-rater reliability. The reliability had not decayed over time (85 - 95% Kappa coefficient). To evaluate inter-rater reliability, five of the twelve videotapes for this study were re-coded by the second trained observer. Before coding data, the second coder also was trained with the three gold standard videotapes until the Kappa coefficient reached 85% or greater. The Kappa coefficients of five feeding observations between the PI and the second coder ranged from 78 to 87%. All Kappa coefficients found in this study suggest excellent reliability (Bakeman & Gottman, 1997).

Procedure

Two study feedings were conducted in a single day for each infant based on a predetermined order of feeding position, within the routine feeding schedule in the nursery. All equipment for monitoring and video recording was set up immediately before the feeding that occurred just prior to the first study feeding to collect pre-feeding data during the inter-feeding period without disturbing the infant (i.e., when the nurse provided pre-feeding care to the infants, such as measuring their temperatures and changing diapers).

To measure the physiological variables, a pulse oximeter sensor was placed on the infant's foot and secured with an opaque sensor wrap. Electrodes were placed on the infant's chest and abdomen, and respiration bands were placed around the infant's chest at the nipple level. A microphone was placed at the suprasternal notch and secured with a hydrogel tape. The camera was attached to the physiologic cart using a flexible arm that allowed the angle of the camera to be changed, which allowed the nurses to access the infant easily and without interruption. The angle of the camera was adjusted to capture a close-up angle of the infant's face and upper body.

The infant began to be monitored and videotaped 30 minutes prior to each study feeding to capture pre-feeding data, and the infant continued to be monitored until the feeding was completed. All equipment remained on the infant until the second study feeding was completed. When the infant exhibited readiness cues for feeding at the scheduled feeding time (i.e., opening mouth and descending tongue in response to presentation of the nipple), the infant was provided routine nursery care by the assigned nurse or mother. The infant was swaddled with a blanket, which allowed a flexed body position. The bib was weighed prior to and after feeding to measure fluid lost from drooling during feeding. Ambient stimuli, such as noise and bright lights, were minimized by controlling unnecessary personnel and pulling the curtain around the infant's bedside if needed.

A neonatal nurse in the NCCC performed bottle-feeding for the infant using a standardized feeding protocol. The infant was placed either in the HES or HEL feeding position according to the predetermined order. The caregiver used a soft voice to maintain the infant's alert state (White-Traut et al., 2002), and then the feeding proceeded. The feeding was stopped briefly at five minutes, and the amount of milk remaining in the bottle (ml) was recorded. The feeding was determined to be 'finished' when the infant had been fed the prescribed amount of breast milk or formula, or no longer engaged in feeding, or 30 minutes had elapsed from bottle-feeding initiation. Following the feeding, the amount of milk consumed, the length of feeding time, and the weight of the bib were recorded. The infant was given the nursery's post-feeding care by the nurse and settled on the bed. This process was repeated for each study feeding. After two study feedings had been completed, all monitoring equipment was removed gently.

Possible confounding factors were standardized as much as possible. The caregiver's approach to feeding between feeding positions was controlled by using a single caregiver for both feedings per infant. All caregivers who fed the infant were asked to follow a standardized feeding protocol (Appendix C). The fidelity of the delivery of the intervention was confirmed by observational measurements to assess whether the assigned position was delivered properly and whether the caregiver consistently followed the feeding protocol within and across the infants. The same type of nipple that the nursery used was used for all study infants. Also, each infant was fed with the same nipple (cleansed properly) for the two study feedings to control for variation in milk flow, because a wide variation in milk flow within and between commercial bottle nipples has been documented (Mathew, 1988).

Three people were involved in data collection during the feeding: the PI, the physiologic equipment research assistant (RA), and the nurse caregiver. (The nurse caregiver was not necessarily the same nurse caregiver throughout the study, however, but was the same person for the two study feedings for the same infant on the same day.) The PI oversaw the data collection, and adjusted the video camera angle to capture the infant's and caregiver's movements. The PI also recorded any other significant events during each feeding. The trained RA managed the physiologic equipment and monitored the data streams. Also, the RA put a mark on the physiologic data streams when the bottle was inserted or removed. A nurse performed the bottle feedings.

Data Preparation

Three types of data were analyzed: physiologic data (HR, SpO_2, and RESCs), descriptive data (infant characteristics and feeding performance), and observational data (intervention fidelity).

The physiologic data include HR, SpO_2, and RESCs. All physiologic data were simultaneously digitized by the amplifier and stored as an analog waveform on a computer using the BioLab Data Acquisition Software . The waveform data were constructed using the BioLab and AcqKnowledge software to facilitate data analysis using the statistical program. The event marks inserted on the physiologic data streams when the bottle was inserted or removed by the RA during data collection, were verified and corrected by the PI, if needed, through examination of the videotape. The verified events were downloaded to a tab-delimited text file and used to separate the pre-feeding, feeding, and bottle-in periods from the total data. ECG signals were imported to the AcqKnowledge software that allows HR data to be extracted from ECG signals as a digitized text file. HR data were extracted for every one second, and the resultant text files were used for analysis. The SpO_2 trends for every one second were extracted as a digitized text file during data acquisition, and these text files were used for analysis. The digitized text files for events, HR, and SpO_2 data were imported to Microsoft Excel and then copied and pasted into a single spreadsheet to create one dataset per feeding (Figure 3.3).

Table 3.2. Illustration of Heart Rate and Oxygen Saturation Dataset for Analysis

Id	Group	Period	Time	Lapse Time[a]	HR (bpm)	SpO_2 (%)
2	1	Baseline	1:24:56 PM	319	143.54	99.36
2	1	Baseline	1:24:57 PM	320	145.28	99.35
Data omitted for illustration						
2	1	Bottle-In	1:53:28 PM	2031	182.93	99.35
2	1	Bottle-In	1:53:29 PM	2032	170.45	99.35
2	1	Bottle-In	1:53:30 PM	2033	153.45	99.35
2	1	Bottle-In	1:53:31 PM	2034	149.25	99.35
2	1	Bottle-In	1:53:32 PM	2035	149.25	99.35
2	1	Bottle-In	1:53:33 PM	2036	154.24	99.35
2	1	Bottle-In	1:53:34 PM	2037	170.45	99.35
Data omitted for illustration						
2	1	Bottle-In	1:59:52 PM	2415	156.25	99.35
2	1	Bottle-In	1:59:52 PM	2416	150.38	99.35
2	1	Bottle-In	1:59:52 PM	2417	147.42	99.35
2	1	Break	1:59:52 PM	2418	148.15	99.35
2	1	Break	1:59:52 PM	2419	153.85	99.34
2	1	Break	1:59:52 PM	2420	159.57	99.35
2	1	Break	1:59:52 PM	2421	163.93	99.35

Note. HR = heart rate; SpO_2 = oxygen saturation. [a]Lapse Time= time in seconds from beginning of file.

For respiratory analysis, the respiratory waveform was imported to the AcqKnowledge software, which allows the peaks and troughs to be marked on the respiratory waveform. The peaks and troughs for breaths were determined based on a consistent rule (Appendix I) and all peaks and troughs were confirmed by listening to the breathing and swallowing sounds on the videotapes as recorded by the microphone attached to the infant's neck. The times and values for each peak and trough marked on the waveform were downloaded to a tab-delimited text file. These text files were translated to Microsoft Excel that was used for calculating the intervals between breaths and the duration and amplitude of breaths (Figure 3.4). Specific procedures for respiratory data management are provided on Appendix J.

Table 3.3. Illustration of Respiratory Characteristics Dataset for Analysis

Period	Peak time (second)	Peak value (volt)	Trough time (second)	Trough value (volt)	Amplitude [a]	Duration [b]	Interval [c]
Baseline	1.168	0.006581	0.884	-0.00614	0.013	0.908	1.112
Baseline	2.280	0.005574	1.792	-0.00894	0.015	1.076	0.868
Baseline	3.148	0.002168	2.868	-0.00667	0.009	0.732	0.704
Baseline	3.852	0.006561	3.600	-0.00448	0.011	1.176	1.184
Baseline	5.036	0.005311	4.776	-0.00462	0.010	0.940	0.912
Data omitted for illustration							
Bottle-In	3065.31	0.016422	3065.06	-0.01675	0.033176	0.508	0.464
Bottle-In	3065.77	0.021767	3065.56	-0.01687	0.038632	0.44	0.433
Bottle-In	3066.21	0.020868	3066.00	-0.01817	0.039034	0.42	0.423
Bottle-In	3066.63	0.024966	3066.42	-0.01836	0.043328	0.432	0.436
Bottle-In	3067.06	0.027645	3066.86	-0.02178	0.049429	0.436	0.444

Note. [a] Amplitude = the next peak value minus the prior trough value. [b] Duration = the time taken from a trough to the next trough. Interval = the time taken from a peak to the next peak.

Data cleaning involved determining a 2-minute period prior to feeding to calculate the pre-feeding levels, and removing physiologic data artifacts. The pre-feeding levels were calculated from the pre-feeding period for each feeding. Two or three 2-minute pre-feeding periods were selected from areas where: (1) minimum variability of HR, SpO_2, and respiratory data occurred; (2) neither increasing nor decreasing patterns of HR, SpO_2, and respiratory data occurred; and (3) the infant was calm and quiet as noted on the videotape. Among several 2-minute segments, the period with the smallest SD for HR and SpO_2 were selected. When the pre-feeding period was not sufficient to find the qualified period for the pre-feeding period criteria because the infant exhibited readiness cues for oral feeding earlier than the scheduled feeding time, the pre-feeding period for another feeding for the same infant was used. Detectable changes in pre-feeding periods between two feedings in a day were not expected to occur. For three feeding observations, the pre-feeding period was insufficient to find the qualified 2-minute segment of pre-feeding period.

Artifacts were determined by comparing the trace of waveform data and the infant's actual activities on the videotapes. *Artifacts for SpO_2* are defined as either: (a) areas of SpO_2 trace that exceed the physiologically possible signal changes from one second to the next ($SpO_2 \geq 5\%$) or (b) areas that show erratic pulse waveforms that do not correspond to ECGs of more than two seconds, accompanied by the infant's large-scale movements (e.g., handling the infant for burping, moving the infant back to the crib, or crying), as determined from the videotapes. Similarly, *artifacts for HR* are defined as either: (a) areas of HR trace that exceed the physiologically possible signal changes from one second to the next ($HR \geq 10$ bpm) or (b) areas that show erratic ECG signals (e.g., noisy baseline, irregular amplitude of QRS peak, and/or irregular R-R interval), accompanied by the infant's large-scale movements as determined from the videotapes. *Artifacts for RESCs* were determined by comparing the traces of respiratory waveform data, the infant's actual activities on the videotapes, and the breathing and swallowing sounds measured by the microphone attached to the infant's neck. All of the artifacts were removed from the physiologic dataset, and the artifact-free physiologic dataset was converted to SAS 9.2 for data analysis.

Descriptive data include infant characteristics and feeding performance data. All descriptive data were entered twice by the PI for cross-verification, and all discrepancies were resolved and corrected by comparing these two datasets. Nominal data were coded numerically to facilitate analysis (e.g., male = 0, female = 1, White = 0, or African-American = 1, etc). Numerical data were entered as they appeared, with no modification. All descriptive data were entered into a single Excel spreadsheet and converted to SAS 9.2 for data analysis.

Observational data were coded using the Noldus Observer XT program, which generated frequencies and durations of all the behavioral codes. Duration was chosen for the codes of infant position and divided by the duration of the bottle-in period (i.e., non-feeding and burping periods removed) to calculate the proportion of feeding time when the infant was held in a semi-upright position for the condition of the HES position (supine) and in a side-lying position for the condition of the HEL position (side-lying). Frequency was chosen for the codes to assess the caregiver's feeding behaviors. The frequency for codes of some caregivers' feeding behaviors was further divided by the total number of bottle-in episodes to calculate the proportion of onsets of feeding based on a caregiver's behavior to prepare the infant (prep) and the infant's readiness (ready). All observational data were converted into a single Excel spreadsheet for calculating descriptive statistics using SAS 9.2.

Data Management

All data collected as part of this study were stored on a laptop computer (dedicated for this research project) that is the property of the PI, under a password-protected system in which two separate passwords are required to access information. The initial password is used to activate the computer, and a different password is required to open any files containing protected health information. Also, data were backed up on a password-protected external hard drive. After being entered into an Excel spreadsheet, hardcopy information was stored in a locked drawer in the PI's office in the School of Nursing at the University of North Carolina at Chapel Hill.

Data Analysis

Several analyses were conducted using SAS 9.2, including descriptive statistics, paired t-tests, linear mixed modeling (LMM), and simulations. *Statistical significance* is defined as a p-value less than .10 for all analyses. With six VP infants, this study may not be powered sufficiently. That is, the paired t-test at a two-sided 0.05 significance level would have 80% power to identify an effect size of 1.44 with six VP infants. A repeated measures analysis of variance over four time points for the difference between measurements in the two positions would generate an effect size of 0.59 with 80% power at a two-sided 0.05 significance level (computed with nQuery Advisor, Statistical Solutions, Inc., Saugus, MA). However, the PI acknowledges that this study will not be powered sufficiently to detect a significant difference between groups. Because this work is a pilot study, the results will be used to provide evidence of trends toward significant difference to justify future study.

Prior to analysis, descriptive statistics (i.e., mean, SD, minimum, and maximum) of the major outcome variables were calculated and tabulated to summarize the variability and distribution of the data. The major outcome variables include HR, SpO_2, some of the RESCs (i.e., intervals between breaths, duration of breath, amplitude of breath, and respiratory rate), and feeding performance.

H1. It is hypothesized that, compared to VP infants bottle-fed in the HES position, VP infants bottle-fed in the HEL position would demonstrate greater physiological stability and better feeding performance during feeding.

To address Hypothesis 1, during the pre-feeding, feeding, and bottle-in periods, the mean, SD, and CV for HR and SpO_2 were calculated. In addition, during the bottle-in periods, the percentages of time with the degrees of change in HR and SpO_2 were calculated. For RESCs, the mean, SD, and CV of breath-to-breath intervals, duration and amplitude of breaths, and respiratory rate were calculated during the pre-feeding and first six minutes of the bottle-in periods. During the first six minutes of the bottle-in periods, the percentage of time with breathing pauses longer than three seconds also was calculated. Paired t-tests were used to assess the differences in each physiologic measure between the feeding positions. A comparison of feeding performance measures between the feeding positions was made using paired t-tests. The normality assumption for all outcome variables was assessed and, if normality was questionable, nonparametric alternative tests (i.e., the Wilcoxon signed rank test and the sign test) were used.

H2. It is hypothesized that, compared to VP infants bottle-fed in the HES position, VP infants bottle-fed in the HEL position would demonstrate fewer physiological changes from the pre-feeding period across the feeding period.

To address Hypothesis 2, three different methods were chosen to create intervals of feeding time, because no clear understanding is currently available to examine changes in physiologic stability across the feeding period in terms of best time and intervals. To remove potentially confounding data, non-feeding and burping periods were eliminated, and the bottle-in periods were examined using three intervals of time: (1) dividing the entire bottle-in period into three equal intervals (which differed in length according to infant and/or feeding observation, e.g., some infants fed for longer periods of time than others); (2) extracting 2-minute intervals from the initial, middle, and final third of the feeding period; and (3) dividing the first six minutes of the bottle-in period into three 2-minute intervals (0-2, 2-4, and 4-6 minutes each) (Figure 3.5).

The mean, SD, and CV for HR and SpO_2 were calculated during the pre-feeding period and for each interval of time. For RESCs, the mean, SD, and CV of the intervals between breaths and breath duration and amplitude were calculated only during the pre-feeding and successive two minutes for the first six minutes of the bottle-in period (i.e., Method 3), because the RESCs variable is new and exploratory. LMM was used for each variable and method to examine whether a significant pattern in physiologic stability was evident across the three time points during feeding by controlling for the pre-feeding period as a covariate, and to determine whether this pattern was different according to feeding position. Covariance structures accounted for possible within-infant correlations for outcomes across time and feeding positions. Residual analysis was conducted for all longitudinal outcome variables to assess if each outcome variable was normally distributed or had no outliers or asymmetry. The transformation of the data and/or sensitivity analyses were performed to resolve the non-normality, outliers, or asymmetry, as needed. Finally, a thousand simulations of LMMs for each longitudinal outcome variable and method were conducted for varying numbers of infants in order to determine the most optimal method, as determined by the method that requires the smallest number of infants to detect a position effect with 80% power.

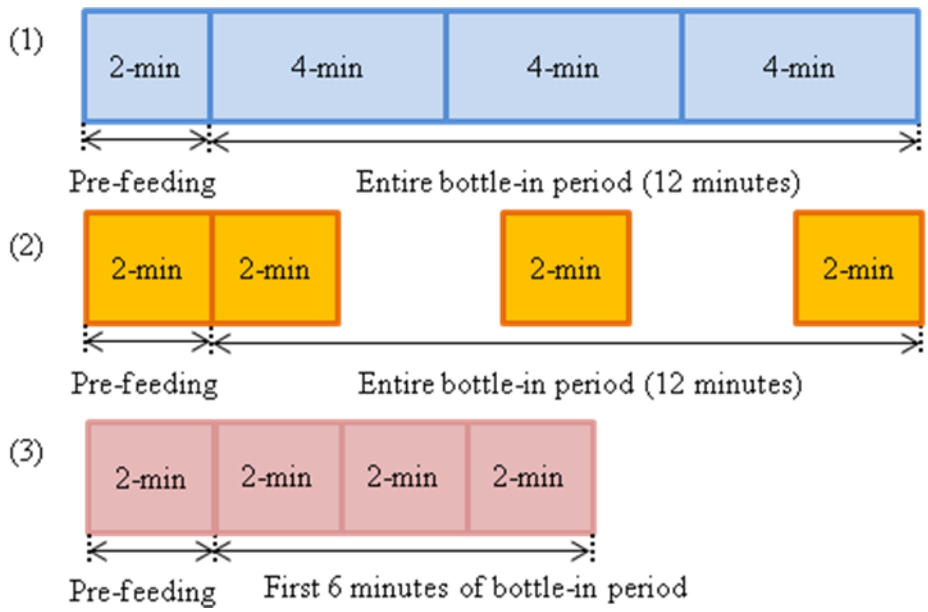

Figure 3.3. Example of the Time Intervals using the Three Methods with 12-Minute Duration Feeding

Intervention Fidelity

To evaluate the intervention fidelity, the entire feeding period was coded for the two infant positions (HES/supine and HEL/side-lying) and the five feeding behaviors implemented by the caregiver (prep, ready, numb rest period, stim suck, and limit flow). Duration was calculated for the codes of the infant position and divided by the duration of the bottle-in periods (i.e., non-feeding and burping periods removed) to calculate the proportion of feeding time when the infant was held in a semi-upright position for the condition of the

HES position and in a side-lying position for the condition of the HEL position. Frequency was calculated for the codes to assess the caregiver's actions. For some codes of caregiver feeding behaviors, the frequency was further divided by total number of bottle-in episodes to calculate the proportion of onsets of feeding based on the caregiver's behavior to prepare the infant and the infant's readiness. Descriptive statistics (i.e., mean, SD, minimum, and maximum) of each behavioral code were calculated and tabulated to assess the variability of the intervention delivery within and across the infants.

CHAPTER IV

RESULTS

This chapter presents the findings of the study. Several analytic strategies are employed in this study. Descriptive statistics of the study infants and major variables are presented first. Following the descriptive statistics, the results of paired t-tests to address Hypothesis 1 and linear mixed modeling to address Hypothesis 2 are presented. Also, simulated sample size results are presented to suggest the optimal method among three candidate methods to examine changes in physiological stability over feeding time. Finally, descriptive statistics to evaluate intervention fidelity are provided.

Characteristics of Study Infants

Six VP infants, who were admitted to the NCCC at North Carolina Children's Hospital in Chapel Hill, North Carolina between June 1, 2011 and September 30, 2011, are the subjects of this study. The infants' characteristics are summarized in Table 4.1. The infants were similar with respect to birth characteristics. Most of the infants were female, and half were white. The infants differed in their PMA and feeding experience but had similar feeding skills at the time of the study. The infants were able to consume on average 58.3% (ranged from 49.4% to 66.1%) of their prescribed milk by mouth for 72 hours prior to the study. Certain types of respiratory support were required prior to the study across infants but only two infants were receiving supplemental oxygen and airflows at the time of the study.

Four infants had either mild or moderate lung disease. One infant had a higher score on the NBRS than the other infants, which indicated an intermediate risk for neurologic problems (Brazy et al., 1993).

Table 4.1. Characteristics of the Study Infants (n = 6)

Variables	Mean ± SD or *n* (%)	Infant 1	Infant 2	Infant 3	Infant 4	Infant 5	Infant 6
Characteristics of the infant							
Gestational age (weeks)	28.1 ± 1.0	26.7	29.4	28	27.3	27.9	29
Birth weight (grams)	1122 ± 233	760	1144	1174	965	1430	1256
APGAR at 1 minute	5 ± 2	5	6	8	3	2	4
APGAR at 5 minutes	8 ± 1	9	7	8	7	9	7
Gender		Female	Female	Male	Female	Male	Female
Male	2 (33.3)						
Female	4 (66.7)						
Race		White	White	Black	Hispanic	Hispanic	White
White	3 (50.0)						
Black	1 (16.7)						
Hispanic	2 (33.3)						
Severity of lung disease [a]		Mild	Moderate	None	Mild	None	Mild
None	2 (33.3)						
Mild	3 (50.0)						
Moderate	1 (16.7)						
Severe	0 (0.00)						
Characteristics of the infant at time of study							
Postmenstrual age at study (weeks)	35.5 ± 2.1	38.6	35.6	32.7	34.1	35.3	36.9
Weight at study (grams)	2262 ± 250	2550	2220	1910	2100	2250	2540
Days on ventilator	1 ± 1	3	0	0	0	2	0
Days on CPAP [b]	15 ± 11	35	9	10	7	19	8
Days on supplemental oxygen or airflow	19 ± 13	6	33	12	34	6	24
Neurobiologic risk score [c]	2 ± 2	6	1	1	1	1	2
Oxygen use during feeding	2 (33.3)	No	Yes	No	Yes	No	No
Feeding experience [d]	79 ± 56	179	48	23	61	103	58
Feeding skill at study [e] (%)	58.3 ± 6.3	54.8	66.1	61.2	49.4	63.2	54.8

Note. [a] Severity of lung disease = diagnostic criteria for bronchopulmonary dysplasia depending on the duration and degree of supplemental oxygen required at 36 weeks of PMA; [b] CPAP = continuous positive airway; [c] Neurobiologic risk score (0 – 28) = scores indicating possible medical conditions that are associated with neurological problems (low, ≤ 4; intermediate, 5-7; high, ≥ 8); [d] Feeding experience = number of cumulative nipple feedings either from the bottle or breast prior to the study; [e] Feeding skill at study = percentage of milk from the prescribed milk consumed by mouth in 72 hours prior to the study.

Descriptive Statistics of Major Variables

Prior to analysis, the variability and distribution of the data were examined by calculating the descriptive statistics. The mean, SD, minimum, and maximum of the major variables were calculated and tabulated per infant by feeding position during the pre-feeding, feeding, and bottle-in periods. *Pre-feeding period* is defined as a 2-minute period prior to feeding when the infant is calm and quiet in the bed and no demands are placed on him or her. *Feeding period* is defined as the period of time from the first time the bottle is placed in the infant's mouth until the last time it is removed. *Bottle-in period* is defined as the period that the non-feeding and burp periods are removed from the feeding period. The major variables include HR, SpO_2, several RESCs (i.e., the interval between breaths, duration of breath, amplitude of breath, and respiratory rate), and feeding performance.

Heart Rate

Table 4.2 presents the mean, SD, minimum, and maximum of individual HR measurements taken during the pre-feeding, feeding, and bottle-in periods by feeding position. During the pre-feeding period, the mean HR for each infant ranged from 149.0 to 165.2 bpm in the HES position and from 143 to 165.2 bpm in the HEL position. The minimum HR for each infant ranged from 140.8 to 155.8 bpm in the HES position and from 135.7 to 155.8 bpm in the HEL position. The maximum HR for each infant ranged from 155.0 to 172.4 bpm in the HES position and from 150.8 to 172.4 bpm in the HEL position. During the pre-feeding period, HR was computed individually for each infant. As a consequence, at least one infant had a mean HR greater than the maximum HR of another infant, and at least one infant had a mean HR lower than the minimum of another infant.

During the feeding period, the mean HR for each infant increased from that of the pre-feeding period, and ranged from 154.1 to 176.0 bpm in the HES position and from 153.6 to 178.0 bpm in the HEL position. Variability in HR also increased from that of the pre-feeding period. The minimum HR for each infant was lower than during the pre-feeding period, and ranged from 75.3 to 100 bpm in the HES position and from 92.0 to 137.0 bpm in the HEL position. The maximum HR for each infant was higher than during the pre-feeding period, and ranged from 174.4 to 200.7 bpm in the HES position and from 173.4 to 196.1 bpm in the HEL position. During the bottle-in periods, the ranges of the mean, minimum, and maximum HR were similar to those during the feeding period.

Table 4.2. Descriptive Statistics for Heart Rate for Each Infant by Position

Infant	Period	HES position				HEL position			
		Mean	SD	Min	Max	Mean	SD	Min	Max
1	Pre-feeding	149.9	2.9	140.8	156.3	143.9	2.8	135.7	150.8
	Feeding [a]	168.7	14.6	86.3	200.7	171.1	10.4	107.3	196.1
	Bottle-in [b]	167.3	13.8	86.3	200.0	170.8	10.2	107.3	196.1
2	Pre-feeding	157.8	2.1	149.3	161.3	155.1	1.7	150.8	157.9
	Feeding	160.1	10.8	96.3	178.6	153.6	9.6	113.9	173.4
	Bottle-in	159.3	11.1	96.3	176.0	152.1	8.9	113.9	166.2
3	Pre-feeding	148.7	2.3	141.8	155.0	149.8	2.3	143.9	155.4
	Feeding	166.3	6.7	88.2	176.5	178.0	4.8	137.0	191.7
	Bottle-in	165.8	7.2	88.2	175.4	178.4	4.0	159.2	191.7
4	Pre-feeding	165.2	3.0	155.8	172.4	165.2	3.0	155.8	172.4
	Feeding	176.0	10.8	94.8	198.0	176.3	6.7	132.2	193.0
	Bottle-in	174.4	12.0	94.8	186.3	176.9	6.5	132.2	193.0
5	Pre-feeding	149.0	3.0	141.5	161.3	151.9	2.5	145.6	159.6
	Feeding	154.9	11.7	100.0	184.6	164.9	7.3	113.6	186.9
	Bottle-in	153.3	12.1	100.0	184.6	163.7	7.0	116.7	178.6
6	Pre-feeding	158.6	5.4	142.2	169.0	158.6	5.4	142.2	169.0
	Feeding	154.1	15.5	75.3	174.4	156.6	10.4	92.0	176.0
	Bottle-in	157.3	10.5	95.7	172.4	156.5	9.7	92.0	174.9

Note. HES = head-elevated supine; HEL = head-elevated side-lying; Min = minimum; Max = maximum. Unit for heart rate is bpm. [a] Feeding period = the period of time from the first time the bottle is placed in the infant's mouth until the last time when it is removed. [b] Bottle-in periods = the non-feeding and burp periods are removed from the feeding period.

Oxygen Saturation

Table 4.3 presents the mean, SD, minimum, and maximum of individual SpO_2 levels during the pre-feeding, feeding, and bottle-in periods by feeding position. During the pre-feeding period, the SpO_2 levels remained over 99% except for infant 6. The mean SpO_2 for infant 6 was 97.9% and had more variability in SpO_2 than the other infants, and ranged from 92.5% to 98.9 percent.

During the feeding period, the mean SpO_2 for each infant decreased from that of the pre-feeding period, and ranged from 93.4% to 99.0% in the HES position and from 93.4% to 99.2% in the HEL position. The variability in SpO_2 increased from that of the pre-feeding period. The minimum SpO_2 for each infant was lower than during the pre-feeding period, and ranged from 41.9% to 86.8% in the HES position and from 52.0% to 89.7% in the HEL position. The maximum SpO_2 for each infant remained similar to that during the pre-feeding period, and ranged from 99.4% to 99.9% in both the HES and HEL positions. During the bottle-in periods, the ranges of the mean, minimum, and maximum SpO_2 were similar to those during the feeding period.

Table 4.3. Descriptive Statistics for Oxygen Saturation for Each Infant by Position

Infant	Period	HES position				HEL position			
		Mean	SD	Min	Max	Mean	SD	Min	Max
1	Pre-feeding	99.3	0.1	98.7	99.4	99.4	0.0	99.3	99.4
	Feeding [a]	97.4	2.5	86.3	99.4	99.0	1.35	89.7	99.4
	Bottle-in [b]	97.4	2.5	86.3	99.4	99.0	1.4	89.7	99.4
2	Pre-feeding	99.8	0.0	99.8	99.8	99.9	0.0	99.9	99.9
	Feeding	96.6	4.6	79.8	99.8	96.7	4.1	80.9	99.9
	Bottle-in	96.7	4.6	79.8	99.8	96.8	4.0	80.9	99.9
3	Pre-feeding	99.8	0.0	99.8	99.9	99.8	0.0	99.8	99.9
	Feeding	99.0	2.0	81.8	99.9	99.2	2.0	84.8	99.9
	Bottle-in	99.1	2.0	81.8	99.9	99.2	2.0	84.8	99.9
4	Pre-feeding	99.8	0.2	98.9	99.9	99.8	0.2	98.9	99.9
	Feeding	98.4	4.4	67.9	99.9	97.1	5.0	69.8	99.9
	Bottle-in	98.1	4.9	68.0	99.9	96.9	5.2	69.8	99.9
5	Pre-feeding	99.8	0.0	99.8	99.8	99.8	0.0	99.8	99.8
	Feeding	98.6	2.3	86.8	99.8	98.7	2.3	85.9	99.8
	Bottle-in	98.5	2.4	86.8	99.8	98.6	2.4	85.9	99.8
6	Pre-feeding	97.9	1.0	92.5	98.9	97.9	1.0	92.5	98.9
	Feeding	93.4	10.6	41.9	99.9	94.4	7.4	52.0	99.9
	Bottle-in	94.2	7.3	57.1	99.9	95.1	5.9	69.1	99.9

Note. HES = head-elevated supine; HEL = head-elevated side-lying; Min = minimum; Max = maximum. Unit for oxygen saturation is %. [a] Feeding period = the period of time from the first time the bottle is placed in the infant's mouth until the last time when it is removed. [b] Bottle-in periods = the non-feeding and burp periods are removed from the feeding period.

Respiratory Characteristics

RESCs were examined as the interval between breaths, breath duration, breath amplitude, respiratory rate, and percentage of feeding time with breathing pauses longer than three seconds. Figure 4.1 depicts examples of variation in interval between breaths, breath duration, and breath amplitude that were frequently observed in the respiratory waveforms during feeding. Individual descriptive statistics were calculated and tabulated for the interval between breaths, breath duration, breath amplitude, and respiratory rate.

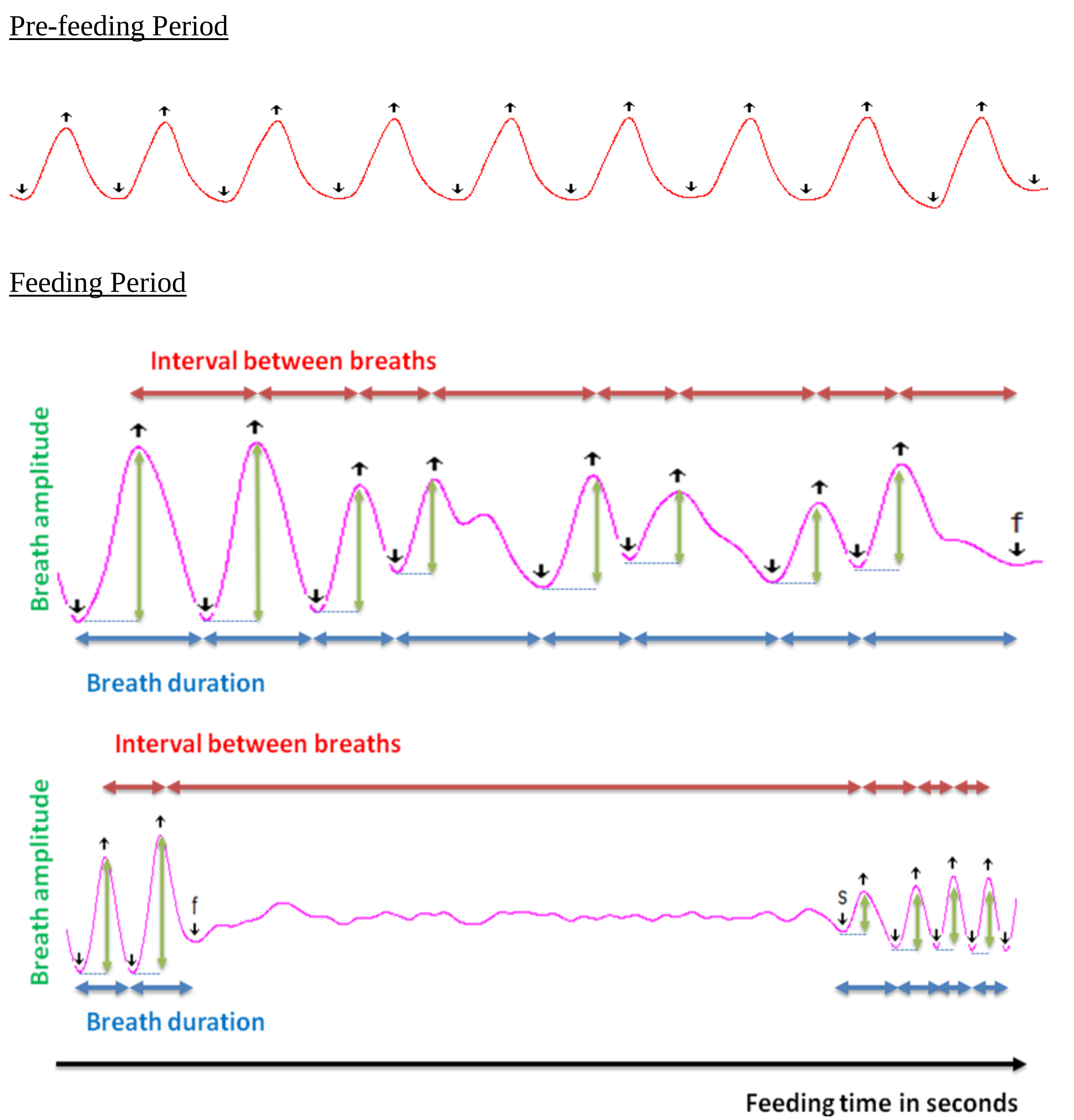

Figure 4.1. Examples of Variation in Respiration during Feeding

Interval between breaths. Table 4.4 presents the mean, SD, minimum, and maximum of the individual intervals between breaths during the pre-feeding and first six minutes of the bottle-in period by feeding position. During the pre-feeding period, the mean interval between breaths for each infant ranged from 0.84 to 1.20 seconds in the HES position and from 0.72 to 1.20 seconds in the HEL position. The minimum interval between breaths for each infant ranged from 0.32 to 0.86 seconds in the HES position and from 0.39 to 0.83 seconds in the HEL position. The maximum interval between breaths for each infant ranged from 1.12 to 4.74 seconds in the HES position and from 1.08 to 4.74 seconds in the HEL position. During the pre-feeding period, the interval between breaths was computed individually for each infant. As a consequence, at least one infant had a mean interval between breaths that was longer than the maximum interval between breaths of another infant, and at least one infant had a mean interval between breaths that was shorter than the minimum of another infant.

During the first six minutes of the bottle-in period, the mean interval between breaths for each infant was longer than during the pre-feeding period, and ranged from 1.11 to 1.64 seconds in the HES position and from 1.03 to 1.45 seconds in the HEL position. The variability in interval between breaths increased from that of the pre-feeding period. The minimum interval between breaths for each infant decreased from that of the pre-feeding period, and ranged from 0.37 to 0.41 seconds in the HES position and from 0.25 to 0.42 seconds in the HEL position. The maximum interval between breaths for each infant increased from that of the pre-feeding period, and ranged from 11.02 to 42.23 seconds in the HES position and from 11.04 to 16.95 seconds in the HEL position.

Table 4.4. Descriptive Statistics for the Interval between Breaths for Each Infant by Position

Infant	Period	HES position				HEL position			
		Mean	SD	Min	Max	Mean	SD	Min	Max
1	Pre-feeding	1.09	0.18	0.83	2.41	1.09	0.18	0.83	2.41
	First 6 min bottle-in	1.33	2.91	0.37	36.06	1.14	1.73	0.34	11.04
2	Pre-feeding	0.84	0.15	0.32	1.12	0.72	0.10	0.48	1.08
	First 6 min bottle-in	1.61	3.05	0.40	21.4	1.27	2.01	0.42	16.91
3	Pre-feeding	1.11	0.11	0.86	1.50	1.00	0.19	0.50	1.56
	First 6 min bottle-in	1.11	1.28	0.39	11.02	1.03	1.36	0.36	11.68
4	Pre-feeding	0.99	0.32	0.39	2.94	0.99	0.32	0.39	2.94
	First 6 min bottle-in	1.64	3.23	0.41	21.90	1.29	2.14	0.25	16.95
5	Pre-feeding	1.18	0.22	0.81	2.35	1.19	0.18	0.68	1.75
	First 6 min bottle-in	1.32	2.11	0.38	14.82	1.45	2.40	0.37	15.14
6	Pre-feeding	1.20	0.45	0.56	4.74	1.20	0.45	0.56	4.74
	First 6 min bottle-in	1.48	3.43	0.38	42.23	1.38	2.08	0.33	12.68

Note. HES = head-elevated supine; HEL = head-elevated side-lying; Min = minimum; Max = maximum. Unit for interval between breaths is second.

Breath duration. Table 4.5 presents the mean, SD, minimum, and maximum of individual breath duration during pre-feeding and the first six minutes of the bottle-in period by feeding position. During the pre-feeding period, the mean duration of breath for each infant ranged from 0.84 to 1.20 seconds in the HES position and from 0.72 to 1.20 seconds in the HEL position. The minimum duration of breath for each infant ranged from 0.24 to 0.84 in the HES position and from 0.39 to 0.84 seconds in the HEL position. The maximum duration of breath for each infant ranged from 1.14 to 5.02 seconds in the HES position and from 1.02 to 5.02 seconds in the HEL position. Again, during the pre-feeding period, duration of breath was computed individually for each infant. As a consequence, at least one infant had a mean duration of breath that was longer than the maximum duration of breath of another infant, and at least one infant had a mean duration of breath that was shorter than the minimum of another infant.

During the first six minutes of the bottle-in periods, the mean breath duration for each infant was shorter than during the pre-feeding period, and ranged from 0.63 to 0.88 seconds in the HES position and from 0.67 to 0.80 seconds in the HEL position. The minimum interval between breaths for most infants decreased from that of the pre-feeding period, and ranged from 0.34 to 0.42 seconds in the HES position and from 0.28 to 0.44 seconds in the HEL position. Changes in the maximum duration of breath from the pre-feeding period showed the opposite direction in most infants by feeding position. In the HES position, the maximum duration of breath was shorter than that during the pre-feeding period, except for infant 2, and ranged from 1.80 to 2.11 seconds; however in the HEL position, the maximum duration of breath was longer than that during the pre-feeding period, except for infant 4 and 6, and ranged from 1.69 to 3.08 seconds. The overall variability in breath duration increased during feeding from the pre-feeding period for most infants.

Table 4.5. Descriptive Statistics for Breath Duration for Each Infant by Position

Infant	Period	HES position				HEL position			
		Mean	SD	Min	Max	Mean	SD	Min	Max
1	Pre-feeding	1.09	0.17	0.84	2.37	1.09	0.17	0.84	2.37
	First 6 min bottle-in	0.63	0.25	0.36	2.07	0.67	0.27	0.35	3.08
2	Pre-feeding	0.84	0.13	0.24	1.14	0.72	0.09	0.52	1.02
	First 6 min bottle-in	0.72	0.20	0.34	1.56	0.80	0.26	0.44	2.27
3	Pre-feeding	1.11	0.15	0.65	1.99	1.00	0.13	0.80	1.44
	First 6 min bottle-in	0.88	0.24	0.42	1.88	0.75	0.22	0.38	1.69
4	Pre-feeding	0.99	0.31	0.38	2.92	0.99	0.31	0.38	2.92
	First 6 min bottle-in	0.70	0.24	0.40	1.87	0.79	0.29	0.28	2.20
5	Pre-feeding	1.18	0.21	0.82	2.42	1.19	0.15	0.81	1.66
	First 6 min bottle-in	0.80	0.24	0.39	2.11	0.76	0.24	0.36	2.13
6	Pre-feeding	1.20	0.45	0.61	5.02	1.20	0.45	0.61	5.02
	First 6 min bottle-in	0.76	0.27	0.36	1.80	0.73	0.26	0.28	2.06

Note. HES = head-elevated supine; HEL = head-elevated side-lying; Min = minimum; Max = maximum. Unit for breath duration is second.

Breath amplitude. Table 4.6 presents the mean, SD, minimum, and maximum of individual breath amplitude during pre-feeding and the first six minutes of the bottle-in period by feeding position. During the pre-feeding period, the mean amplitude of breath for each infant ranged from 0.010 to 0.028 volts in the HES position and from 0.010 to 0.027 volts in the HEL position. The minimum amplitude of breath for each infant ranged from 0.003 to 0.008 volts in both the HES and HEL positions. The maximum amplitude of breath for each infant ranged from 0.012 to 0.145 volts in the HES position and from 0.014 to 0.179 volts in the HEL position. During the pre-feeding period, amplitude of breath also was computed individually for each infant. As a consequence, at least one infant had a mean amplitude of breath that was greater than the maximum amplitude of breath of another infant, and at least one infant had a mean amplitude of breath that was lower than the minimum of another infant.

During the first six minutes of the bottle-in period, the mean amplitude of breath for each infant increased from that of the pre-feeding period, and ranged from 0.050 to 0.181 volts in the HES position and from 0.037 to 0.129 volts in the HEL position. The variability in breath amplitude increased from that of the pre-feeding period. The minimum amplitude of breath for each infant was similar to that during the pre-feeding period, and ranged from 0.004 to 0.030 volts in the HES position and from 0.009 to 0.020 volts in the HEL position. However, the maximum amplitude of breath for each infant increased from the pre-feeding period, ranging from 0.158 to 0.609 volts in the HEL position and from 0.120 to 0.474 volts in the HES position.

Table 4.6. Descriptive Statistics for Breath Amplitude for Each Infant by Position

Infant	Period	HES position				HEL position			
		Mean	SD	Min	Max	Mean	SD	Min	Max
1	Pre-feeding	0.011	0.001	0.008	0.014	0.011	0.001	0.008	0.014
	First 6 min bottle-in	0.061	0.040	0.006	0.372	0.087	0.047	0.020	0.337
2	Pre-feeding	0.010	0.002	0.007	0.020	0.011	0.002	0.005	0.015
	First 6 min bottle-in	0.050	0.024	0.004	0.158	0.037	0.014	0.009	0.120
3	Pre-feeding	0.010	0.001	0.004	0.012	0.010	0.002	0.006	0.020
	First 6 min bottle-in	0.066	0.024	0.011	0.178	0.092	0.035	0.017	0.232
4	Pre-feeding	0.011	0.007	0.003	0.044	0.011	0.007	0.003	0.044
	First 6 min bottle-in	0.074	0.033	0.021	0.245	0.129	0.070	0.012	0.474
5	Pre-feeding	0.028	0.016	0.006	0.145	0.020	0.018	0.003	0.179
	First 6 min bottle-in	0.111	0.061	0.016	0.458	0.079	0.038	0.013	0.346
6	Pre-feeding	0.027	0.013	0.005	0.090	0.027	0.013	0.005	0.090
	First 6 min bottle-in	0.181	0.080	0.030	0.609	0.113	0.049	0.011	0.442

Note. HES = head-elevated supine; HEL = head-elevated side-lying; Min = minimum; Max = maximum. Unit for breath amplitude is volt.

Respiratory rate. Table 4.7 presents individual respiratory rates per minute during the pre-feeding and the first six minutes of the bottle-in period by feeding position. During the pre-feeding period, the respiratory rate for each infant ranged from 51 to 70 per minute in the HES position and from 50 to 82 per minute in the HEL position. During the first six minutes of the bottle-in period, the respiratory rate for each infant decreased from that of the pre-feeding period, and ranged from 36 to 53 per minute in the HES position and from 41 to 53 per minute in the HEL position.

Table 4.7. Descriptive Statistics for Respiratory Rate for Each Infant by Position

Infant	HES position		HEL position	
	Pre-feeding period	First 6 min of bottle-in period	Pre-feeding period	First 6 min of bottle-in period
1	54	46	54	53
2	70	36	82	47
3	54	53	60	58
4	60	36	60	46
5	51	44	50	41
6	50	40	50	43
Mean	56	42	59	48
SD	8	6	12	6
Min	51	36	50	41
Max	70	53	82	53

Note. HES = head-elevated supine; HEL = head-elevated side-lying; Min = minimum; Max = maximum. Respiratory rate is calculated per minute.

Feeding Performance

Feeding performance was examined in terms of the overall milk transfer, proficiency, efficiency, and duration of the feeding time in minutes. Overall milk transfer was calculated as the percentage of milk consumed from the prescribed amount of milk (%). Efficiency was calculated as the amount of milk in milliliters consumed by total feeding time in minutes (ml/min). Proficiency was calculated as the percentage of milk consumed during the first five minutes of the feeding period (%). Duration of feeding time was calculated as the minutes of the feeding time after removing the non-feeding and burping periods. Individual feeding performance measures are described in Table 4.8. All infants consumed almost all their prescribed milk; this overall milk transfer ranged from 80% to 100% for both positions. During the first five minutes of feeding, the infants consumed an average 44.3% in the HES position, ranging from 25.5% to 86.5%, and 42.3% in the HEL position, ranging from 24.3 to 57.5 percent. Efficiency ranged from 1.5 to 3.1 ml/min in the HES position and from 1.8 to

3.7 ml/min in the HES position. Duration of feeding time ranged from 7.4 to 14.8 minutes in the HES position and from 10.3 to 18.0 minutes in the HEL position.

Table 4.8. Descriptive Statistics for Feeding Performance for Each Infant by Position

Infant	HES position				HEL position			
	Overall milk transfer (%)	Effi-ciency (ml /min)	Pro-ficiency (%)	Duration of feeding time (min)	Overall milk transfer (%)	Effi-ciency (ml /min)	Pro-ficiency (%)	Duration of feeding time (min)
1	86.7	2.4	37.8	13.3	80.0	1.8	37.8	18.0
2	100.0	2.6	29.7	14.0	100.0	2.8	24.3	13.4
3	80.0	1.5	28.6	14.8	91.4	2.0	37.1	14.2
4	100.0	3.1	86.5	7.4	100.0	2.3	45.9	10.9
5	100.0	3.0	57.5	10.0	100.0	2.6	57.5	10.3
6	89.4	1.9	25.5	10.2	100.0	3.7	51.1	11.2
Mean	92.7	2.4	44.3	11.6	95.2	2.5	42.3	13.0
SD	8.6	0.6	23.7	2.9	8.2	0.7	11.8	2.9
Min	80.0	1.5	25.5	7.4	80.0	1.8	24.3	10.3
Max	100.0	3.1	86.5	14.8	100.0	3.7	57.5	18.0

Note. HES = head-elevated supine; HEL = head-elevated side-lying; Min = minimum; Max = maximum.

Hypothesis 1: When compared to infants bottle-fed in the HES position, VP infants bottle-fed in the HEL position would demonstrate greater physiological stability and better feeding performance.

Hypothesis 1 was tested using paired t-tests to assess the differences in physiological stability and feeding performance between the two feeding positions. Because this is a pilot study, the significance level was set at p = .10, and p-values less than .20 were considered to be indicative of trends. Results from nonparametric alternative tests (i.e., the Wilcoxon signed rank test and the sign test) also were computed. The conclusions for the alternative tests were the same as for the paired t-tests except that some cases no longer indicated possible trends. Consequently, only results for the paired t-tests are reported (Tables 4.9 - 4.17).

Comparisons of Physiological Stability

The physiological variables include HR, SpO_2, and RESCs. Physiological stability was examined by calculating the mean, SD, and CV (the ratio of the SD divided by the mean for the assigned period) of each physiological variable. For HR and SpO_2, the percentages of feeding time with degrees of changes from an individual infant's pre-feeding level also were calculated.

Heart Rate

The mean, SD, and CV of HR during the pre-feeding, feeding, and bottle-in periods are described in Table 4.9. During the pre-feeding period, no significant differences were found in the mean, SD, and CV of HR prior to each of the infant's two feeding observations, and only the trend of a lower SD of HR was observed prior to the feeding condition in the

HEL position compared to that of the HES position. Therefore, the study infants exhibited comparable HR states prior to the experimental conditions. During the feeding period, no difference in the means for HR was observed; however, the infants showed significantly less variation in HR (i.e., lower SD and CV of HR) when fed in the HEL position compared to the HES position. Similarly, during the bottle-in periods, no difference in the means for HR was observed; however, the infants showed significantly less variation in HR (i.e., lower SD and CV of HR) when fed in the HEL position compared to the HES position.

Table 4.9. Comparisons of Heart Rate between Feeding Positions (n = 6)

Variables	Feeding Position		*t*	*p*-value
	HES	HEL		
Pre-feeding period				
Mean of HR (bpm)	154.9 ± 6.7	154.1 ± 7.4	-0.62	.564
SD of HR	3.1 ± 1.2	3.0 ± 1.3	-1.62	.166
CV of HR	0.02 ± 0.01	0.02 ± 0.01	-1.37	.229
Feeding period				
Mean of HR (bpm)	163.3± 8.5	166.7 ± 10.2	1.26	.264
SD of HR	11.7 ± 3.1	8.2 ±2.3	-5.55	.003
CV of HR	0.07 ± 0.02	0.05 ± 0.02	-4.92	.004
Bottle-in periods				
Mean of HR (bpm)	162.9± 7.7	166.4 ± 10.8	1.18	.292
SD of HR	11.1 ± 2.2	7.7 ±2.4	-4.67	.005
CV of HR	0.07 ± 0.01	0.04 ± 0.02	-4.33	.007

Note. HES = head-elevated supine; HEL = head-elevated side-lying; CV = coefficient of variation; HR = heart rate. Data are expressed as mean ± SD.

Changes in Heart Rate

Both increases in HR and decreases in HR during feeding were examined. Increases in HR are defined as HRs at least 10% (mild), 15% (moderate), and 20% (severe) above those of the pre-feeding period, and decreases in HR are defined as HRs at least 10% (mild), 15% (moderate), and 20% (severe) below those of the pre-feeding period, and HRs below

100 bpm. HR cutoffs for each category were calculated per feeding observation based on the pre-feeding period for a given feeding; these cutoffs were used to calculate the percentage of feeding time for each category. Using infant 1 as an example, the percentages of feeding time with HRs greater than 164.9, 172.4, and 179.9 were calculated for HRs at least 10%, 15%, and 20% above the pre-feeding period, respectively. Similarly, the percentages of feeding time with HRs less than 134.9, 127.4, and 119.9 were calculated for HRs at least 10%, 15%, and 20% below the pre-feeding period, respectively. Individual HR cutoffs that were used to define the degrees of changes in HR per feeding position are presented in Table 4.10.

Table 4.10. Individual Cutoffs Used for Defined Changes in Heart Rate from the Pre-feeding periods per Position

Infant	HES position						HEL position					
	1	2	3	4	5	6	1	2	3	4	5	6
Mean HR during pre-feeding period	149.9	157.8	148.7	165.2	149.0	158.6	143.9	155.1	149.8	165.2	151.9	158.6
HR at 10% above pre-feeding mean	164.9	173.6	163.6	181.7	163.9	174.5	158.3	170.6	164.8	181.7	167.1	174.5
HR at 15% above pre-feeding mean	172.4	181.5	171.0	190.0	171.4	182.4	165.5	178.4	172.3	190.0	174.7	182.4
HR at 20% above pre-feeding mean	179.9	189.4	178.4	198.2	178.8	190.3	172.7	186.1	179.8	198.2	182.3	190.3
HR at 10% below pre-feeding mean	134.9	142.0	133.8	148.7	134.1	142.7	129.5	139.6	134.8	148.7	136.7	142.7
HR at 15% below pre-feeding mean	127.4	134.1	126.4	140.4	126.7	134.8	122.3	131.8	127.3	140.4	129.1	134.8
HR at 20% below pre-feeding mean	119.9	126.2	119.0	132.2	119.2	126.9	115.1	124.1	119.8	132.2	121.5	126.9

Note. HES = head-elevated supine; HEL = head-elevated side-lying; HR = heart rate. Unit for heart rate is bpm.

The percentages of feeding time with defined changes in HR are described in Table 4.11. Compared to being fed in the HES position, infants fed in the HEL position tended to spend more time with an increase in HR from the pre-feeding period; however, a significant difference was found only in mild increases in HR between the feeding positions. When fed in the HEL position, infants tended to spend less time with a decrease in HR from that of the pre-feeding period; however, a significant difference was found only in severe decreases in HR between the feeding positions. Using clinically significant criteria for bradycardia (i.e., HR below 100 bpm), when fed in the HEL position, infants spent significantly less time with a decrease in HR below 100 bpm than in the HES position.

For some cases, even when the mean percentage of feeding time for the two feeding positions were not very close, the difference in mean values was not statistically significant. This occurrence is a consequence of large variability (e.g., the percentage of feeding time with a moderate increase in HR has means of 7.9 and 30.1 for the two positions and p = .190, but the SD for the HEL position is 45.7).

Table 4.11. Comparisons of Percentage of Feeding Time with Defined Changes in Heart Rate between Feeding Positions (n = 6)

Variables	Feeding Position		*t*	*p*-value
	HES	HEL		
% of feeding time with increases in HR				
10% above pre-feeding period (mild)	26.5 ± 32.1	39.7 ± 45.0	2.33	.068
15% above pre-feeding period (moderate)	7.9 ± 12.4	30.1 ± 45.7	1.52	.190
20% above pre-feeding period (severe)	1.0 ± 2.1	12.9 ± 20.9	1.52	.190
% of feeding time with decreases in HR				
10% below pre-feeding period (mild)	5.0 ± 3.3	3.3 ± 3.8	-1.31	.246
15% below pre-feeding period (moderate)	3.3 ± 1.7	2.2 ± 1.8	-0.98	.373
20% below pre-feeding period (severe)	2.2 ± 1.2	0.8 ± 0.7	-3.46	.018
less than 100 bpm	0.7 ± 0.6	0.3 ± 0.5	-5.08	.004

Note. HES = head-elevated supine; HEL = head-elevated side-lying; HR = heart rate. Data are expressed as mean ± SD.

Oxygen Saturation

The mean, SD, and CV of SpO_2 during the pre-feeding, feeding, and bottle-in periods are described in Table 4.12. No differences in the mean, SD, and CV of SpO_2 were found prior to each of the infant's two feeding observations. Therefore, the infants exhibited comparable SpO_2 states prior to the experimental conditions. Both during the feeding and bottle-in periods, no significant differences in mean, SD, and CV of SpO_2 between the feeding positions were found. However, during the bottle-in periods, trends of less variation in SpO_2 (i.e., lower SD and CV of SpO_2) were observed in the HEL position than in the HES position.

Table 4.12. Comparisons of Oxygen Saturation between Feeding Positions (n = 6)

Variables	Feeding Position		*t*	*p*-value
	HES	HEL		
Pre-feeding period				
Mean of SpO_2 (%)	99.4 ± 0.8	99.4 ± 0.8	1.19	.288
SD of SpO_2	0.2 ± 0.4	0.2 ± 0.4	-1.03	.351
CV of SpO_2	0.00 ± 0.00	0.00 ± 0.00	-1.03	.351
Feeding period				
Mean of SpO_2 (%)	97.2 ± 2.1	97.5 ± 1.8	0.76	.483
SD of SpO_2	4.4 ± 3.2	3.7 ± 2.3	-1.34	.237
CV of SpO_2	0.05 ± 0.04	0.04 ± 0.02	-1.31	.246
Bottle-in period				
Mean SpO_2 (%)	97.3 ± 1.8	97.6 ± 1.6	0.71	.511
SD of SpO_2	3.9 ± 2.0	3.5 ± 1.9	-1.67	.155
CV of SpO_2	0.04 ± 0.02	0.04 ± 0.02	-1.61	.169

Note. HES = head-elevated supine; HEL = head-elevated side-lying; CV = coefficient of variation; SpO_2 = oxygen saturation. Data are expressed as mean ± SD.

Changes in Oxygen Saturation

Changes in SpO_2 are defined as SpO_2 levels at least 5% below those of the pre-feeding period and below 85 percent. The changes in SpO_2 at least 5% below those of the pre-feeding period were further classified as mild (5-10%), moderate (10-15%), or severe

(>15%) decreases in SpO_2. SpO_2 cutoffs for each category were calculated based on the pre-feeding period for a given feeding and were used to calculate the percentage of feeding time for each category. Using infant 1 as an example, the percentage of feeding time with SpO_2 levels less than 94.3% was calculated first and was classified as the percentage of feeding time with SpO2 levels between 89.4% and 94.3% (i.e., mild), between 84.4% and 89.4% (i.e., moderate), and less than 84.4% (i.e., severe). Individual SpO_2 cutoffs used to define degrees of changes in SpO_2 per feeding position are presented in Table 4.13.

Table 4.13. Individual Cutoffs Used for Defined Changes in Oxygen Saturation from the Pre-feeding Periods per Position

	HES position						HEL position					
Infant	1	2	3	4	5	6	1	2	3	4	5	6
Mean SpO_2 during pre-feeding period	99.3	99.8	99.8	99.4	99.8	99.8	97.9	99.8	99.8	97.9	99.9	99.8
SpO_2 at 5% below pre-feeding mean	94.3	94.8	94.8	94.4	94.8	94.8	93.0	94.8	94.8	93.0	94.9	94.8
SpO_2 at 10% below pre-feeding mean	89.4	89.8	89.8	89.5	89.8	89.8	88.1	89.8	89.8	88.1	89.9	89.8
SpO_2 at 15% below pre-feeding mean	84.4	84.8	84.8	84.5	84.8	84.8	83.2	84.8	84.8	83.2	84.9	84.8

Note. HES = head-elevated supine; HEL = head-elevated side-lying; SpO_2 = oxygen saturation. Unit for oxygen saturation is %.

The percentages of feeding time with changes in SpO_2 are described in Table 4.14. No significant differences were found in the percentages of feeding time with SpO_2 levels at least 5% below the pre-feeding level between feeding positions. Even after the percentages of feeding time with SpO_2 levels at least 5% below the pre-feeding level were classified as mild, moderate, and severe decreases in SpO_2, no significant differences in each classification were found between the feeding positions. Similarly, using clinically significant criteria for desaturation (i.e., SpO_2 less than 85%), no significant differences between the feeding positions were evident.

Table 4.14. Comparisons of Percentage of Feeding Time with Defined Changes in Oxygen Saturation between Feeding Positions (n = 6)

Variables	Feeding Position		t	p-value
	HES	HEL		
% of feeding time with SpO_2 at least 5% below pre-feeding period	14.9 ± 8.7	14.6 ± 10.3	-0.11	.914
Mild desaturation [a]	8.9 ± 3.8	8.1 ± 4.5	-0.53	.618
Moderate desaturation [b]	3.2 ± 3.0	4.1 ± 3.5	1.04	.346
Severe desaturation [c]	2.8 ± 3.3	2.4 ± 3.0	-0.75	.489
% of feeding time with SpO_2 less than 85%	3.1 ± 3.8	2.9 ± 3.7	-0.40	.708

Note. HES = head-elevated supine; HEL = head-elevated side-lying; SpO_2 = oxygen saturation. Data are expressed as mean ± SD. [a] Decreases in SpO_2 between 5-10% below pre-feeding period, [b] decreases in SpO_2 between 10-15% below pre-feeding period, [c] decreases in SpO_2 at least 15% below pre-feeding period.

Respiratory Characteristics

RESCs were examined in terms of the interval between breaths, breath duration, breath amplitude, respiratory rate, and percentage of feeding time with breathing pauses longer than three seconds. During the pre-feeding and first six minutes of the bottle-in periods, the mean, SD, and CV of the intervals between breaths, breath duration, breath amplitude, and respiratory rate were calculated. During the first six minutes of the bottle-in period, the percentages of feeding time with breathing pauses longer than three seconds also were calculated.

The mean, SD, and CV of RESCs during the pre-feeding and first six minutes of the bottle-in period are described in Tables 4.15 and 4.16. No significant differences were found for all RESCs prior to each of the infant's two feeding observations, and only the trend of less variation of breath amplitude (i.e., lower SD of breath amplitude) and less variation of breath duration (i.e., lower SD and CV of breath duration) were observed prior to the condition for the HEL position, compared to prior to that of the HES position. Therefore, infants were in comparable respiratory states prior to the experimental conditions. During the first six minutes of the bottle-in period, the infants showed significantly shorter intervals between breaths and less variation in interval lengths between breaths (i.e., lower SD of interval between breaths) when fed in the HEL position compared to the HES position. In addition, the trend of lower CV of intervals between breaths that also indicates less variation in intervals between breaths was observed in the HEL position. No significant differences in mean and SD of breath duration were found; however, the infants showed significantly greater variation in breath duration (i.e., higher CV of breath duration) when fed in the HEL position compared to the HES position. No significant differences in mean, SD, and CV for breath amplitude between the feeding positions were found. The respiratory rate was significantly higher in the HEL position than in the HES position. Infants tended to spend less time with breathing pauses that were longer than three seconds in the HEL position; however, no significant difference between the feeding positions was found. Therefore, infants in the HEL position breathed with significantly shorter breaths and more regular intervals between breaths, with higher frequency that is closer to the pre-feeding states, and more variation in durations of breath compared to being fed in the HES position.

Table 4.15. Comparisons of Respiratory Characteristics during the Pre-feeding Period (n = 6)

Variables	Feeding Position That Followed		t	p-value
	HES	HEL		
Interval between Breaths				
Mean (seconds)	1.07 ± 0.13	1.04 ± 0.18	-1.41	.219
SD	0.24 ± 0.13	0.24 ± 0.13	-0.00	.997
CV	0.22 ± 0.10	0.22 ± 0.10	0.21	.843
Breath Duration				
Mean (seconds)	1.07 ± 0.13	1.03 ± 0.18	-1.42	.214
SD	0.23 ± 0.12	0.22 ± 0.14	-2.00	.102
CV	0.22 ± 0.10	0.20 ± 0.11	-1.71	.148
Breath Amplitude				
Mean (volts)	0.016 ± 0.009	0.015 ± 0.007	-0.81	.456
SD	0.007 ± 0.006	0.007 ± 0.007	1.50	.193
CV	0.342 ± 0.228	0.407 ± 0.296	1.27	.261
Respiratory Rate (per minute)	56 ± 8	59 ± 12	1.34	.236

Note. HES = head-elevated supine; HEL = head-elevated side-lying; CV = coefficient of variation. Data are expressed as mean ± SD.

Table 4.16. Comparisons of Respiratory Characteristics between Feeding Positions during the First Six Minutes of Bottle-in Period (n = 6)

Variables	Feeding Position		t	p-value
	HES	HEL		
Interval between Breaths				
Mean (seconds)	1.41 ± 0.20	1.26 ± 0.15	-2.13	.087
SD	2.67 ± 0.82	1.95 ± 0.36	-2.47	.056
CV	1.86 ± 0.43	1.55 ± 0.13	-1.96	.107
Breath Duration				
Mean (seconds)	0.75 ± 0.09	0.75 ± 0.05	0.06	.953
SD	0.24 ± 0.02	0.26 ± 0.02	1.10	.321
CV	0.33 ± 0.05	0.34 ± 0.04	2.37	.064
Breath Amplitude				
Mean (volts)	0.091 ± 0.049	0.089 ± 0.032	-0.06	.955
SD	0.044 ± 0.022	0.042 ± 0.018	-0.13	.898
CV	0.490 ± 0.098	0.462 ± 0.069	-0.85	.434
Respiratory Rate (per minute)	42 ± 6	48 ± 6	2.67	.044
% Feeding time with Breathing pauses > 3 seconds (%)	48.4 ± 14.7	41.9 ± 8.6	-1.32	.245

Note. HES = head-elevated supine; HEL = head-elevated side-lying; CV = coefficient of variation. Data are expressed as mean ± SD.

Comparisons of Feeding Performance

Feeding performance measures are described in Table 4.17. Compared to being fed in the HES position, infants fed in the HEL position tended to consume slightly more milk and showed slightly lower proficiency and higher efficiency; however, none of these effects were significant. Only the trend of longer feeding time was observed in the HEL position compared to the HES position.

Table 4.17. Comparisons of Feeding Performance between Feeding Positions (n = 6)

Variables	Feeding Position		t	*p-value*
	HES	HEL		
Overall milk transfer (%)	92.7 ± 8.6	95.2 ± 8.2	0.89	.414
Proficiency (%)	44.3 ± 23.7	42.3 ± 11.8	-0.22	.833
Efficiency (ml/min)	2.4 ± 0.6	2.5 ± 0.7	0.33	.756
Duration of feeding time (minutes)	11.6 ± 2.9	13.0 ± 2.9	1.55	.182

Note. HES = head-elevated supine; HEL = head-elevated side-lying. Data are expressed as mean ± SD.

Conclusions for Hypothesis 1

Hypothesis 1 is partially supported. Compared to the HES position, study infants fed in the HEL position exhibited significantly less variation in HR. In the HEL position, the infants spent significantly less time with severe decreases in HR (i.e., decreases in HR below 20% pre-feeding levels), bradycardia (i.e., less than 100 bpm), and more time with mild increases in HR (i.e., an increase in HR above 10% pre-feeding levels) compared to being fed in the HES position. In addition, infants breathed with significantly shorter breaths and more regular intervals between breaths, higher frequency that was closer to the pre-feeding states, and more variation in durations of breath in the HEL position compared to when they were fed in the HES position. No significant findings for SpO_2 and feeding performance were evident; however, trends of less variation in SpO_2 and longer duration of feeding were evident in the HEL position compared to the HES position.

Hypothesis 2: When compared to infants bottle-fed in the HES position, VP infants bottle-fed in the HEL position would demonstrate fewer physiological changes from the pre-feeding period across the feeding period.

To measure physiological changes over time, three methods were chosen to create three intervals for the feeding time. To remove potentially confounding data, non-feeding and burping periods were eliminated, and the summed bottle-in periods were examined using three intervals of time: (1) dividing the entire bottle-in period into three equal intervals, (2) extracting 2-minute intervals from the initial, middle, and final third of the bottle-in period, and (3) using successive 2-minute intervals during the first six minutes of the bottle-in period (see Figure 3.4). The mean, SD, and CV for HR and SpO_2 were calculated for the pre-feeding period and for each interval of feeding time. The changes in RESCs over time were examined using only Method 3 (i.e., successive two minutes during the first six minutes of the bottle-in period) because the RESCs were calculated only during the first six minutes of the bottle-in period. Individual data using each physiologic variable and method were plotted by feeding position and are presented in Appendices K, L, and M.

LMM was used to examine whether a significant pattern could be found in all the physiologic variables across the three time points during feeding by controlling for the pre-feeding level as a covariate, and to determine whether this pattern was different according to the feeding position. LMMs were calculated separately for each physiologic variable and method by taking the following steps. First, all possible fixed and random effect components were included in the preliminary LMMs. The fixed effect components include time, feeding position, and interaction between time and feeding position. To examine the effect of feeding position on the feeding period more accurately, the physiologic variables during the feeding period were modeled, controlling for the pre-feeding period as a covariate. Time and feeding position also were considered as random effect components to account for possible within-infant correlations of physiological variables across time and feeding positions. Random effect components were treated as either random ANOVA factors or random regression coefficients, and one of these was chosen based on Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) scores. Second, the preliminary LMMs were reduced by removing non-significant fixed components, except for feeding position, as long as both AIC and BIC scores improved. Because this is a pilot study, the significance level was set at $p = .10$ so that significant components remained in the final reduced models. Also, p-values less than .20 were considered indicative of trends. Third, when the final reduced LMMs still had non-significant fixed effect components, adjusted LMMs were considered to account for the possible different effects of feeding position at each time point based on the plots. Only when both AIC and BIC scores improved were the adjusted LMMs reported. Finally, residual analysis was conducted using the final reduced LMMs for each physiologic variable and method.

Changes in Heart Rate over Feeding Time

Method 1: Dividing the entire bottle-in period into three equal intervals

The averages of the mean HRs over time by feeding position using Method 1 are plotted in Figure 4.2, and the associated LMM results are reported in Table 4.18. In the full LMM for the HR mean, no significant effects were found for time, feeding position, interaction between time and feeding position, and pre-feeding covariate. Even after removing all non-significant fixed effect components except for feeding position, no significant effect of feeding position was found ($F_{1, 5} = 1.53$; $p = .272$).

The averages of SD for HR over time by feeding position using Method 1 are plotted in Figure 4.2, and the associated LMM results are reported in Table 4.18. In the full LMM, the SD for HR significantly decreased over time ($F_{2, 10} = 5.02$; $p = .031$), and this pattern is significantly different by feeding position ($F_{1, 5} = 6.80$; $p = .048$). Also, a trend toward an interaction effect between time and feeding position ($F_{2, 10} = 2.69$; $p = .116$) was found. After removing the pre-feeding covariate, a significant effect remained for time ($F_{2, 10} = 5.02$; $p = .031$), feeding position ($F_{1, 5} = 7.54$; $p = .041$), and a trend toward an interaction effect between time and feeding position ($F_{2, 10} = 2.71$; $p = .115$) was found. The adjusted LMM considered a possible difference in SD for HR between the feeding positions during the first third feeding interval. The adjusted LMM suggested that, compared to the HES position, the SD for HR was significantly lower in the HEL position, especially during the first third feeding interval ($F_{1, 29} = 19.33$; $p = < .001$).

The averages of the CV for HR over time by feeding position using Method 1 are plotted in Figure 4.2, and the associated LMM results are reported in Table 4.17. In the full LMM, the CV for HR significantly decreased over time ($F_{2, 10} = 4.57$; $p = .039$), and this pattern was significantly different by feeding position ($F_{1, 5} = 5.50$; $p = .066$). Also, a trend toward an interaction effect between time and feeding position ($F_{2, 10} = 1.92$; $p = .197$) was found. After removing the pre-feeding covariate and the interaction term, a significant effect remained for time ($F_{2, 10} = 4.12$; $p = .049$), and feeding position ($F_{1, 5} = 5.37$; $p = .068$). The adjusted LMM considered a possible difference in the CV for HR between the feeding positions during the first third feeding interval. This adjusted LMM suggested that the CV for

HR was significantly lower in the HEL position, especially during the first third feeding interval ($F_{1, 29} = 16.20$; $p < .001$), than in the HES position.

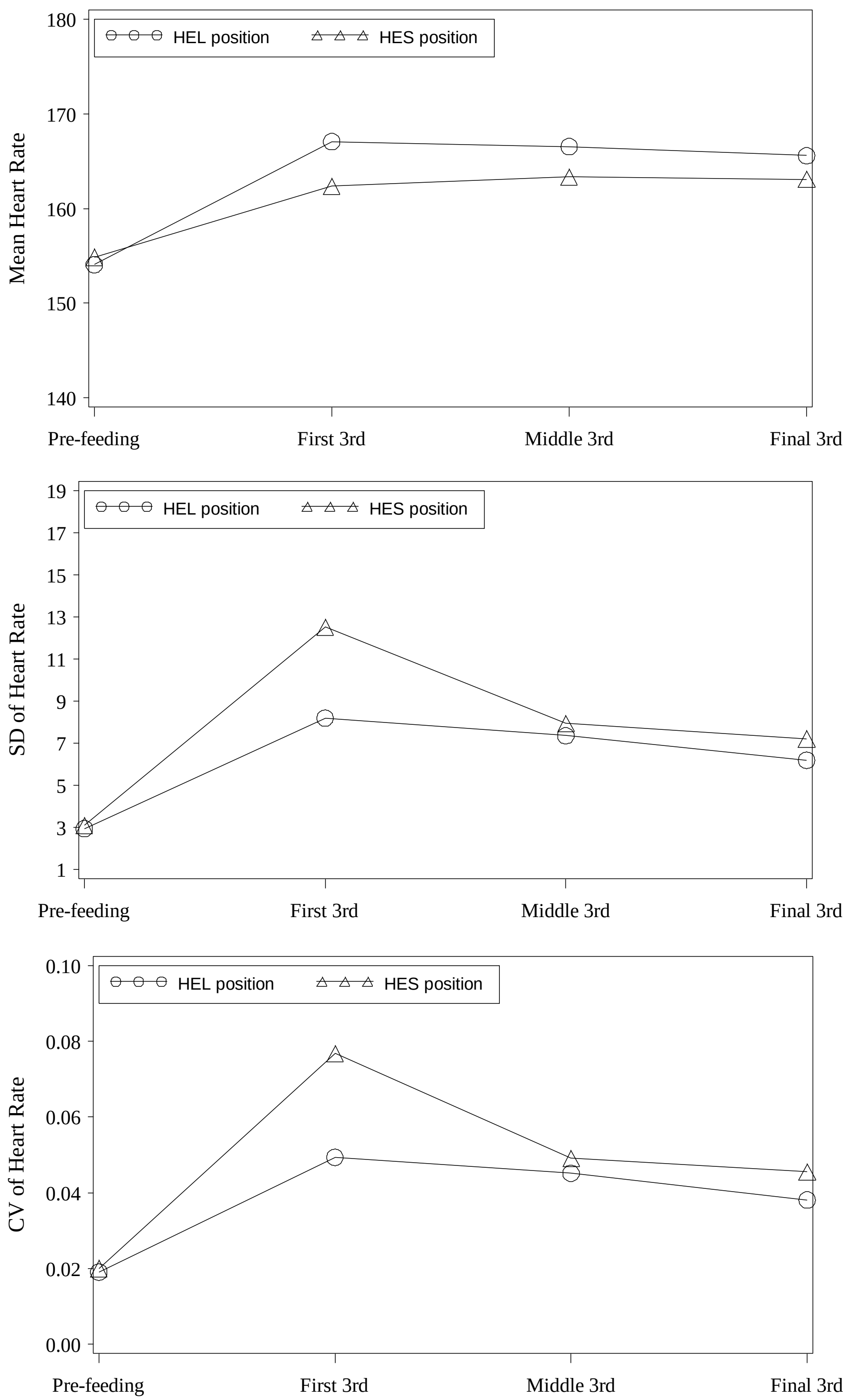

Figure 4.2. Changes in Heart Rate over Time using Method 1. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance.

Method 2: Extracting 2-minute intervals from the initial, middle, and final third of the bottle-in period

The averages of the mean HR over time by feeding position using Method 2 are plotted in Figure 4.3, and the associated LMM results are reported in Table 4.18. In the full LMM for the HR mean, no significant effects of time, feeding position, interaction between time and feeding position, and pre-feeding covariate were found. Even after removing all non-significant fixed effect components except for feeding position, no significant effect of feeding position was found ($F_{1, 5} = 1.58$; $p = .265$).

The averages of the SD for HR over time by feeding position using Method 2 are plotted in Figure 4.3, and the associated LMM results are reported in Table 4.18. In the full LMM, the SD for HR significantly decreased over time ($F_{2, 10} = 6.88$; $p = .013$), but this pattern is not significantly different by feeding position ($F_{1, 5} = 1.45$; $p = .282$). No significant effects of interaction between time and feeding position and pre-feeding covariate were found. After removing the interaction term and pre-feeding covariate, a significant effect of time ($F_{2, 10} = 6.41$; $p = .016$) was still evident, but no significant effect of feeding position ($F_{1, 5} = 1.55$; $p = .268$) was found. The adjusted LMM considered a possible difference in SD for HR between the feeding positions during the first and final 2-minute feeding intervals. This suggested that compared to the SD for HR for the HES position, the SD for HR in the HEL position was significantly lower only during the first and final 2-minute feeding intervals with the same amount of difference between the feeding positions ($F_{1, 29} = 14.19$; $p = < .001$).

The averages of the CV for HR over time by feeding position using Method 2 are plotted in Figure 4.3, and the associated LMM results are reported in Table 4.18. In the full

LMM, the CV for HR significantly decreased over time ($F_{2, 10} = 5.59$; $p = .024$), but this pattern is not significantly different by feeding position ($F_{1, 5} = 1.61$; $p = .260$). No significant effects of interaction between time and feeding position and pre-feeding covariate were found. After removing the interaction term, a significant effect of time ($F_{2, 10} = 4.12$; $p = .049$) was found, but no significant effects of feeding position ($F_{1, 5} = 1.51$; $p = 0.273$) and pre-feeding covariate ($F_{1, 26} = 0.92$; $p = .346$) were found. The adjusted LMM considered a possible difference in the CV for HR between the feeding positions during the first and final 2-minute feeding intervals. This model suggested that compared to the CV for HR in the HES position, the CV for HR in the HEL position was significantly lower only during the first and final 2-minute feeding intervals with the same amount of difference between the feeding positions ($F_{1, 29} = 12.20$; $p = .002$).

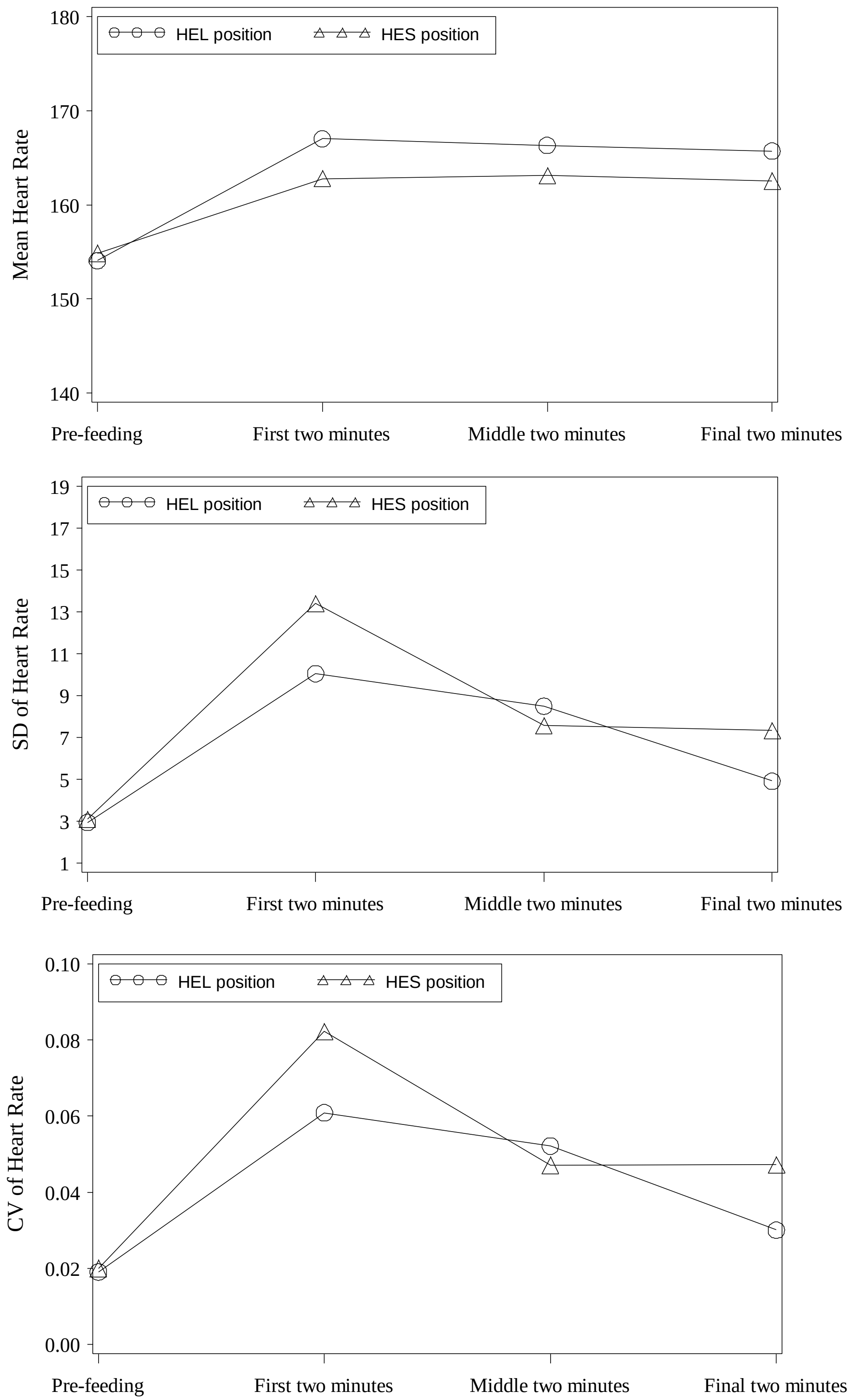

Figure 4.3. Changes in Heart Rate over Time using Method 2. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance.

Method 3: Successive two minutes during the first six minutes of the bottle-in period

The averages of the mean HR over time by feeding position using Method 3 are plotted in Figure 4.4, and the associated LMM results are reported in Table 4.17. In the full LMM for the mean for HR, only a trend toward the effect of feeding position ($F_{1, 5} = 3.78$; $p = .111$) was found, and no significant effects of time, interaction between time and feeding position, and pre-feeding covariate were found. After removing all non-significant fixed effect components except for feeding position, a trend toward the effects of feeding position ($F_{1, 5} = 2.33$; $p = .188$) was still evident.

The averages of the SD for HR over time by feeding position using Method 3 are plotted in Figure 4.4, and the associated LMM results are reported in Table 4.17. In the full LMM, the SD for HR significantly decreased over time ($F_{2, 10} = 10.26$; $p = .004$), and the SD for HR was significantly lower across all time points in the HEL position compared to the HES position ($F_{1, 5} = 6.73$; $p = .049$). After removing the interaction term, significant effects of time ($F_{2, 10} = 10.18$; $p = .004$) and feeding position ($F_{1, 5} = 6.67$; $p = .049$) were still evident, but no significant effect of the pre-feeding covariate ($F_{1, 26} = 0.48$; $p = .494$) was evident.

The averages of CV for HR over time by feeding position using Method 3 are plotted in Figure 4.4, and the associated LMM results are reported in Table 4.17. In the full LMM, the CV for HR significantly decreased over time ($F_{2, 10} = 9.51$; $p = .006$), and the CV for HR was significantly lower across all time points in the HEL position compared to the HES position ($F_{1, 5} = 7.16$; $p = .040$). After removing the pre-feeding covariate and interaction term, significant effects of time ($F_{2, 10} = 8.91$; $p = .006$) and feeding position ($F_{1, 5} = 7.98$; $p = .037$) were still evident.

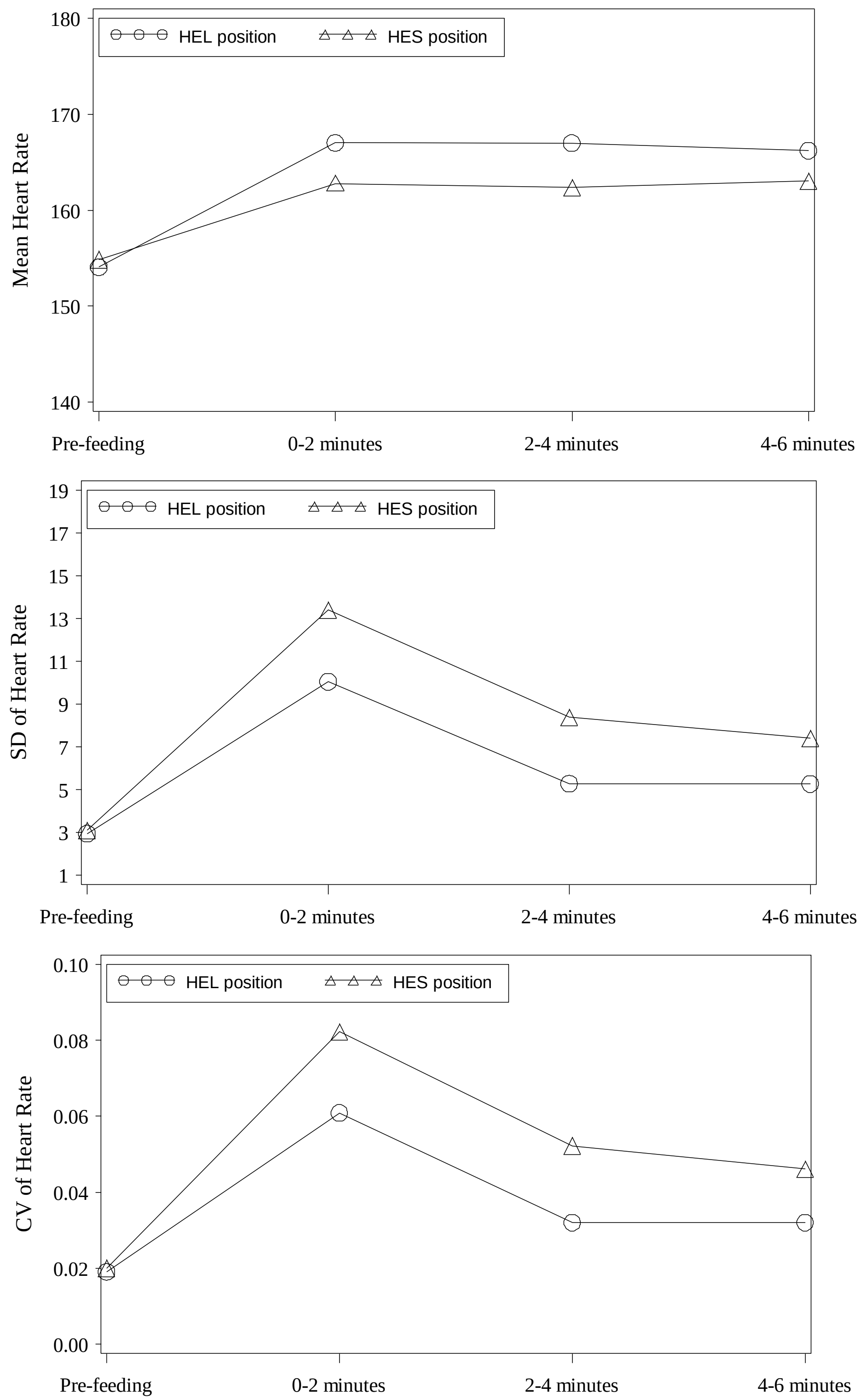

Figure 4.4. Changes in Heart Rate over Time using Method 3. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance.

Table 4.18. Changes in Heart Rate over Time by Feeding Position using Three Methods of Feeding Time Intervals

	Method 1 [a]			Method 2 [b]			Method 3 [c]		
	Mean	SD	CV	Mean	SD	CV	Mean	SD	CV
Full model									
Time	.940	.031	.039	.970	.013	.024	.984	.004	.006
Position	.257	.048	.066	.252	.282	.260	.111	.049	.040
Time * Position	.749	.116	.197	.963	.378	.401	.854	.888	.889
Pre-feeding period	.817	.463	.336	.861	.450	.344	.298	.495	.624
Reduced model									
Time	-	.031	.049	-	.016	.028	-	.004	.006
Position	.272	.041	.068	.265	.268	.273	.188	.050	.037
Time * Position	-	.115	-	-	-	-	-	-	-
Pre-feeding period	-	-	-	-	-	.346	-	.494	-

Note. CV = coefficient of variance. Data are expressed as *p*-values. [a] Method 1 = Dividing the entire bottle-in period into three equal intervals. [b] Method 2 = Extracting 2-minute intervals from each third of the bottle-in period. [c] Method 3 = successive 2-minute intervals for the first six minutes of the bottle-in period.

Changes in Oxygen Saturation over Feeding Time

Method 1: Dividing the entire bottle-in period into three equal intervals

For all the LMMs for SpO_2 using Method 1, a significant effect for the pre-feeding covariate was found, which indicates that lower values for each mean, SD, and CV of SpO_2 during the pre-feeding period are associated with lower values for each mean, SD, and CV of SpO_2 across the feeding period (Table 4.19).

The averages of the mean SpO_2 levels over time by feeding position using Method 1 are plotted in Figure 4.5, and the associated LMM results are reported in Table 4.19. In the full LMM for the mean of SpO_2, no significant effects of time, feeding position, and interaction between time and feeding position were evident. Even after removing all non-significant fixed effect components except for feeding position, no significant effect of feeding position was found ($F_{1, 5} = 0.39$; $p = .561$). The adjusted LMM considered a possible difference in the mean of SpO_2 between feeding positions during the first third feeding interval; however, no significant difference was found ($F_{1, 28} = 1.09$; $p = .306$).

The averages of SD for SpO_2 over time by feeding position using Method 1 are plotted in Figure 4.5, and the associated LMM results are reported in Table 4.19. In the full LMM for the SD of SpO_2, only a trend toward the effect of time ($F_{2, 10} = 2.62$; $p = .122$) was evident, and no significant effects of time, feeding position, and interaction between time and feeding position were found. After removing the interaction term, a trend toward the effect of time ($F_{2, 10} = 2.52$; $p = .130$) was evident, but no significant effect of feeding position ($F_{1, 5} = 0.05$; $p = .838$) was found. The adjusted LMM considered a possible difference between feeding positions during the first third feeding interval and a decreasing pattern for the SD of SpO_2 at the final third feeding interval. This model suggested that no significant difference was evident between the feeding positions during the first third feeding interval ($F_{1, 27} = 1.04$; $p = .317$). After removing that term, the SD of SpO_2 significantly decreased at the final third feeding interval from that of the first and middle third feeding intervals ($F_{1, 28} = 4.87$; $p = .036$).

The averages of CV for SpO_2 over time by feeding position using Method 1 are plotted in Figure 4.5, and the associated LMM results are reported in Table 4.19. In the full LMM for the CV of SpO_2, only a trend toward the effect of time ($F_{2, 10} = 2.41$; $p = .140$) was found, and no significant effects of time, feeding position, and interaction between time and feeding position were found. After removing the interaction term, a trend toward the effect of time ($F_{2, 10} = 2.32$; $p = .148$) was still evident, but no significant effect of feeding position ($F_{1, 5} = 0.07$; $p = .807$) was found. The adjusted LMM considered a possible difference in CV of SpO_2 between the feeding positions during the first third feeding interval and a decreasing pattern of CV of SpO_2 at the final third feeding interval. This model suggested that no significant differences in the SD of SpO_2 between the feeding positions during the first third feeding interval ($F_{1, 27} = 0.93$; $p = .344$) were evident. After removing that term, the CV for SpO_2 significantly decreased at the final third feeding interval from that of the first and middle third feeding intervals ($F_{1, 28} = 4.55$; $p = .042$).

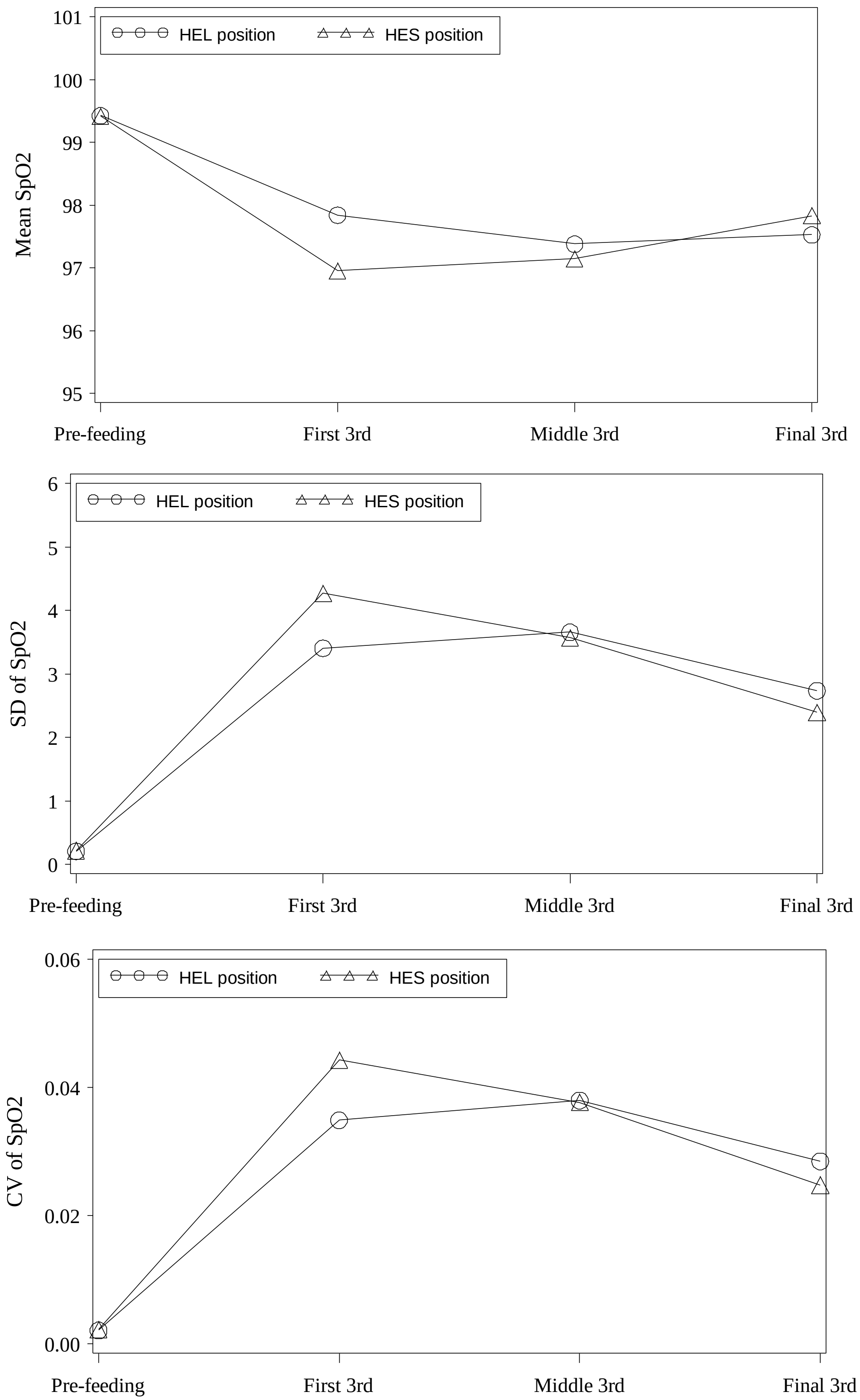

Figure 4.5. Changes in Oxygen Saturation over Time using Method 1. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance; SpO_2 = oxygen saturation.

Method 2: Extracting 2-minute intervals from the initial, middle, and final third of the bottle-in period

For all the LMMs for SpO_2 using Method 2, a significant effect of the pre-feeding covariate was found, which indicates that lower values for each mean, SD, and CV of SpO_2 during the pre-feeding period are associated with lower values for each mean, SD, and CV of SpO_2 across the feeding period (Table 4.19).

The averages of the mean SpO_2 over time by feeding position using Method 2 are plotted in Figure 4.6, and the associated LMM results are reported in Table 4.19. In the full LMM for the mean of SpO_2, no significant effects of time, feeding position, and interaction between time and feeding position were found. Even after removing all non-significant fixed effect components except for feeding position, no significant effect of feeding position was found ($F_{1, 5} = 0.55$; $p = .493$). The adjusted LMM considered a possible difference in mean SpO_2 between the feeding positions during the first 2-minute feeding interval and an increasing pattern of mean SpO_2 toward the final 2-minute feeding interval; however, no significant effects were found.

The averages of SD for SpO_2 over time by feeding position using Method 2 are plotted in Figure 4.6, and the associated LMM results are reported in Table 4.19. In the full LMM for the SD of SpO_2, a significant effect of time ($F_{2, 10} = 3.55$; $p = .069$) was found; however, no significant effects of feeding position and the interaction between time and feeding position were found. After removing the interaction term, a significant effect of time ($F_{2, 10} = 3.49$; $p = .071$) was still evident, but no significant effect of feeding position ($F_{1, 5} = 0.29$; $p = .614$) was found. The adjusted LMM considered a possible difference in SD of SpO_2 between the feeding positions during the first 2-minute feeding interval and a decreasing pattern of SD of SpO_2 toward the final 2-minute feeding interval. This model suggested that no significant difference in the SD of SpO_2 was evident between the feeding positions during the first 2-minutefeeding interval ($F_{1, 27} = 0.39$; $p = .540$). After removing that term, the SD of SpO_2 significantly decreased at the final 2-minutefeeding interval from that of the first and middle third feeding intervals ($F_{1, 28} = 6.93$; $p = .014$).

The averages of CV for SpO_2 over time by feeding position using Method 2 are plotted in Figure 4.6, and the associated LMM results are reported in Table 4.19. In the full LMM for CV of SpO_2, a significant effect of time ($F_{2, 10} = 2.98$; $p = .097$) was found; however, no significant effects of feeding position and the interaction between time and feeding position were found. After removing the interaction term, a significant effect of time ($F_{2, 10} = 2.98$; $p = .097$) was evident, but no significant effect of feeding position ($F_{1, 5} = 0.37$; $p = .568$) was found. The adjusted LMM considered a possible difference in CV of SpO_2 between the feeding positions during the first 2-minute feeding interval and a decreasing pattern of CV of SpO_2 toward the final 2-minutefeeding interval. This model suggested that no significant difference in the SD for SpO_2 was evident between the feeding positions during the first 2-minutefeeding interval ($F_{1, 27} = 0.34$; $p = .567$). After removing that term, the CV for SpO_2 significantly decreased at the final 2-minutefeeding interval from that of the first and middle third feeding intervals ($F_{1, 28} = 5.94$; $p = .021$).

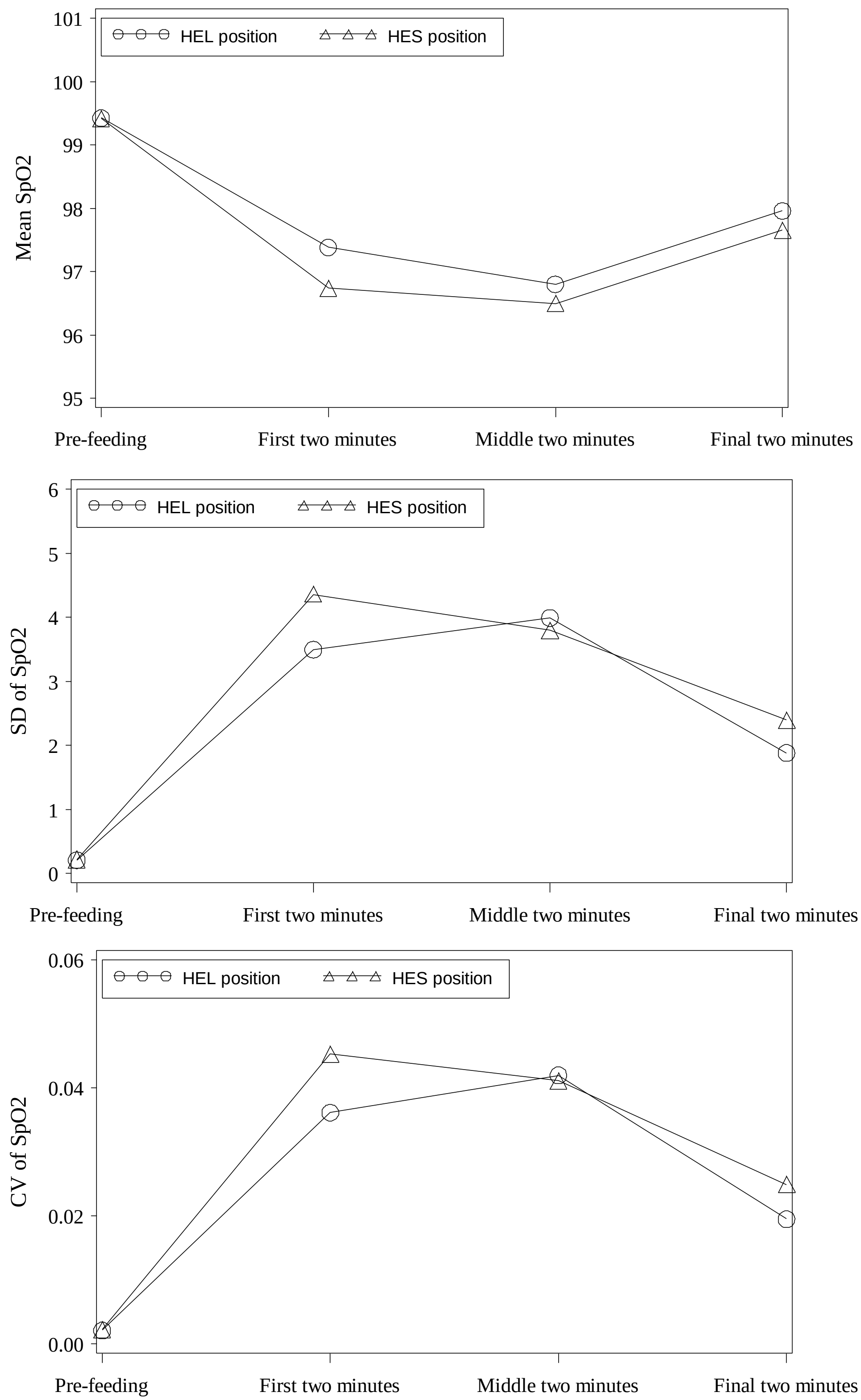

Figure 4.6. Changes in Oxygen Saturation over Time using Method 2. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance; SpO_2 = oxygen saturation.

Method 3: Successive two minutes during the first six minutes of the bottle-in period

For all the LMMs for SpO_2 using Method 3, a significant effect of the pre-feeding covariate was found, which indicates that lower values for each mean, SD, and CV of SpO_2 during the pre-feeding period are associated with lower values for each mean, SD, and CV of SpO_2 across the feeding period (Table 4.19).

The averages of the mean SpO_2 levels over time by feeding position using Method 3 are plotted in Figure 4.7, and the associated LMM results are reported in Table 4.19. In the full LMM for the mean of SpO_2, only a trend toward the effect of time ($F_{2, 10} = 2.01$; p = .185) was evident, and no significant effects of time, feeding position, and interaction between time and feeding position were found. After removing the interaction term, a trend toward the effect of time ($F_{2, 10} = 2.00$; p = .185) was still evident, but no significant effect of feeding position was found ($F_{1, 5} = 2.03$; p = .213). The adjusted LMM considered a possible difference in the mean SpO_2 between feeding positions across the three successive 2-minute feeding intervals by considering an increasing pattern of mean SpO_2 at the 2- 4-minute feeding interval. This model suggested that the mean SpO_2 significantly increased during the 2- 4-minute feeding interval ($F_{1, 27} = 4.00$; p = .056), and a trend of higher SpO_2 levels in the HEL position compared to in the HES position across the three successive 2-minute feeding intervals was observed ($F_{1, 27} = 2.03$; p = .166).

The averages of SD for SpO_2 over time by feeding position using Method 3 are plotted in Figure 4.7, and the associated LMM results are reported in Table 4.19. In the full LMM for the SD for SpO_2, only a trend toward the effect of time ($F_{2, 10} = 2.57$; p = .126) was found, and no significant effects of time, feeding position, and interaction between time and feeding position were found. After removing the interaction term, a trend toward the effect of time ($F_{2, 10}$ = 2.54; p = .128) was still evident, but no significant effect of feeding position ($F_{1, 5}$ = 0.62; p = .468) was found. The adjusted LMM considered a possible difference in the SD of SpO_2 between the feeding positions during the 0-2 and 2-4 minutes of feeding intervals by considering a decreasing pattern of SD for SpO_2 at the 2- 4-minute feeding interval. This model suggested that the SD of SpO_2 significantly decreased during the 2- 4-minute feeding interval ($F_{1, 27}$ = 3.85; p = .060), but no significant difference of SD for SpO_2 between feeding positions during the 0-2 and 2-4 minutes of feeding intervals ($F_{1, 27}$ = 0.82; p = .373) was found.

The averages of the CV for SpO_2 over time by feeding position using Method 3 are plotted in Figure 4.7, and the associated LMM results are reported in Table 4.19. In the full LMM for the CV of SpO_2, only a trend toward the effect of time ($F_{2, 10}$ = 2.52; p = .130) was found, and no significant effects of time, feeding position, and interaction between time and feeding position were found. After removing the interaction term, a trend toward the effect of time ($F_{2, 10}$ = 2.50; p = .132) was found, and no significant effect of feeding position ($F_{1, 5}$ = 0.72; p = .435) was found. The adjusted LMM considered a possible difference in the CV of SpO_2 between the feeding positions during the 0-2 and 2-4 minutes of feeding intervals by considering a decreasing pattern of CV of SpO_2 at the 2- 4-minute feeding interval. This model suggested that the CV of SpO_2 significantly decreased during the 2- 4-minute feeding interval ($F_{1, 27}$ = 3.75; p = .063), but no significant difference of CV of SpO_2 between feeding positions during the 0-2 and 2-4 minutes of feeding intervals ($F_{1, 27}$ = 0.86; p = .363) was found.

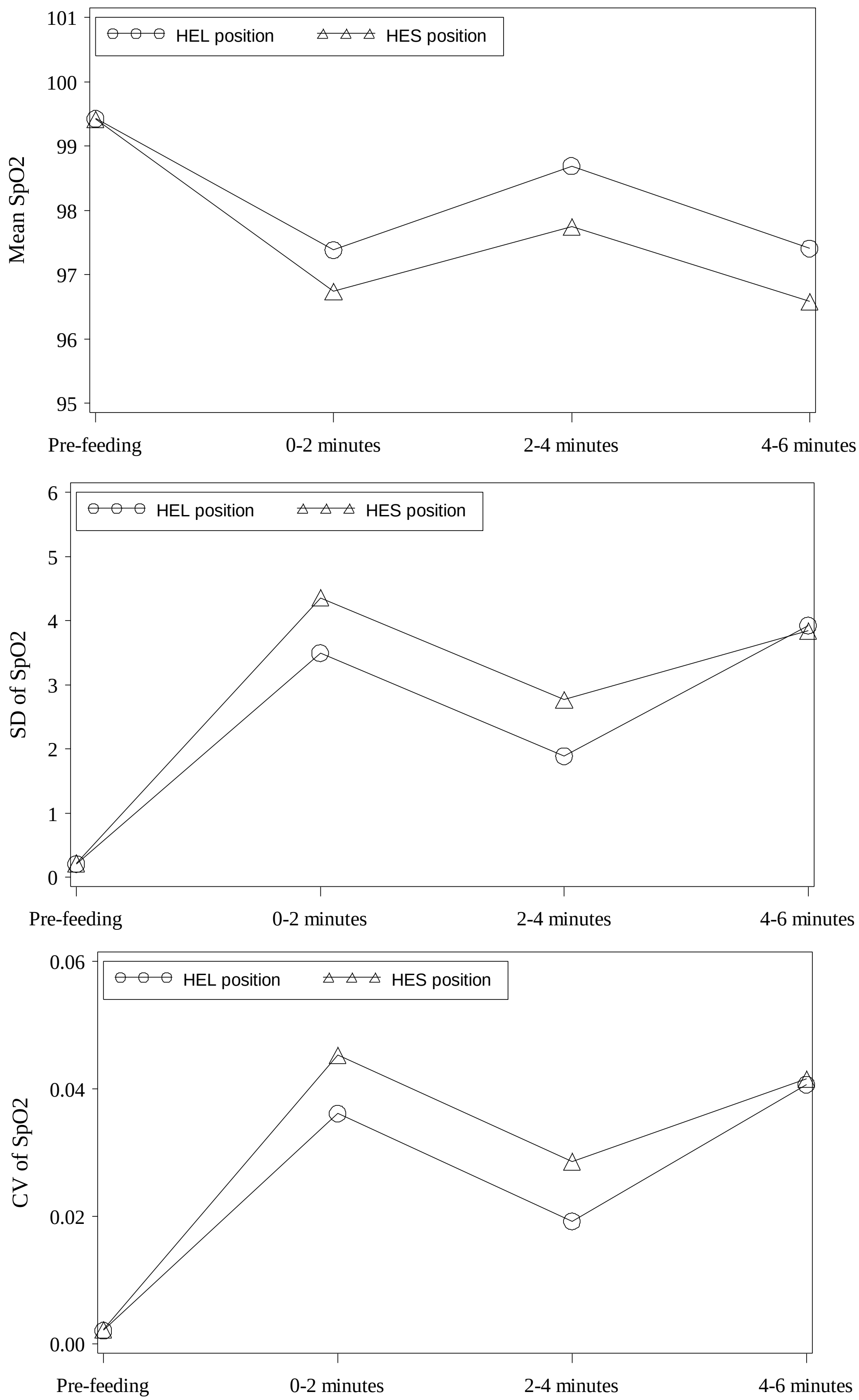

Figure 4.7. Changes in Oxygen Saturation over Time using Method 3. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance; SpO_2 = oxygen saturation.

Table 4.19. Changes in Oxygen Saturation over Time by Feeding Position using Three Methods of Feeding Time Intervals

	Method 1 [a]			Method 2 [b]			Method 3 [c]		
	Mean	SD	CV	Mean	SD	CV	Mean	SD	CV
Full model									
Time	.710	.122	.140	.337	.069	.097	.185	.126	.130
Position	.548	.835	.804	.492	.612	.564	.213	.465	.433
Time * Position	.518	.580	.587	.958	.788	.829	.976	.794	.859
Pre-feeding period	.002	<.001	<.001	.005	<.001	<.001	.004	<.001	<.001
Reduced model									
Time	-	.130	.148	-	.071	.097	.185	.128	.132
Position	.561	.838	.807	.493	.614	.568	.213	.468	.435
Time * Position	-	-	-	-	-	-	-	-	-
Pre-feeding period	.002	<.001	<.001	.004	<.001	<.001	.004	<.001	<.001

Note. CV = coefficient of variance. Data are expressed as *p*-values. [a] Method 1 = Dividing the entire bottle-in period into three equal intervals. [b] Method 2 = Extracting 2-minute intervals from each third of the bottle-in period. [c] Method 3 = successive 2-minute intervals for the first six minutes of the bottle-in period.

Changes in Respiratory Characteristics over Feeding Time

Interval between Breaths

The averages of the mean intervals between breaths over successive 2-minute intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.8, and the associated LMM results are reported in Table 4.20. In the full LMM, the mean interval between breaths was significantly longer over time in the HEL position compared to the HES position ($F_{1,5} = 7.87$; $p = .038$), and a trend toward the effect of time was found ($F_{2,10} = 2.71$; $p = .115$). No significant effects of interaction between time and feeding position and pre-feeding covariate were evident. After removing the interaction term and pre-feeding covariate, a significant effect of feeding position ($F_{1,5} = 8.25$; $p = .035$) was still evident, and a trend toward the effect of time ($F_{2,10} = 2.71$; $p = .115$) was found.

The averages of the SD for the intervals between breaths over successive 2-minute intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.8, and the associated LMM results are reported in Table 4.20. In the full LMM, the SD for interval between breaths was significantly lower over time in the HEL position compared to the HES position ($F_{1,5} = 7.64$; $p = .040$), and a significant effect of the pre-feeding covariate ($F_{1,24} = 3.54$; $p = .072$) was found. No significant effects of time and interaction between time and feeding position were evident. After removing the time and interaction terms, a significant effect of feeding position ($F_{1,5} = 6.91$; $p = .047$) and pre-feeding covariate ($F_{1,28} = 3.49$; $p = .072$) were found.

The averages of the CV for the intervals between breaths over successive 2-minute feeding intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.8, and the associated LMM results are reported in Table 4.20. In the full

LMM, the CV of the interval between breaths was significantly lower over time in the HEL position compared to the HES position ($F_{1, 5} = 4.67$; $p = .083$), and a trend toward the effect of the pre-feeding covariate ($F_{1, 24} = 2.51$; $p = .126$) was found. No significant effects of time and interaction between time and feeding position were found. After removing the time and interaction terms, a significant effect of feeding position ($F_{1, 5} = 4.19$; $p = .096$) and a trend toward the effect of pre-feeding covariate ($F_{1, 28} = 2.42$; $p = .131$) were still evident. The adjusted LMM considered a possible difference in the CV of intervals between breaths between the feeding positions, especially during the 2-4 and 4-6 minutes of feeding intervals. This adjusted model suggested that compared to the HES position, the CV for intervals between breaths was significantly lower in the HEL position, especially during the 2-4 and 4-6 minutes of feeding intervals ($F_{1, 29} = 6.15$; $p = .019$).

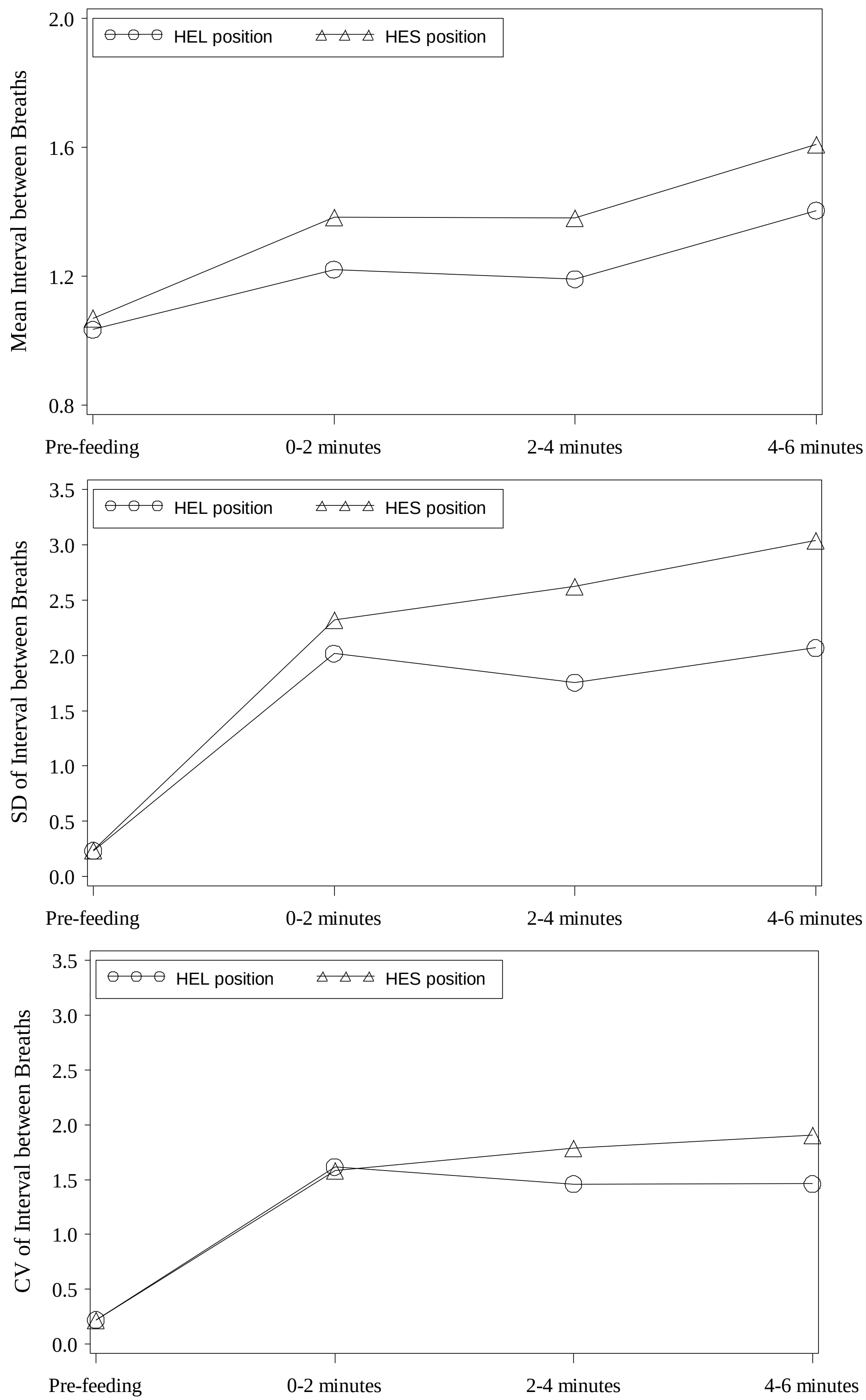

Figure 4.8. Changes in Interval between Breaths over Time using Method 3. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance.

Breath Duration

The averages of the mean for breath duration over successive 2-minute intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.9, and the associated LMM results are reported in Table 4.20. In the full LMM for mean breath duration, a significant effect of time ($F_{2, 10} = 3.75$; $p = .061$) is evident; however, no significant effects of feeding position, interaction between time and feeding position, and pre-feeding covariate were found. After removing the interaction term and pre-feeding covariate, a significant effect of time ($F_{2, 10} = 3.64$; $p = .065$) and no significant effect of feeding position ($F_{1, 5} = 0.00$; $p = .956$) were found.

The averages of the SD for breath duration over successive 2-minute intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.9, and the associated LMM results are reported in Table 4.20. In the full LMM for SD of breath duration, only a trend toward the effect of pre-feeding covariate ($F_{1, 24} = 2.01$; $p = .169$) was evident, and no significant effects of time, feeding position, and interaction between time and feeding position were found. After removing the time and interaction terms, a trend toward the effect of the pre-feeding covariate ($F_{1, 28} = 1.77$; $p = .194$) and no significant effect of feeding position ($F_{1, 5} = 1.70$; $p = .249$) were found. The adjusted LMM considered a possible difference in the SD of breath duration between the feeding positions only during the 0-2 and 4-6 minutes of feeding intervals. This adjusted model suggested that compared to the HES position, the SD for breath duration was significantly higher during the 0-2 and 4-6 minutes of feeding intervals in the HEL position ($F_{1, 29} = 5.48$; $p = .026$).

The averages of the CV for breath duration over successive 2-minute intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.9, and the associated LMM results are reported in Table 4.20. In the full LMM for CV of breath duration, a significant effect of time ($F_{2, 10}$ = 3.64; p = .065) was found; however, no significant effects of feeding position, interaction between time and feeding position, and pre-feeding covariate were found. After removing the interaction term and pre-feeding covariate, a significant effect of time ($F_{2, 10}$ = 3.45; p = .073) and no significant effect of feeding position ($F_{1, 5}$ = 1.38; p = .293) were still evident. The adjusted LMM considered a possible difference in the CV for breath duration between the feeding positions only during the 0-2 and 4-6 minutes of feeding intervals. This adjusted model suggested that compared to the HES position, the CV of breath duration was significantly higher during the 0-2 and 4-6 minutes of feeding intervals in the HEL position ($F_{1, 29}$ = 6.03; p = .020).

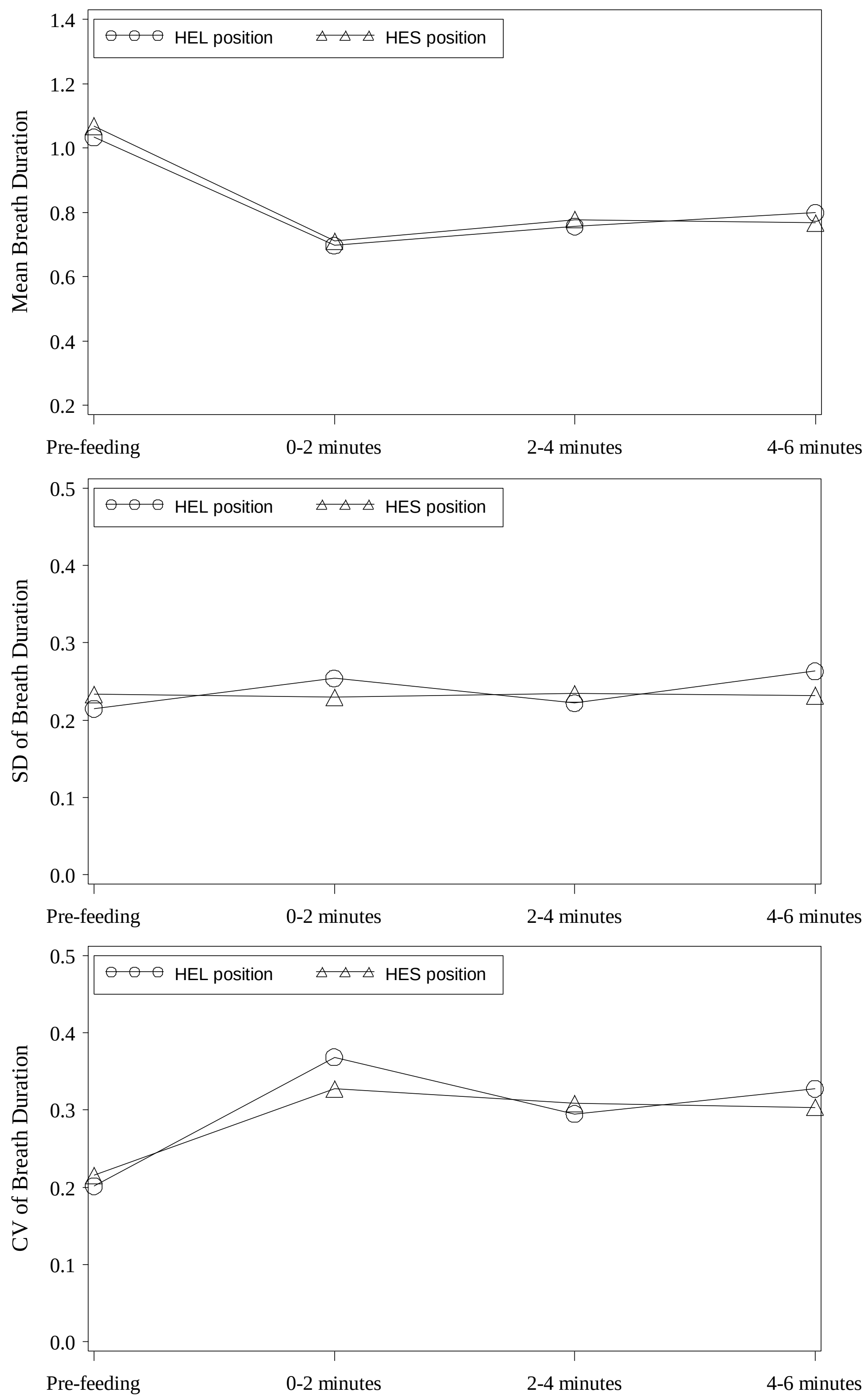

Figure 4.9. Changes in Breath Duration over Time using Method 3. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance.

Breath Amplitude

The averages of mean breath amplitude over successive 2-minute intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.10, and the associated LMM results are reported in Table 4.20. In the full LMM for mean breath amplitude, a significant effect of time ($F_{2, 10} = 3.99$; $p = .053$) and pre-feeding covariate ($F_{1, 24} = 9.01$; $p = .006$) were evident; however, no significant effects of feeding position and interaction between time and feeding position were found. After removing the interaction term, a significant effect of time ($F_{2, 10} = 3.70$; $p = .063$) and pre-feeding covariate ($F_{1, 26} = 9.01$; $p = .006$) were still evident, but no significant effect of feeding position ($F_{1, 5} = 0.04$; $p = .844$) was found.

The averages of the SD for breath amplitude over successive 2-minute intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.10, and the associated LMM results are reported in Table 4.20. In the full LMM for the SD of breath amplitude, a significant effect of time ($F_{2, 10} = 5.04$; $p = .031$) and pre-feeding covariate ($F_{1, 24} = 5.34$; $p = .030$) were found; however, no significant effects of feeding position and interaction between time and feeding position were found. After removing the interaction term, a significant effect of time ($F_{2, 10} = 4.58$; $p = .039$) and pre-feeding covariate ($F_{1, 26} = 5.34$; $p = .029$) were still evident, but no significant effect of feeding position ($F_{1, 5} = 0.07$; $p = .807$) was found.

The averages of the CVs for breath amplitude over successive 2-minute intervals during the first six minutes of the bottle-in period by feeding position are plotted in Figure 4.10, and the associated LMM results are reported in Table 4.20. In the full LMM for the CV of breath amplitude, no significant effects of time, feeding position, interaction between time and position, and pre-feeding covariate were evident. After removing all non-significant fixed components except for feeding position, no significant effect of feeding position was found ($F_{1, 5} = 1.55$; $p = .268$). The adjusted LMM considered a possible difference in CV of breath amplitude between the feeding positions only during the 0-2 and 2-4 minutes of feeding intervals. This adjusted model suggested that compared to the HES position, only a trend of lower CV of breath amplitude during the 0-2 and 2-4 minutes of feeding intervals was observed in the HEL position ($F_{1, 29} = 2.71$; $p = .111$).

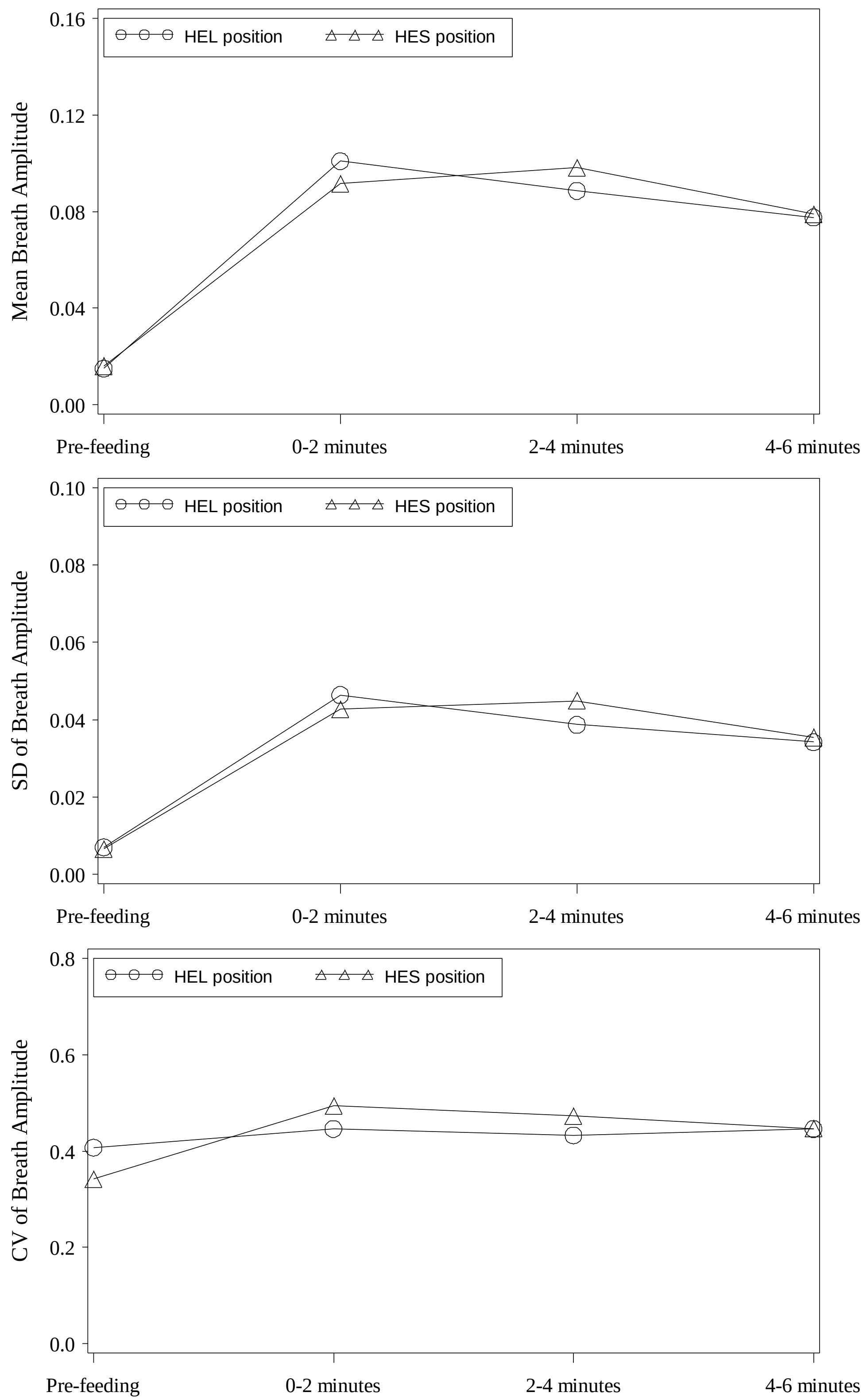

Figure 4.10. Changes in Breath Amplitude over Time using Method 3. HEL = head-elevated side-lying; HES = head-elevated supine; CV = coefficient of variance.

Table 4.20. Changes in Respiratory Characteristics over Time by Feeding Position using Method 3

	Interval between Breaths			Breath Duration			Breath Amplitude		
	Mean	SD	CV	Mean	SD	CV	Mean	SD	CV
Full model									
Time	.115	.423	.834	.061	.388	.062	.053	.031	.699
Position	.038	.040	.083	.975	.223	.254	.844	.807	.293
Time * Position	.942	.546	.262	.663	.290	.312	.417	.337	.680
Pre-feeding period	.990	.072	.126	.903	.169	.547	.006	.030	.830
Reduced model									
Time	.115	-	-	.065	-	.073	.063	.039	-
Position	.035	.047	.096	.956	.249	.293	.844	.807	.268
Time * Position	-	-	-	-	-	-	-	-	-
Pre-feeding period	-	.072	.131	-	.194	-	.006	.029	-

Note. CV = coefficient of variance. Data are expressed as *p*-values.

Residual Analysis

Changes in Heart Rate over Time

Residual analysis was conducted using the final reduced model separately for each HR measure and method. Most HR measures were normally distributed and had no outliers. However, the Shapiro-Wilk tests of normality were significant for the CV of HR using Method 1 (W = 0.93, $p = .027$) and the SD and CV of HR using Method 2 (SD: W = 0.89, $p = .002$; CV: W = 0.91, $p = .007$), indicating that these measures were not normally distributed and the associated LMM results are questionable. To resolve the non-normality, data were transformed using 0.35, 0.6, and 0.6 powers, respectively. After transformation, the Shapiro-Wilk tests of normality were no longer significant for the CV of HR using Method 1 (W = 0.97, $p = .309$) and the SD and CV of HR using Method 2 (SD: W = 0.95, $p = .090$; CV: W = 0.95, $p = .110$). The final reduced LMMs for these measures were recalculated for the transformed data. The conclusions were the same as the results for the untransformed data. These results suggest that the effects of time and feeding position for the CV of HR using Method 1 and for the SD and CV of HR using Method 2 are not affected by the non-normality, and it is reasonable to report the results for the untransformed data.

Changes in Oxygen Saturation over Time

Residual analysis was conducted using the final reduced model separately for each SpO_2 measure and method. Most SpO_2 measures were normally distributed and had no outliers. However, the Shapiro-Wilk tests of normality were significant for the mean SpO_2 using Method 2 (W = 0.92, $p = .014$) and the mean SpO_2 using Method 3 (W = 0.92, $p = .013$), indicating that these measures were not normally distributed and the associated LMM results are questionable. To resolve the non-normality, the data were transformed using 5.5 and 5.0 powers, respectively. After the transformation, the Shapiro-Wilk tests of normality were no longer significant for the mean SpO_2 using Method 2 (W = 0.94, p = .063) and for the mean SpO_2 using Method 3 (W = 0.94, p = .064). The final reduced LMMs for these measures were recalculated for the transformed data. The conclusions were the same as the results for the untransformed data. These results suggest that the effects of time and feeding position on the mean SpO_2 using Methods 2 and 3 are not affected by the non-normality, and it is reasonable to report the results for the untransformed data.

Changes in Respiratory Characteristics over Time

Residual analysis was conducted using the final reduced model separately for each RESCs measure that was used for the linear mixed modeling. Most RESCs measures were normally distributed and have no outliers. However, the Shapiro-Wilk tests of normality were significant for the mean breath amplitude (W = 0.87, $p < .001$), indicating that this measure was not normally distributed and the associated LMM results are questionable. To resolve the non-normality, data were transformed through 0.9 power. After the transformation, the Shapiro-Wilk tests of normality were no longer significant for the mean breath amplitude (W = 0.97, p = .456). The final reduced LMM for mean breath amplitude was recalculated for the transformed data. The conclusion was the same as the result for the untransformed data. This finding suggests that the effects of time and feeding position on mean breath amplitude are not affected by the non-normality, and it is reasonable to report the results for the untransformed data.

Conclusions for Hypothesis 2

Hypothesis 2 is partially supported. When the study infants were fed in the HEL position compared to the HES position, they exhibited significantly less variation in HR across the feeding period. Specifically by method, Method 1 (i.e., dividing the entire bottle-in period into three equal intervals) demonstrated that variation in HR significantly decreased over time in both positions; however, in the HEL position, the infants exhibited significantly less variation in HR across the feeding period, compared to being fed in the HES position. When considering the adjusted model based on the plot, the difference of variation in HR between the feeding positions appears to derive mostly from the difference during the first third of the feeding period. In Method 2 (i.e., extracting 2-minute intervals from the initial, middle, and final third of the bottle-in period), variation in HR also significantly decreased over time in both positions; however, this pattern did not significantly differ according to feeding position. When considering the adjusted model based on the plot, the infants exhibited significantly less variation in HR in the HEL position only during the first two minutes and the final two minutes of the feeding period compared to when fed in the HES position. In Method 3 (i.e., successive two minutes during the first six minutes of the bottle-in period), variation in HR also significantly decreased over time in both positions; however, in the HEL position, the infants exhibited significantly less variation in HR across all time points with a similar amount of difference between the feeding positions compared to when fed in the HES position.

The RESCs findings reveal that compared to the HES position, the infants breathed with significantly shorter breaths and more regular intervals between breaths across the feeding period when fed in the HEL position. When considering the adjusted model based on the plot, the difference in variation in intervals between breaths between the feeding positions appears to derive mostly from the difference during the last four minutes of the first six minutes of the bottle-in period. Breath duration became significantly more regular over time in both positions; however, this pattern did not significantly differ according to feeding position. When considering the adjusted model based on the plot, the infants fed in the HEL position exhibited significantly more irregularity in breath duration only during the 2-4 and 4-6 minutes of feeding intervals compared to when fed in the HES position. No significant findings of breath amplitude were found, but considering the adjusted model based on the plot, a trend of lower variation in breath amplitude only during the 0-2 and 2-4 minutes of the feeding intervals was found for the HEL position.

No significant findings for SpO_2 were found to support Hypothesis 2; however, in Method 3 (i.e., successive 2 minute intervals during the first six minutes of the bottle-in period), the adjusted model based on the plot, that considered an increasing pattern during the 2- to 4-minute feeding interval, suggested a trend of higher SpO_2 levels across the three successive 2-minute intervals in the HEL position.

Power Analysis Simulations

Simulations were conducted to address power for longitudinal measures of HR, SpO_2, and RESCs analyzed with linear mixed modeling. The purpose was to suggest the optimal method to detect position effects among the three candidate methods that were used for examining physiologic changes over time as determined by requiring the smallest number of infants to detect a position effect with 80% power. The findings may also suggest estimated sample sizes for future study.

Using mean and covariance estimates based on observed data for each outcome measure and method, a thousand simulations of full factorial LMMs for values during the feeding period, controlling for the pre-feeding period as a covariate, were computed for varying numbers of infants. The number of infants was increased until the estimated probability of a significant position effect reached 80%. In this way, the necessary sample size was estimated to achieve 80% power for detecting a position effect that allowed for within-infant correlations for outcomes across time and feeding positions. If the estimated probability did not reach 80% by 100 infants, the search was stopped, and the associated method was considered impractical for the current outcome. For the physiologic stability measures that did not meet the normality assumption in the residual analysis (i.e., the SD of HR using Method 1, the SD and CV of HR using Method 2, the mean SpO_2 using Method 2 and Method 3, and mean breath amplitude), power-transformed data (using the powers reported earlier) were used for the simulations.

Table 4.21 describes the minimum numbers of infants required for an estimated power of 80% for a significant position effect for each physiological variable and method. Overall, the HR and interval between breaths variables have enough power to detect a significant position effect with the smallest number of infants. The SpO_2 and breath duration and amplitude variables do not have enough power, even with over 100 infants for some methods.

In terms of choosing the most useful method for HR, Methods 1 and 3 have enough power to detect a significant position effect with a smaller number of infants than with Method 2. Especially for the SD and CV for HR, Method 3 requires the smallest number of infants to detect a significant position effect. For SpO_2, only Method 3 has 80% power to detect a significant position effect with fewer than 100 infants. When using Methods 1 and 2, the SpO_2 variable does not have enough power even with over 100 infants. Therefore, the results suggest that Method 3 may be the most useful method to detect a significant effect of feeding position on changes in HR and SpO2 over time while requiring the smallest number of infants.

Table 4.21. Number of Infants Required for an Estimated Power of 80%

	Method 1 [a]	Method 2 [b]	Method 3 [c]
Heart Rate			
Mean	29	37	27
SD	11	32 [d]	8
CV	14 [d]	28 [d]	8
Oxygen Saturation			
Mean	> 100	> 100 [d]	36 [d]
SD	> 100	> 100	80
CV	> 100	> 100	75
Interval between Breaths			
Mean	-	-	10
SD	-	-	7
CV	-	-	10
Breath Duration			
Mean	-	-	> 100
SD	-	-	> 100
CV	-	-	> 100
Breath Amplitude			
Mean	-	-	> 100 [d]
SD	-	-	> 100
CV	-	-	> 100

Note. CV = coefficient of variance. [a] Method 1 = Dividing the entire bottle-in period into three equal feeding intervals. [b] Method 2 = Extracting 2-minute intervals from each third of the bottle-in period. [c] Method 3 = Successive 2-minute intervals for the first six minutes of the bottle-in period. [d] Because normality was questionable, the transformed data were used.

Intervention Fidelity

Intervention fidelity was assessed by determining whether the assigned position was delivered properly, and whether the caregiver's feeding strategies were consistently carried out across and within the infants based on the feeding protocol (Table 4.22). To evaluate whether the assigned position was delivered properly, the proportion of feeding time that the infants were in the HES position (supine) and in the HEL position (side-lying) were calculated. For both conditions, the infants were placed in each of the assigned positions for the majority of the feeding time (mean 97.3% of feeding period for HES position; 99.7% of feeding period for HEL position).

To evaluate whether the caregiver's feeding strategies were consistently carried out across and within the infants based on the feeding protocol, five caregivers' feeding behaviors, as described in the feeding protocol, were assessed. For both conditions (HES and HEL), the caregivers consistently prepared the infants for the feeding before placing the nipple in their mouth (prep). However, high variability was observed in the caregivers' feeding behaviors of placing the nipple in the mouth based on the infant's behavioral cues of readiness (ready), moving the nipple to stimulate sucking (stim suck), allowing time for the infants to minimize sucking and resume breathing by limiting the flow of milk (limit flow), and providing rest periods with the bottle out of the mouth (numb rest periods) across infants and feeding conditions. Overall, in the HEL position, the caregivers were more likely to provide fewer rest periods with the bottle out of the mouth (numb rest periods), more likely to stimulate sucking by moving the nipple (stim suck), and more likely to initiate feedings when infants demonstrated readiness (ready). In terms of the caregivers' feeding behaviors of limiting the flow of milk, for infants 1 and 2, the designated caregivers provided fewer opportunities to allow time for the infants to minimize sucking and resume breathing when they were fed in the HEL position; but for infants 4, 5, and 6, the caregivers provided slightly fewer actions to limit the flow of milk (limit flow) in the HEL position. However, the mean frequency of this behavior was slightly higher in the HES position. Therefore, the intervention of feeding position was delivered properly; however, the caregivers' feeding behaviors were different between conditions.

Table 4.22. Descriptive Statistics for Intervention Fidelity

Condition \ Infant		1	2	3	4	5	6	Mean	SD
Supine Side-lying [a]	HES	94	100	100	100	91	100	97.3	4.0
	HEL	100	100	100	100	99	99	99.7	0.4
Prep [b]	HES	100	100	100	100	100	100	100	0
	HEL	100	100	100	100	100	100	100	0
Ready [c]	HES	0	0	25	50	0	75	25.0	31.6
	HEL	100	33	50	67	100	100	75.0	29.3
Stim Suck Events [d]	HES	58	35	108	30	35	35	50.2	30.0
	HEL	99	32	114	40	65	46	66.0	33.5
Limit Flow Events [e]	HES	43	14	1	4	6	34	17.0	17.4
	HEL	21	2	1	9	9	37	13.2	13.7
Numb Rest Periods [f]	HES	5	4	3	1	1	3	2.8	1.6
	HEL	1	2	3	2	2	2	2.0	0.6

Note. HES = head-elevated supine; HEL = head-elevated side-lying. [a] Proportion of the feeding time (using the bottle-in period) that the infant is held in a semi-upright position for the condition of the HES position (Supine) and in a side-lying position for the condition for the HEL position (Side-lying); [b] Proportion of onset of feeding episodes that the caregiver prepared the infant for feeding; [c] Proportion of onset of feeding episodes that the infant demonstrated readiness; [d] Number of times the caregiver stimulated infant sucking; [e] Number of times the caregiver limited the flow of milk; [f] Number of rest periods provided by the caregiver.

CHAPTER V

DISCUSSION

This final chapter interprets the results presented in Chapter IV. This study examines the preliminary effects of the HEL feeding position on physiologic stability and feeding performance, as compared to the HES feeding position, for VP infants (≤ 30 weeks of GA) who are transitioning from gavage feeding to full oral feeding. In addition, methods for measuring changes in physiologic stability across the feeding time are examined.

To examine the preliminary effects of the HEL position, two hypotheses were tested by examining physiologic stability and feeding performance during and across the feeding time. To examine methods for measuring changes in physiologic stability across the feeding time, three methods to create intervals of feeding time were chosen and examined. Simulations for each method were conducted to determine the most optimal method, as determined by which method requires the smallest number of infants to detect a position effect with 80% power. Finally, intervention fidelity was evaluated.

This chapter is organized as follows: interpretation of the results of the two hypotheses, power simulations analysis, discussion of intervention fidelity, description of the study's strengths, limitations, and implications, and, finally, presentation of conclusions.

Hypothesis 1

Hypothesis 1 premises that VP infants would have greater physiologic stability and better feeding performance when they are fed in the HEL position compared to the HES position. Physiologic stability was measured in terms of HR, SpO_2, and RESCs (i.e., breath-to-breath intervals, duration and amplitude of breaths, respiratory rate, and breathing pauses > 3 seconds). Feeding performance was measured in terms of overall milk transfer, proficiency, efficiency, and duration of feeding.

Heart Rate

It is well known that during oral feeding, normal breathing patterns are modulated by the act of sucking and swallowing. Several studies involving both term and preterm infants have shown that breathing alternation while feeding reduces minute ventilation by decreasing inspiration time, breathing frequency, and tidal volume (Bamford et al., 1992; Koenig et al., 1990; Mathew et al., 1985; Shivpuri et al., 1983). However, the decrease in ventilation has a greater impact on VP infants than healthy full term infants because of their reduced capacity to self-organize changes in ventilation due to immaturity and/or compromised lung function (Gewolb & Vice, 2006; Mizuno et al., 2007).

One of the strategies neonates employ to self-organize physiologic changes during activities such as feeding is to increase their HR to provide the necessary oxygen and nutrients to tissues in response to increased respiratory efforts (Blackburn, 2007). The increase in HR is considered a compensatory process, possibly indicating that the infant is coping with the physiologic demands of feeding to maintain homeostasis. Large increases in HR may indicate that feeding is placing excessive physiologic demands on the infant.

However, for VP infants, especially those with respiratory problems, decreased ventilation while feeding may be too great to be recovered through the compensatory process and can be frequently associated with decreases in HR. The decrease in HR is considered a potentially life-threatening event, which could result from stimulation of the sensory receptors in the pharyngeal-largyngeal area by microaspiration of food, gastro-esophageal reflux, or a large bolus of milk, or stimulation of carotid body chemoreceptors caused by a decrease in oxygen saturation (Glass & Wolf, 1994). Although the degree of change in HR that can be tolerated by VP infants while feeding is unknown, it is not uncommon to see changes in HR within 10% above or below the resting HR. In this study, VP infants exhibited significantly less variation in HR, spent less time with severe decreases in HR (i.e., at least 20% below that of the pre-feeding period) and bradycardia (i.e., less than 100 bpm), and spent more time only with mild increases in HR (i.e., at least 10% above that of the pre-feeding period) when fed in the HEL position as compared to the HES position. The findings suggest that VP infants fed in the HEL position are able to handle the physiologic demands of feeding more effectively by modulating their HR through a compensatory process. However, when fed in the HES position, VP infants may not be able to handle the physiologic challenges by modulating their HR through a compensatory process, thereby resulting in increased variation in HR, and more time with severe decreases in HR and bradycardia (i.e., less than 100 bpm). These findings may be a consequence of the increased physiologic challenges faced by VP infants when they are fed in the HES position as compared to the HEL position.

Oxygen Saturation

Another major physiologic variable used in this study is SpO_2. In this study, no statistically significant difference in SpO_2 between the feeding positions was found. Only a trend towards less variation in SpO_2 in the HEL position as compared to the HES position was evident. These SpO_2 findings can be explained in several possible ways. The VP infants in this study had relatively healthy cardio-respiratory conditions (i.e., two infants had no lung disease, three infants had mild lung disease, and one infant had moderate lung disease). Thus, the study infants might have been able to modulate their breathing or HR in response to the demands of feeding without severely compromising their cardio-respiratory status which could cause oxygen desaturation. Another explanation of no significant differences in SpO_2 levels is that the number of observations was relatively small, so statistically significant differences were not evident. However, a trend towards less variation in SpO_2 levels in the HEL position suggests further examination of the effect of the HEL position on SpO_2.

Respiratory Characteristics

The RESCs findings indicate that VP infants show decreased breathing frequency, longer and more irregular intervals between breaths, and shorter breath durations during the feeding period than during the pre-feeding period in both feeding positions. These findings are concordant with previous findings that suggest that during oral feeding, normal breathing patterns are modulated by the act of sucking and swallowing, resulting in decreased inspiration time, decreased respiratory frequency, decreased minute ventilation, and decreased tidal volume (Bamford et al., 1992; Koenig et al., 1990; Mathew et al., 1985; Shivpuri et al., 1983). However, when VP infants were fed in the HEL position, decreased breathing was significantly less marked than in the HES position, especially for breathing frequency and intervals between breaths. That is, in the HEL position, VP infants breathed with significantly higher frequency that is closer to that of the pre-feeding state, and with shorter breaths and more regular intervals between breaths, suggesting that they were able to breathe better and with less interruption than in the HES position. In addition, VP infants, who show higher respiratory rates during the pre-feeding period, tend to have more benefits from the HEL position, i.e., the differences in respiratory rate during feeding between the feeding positions were more remarkable for those infants with higher respiratory rate during the pre-feeding period, than that of other infants. This observed pattern suggests that this intervention may be best targeted to those infants who have increased respiratory requirements in a resting state (i.e., a marker of a rate limiter). Further study is warranted to examine a moderate effect of pre-feeding respiratory states on the relationship between the HEL position and physiologic outcomes.

Another RESCs finding from this study is that breath duration is significantly more irregular in the HEL position than in the HES position. Increased irregularity in breathing duration can be explained by a feeding pattern that is frequently observed in preterm infants. Normally, infants coordinate breathing with sucking and swallowing during feeding. That is, they are able to properly and efficiently integrate breathing into sucking and swallowing rhythms. However, VP infants have difficulty integrating sufficient breathing while sucking and swallowing the milk, so they often adopt a less complex pattern of coordination, which presents only a suck-swallow dyad during the sucking bursts with breathing that follows in an alternating fashion (Palmer, 1993). This feeding pattern may be a functional strategy to protect the airway when the proper coordination of sucking, swallowing, and breathing is too difficult; however, this pattern may cause longer cessations of breathing that could increase the cardio-respiratory load during feeding, especially during long sucking bursts.

This study finds that in the HES position, VP infants are more likely to adopt a less complex pattern of coordination (i.e., alternating clusters of sucks and breaths)), which may contribute to longer cessation of breathing. In the HEL position, infants were more likely to demonstrate a more complex coordination pattern (i.e., integrating breathing into sucking bursts)), as depicted in Figure 5.1. Craig et al. (1999) report that during the sucking bursts, breathing is constantly interrupted by the need to defend the airway when swallowing the milk than during the period when the infant is not sucking, which causes irregular breath durations and shallow breath depths. Therefore, in this study, VP infants' efforts to adopt a more mature, more complex feeding patterns (i.e., integrating more breathing into the sucking bursts) in the HEL position may increase variation in breath duration during the sucking bursts, which also can increase the average variation in breath durations during the overall feeding period. As a consequence, the RESCs findings from this study suggest that the HEL position may create a condition that supports improved regulation of breathing while sucking and swallowing and that minimizes the long cessations of breathing. Therefore, in the HEL position, the cardio-respiratory load during feeding is decreased, which allows for infants to maintain greater physiologic stability throughout the feeding, as demonstrated by the findings of HR and SpO_2, i.e., less variation in HR, less severe and fewer decreases in HR, and trend towards less variation in SpO_2. Also, the HEL position may facilitate the practice of a more mature and complex feeding pattern as compared to the HES position. Therefore, the HEL position may be a strategy to improve feeding outcomes by supporting a breathing (i.e., a rate-limiter), which limits VP infants' capacity to self-organize the entire feeding system.

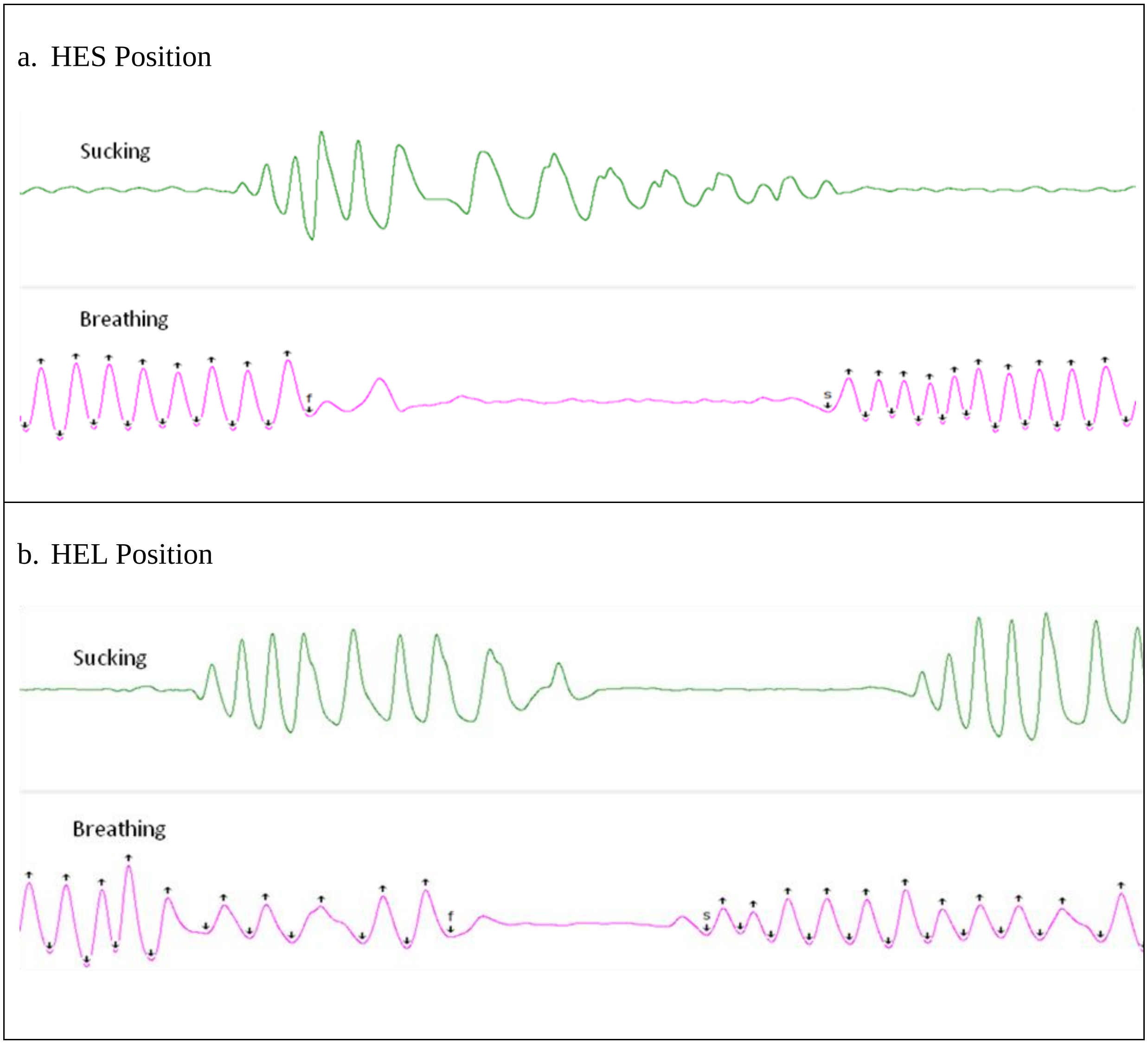

Figure 5.1. Example of Tracing of Sucking and Breathing Pattern in Two Different Positions. HES = head-elevated supine; HEL = head-elevated side-lying.

Two major mechanisms of the HEL position may contribute to the physiological benefits over the HES position. First, the HEL position is the natural position that is assumed by infants when they are fed at the breast. The physiologic benefits of breastfeeding for preterm infants are well documented. Previous researchers have found that during breastfeeding, as compared with bottle feeding, preterm infants better coordinate breathing with swallowing (Goldfield et al., 2006), resulting in less disruption of breathing (Blaymore Bier et al., 1997; Chen, Wang, Chang, & Chi, 2000; Dowling, 1999; P. Meier, 1988). This study's findings reveal that VP infants are better able to regulate breathing during feeding by demonstrating a respiratory rate that is closer to their pre-feeding respiratory rate, shorter and more regular intervals between breaths, and more variation in duration of breath in the HEL position compared with the HES position. These findings are somewhat similar to those of previous studies that demonstrate the physiologic advantages of breastfeeding as compared to bottle-feeding (Blaymore Bier et al., 1997; Chen et al., 2000; Dowling, 1999; Goldfield et al., 2006; P. Meier, 1988). Although this study does not include a direct comparison of the physiologic responses to feeding between the HEL position and breastfeeding, the findings suggest that the HEL position, which better mimics the natural position of breastfeeding than the HES position, might contribute to the physiologic advantages of breastfeeding over bottle feeding.

The second potential mechanism of the HEL position is that it may create conditions for infants to better manage the flow of milk. Several research studies have consistently demonstrated that under more rapid milk flow conditions, breathing is more interrupted as a consequence of the increased bolus size of each suck and swallowing frequency (Al-Sayed et al., 1994; Mathew, 1991a). This study premises that in the HEL position, the lowered angle of the bottle may slow the gravitational milk flow by decreasing the hydrostatic pressure generated by the volume of milk in the inverted bottle. Although this study does not include a direct measure of the rate of milk flow in each position, the potentially slower flow of milk by gravity in the HEL position may permit infants to swallow less, and in turn, have fewer interruptions of breathing. In addition, in the HEL position, gravitationally the milk is directed toward the cheek rather than directly to the back of the oral cavity, so that infants may have more time to form a bolus and control its movement for safe and efficient swallowing which minimize breathing interruptions. This additional time may also allow the infant to raise the distal portion of the tongue in order to slow the flow of milk and delay swallowing, thereby providing additional time for breathing. Therefore, better fluid management by several potential mechanisms of the HEL position may minimize the interruption of breathing during feeding, which allows the infant to maintain greater physiologic stability throughout the feeding.

Feeding Performance

In this study, no significant findings for any of the feeding performance measures were found; however, a trend toward longer duration of feeding was observed for the HEL position. Several factors of the trend of longer duration of feeding in the HEL position can be explained and support further examination. The longer duration of feeding may indicate that infants are able to maintain engagement in the activity of feeding for a longer period of time. Als (1986), in her synactive theory of development, proposed that the first task of preterm infant development is to achieve control over the autonomic system, and that this autonomic system development affects and supports the development of an infant's motor and state systems. Thoyre and Brown (2004) also report that physiologic conditions that occur during feeding have a significant effect on infants' engagement in feeding. In the current study, when fed in the HEL position as compared to the HES position, VP infants exhibited greater physiological stability as demonstrated by less variation in HR, less severe and fewer decreases in HR, frequency of breathing that is closer to that of the infant's pre-feeding state, and shorter breaths and more regular intervals between breaths. The greater physiologic stability in the HEL position over that observed in the HES position may serve to conserve the necessary energy that supports an infant's engagement in feeding at the behavioral level for a longer period of time.

In addition, even if VP infants were able to consume similar amounts of their prescribed milk in both feeding positions, i.e., mean 92.7% and 95.2% of the prescribed milk in the HES and HEL positions, respectively, VP infants tended to spend more time consuming a similar amount of milk when being fed in the HEL position. This finding may support the fact that the potentially faster flow of milk in the HES position, compared to the HEL position, may encourage infants to consume the milk faster. In other words, when fed in the HEL position, infants may be allowed to feed at a slower pace, which may provide additional time to better control the bolus for safe and efficient swallowing, possibly contributing to greater physiologic stability throughout the feeding as evidenced in the findings for the physiologic parameters. This longer duration of feeding may also indicate that the infant's stomach fills more slowly and with less gastric distention. Rapid stomach filling may be associated with gut hyperperfusion and peripheral hypoperfusion after feeding (Yao, Wallgren, Sinha, & Lind, 1971). Although this study did not measure physiologic responses after feeding, the physiology of slower feeding leads to the consideration that the longer duration of feeding in the HEL position may have different physiologic impacts after feeding.

Conclusions of Hypothesis 1

The findings of this study partially support Hypothesis 1 that VP infants would have greater physiologic stability when they are fed in the HEL position, compared to the HES position, by demonstrating less variation in HR, less severe and fewer decreases in HR, shorter breaths and more regular intervals between breaths, respiratory rates that are closer to the the pre-feeding state, and more variation in breath duration. Although the findings for SpO_2 and feeding performance are statistically non significant, the trends of less variation in SpO_2 and longer duration of feeding in the HEL position support further examination of the HEL position using these variables. In conclusion, the HEL position may be a feeding strategy that can reduce the physiologic work by supporting a breathing (i.e., a rate-limiter) during feeding which may allow VP infants to better handle the physiologic challenges of feeding.

Hypothesis 2

Hypothesis 2 premises that VP infants would demonstrate fewer physiologic changes from the pre-feeding period across the feeding period when they are fed in the HEL position, compared to the HES position. Infants' feeding behaviors emerge from the continuous interaction within and between the subsystems that are involved in the feeding process and, thus, can change across the feeding period (Goldfield, 2007). Therefore, different feeding dynamics over time can reflect different infants' adaptive capacities in response to the demands of feeding. Hypothesis 2 was established to examine more precisely the different feeding dynamics according to feeding position by taking into account the non-stationary state of infants' feeding responses across the feeding period. To examine changes in physiologic stability over time, three methods were chosen to explore the optimal way to divide the feeding for across-feeding analysis: (1) dividing the entire bottle-in period into three equal intervals; (2) extracting 2-minute intervals from the initial, middle, and final third of the bottle-in period; and (3) using successive two minutes during the first six minutes of the bottle-in period (see Figure 3.4). All three methods were used to examine changes in HR and SpO_2 over time. Because RESCs measures are new and exploratory, some of the RESCs (i.e., intervals between breaths, breath duration and amplitude) were calculated for the first six minutes of the bottle-in period, and only Method 3 was used to examine the change of RESCs over time.

Heart Rate

In this study, statistically significant differences between the HES and HEL positions were evident only for variation in HR. Overall, variation in HR was the highest in the initial minutes of feeding and decreased as the feeding progressed in both positions; however, in the HEL position, VP infants exhibited significantly less variation in HR across the feeding period, including the early minutes, compared with the HES position. Specifically by method, when the entire bottle-in period was divided into three equal intervals (i.e., Method 1), the VP infants exhibited significantly less variation in HR, especially during the first third period (see Figure 4.2). When 2-minute intervals were extracted from the initial, middle, and final third of the bottle-in period (i.e., Method 2), variation in HR was not significantly different by feeding position over time; but, when considering the adjusted model to examine possible differences of variation in HR at each time point based on the plot, significantly less variation in HR was observed during the first and final 2-minute intervals when fed in the

HEL position (see Figure 4.3). When the successive 2- minute intervals during the first six minutes of the bottle-in period (i.e., Method 3) were examined, variation in HR was significantly less across all time points with a constant amount of difference between the feeding positions (see Figure 4.4).

Despite the statistically non significant findings derived from Method 2, the overall findings partially support Hypothesis 2 that VP infants would demonstrate fewer physiologic changes from pre-feeding across the feeding period when they are fed in the HEL position, compared to the HES position, by demonstrating a more stable HR over time in the HEL position. One explanation of the statically non-significant difference of HR patterns between the feeding positions in Method 2 is that the three 2-minute intervals extracted from the initial, middle, and final third of the bottle-in period may not sufficiently reflect the conditions of the feeding dynamics; i.e., meaningful data may be lost through this method.

For all the methods and in both positions, variation in HR was found to be the highest in the initial minutes of the bottle-in period, and this variation declined as infants adapted to the feeding process. This pattern may indicate that more physiologic adjustments, through modulation of HR, were required when infants began feeding. This finding is somewhat similar to that of a previous study that reports that the initial minutes of feeding are the physiologically most vulnerable period, as demonstrated by more frequent desaturation events (Thoyre & Carlson, 2003). Changes in HR can indicate the physiologic load of coping with the demand of feeding activity. Therefore, the finding in Method 1, which shows that the biggest difference in variation of HR between the feeding positions is during the first third bottle-in period, further suggests that the HEL position may reduce physiologic work, especially during the beginning of the feeding, which possibly is the time when infants require the most physiologic adjustments.

The findings of this study are inconsistent with a previous study that found no difference in variation in HR of VP infants over time between the HES and HEL positions (L. Clark et al., 2007). Despite statistical non significance, from a visual inspection, these previous researchers observed a pattern of increased variation in HR in the first three minutes of feeding from the pre-feeding period, then recovery of variation in HR near to the pre-feeding period in the middle three minutes of feeding, with a more marked recovery of HR in the HEL position. One explanation for discrepancies in the findings may be the different period and interval of time when the measurements were taken in the two studies. Also, during a typical feeding observation, infants have periods of feeding and periods of resting or burping, during which the nipple is not in the infant's mouth. In this study, in order to remove potentially confounding data, the resting and burping periods were eliminated, and combined bottle-in periods were used for creating intervals of feeding time. However, L. Clark et al. (2007) do not clarify whether they include non-feeding and burping periods in taking their measurements at the beginning and middle point of feeding. This fact may further contribute to the difference of the findings between the two studies.

Oxygen Saturation

No significant pattern for SpO_2 over time by feeding position was found for any of the analysis methods. Although statistically non significant differences in SpO_2 were found between the feeding positions, from visual inspection based on the plots, in Method 1 (i.e., dividing the entire bottle-in period into three equal intervals) and Method 2 (i.e., extracting 2-

minute intervals from each third of the bottle-in period), the mean SpO_2 decreased and the variation in SpO_2 increased from the pre-feeding period in the initial minutes of the bottle-in period. Then, they partially recovered over time toward the pre-feeding period as the infants adapted to the feeding process with slightly higher and more stable SpO_2 levels in the HEL position over time (see Figures 4.5 and 4.6). However, when successive 2-minute intervals during the first six minutes of the bottle-in period (i.e., Method 3) were observed, the mean and variation of SpO_2 moved in the opposite direction at the 4-6 minutes interval, thereby decreasing the mean SpO_2 and increasing the variation in SpO_2 again (see Figure 4.7). When the adjusted model considered this nonlinear pattern of SpO_2 over time in Method 3, a trend towards a higher mean SpO_2 across all time points in the HEL position, compared to the HES position, was observed.

This finding differs from the Clark study that showed a significant interaction effect of time and position, suggesting that the mean SpO_2 decreases in the first three minutes of feeding in both feeding positions; however, in the middle three minutes of feeding, the mean SpO_2 increases in the HEL position and decreases further in the HES position (L. Clark et al., 2007). Again, the difference in the findings from these two studies can be explained by the different periods and intervals of feeding time that were used for taking the measurements. Another explanation is the different cardio-respiratory conditions of the study infants, even if in the Clark study, the severity of lung disease of the sample was not specified. In this study, the cardio-respiratory conditions of the study infants reflect relatively healthy infants (i.e., two infants had no lung disease, three infants had mild lung disease, and one infant had moderate lung disease), which may have allowed the study infants to cope with the demands of feeding without severely compromising their cardio-respiratory status, which could result in a decrease in SpO_2. Finally, the number of observations in the current study was smaller than that in the Clark's study (6 feeding observations per position in the current study and 18 feeding observations per position in Clark's study), so that statistically significant differences may not be evident in the current study.

Even if all of the changes in SpO_2 observed in the current study were slight and statistically non significant and occurred within the normal range, the trend towards higher and visually more stable SpO_2 over time in the HEL position compared to the HES position suggest further examination in a different and larger sample to clarify the patterns of SpO_2 over time across the methods.

Respiratory Characteristics

In this study, VP infants breathed with significantly shorter breaths and more regular intervals between breaths across all successive 2-minute intervals during the first six minutes of bottle-in periods when being fed in the HEL position as compared to the HES position (see Figure 4.8). When considering the adjusted model to examine the possible difference of variation in intervals between breaths at each time based on the plots, the significant difference of variation in intervals between breaths between the feeding positions may derive from a difference during the last four minutes of the first six minutes of the bottle-in period. That is, variation in intervals between breaths was likely to increase over time in the HES position, whereas in the HEL position, such variation remained approximately at the same level. This finding suggests that the HEL position may support VP infants in consistently regulating their breathing over time by sustaining the regularity of intervals between breaths.

No statistically significant difference in breath duration and amplitude over time by feeding position was observed in this study. However, when the adjusted model was considered for examining the possible differences in variations in breath duration at each time based on the plot, VP infants exhibited more irregular breath duration in the HEL position only in the 0-2 and 4-6 minutes of the bottle-in period (see Figure 4.9). Like the previous description of increased irregularity of breath duration in Hypothesis 1, this finding suggests that the integration of breathing into sucking and swallowing rhythms is less compromised when VP infants are fed in the HEL position (see Figure 5.1). Therefore, all the findings for longitudinal RESCs measures further strengthen the potential mechanisms of the HEL position to support breathing over time by demonstrating better modulation of breathing over time.

Conclusions of Hypothesis 2

The findings of longitudinal measures partially support Hypothesis 2 that VP infants would demonstrate fewer physiologic changes from the pre-feeding period across the feeding period when fed in the HEL position, compared to the HES position, by demonstrating more stable HR over time in the HEL position, especially during the early minutes of feeding. Although statistically non significant findings were found for SpO_2, the trend of higher and visually more stable SpO_2 over time in the HEL position supports further examination of the HEL position with regard to this variable. In addition, although RESCs measures used for this study are new and exploratory, the significant findings for some of the measures (i.e., shorter breaths and more regular intervals between breaths over time and increased variation in breath duration at the first and last two minutes of the first six minutes of the bottle-in periods) strengthen the findings of other physiologic parameters and supports further examination as an indicator of physiologic work during feeding.

Comparisons of Methods for Examining Feeding Over Time

Examining infants' physiologic responses to feeding over time may better reflect the conditions of feeding dynamics by taking into account the non-stationary state of infants' feeding responses. In addition, the values divided by small intervals of feeding time can provide trend information and counter the criticism that an averaged value smoothes too much of the data streams and loses too much information. However, no clear understanding of the optimal period and intervals of feeding for across-feeding analysis currently exists. Therefore, this study employs three methods to create intervals of feeding time and examines changes in physiologic stability over time using HR, and SpO_2.

Somewhat different patterns of change in HR and SpO_2 across the methods were observed in this study, which may imply potential advantages and disadvantages of each method. In the HR findings using each method as an example, Method 1 (i.e., dividing the entire bottle-in period into three equal intervals) shows that variation in HR increase in the first third bottle-in period, decline in the middle third period, and remain approximately at a similar level during the final third period. The difference in variation of HR between feeding positions was most remarkable during the first third period (see Figure 4.2.). For Method 2 (i.e., extracting 2-minute intervals from the initial, middle, and final thirds of the bottle-in period), variation in HR also were the highest during the initial two minutes in both positions, but in the HES position, it declined further during the middle two minutes and remained steady during the final two minutes, whereas in the HEL position, the variation in

HR declined slightly less during the middle two minutes, but further declined during the final two minutes (see Figure 4.3). The different HR pattern in Method 2 indicates that 2-minute intervals extracted from each third of the bottle-in period may not be sufficient to reflect the whole of the feeding dynamics. Method 3 (i.e., successive 2-minute intervals during the first six minutes of the bottle-in period) closely reflects the decreased variation in HR from the 0-2 minutes to the 2-4 minutes in the HES position that are missing in the other methods, resulting in a constant amount of difference in variation of HR between feeding positions across all time points (see Figure 4.4). This finding suggests that Method 3 may provide more precise variability.

Therefore, different physiologic patterns over time across the methods may indicate both advantages and disadvantages. In Method 1, the overall feeding dynamics can be presented, but true variability may be smoothed, especially for feedings of long duration. Method 2 can provide comparable interval lengths in each period across feedings to be cross-compared, regardless of feeding time. However, meaningful data may be left out. In Method 3, the smaller epochs may allow for more precision to reflect continuous feeding dynamics, but do not demonstrate the whole dynamics of feeding by not including the data after the first six minutes of the bottle-in periods.

The most useful method, as determined by the method that requires the least number of infants to detect a position effect with 80% power, can be recommended by conducting simulations of LMMs for each method and variables for varying numbers of infants. The findings from these simulations suggest that Method 3 may be the optimal, most efficient method to examine changes in both HR and SpO_2 over time by feeding position since it requires the least number of infants. Therefore, the first six minutes of bottle-in periods may be sufficient to examine dynamics of feeding over time according to feeding position, which may allow for less cost and effort in collecting and analyzing data.

Intervention Fidelity

Intervention fidelity was assessed in this study by determining whether the assigned position is delivered properly, and whether the caregiver's feeding strategies were consistent across the two feeding conditions. In both feeding conditions, the assigned feeding position was properly delivered for most of the feeding time (mean 97.3% of feeding period for HES; 99.7% of feeding period for HEL). Five caregivers' feeding behaviors, based on the feeding protocol that the nurse caregivers were asked to follow during the study (Appendix B), were assessed. For both feeding conditions, the caregiver consistently prepared the infants for the feeding before placing the nipple in their mouths across infants and feeding conditions. However, in the condition of the HEL position, caregivers provided fewer rest periods with the bottle out of the infant's mouth, stimulated sucking by moving the nipple more often, and initiated feedings when infants demonstrated behavioral cues of readiness more often. Caregivers' feeding behaviors of limiting the flow of milk varied across infants and feeding conditions. For some infants, the caregiver was more likely to tip the bottle back to limit the flow of milk in the HES position; and for some infants, the caregiver was slightly more likely to tip the bottle back in the HEL position. However, the mean frequency of this behavior was slightly higher in the HES position than in the HEL position.

Even if the assigned position was delivered properly, part of the feeding protocol was not consistently followed during the study, as demonstrated by high variability in some of the caregivers' feeding behaviors within and between infants. Several factors may contribute to these findings. First, even if nurses were asked to read and follow the feeding protocol as much as they could before the study commenced, they were not systematically trained to use the feeding protocol. Also, a single nurse caregiver performed both feedings per infant for the comparable feeding strategies between two experimental conditions; however, three different nurse caregivers were used for all study infants. Possibly, different feeding strategies across the caregivers may have contributed to the variability of the caregivers' feeding behaviors across the infants. Finally, based on the feeding protocol, the designated caregiver's feeding behavior to limit the flow of milk and provide rest periods should be offered contingent upon the infant's needs while feeding. Therefore, the variability of these feeding behaviors between feeding conditions suggests that infants may demonstrate different needs for external support to regulate breathing with sucking and swallowing in each feeding position, rather than indicating the caregiver's poor compliance with the protocol.

The inconsistency of the caregivers' feeding behaviors may confound the study findings in several ways. The designated caregiver's feeding behavior to stimulate sucking can cause the infant to increase sucking and potentially cause more milk to be expelled into his or her mouth, thus contributing to physiologic distress, especially if this event occurs when the infant is regulating his or her breathing after a sucking burst. Thus, the higher frequency of this behavior in the HEL position may mask some of the physiologic benefits of the HEL position. In addition, the more onsets of feeding when the infant demonstrates readiness in the HEL position may increase the infant's ability to maintain engagement and to maintain more physiologic stability throughout the feeding in the HEL position compared to the HES position. Therefore, further testing is warranted to examine the effect of the HEL position by controlling the possible confounding variables. Also, in future studies, a single and better trained interventionist, and better monitoring of the caregiver's strategies to feed during the study would increase confidence in the findings. Even if the feeding protocol was not consistently followed during the study, variation in ways the caregivers fed the infants in this study may mimic actual conditions of how infants are fed in the NICU.

Strengths of the Study

This study is one of the first studies to examine the effect of the HEL position on feeding outcomes. So far, only one pilot study has been published that examines the effect of the HEL position. Moreover, this study includes more specific and new measures to examine physiologic stability than are found in previous studies. For example, the CV is used to quantify the variability of the physiologic parameters in this study. In addition, this study is the first to include specific and systematic approaches to examine RESCs, including intervals between breaths, breath duration and amplitude, respiratory rate, and breathing pauses longer than three seconds. Breath-by-breath analysis was conducted to quantify all the RESCs measures. Also, in order to control movement artifacts of respiratory signals that were detected by chest movements associated with respiratory effort, all respiratory signals were validated by the amplified breathing and swallowing sounds that were measured from the microphone attached to the infant's neck. Finally, this study is the first to analyze and compare several methods to examine patterns of physiologic stability across the feeding time.

Limitations of the Study

The limitations of this study include its small sample size and different caregiver feeding behaviors within and across the infants, which may confound the effects of the HEL position on the infants' responses to feeding. A larger sample and replication would increase confidence in the findings as well as allow potential covariates to be tested. A single and better trained caregiver is also recommended for future studies. In addition, the RESCs measures and methods used to examine the patterns of physiologic stability over time in this study are new and exploratory and, therefore, all of these measures and methods should be replicated with a larger population and different feeding conditions for further clarification. In particular, the mediating effect of RESCs measures on other physiologic parameters could become an important area for further study. Finally, although physiologic benefits are found in this study, long-term benefits for infants who are consistently fed in this way are still unknown, because this study examines only two feeding observations per infant by alternating feeding position. Therefore, subsequent study to extend these findings also is needed.

Implications of the Study

The results of this study have several implications for both clinical practice and research. Feeding position is a feeding strategy that can readily be applied to neonatal care. However, because of limited experimental evidence, no precise and consistent feeding position has been recommended for health care professionals to follow. Therefore, the findings from this study that demonstrate evidence of greater physiologic stability when VP infants are fed in the HEL position can lead to changed practice for feeding infants in the NICU, especially those infants who have difficulty maintaining physiologic stability during feeding. This study also can provide a foundation for developing a randomized controlled trial in a larger group to investigate the effects of the HEL position more definitively.

In addition, the RESCs measures and methods used to measure the patterns of physiologic stability across the feeding time provide valuable information that could be used to design a future study to understand feeding difficulties, both for researchers as well as to help clinicians better understand feeding difficulties and potentially bring more precision and effectiveness to the application of this feeding intervention.

Conclusions

This study finds that the HEL position has significant short-term physiologic benefits over the HES position. In the HEL position, as compared to the HES position, VP infants maintain more physiologic stability by demonstrating less variation in HR, less severe and fewer decreases in HR, shorter breaths and more regular intervals between breaths, a higher respiratory rate that is closer to that of the pre-feeding state, and more variation in breath duration. When the feeding period is divided into small intervals using three methods, in the HEL position, VP infants demonstrate more stable HR over time, especially during the early minutes of feeding, and better regulated breathing over time by demonstrating shorter breaths and more regular intervals between breaths and more variation in breath duration across the feeding period than in the HES position. Therefore, all the study findings suggest that the HEL position may be a feeding strategy to modulate a rate-limiter by supporting better regulation of breathing that could allow VP infants to better maintain physiologic stability throughout the feeding. In addition, the first six minutes of bottle-in periods is suggested to be sufficient for effectively examining significantly different changes in physiologic stability over time according to the feeding position that requires the smallest number of infants to demonstrate an effect. Because this is a small-sized study, all of the findings and methods used in this study should be further investigated in a larger study.

SUMMARY OF APPENDICES

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Appendix B	Study Consent
Appendix C	Intervention Protocol
Appendix D	Neuro-Biological Risk Score (NBRS)
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Appendix A. Feasibility Study

The purpose of this study is to test the feasibility and acceptability of data collection plans for examining physiologic stability and feeding performance of VP infants (≤ 30 weeks of gestational age [GA]) when bottle-fed in the head-elevated side-lying (HEL) and the head-elevated supine (HES) positions. This study also examines data analysis plans: (1) to determine physiologic data artifacts, (2) to determine pre-feeding baselines, (3) to measure feeding performance and physiologic stability, and (4) to trial approaches for measuring changes in physiologic stability across the feeding period.

Study Design

Using a within-subject cross-over design, one infant was fed in both the HEL and the HES positions over the course of two days; the order of the feeding position was randomly assigned.

Subject

One infant who met the following criteria was selected from the Newborn Critical Care Center (NCCC) at North Carolina Children's Hospital in Chapel Hill, North Carolina: (a) born at less than or equal to 30 weeks GA, and (b) orally fed at least once per day for three consecutive days prior to the study. Infants were excluded if they had congenital or acquired medical conditions that may be associated with feeding difficulties beyond the scope of this intervention, e.g., a congenital anomaly that interferes with oral feeding (e.g., cleft palate or paralysis of facial muscles), grade IV intraventricular hemorrhage, high risk for neurological impairments (≥ 8 neuro-biologic risk score [NBRS]), ventilator-dependence beyond 60 days of life, and/or inability to begin oral feeding prior to 40 weeks postmenstrual age (PMA). Details of the infant characteristics are given in the Table A. 1.

Table A. 1. Infant Characteristics

Level of Maturity	
GA (weeks)	27.7
PMA (weeks)	34.3
Health condition	
NBRS[a]	1
Oxygen in use during feeding	Yes
Feeding experience	
Days since first oral feeding	13
Number of oral feedings prior to the study	24
Additional descriptors	
Gender	Male
Race	White
Birth weight (grams)	920
Weight at the study (grams)	1,885
1-minute APGAR	3
5-minute APGAR	7
Days on ventilator	1
Days on CPAP[b]	26
Days on oxygen	39

Note. [a]This score is used to identify the degree of neurological risk of the infant based on the duration and severity of medical events that may affect brain injury (range 0-28).
[b]CPAP=continuous positive airway pressure

Intervention

The infant was bottle-fed in two feeding positions according to the predetermined order. In the HES position, the infant was placed in a reclining position at a 45-degree angle to the buttocks on the caregiver's lap. In the HEL position, the infant was placed in the side-lying position on the caregiver's lap with one ear facing the ceiling and the head elevated at a 45 degree angle. In both feeding positions, the infant's head and trunk was in neutral straight alignment, and the infant's head and neck was supported by the caregiver's hand in neutral flexion, i.e., chin tilted down slightly, without the head being extended and without excessive flexion. The infant was swaddled with a blanket, providing a flexed body position, but the lower arms were not constrained for behavioral observation (Figure A. 1).

HES position (Feeding 1)

HEL position (Feeding 2)

Figure A. 1. Intervention

Variables and Measures

Physiologic stability includes heart rate (HR) and oxygen saturation (SpO_2). These variables were measured continuously using a pulse oximeter (Ohmeda 4700, Boulder, CO) prior to and during feeding, sampling at 91 samples per second and averaging set at 3 seconds. Oximeter-generated HR and SpO_2 were confirmed using an electrocardiogram (ECG) (Gould Electronics, Valley View, OH) to determine artifacts. Feeding performance includes overall milk transfer (%), efficiency (ml/min), and proficiency (%). Overall milk transfer was measured by determining the percentage of prescribed volume taken over the total feeding time. Efficiency is the total volume taken over the total feeding time. Proficiency was measured by determining the percentage of prescribed volume taken in the first 5 minutes of the feeding. Each feeding was also video-recorded using a Sony Digital Video Camera DCR-VX2100 to test the videotaping procedures.

Data Collection

After the approval from both the Institutional Review Board at the University of North Carolina at Chapel Hill and the Nursing Research Council at the North Carolina Children's Hospital has been obtained, one mother was approached to consent for her infant. After one infant was enrolled, data collection was completed over the course of two days. Three scheduled feeding times for the study were attempted. For the first expected feeding observation, the infant was not ready for oral feeding, so feeding was not attempted. The study feeding was attempted at the next scheduled oral feeding; however immediately after the first feeding observation, the infant had to undergo an eye exam. Eye exams can be upsetting for the infant, leading to fatigue. Also, eye drops used for eye exams can slow gastric mobility, thereby decreasing an infant's appetite. Thus, on the second expected feeding observation, the infant's ability to perform oral feeding was decreased significantly. The infant engaged in predominantly non-nutritive sucking with only a brief period of suckling, which led to only 1 cc of intake. The third feeding observation was conducted on the next day.

For each study feeding, the process described below was repeated. All equipment for monitoring and video recording was set up after completion of the feeding immediately prior to the study feeding (i.e., when the infant was being burped) to collect pre-feeding baseline data without disturbing the infant. To measure the physiologic variables, a pulse oximeter probe was placed on the infant's foot and the infant's own ECG leads were used. The camera and tripod were set up to capture a close-up angle of the infant's face and upper body. During the pre-feeding period, the camera was placed in front of the incubator, and during the feeding, it was placed by the chair where the infant was fed.

The infant began to be monitored and videotaped 30 minutes prior to each study feeding to capture baseline data, and this monitoring and videotaping continued until the feeding was completed. All equipment remained on the infant until all study feedings were completed on the same day. When the infant exhibited readiness cues for feeding at the scheduled feeding time (i.e., opening mouth and descending tongue in response to presentation of the nipple), the infant was given routine nursery care and swaddled with a blanket, allowing a flexed body position with the lower arms visible for behavioral observation. The bib was weighed to identify the fluid lost from drooling during feeding. The infant was placed either in the HES or HEL feeding position according to predetermined order. A trained RA performed bottle-feeding using a standardized feeding protocol. The feeding was stopped briefly at five minutes to record the amount of milk remaining in the bottle (ml). The feeding was finished when the infant no longer engaged in feeding. Following the feeding, the amount of milk consumed, the length of feeding time, and the weight of the bib were recorded. The infant was given the nursery's post-feeding care and settled on the bed.

Feasibility of Data Collection Procedures

Overall, the data collection procedures are feasible; however three notable issues were raised from the feasibility study and, as a result, modifications were made for the final study.

First, an unpredictable clinical event occurred prior to the study that may have affected the infant's ability to perform oral feeding, thus threatening the internal validity of the study. Prior to the second feeding observation, the infant underwent an eye exam. An eye exam can tire an infant as well as affect their appetite because the eye drops (i.e., cyclomydril) used for pupil dilatation have an adverse effect on gastric mobility. Thus, the infant's decreased oral feeding performance on the second feeding observation may be attributable to this stressful clinical event, rather than the feeding position. To reduce the potential problems associated with such an event, the data collection period will be extended over a two-day period, if necessary, so that two feedings can be captured under stable conditions for each infant.

Second, the study implementation was not valid for one of the feeding observations. For the second observation, the infant engaged in predominantly non-nutritive sucking with only a brief period of suckling, which led to only 1 cc intake. Oral feeding requires three major components—sucking, swallowing, and breathing; however this feeding observation did not have a sufficient amount of sucking and swallowing to test the effects of the feeding position on feeding outcomes. Thus, to address the validity of a feeding observation with little intake, two criteria were set to define a valid feeding observation. The infant must demonstrate at least 0.5 ml/min of sucking efficiency over the course of the entire observation to ensure that a sufficient amount of sucking and swallowing occurs that will validate the testing of the effect of position. In addition, the bottle-in periods of the observation must total at least six minutes to ensure the sufficient duration of feeding to examine the changes in infants' responses to feeding over time adequately. Moreover, to increase the likelihood that the infant is ready to engage in feeding, the inclusion criteria for controlling the infant's oral feeding experience will be changed to oral feeding at least four times per day for three consecutive days prior to the study (instead of the originally planned once per day for three consecutive days). It is anticipated that a more experienced infant will be more likely to engage in feeding twice during the observation period. Finally, the data collection period for each infant will be extended to a two-day period, if necessary, to be able to collect two valid observations.

The third issue encountered during the feasibility study was a potential problem identified at the clinical site. In order to videotape the pre-feeding condition, the camera was placed in front of the incubator to capture a close-up angle of the infant's face and upper body. The camera and tripod took up half the amount of space of the incubator itself, so the camera and tripod interfered with the nurses' access to the infant in the incubator. A smaller camera with a smaller tripod, which can be placed either on the incubator or the physiologic cart, is now planned for use in the final study.

Feasibility of Data Preparation

Physiologic data were simultaneously digitized by the A-D converter and stored in analog waveform using the Windaq Data Acquisition Software (DATAQ Instrument, Akron, OH) on a computer. The waveform data file, sampling at 91 samples per second, was compressed into 1 sample per second using the Windaq software and converted to a digital Excel file for analysis. Physiologic data artifacts were removed from the data by comparing the trace of waveform data and the infant's actual activities as shown on the videotapes. To set up the criteria for artifacts, two researchers examined the data to define the artifacts and discuss the rationale for decisions to be made regarding the artifacts. Based on these discussions, artifacts were defined as: (a) areas of HR and/or SpO_2 trace that exceed physiologically possible signal changes (HR $\geq$ 10 bpm and/or SpO2 $\geq$ 5%), and/or (b) areas that show erratic pulse waveforms that do not correspond to ECGs of more than 3 seconds, accompanied by large-scale movement (e.g., handling infants for burping, moving infant back to the crib, or infant crying), as determined from the videotapes. Data considered as artifacts were removed by considering a lag between changes in pulse waveforms and data of HR and SpO2 due to an averaged time of 3 seconds. That is, the artifacts were removed from 2 seconds after the start of problematic pulse waveforms to 2 seconds after the end of problematic pulse waveforms (Table A. 2). Using these criteria, one feeding observation could be examined by two observers to determine inter-observer agreement, and 99% agreement was demonstrated. Feeding 1 contained 10% artifact signals during the feeding period; and feeding 2 showed that 13.5% of recordings contained artifact signals.

Table A. 2. Methods of Artifact Removal

Original data		Rationale		Data artifact removed	
HR	SpO2	Videotape	Pulse waveforms	HR	SpO2
132.78	87.21			132.78	87.21
136.50	87.94			136.50	87.94
140.22	88.67			140.22	88.67
148.52	89.40			148.52	89.40
156.82	90.01	burping	erratic	156.82	90.01
160.26	90.50	burping	erratic	160.26	90.50
163.69	90.87	burping	erratic		
165.12	90.74	burping	erratic		
166.55	90.62	burping	erratic		
166.55	90.50	burping	erratic		
166.55	90.38	burping	erratic		
166.55	90.13	burping	erratic		
166.55	89.89	burping	erratic		
165.98	89.65	burping	erratic		
165.69	89.40	burping	erratic		
160.83	89.16	burping	erratic		
156.25	88.92	burping	erratic		
28 seconds of data were omitted					
124.48	86.85	burping	erratic		
125.91	86.48	burping	erratic		
127.34	86.11	burping	erratic		
128.77	85.99	burping	erratic		
129.91	85.99	burping	erratic		
131.06	85.99	burping	erratic		
131.06	85.99	burping	erratic		
131.06	85.99	stroking			
133.64	86.11	stroking			
136.21	86.24			136.21	86.24
138.22	86.48			138.22	86.48
140.22	86.72			140.22	86.72
138.22	86.85			138.22	86.85

Feasibility of Data Analysis Plans

Feeding Performance

The feeding performance outcomes of the infant when bottle-fed in two different feeding positions are provided in Table A. 3. As expected, feeding performance outcomes for feeding 1 confirm the fact that this feeding was not valid in terms of implementation in order to examine the effects of feeding position on feeding outcomes.

Table A. 3. Feeding Performance

	Feeding 1	Feeding 2
Feeding characteristics		
Prescribed milk (ml)	34	34
Consumed milk (ml)	1	10
Consumed milk at 5 minutes of the feeding (ml)	1	3
Length of total feeding time (min)	8	17.93
Feeding performance		
Overall milk transfer (%)	2.94	29.41
Proficiency (%)	2.94	8.82
Efficiency (ml/min)	0.13	0.56

Physiologic Stability

Pre-feeding Baseline

Pre-feeding baselines were calculated from the pre-feeding period of each feeding. Three two-minute pre-feeding periods were selected from periods that exhibited: (1) minimum variability in HR and SpO_2; (2) neither increasing nor decreasing patterns of HR and SpO2; and (3) the infant being calm and quiet, as seen on the videotape. Among these three 2-minute segments from the pre-feeding periods, the period with the smallest SD of HR and SpO_2 was selected. The mean, SD, and CV (the ratio of the SD divided by the mean for the assigned period) were calculated (Table A. 4). However, for feeding 2, because the infant exhibited readiness cues for oral feeding earlier than the scheduled feeding time, the pre-feeding period was observed only for 10 minutes, which was insufficient for determining 2-minute periods that qualified for the baseline criteria. Thus, the criteria for the pre-feeding baseline need to be assessed to for further validation for the final study and refined, as needed.

Table A. 4. Pre-feeding Baseline

	HR			SpO_2		
	Mean	SD	CV	Mean	SD	CV
Feeding 1	174.04	0.76	0.00	97.82	0.80	0.01
Feeding 2	164.98	2.18	0.01	96.93	1.31	0.01

Physiologic Stability

Physiologic stability was measured using mean, SD, and CV during the entire feeding period. Because the CV is calculated using the SD normalized by the mean of the data, this measurement may provide a more appropriate measure of the rhythmic variability of infants' physiologic responses to feeding (Table A. 5).

Table A. 5. Physiological Stability

	HR			SpO_2		
	Mean	SD	CV	Mean	SD	CV
Feeding 1	166.24	12.20	0.07	88.15	4.66	0.05
Feeding 2	183.06	7.98	0.04	92.16	4.44	0.05

Physiologic stability was also measured in terms of physiologic distress events, identified as hypoxemic events and problematic changes in HR (i.e., bradycardia or tachycardia). Hypoxemic events are defined as the proportion of feeding time where two classifications are met: (1) SpO_2 > 5% below the baseline and less than 85%, and (2) SpO_2 > 5% below the baseline and classified as mild (5-10%), moderate (10-15%), or severe (>15%). Both classifications were able to demonstrate the differences between feedings and provide useful information. Classification 1 provided clinically significant information by using criteria used by clinicians to define desaturation (< 85%), and classification 2 provided information regarding the level of severity by separating SpO2 > 5% below the baseline into three levels (Figure A. 2 and A. 3).

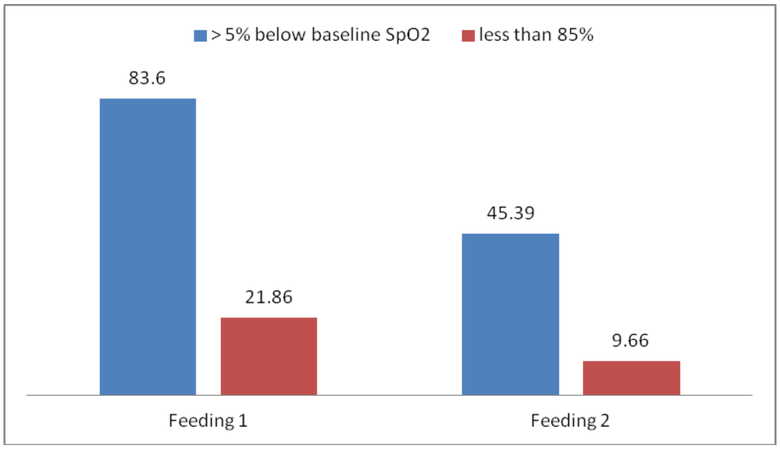


Figure A. 2. Proportion of Feeding Time with Hypoxemic Events using Classification 1

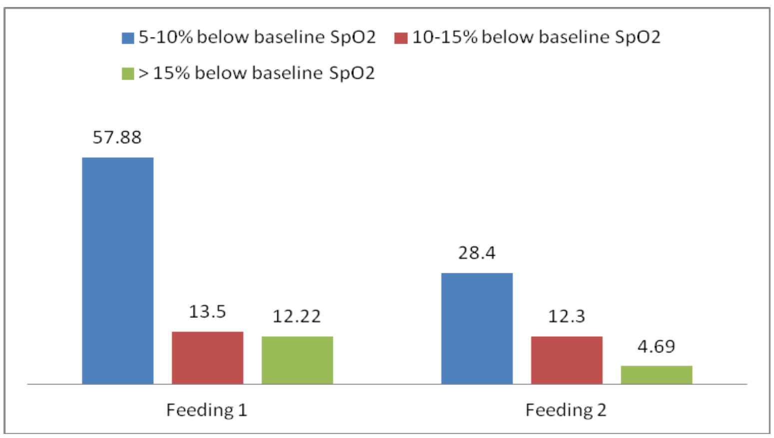


Figure A. 3. Proportion of Feeding Time with Hypoxemic Events using Classification 2

Problematic changes in HR are defined as (1) changes of HR > and < 5% baseline, (2) > and < 10% baseline, and (3) less than 100 bpm. Each cut-off describes the level of HR changes and can discriminate the differences between feedings, with the exception of less than 100 bpm because this cut-off parameter did not occur in either feeding (Figure A. 4).

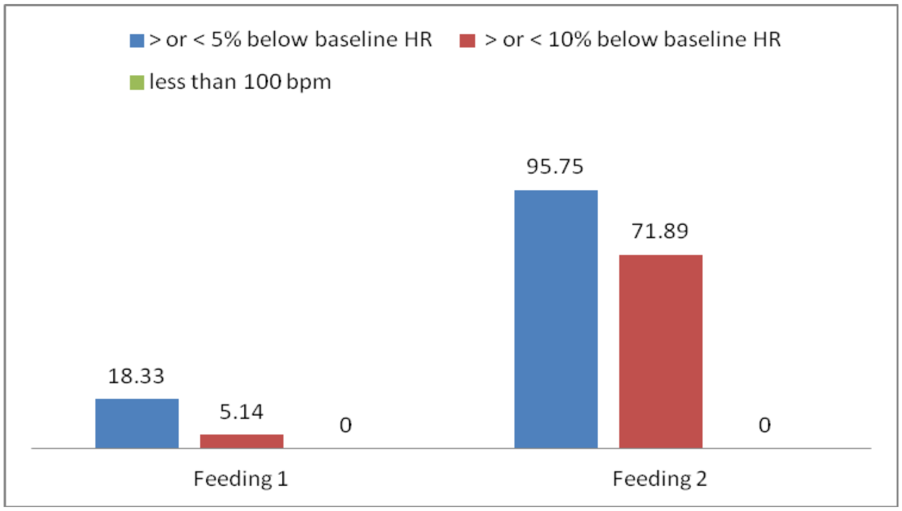


Figure A. 4. Proportion of Feeding Time with Problematic Changes in HR Using Three Cut-off Parameters

Changes in Physiologic Stability

Three methods were trialed to measure changes in physiologic stability over time as the infant becomes accustomed to bottle feeding or becomes fatigued. The hypothesis is that infant feeding behavior can change as the infant becomes fatigued and/or accustomed to the demands of the feeding; these changes can be affected by the feeding positions. That is, the infant who feeds in the HEL position, which may provide a better physiologic support during feeding than the HES position, may adjust better to physiologic challenges throughout the feeding; thus, physiologic stability would be maintained better in the HEL position. To examine changes in physiologic stability only during the feeding period, potentially confounding data (i.e., non-feeding and burp periods) were eliminated and bottle-in periods were summed. Changes in physiologic stability during summed bottle-in periods were examined using three intervals of time: (1) 2-minute intervals with removal of the last period of data with less than 2 minutes; (2) three equal periods by dividing total bottle-in periods into three periods; and (3) 2-minute periods extracted each from initial, middle, and final third of feeding period (Figure A. 5). The three time intervals were selected by taking into account two exploratory questions: (1) what time epoch would reflect the most precise variability of physiologic variables across a given feeding, and (2) what periods of feeding time would allow for comparisons of changes in physiologic variables across feedings in terms of the different durations?

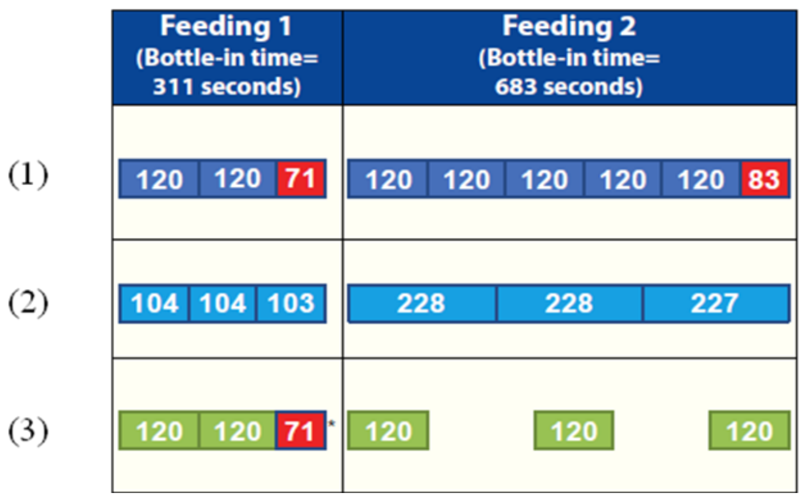
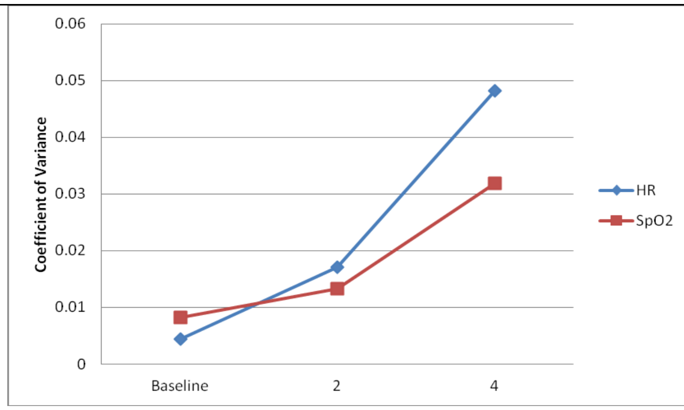


Figure A. 5. Three Sets of Time Intervals

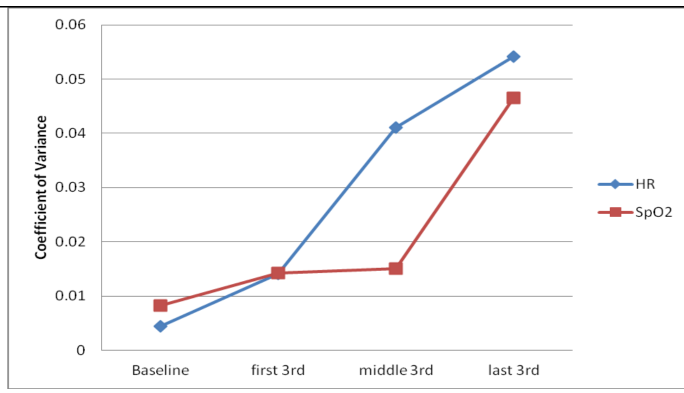
Note. Numbers indicate seconds. *Feeding 1 does not meet the criteria that are required for this method.

Each method offers advantages and disadvantages (Figure A. 6 and A. 7). In method 1, the smaller epoch allows for more precision, but the larger number of intervals with longer feeding observations may make the pattern difficult to interpret. Further, the statistical approach needs to support comparisons of feedings of different durations. Method 2 ensures three time points during feeding, regardless of length of feeding time; however true variability will be smoothed with longer feedings. Method 3 provides comparable interval lengths in each period across feedings, regardless of length of feeding time. However, meaningful data may be left out, and this method requires at least 6 minutes of bottle-in time to cross-compare each interval and avoid missing data.

Method 1



Method 2



Method 3

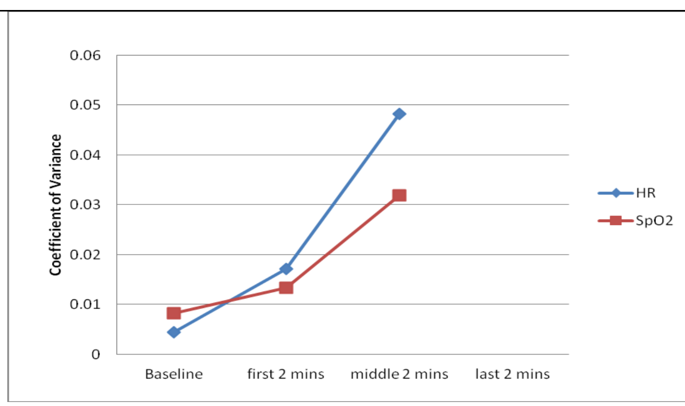
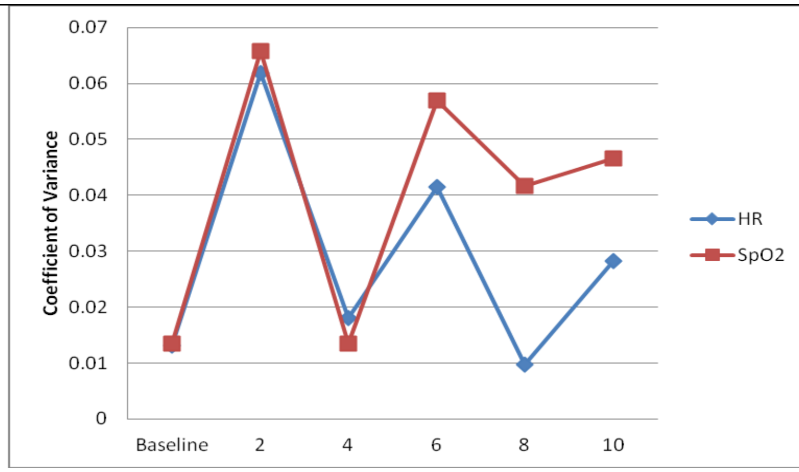


Figure A. 6. Changes in Physiologic Stability over Time in Feeding 1

Note. Feeding 1 does not meet the criteria that are needed for method 3.

<table>
<tr><td>Method 1</td><td>
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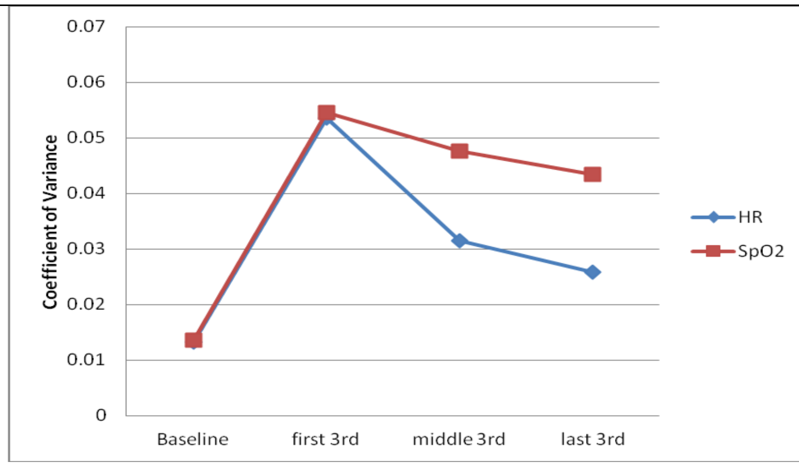
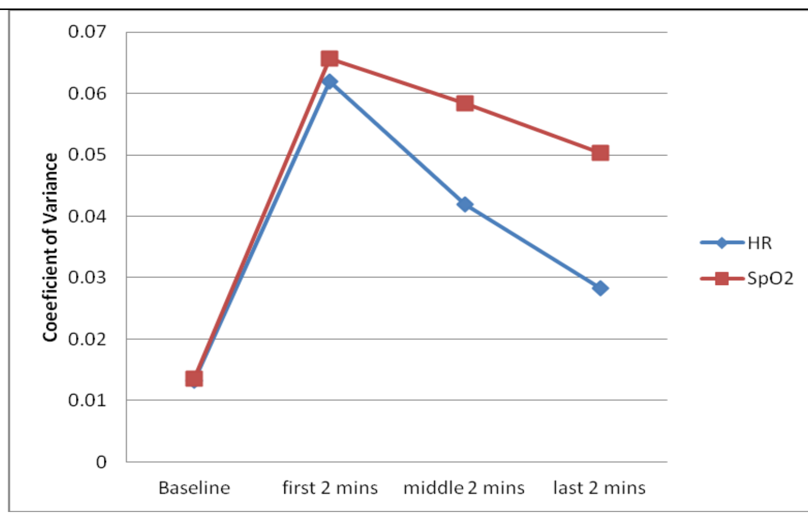
<tr><td>Method 2</td><td>
</td></tr>
<tr><td>Method 3</td><td>
</td></tr>
</table>

Figure A. 7. Changes in Physiologic Stability over Time in Feeding 2

In summary, the overall data analysis plans are feasible and useful for examining the effects of feeding position. However, feeding 1 was not a valid feeding observation that may not represent infants' physiologic responses to feeding. Furthermore, method 3 (to measure changes in physiologic stability) could not be trialed in feeding 1 because of insufficient length of feeding. Thus, the usefulness of all the data analysis plans to detect the differences between feedings that are considered valid remains unknown. Therefore, all the methods for data analysis, with modifications as needed, should be assessed further in order to validate the final study design.

Conclusion

Overall, data collection procedures are feasible; however some modifications will make the future study more valid. All measures for description of physiologic stability, such as mean, SD, CV, and physiologic distress events, may be useful for evaluating the effectiveness of feeding position. Each method to examine changes in physiologic stability offers advantages and disadvantages. However, this feasibility study is based on two feeding observations from one infant and one feeding observation was not valid. Thus, all measures for physiologic stability and all three methods for changes in physiologic stability across the feeding time need further assessment with more valid and increased number of feeding observations.

Appendix B. Study Consent

University of North Carolina-Chapel Hill
Parental Permission for a Minor Child to Participate in a Research Study
Social Behavioral Form

IRB Study # 11-1017
Consent Form Version Date: 8/2/2011

Title of Study: Bottle Feeding Outcomes in Very Preterm Infants: Effects of Positioning

Principal Investigator: Jinhee Park, PhD(c), MSN, RN
UNC-Chapel Hill Department: School of Nursing
UNC-Chapel Hill Phone number: (919) 966-8418
Email Address:
Faculty Advisor: Suzanne Thoyre, PhD, RN
Funding Source and/or Sponsor: Funded by Linda Waring Mathews Research Fund Scholarship from the UNC's School of Nursing

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What are some general things you should know about research studies?

You are being asked to allow your baby to take part in a research study. To join the study is voluntary. You may refuse to give permission, or you may withdraw your permission for your baby to be in the study, for any reason.

Research studies are designed to obtain new knowledge. This new information may help people in the future. Your baby may not receive any direct benefit from being in the research study. There also may be risks to being in research studies.

Deciding not to be in the study or leaving the study before it is done will not affect you and your baby's relationship with the researcher, your baby's health care provider, or the University of North Carolina-Chapel Hill. If your baby is a patient with an illness, your baby does not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you and your baby can make an informed choice about being in this research study.
You will be given a copy of this permission form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to learn more about how we can help very early born preterm infants learn to feed safely.

How many people will take part in this study?

If your baby is in this study, your baby will be one of approximately 10 babies in this research study.

How long will your baby's part in this study last?

Your baby's participation will be for two bottle feedings across one or two days, depending on how many times he or she is being fed by mouth at the time of the study. We will collect information about how your baby is breathing, heart rate, oxygenating, sucking, and swallowing while your baby is feeding in two different positions: a semi-upright in front position and a side-lying position. We will also collect information about how your infant is breathing, heart rate, and oxygenating while he/she is sleeping between feedings.

What will happen if your baby takes part in the study?

During the course of this study, the following will occur: We will plan to observe two bottle feedings that occur between 9 am and 6 pm on one day when your baby is early in their learning to feed. If your baby is not able to do two bottle feedings during this time, we will return the following day. For the two study feedings, a nurse will feed your baby with a bottle in two different positions: (1) one feeding in the semi-upright in front position (i.e. providing head-elevation at a 45 degree angle to the buttocks with baby facing the feeder) and (2) the second feeding in a side-lying position (i.e. providing head-elevation at 45 degree angle to buttocks placed on the side-lying position). The semi-upright in front position has been typically used in Neonatal Intensive Care Units when preterm infants are fed and the head-elevated side-lying position has been recently recognized to potentially be effective for some preterm infants. We will start the study feeding only when/if your baby looks ready to eat and when you do not plan to breast feed your baby. We will feed your baby in both positions using the nursery's techniques that aim to support your baby during feeding.

On the day(s) of the study we will collect three types of information: medical record data, videotaped observational data, and physiologic data. We will write down information that is in your baby's medical record to describe your baby's age, size, and health condition. Second, we will videotape your baby while he or she is being fed and while he or she is sleeping between feedings. During the feeding, the camera will focus on your baby's face and upper body so we can record your baby's responses to the feeding. Prior to and after the feedings, the camera will focus on your baby's entire body so that we can collect the general movement of his/her body during a time when they are calm. Third, we will collect information about your baby's breathing, heart rate, oxygenation prior to, during (including information about sucking and swallowing) and after feeding. This will help us further understand your baby's responses to these two feeding positions.

Each feeding will be done at your baby's bedside. Your baby's heart rate and oxygen will be monitored as they usually are in the nursery. Breathing will be measured with a stretchy band that is about 1 inch wide that wraps around your baby's chest to measure breathing. The band is not tight and does not stick to your baby's skin. To prevent potential risks to your baby's skin irritation by the band, these bands will be covered with silky fabric and then placed on the top of your baby's clothes. A small, flat microphone will be placed on your baby's neck during the feeding so we can hear your baby swallowing and breathing. Hydrogel tape will be used to attach this microphone which will ensure no skin irritation when it is removed. If your baby has skin breakdown around the neck, the microphone will be placed on your baby's upper chest. The sounds from the microphone will be transmitted to the videotape for later assessment of your baby's feeding responses. For the bottle feedings, we will place a small pressure sensor inside the bottle that will detect your baby's sucking. This sensor does not change the flow of milk from the bottle and your baby will not sense that it is there. If your baby has a feeding tube in their nose we will gently remove it, without untaping it, before the study feedings. The tube will be gently re-placed prior to your baby's next tube feeding. After each feeding your baby will be settled in their bed as they usually are in the nursery.

The research team for data collection will include the principal investigator, Jinhee Park advised by Dr. Thoyre and two research assistants from the School of Nursing. Dr. Thoyre has 19 years experience as a neonatal nurse and 17 years experience studying preterm infant feeding. Jinhee Park is a neonatal nurse who has cared for preterm infants for over 3 years and has acquired techniques and approaches for studying preterm infants feeding by working with Dr. Thoyre since 2007. Since we want all babies to have similar support during the feeding, a nurse from the nursery will feed your baby during the study.

What are the possible benefits from being in this study?

The benefits to you and your baby of participating in this study may be that the research nurses will formally assess your baby's feeding skills and be able to discuss these skills with you and your baby's nurses. You will also be helping us to understand the effect that a baby's position has on their ability to eat.

What are the possible risks or discomforts involved from being in this study?

There are no known risks or discomforts for you and your baby. The two feeding positions being compared in this study are commonly used positions for feeding preterm infants. Your baby's breathing, heart rate, and oxygenation will be monitored before, during, and after the feeding to ensure safety throughout the feeding study. Potential skin irritation by the microphone or breathing band will be avoided by attaching the microphone on your baby's neck using hydrogel tape or covering the breathing band with silky fabric and then placing it on the top of your baby's clothes. Before feeding your baby we will check with your baby's nurse to make sure their feeding plan allows for bottle feeding at that time. We will not be changing what your baby eats. We do not want to interfere in any way with your visitation or your breastfeeding your baby. You may hold your baby between feedings as you normally would. You will not be able to feed your baby for the two study bottle feedings. However, you are welcome to sit near your baby while we trial the two feeding positions. In addition, there may be uncommon or previously unrecognized risks that might occur.

How will your baby's privacy be protected?

No infants' or mothers' names will be identified in any report or publication about this study. All forms and files including videotapes will be identified with an ID number, rather than a name. When we report this information we will not report any names. A document connecting your baby's name with the ID number will be kept in a locked file cabinet in Dr. Thoyre's office in the School of Nursing. Videotapes will be stored on the secured server with a password protection. Upon completion of the study the file will be destroyed unless you agree to their use for educational purposes (see below). Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-CH will take all steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety. A copy of this consent form will be placed in your baby's medical record.

We would like to use video examples of your baby feeding to teach nurses and mothers in the future about common feeding issues for preterm infants. You are being asked for permission to use videotapes with your baby for teaching purposes. Please put your initials on one of the following options:

___Yes, I agree. Videotapes taken during this study of my baby can be used in the future for teaching purposes.
___No, I do not agree. Videotapes taken during this study can only be used for this study's purposes.

We would like to be able to contact you in the future for a follow-up research study to learn more about feeding issues for older preterm infants. You are being asked for permission for us to contact you in the future about another study. To do this we would need to save your address and phone number. Please put your initials on one of the following options:

___Yes, I agree. My address and phone number can be saved and you may contact me to tell me about a future research study .
___No, I do not agree. Please do not contact me about a future study and do not save my address and phone number.

Will you or your baby receive anything for being in this study?

You and your baby will not be paid for participating in this study but you will be given a photograph of your baby during the study in appreciation of you and your baby's participation in the study. If you desire, after the study the research nurse will talk to you about what she has learned about your baby's feeding skills.

What if you want to stop before your baby's part in the study is complete?

Your baby can withdraw from this study at any time, without penalty. The investigators also have the right to stop your baby's participation at any time. This could be because your baby has had unexpected reaction, or has failed to follow instructions, or the entire study has been stopped.

Will it cost you anything for your baby to be in this study?

There will be no costs to you for participating.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions, complaints or concerns, you should contact the researchers listed on the first page of this form.

What if you have questions about your baby's rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you or your baby has questions or concerns about your baby's rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

- -

Title of Study: Bottle Feeding Outcomes in Very Preterm Infants: Effects of Positioning

Principal Investigator: Jinhee Park, PhD(c), MSN, RN

Parent's Agreement:
I have read the information provided above. I have asked all the questions I have at this time. I voluntarily give permission to allow my child to participate in this research study.

____
Printed Name of Research Participant (Child)

____ ______________
Signature of Parent Date

____
Printed Name of Parent

____ ______________
Signature of Research Team Member Obtaining Permission Date

____
Printed Name of Research Team Member Obtaining Permission

Appendix C. Intervention Protocol

Standardized Feeding Protocol

Pre-Feeding Preparation:

1. Hold infant supported at shoulders with blanket and caregiver's hands.
2. Hold infant in a flexed body position (shoulders adducted, hips and knees flexed).
3. Provide minimal movement of the infant's body.
4. Bring infant to an alert state and maintain the alert state (by vocalizing).

General Feeding Strategies:

1. Hold infant in left or right arm supported at the shoulders with blanket.
2. Hold infant in a flexed body position (shoulders adducted, hips and knees flexed)
3. Hold infant in either a HEL position or a HES position.
    - HEL position
      The caregiver should be seated comfortably creating a lap that provides head elevation at a 45 degree of angle to the buttocks. A pillow can be used to support head elevation. The infant will be placed in a side-lying position (i.e., one ear facing toward the ceiling and another ear facing the caregiver's lap) on the caregiver's lap, with the head at the knee end of the lap and bottom against the caregiver's stomach. The infant's head and trunk should be in a natural straight alignment, and the infant's head and neck should be supported by the caregiver's hand in a neutral flexion (chin tilted down slightly, not with the head extended or with excessive flexion).

      

    - HES position
      The infant sits in a reclining position at a 45 degree of angle to the buttocks on the caregiver's lap. The caregiver supports the infant's head, neck and trunk with one hand while holding the bottle with the other. The infant's head and trunk should be in a natural straight alignment, and the infant's head and neck should be supported by the caregiver's hand in a neutral flexion (chin tilted down slightly, not with the head extended or with excessive flexion).

4. Allow minimal movement of the infant's body.
5. Avoid any prodding techniques to encourage sucking.
6. Avoid any movements of the nipple that would increase the milk flow from the nipple.

Contingently Structured Feeding Strategies:

1. Infant is prepared for feeding by stroking the infant's lips with the bottle nipple.
2. Nipple placed into infant's mouth at outset of each feeding contingent upon infant cues of readiness to feed (infant opens mouth and descends tongue in response to presentation of the nipple, arms flexed and close in to the body)
3. Prevent prolonged breathing pauses.
   - When infant has not had sufficient breaths (number depends on the infant's baseline respiratory rate), move the nipple of the bottle to the roof of the infant's mouth to stop the infant's sucking and cue the infant to breathe.
   - If infant does not respond with cessation of sucking and resumption of breathing, remove the nipple from the infant's mouth.
   - Resume feeding when infant provides cues of readiness to feed and is physiologically stable.
4. Prevent fatigue prior to and during the feeding.
   - When infant displays early signs of fatigue (infant body tone decreasing, milk coming out of infant's mouth, and prolonged sucking pauses), remove the nipple from the infant's mouth, minimize movement of the infant and rest the infant.
   - Resume feeding when infant provides cues of readiness to feed and is physiologically stable.
5. Maintain the infant's engagement in feeding.
   - Respond to cues of physiologic or behavioral distress (head moving away from the nipple, arms extending outward, color change, noisy respirations, coughing, choking, double swallowing, prolonged apnea, desaturation) and cues of fatigue (infant body tone decreasing, milk coming out of the infant's mouth, and prolonged sucking pauses) by removing the nipple.
   - Resume feeding when infant provides cues of readiness to feed and is physiologically stable.
6. Discontinue feeding if the infant has taken the prescribed amount of milk, if 30 minutes have elapsed from the first time the bottle was placed in the infant's mouth, or if the infant does not re-initiate feeding after the feeding has been paused.

Appendix D. Neuro-Biological Risk Score (NBRS)

Neuro-Biological Risk Score (NBRS)

Total score: __________ (≤ 4 low risk; 5-7 intermediate risk; ≥8 high risk)

Points	0	1	2	4
Ventilation	No mechanical ventilation	≤ 7 days	8-28 days	> 28 days
PH	Never < 7.15	<7.15 for ≤ 1 hr (<7.15 for 2x) or < 7.15 all respiratory, any duration	< 7.15 metabolic for > 1hr (<7.15 for 2x) or < 7.00 metabolic, any duration	Cardiorespiratory arrest
Seizures	None	Controlled on one drug and normal interictal EEG	Not controlled on one drug or abnormal interictal EEG	Status epilepticus ≥ 12 hr
Intraventricular hemorrhage	None	Germinal matrix only	Blood in one or both ventricles	Intra parenchymal blood or development of overt hydrocephalus
Periventricular leukomalacia	None	Questionable changes that resolve	Moderate or definite changes that resolve	Cyst formation or cerebral atrophy with large ventricles
Infection	None or antibiotics for possibility of infection with negative cultures	Highly suspicious or documented infection without changes in blood pressure	Septic shock (documented sepsis and hypotension)	Meningitis
Hypoglycemia	No glucose < 30 mg/dL	< 30 mg/dL asymptomatic and ≤ 6 hr duration	< 30 mg/dL asymptomatic and > 6 hr or symptomatic any duration	< 30 mg/dL ≥ 24 hr and symptomatic

Note. Adapted from "Nursery Neurobiologic Risk Score: Levels of Risk and Relationships with Nonmedical Factors" by J. E. Brazy et al., 1993, *Developmental and Behavioral Pediatrics*, 14, p. 376.

Appendix E. Diagnostic Criteria for Bronchopulmonary Dysplasia

Diagnostic Criteria for Bronchopulmonary Dysplasia

Gestational Age	< 32 weeks
Time point of assessment	36 wk PMA or discharge to home, whichever comes first
None	Treatment with oxygen > 21% for less than 28 day, no supplemental oxygen therapy at 36 wk PMA or discharge, whichever comes first
Mild BPD	Treatment with oxygen > 21% for at least 28 day **plus** breathing room air at 36 wk PMA or discharge, whichever comes first
Moderate BPD	Treatment with oxygen > 21% for at least 28 day **plus** need for < 30% oxygen at 36 wk PMA or discharge, whichever comes first
Severe BPD	Treatment with oxygen > 21% for at least 28 day **plus** need for ≥ 30% oxygen and/or positive pressure (positive-pressure ventilation or nasal continuous positive airway pressure) at 36 wk PMA or discharge, whichever comes first

Note. Adapted from “Bronchopulmonary Dysplasia” by A. H. Jobe and E. Bancalari, 2001, *American Journal of Respiratory and Critical Care Medicine*, 163, p. 1,726.

Appendix F. History of Hospitalization Form

ENT	DATE / /	VER	DATE / /
	INITIAL		INITIAL

History of Hospitalization

SUBJECT ID ___________
Today's date (e.g., 05/15/2010) ___/___/___
Research Team today ____

GENERAL CHARACTERISTICS

Infant's Gender: *1-M* *0-F*

Mother's race: 1-African-American 2-Euro-American 3-Latino
4-American Indian 5-Other (specify) ___________

Father's race: 1-African-American 2-Euro-American 3-Latino
4-American Indian 5-Other (specify) ___________

BIRTH HISTORY

MOTHER:

ObstetEDC ___________G ___ P___
Fullterm ___ # Preterm ___ # AB ___ # Living Children ___

Pregnancy complications ____
Labor/delivery Complications____

INFANT:

Apgar: 1" ________ *5"* _________
Birthweight (g) __________
Size (Circle one) LGA AGA SGA
HC (cm) _________ Length (cm) _________
Gestational Age at Birth ______________
How was gestational age determined? ________________________________
GA by Ballard _____________wks.

PMA at discharge: ___________ Weight at discharge: ___________

Infant Abnormalities ____

RESPIRATORY

Treatment:

Ventilator	*#days* ________
CPAP	*#days* ________
Supplemental O_2 and/or airflows	*#days* ________

Comments/Diagnoses____

CARDIOVASCULAR

PDA	Y (1)	N (0)	Treated Y (1) N (0)
CHF	Y (1)	N (0)	

Other ____

NEUROLOGICAL

IVH Y (1) N (0) *IVH Grade (1-4)* _________ PVL Y (1) N(0)

Comments/Findings/US____

OTHERS

NEC Y (1) N (0)
Comments____
____

INFECTIONS Y (1) N (0)
Comments____
____

JAUNDICE Y (1) N (0)
Comments____
____

METABOLIC Y (1) N (0)
Comments____
____

SURGERY Y (1) N (0)
Comments____
____

<u>NEUROBIOLOGICAL RISK SCORE</u> (NBRS) = ____

Points	0	1	2	4
Ventilation	No mechanical ventilation	≤ 7 days	8-28 days	> 28 days
PH	Never < 7.15	<7.15 for ≤ 1 hr (<7.15 for 2x) or < 7.15 all respiratory, any duration	< 7.15 metabolic for > 1hr (<7.15 for 2x) or < 7.00 metabolic, any duration	Cardiorespiratory arrest
Seizures	None	Controlled on one drug and normal interictal EEG	Not controlled on one drug or abnormal interictal EEG	Status epilepticus ≥ 12 hr
Intraventricular hemorrhage	None	Germinal matrix only	Blood in one or both ventricles	Intra parenchymal blood or development of overt hydrocephalus
Periventricular leukomalacia	None	Questionable changes that resolve	Moderate or definite changes that resolve	Cyst formation or cerebral atrophy with large ventricles
Infection	None or antibiotics for possibility of infection with negative cultures	Highly suspicious or documented infection without changes in blood pressure	Septic shock (documented sepsis and hypotension)	Meningitis
Hypoglycemia	No glucose < 30 mg/dL	< 30 mg/dL asymptomatic and ≤ 6 hr duration	< 30 mg/dL asymptomatic and > 6 hr or symptomatic any duration	< 30 mg/dL ≥ 24 hr and symptomatic

<u>SEVERITY OF LUNG DISEASE</u> = _______

**Time point of assessment*	*36 wk PMA or discharge to home, whichever comes first*
None	Treatment with oxygen > 21% for less than 28 day, no supplemental oxygen therapy at 36 wk PMA or discharge, whichever comes first
Mild BPD	Treatment with oxygen > 21% for at least 28 day plus breathing room air at 36 wk PMA or discharge, whichever comes first
Moderate BPD	Treatment with oxygen > 21% for at least 28 day plus need for < 30% oxygen at 36 wk PMA or discharge, whichever comes first
Severe BPD	Treatment with oxygen > 21% for at least 28 day plus need for ≥ 30% oxygen and/or positive pressure (positive-pressure ventilation or nasal continuous positive airway pressure) at 36 wk PMA or discharge, whichever comes first

Appendix G. Feeding Data Collection Form

ENT	DATE / /	VER	DATE / /
	INITITAL		INITIAL

Feeding Data Collection Form

SUBJECT ID ___________
Today's date (e.g., 05/15/2010) ___/___/___
Research Team today ____

<u>FEEDING HISTORY</u>
Date of first gavage feeding ___/___/___
Day of Life_______ NGWT(g) _________ NGPCA ___________
Date of first PO feeding ___/___/___
Day of Life_______ PO1WT(g) ________ PO1PCA __________
Date of full PO feeding ___/___/___
Day of Life_______ FULLWT(g) ________ FULLPCA __________

Date of onset	BM/Formula History	Date of onset	BM/Formula History

EXPNIPP (# of cumulative oral feedings from either bottle or breast since first oral feeding)
= ________________

	DATE / /		DATE / /		DATE / /	
Feeding Time	Milk taken by mouth	Milk taken by tube	Milk taken by mouth	Milk taken by tube	Milk taken by mouth	Milk taken by tube
2AM						
5AM						
8AM						
11AM						
2PM						
5PM						
8PM						
11PM						
	DATE / /		DATE / /		DATE / /	
2AM						
5AM						
8AM						
11AM						
2PM						
5PM						
8PM						
11PM						

Feeding Time	DATE / /		DATE / /		DATE / /	
	By mouth	By tube	By mouth	By tube	By mouth	By tube
2AM						
5AM						
8AM						
11AM						
2PM						
5PM						
8PM						
11PM						
	DATE / /		DATE / /		DATE / /	
2AM						
5AM						
8AM						
11AM						
2PM						
5PM						
8PM						
11PM						
	DATE / /		DATE / /		DATE / /	
2AM						
5AM						
8AM						
11AM						
2PM						
5PM						
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11PM						
	DATE / /		DATE / /		DATE / /	
2AM						
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8AM						
11AM						
2PM						
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8PM						
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	DATE / /		DATE / /		DATE / /	
2AM						
5AM						
8AM						
11AM						
2PM						
5PM						
8PM						
11PM						
	DATE / /		DATE / /		DATE / /	
2AM						
5AM						
8AM						
11AM						
2PM						
5PM						
8PM						
11PM						

SUBJECT CHARACTERISTICS AT THE STUDY

Recorded apnea in past 24 hours: ____________
Recorded bradycardia in past 24 hours: ______
Last dose of theophylline or caffeine: amount ________time given ______
Recorded clinical events that affect oral feeding skills (e.g., eye exam) in past 24 hours:
Y (1) ________________ N (0)
Supplemental Oxygen and/or airflow Prior to Feeding (O2DOS)
Y (1): Amount ________ N (0): Setting ______
Last recorded hematocrit________
Study weight (STUWG): ________ gm Study PMA (STUPMA): _________

STUDY FEEDING 1:

Feeding Position: HES / HEL
Prescribed feeding today: amount __________ formula/MBM __________
Auxiliary Temperature: ______
Supplemental 02 and/or airflow during feeding 1: Y(1) No(0) If Yes, Amount:_______
Initial Bottle in Time: _______________ Final Bottle out Time: _______________
Total Feeding Time: ________________
Amount Consumed at 5 minute (mL): _________ Amount Consumed (mL): ____________

Overall Milk Transfer (%, amount consumed/prescribed milk * 100): __________
Efficiency (mL/min, amount consumed/total feeding time): ___________
Proficiency (%, amount consumed at 5 minute/prescribed milk * 100): _________

Notes:

Time	Events

STUDY FEEDING 2:

Feeding Position: HES / HEL
Prescribed feeding today: amount ___________ formula/MBM ___________
Auxiliary Temperature: _______
Supplemental 02 and/or airflow during feeding 1: Y(1) No(0) If Yes, Amount:_______
Initial Bottle in Time: ________________ Final Bottle out Time: ________________
Total Feeding Time: _________________
Amount Consumed at 5 minute (mL): _________ Amount Consumed (mL): ____________

Overall Milk Transfer (%, amount consumed/prescribed milk * 100): __________
Efficiency (mL/min, amount consumed/total feeding time): ____________
Proficiency (%, amount consumed at 5 minute/prescribed milk * 100): _________

Notes:

Time	Events

Appendix H. Intervention Fidelity

Modified Dynamic-Early Feeding Skills Coding Scheme (D-EFS)

Categories	Description
1. Caregiver Feeding Actions	
1.1. Nipple in	Nipple in: coded when nipple is fully seated in mouth; modified as infant's readiness to feed and preparation provided for a feeding. *Ready to feed*- infant is ready for participating in the feeding (it is different from hunger cues—e.g., crying or fussing, just sucking on lips, tongue, or figure) :opening mouth to seek the nipple, moving head toward the nipple, bringing both arms close to the mouth, having flexed & toned body or facial tone for feeding activity *Not ready to feed*- infant is not showing any initiation cues for participating in the feeding : infant remains a sleep, tired, passive, or does not take the nipple voluntarily or may be accept the nipple but sucking is weak and intermittent or actively avoiding the feeding, using energy to move away from nipple, to signal the caregiver to stop, pushing away, pulling away, turning away *Unable to determine (UTD) readiness*- when the video angle is not good enough or this moment went so fast to figure out. *Prepared for a feeding* - caregiver inducing rooting responses by touching the nipple, finger, or pacifier across the infant's lips or cheeks. *Not prepared for a feeding*- caregiver not inducing rooting responses. *Unable to determine (UTD) preparation*- when the video angle is not good enough or this moment went so fast to figure out.
1.2. Nipple out	Nipple out; code when space is visible between the infant's lips and the bottle nipple
1.3. Stimulating infant sucking	Any movement of the nipple <u>*by the feeder*</u> that may stimulate a suck; intention is not assumed : the feeder may be adjusting the nipple to hold the bottle better or to seat the nipple on the tongue better, may occur in the process of checking to see if the infant is drooling or the amount of milk left in the bottle, or trying to arouse the infant or stimulate the infant to engage in sucking by moving the nipple (do not code when the bottle is moving by the infant's sucking)

	**Note. From the infant's perspective, the nipple has moved in the mouth and this reflexively may stimulate sucking; it may also cause fluid to drip into the mouth placing a demand on the infant to manage the fluid.* **Note. When the caregiver moves the nipple to reduce the vacuum pressure in the mouth in order to take the nipple out, do not code "stimulating infant sucking".*
1.4. Limiting milk flow	Moving nipple downward (or to side if infant is side-lying) <u>with enough time</u> allowing for infants to breath and swallow accumulated milk in the oral cavity. : limits bottle nipple from dripping milk into infant's mouth; breaks infant's seal on nipple/stop sucking; the changed angle of the milk in the bottle against the gravity. **Note. If after the nipple is tip back to limit the milk flow the caregiver tips the nipple back up <u>after</u> the infant has initiated sucking then it is just limiting milk flow (do not code for "stimulating infant sucking" when the nipple is back up).* *If the caregiver tips the nipple back up <u>before</u> the infant has initiated sucking, then there is stimulating sucking after the limiting milk flow (code for " stimulating infant sucking" when the nipple is back up)*
2. Infant Position	
2.1. Non feeding position	Position when the nipple is not placed in the infant's mouth. (e.g., during burping and break or during pre-and post-feeding period)
2.1. Supine position	Infant placed in a supine position on the caregiver's lap with upper forehead facing the ceiling and the upper body elevated at least a 45 degree angle; the infant's head, chin, and sternum in a straight alignment with chin tilted down slightly.
2.2. Side-lying position	Infant placed in a side-lying position on the caregiver's lap with one ear facing the ceiling and the upper body elevated at least a 45 degree angle; the infant's head, chin, and sternum in a straight alignment with chin tilted down slightly.
2.3. Not in supine position	Infant placed in a supine position but the infant's head turns toward the shoulder; the infant's chin elevated.
2.4. Not in side-lying position	Infant placed in a side-lying position but the infant's head turns toward the shoulder; the infant's chin elevated.
2.5. Out of screen	Code when the infant's position changed after the angle of the video is back; not code when the infant's position remained the same after the angle of the video is back (need to choose other codes under infant position).

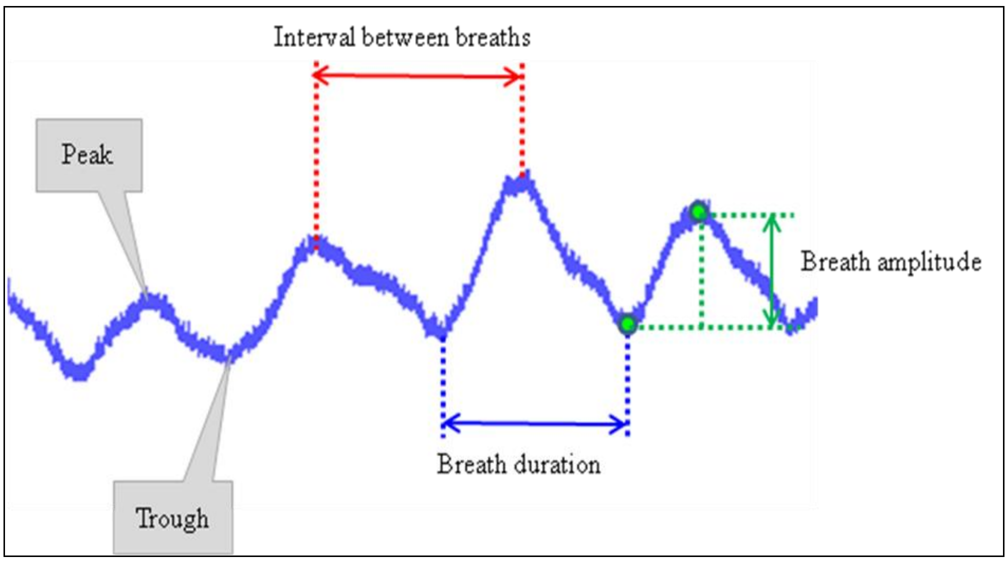
Note. Revised from "Dynamic Early Feeding Skills Coding Scheme" developed by S. Thoyre (2009), with permission.

Appendix I. Protocol for Respiratory Data Management

Protocol for Respiration Analysis Using the Acknowlege 4.1.

Definitions of Respiratory Characteristics

- *Intervals between breaths*: distance between a peak and the next peak
- *Breath duration*: distance between a trough to the next trough
- *Breath amplitude*: distance between a trough and the next peak



STEP 1. Converting a biolab file (.mw) into a acqKnowledge file (.acq)

1. Open the file collected with the BioLab 3.0.4.
2. In the configuration window, cancel the channels except for respiration by clicking ON/OFF button on the left side of each channel.
3. Click VIEW and you can see the respiration channel only.
4. Click SAVE ALL TEXT to save the respiration channel as a text file. Save this with the same name plus _resp (i.e., xxxxx_resp.txt).
5. Open the AcqKnowledge 4.1.
6. Click FILE > OPEN and select the text file you saved from the BioLab program
7. Put wave data start on the line (**3**), sample rate interval (**1 milisecs**), column delimiter (**tab**) when the window pops up to ask these. _*Make sure the line data start by opening the text file with word pad_
8. Two channels will be opened: Channel 0 (Time) and Channel 1 (Respiration)
9. Save this waveform file as xxxxx_resp.acq

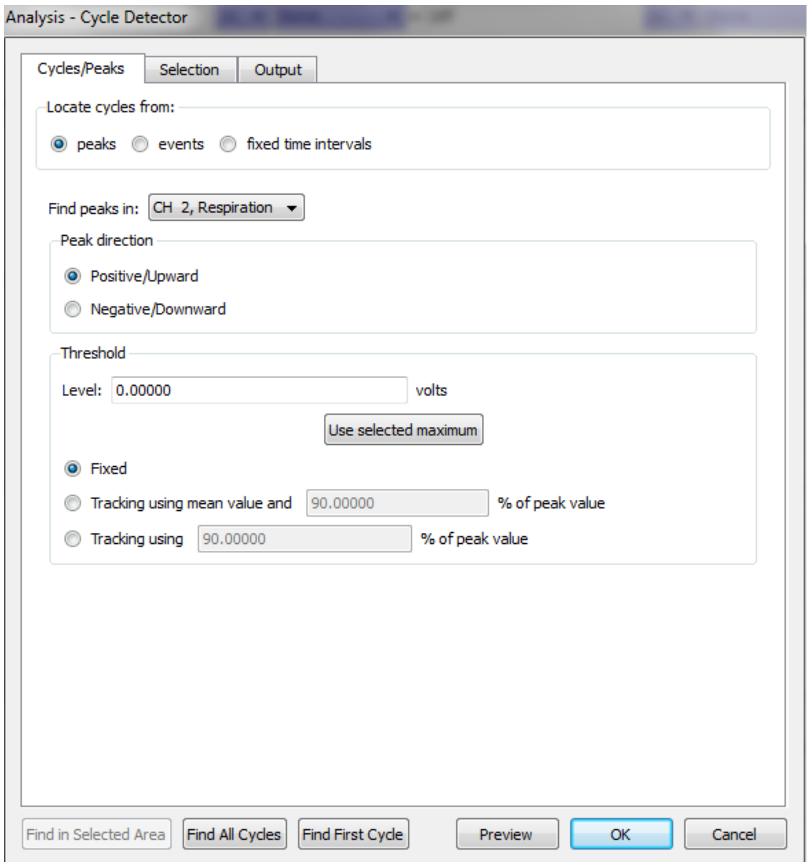
STEP 2. Mark the peak and trough on the respiratory waveform

File preparation

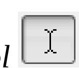
1. Open the acqknowledge file (xxxxx_resp.acq) that converted from the BioLab.
2. Take off the visibility of channel 0 on the screen by clicking channel icon with holding down ALT key in the upper part of graph display.
3. When you see only channel 1(Respiration), duplicate the respiration channel on channel 2 to work on (EDIT<DUPLICATE WAVEFORM)
4. Take off the visibility of original waveform and then you can only see the duplicated respiration channel on the channel 2.
5. Filter the waveform to adjust the file adequately to mark peaks and troughs (TRANSFORM<DIGITAL FILTER<FIR<HIGH PASS) and fix the frequency cutoff at "0.5" Hz then click OK. *Make sure if the frequency cutoff is too high, the peak will be swashed down.*
6. Smooth the waveform to remove noisy points on the waveform (TRANSFORM<SMOOTHING)
7. In the field for smoothing factor, put the number that multiply 0.1 by the sample rate of the waveform (i.e., sampling rate * 0.1=1000*0.1=100) and choose mean value and transform entire waveform.
8. Resample the waveform to appropriate rate for respiration. It would be recommended to use the number that multiply maximum signal of respiration of preterm infants by 4 (i.e., 60 per minute * 4 = 240). So, resample to **250**. (TRANSFORM<RESAMPLE WAVEFORM)

Mark the peak and trough

Run cycle detector (ANALYSIS<FIND CYCLE or Click  on the toolbar). Set up the dialog box as the below. *Make sure the cursor need to be at the beginning of the waveform before running cycle detector.*



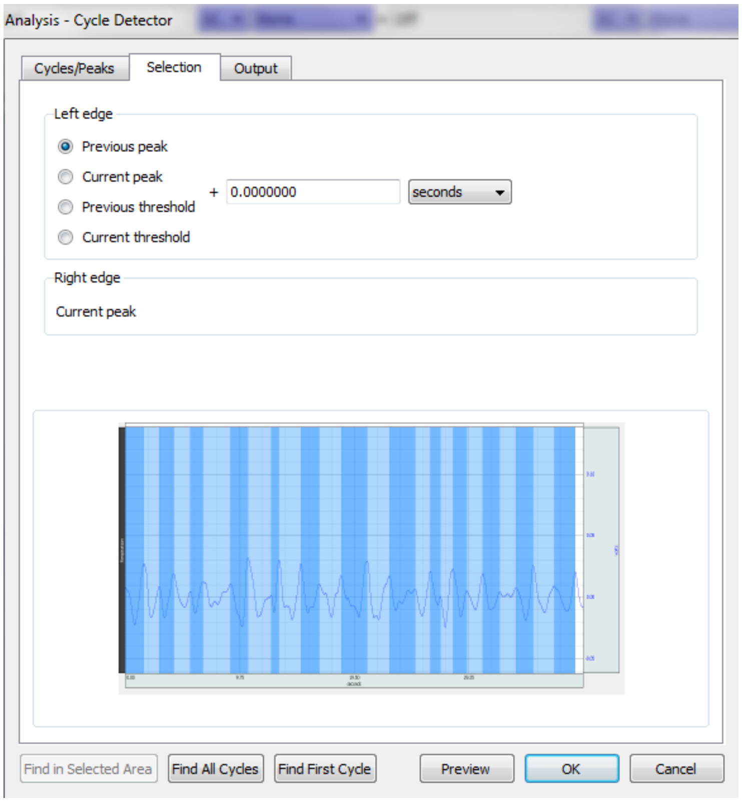
Note.

You can move cursor or make selection on the waveform using I-beam tool  *on the toolbar.*

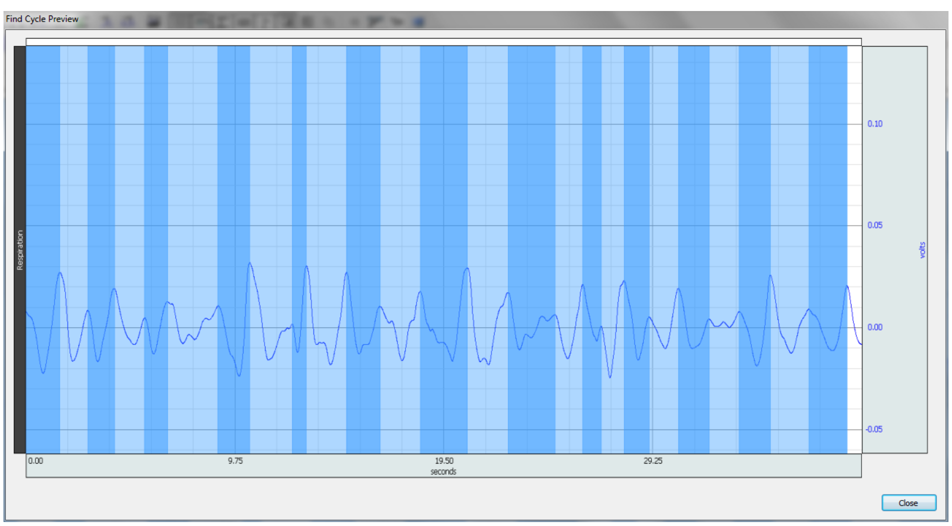
You can autoscale the waveform vertically using  *on the toolbar.*

You can autoscale the waveform vertically using  *on the toolbar.*

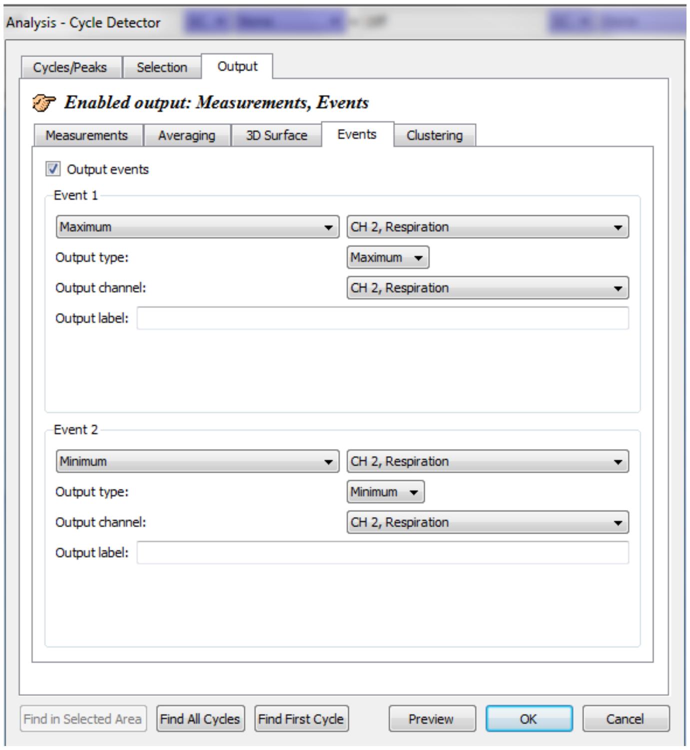
Next, choose the selection tab and set it up as the below.



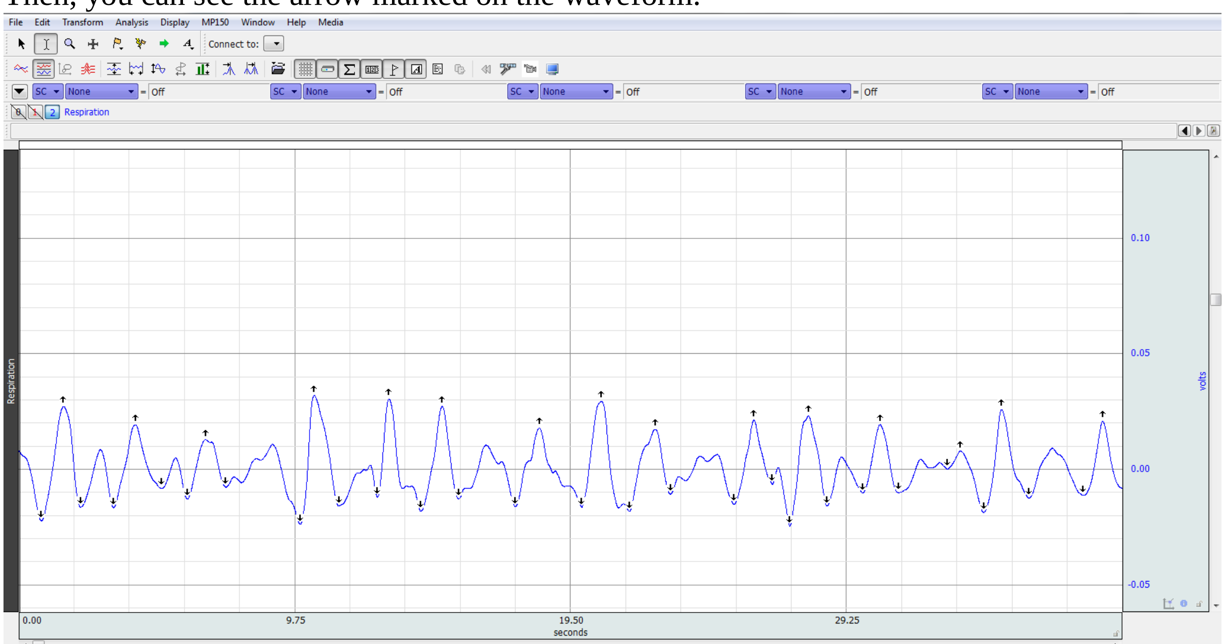
Then, click "PREVIEW" to see if the peaks and troughs are captured adequately. Play with the data until a majority of peaks are captured by adjusting threshold.



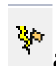
When you are satisfied with the peaks and troughs captured, choose output tab to mark the peaks and troughs on the waveform and set it up as the below.



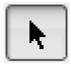
Then, you can see the arrow marked on the waveform.

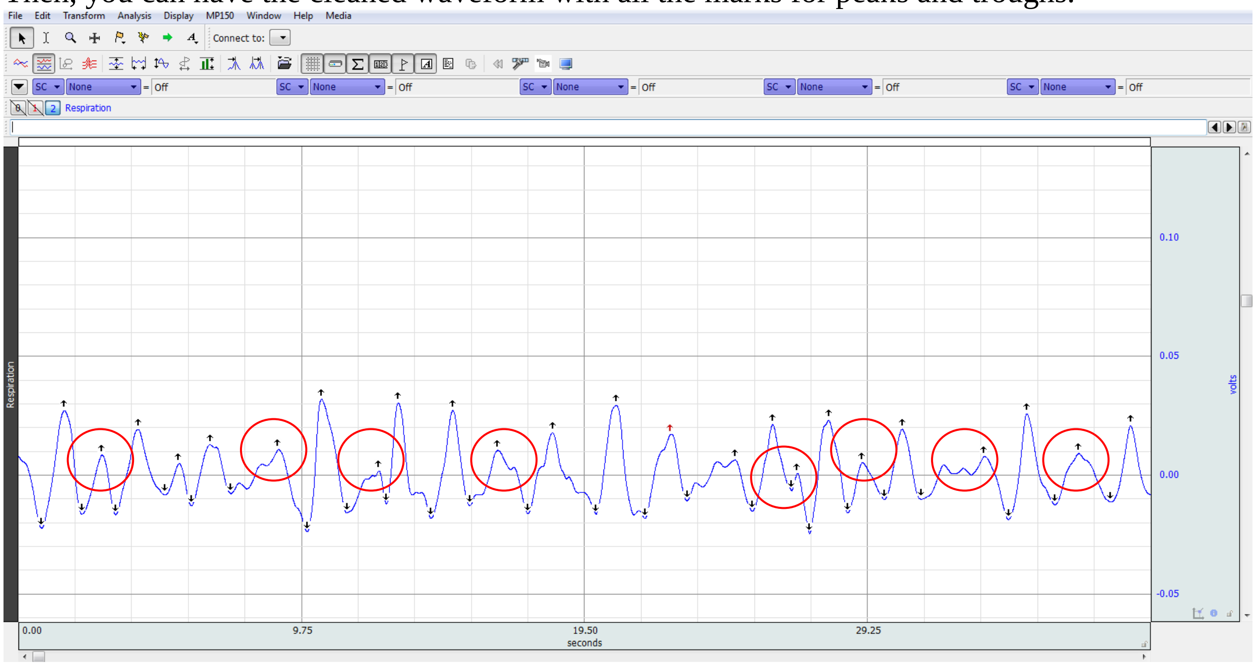


Clean artifacts by removing and adding marks manually.

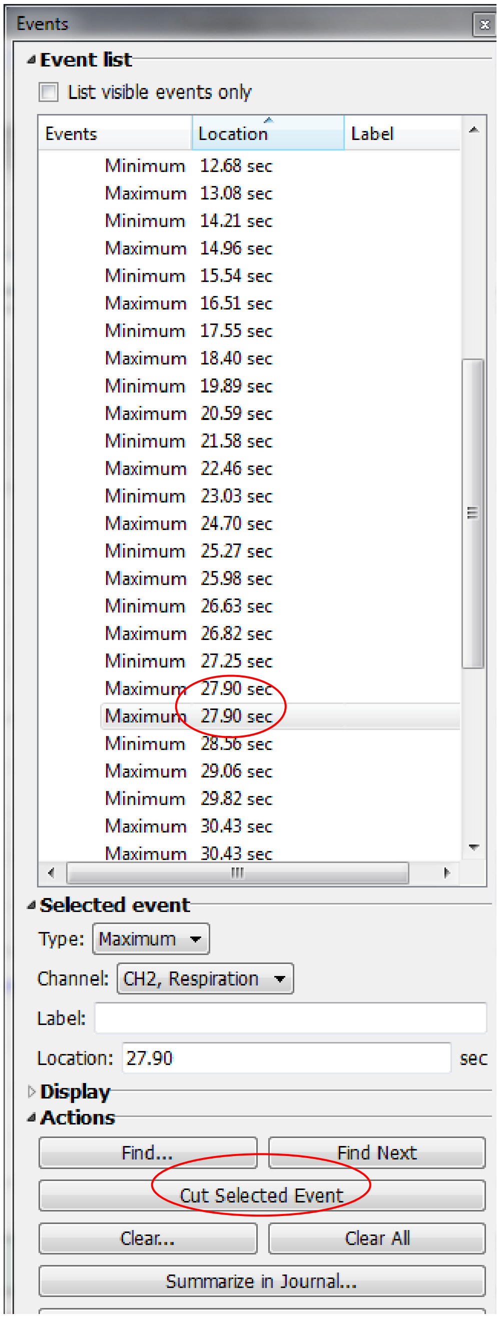
To remove the mark, click event zap tool  and put the cursor on the mark you want to remove and click.

To add the mark, click and hold event tool  and choose event type (GENERAL<MINIMUM to add the peak and GENERAL<MAXIMUM to add the trough). Then, put the cursor on the point where you wan to add the mark and click.

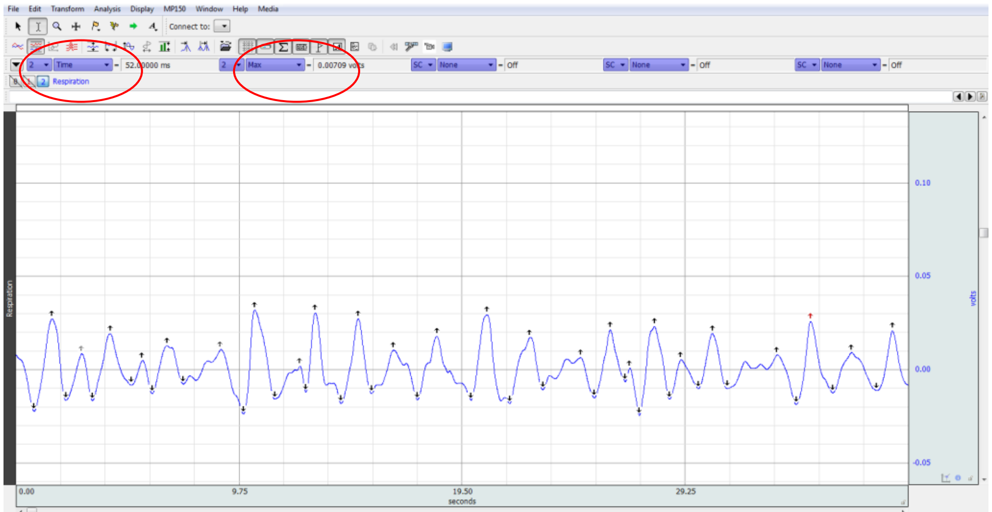
To move the mark, click  and put the cursor on the mark that you want to move and click. When it turns red, you can move the mark with holding down ALT key.
Then, you can have the cleaned waveform with all the marks for peaks and troughs.



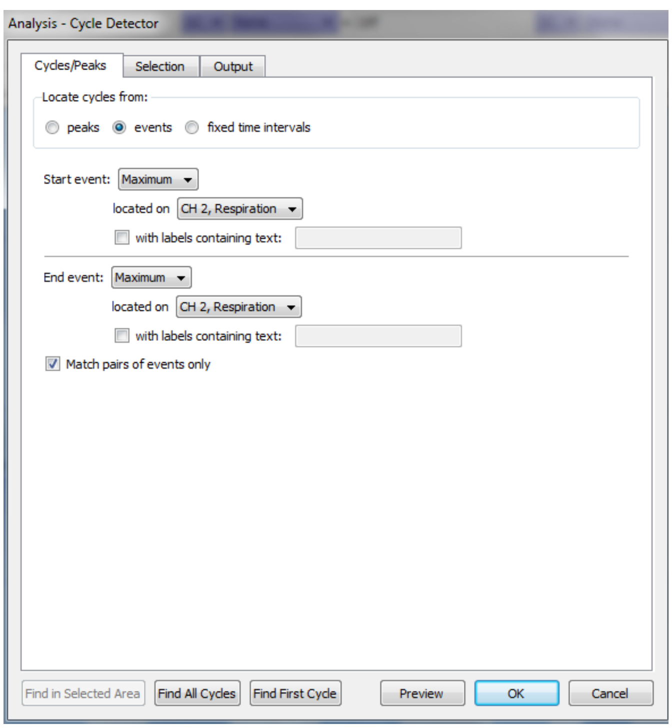
To check if all peaks and troughs that you really want are marked, click event palette tool  or go DISPLAY<SHOW<EVENT PALETTE. Sometimes one peak or trough is double marked even if we cannot see this on the screen. Thus, you need to go over all the marks and clean them manually if it is doubled using event palette tool.



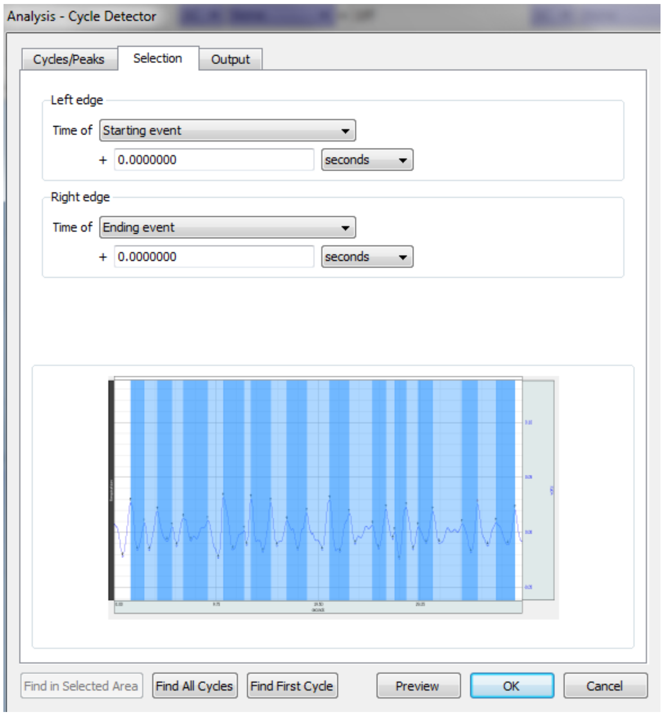
STEP 3. Export the time and value of each peak and trough into excel file
To export the time and voltage of each peak, select Time and Max on the measurement box and select channel 2.



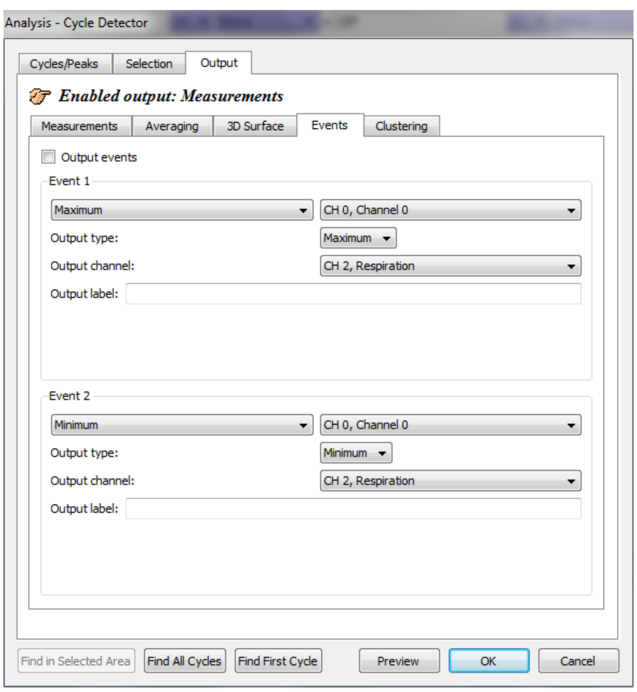
Next, run cycle detector, again. Set up the dialog box as below at this time (i.e., select events and maximum to maximum). *Make sure the cursor need to be at the beginning of the waveform before running cycle detector*.



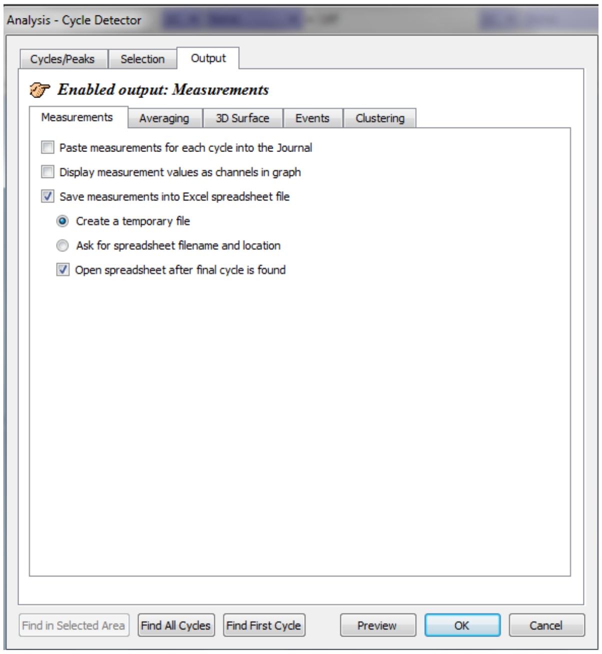
Under selection tab, set up as below.



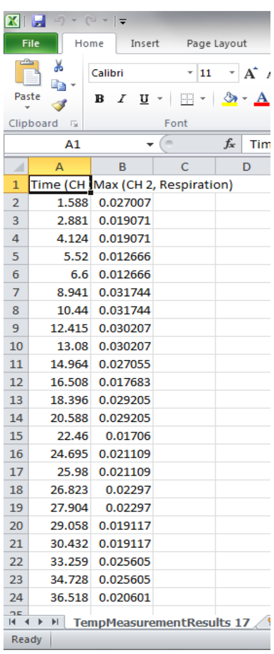
On Events under Ouput tab, uncheck the output events because we don't want to mark peaks and troughs on the waveform at this time.



Under measurement tab, set it up as the below. Check “save measurements into excel spreadsheet file”. Then, click “FIND ALL CYCLES”. *If you also want to have a waveform on subsequent channel for time and voltage of each peak, then check “display measurement values” as channels in graph.*

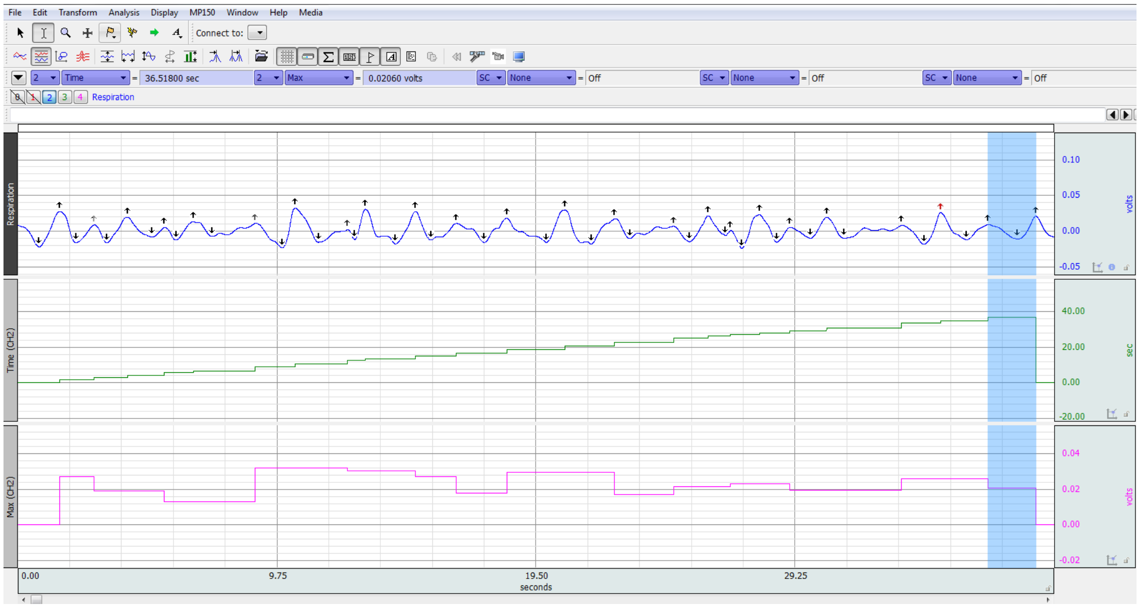


Now, you have an excel spread sheet to have time and voltage of each peak. Save this excel file for analysis.

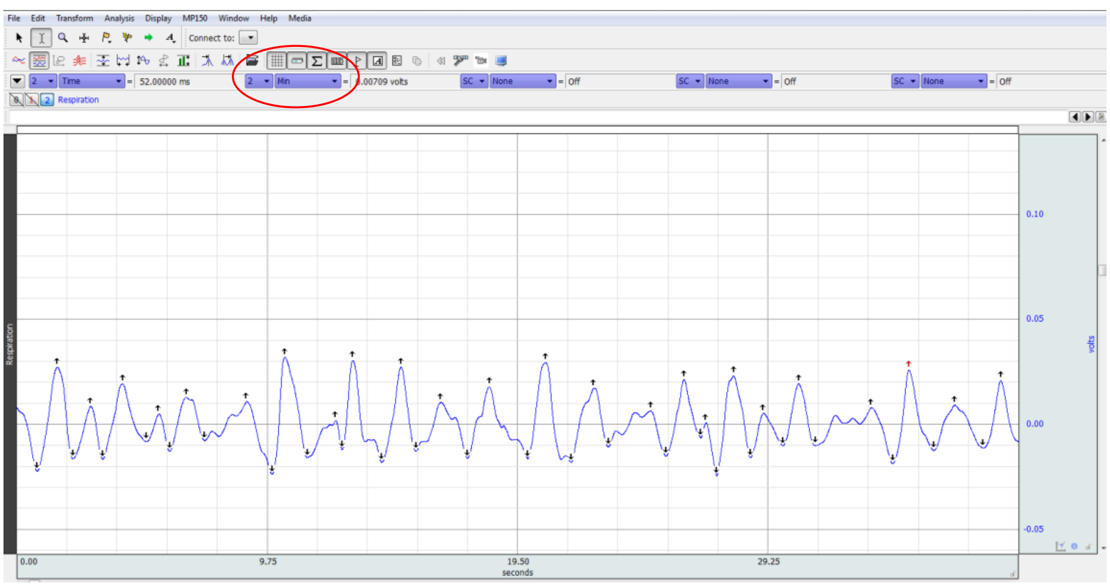


	A	B
1	Time (CH	Max (CH 2, Respiration)
2	1.588	0.027007
3	2.881	0.019071
4	4.124	0.019071
5	5.52	0.012666
6	6.6	0.012666
7	8.941	0.031744
8	10.44	0.031744
9	12.415	0.030207
10	13.08	0.030207
11	14.964	0.027055
12	16.508	0.017683
13	18.396	0.029205
14	20.588	0.029205
15	22.46	0.01706
16	24.695	0.021109
17	25.98	0.021109
18	26.823	0.02297
19	27.904	0.02297
20	29.058	0.019117
21	30.432	0.019117
22	33.259	0.025605
23	34.728	0.025605
24	36.518	0.020601

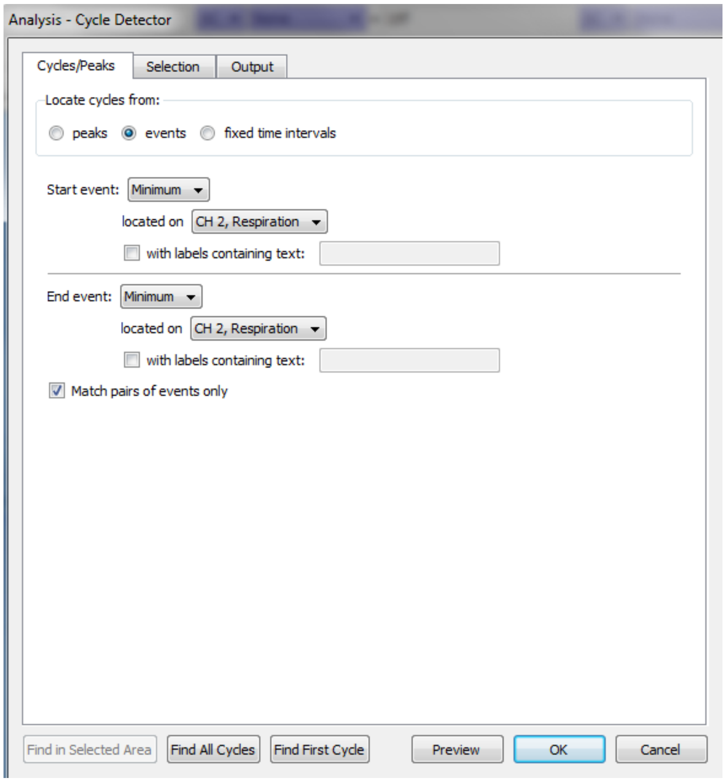
When you check "display measurement values" as channels in graph, you will also have the subsequent graph on the window.



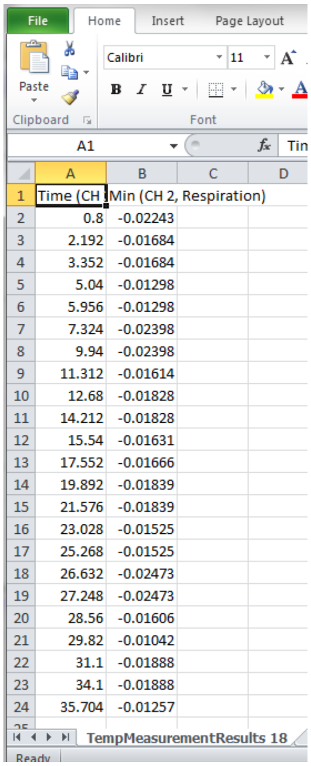
To export the time and voltage of each trough, select Time and **Min** on the measurement box and select channel 2.



Next, run cycle detector, again. Set up the dialog box as below at this time (i.e., select events and minimum to minimum). *Make sure the cursor need to be at the beginning of the waveform before running cycle detector*. Set up the selection tab and output tab as same as the one when you generate time and voltage for each peak. Click "FIND ALL CYCLES".

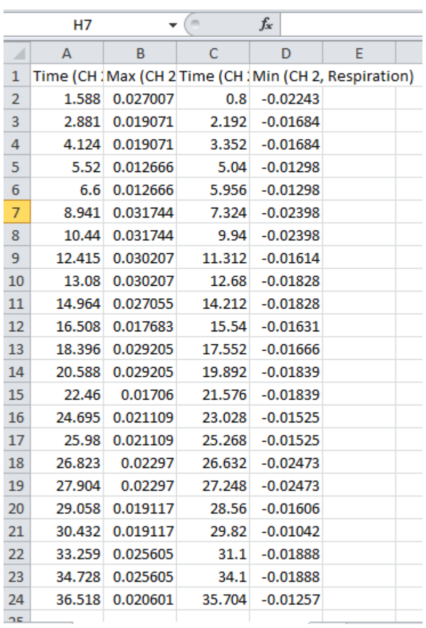


Now, you have an excel spread sheet to have time and voltage of each trough. Save this excel file for analysis. Merge the excel files of peak and trough for analysis.



	A	B	C	D
1	Time (CH	Min (CH 2, Respiration)		
2	0.8	-0.02243		
3	2.192	-0.01684		
4	3.352	-0.01684		
5	5.04	-0.01298		
6	5.956	-0.01298		
7	7.324	-0.02398		
8	9.94	-0.02398		
9	11.312	-0.01614		
10	12.68	-0.01828		
11	14.212	-0.01828		
12	15.54	-0.01631		
13	17.552	-0.01666		
14	19.892	-0.01839		
15	21.576	-0.01839		
16	23.028	-0.01525		
17	25.268	-0.01525		
18	26.632	-0.02473		
19	27.248	-0.02473		
20	28.56	-0.01606		
21	29.82	-0.01042		
22	31.1	-0.01888		
23	34.1	-0.01888		
24	35.704	-0.01257		

Merge the excel files of peak and trough and save it for analysis.



	A	B	C	D	E
1	Time (CH :	Max (CH 2	Time (CH :	Min (CH 2, Respiration)	
2	1.588	0.027007	0.8	-0.02243	
3	2.881	0.019071	2.192	-0.01684	
4	4.124	0.019071	3.352	-0.01684	
5	5.52	0.012666	5.04	-0.01298	
6	6.6	0.012666	5.956	-0.01298	
7	8.941	0.031744	7.324	-0.02398	
8	10.44	0.031744	9.94	-0.02398	
9	12.415	0.030207	11.312	-0.01614	
10	13.08	0.030207	12.68	-0.01828	
11	14.964	0.027055	14.212	-0.01828	
12	16.508	0.017683	15.54	-0.01631	
13	18.396	0.029205	17.552	-0.01666	
14	20.588	0.029205	19.892	-0.01839	
15	22.46	0.01706	21.576	-0.01839	
16	24.695	0.021109	23.028	-0.01525	
17	25.98	0.021109	25.268	-0.01525	
18	26.823	0.02297	26.632	-0.02473	
19	27.904	0.02297	27.248	-0.02473	
20	29.058	0.019117	28.56	-0.01606	
21	30.432	0.019117	29.82	-0.01042	
22	33.259	0.025605	31.1	-0.01888	
23	34.728	0.025605	34.1	-0.01888	
24	36.518	0.020601	35.704	-0.01257	

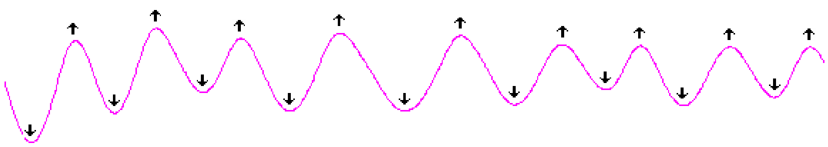
Appendix J. Rules to Mark Peaks and Troughs on Respiratory Waveforms

How to mark the peak and valley on the respiratory waveform

Variation of Breathing <u>when not Sucking</u>

** All breathing signals should be confirmed by listening to the breathing sounds on video clips*

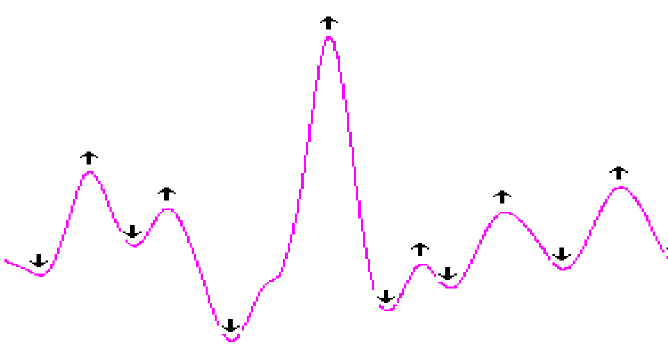
1. **Uninterrupted/ideal Breaths**



- Peak=the point of maximum chest circumference, between inspiration and expiration
- Valley=the point of minimum chest circumference, between inspiration and expiration

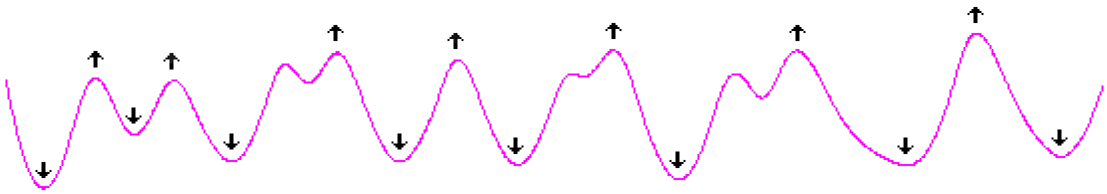
2. **Gasp or big breaths:** mark them as a valid breath because it is also a respiratory effort to achieve oxygen.

- Peak=the point of maximum chest circumference, between inspiration and expiration
- Valley=the point of minimum chest circumference, between inspiration and expiration



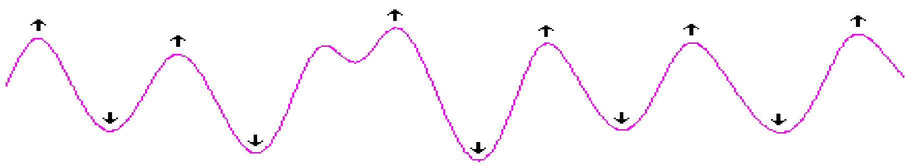
3. Breaths with double peaks

If you clearly hear separate inspiration and expiration sound for each breath; they have wide enough intervals between peaks to achieve air flow from each breath, then mark each peak and valley based on the rules for ideal breaths.



If not, consider them as one breath.

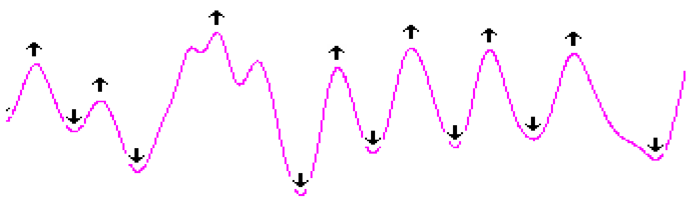
- Peak= the highest point
- Valley= the minimum point between inspiration and expiration

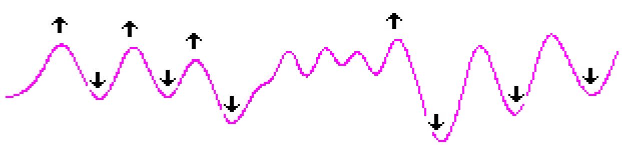


4. Breaths with multiple shallow peaks (by several shallow inspirations and expirations)

Mark it as one breath.

- Peak= the highest point
- Valley= the minimum point between inspiration and expiration





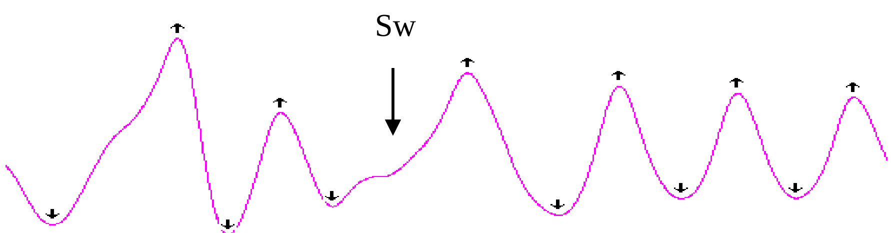
Variations of Breathing <u>during Sucking Bursts</u>

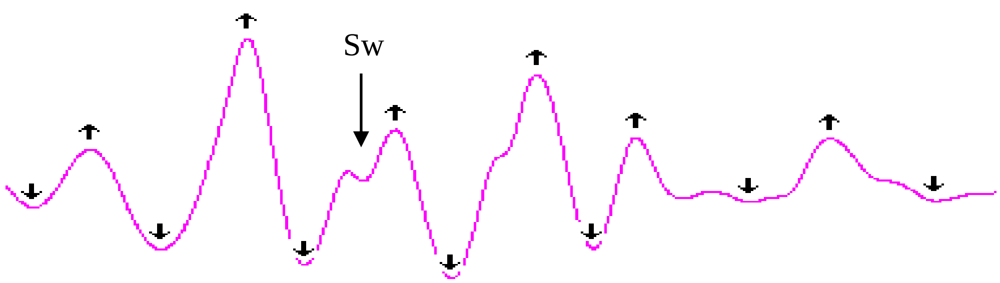
**All interrupted breathing should be confirmed by listening to the breathing and swallowing sounds on the video clips.*

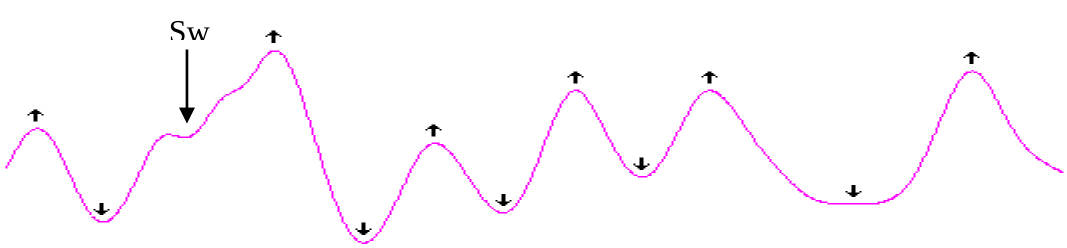
1. Interrupted inspiration

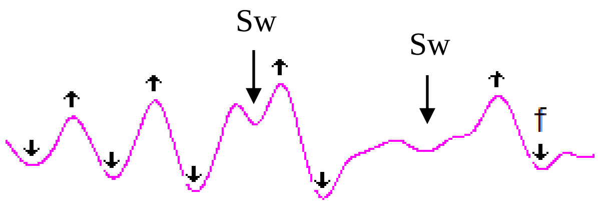
- Peak=the point when the inspiration is completed (no more increasing pattern follow-highest point)
- Valley=the point at the end of expiration
- For breaths with the double peaks, apply the same rule for breaths with double peaks when not sucking in order to decide if they need to be marked as one breath or not.

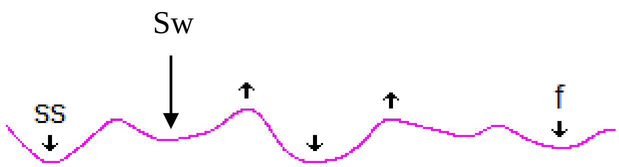
Note.
Sw=swallow sound
S= the start of breathing burst
SS= the start of breathing burst right after the bottle is inserted
F= the end of breathing burst







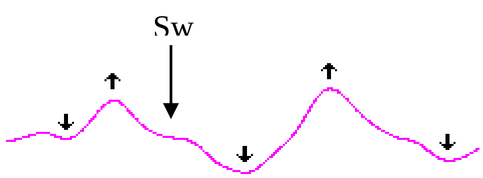


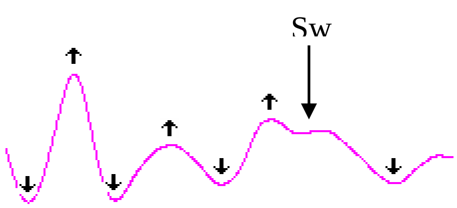


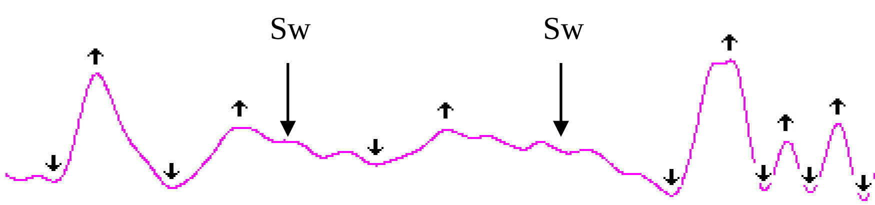
2. Interrupted expiration

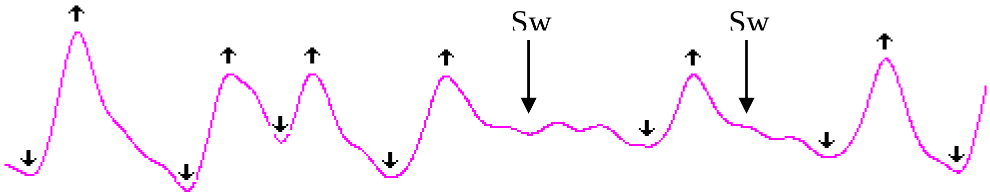
- Peak=the point at the end of inspiration (highest point)
- Valley=the point when the expiration is completed (no more decreasing pattern follow)

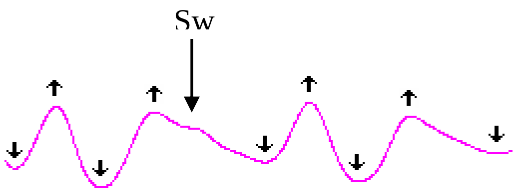
Note.
Sw=swallow sound
S= the start of breathing burst
SS= the start of breathing burst right after the bottle is inserted
F= the end of breathing burst

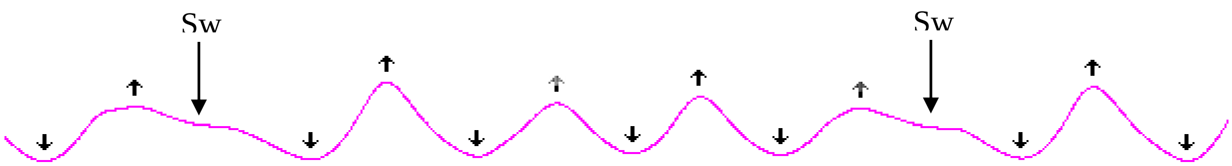










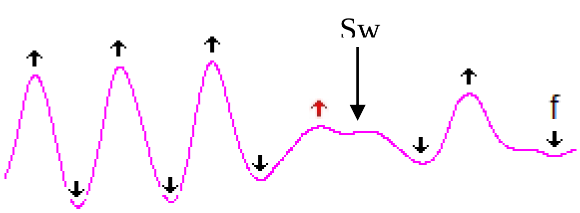


3. Interrupted peak (at the end of inspiration/ the start of expiration)

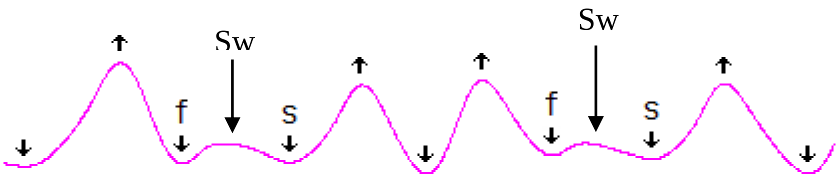
- Peak=the point of maximum chest circumference, between inspiration and expiration
- Valley=the point of minimum chest circumference, between inspiration and expiration

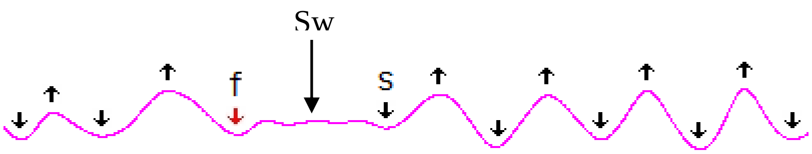
Note.
Sw=swallow sound
S= the start of breathing burst
SS= the start of breathing burst right after the bottle is inserted
F= the end of breathing burst

If you hear inspiration and expiration sound before and after swallowing sound, then mark it as a breath.



If you do not hear any breathing sound during this period, then do not mark it as a breath.

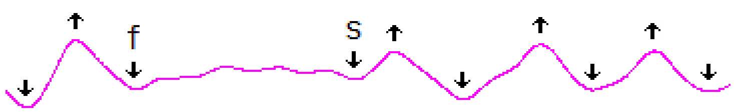


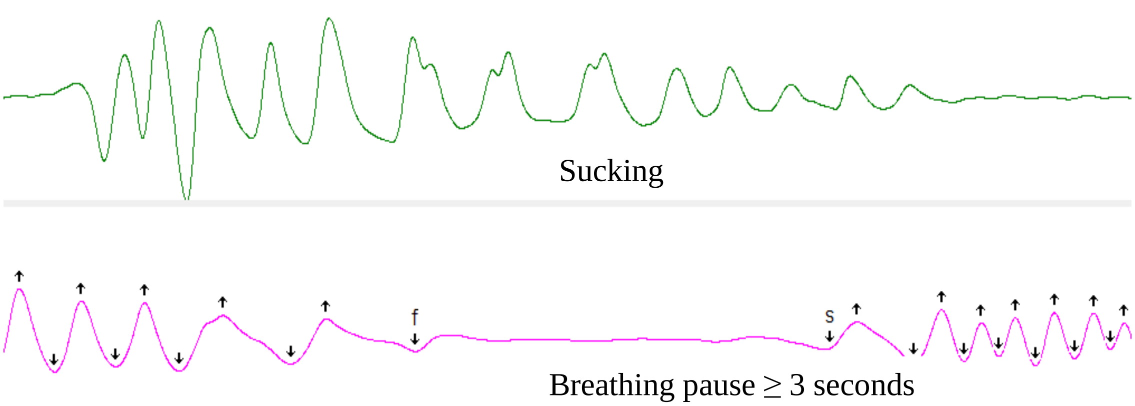


5. Interrupted breaths more than 3 seconds

Do not mark the peak during breathing pause

Note.
Sw=swallow sound
S= the start of breathing burst
SS= the start of breathing burst right after the bottle is inserted
F= the end of breathing burst



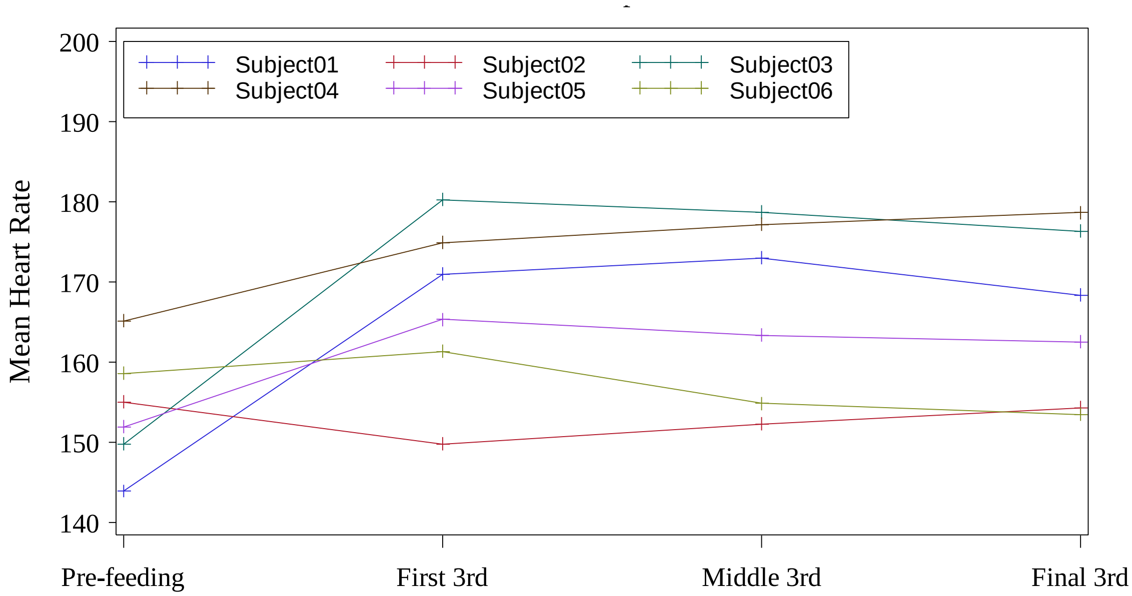


Created and updated by Jinhee Park on 11/24/2011

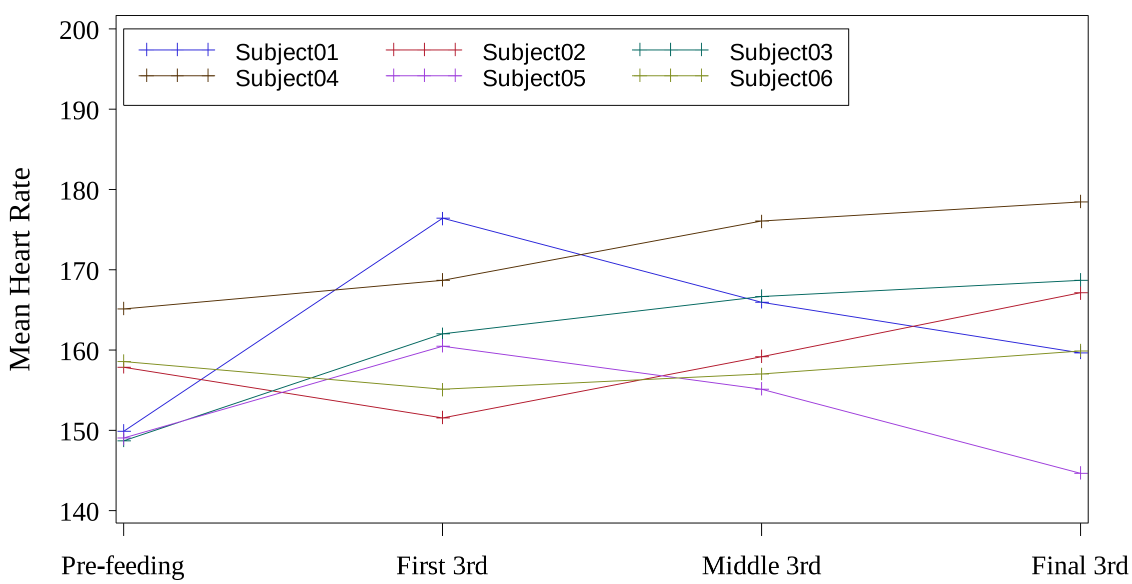
Appendix K. Plots of Individual Heart Rate using Each Method

1. Method 1: dividing the entire bottle-in periods into three equal periods

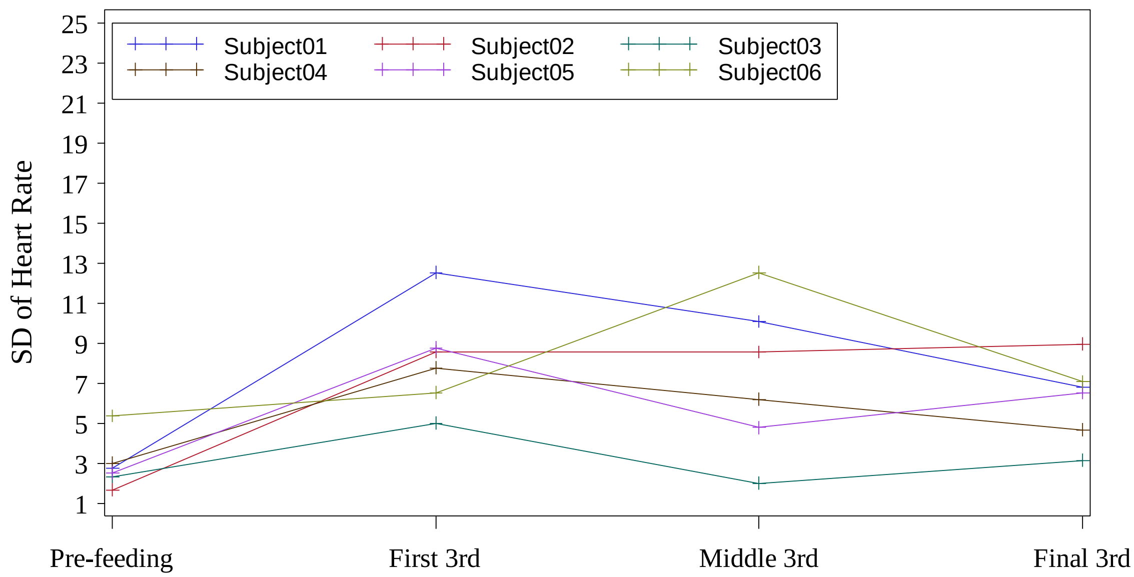
Mean Heart Rate in the HEL position



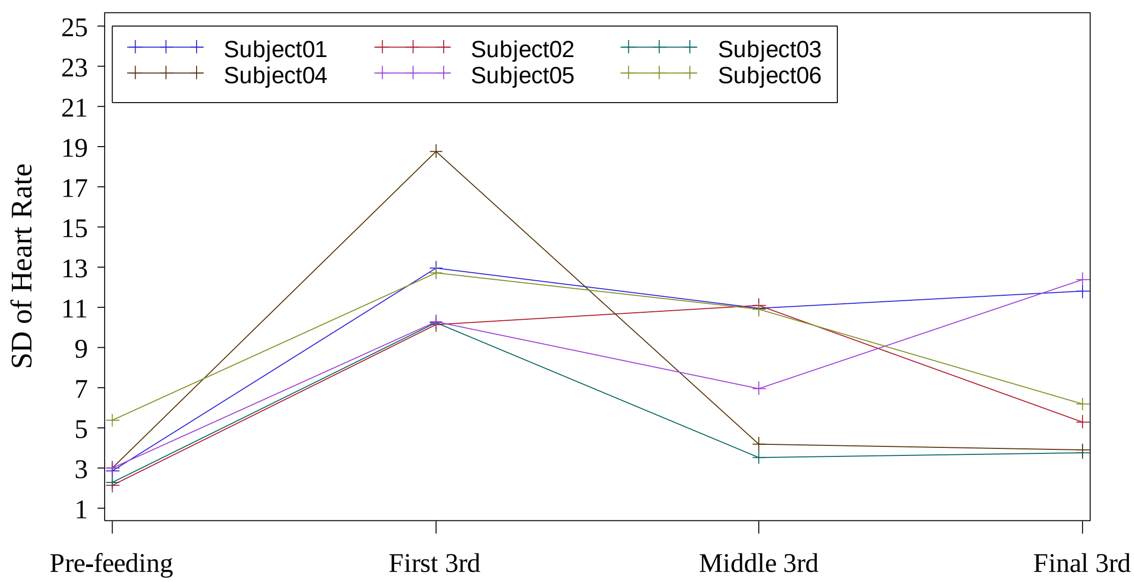
Mean Heart Rate in the HES position

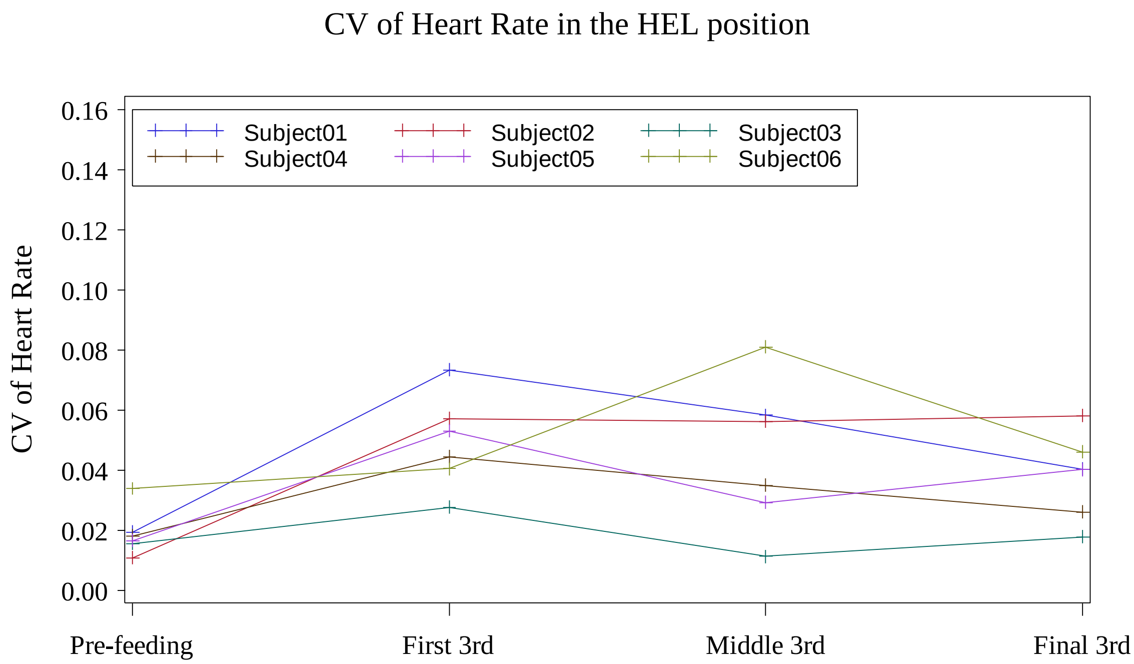


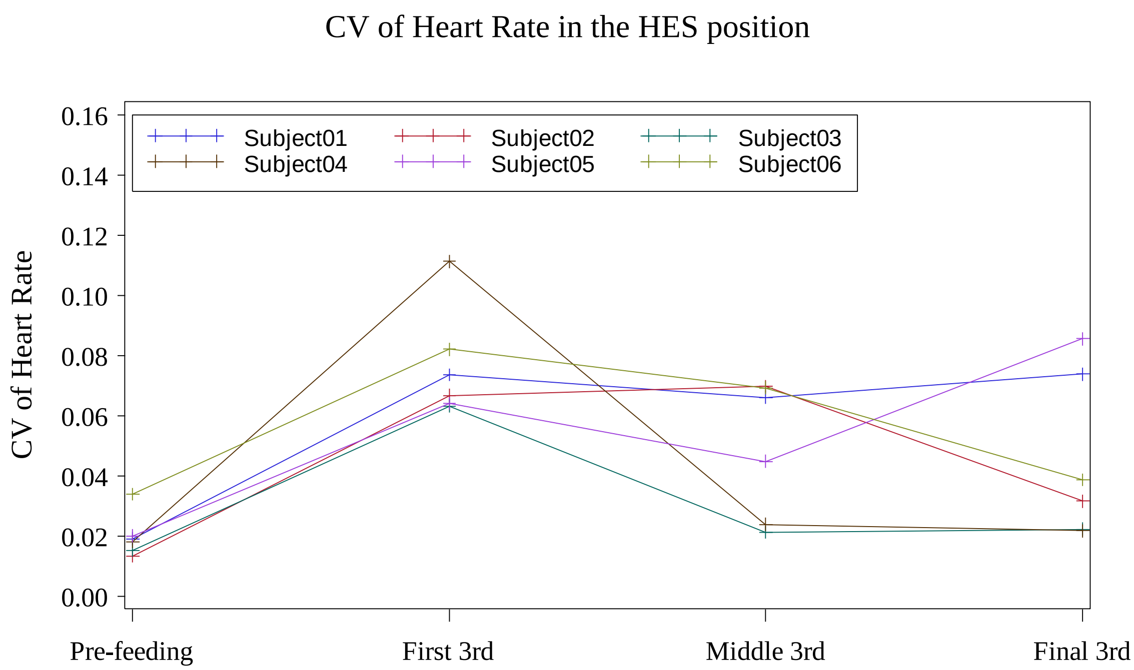
SD of Heart Rate in the HEL position



SD of Heart Rate in the HES position

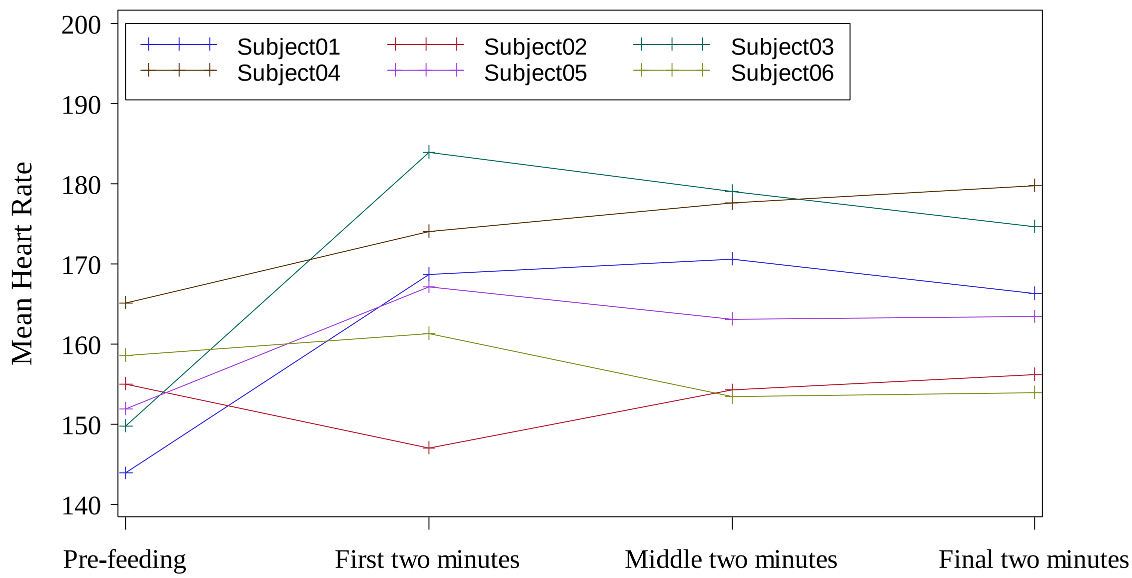



CV of Heart Rate in the HEL position
Subject01
Subject02
Subject03
Subject04
Subject05
Subject06
CV of Heart Rate
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
Pre-feeding
First 3rd
Middle 3rd
Final 3rd

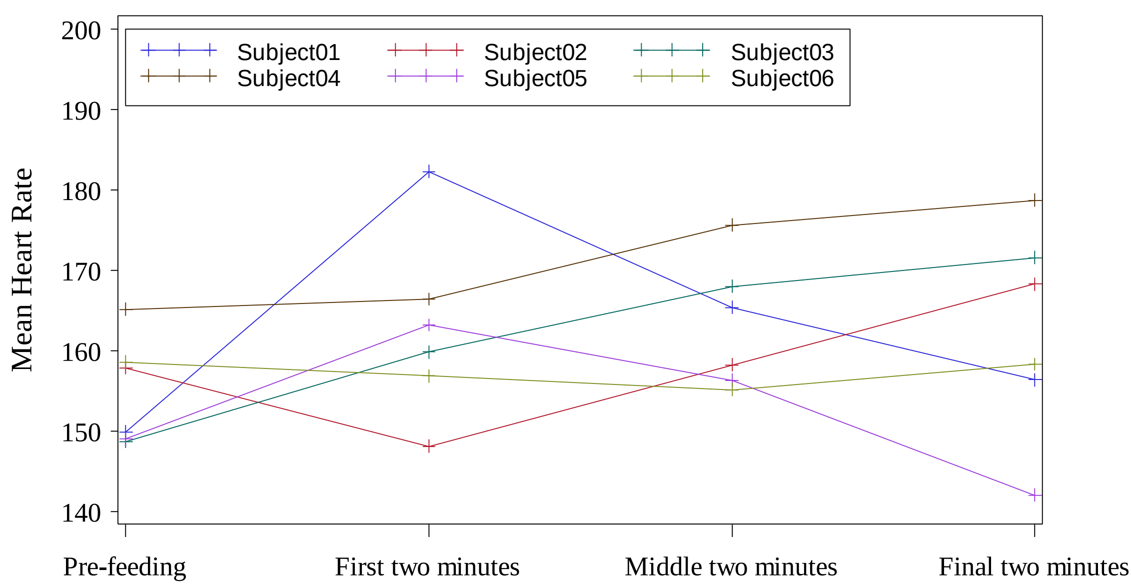

CV of Heart Rate in the HES position
Subject01
Subject02
Subject03
Subject04
Subject05
Subject06
CV of Heart Rate
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0.00
Pre-feeding
First 3rd
Middle 3rd
Final 3rd

2. Method 2: extracting 2-minute periods from the initial, middle, and final third of the bottle-in periods

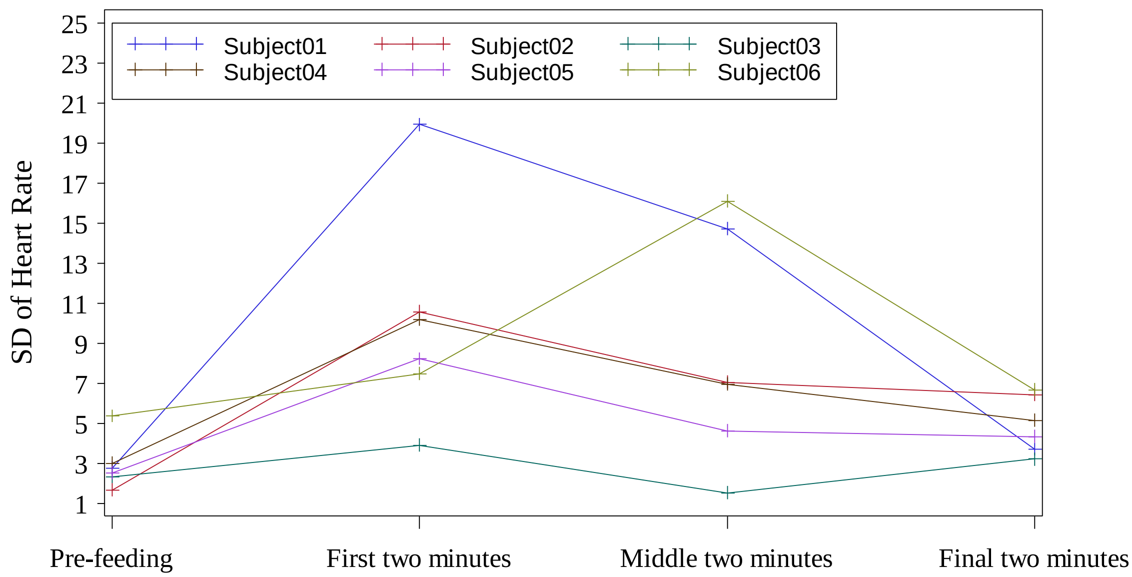
Mean Heart Rate in the HEL position



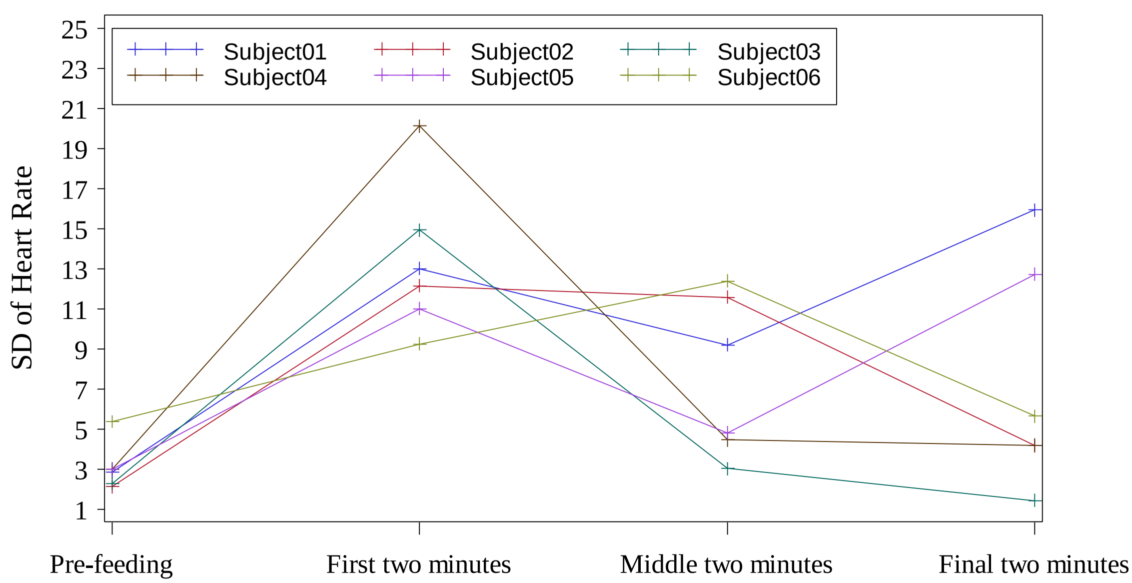
Mean Heart Rate in the HES position



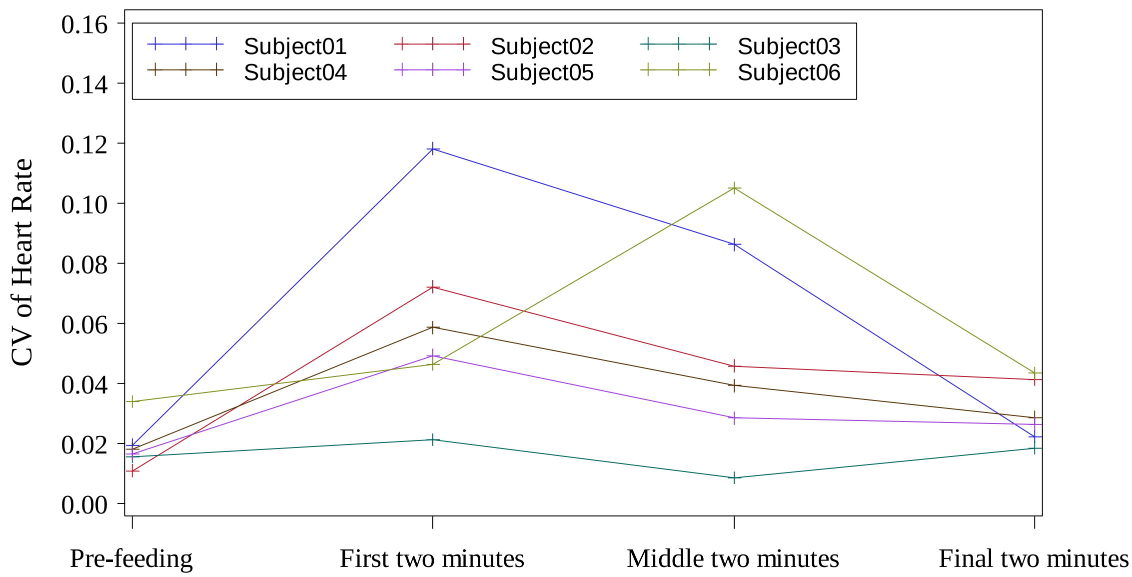
SD of Heart Rate in the HEL position



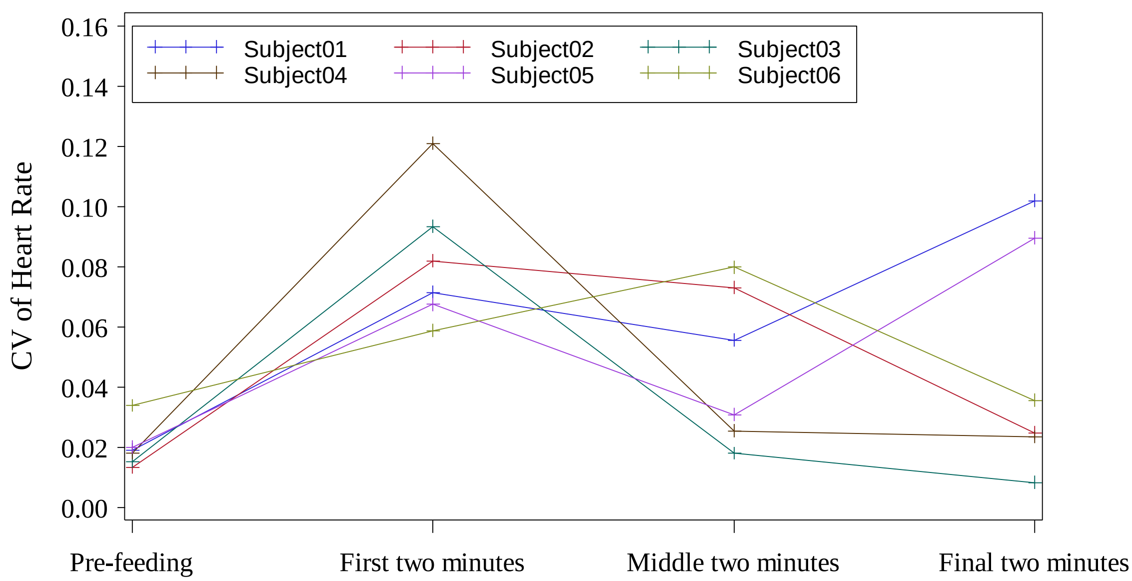
SD of Heart Rate in the HES position



CV of Heart Rate in the HEL position

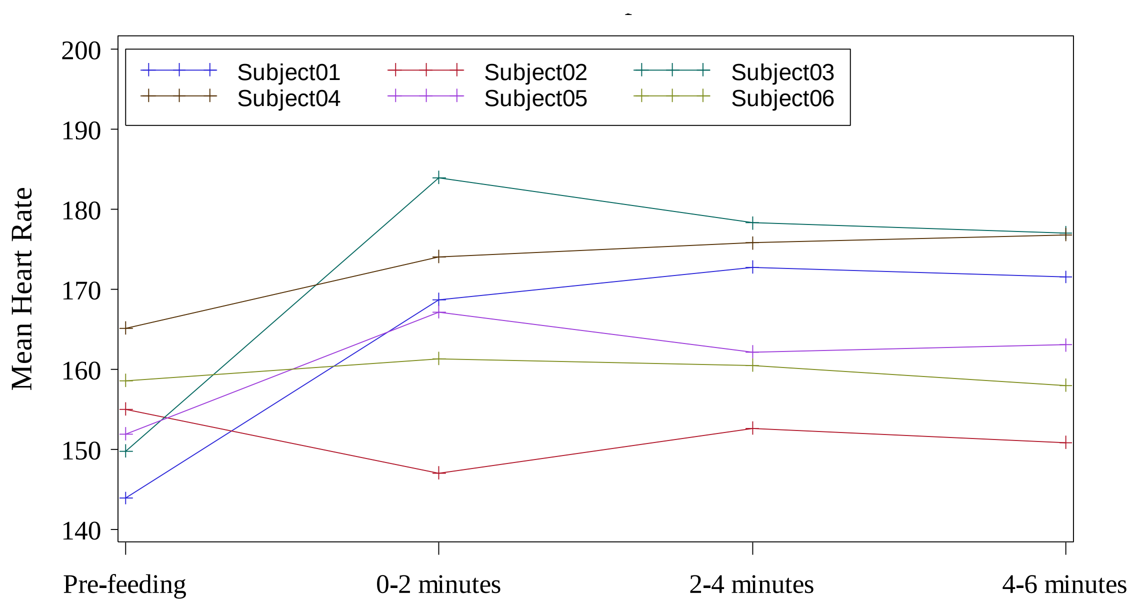


CV of Heart Rate in the HES position

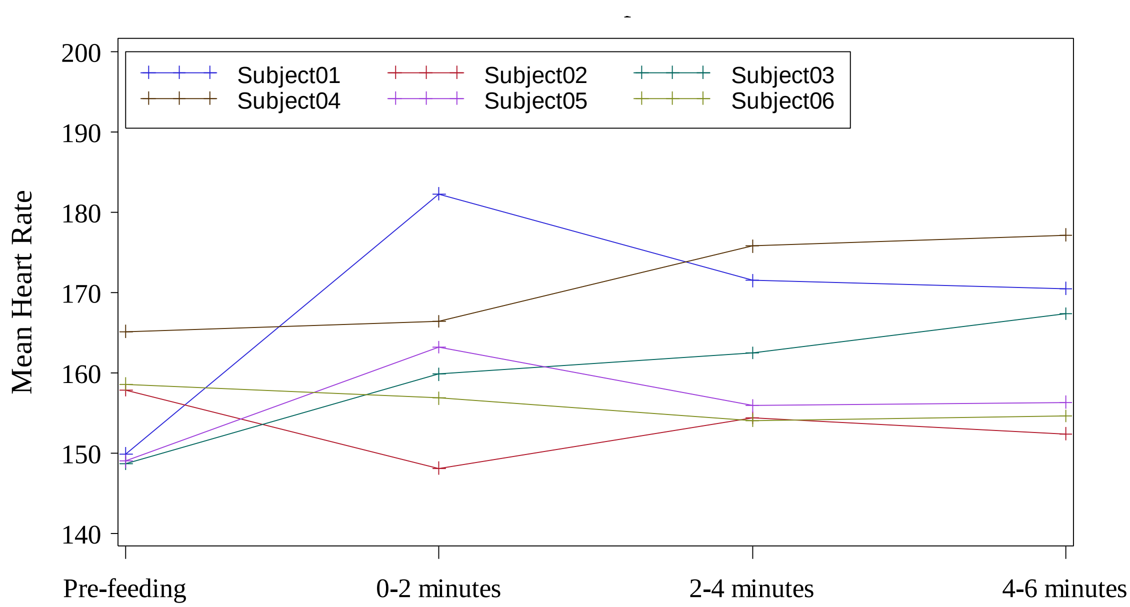


3. Method 3: successive 2 minutes during the first 6-minute bottle-in periods

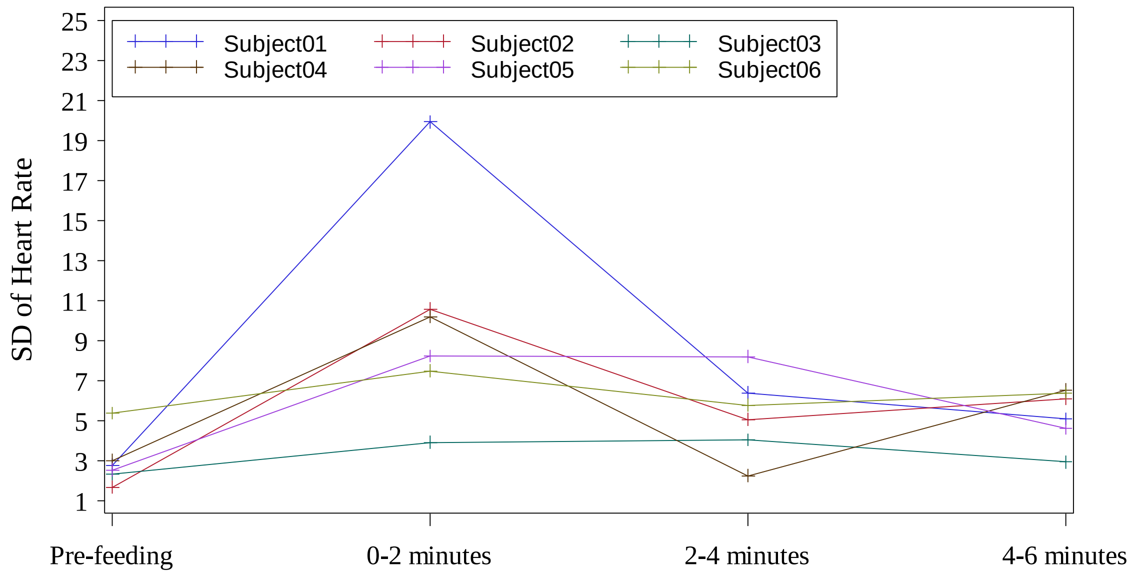
Mean Heart Rate in the HEL position



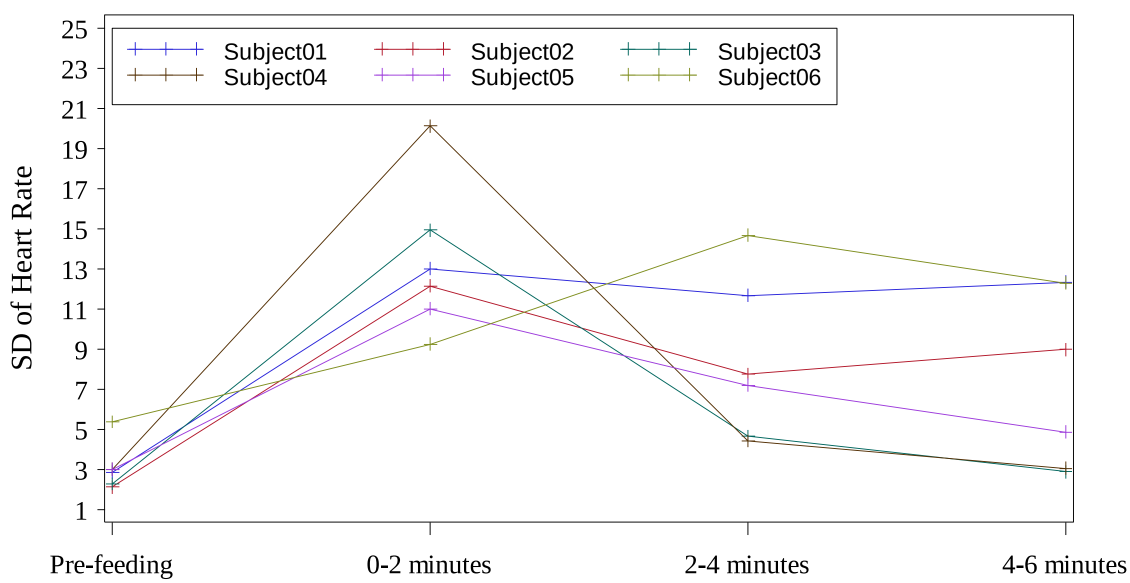
Mean Heart Rate in the HES position



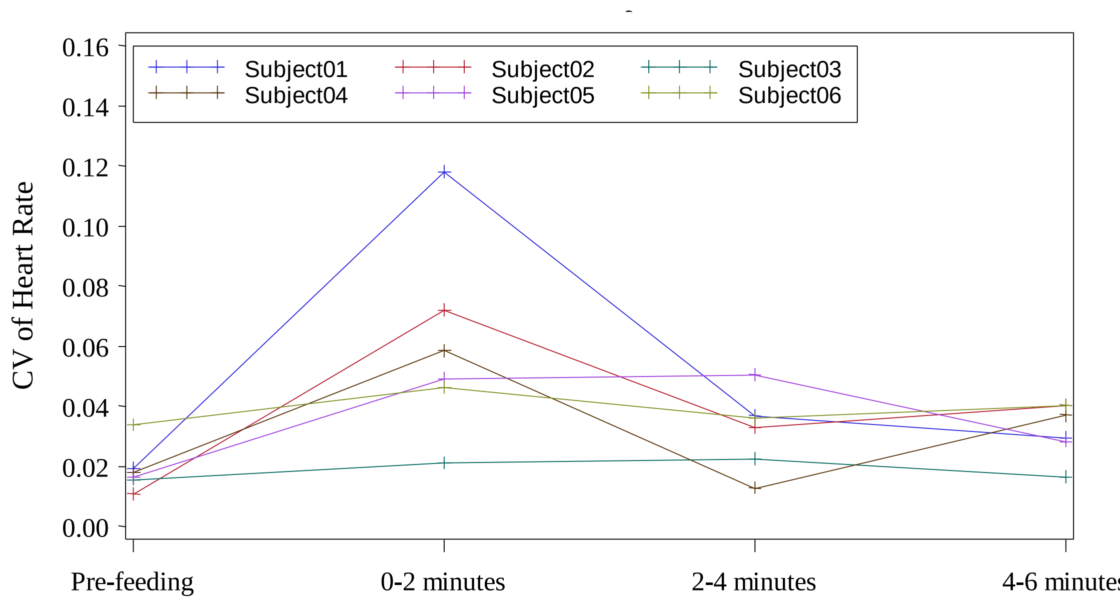
SD of Heart Rate in the HEL position



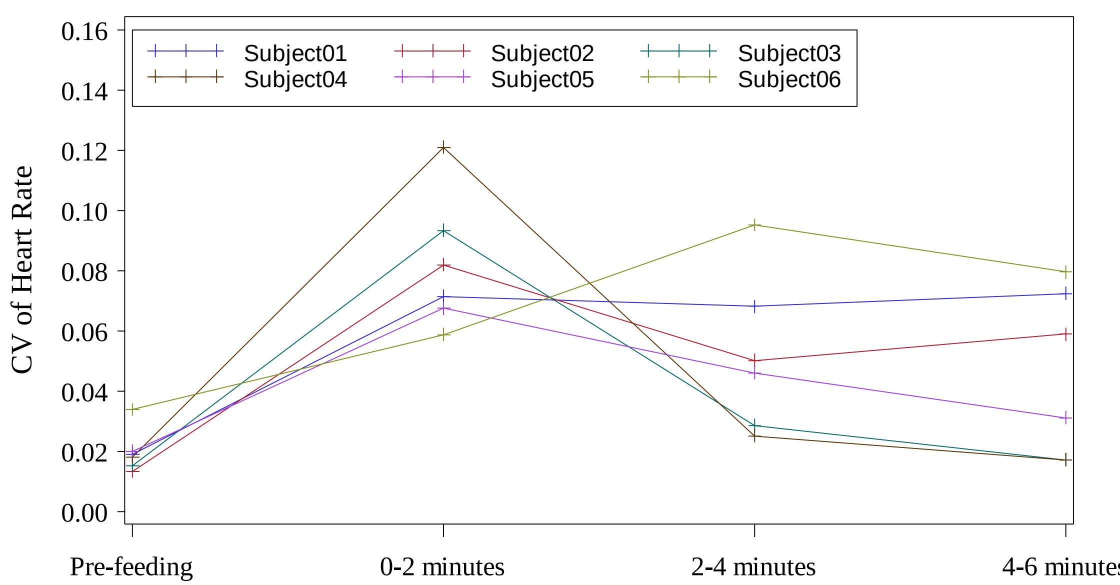
SD of Heart Rate in the HES position



CV of Heart Rate in the HEL position



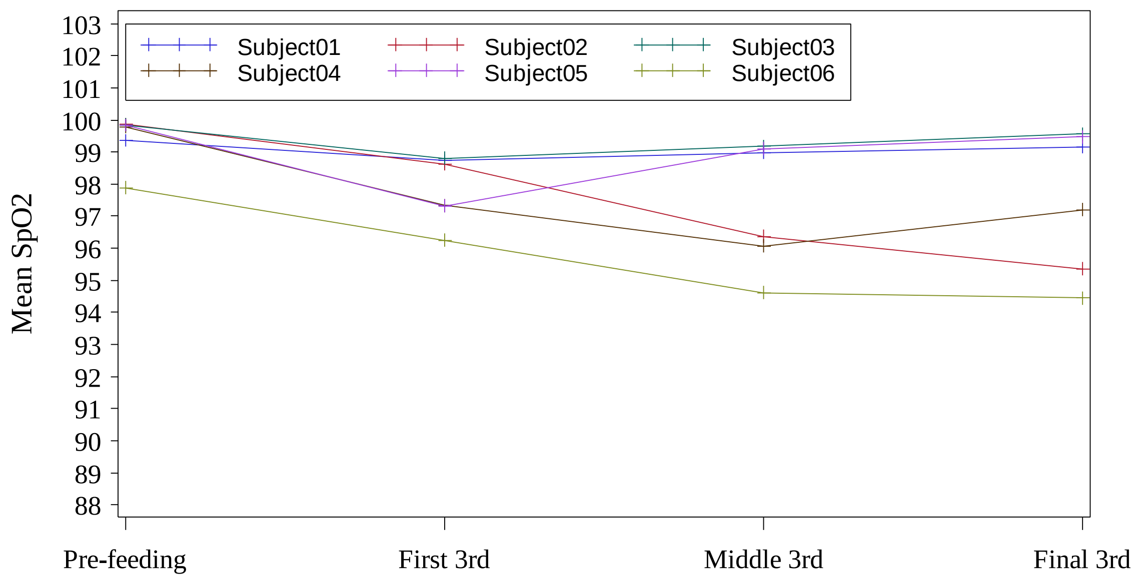
CV of Heart Rate in the HES position



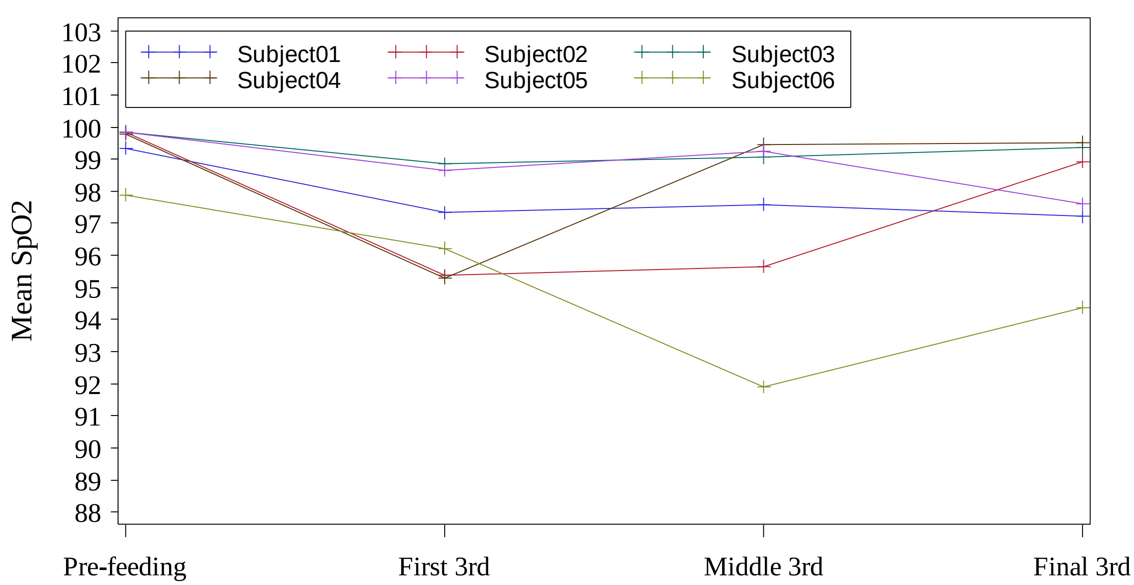
Appendix L. Plots of Individual Oxygen Saturation using Each Method

1. Method 1: dividing the entire bottle-in periods into three equal periods

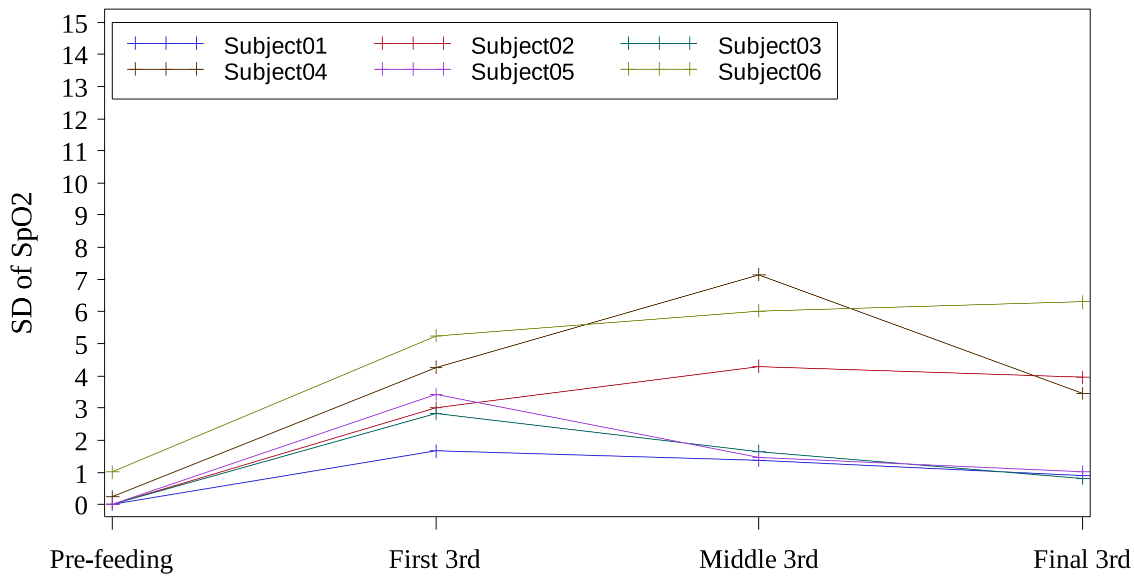
Mean SpO_2 in the HEL position



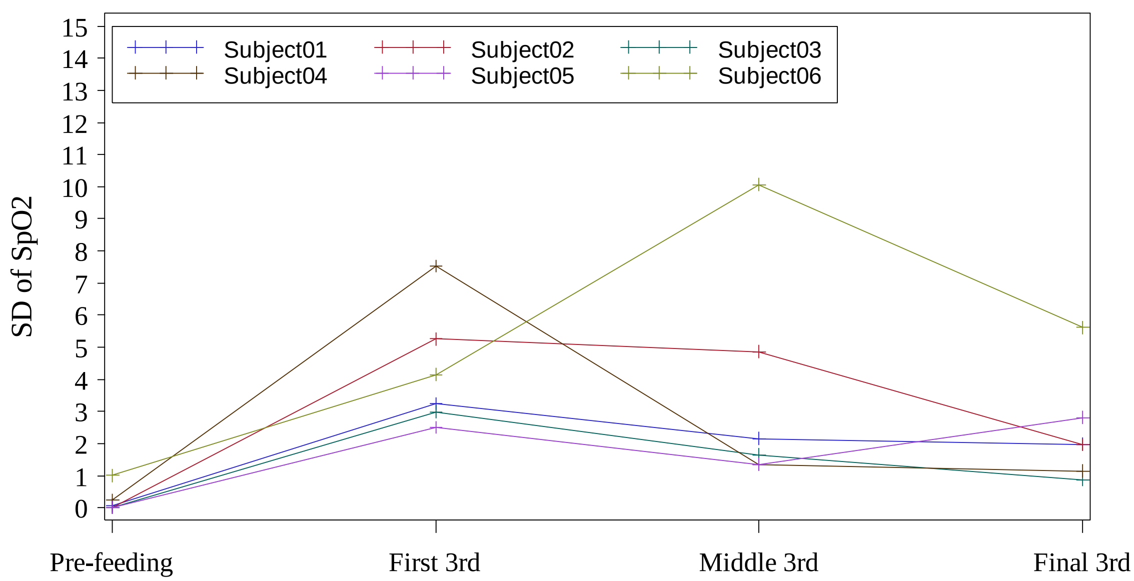
Mean SpO_2 in the HES position



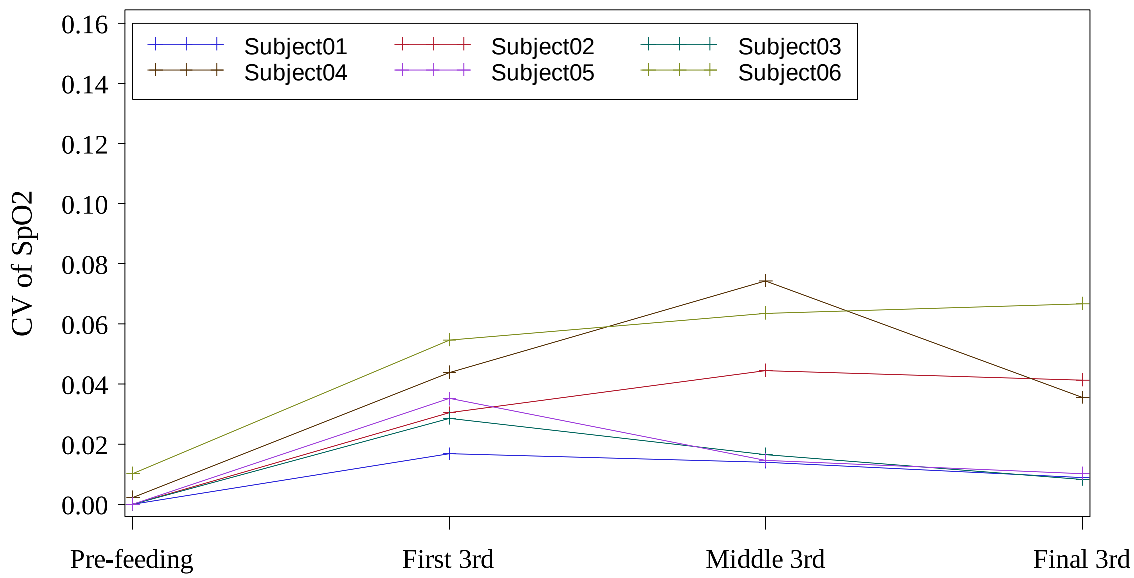
SD of SpO_2 in the HEL position



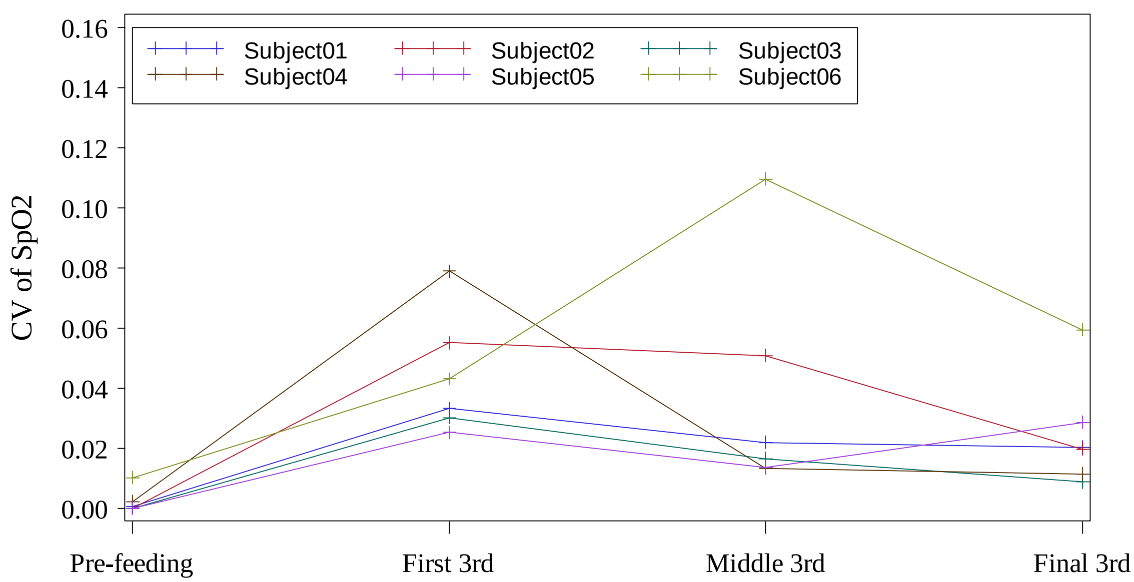
SD of SpO_2 in the HES position



CV of SpO_2 in the HEL position

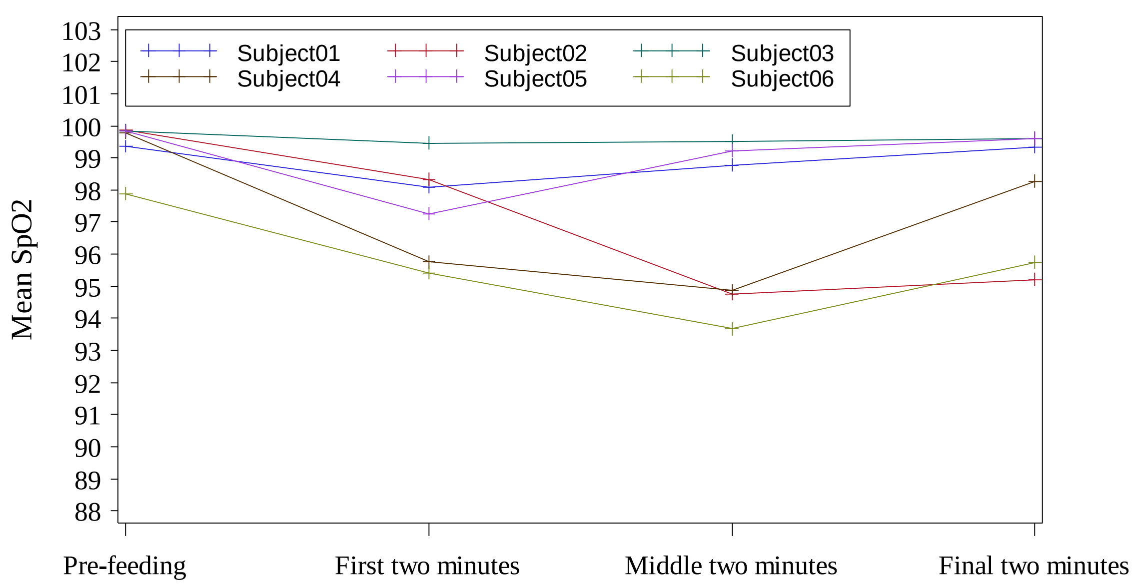


CV of SpO_2 in the HES position

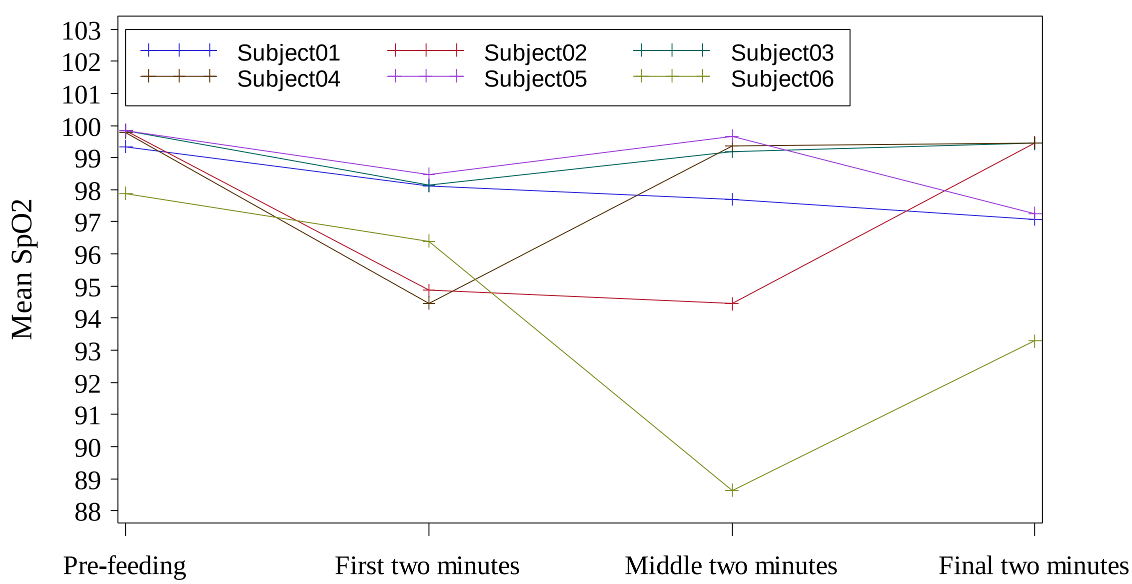


2. Method 2: extracting 2-minute periods from the initial, middle, and final third of the bottle-in periods

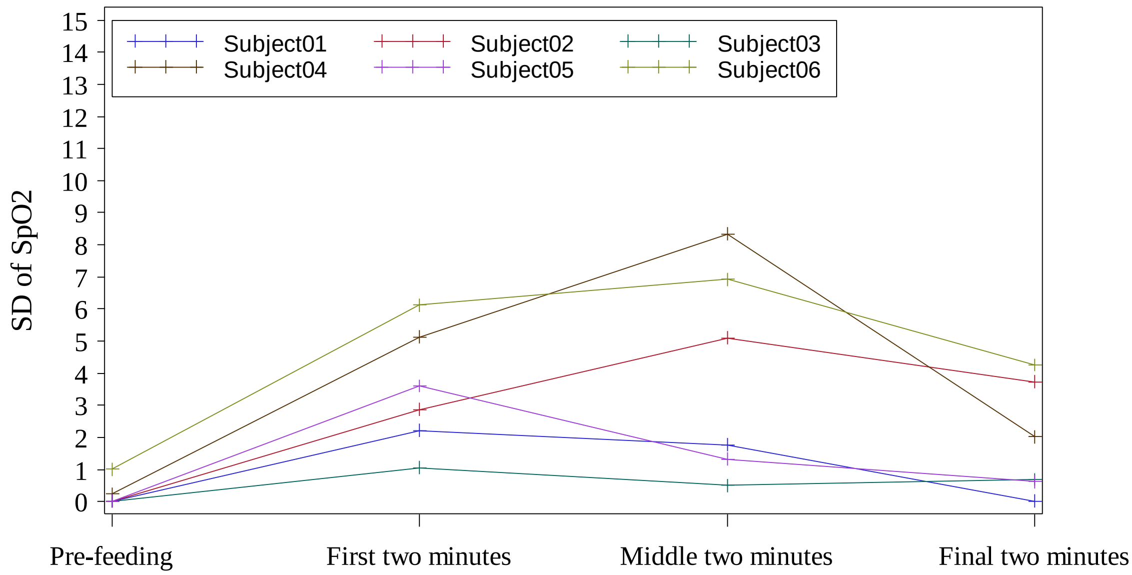
Mean SpO_2 in the HEL position



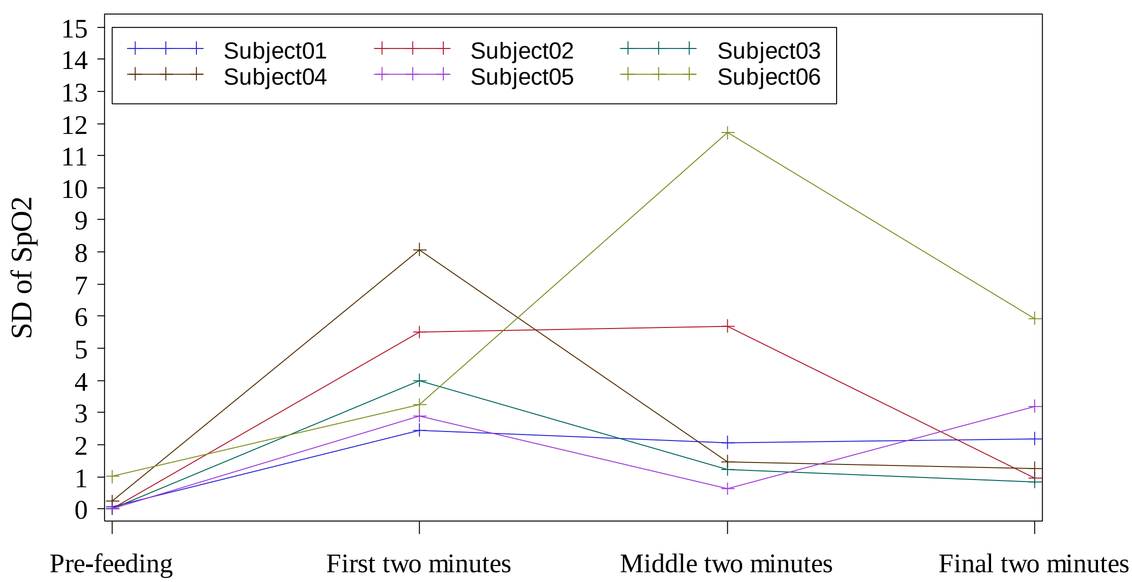
Mean SpO_2 in the HES position



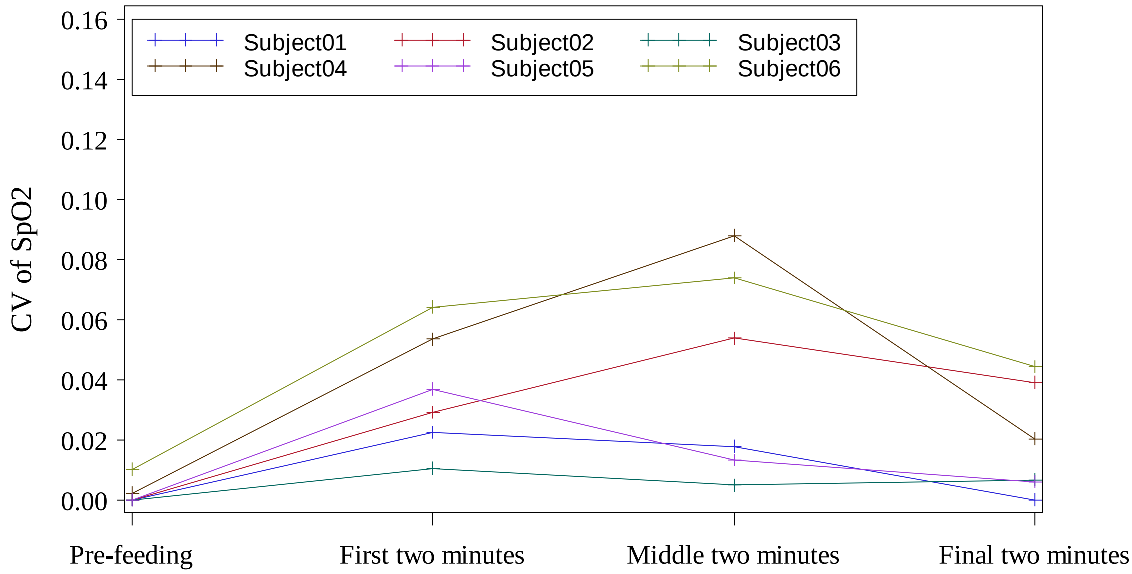
SD of SpO_2 in the HEL position



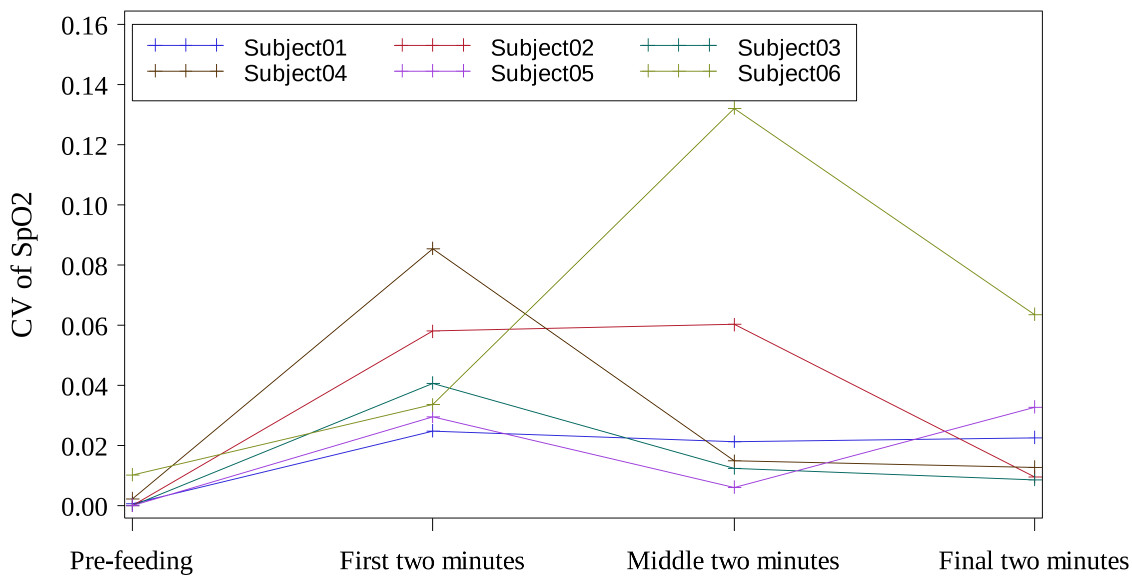
SD of SpO_2 in the HES position



CV of SpO_2 in the HEL position

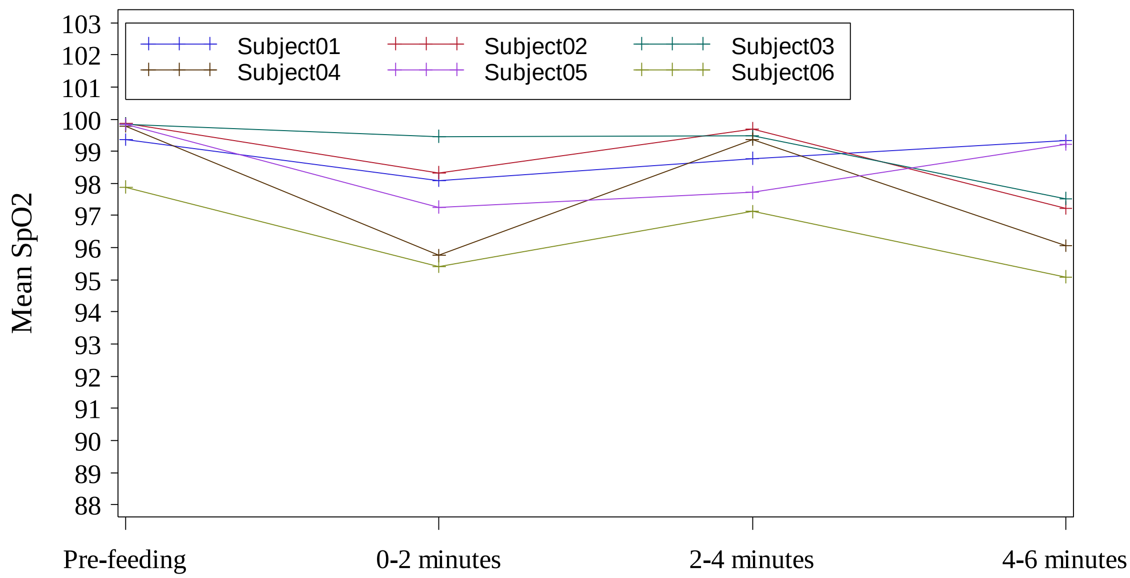


CV of SpO_2 in the HES position

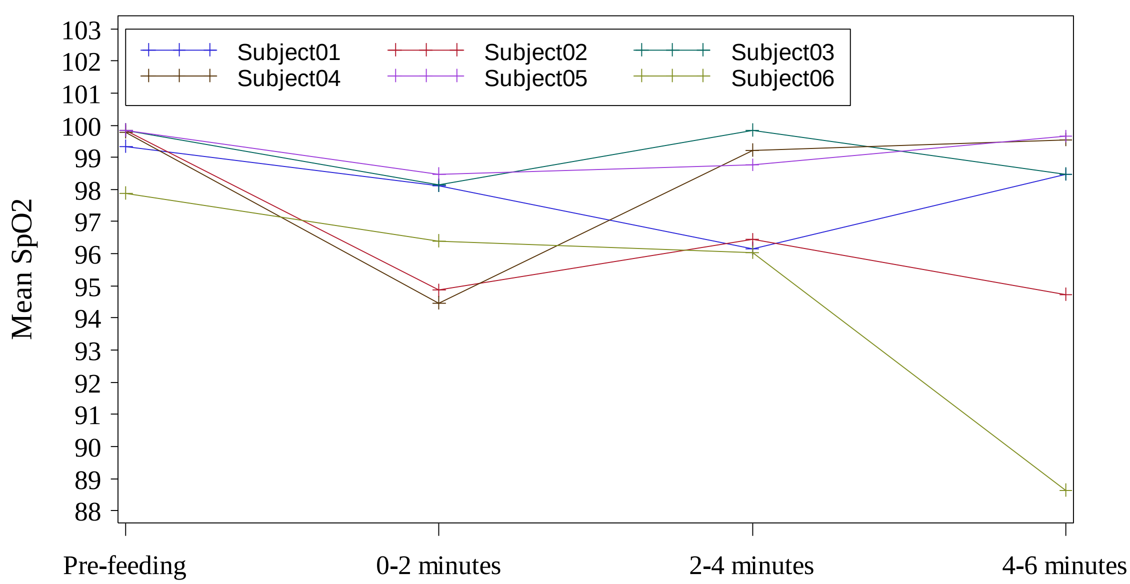


3. Method 3: successive 2 minutes during the first 6-minute bottle-in periods

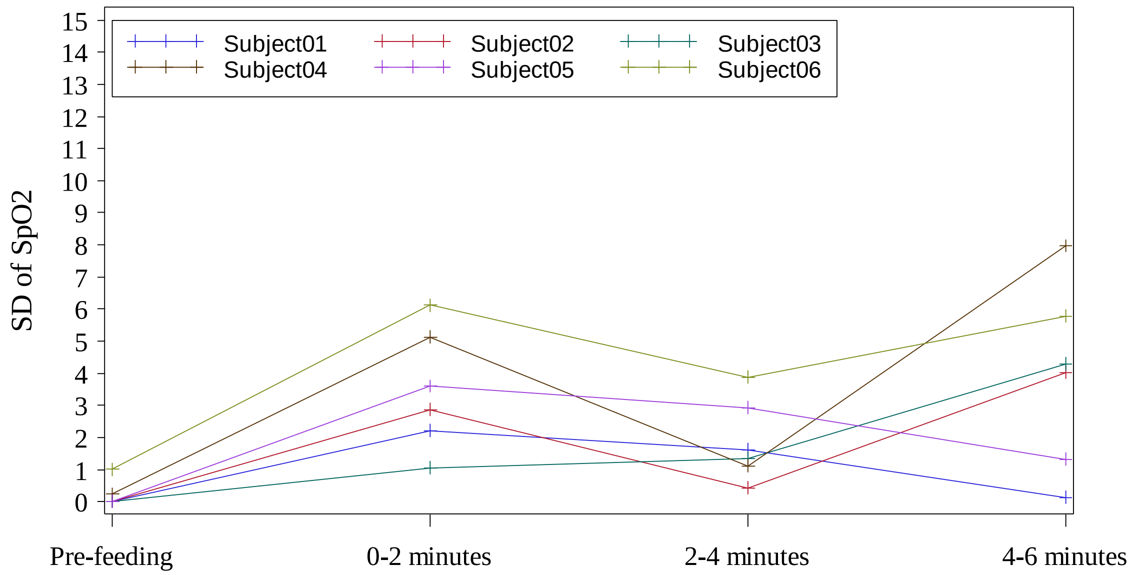
Mean SpO_2 in the HEL position



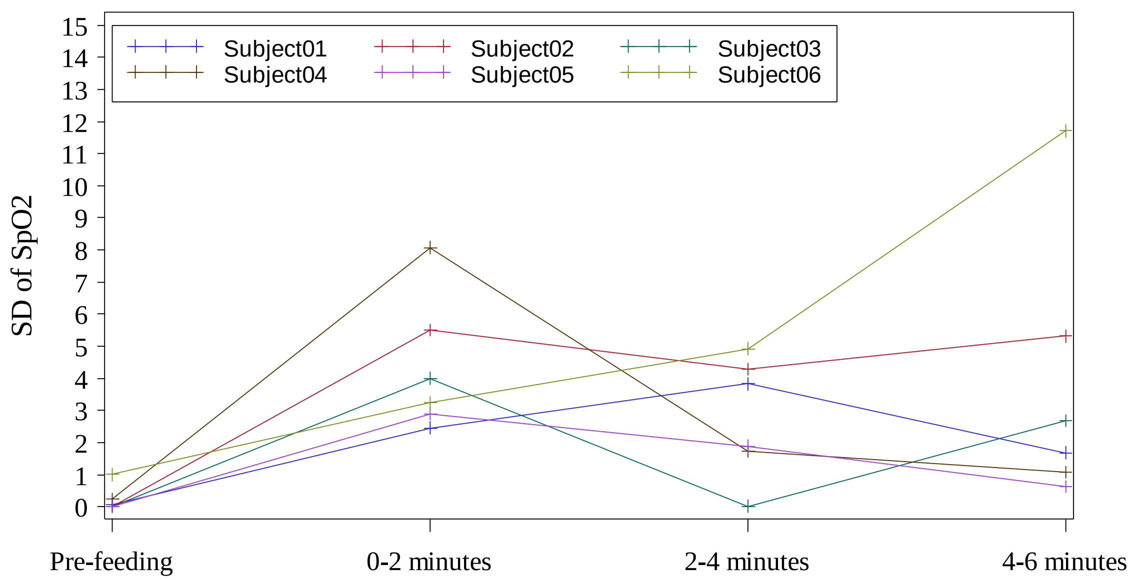
Mean SpO_2 in the HES position



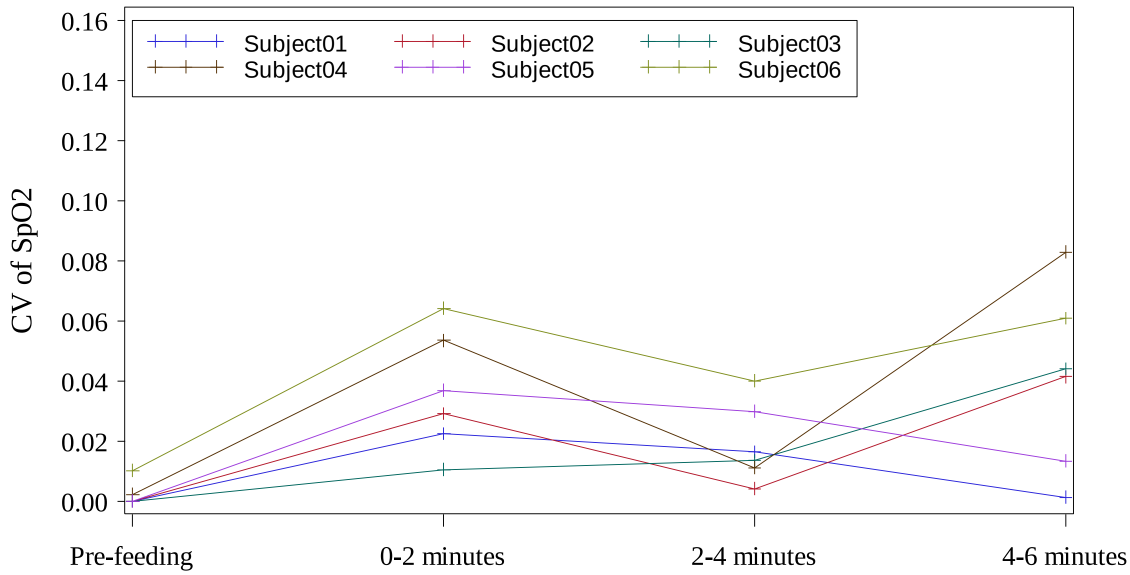
SD of SpO_2 in the HEL position



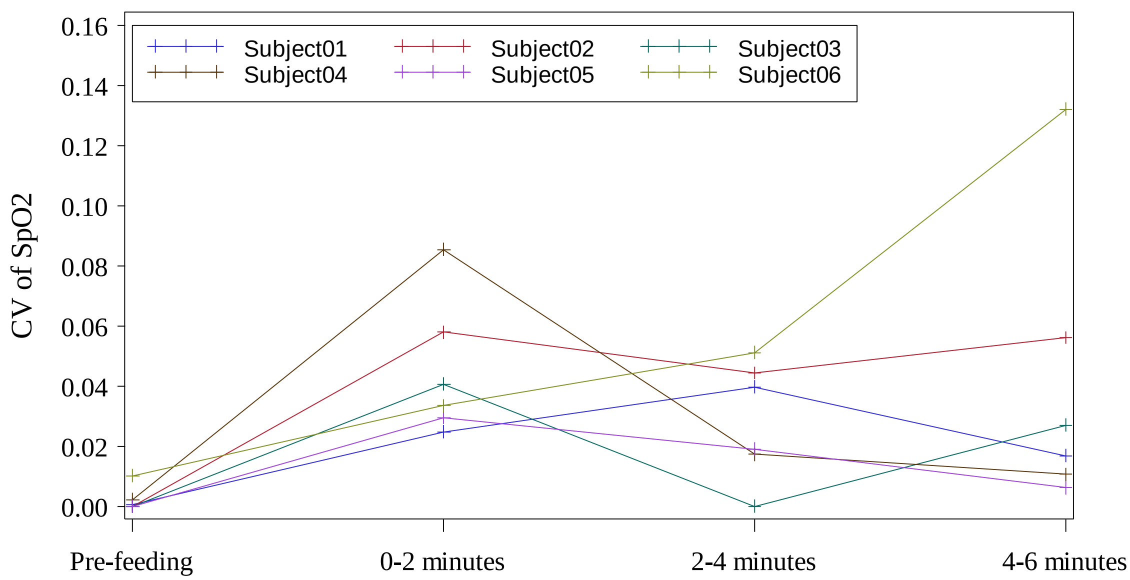
SD of SpO_2 in the HES position



CV of SpO_2 in the HEL position



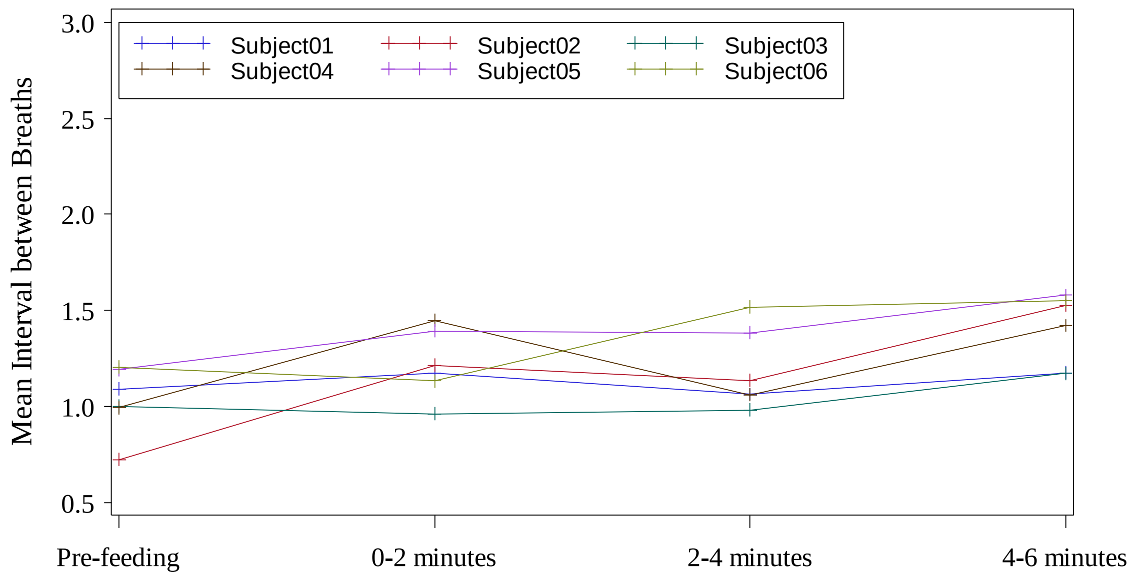
CV of SpO_2 in the HES position



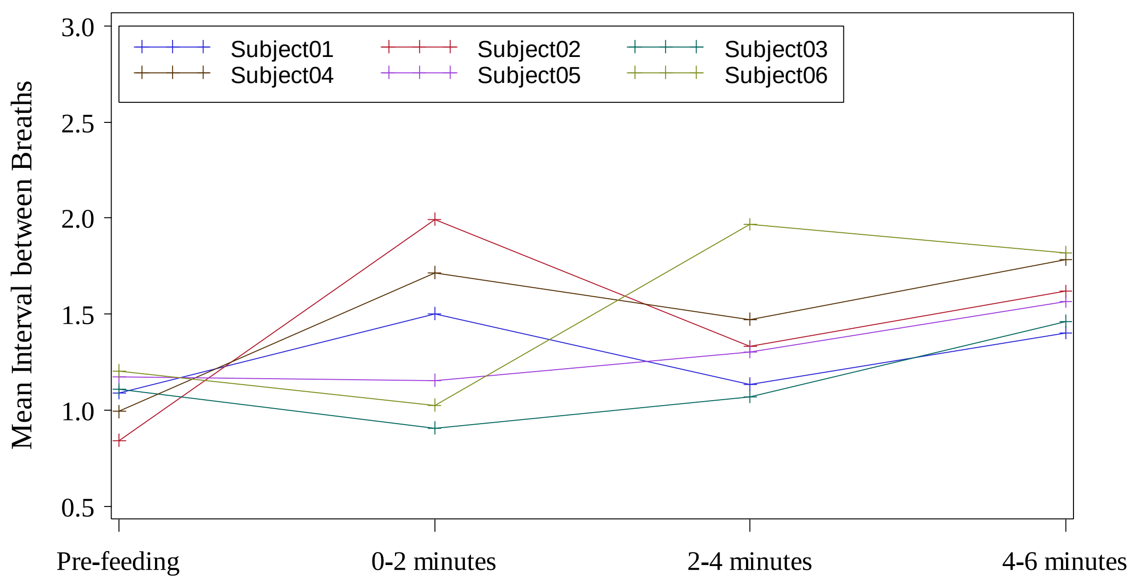
Appendix M. Plots of Individual Respiratory Characteristics

1. Interval between Breaths

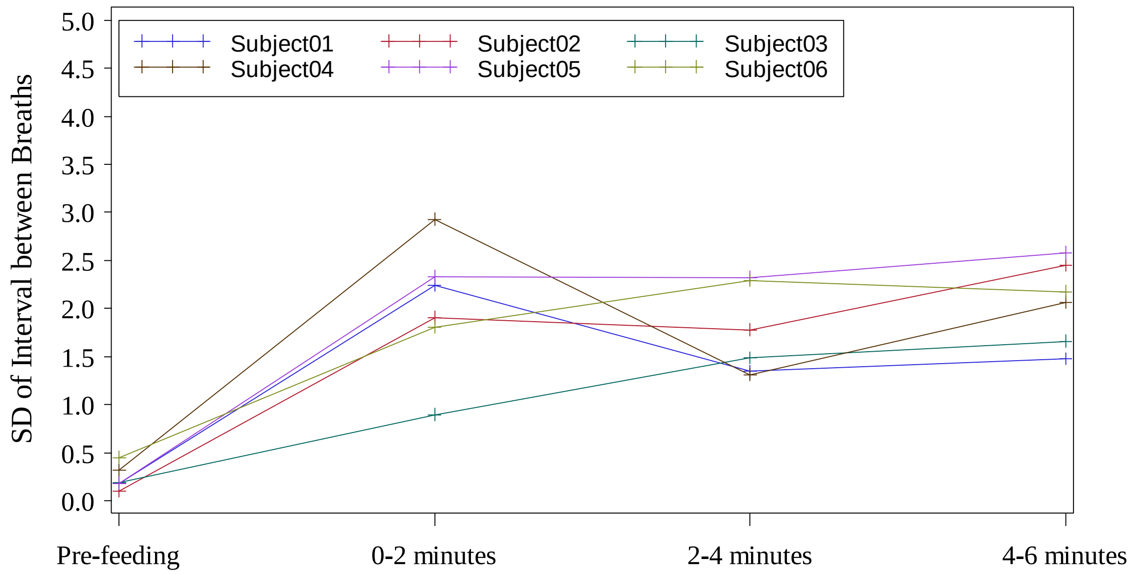
Mean Intervals between Breaths in the HEL position



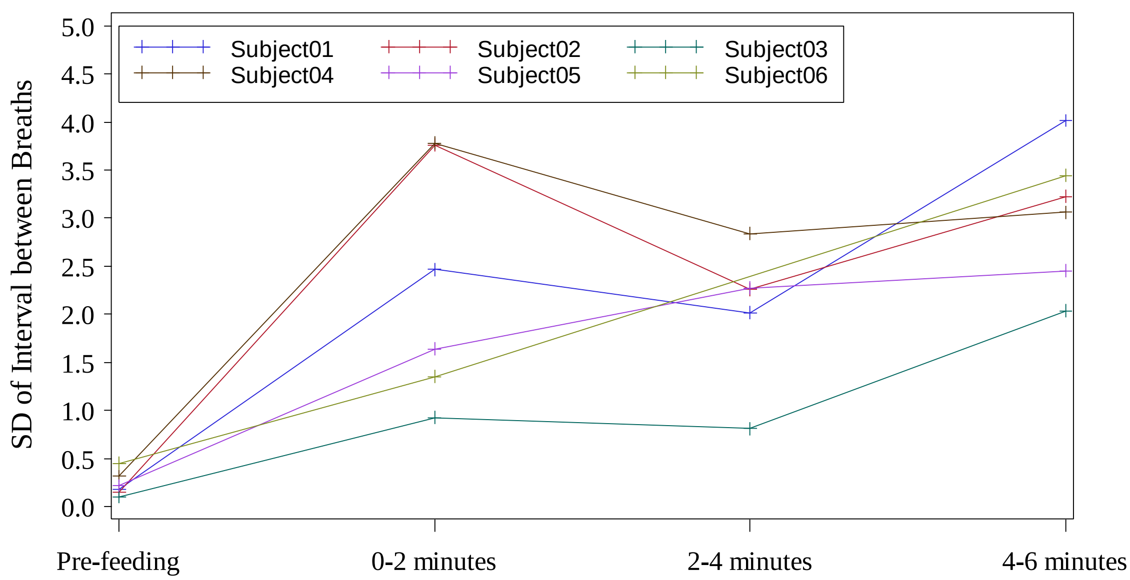
Mean Intervals between Breaths in the HES position



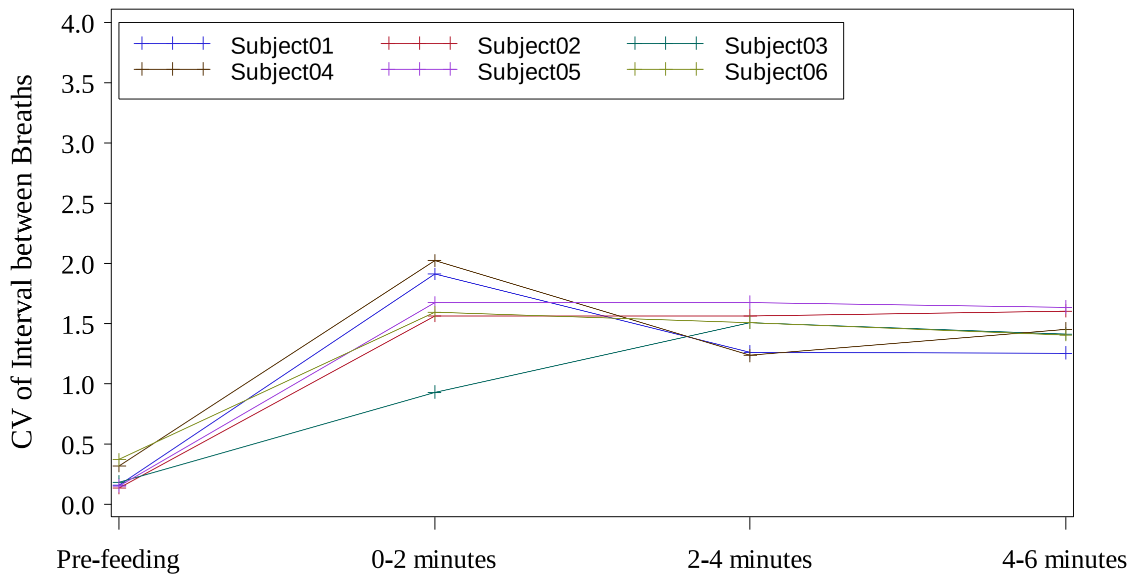
SD of Intervals between Breaths in the HEL position



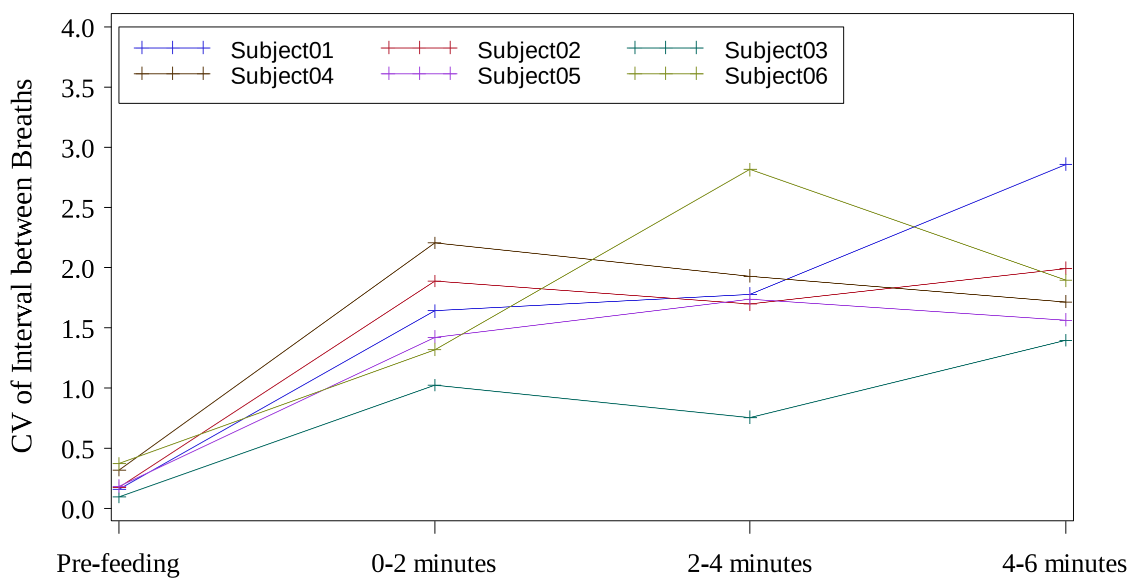
SD of Intervals between Breaths in the HES position



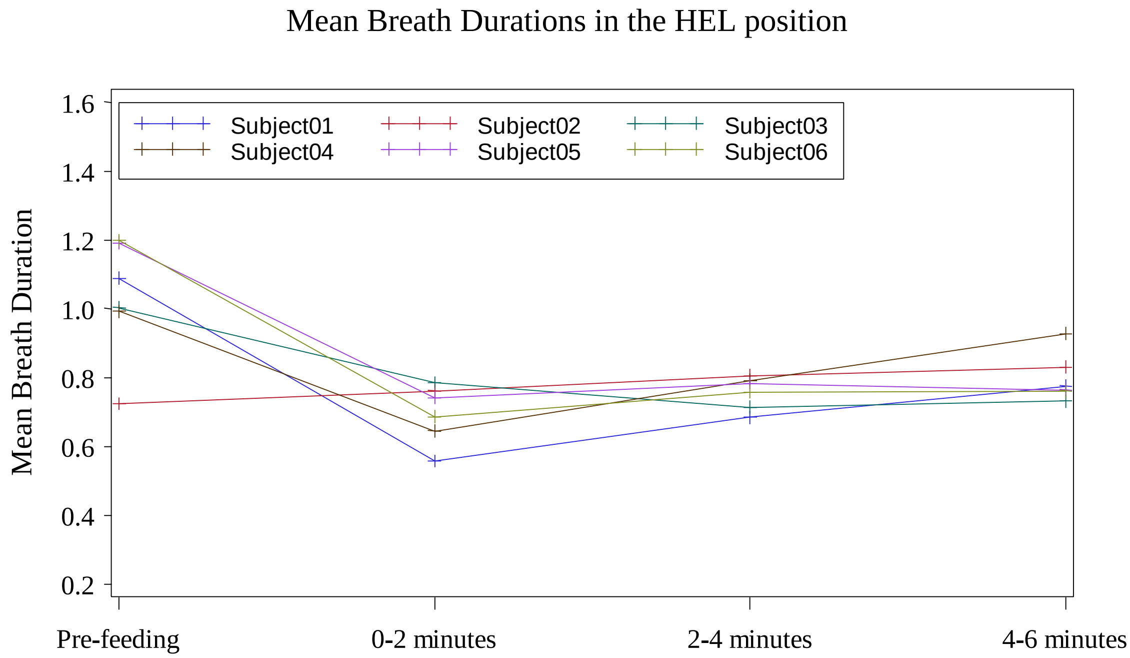
CV of Intervals between Breaths in the HEL position

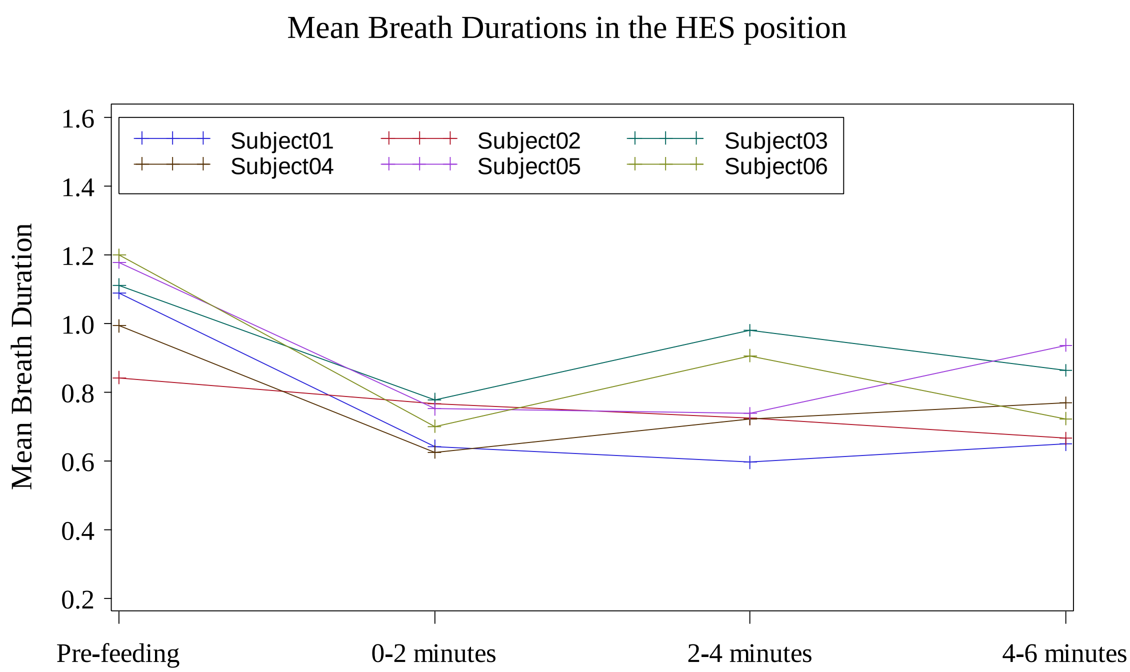


CV of Intervals between Breaths in the HES position

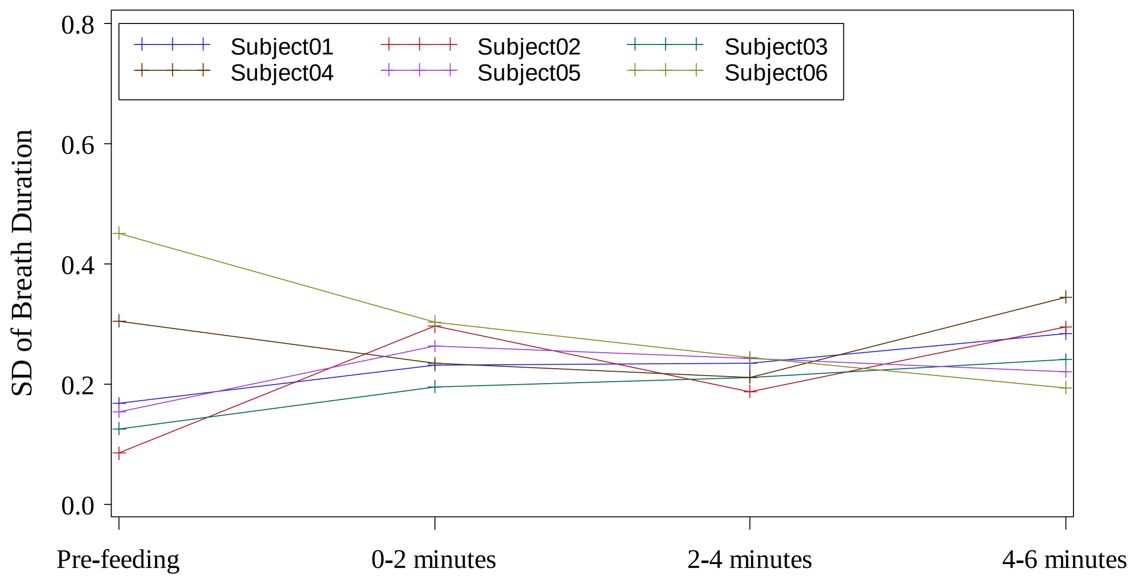


2. Breath Duration

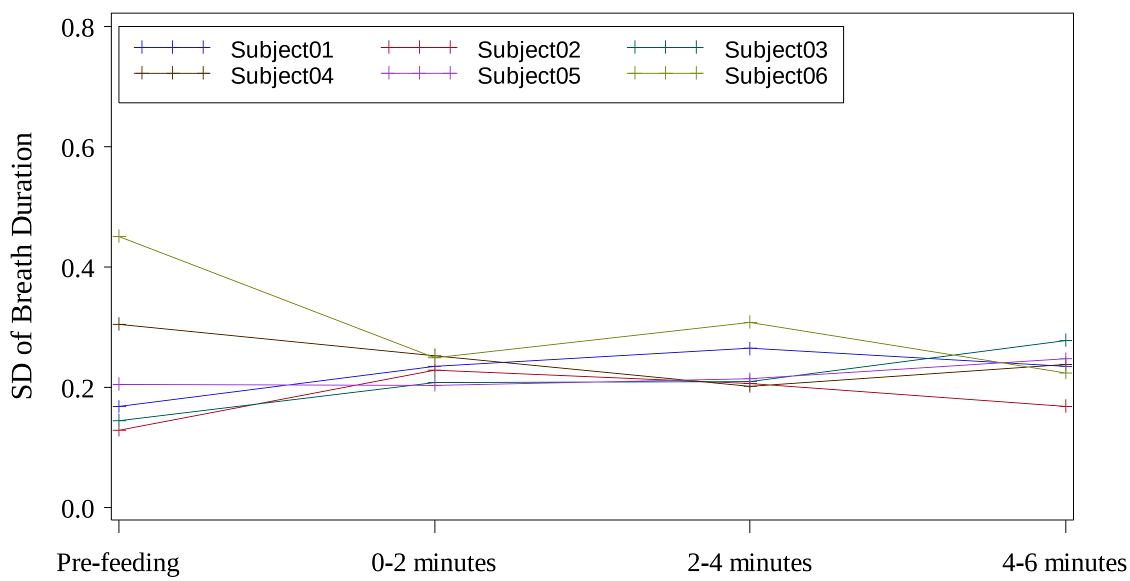




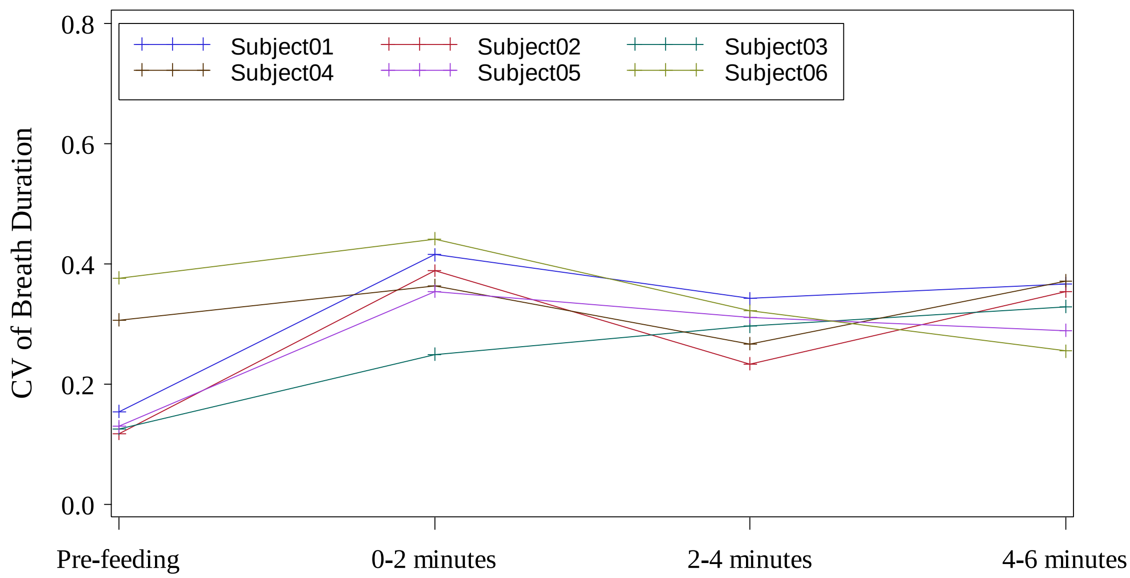
SD of Breath Durations in the HEL position



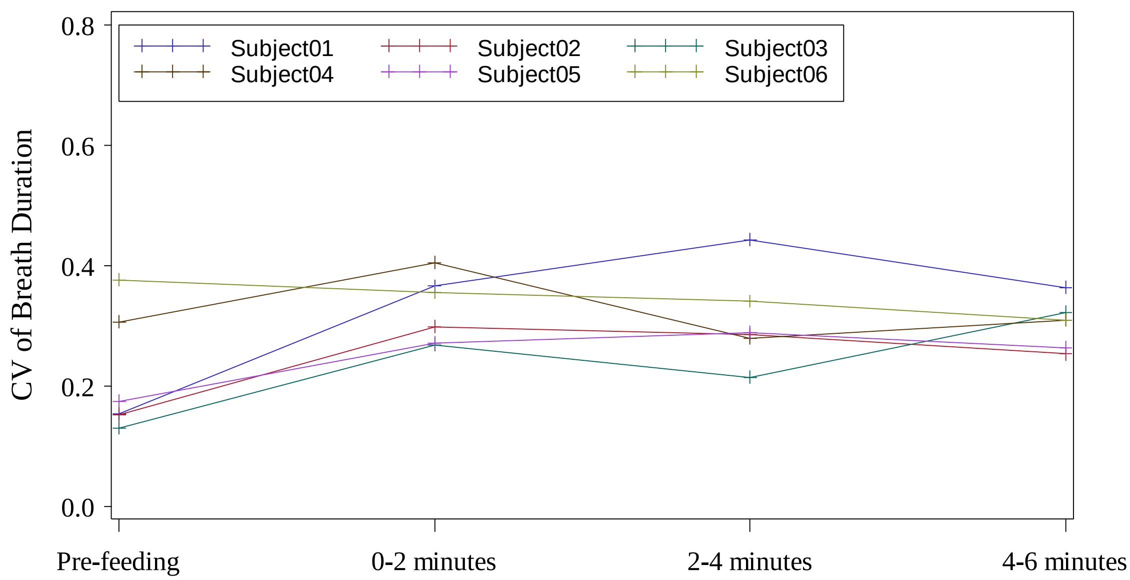
SD of Breath Durations in the HES position



CV of Breath Durations in the HEL position

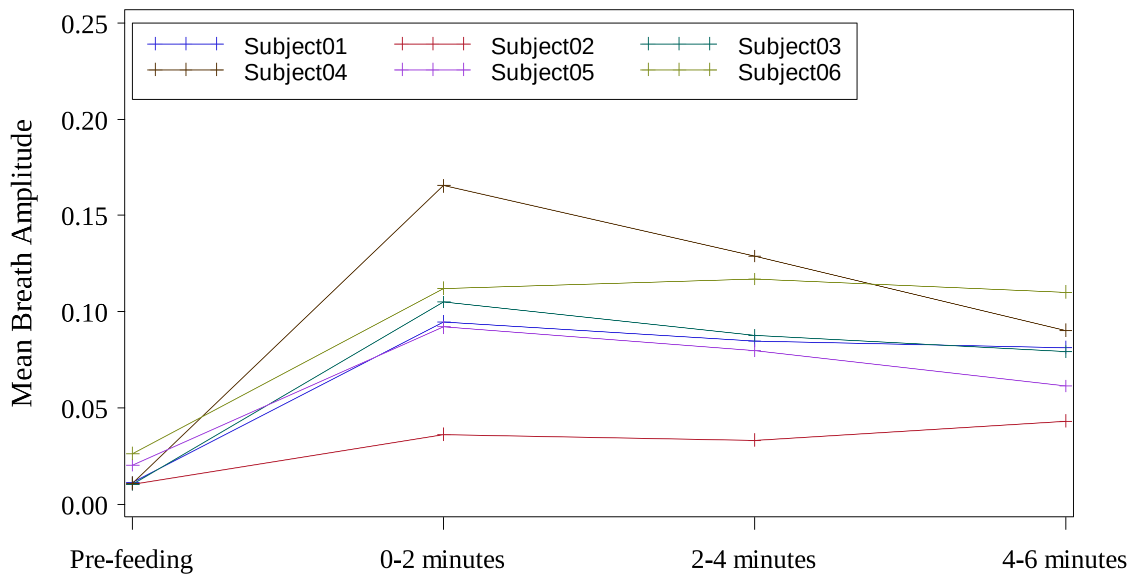


CV of Breath Durations in the HES position

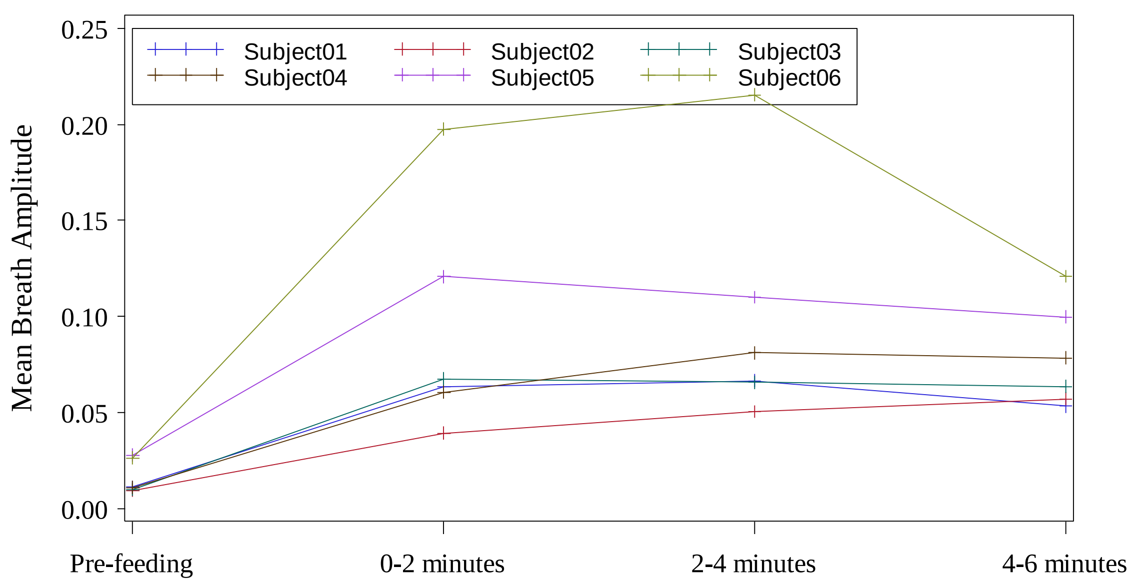


3. Breath Amplitude

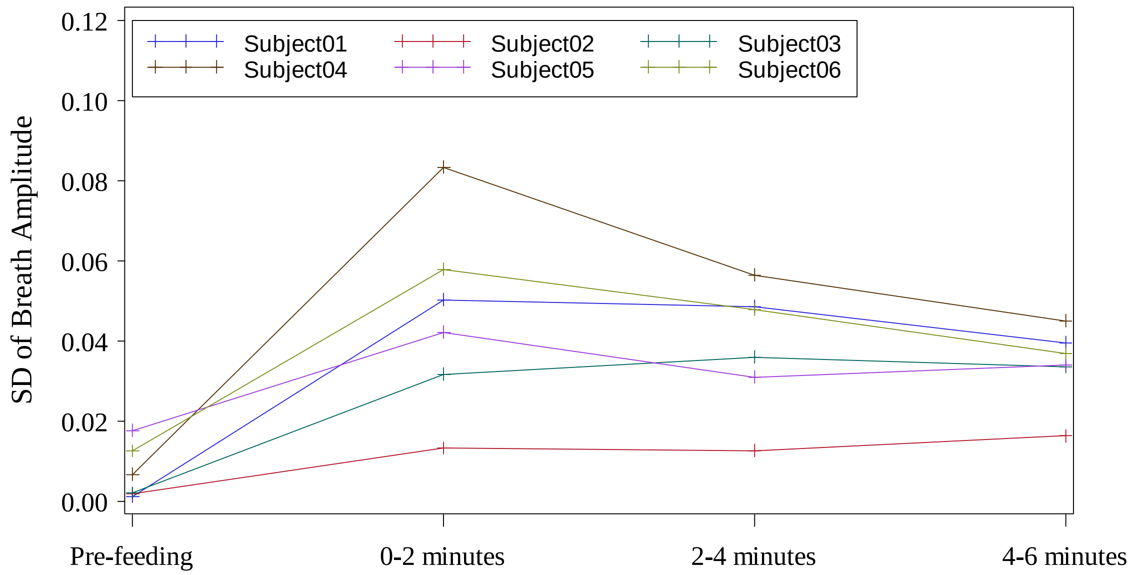
Mean Breath Amplitudes in the HEL position



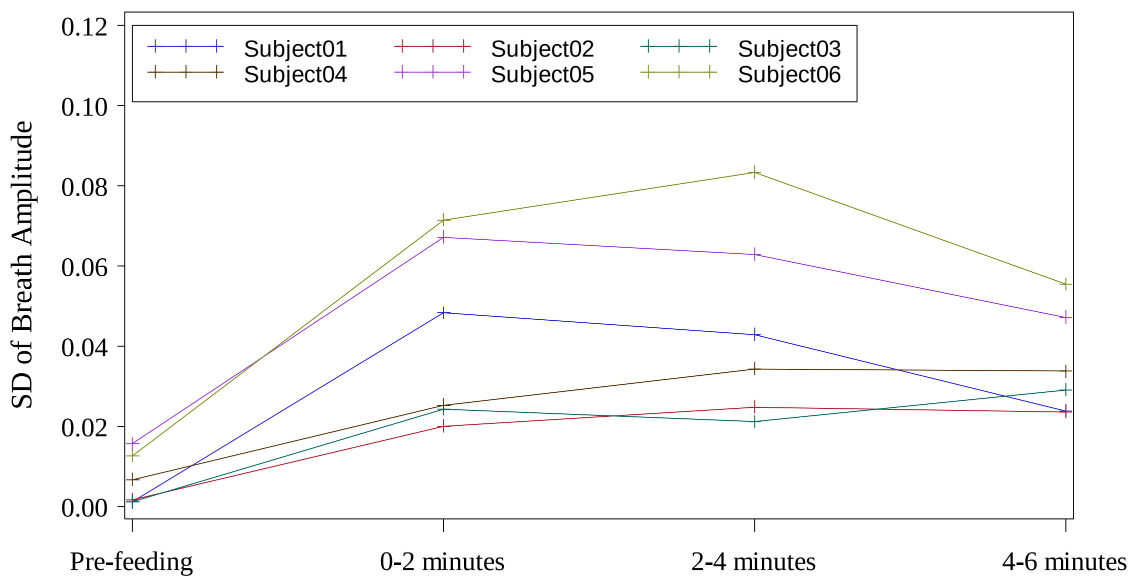
Mean Breath Amplitudes in the HES position



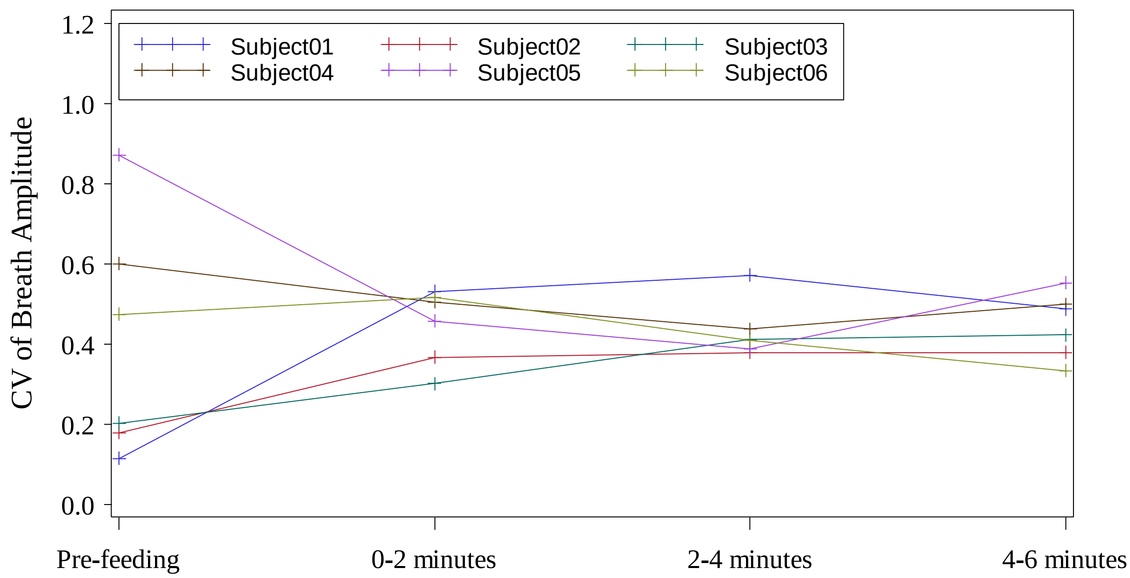
SD of Breath Amplitudes in the HEL position



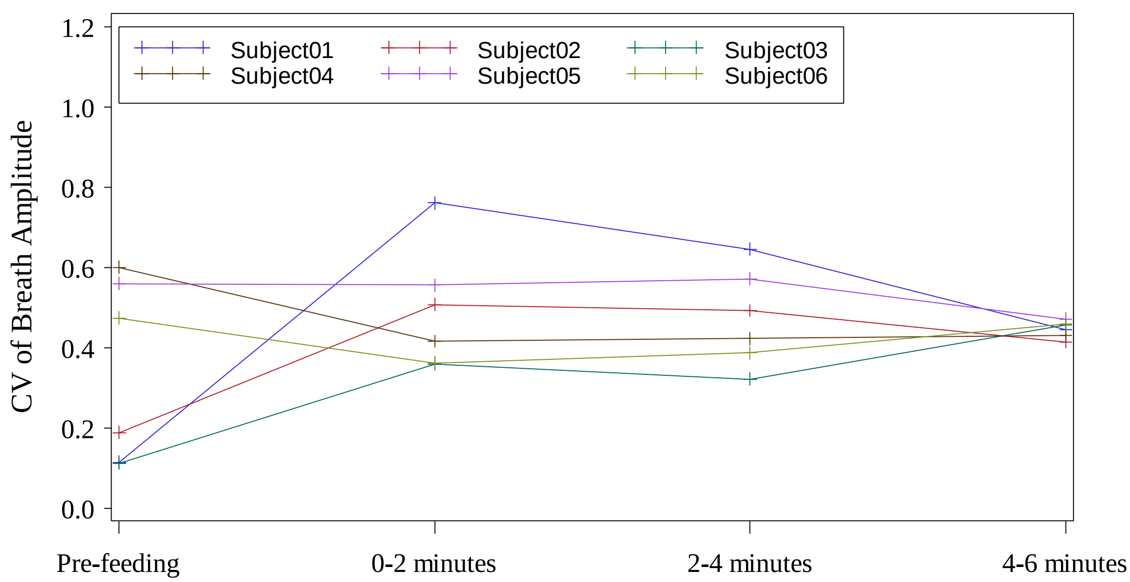
SD of Breath Amplitudes in the HES position



CV of Breath Amplitudes in the HEL position



CV of Breath Amplitudes in the HES position



Appendix N. Protocol to Set up Infant Feeding Data Collection Cart

STEP 1. PREPARATION

Check out everything that belongs on the feeding cart.
If there is missing or broken items, purchase or make the new one.
Before going to the nursery, disassemble all equipment from the cart and clean them all with disinfectant wipes, then re-assemble them.

Equipment		Laptop & wireless mouse
		BioNex Chassis
		Masimo Radical-7 Pulse Co-Oximeter
		Panasonic HDC-TM700
		Samba 201 Micro Pressure Measurement System
Instrument		<Primary>
Sucking		Feeding bottle
		Storage bottle
		Transducer sensor
		Measured bibs (2x)
Respiration		Piezo Respiration band
		Pulse oximeter cable & adhesive sensor
		Adhesive placement wraps (Red)
Hear rate		EGC leads
		Wet electrodes
Swallowing		Microphone set (mic, power supply, earphone, & 2 cables)
		Hydro gel tape
		Double sided tape
Others		Stopwatch
		Alcohol swabs
		Zip bag
		Tool bag (tapes, screwdrivers, cable ties, 2 AA batteries, 2 9v batteries, scissors, and hemostats)
		Extension cord
		<Extra>
		Feeding bottle
		Measured bibs
		Piezo Respiration band
		Wet electrodes
		Pulse oximeter adhesive sensor
		Pulse oximeter replacement wrap
		Hydrogel tape and double sided tape for the mic
File folder		History of Hospitalization & Feeding Data Collection Form with stamp from IRB
		Protocols (intervention & data collection) with stamp from IRB
		Informed consent form with Stamp from IRB
		HIPPA authorization form with Stamp from IRB

STEP 2. SET UP THE BIONEX CHASSIS

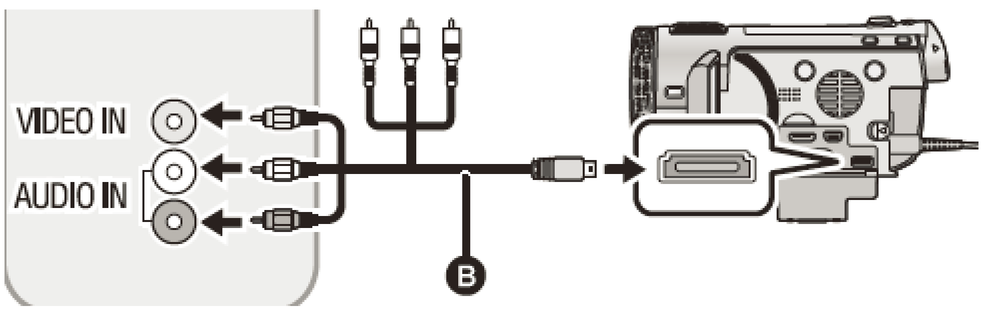
Connect the BioNex Chassis to power
Connect to power, using the DC IN post on the back panel of the BioNex Chassis. *Press the power button on the back panel of the BioNex Chassis. Make sure the green power light on the front panel is on.*

Connect the BioNex Chassis to the Lenovo laptop.
Use the USB cable to connect the BioNex Chassis to the USB port on the laptop.

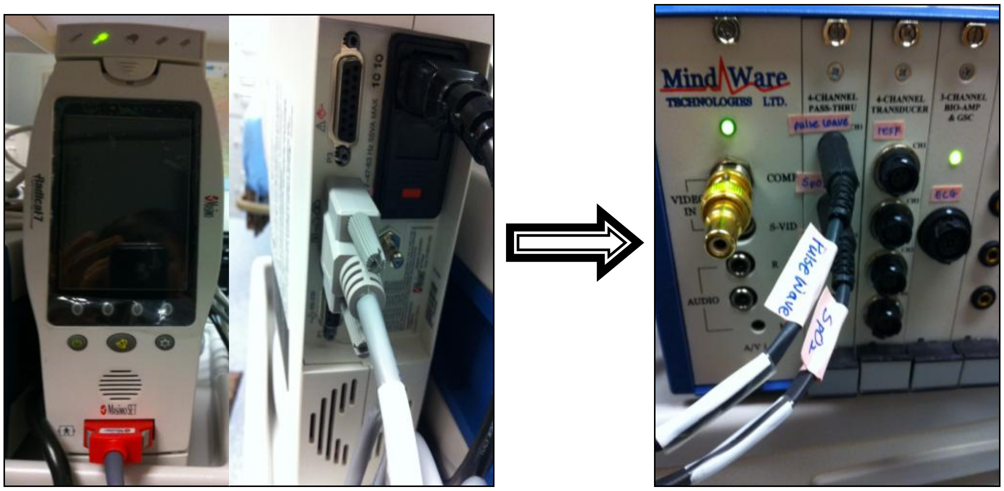
Connect the equipment to the BioNex Chassis

<u>Panasonic HDC-TM700</u>

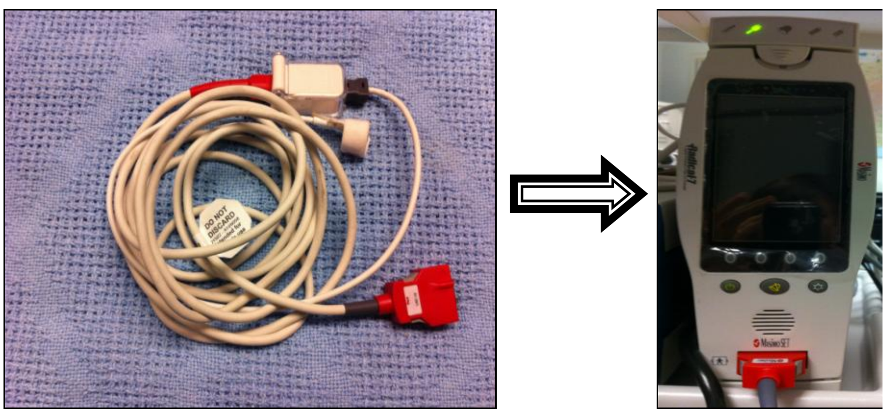
: Using AV multi-cable, connect video cable (Yellow) to the COM port on the video amplifier and connect audio cables (Red and white) to either R or L on the video amplifier. Connect the other side of the cable to the AV multi connecter on the right bottom of the Panasonic HDC-TM700.



<u>Masimo Radical-7 pulse co-oximeter</u>
: Using analog output cable, connect the two mono jack to channel 1 (pulse wave), channel 2 (SpO_2) on the 4-channel pass-thru amplifier. Connect the serial output cable to the analog output connecter on the back of the Masimo Radical-7 pulse co-oximeter.

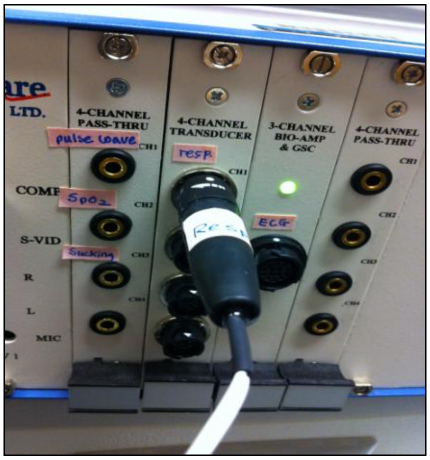


Connect the pulse oximeter cable and sensor to Masimo pulse oximeter.

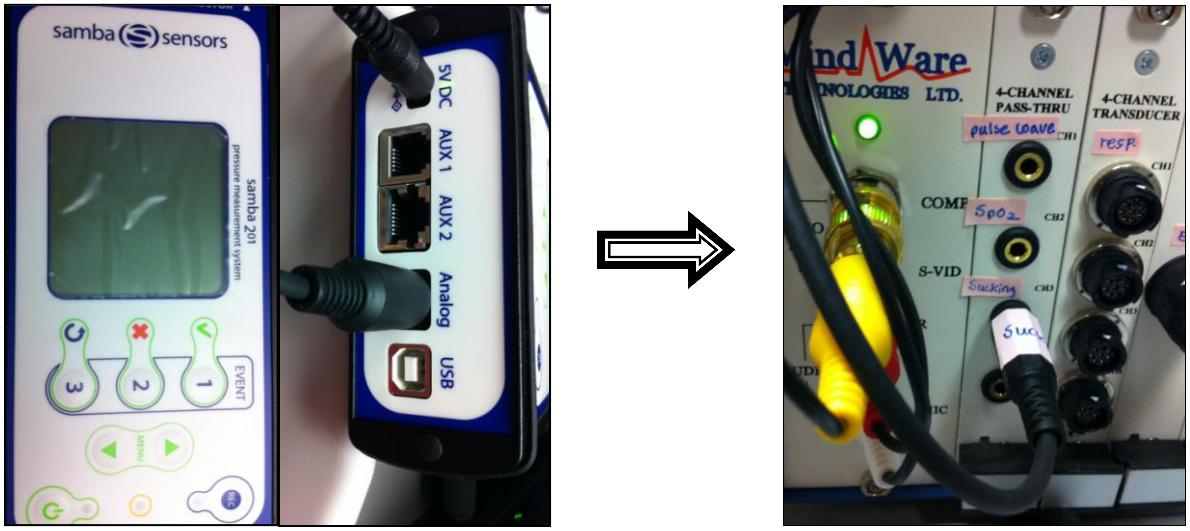


Respiratory effort system

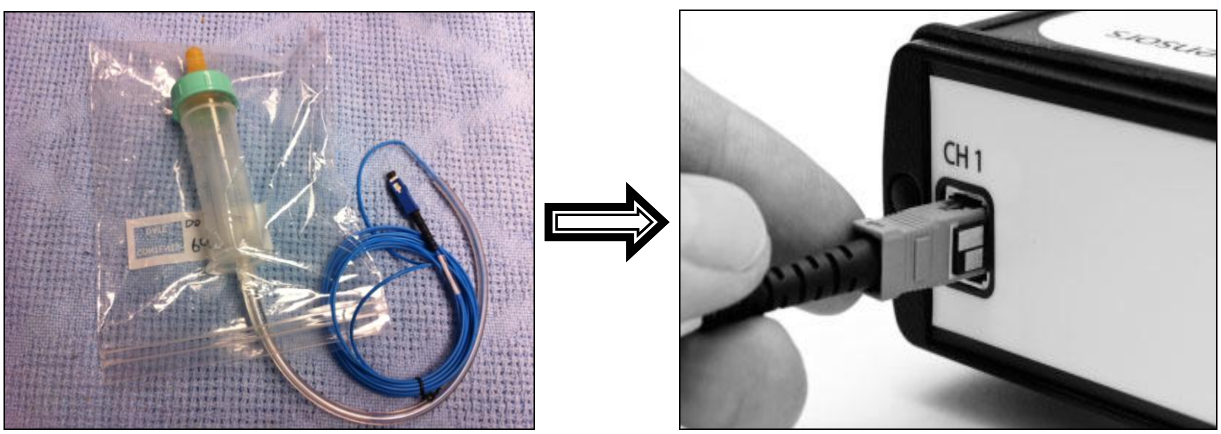
: Connect the respiration band to the first channel (respiration) on the transducer amplifier.



<u>Samba 201 micro pressure measurement system</u>
: Connect the analog output cable from micro pressure measurement system to channel 3 (sucking) on the 4-channel pass-thru amplifier.

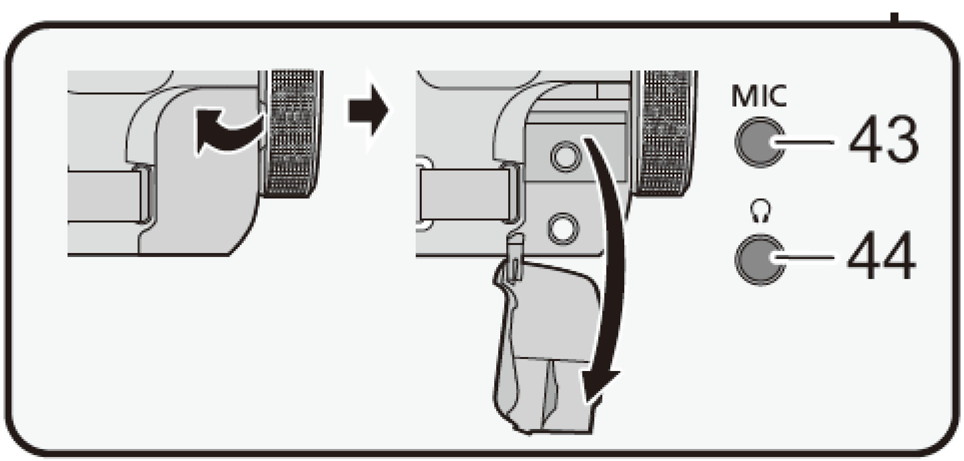


Connect the transducer to the optical connector on the side of the Samba 201 control unit. *Note. The caps to protect the optical sensor need to be uncovered and re-caped after the completion of data collection.*



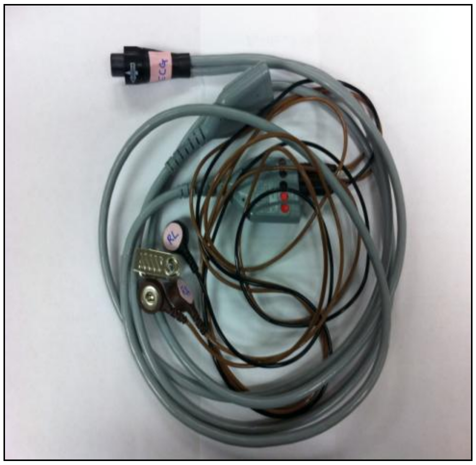
Audio Trainer
: Connect the microphone to the camcorder (mic-see 43 on the picture at the bottom of this page) to transmit the sound into the video clips.

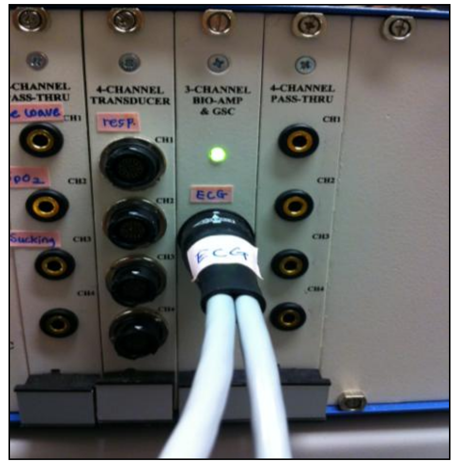
To send the microphone signal out, connect the analog out cable to mono jack connected to headphone terminal [🎧] (see 44 on the picture at the bottom of this page) and connect the other side of the cable to channel 3 (swallowing) on the 4-channel pass-thru amplifier. To hear the sound during feeding, connect the earphone to stereo jack.



BioNex 3-Channel Bio-Potential and GSC amplifier

: Connect the ECG cable to the 3-Channel Bio AMP &GSC amplifier.

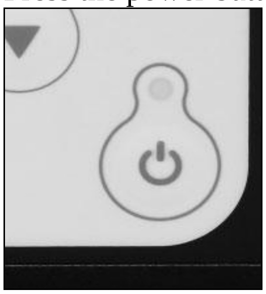




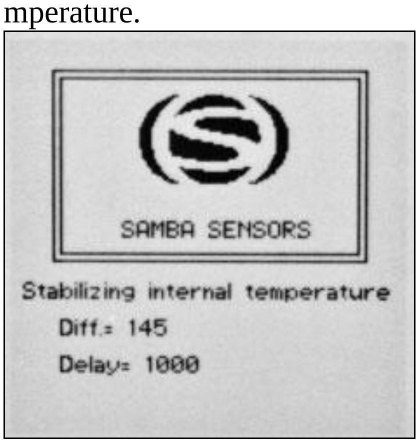
STEP 3. SET UP INITIAL SETTING FOR THE EQUIPMENT

Samba 201 Micro Pressure Measurement System

- Press the power button and hold it down for 5 seconds to turn it on.

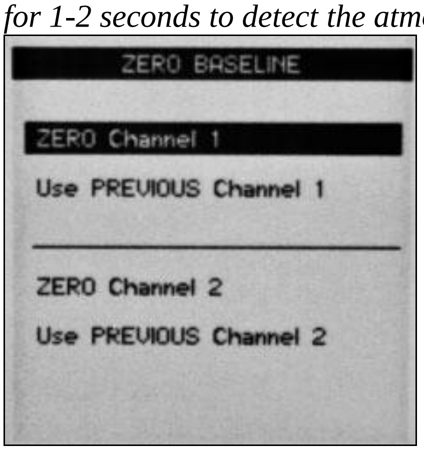


- The warming up process takes between 1 and 2 minutes depending on the ambient te mperature.

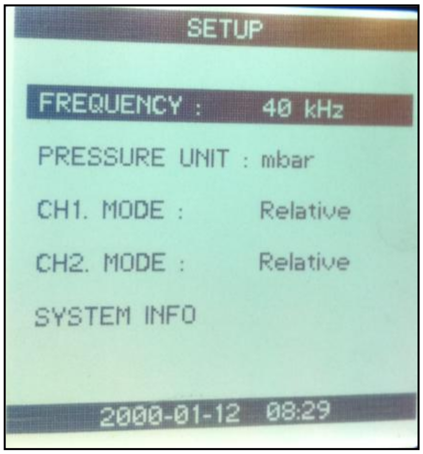


- After warming up, the Samba 201 will search for the connected transducer.

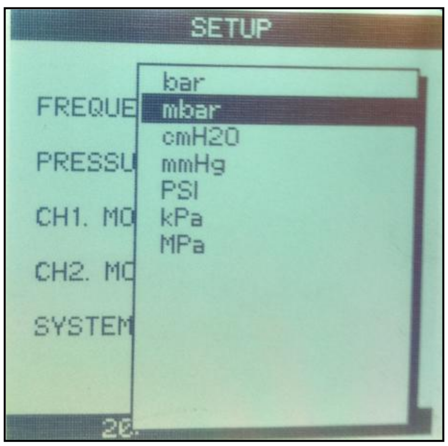
- When the Zero Baseline setting window appears, highlight 'ZERO Channel 1' and pr ess button 1 to synchronize the pressure value received from the transducer sensor an d the value registered by the internal barometer. *Note. Detach the nipple from the bott le before you press button 1 because the transducer tip needs to be exposed to the air for 1-2 seconds to detect the atmosphere pressure as a zero baseline.*

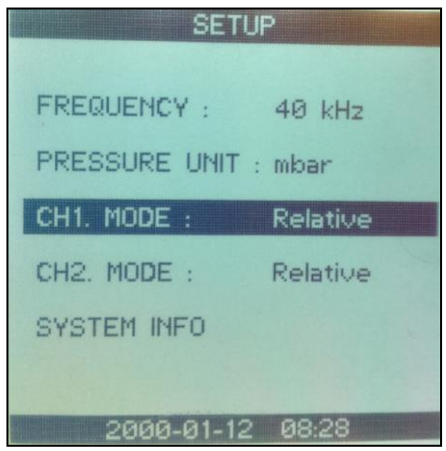


- Enter Menu<SETUP, highlight frequency 40Hz using the menu navigation keys and press 1 to confirm.

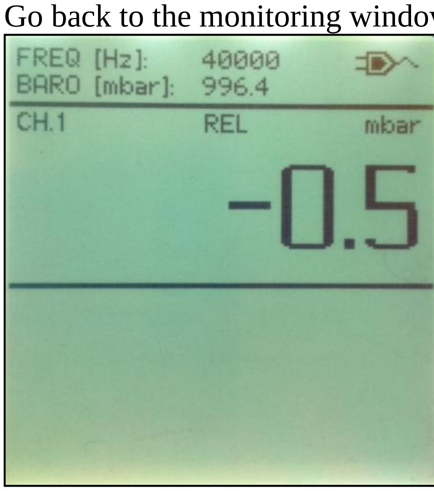


- In the same manner, set pressure unit (mbar), and measurement mode (relative). *Note. 'Relative value' is a change from the zero baseline which will be atmosphere pressur e and 'Absolute value' is a value that adds a change of pressure to the zero baseline.*



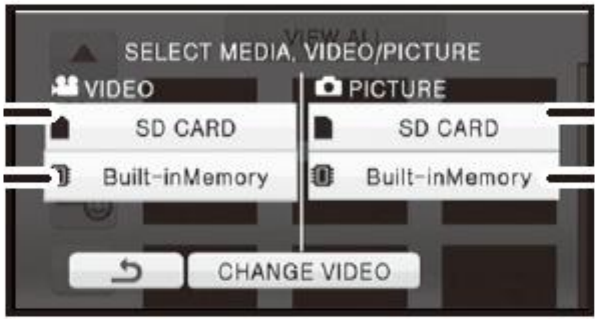


- Go back to the monitoring window by pressing button 3.

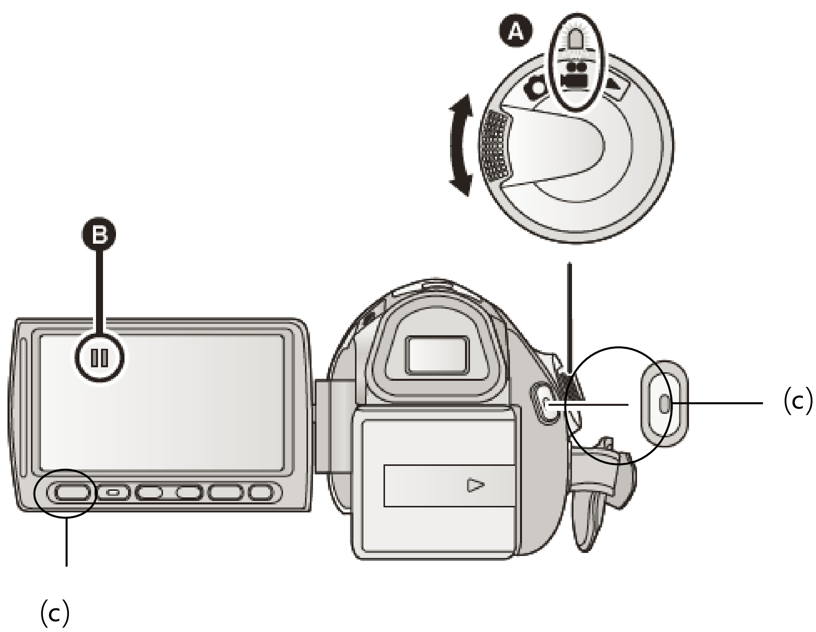


Panasonic HDC-TM700

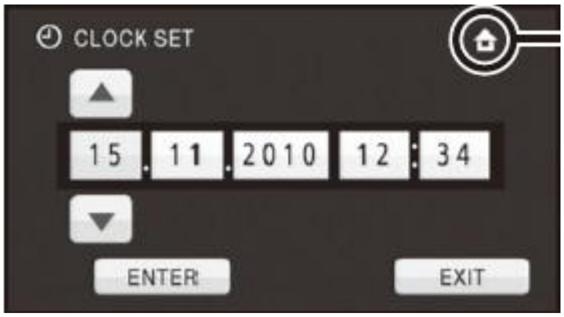
- Open LCD monitor and hit the power button [⏻/I] .
- If you see the screen to ask the output mode, then touch ‘A/V output’.
- If you see the screen to ask the type of memory, then touch ‘Built-in Memory’.



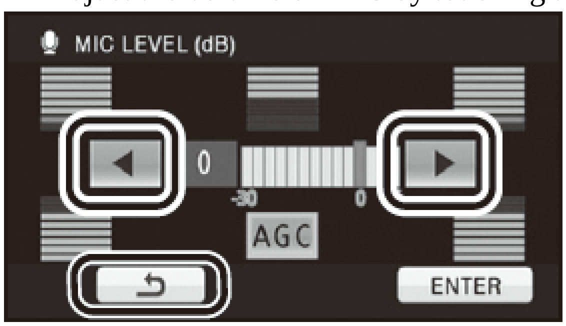
- Select a motion picture recording mode
  - ✓ Select the motion picture recording mode (A) by turning a mode dial.
  - ✓ Press record start/stop button to start recording (C). *When you begin recording, will change to* (B).



- Set date and time
  - ✓ MENU<SETUP<CLOCK SET
  - ✓ Touch the date and time to be set, and then set the desired value using the arrow b utton▲/▼.



- Adjust the MIC volume
  - ✓ MENU<RECORD SETUP<MIC LEVEL<SET+AGC
  - ✓ Adjust the volume of MIC by touching arrows and touch ‘ENTER’ to confirm.



  - ✓ Touch ‘EXIT’ to go back to recording window.

- Adjust the headphone volume
  - ✓ Touch the LCD screen and you can see ‘F’ arrow on the left bottom of the screen.

  - ✓ Touch the ‘F’ arrow and go next using the arrow on the right side until you can se e the symbol of headphone.

✓ Touch the symbol of headphone and adjust the volume using the arrows.

✓ After adjusting the volume, touch the ‘F’ arrow again to exit.

Masimo Radical-7 pulse co-oximeter

- Turn the power on.
- Set the averaging time as 2 seconds.
  - ✓ Press menu button
  - ✓ Press the next icon until "general" is highlighted and then press the menu button to select this parameter
  - ✓ Select "averaging time" by hitting the menu button again and then change averaging time to 2 second using or icon and hit to confirm.
  - ✓ Press check icon to accept this setting and then exit .

- Decrease the volume of the pulse beep
  - ✓ Press and press the decrease loudness button until the volume of the pulse beep is gone.

- Alarm off.
  - ✓ Press menu button , select alarm, and set the alarm condition as 'all mute'. *Note. Alarm will be indicated by the alarm sign flashing on the left side of the Masimo machine.*

- Set up the clock if you want to download the trend data
  - ✓ Press menu button
  - ✓ Press the next icon until "clock" is highlighted and then press the menu button to select this parameter
  - ✓ Select the desired value using or icon and press check icon to accept each value and then exit .

- Erasing trend memory before each data collection (Optional, if you want to download the trend data from the Masimo)
  - ✓ Press to access the trend menu
  - ✓ Press to enter the trend menu
  - ✓ Press two times to access the "clear trend" button
  - ✓ Press to delete trend data

STEP 4. SET UP CONFIGURATION OF THE BIOLAB 3.0.6 DATTA ACQUISITION PROGRAM

Turn on the Lenovo computer and select ‘computer log in only’ (put id:bnix and pw:kathy@24)

Turn on the BioNex Chassis and double click on the BioLab 3.0.6 icon. 

The configuration window will open.

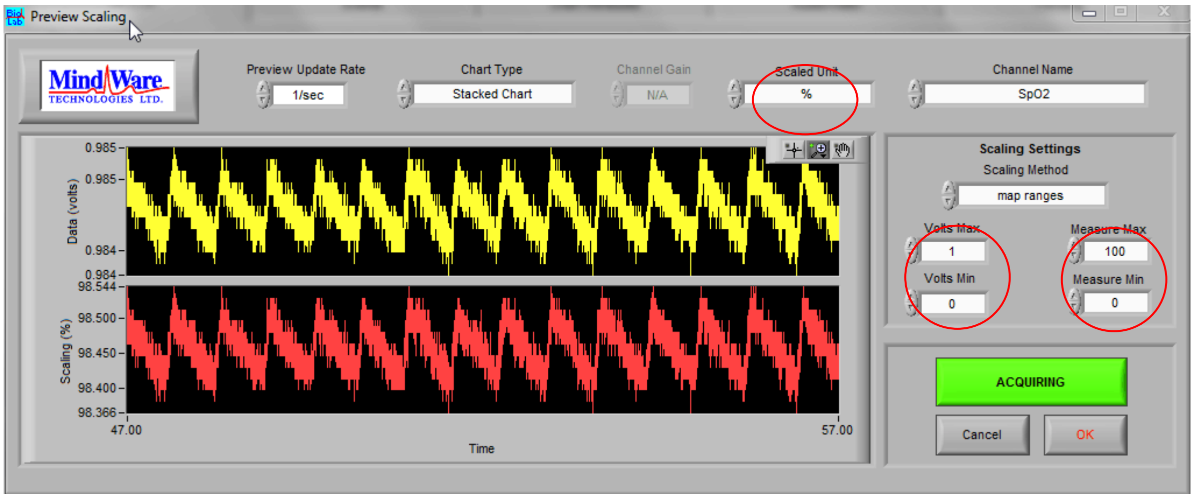
General Setting
Select sample rate (1000), acquisition mode (Continuous), and file mode (Auto Name). Under Chart Attribute tab, choose plot type as Stacked Chart.

Channel Setting

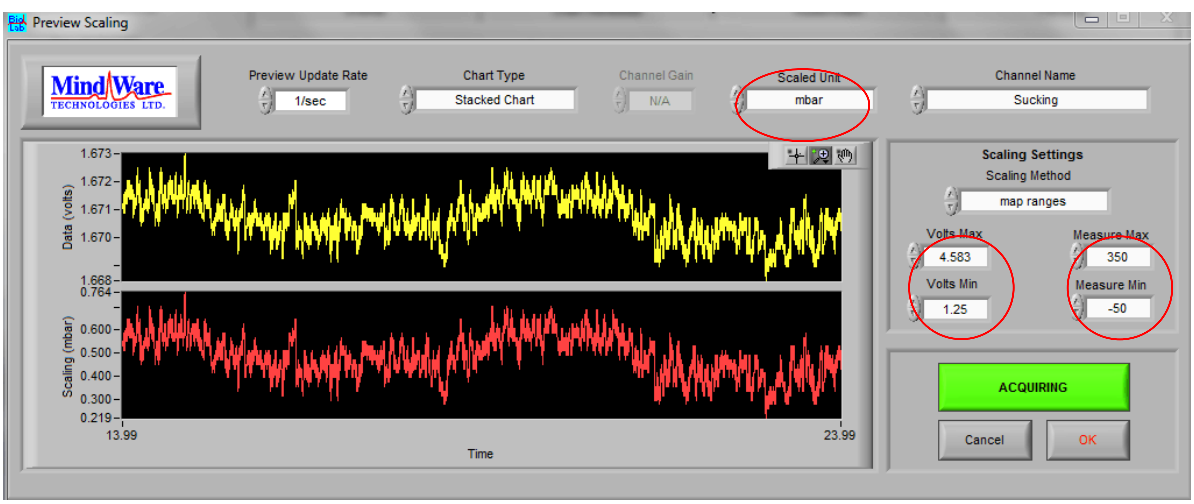
Enable channels needed by clicking ON/OFF on the left side of the configuration window and assign each channel as follows: channel 1(Pulse Wave), channel 2 (SpO_2), channel 3 (Sucking), channel 4 (Swallowing), channel 5 (Respiration), channel 9 (ECG).
Select the smallest amount of gain for channel 5 (50) and channel 9 (100).
Select the filter type as ECG for Channel 9.

Set up scaling for SpO_2 and Sucking channel

Channel 2 (SpO_2)
: Select 'Map range' to map voltage range to scale unit of SpO_2 and click view scale to open the preview scaling window. Set up scaling settings (scaled units: %, scaling method: map range, Volt max:1, Volt min:0, Measure Max: 100, Measure Min: 0) and click OK to confirm.

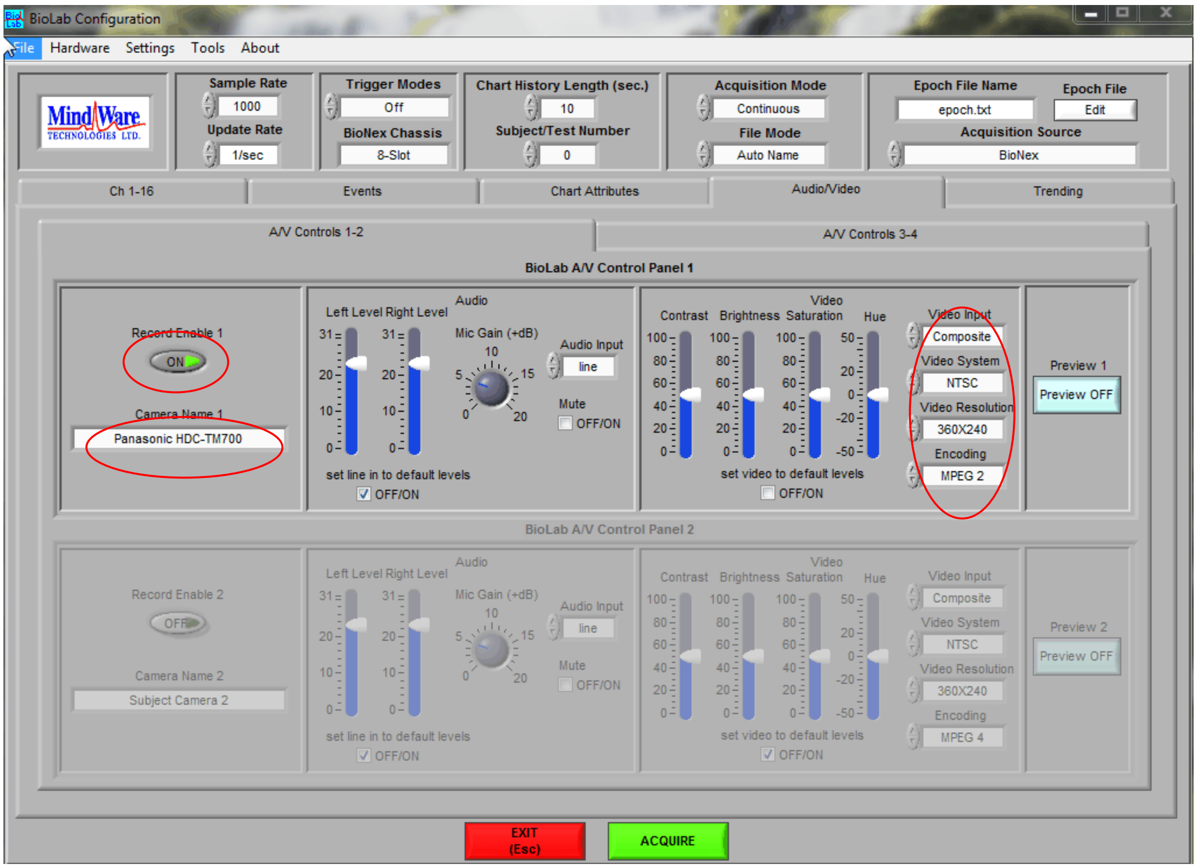


Channel 3 (Sucking)
: Select 'Map range' to map voltage range to scale unit of Sucking and click view scale to open the preview scaling window. Set up scaling settings (scaled units: mabr, scaling method: map range, Volt max: 4.583, Volt min: 1.25, Measure Max: 350, Measure Min: -50) and click OK to confirm.



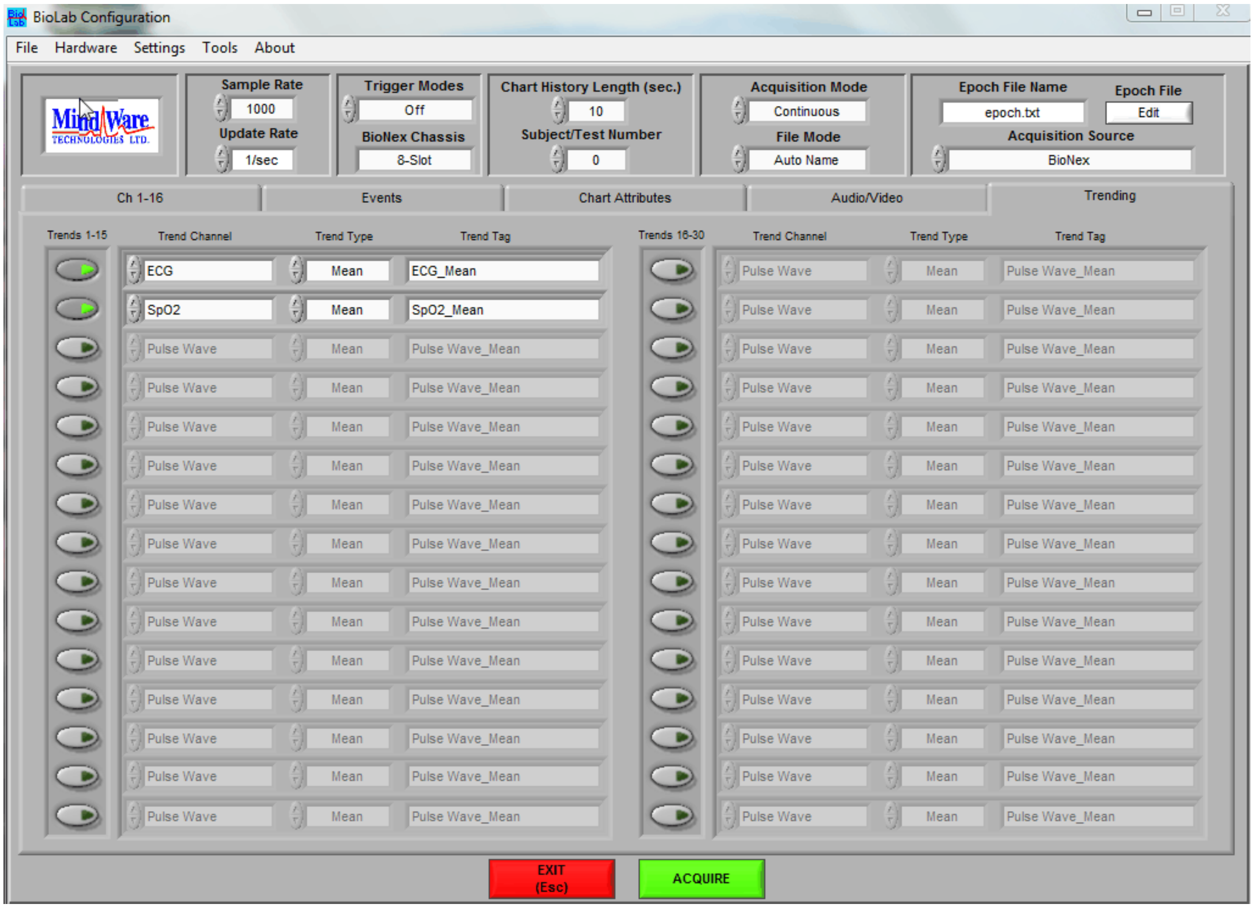
Audio/Video Setting

: Click ‘Audio/Video’ tap to set up module for video camera.
Enable Camera 1 by clicking ON.
Put Camera Name as “Panasonic HDC-TM700”
Set up Audio input (Audio input: line) and Video input (Video input: Composite, Video system: NTSC, Video resolution: 360*240, Encoding: MPEG2)
Check the video file by clicking preview and adjust the quality of the video if needed.



Set up Trending

Click 'Trending' tab to extract the trending data for HR and SpO2 every second from ECG and SpO_2 waveform sampling at 1000 samples per second. Enable the first two trends by clicking ON/OFF button. For the first trend for HR, select 'ECG' for the trend channel, 'mean' for the trend type. For the second trend for SpO_2, select 'SpO2' for the trend channel, 'mean' for the trend type.



Save all setting (Setting<Save Configuration as).

Created and updated by Jinhee Park on 6/27/2011

Appendix O. Protocol for Data Collection

Before leaving the lab

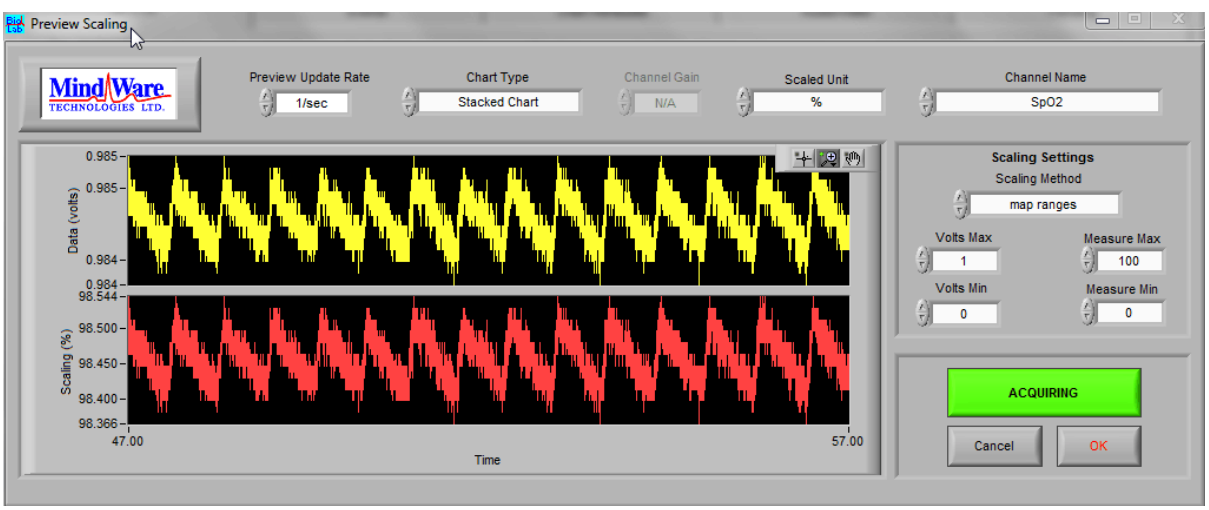
- Check out everything that belongs on the feeding cart (use the check list)
- Turn on the Lenovo computer and select 'computer only log on' (put id:bnix and pw: kathy@24)
- Turn on the BioNex Chassis and all the equipment and open the BioLab 3.0.6 icon.
- Open the BioLab 3.0.6.
- Open the configuration file (JP MW cfg.nwcfg) that previously set up and saved on th e JP dissertation folder on the desktop.
- Check out the initial setting of the equipment
  - ✓ *Samba 201:* Frequency (40Hz), Unit (mbar), Measurement mode (Relative)
  - ✓ *Panasonic HDC TM700:* Check out the date and time.
  - ✓ *Masimo pulse oximeter:* Averaging time (2 seconds), alarm and pulse beep sound (off), the date and time

- Check out the setting of the configuration window.

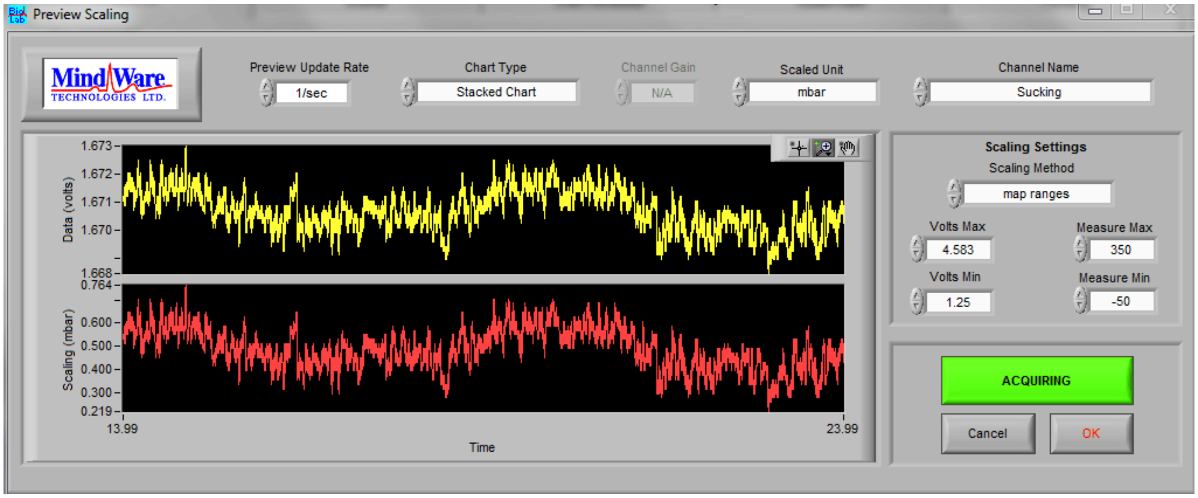
<u>General setting</u>

Channel setting

Scale setting for SpO2 channel

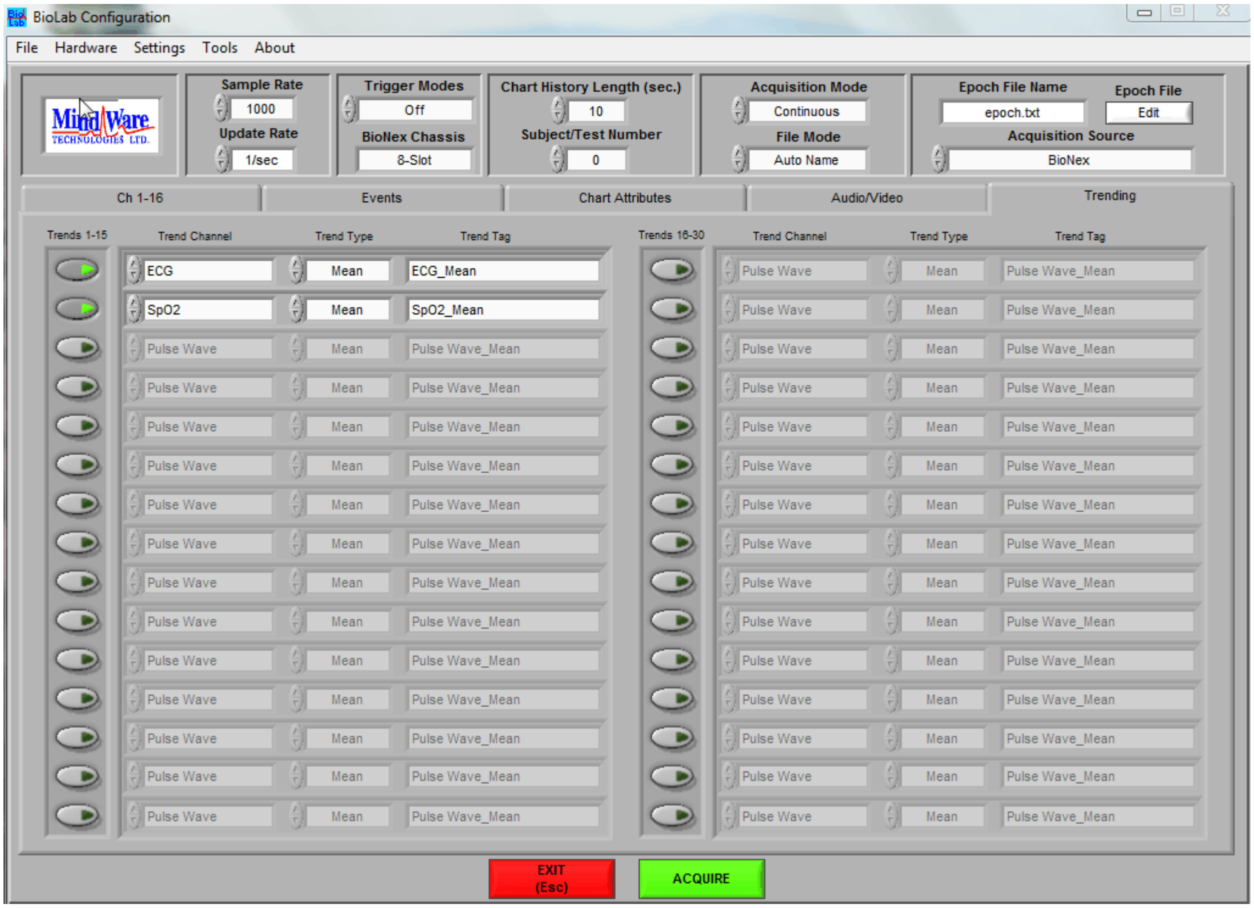


Scale setting for Sucking channel



Audio/Video Setting

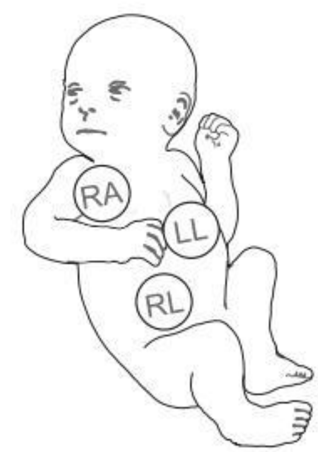
Trending setting



- Exit the BioLab program.
- Shunt down the all equipment and computer.
- Disconnect the pulse oximeter sensor, transducer, respiration band, EKC leads, and microphone set from the equipment and put them back into the first drawer.
- Fold the camera up inside the room under the top of the cart.
- Remind which position will be the first. *Note. Determine if which position would be the first by picking a paper from the envelop for the first subject. From the second subject, the order of the position will be alternated.*

In the nursery

- Make environment be as quite as possible (Pull the curtain down, Dim the light etc)
- Connect the cables to the BioNex Chassis and to the equipment
- Turn the computer on (*The receiver of wireless mouse must be unplugged from the U SB port before you turn on the computer*).
- Turn on the power of the BioNex Chassis and all equipment (Pulse oximeter, Pressure measurement system, Microphone, ECG, and camera)
- Open BioLab 3.0.6.
- Open the configuration file (JP MW cfg.nwcfg) that previously set up and saved on th e JP dissertation folder on the desktop.
- Put sensors to a baby
  - ✓ *Pulse oximeter: Place pulse oximeter sensor on the infant's foot without their own pulse oximeter sensor and secure with additional placement wrap.*
  - ✓ *ECG: place electrodes on the infant's chest as below. Note. Do not remove the inf ant's own electrodes if he/she has but you can move them if needed.*



  - ✓ *Respiration: Place respiratory band around the infant's chest at nipple level on th e top of the infant's clothes.*
  - ✓ *Microphone: Place the mic on the infant's mid neck at the suprasternal notch wit h a double-sided tape and secure with a hydrogel tape.*

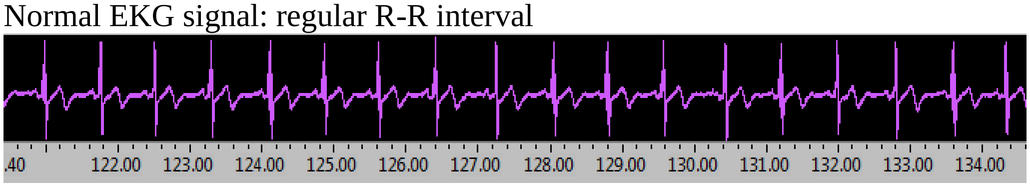
- Make sure the signals are all good before the infant is settled.
- Let all instruments warm up 30 min

Baseline data collection

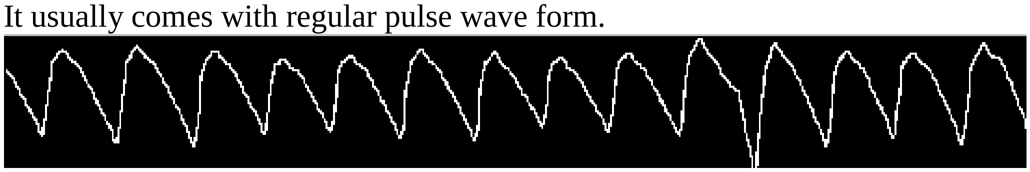
- Begin to record at least 30 minutes before scheduled feeding time (When recording, you can see green light on the right bottom)
  - ✓ *Click AQUIRE on the bottom of the configuration window*
- Enter the name of the file in the Jinhee's dissertation folder based on the following order: study name, subject ID, the order of feeding, condition. (i.e., JP01F1HES: JP=Jinhee Park's dissertation, 01=the first subject, F1=the first feeding on that infant, HES=head elevated supine position).
- Hit START/STOP button on the upper left of the BioLab acquisition screen to start recording.
- Hit record button on the video camera
- Send the analog out calibration signals <u>from the Masimo to the BioNex Chassis.</u>
  - ✓ *Pulse wave: Hit menu , select 'output', and set 'Analog 1' to '0V Signal'. Verify that the BioLab shows a voltage of approximately 0V on pulse wave channel. Set 'Analog 1' to '1V Signal' and then verify that the BioLab shows a voltage of approximately 1V on pulse wave channel.*
  - ✓ *Hit menu , select 'output', and set 'Analog 2' to '0V Signal'. Verify that that the BioLab shows an approximately 0% of SpO2 on the second channel. Set 'Analog 2' to '1V Signal' and then verify that the BioLab shows approximately 100% of SpO2 on the second channel.*
- Send the analog out calibration signals <u>from the Samba 201 to the BioNex Chassis.</u>
  - ✓ *Press menu button and navigate to 'ANALOG CALIB' using the menu navigation keys and confirm by pressing button 1.*
  - ✓ *Highlight the minimum value (MIN) in the Analog Calibration window and then the displayed voltage is being sent to the analog port (Verify the signal is approximately -50 mbar).*
  - ✓ *Highlight the maximum value (MAX) and then the displayed voltage is being sent to the analog port (Verify the signal is approximately 350 mbar).*
- Continue to record until the feeding is completed.
- Physiologic operator needs to monitor that signals of all channels look good. If the signal is lost or has too many noise, then let the PI knows and troubleshoots.

  - ✓ <u>Pulse wave & EKG</u>

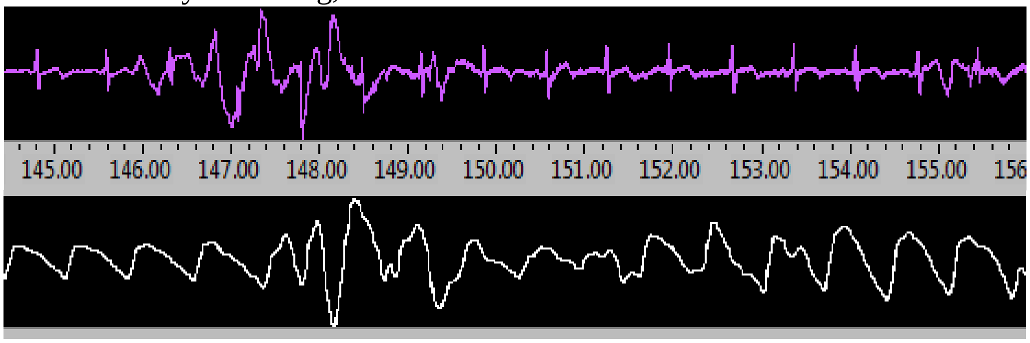
Normal EKG signal: regular R-R interval



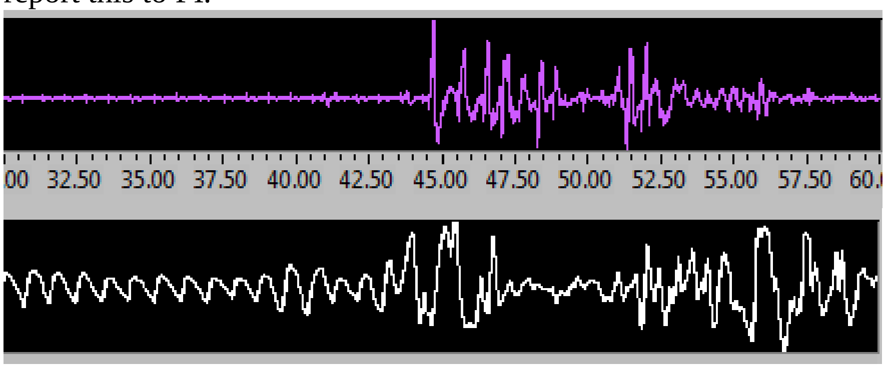
It usually comes with regular pulse wave form.



When the baby is moving, EKG can be disturbed a bit.

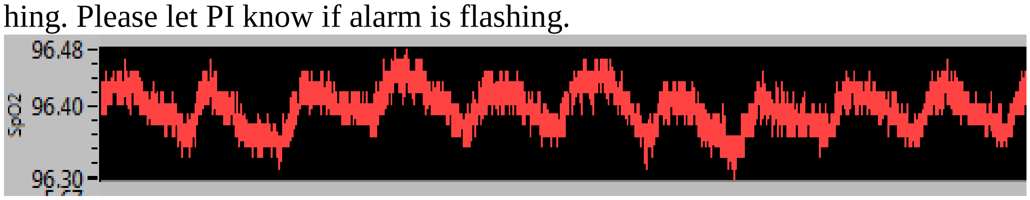


BUT, the signal goes flat or has irregular waveform for few seconds, report this to PI.

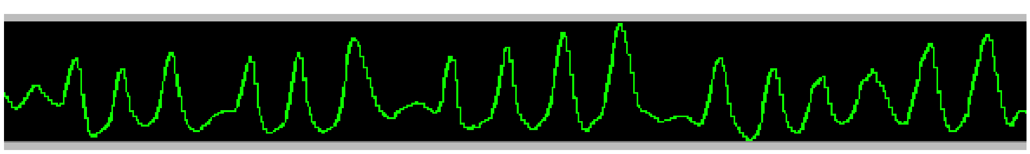


- ✓ <u>SpO2</u>

Signals on the masimo and the BioLab need to be corresponding each other.
Note. The alarm of the Masimo will be indicated only by the symbol of alarm flas hing. Please let PI know if alarm is flashing.

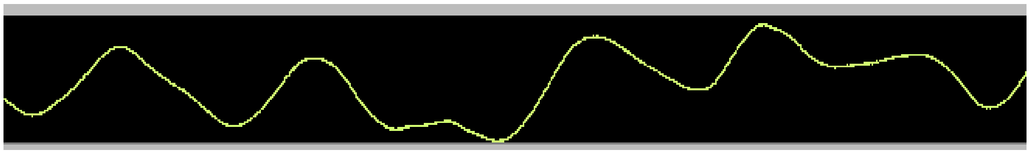


- ✓ <u>Sucking:</u> When the nipple is pressed and released, the signal goes up and down.



- ✓ <u>Swallowing</u>

✓ Respiration: When infants breathe, the signal goes up and down by associating wi th the chest movement for breathing.



Data collection during feeding

- When the infant wakes up for feeding, provide routine nursery care by his/her assigne d nurse.
- If NG tube is in place, it will be gently removed without untaping.
- Swaddle the infant with the blanket and place him/her in the predetermined position.
- Weigh a bid and put it around the neck.
- Write down the amount of prescribed milk
- Set up the stopwatch for 5 minutes
- Begin to feed.
- Write a memo when significant events were occurred using Journal (F12) of the BioL ab program.
- When alarm is ringing, briefly take the bottle out and measure the amount of the milk remained in the bottle.
- When feeding is determined to be finished, record the amount of milk consumed, the l ength of feeding time, the weight of the bib.
- Pour the milk remained out of the bottle.
- Take the transducer tip out of the bottle and put it back into the storage bottle filled w ith the distilled water.
- If you can see proteins on the tip, physiologic operator to go to the BBL, to clean the t ransducer tip based on the protocol, and to bring it back to the nursery for the second feeding.
- Provide post feeding nursery care and settle back the infant on the crib.

Data collection after feeding

- Set up the stopwatch for 30 minutes
- Click STOP on the bottom of the configuration window when alarm is ringing.
- Shutting down all equipment.
- Remain all equipment on the infant until the second feeding observation is completed.
- Repeat the procedure from warming up all instruments for 30 minutes for the second f eeding.

After Data collection

- Shutting down all equipment, computer, and BioNex Chassis.
- Gently remove all monitoring equipment.
- Wipe down all cables and monitoring equipment as it is put away from the baby and p ut it back into the drawer in the physiologic cart. *Note. Put the research stuffs being c*

onsidered as dirty to the zip bag (like used bottle, nipple, resp. band).

- Report any meaningful events during the study.
- Ask nurse to re-insert NG tube right before the next gavage feeding

fter arriving at the lab

- Clean up all the equipment or throw away if it is disposable.

  <Transducer tip>
  - ✓ *Pour distilled water into the cylinder in the lab.*
  - ✓ *Put an enzyme mixture into the cylinder.*
  - ✓ *Submerge the transducer tip in distilled water.*
  - ✓ *Place the cylinder on the center of the magnetic stirring plate.*
  - ✓ *Set the speed to 3-4 level.*
  - ✓ *Soak the transducer tip in this mixture for 10 to 20 minutes.*
  - ✓ *Rinse it again with a clean distilled water for 10 to 20 minutes with the magnetic s tirring plate.*
  - ✓ *Put it back into a cleaned and dry storage bottle.*

  <Bottle>
  - ✓ *Clean with the soap and put it on the dry rack.*
  - ✓ *After drying, put it into a cleaned zip bag and put it back into the first drawer.*

  <Pulse oximeter sensor and cable>
  - ✓ *Washing the light blue band.*
  - ✓ *Wipe down the black band and the crystal sensor with alcohol swab or disinfectan t wipes.*

  <Respiration band>
  - ✓ *Washing the light blue band.*
  - ✓ *Wipe down the black band and the crystal sensor with alcohol swab or disinfectan t wipes.*

  <Others>
  - ✓ *Wipe down other equipment with alcohol swab or disinfectant wipes.*

- Look through the data if it is properly collected and decide if re-collecting data is nee ded on the following day.
  #1. At least 0.5 ml/min of sucking efficiency
  #2. At least six minutes duration of the bottle-in periods of the observation

- Back up the data to two places: Archive (on the secured server) and Working data (on the personal computer or external hard driver)
- Erase all data on the laptop that used for data acquisition after back up.

- Download the trend data from the Masimo Radical-7 pulse co-oximeter if needed.
  - ✓ *Assure that the Radical-7 serial output mode is set to "ASCII2" (MENU <OU*

PUT).

- ✓ *Open Trendcom software on the computer.*
- ✓ *Under the 'instrument' menu in Trendcom, select 'Radical-7 (V7619 or greater)'.*
- ✓ *Under the 'COM Port' menu, select 'COM5'.*
- ✓ *Click on 'Retrieve Trend'. The following message may appear: "please make sure the Radical is set to ASCII2 output mode" and click OK.*
- ✓ *Name the file.*
- ✓ *Save the file to the appropriated folder.*
- ✓ *You will have date, time, SpO2, pulse rate and perfusion index (PI) every 2 seconds that is same as averaging rate you set.*

- Download the video files from the Panasonic HDC-TM700 if you need a high resolution AVCHD video file.
  - ✓ *Assure that HD Writer AE 2.1 is installed in the computer.*
  - ✓ *Connect the video camera to the computer with the USB cable.*
  - ✓ *Turn the video camera on.*
  - ✓ *Open HD Writer AE 2.1.*
  - ✓ *Click 'Copy to PC'< 'Video Camera (E)'< 'Next'.*
  - ✓ *Select the video file what you want to download.*
  - ✓ *Assign the folder and name the file.*
  - ✓ *Click 'Execute'.*

- After downloading the video files, format built-in memory on the Panasonic camera
  - ✓ *MENU<SETUP<FORMAT MEDIA<BUILT-IN MEMORY.*
  - ✓ *When formatting is complete, touch 'EXIT' to exit the message screen.*

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