Describing and differentiating pain responses from non-pain responses in low birth weight pre-term infants

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Describing and Differentiating Pain Responses from Non-pain Responses in Low Birth Weight, Pre-term Infants

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DEDICATION

I strongly believe that all accomplishments are the result of a group effort, that no one person is successful entirely through individual effort. In that vein I would like to dedicate this work to my loving wife, Vicki. I could not have accomplished this goal without her whole-hearted support. She has tolerated being on her own while I was occupied at school or work these past 3 years exceedingly well. She has always been quick and generous with her enthusiasm, generosity and affection. She has boosted my spirits and kept me from giving up many times.

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CHAPTER I

Introduction

Unfortunately, pain was a common experience for the hospitalized pre-term neonate. This population underwent frequent invasive tissue damaging procedures that were considered painful, such as heel lancing to obtain blood. The long-term consequences of frequent pain had possibly far reaching effects by deleteriously affecting brain development (Avchen, Scott & Mason 2001; Grunau 2000). There was considerable evidence that infants reacted differently to pain as they matured (Johnston, Stevens, Craig & Grunau 1993). Also, current work has shown that pre-term infants often manifest behavioral and physiological reactions to painful and non-painful interventions in similar ways (Johnston et al. 1993; Grunau, Oberlander, Holsti & Whitfield 1998; Zahr & Balian 1995; Evans, Vogelpohl, Bourguignon & Morcott 1997). For these reasons, physiologically based assessment tools that measured heart rate and behavior based pain scales developed and used to assess pain in term infants may not accurately assess pain in pre-term infants. This chapter provided an overview of a research project that investigated the pain responses of pre-term infants. Problems encountered in pain assessment in pre-term infants were discussed and followed by a statement of purpose for this research. The nursing theory used to guide this research was summarized (Roy & Andrews, 1999). Research questions related to this project will be stated and variables and terms will be conceptually and operationally defined. The research hypothesis was presented. The significance of this research for nursing, health care and the general public...
was discussed. And lastly, assumptions and limitations inherent in the research were introduced.

Statement of the Problem

The NICU personnel had difficulty ascertaining when low birth weight premature infants were in pain for a variety of different reasons. Facial pain responses were transitory and changed rapidly (Evans et al., 1997). Although many of the facial movements associated with pain were present as early as 25 weeks gestational age (Grunau & Craig, 1987), in general, younger infants displayed less vigorous physical reactions to painful stimuli (Johnston et al. 1993). Behavior based pain scales required interpretation and scoring by personnel trained in that assessment tool and relied on subjective interpretation by the person doing the pain scoring. For these reasons, researchers looked for a practical method capable of giving instantaneous and objective information to medical personnel regarding pain assessment of pre-term, low birth weight infants.

Promising but preliminary discoveries were made regarding the development of an objective pain measurement tool based on changes in heart rate and heart rate variability. Lindh, Wiklund & Hakansson (1999) noted that total heart rate variability, low frequency heart rate variability and high frequency heart rate variability decreased during heel squeezing after lancing. These researchers converted the instantaneous heart rate into frequency-based data via a Wavelet Transform. The resulting curve was broken down into different frequency bands that represented different influences on heart rate variability. The high frequency band, greater than 0.15 Hz, reflected respiratory activity
and was mostly mediated by parasympathetic tone (Lindh, Wiklund & Hakansson, 2000). The baroreceptor loop reflex modulated the very low frequency band, which was less than 0.04 Hz (Lindh et al., 2000). The low frequency band, 0.04- 0.15 Hz, reflected thermoregulatory influences (Lindh et al., 2000). The very low and low frequency bands were modulated by both the sympathetic and parasympathetic nervous systems (Lindh et al., 2000). The low frequency to high frequency ratio gave a measure of the relationship between parasympathetic and sympathetic tone. (Mazursky, Birken, Bedell, Ben- Haim and Segar, 1998).

Statement of Purpose

This study examined whether or not total heart rate variability (the sum of very low, low and high frequency variability), high frequency heart rate variability and the ratio of low frequency to high frequency variability were useful in differentiating between procedures that were presumed to be painful and other routine care giving interventions that were presumed to be non-painful in pre-term, low birth weight infants. Heel sticks represented the painful procedures and axillary temperature measurements represented the non-painful procedures. Total heart rate variability, high frequency heart rate variability and the low/high frequency heart rate variability ratio before and after the heel sticks and axillary temperature measurements were compared using paired T tests. This discussion took place within the framework of the Roy Adaptation Model (Roy & Andrews, 1999).
Theoretical Framework

The Roy Adaptation Model (Roy & Andrews, 1999) was well suited to guide this work for several reasons. Roy provided a practical and useful, system based framework for classifying and discussing how individual systems cope with various environmental stimuli. The model discussed the product of the interaction of the individual with the environment in terms of level of coping or success in dealing with new problems. The division of the individual system into regulator and cognator subsystems fit with widely accepted views of how an individual functions. The Roy Adaptation Model was not strictly mechanistic in its approach to explaining human reactions to internal and external stimuli. It did a very good job of synthesizing complex and as yet incompletely explained phenomena with known facts about human anatomy and physiology, biochemistry and expression of genetic traits. One often thought that humans had a largely automatic set of physiological regulatory processes (the regulator subsystem) and another, integrated group of control processes involved in learning, memory and conscious thought (the cognator subsystem). Roy and Andrews (1999) described individual reactions to the environment in terms of relative success or failure. Was the individual reacting relatively positively and constructively? Was the stimulus harmful? Was the individual reacting relatively ineffectively? This explanation of adaptive behavior fit well with the structure and purposes of this study. For example, a high degree of heart rate variability was a sign that a premature infant was adapting well to life outside the womb and may be an indicator of the infant’s ability to recover from a serious illness.
Griffin, Scollan and Moorman (1994) found that while infants were severely ill, they exhibited little heart rate variability, but that when they began to recover, heart rate variability significantly increased. The authors also noted that low heart rate variability was correlated with a poor prognosis in infants recovering from cardiac and respiratory distress syndrome. The present study examined the relationship between a focal stimulus, a heel stick, and any change in heart rate variability it evoked. Roy’s concept of the regulator subsystem provided a useful framework to discuss and explain this relationship.

Research Questions

A narrow scope of inquiry was required in order to describe and understand the pain response in pre-term, low birth weight infants less than 28 weeks gestation. This study examined three research questions:

1) Was there a difference in total heart rate variability (total HRV) responses before and after what was considered a painful stimulus (a heel stick) and a non-painful stimulus (an axillary temperature measurement) in low birth weight, pre-term infants?

2) Was there a difference in high frequency heart rate variability (HF HRV) before and after what was considered a painful stimulus (a heel stick) and what is considered a non-painful stimulus (an axillary temperature measurement) in low birth weight, pre-term infants?

3) Was there a difference in the low frequency/ high frequency heart rate variability ratio (LF/HF HRV) before and after what is considered a painful stimulus (a heel
stick) and what is considered a non-painful stimulus (an axillary temperature measurement) in low birth weight, pre-term infants?

Definition of Terms

The conceptual definition of pain was a complex, multidimensional phenomenon that was most often expressed subjectively (Stevens and Johnston, 1994). Pain was an unpleasant sensation mediated by neurochemical events and accompanied by an involuntary cascade of adaptive physiological, emotional and other communication behaviors that served to protect the infant from actual or potential tissue damage (Evans, Vogelpohl, Bourguignon & Morcott, 1997; Mines & Rosenzweig, 1996). The operational definition of pain was a decrease in total heart HRV (the sum of very low, low and high frequency variability), decreased HF HRV and increased LF/HF HRV. The definition of the LF/HF HRV did not include any contribution from the very low frequency band.

The conceptual definition of a painful procedure was a tissue-damaging event causing a reaction mediated by neurochemical events and accompanied by an involuntary cascade of adaptive physiological, emotional and communication behaviors. The operational definition of a painful procedure used in this study was heel lancing to obtain a blood sample for lab analysis.

The conceptual definition of a non-painful procedure was a routine care giving procedure that did not involve tissue damage and did not evoke a pain response. The operational definition of a non-painful procedure in this study was axillary temperature measurement.
The conceptual definition of heart rate variability (HRV) was defined in terms of the QRS complex on EKG, specifically as changes in successive R-to-R intervals over time (Porges, 1992). Total heart rate variability was the sum of very low, low and high frequency heart rate variability (Lindh et al., 2000). High frequency heart variability was a measure of parasympathetic nervous system activity (Lindh et al. 2000). Low frequency variability and very low frequency heart rate variability reflected both parasympathetic and sympathetic nervous system activity (Lindh et al. 2000). The LF/HF HRV was a measure of parasympathetic and sympathetic nervous system balance (Mazursky et al. 1998). The operational definition of total heart rate variability was the total area under the curve of a Fast Fourier Transform of a continuous ECG recording of the instantaneous heart and was the sum of very low, low and high frequency heart rate variability. Very low frequency heart rate variability was the area under the curve of a Fast Fourier transform of a continuous ECG recording of instantaneous heart rate that lay in the frequency band less than 0.04 Hz. LF HRV was the area under the curve of a Fast Fourier Transform of a continuous ECG recording of instantaneous heart rate that lay in the frequency band 0.04-0.15 Hz. HF HRV was the area under the curve of a Fast Fourier Transform of a continuous ECG recording of instantaneous heart rate lying in the frequency band of >0.15 Hz. The LF/HF HRV was the result of dividing the low frequency heart rate variability by the high frequency variability.

Significance

The ability to accurately distinguish pain from other responses was useful to NICU personnel in assessing and treating pain in premature low birth weight infants.
Shapiro (1993) found that Neonatal Intensive Care Units (NICUs) nurses tended to rate the intensity of pain experienced by pre-term, low birth weight infants during heel lancings to be significantly less than pain experienced by term infants who underwent identical procedures. The basis for this difference may have been grounded in incomplete or inaccurate knowledge of basic and very real differences in the neuromuscular, biochemical and anatomical substrate of pre-term, low birth weight infants as compared to term infants. It also may be true that a few weeks difference in post-conceptional age could result in substantially significant differences in these same parameters.

Reducing the severity and/or frequency of pain may improve developmental and behavioral outcomes later in life. Avchen, Scott and Mason (2001) found that 17% of children who had been low birth weight, pre-term infants developed learning disabilities and behavior problems. Lindeke, Mills, Georgieff and Wrbsky (1998) had evidence those children who experienced NICU care as infants needed more community health care services during their school age years. While it was not proven that frequent, intense pain experienced in Neonatal Intensive Care Units caused these problems, Grunau (2000) hypothesized that frequent pain during the third trimester of brain development significantly altered the course of this development and adversely affected brain function. Accurate assessment of pain in this group of patients may be difficult since they are preverbal.

Assumptions

It was assumed that each infant reacted to the heel stick in the same way regardless of who performed the procedure. It was assumed that axillary temperature
measurement was not a painful experience for the pre-term, low birth weight infant. It was assumed that each infant had similar abilities to vary heart rate. This study assumed that using data from heel sticks and axillary temperature measurements that were obtained within two weeks of each other minimized the effects of ongoing developmental changes in the functioning of the autonomic nervous system.

Limitations

It was a limitation of this study that more than one nurse performed the heel sticks and axillary temperature measurements. This may have caused variability in the way that each procedure was performed and was a possible source of error. An infant may habituate to painful stimuli and become less sensitive to pain after repeated procedures. This habituation, together with changes in growth and development, may alter how each infant responded to pain over time. There also may be gender and racial differences in pain sensitivity and responses. Infants who were more severely ill display less heart rate variability at rest and while under stress (Griffin, Scollan & Moorman, 1994). Although exclusion criteria eliminated infants with certain conditions and histories, this study did not compensate for this effect.

Summary

Pain has been a serious consequence of care in a typical NICU. The consequences of severe, frequent and untreated pain may have long-term consequences in terms of learning problems and behavioral disorders. These long-term sequelae may impose a burden on society in terms of increased costs and loss of potential positive contributions from these children. The results of frequent pain may be increased morbidity and
mortality of pre-term, low birth weight infants. It may be necessary to monitor the amount of stress from pain infants experience in order to improve outcomes. Current assessment tools may be inaccurate when used for low birth weight, preterm infants. This study seeks to establish the utility of heart rate variability measurement as an additional measure to be used in the assessment of pain in low birth weight preterm infants. It aims to do so within the conceptual framework of the Roy Adaptation Model (Roy & Andrews, 1999).
CHAPTER II

Literature

This study investigated the question of whether heart rate variability was a useful tool in distinguishing between painful, invasive procedures and those routine care-giving procedures that are not painful to low birth weight premature infants. This question was researched using the Roy Adaptation Model as a framework for understanding the relationship between pain and heart rate variability. This chapter began with a discussion of the Roy Adaptation Model. This chapter included an outline of the model, the conceptual basis for the use of high frequency heart rate variability as an indicator of pain and a schematic diagram of the model and how it applied to this research question. This was followed by a review of research relevant to this study.

Theoretical Framework

According to Roy, human beings were conceptualized as adaptive systems (Roy & Andrews, 1999). The model was based on systems theory. The individual was an open, adaptive system interacting with the environment. The system/individual sought to maintain equilibrium. Each individual was comprised of two subsystems, the regulator and the cognator subsystems. This study was concerned with the regulator subsystem. There were four adaptive modes. These were the physical, self-concept, role function and interdependent modes. This study focused on the physical adaptive mode. The physical mode controlled behavioral manifestations of the body. Within the physical mode there were five basic needs. These needs were oxygenation, food, elimination, activity/rest and protection. The physical mode also included four physiological processes that function to
meet the body’s needs. These were the five senses, fluid/electrolyte/acid-base balance, neurological functions and endocrine functions. The behavioral outcomes were classified into three levels of adaptation. These are the integrated, compensatory and compromised adaptation levels.

According to the Roy Adaptation Model, the levels of adaptation were used to describe the life processes of the individual and how well the organism was meeting the challenges of living. An integrated level of adaptation described the structures and functions of the life process working smoothly to meet the system’s needs. It was a description of a healthy state where everything was in balance. The system was in equilibrium. The second adaptation level was called compensatory and operated when the system was disturbed and was temporarily out of balance. It was working to restore that balance. A frequently used example was fever. Fever was seen as a manifestation of the body’s attempt to fight off an infection and speed healing. The third level of adaptation was termed compromised. This was where the system was out of balance and the organism may or may not be able to recover. When illness and disease occurred, the compromised adaptive level was in operation. For example, if the pre-term infant developed respiratory distress syndrome or became septic. The infant attempted to compensate but did not do it well enough to survive.

Various types of stimuli sent information to the system and the system reacted in a coordinated fashion with a purpose, the maintenance of equilibrium. According to Roy, there were three major groups of stimuli. They were called focal, contextual and residual stimuli. Focal stimuli were those that primarily occupied the individual’s attention at that
time. They were internal or external stimuli. The adaptation level of an organism was a type of internal stimulus within the Roy Adaptation Model. In this study there were two focal stimuli; a presumably painful invasive procedure (the heel stick) or a standard caregiving procedure assumed to be non-painful (axillary temperature measurement).

Contextual stimuli were other stimuli present in a given situation that contributed to the effect of the focal stimulus. Contextual stimuli increased or decrease the impact of the focal stimulus. In this study gestational age and post-natal age were contextual stimuli.

Residual stimuli were all other stimuli present within the individual or the environment whose contribution was unclear at this time. One may or may not be aware of the presence of a residual stimulus. Even if one knew the stimulus was present, its influence was unclear. The environment presented an array of stimuli to the system. The environment was always in a state of flux. What may be a focal stimulus at one moment may become contextual or residual in the next moment. The environment and how the person was able to react to it were constantly changing.

An infant’s capability to deal with a particular situation was based upon two factors, the intensity of the demands placed on it (stimuli) and the internal resources it had available (regulator and cognator subsystems). Behavior was the measurable, observable response of the individual in a given situation. It can be effective or ineffective. Effective behavior contributed positively to the survival, growth, reproduction and mastery of the new circumstances. Ineffective behavior was that which did not contribute positively to the survival, growth or goals of the individual.
According to the Roy Adaptation Model, humans had two major subsystems, the regulator and cognator subsystems. The regulator subsystem was mainly an automatic system. It was seen to act primarily through the neural and endocrine systems. Sensory stimuli from the internal and external environment acted as input to the nervous system and the regulator subsystem acted to alter the fluid, electrolyte and acid-base balance of the body and drive the appropriate endocrine and autonomic responses in an automatic unconscious manner. This was the subsystem that was most often used by pre-term infants when they responded to stimuli in their environment, particularly painful and/or annoying stimuli.

The cognator subsystem was manifested as conscious thought processes, memory and emotion. It was used as the individual thinks through what has happened to them and then tried to reason out the most appropriate responses. It was thought to be how we learned and how we processed this learning into judgment for future use in similar situations. This subsystem was poorly developed in pre-term infants and was not an important factor in their responses to painful or annoying stimuli. It was important however in that it appeared that the development and maturation of the cognator system was deleteriously affected by the intensity and frequency of painful stimuli inflicted upon pre-term infants.

According to Roy (Roy & Andrews 1999), it was not possible to directly observe the function of the regulator subsystem. It was possible to observe the behaviors that resulted from the regulator control processes by observing the adaptive modes and using these observations as a basis for an assessment. There were four adaptive modes: the...
physical, self-concept, role function and interdependent modes. Only the physiological mode was of interest here. This mode was the behavioral manifestation of all the physiological activities of the body. The physiologic mode was comprised of nine parts. The five basic needs were the needs for adequate oxygenation, food, elimination, activity, rest and protection. There were also four complex processes involved in physiological adaptation. These were the use of the five senses; fluid/electrolyte and acid/base balance; neurological function and endocrine function. The system maintained the physiological integrity of the individual when all nine of these components functioned together. Any individual experienced different performance capabilities of these nine components over time. Prolonged inability to meet physiological needs did result in serious and perhaps life threatening consequences. It was the physiologic mode where the premature infant was vulnerable to serious and perhaps life threatening challenges and had not yet achieved optimal functioning. The pre-term infant was at increased risk for fluid and electrolyte imbalances. It has not yet fully developed its nervous system (Mazursky et al. 1998; Evans 2001). The nervous system functions that were present were markedly different from older term infants (Evans 2001; Johnston, Stevens, Craig & Grunau 1993). The ability to meet the need for adequate oxygenation is often impaired due to immature lung function. Infants were completely unable to independently meet the needs for food and rest/protection. The physiologic mode was seriously affected by the consequences of painful invasive procedures and routine care giving activities experienced by the pre-term neonate in the NICU.
Another major component of the Roy Model (Roy & Andrews, 1999) was the environment. According to Roy, human systems confronted an ever-changing environment and sought to adapt successfully to its demands. Adaptation was a measure of the degree of change that was occurring and the human system’s adaptation level. Adaptation level has been previously described as part of the internal environment of integrated, compensatory or compromised life processes. All of the focal, contextual and residual stimuli coalesced to impact the adaptation level of the individual at that particular point in time. Environment can be seen in the influences that surround and affect the development and behavior of human systems. For the pre-term infant, the environment may be seen as all of the experiences in the NICU.

The Roy Adaptation Model was chosen as a framework for this study because it provided a sound basis for discussing how low birth weight premature infants react to painful or annoying stimuli. This study was primarily concerned with the usefulness of heart rate variability in distinguishing between pain and other stimuli. It was focused on how the infant reacts in the physiological mode within the regulator subsystem. Figure 1 is a diagram of the physiological mode that represents the impact of painful and annoying stimuli on the behavior of low birth weight premature infants within the context of the Roy Adaptation Model.
Review of Research

Observations of verbal human beings revealed that certain experiences are painful. The experience of pain results in physiological changes and behaviors unique to pain. Heart and respiratory rates accelerated and blood pressure increased when adults
and children were in pain. Certain facial expressions were often seen during the pain response. These same changes were often seen in term infants undergoing what was assumed to be a painful stimulus. However, in pre-term infants, facial and other body movements were less reliable pain indicators (Johnston et al., 1993). The investigation of heart rate variability as an objective, measurable pain indicator was an effort to develop a better way to assess the presence or absence of pain in pre-term infants. This review looked at the work that has been done to evaluate and measure pain in term and pre-term infants using physiological response based tools and models.

Similarities in Response to Painful and Non-painful Stimuli:

Investigators found many similarities in the physiological responses of infants to painful and non-painful stimuli. Zahr and Balian (1995) found that about 20% of infants displayed increased heart rate, increased respiratory rate and decreased oxygen saturation in response to noise combined with routine non-invasive nursing interventions. Grunau, Oberlander, Holsti and Whitfield (1998) measured heart rate during a baseline resting period, contact with the infant, heel swabbing, lancing, heel squeezing and a recovery phase in 40 infants of 32 weeks gestational age. There was a significant increase in heart rate between lancing and squeezing indicating that squeezing may be more painful than lancing. However it was interesting to note that heart rate was also seen to significantly increase during the unwrapping phase compared to the baseline and during heel swabbing compared to the unwrapping phase. In fact, these supposedly non-painful events accounted for much of the increased heart rate. The highest heart rates were seen during
lancing and squeezing. There was, of course a significant increase in heart rate during the lancing and squeezing phases compared to baseline.

Craig, Whitfield, Grunau, Linton and Hadjistavropoulos (1993) examined physiological measures (heart rate, respiratory rate and oxygen tension) in 56 pre-term and full term infants during painful and non-painful events. The painful event was heel lancing and the non-painful event was heel swabbing. They did not consider first contact as a non-painful event. The infants were divided into groups based on gestational age, Group one was 25-27 weeks, group two was 28-30 weeks, group three was 31-33 weeks, group four was 34-36 weeks and group five was 37-41 weeks. In general, there was a steady increase in heart rate from the resting baseline period to first contact with the infant, heel swabbing and heel lancing in groups 1 through 3. There were no significant differences in heart rate across adjacent events (baseline compared to first contact, first contact compared to heel swabbing and lancing compared to heel swabbing), with a few exceptions. Group 5 actually had a significantly higher heart rate during the recovery phase than at any other time. Groups 2 and 3 also exhibited their highest heart rates during the recovery period, but this difference was not statistically significant Group 4 had a significantly lower heart rate during the recovery period compared to heel lancing. When heart rate during lancing was compared to heart rate during the baseline period, all five groups of infants had significantly higher heart rates. In summary, the results indicated that heart rate significantly increased during pain compared to baseline, but there were no significant difference in heart rate when comparing lancing to heel swabbing, an event assumed to be non-painful. Furthermore, heart rate steadily increased
from baseline through first contact and heel swabbing, both of which were not considered painful.

Johnston, Stevens, Yang and Horton (1995) used the Standard Deviation method to compare heart rate variability in a group of 40 pre-term infants less than 29 weeks gestational age. Their goal was to compare these infants’ responses to presumably non-painful and painful events. These investigators used sham heel lancing as a non-painful event and actual heel lancing as a painful event.

The Standard Deviation method for calculating heart rate variability was done in the following way. They recorded the instantaneous heart rate over a period of time. The mean instantaneous heart rate (IHR) and the standard deviation of the mean instantaneous heart rate were calculated. Johnston et al. (1995) attempted to standardize the entire recording period for both sham and real conditions to be approximately 315 seconds from beginning to end. This standard deviation of the mean IHR was then used as a measure of heart rate variability. A larger standard deviation meant greater heart rate variability. Conversely, a smaller standard deviation meant less heart rate variability.

Real heel lancing involved a standardized procedure culminating in actually puncturing the infant’s heel for a blood sample. The sham procedure was identical to the real procedure except that a dummy lancet device was used so that no actual puncture occurred. The sham and real conditions also differed with respect to the amount of time dedicated to heel squeezing. They limited heel squeezing following sham lancing to 120 seconds. They limited heel squeezing after real lancing to a variable period of time necessary to obtain a blood sample (Johnston et al., 1995).
Johnston et al. (1995) divided the infants into two age groups based on a median post-conception age equal to 29 weeks. They then used repeated measures ANOVA to examine the effects of treatment (non-painful versus painful) and post-conception age. Interestingly, they found that the younger group responded differently in terms of heart rate variability and mean IHR regardless of treatment condition. The younger infants responded less robustly to heel sticks compared to the older infants and they concluded that age was a very important factor to consider when assessing pain in very low birth weight, pre-term infants. Johnston et al. (1995) also found that heart rate variability, by the standard deviation method, did not distinguish pain from non-pain when the groups’ responses were examined without age distinctions.

Behavioral indices were variable as well. Johnston et al. (1995) also compared facial activity in 40 pre-term infants less than 29 weeks gestational age in response to sham and real heel lancing. These researchers again divided the infants into two groups based on a median age of 29 weeks post-conception. The researchers concluded that while facial activity was useful in differentiating real heel lancing from the sham condition, the response was less obvious in the younger infants.

Grunau et al. (1998) scored 40 infants of 32 weeks gestational age on the Neonatal Facial Coding System (NFCS) as they experienced first contact, swabbing, lancing, squeezing and recovery. The NFCS score remained less than or equal to 1 during the non-painful events including baseline, first contact and swabbing but jumped to 3.5 during lancing and 4.5 during squeezing. Grunau et al. (1998) concluded that the NFCS is able to distinguish pain from non-pain in this age group. The NFCS dropped to 1.5 during
the recovery period. This is further evidence supporting the validity of the NFCS. Craig et al. (1993) also examined facial activity and body movements in a study of 56 pre-term and full term neonates. Their research group found that the full term infants exhibited more baseline facial and general body activity than the pre-term infants. Also, full term infants displayed greater facial responses and higher NFCS scores to the various stimuli than did the pre-term infants. The youngest gestational age infants (25-27 weeks) did not display significantly different NFCS scores to swabbing and lancing compared to baseline. All of the older groups of infants (more than 28 weeks gestation) displayed a significant increase in NFCS scores during swabbing and lancing compared to baseline.

Craig et al. (1993) also used the Infant Body Coding System (IBCS) to score the responses of 56 pre-term and term infants during swabbing and heel lancing. Interestingly, the youngest infants (25-27 weeks gestational age) displayed as much body activity response to swabbing and lancing as did infant groups 2-4 (28-36 weeks gestational age). There were no significant differences in IBCS scores during swabbing compared to lancing until the infants were greater than 36 weeks gestational age.

Lindh, Wiklund, Sandman and Hakansson (1997) also compared facial activity in a sample of 10 pre-term infants having 27-35 weeks gestational age. Experienced NICU nurses classified infants as undisturbed, stimulated or in pain based on videotaped facial activity. Experts using the Neonatal Facial Coding System (NFCS) scored the same videotapes. The authors concluded that there was agreement between the experienced NICU nurses and the NFCS experts and that both were able to distinguish infants in the undisturbed state, the stimulated state and the painful state. There was no distinction
between the younger and older infants due to small sample size. These authors did not use any infants less than 27 weeks gestational age. Therefore, it was difficult to compare these results to those of Craig et al. (1993).

Zahr and Balian (1995) noted that about 79% of the infants in their sample changed their behavioral state in response to noise and handling and often this change was from sleeping to a crying/fussy state. These same behaviors were frequently seen in infants undergoing painful procedures. Evans et al. (1997) found infants subjected to painful and non-painful procedures exhibited considerable overlap in the expression of four pain behaviors. The authors found that four pain expressions were present 75-100 % of the time following suctioning, NG insertion, skin puncture, dressing change/ removal and discontinuation of an IV line. These procedures were assumed to be painful. The four pain behaviors were grimace, slight cry expression, increased cry expression and knee/leg flexion. Evans et al. (1997) found these pain behaviors to be present 49-69% of the time following non-painful procedures including total position change, addition/withdrawal of fluid from an umbilical catheter and IV drug administration. However, it may be that tension on umbilical lines during position change, administration of certain IV drugs and withdrawal or addition of fluid to or from an umbilical line is painful. Either way it was clear that many procedures thought to be non-painful resulted in responses that can be interpreted as pain.

A significant source of variability in pain response may be related to developmental age. Johnston et al. (1993) examined developmental changes in pain expression in pre-term, full term, two-month-old and four month old infants. These
researchers found that the pre-term group expressed pain differently from the other
groups. These differences manifested in different facial movements and different cry
frequencies. It may be necessary to monitor heart rate variability and combine it with
other pain assessment criteria to accurately assess and ultimately treat pain in pre-term
infants.

Pre-term Infants and Long Term Sequelae:

Avchen, Scott and Mason (2001) found a significant proportion of low birth
weight and extremely low birth weight infants developed some school-identified
disability. Lindeke, Mills, Georgieff and Wrbsky (1998) found that infants who
experienced care in a NICU had more chronic health problems and required a greater
amount of community services than did children who did not require NICU care. While it
cannot yet be proven that frequent painful experiences while in a NICU directly caused
brain abnormalities, behavioral problems and learning disabilities later in life, there was
general agreement that the period of time corresponding to final brain development may
be a vulnerable time in an infant’s life. Grunau (2000) hypothesized that the long term
sequelae resulting from multiple painful procedures and prolonged pain experienced
during a period that corresponded to what would have been the third trimester of fetal life
may alter the way that the brain developed and may have predisposed the child to
deleterious consequences in terms of intelligence, personality and behavior.

Heart Rate Variability as a Health Indicator:

Griffin, Scollan and Moorman (1994) sought to analyze heart rate variability in
eight pre-term and full term infants who recovered from severe illness. The diagnoses
included pneumonia/sepsis, respiratory distress syndrome, meconium aspiration, diaphragmatic hernia repair and pulmonary hypoplasia/ hypertension. These authors found that total heart rate variability was low during severe illness and increased significantly during recovery. This corresponded with findings of Rosenstock, Cassuto and Zmora (1999) and Van Ravenswaaij-Arts, Hopman, Kollee, Stoelinga and Van Geijn (1995) who had supported the contention that low heart rate variability was a sign of stress and was correlated with poor outcome, morbidity and increased mortality if it remained low. According to Porges (1992), another supporter of the link between low heart variability and poor outcomes “stress is assumed to be a physiological construct (in pediatric patients) that is observed when behavior becomes disorganized and homeostatic processes are disrupted. In clinical settings, this is often labeled physiological instability.”

Heart rate variability was the result of fluctuating levels of sympathetic and parasympathetic stimulation of the heart (Porges, 1992; Lindh et al., 1997). When sympathetic tone dominated heart rate speeds up and when it was unopposed heart rate variability decreased (Lindh et al. 1999). Parasympathetic stimulation of the heart has been called vagal tone and when it predominated heart rate slows down (Porges, 1992). The physiological health of an infant can be measured as the degree of heart rate variability exhibited. Porges (1992) stated, “Efficient neural control is manifested as rhythmic physiologic variability, and within normal parameters, the greater the amplitude of oscillation, the healthier the individual.”

This greater variability in heart rate has been thought to reflect the flexibility of cardiovascular responses to stress. Porges advocated the use of vagal tone monitoring
(i.e., heart rate variability) as an objective means to assess the degree of stress a neonate had experienced and allow for comparison of the stress response between individuals by application of statistical analyses (Porges, 1992). He also noted that in general, pre-term neonates had much less vagal tone (parasympathetic stimulation) than full term infants. Pre-term neonates were therefore less able to adapt successfully to stress such as frequent and intensely painful stimuli.

*Pain and Heart Rate Variability:*

Owens and Todt (1984) measured heart rate every 3 seconds in 10 male and 10 female full term infants. These researchers made qualitative observations of changes in heart rate variability when comparing heart rate measurements during resting baseline state, tactile handling phase and heel lancing phase. They visually compared the recordings of instantaneous heart rate during the rest, tactile stimulation and heel lancing periods and concluded that there was a decrease in heart rate variability during heel lancing. However, they did not apply any quantitative analysis to the heart rate recordings.

Lindh et al. (1997) studied a sample consisting of ten pre-term infants aged 24-33 weeks gestation and 27-35 weeks post-conception. This was a sample with a wide age range. Four of the infants required ventilator support with nasal CPAP and three of these four required supplemental oxygen. The purpose of the study was to investigate and compare changes in heart rate variability in pre-term infants during a resting state, stimulation with Von Frey’s hairs and blood sampling by heel lancing. The stimulation of an infant’s flexor muscle response using Von Frey’s hairs has been thought to produce a
reaction that may be similar to that induced by a painful stimulus. Lindh et al. (1997) defined this as limb withdrawal due to flexor muscle contraction.

Lindh et al. (1997) took the reciprocal of the R-to-R interval as the instantaneous heart rate. They then performed a Wavelet Transform to convert a graph of the instantaneous heart rate from time based data to frequency based data. They then integrated the resulting graph and derived the total area under the curve. The total area under the curve was the total heart rate variability. This was then divided into low and high frequency bands. The investigators performed a spectral analysis and calculated the total heart rate variability (HRV), the low frequency HRV and the high frequency HRV. These were then logarithmically transformed and converted into a three dimensional plot. These authors then applied principal component analysis (vector analysis) to study the patterns obtained from this three dimensional representation of the spectral analysis.

Analysis of the results demonstrated that there were significant increases in mean heart rate as the infants were stimulated with the Von Frey’s hairs or lanced. Additionally it was found that there were significant changes in total HRV and low frequency HRV only during the blood-sampling situation. Principal component analysis supports this conclusion (Lindh et al. 1997). In summary; there were significant decreases in total HRV and low frequency HRV only during heel lancing and blood sampling. This supported the theory that pain caused a loss of vagal tone and resulted in predominantly sympathetic nervous system control of heart rate and decreased HRV.

Lindh et al. (1999) repeated the above findings in a subsequent study that examined changes in heart rate variability after a sham and real heel lancing procedure in
a sample consisting of 23 term infants. This study again utilized principal component analysis (vector analysis) to graphically demonstrate changes in heart rate variability. What was different about this study was that the investigators analyzed the changes in heart rate variability following lancing and during heel squeezing separately. After preparing and warming the heel, a sham lancing was performed on 11 of the infants, followed by a repeat warming and preparation of the heel and a real lancing. A delay of 40 seconds between lancing and squeezing was inserted in an attempt to separate effects of the sharp lancing from heel squeezing. These authors used paired t tests to compare total heart rate variability (HRV), low frequency HRV, high frequency HRV and mean heart rate during sham lancing and actual heel lancing without heel squeezing. Lindh et al. (1999) found no significant changes in total heart rate HRV, low frequency HRV, high frequency HRV or mean heart when comparing sham lancing to sharp lancing without heel squeezing.

Lindh et al. (1999) then used ANOVA to compare heart rate, total heart rate variability (HRV), low frequency HRV and high frequency HRV. They compared data obtained during a resting state, heel lancing and heel squeezing. During and after squeezing, mean heart rate increased and total heart rate variability, low frequency power and high frequency power decreased significantly compared to lancing and the resting state. This suggests that the heel squeezing and not lancing is the most stressful and painful part of the procedure.

Another difference noted between the responses of the pre-term infants in Lindh et al. (1997) and the full term infants in Lindh et al. (1999) was that high frequency heart
rate variability (HRV) did not change significantly in the pre-term group during heel lancing without heel squeezing. High frequency HRV dropped significantly following heel lancing followed by squeezing in the full term group. It was possible that the decrease in variability following lancing alone may take more than 40 seconds to appear and the effect of lancing on heart rate and HRV may run over into the heel squeezing phase. However the lancing puncture would probably clot if the gap were extended. While it would be interesting to see what would happen after lancing without squeezing the heel at all, this practice would be prohibited due to ethical problems.

McIntosh, Van Veen and Brameyer (1993) measured the variability of four physiological variables during a resting state, sham heel squeezing and heel lancing and squeezing. Thirty-five pre-term infants ranging from 26-34 weeks gestational age were sampled. All infants had heart rate data analysis, 28 infants had respiratory rate data analysis, 30 had transcutaneous oxygen tension data analysis and 17 had transcutaneous carbon dioxide data analysis. Variability was measured slightly differently than the preceding studies. This group calculated heart rate variability as the standard error of the mean. The test procedure occurred as follows. Data was recorded during a rest period. Then the infants were subjected to a sham lancing. This was always the first treatment. This sham lancing was then followed by a rest period then an actual lancing and squeezing.

The results demonstrated that the variability of all four physiological variables increased significantly after heel lancing and squeezing. There were a few problems with the McIntosh et al. (1993) study. There was an 8-week range in gestational age and a
four-week range in age of the subjects. Since there was an apparent developmental factor in the pain response, this wide range in age may dilute the validity of this study. Also, the sham procedure was always first. It would have been better to alternate the sham and the real procedures in order to compensate for any carry over effect from the sham procedure.

Johnston et al. (1995) designed a study to examine the behavioral and physiological responses of premature infants to real and sham heel stick conditions. In this respect it was similar to the McIntosh et al. (1993) study. There were some important differences in subjects and design. Their pool of subjects included 48 pre-term infants who were between 26-31 weeks gestational age and 3-27 days old compared to the McIntosh et al. (1993) study pool with 26-34 weeks gestational age and 7-35 days of age. This study also alternated the order of the sham and real heel lancing whereas in McIntosh et al. (1993), the sham condition always came first. Johnston et al. (1995) conclusions were that mean heart rate was significantly higher in the real condition compared to the sham heel lancing but that heart rate variability, as measured by mean HR plus or minus 1 standard deviation, was a not a useful pain indicator.

Gonsalves and Mercer (1993) aimed to compare physiological responses of 35 pre-term infants during painful and non-painful procedures. The infants were 28 weeks plus/minus 3.1 weeks gestational age and 10.4 days plus/minus 15.5 days old. Non-painful procedures included handling, talking, temperature taking, swabbing skin with alcohol, patting, tapping a tube, increasing oxygen, diapering, bandaging, feeding and pacifier placement. Painful procedures included heel lancing, heel squeezing after
lancing, injection, tape removal and suctioning. Gonsalves and Mercer (1993) found that heart rate was higher after painful procedures but the size of one standard deviation was less during the painful procedure. This suggests a decrease in heart rate variability with pain, a finding in direct contrast to McIntosh (1993). Johnston et al. (1995) also found that heart rate increased with pain but, in contrast, concluded that there was no change in heart rate variability during pain. McIntosh et al. (1993) and Johnston et al. (1995) used definitions of painful and non-painful procedures that were different than those used by Gonsalves and Mercer (1993).

Stevens and Johnston (1994) attempted to describe the physiological responses of pre-term infants to heel lancing. These researchers measured heart rate variability as the standard deviation around the mean heart rate. The Stevens and Johnston (1994) sample consisted of 124 neonates between 32-34 weeks of age and less than 5 days old. Additionally, the neonates were free of major congenital or neurological defects and did not require a ventilator or surgery. These authors found that while mean and maximum heart rates were sensitive indicators of pain, heart rate variability, as defined above, was not. The only significant difference in heart rate variability was between baseline measurement and heel warming. Stevens and Johnston (1994) go on to conclude that physiological measures alone were not sufficient to assess pain and they must be combined with a behavioral scale (i.e. the Premature Infant Pain Profile or the NFCS).

Porter, Porges and Marshall (1988) looked at the relationship between cry pitch, vagal tone (parasympathetic stimulation) and pain during circumcision. Their sample consisted of 49 full term infants (32 experimental and 17 control subjects) between 24-48
hours old. Full term gestation was defined as greater than 37 weeks. This study used the standard deviation method. The instantaneous heart rate was recorded for one minute. A mean instantaneous heart rate was calculated. Heart rate variability was defined as one standard deviation. Porter et al. (1988) concluded that heart rate variability decreased significantly during circumcision but quickly returned to baseline levels. Infants who displayed more heart rate variability at baseline lost more heart rate variability during circumcision, compared to those infants who had less heart rate variability at baseline. Infants who had less heart rate variability at baseline lost less heart rate variability during circumcision.

If a decrease in heart rate variability is a useful measure of pain, then measures taken to reduce pain such as analgesia or anesthesia should preserve heart rate variability. This is what Lindh, Wiklund and Hakansson (2000) set out to do when they assessed the effects of EMLA on heart rate variability during venipuncture. Their sample included 60 full-term infants. Therefore, the results cannot be directly applied to pre-term, very low birth weight infants. One gram (1 cc) of EMLA cream or the placebo was applied to the dorsum of the left hand and covered with tegaderm for 60 minutes. Heart rate, total heart rate variability, low and high frequency heart rate variability were calculated using a wavelet transform. Principal component analysis was used to graphically display trends in the data. If the vector points down and to the left, this represents a decrease in heart rate variability. The placebo group experienced a larger mean heart rate, significantly decreased total HRV and significantly decreased low frequency heart rate variability. Principle component analysis confirms this result, revealing a greater trend down and to
the left in the placebo group. Incidentally, more babies cried and more cried immediately (within 30 seconds of venipuncture) in the placebo group. Overall, the results show that EMLA cream relieved the stress related to venipuncture by preventing pain.

Since pre-term infants are often artificially ventilated, it is important to know the effects of artificial mechanical ventilation on heart rate variability. Van Ravenswaaij-Arts, Hopman, Kollee, Stoelinga, and Van Geijn (1995) examined the effect of artificial ventilation on heart rate variability in very pre-term infants. They recorded ECG signals and respiratory impedance curves four times each day in 20 pre-term infants less than 33 weeks gestational age within the first 72 hours of life over a wide range of artificial respiratory rates. Respiratory distress syndrome (RDS) severity was assessed at each measurement. High frequency band heart rate variability in artificially ventilated infants was similar to that seen in the control group who were spontaneously breathing. As the ventilator rate was decreased, the high frequency band variability increased. High frequency heart rate variability also increased in spontaneously breathing infants as their respiratory rate decreased. Decreases in heart rate variability in the low frequency band followed the severity of respiratory distress syndrome assessments. The loss of heart rate variability in the low frequency band occurred as RDS worsened and therefore is probably not due to the effects of artificial ventilation.

Van Ravenswaaij-Arts, Hopman, Kollee, Stoelinga, and Van Geijn (1994) examined pre-term infants who were breathing spontaneously with the purpose of determining the influence of physiological maturation over a 72-hour period, sleep state and respiration on heart rate variability. Their sample consisted of 16 pre-term infants.
less than 33 weeks gestational age during the first three days of life. This group served as
the control group in the above study. They found that heart rate variability increased with
gestational age and reflected maturation of the autonomic nervous system. High
frequency heart rate variability increased with age and reflected growing influence of the
parasympathetic nervous system.

Summary

This review of the literature demonstrated that the assessment and measurement
of pain in term and pre-term infants was complex and the results were often
contradictory. The tools used to measure pain fall into two categories. These were the
physiologically based methods and behavior based methods. The physiologically based
methods used heart rate and heart rate variability as variables to measure pain.
Additionally, there were two methods to calculate heart rate variability discussed so far.
These were the Standard Deviation method and the Wavelets Transform method. The
Fast Fourier Transform (FFT) is a third method that has not yet been discussed. This
study utilized the FFT. These methods measured variation in the R-R interval on EKG
tracings. The superiority of either method has not been clearly established at this time.
Behavior based methods looked at changes in facial activity and body movements.
Examples included the Neonatal Facial Coding System (Grunau et al. 1998), the
Premature Infant Pain Profile (Johnston et al. 1993) and the Infant Body Coding System
(Craig et al. 1993). There are many others but these are examples of commonly used
behavior pain scales.
Different groups of researchers who used the physiologically based methods often reached different conclusions. Lindh et al. (1997) and Lindh et al. (1999, 2000) were the only groups that used the frequency-based wavelet transform to measure heart rate variability during a painful procedure. Lindh et al. (1997) studied pre-term infants and concluded that acute pain resulted in a drop in total HRV and low frequency HRV. Lindh et al. (1999, 2000) examined term infants and concluded that acute pain in this group results in consistent decreases in total HRV, low frequency HRV and high frequency HRV during the pain response. The groups who used the standard deviation approach had mixed results. McIntosh et al. (1993) found that heart rate variability increased during pain in pre-term infants. Johnston et al. (1995) and Stevens and Johnston (1994) saw no significant changes in heart rate variability and concluded it was not a useful measure. Gonsalves and Mercer (1993), Porges (1992), Porter et al. (1988) and Owens and Todt (1984) all found heart rate variability decreased during the pain response.

Grunau et al. (1998), Craig et al. (1993), Stevens and Johnston (1994) Johnston et al. (1995) and Lindh et al. (1999, 2000) found that heart rate increased significantly compared to baseline during painful procedures. However, Craig et al. (1993) found that the peak heart rates in three out of five of their infant sub-groups occurred during the recovery phase. All of the groups displayed increased heart rates resulting from non-painful handling of the infants in preparation for heel lancing. Evans et al. (1997) found increased heart rates in many infants who were receiving routine care giving procedures. Zahr and Balian (1995) concluded that many infants expressed increased heart rate in response to light and noise.
Craig et al. (1993), Grunau et al. (1998), Johnston et al. (1993), Johnston et al. (1995) Lindh et al. (1997) and Shapiro (1993) all concluded that facial activity scores correlated well with the pain response in infants greater than 27 weeks gestation. Johnston et al. (1993) saw that pre-term infants used different facial expressions than did term, 2-month old and 4-month old infants. However, Craig et al. (1993) discovered that facial activity scores were not useful in distinguishing pain if the infant was less than 27 weeks gestation. The other groups did not use infants who were that young in their studies. Zahr and Balian (1995) noted that significant numbers of pre-term infants started crying in response to noise and light in the NICU.

Van Ravenswaaij-Arts et al. (1994) found that heart rate variability, as measured by the frequency-based method, increased in spontaneously breathing pre-term infants over their first 72 hours of extra-uterine life. They concluded that this was a result of physiological maturation. Van Ravenswaaij-Arts et al. (1995) found that the degree of heart rate variability of artificially ventilated pre-term infants was basically the same as spontaneously breathing pre-term infants.

There is very little doubt that low heart rate variability is strongly correlated with stress. Porges (1992), Rosenstock et al. (1999) and Van Ravenswaaij-Arts et al. (1995) all support this contention. Griffin et al. (1994) and Rosenstock et al. (1999) studied infants who were seriously ill and found low heart rate variability strongly correlated with the severity of illness. Furthermore, they saw that heart rate variability increased as the
infants’ clinical pictures improved. They also saw an increase in mortality in infants who did not experience an increase in variability.

Two studies supported the position that low heart rate variability was linked to stress and pain. While it wasn’t directly proven yet, Grunau (2000) believed that excessive stress during this vulnerable period of brain development had long-term consequences for these children. Avchen et al. (2001) found that many school age children who were pre-term infants experienced learning and behavior problems and needed more health services than their counterparts who were full term.

The NICU personnel need an objective, reliable, accurate and precise method to measure pain in pre-term, low birth weight infants who are less than 28 weeks gestation. There has not been much work done involving the study of pain with this population group. This study examined whether or not total heart rate variability (the sum of very low, low and high frequency variability), high frequency heart rate variability and the ratio of low frequency to high frequency variability were useful in differentiating between procedures that were painful and other routine care giving interventions that were non-painful in pre-term, low birth weight infants.
CHAPTER III

Methods

This study examined whether or not total heart rate variability, high frequency heart rate variability and the low/ high frequency heart rate variability ratio were useful in differentiating between procedures that were painful and other routine care giving interventions that were non-painful in pre-term, low birth weight infants. The study design, subjects, materials, data collection and data analysis are discussed in this chapter.

Design

This study was a secondary analysis of heart rate variability derived from continuous ECG recordings performed on a subgroup of preterm infants participating in a larger NIH study (Evans, McCartney & Lawhon, 2001). The design of this larger study involved the observation of premature infants in routine care giving situations over time. This study compared heart rate variability responses during heel stick procedures to those seen during axillary temperature measurements. These infants’ responses were compared using a repeated measures design.

Subjects

The setting for the original study was a regional level III neonatal intensive care unit. The unit was one of the largest in a mid-western state and served an 18 county area. The unit averaged 745 pre-term infant admissions per year, 232 of which had birth weights less than 2000 grams. For the larger study (Evans et al., 2001), infants had to be less than 37 weeks gestational age. Inclusion criteria included appropriate size for
gestational age and less than 72 hours elapsed time since birth. Exclusion criteria included known cardiovascular or CNS abnormalities, evidence of sepsis, major surgery and infants receiving tranquilizers or neuromuscular blocking agents at the time of entry into the study.

For this sub-group used in the present study, infants must have met the above criteria and gestated less than 28 weeks. This group was chosen because they were most likely to have both heel sticks and axillary temperature measurements. Of this subset, it was decided to include only those infants who experienced a heel stick or axillary temperature measurement as the first or only event in a cluster and who had these heel sticks and axillary temperature measurements performed within 14 days of each other. 10 infants met those criteria. Protection of human rights was observed and approval was obtained from the Institutional Review Boards (IRBs) at the Medical College of Ohio and the hospital where the data were collected. This was a naturalistic observation. No manipulation was done to equalize the number of painful and non-painful procedures.

Material

The larger study (Evans et al., 2001) videotaped the infants and collected continuous physiological data. A Hewlitt-Packard Merlin monitor was used to record EKG information and S+ software was used to perform Fourier Transformations and analysis to derive power spectral data for analysis of heart rate variability. Each infant served as his or her own control. Instantaneous heart rates were recorded for 128 seconds before and after a heel stick or an axillary temperature measurement. The data were stored in the computer. The real time videotape was synchronized so that physiological
and behavioral variables were observed in the exact time sequence. For this study, the physiological data included heart rate and EKG. Calculated variables included the mean heart rate, the standard deviation of the mean heart rate, the total heart rate variability, the very low frequency heart rate variability, the low frequency heart rate variability, the high frequency heart rate variability and the ratio of low frequency to high frequency heart rate variability ratio before and after painful procedures and standard care giving procedures. The presumed painful procedure was a heel stick. The presumed standard, non-painful care giving procedure was an axillary temperature measurement. This study examined whether or not high frequency heart rate variability, the ratio of low frequency to high frequency heart rate variability and total heart rate variability were useful in differentiating between procedures that were painful and other routine care giving interventions that were non-painful in pre-term, low birth weight infants. ECG recordings were analyzed using a Fourier Transform and a power spectrum analysis to determine the amount of total heart rate variability, very low frequency heart rate variability, low frequency heart rate variability and high frequency heart rate variability.

Data Collection

ECG recordings were made in daily sessions of 2-4 hours in length for the first week of the infant’s life and in weekly sessions thereafter. These time blocks were in the morning and the evening and were selected to correspond with the timing of most lab work and nursing assessments. These time blocks allowed a rest period over shift change. A computer program was written to extract those instances where an axillary temperature measurement or a heel stick was the first or only event in a cluster of care
giving activities. This was done to isolate these events and it minimized cumulative effects from preceding events. It ensured that each infant had a resting baseline prior to the heel stick or axillary temperature measurement.

This study utilized a subset of data from the larger study (Evans et al., 2001). This study focused only on those infants who had a gestational age of 28 weeks or less. The infants who experienced an axillary temperature measurement or a heel stick as the first or only event in a cluster of care giving activities and who experienced both types of stimuli within a 14-day period were included. This left a sample size of 10 infants with at least one pair of observations. Each observation consisted of 128 seconds before each infant was touched for the procedure and 128 seconds after the heel stick or insertion of the axillary thermometer. The data were grouped as having occurred either before or after an axillary temperature measurement or a heel stick. Calculated variables of interest included high frequency HRV, the low/high frequency HRV ratio and total HRV.

External validity was limited by a convenience sample and one data collection site. A variety of personnel performed the treatments and the treatment regimen wasn’t standardized. This caused a threat to internal validity. Sample size was not a threat to external validity. Hinkle, Wiersma and Jurs (1998) stated that 8 subjects achieved a power= 0.8 with 2 treatment levels. Threats to internal validity were controlled through admission and exclusion criteria and included signs of sepsis, known cardiovascular and CNS abnormalities, major surgery and certain medications. Measurement reliability was obtained by using the same program to analyze all ECG and HRV data. There was no way to control for maturation as each infant received different numbers of painful
procedures based on medical necessity and it was unethical to submit infants to unnecessary painful procedures. External validity was improved by seeking a study sample that was representative of the entire population in terms of minority membership and gender.

Data Analysis

In the original study, the data were collected. Data were cleaned and prepared for analysis. Data then were coded. The descriptive phase of the data analysis included calculation of mean heart rate and standard deviation, total heart rate variability, very low frequency heart rate variability, low frequency heart rate variability, high frequency heart rate variability and the low to high frequency heart rate variability ratio before and after a heel stick or an axillary temperature measurement. The Medical Graphics recorder detected and measured R-R wave intervals in milliseconds. An artifact correction procedure was used in the larger study to correct the arrays of R-R intervals for artifacts and spurious or missed R waves. This study then utilized a Fast Fourier Transform and a spectral analysis to obtain total heart rate variability, very low frequency heart rate variability, low frequency heart rate variability, high frequency heart rate variability and the low to high frequency heart rate variability ratio.

In the present study this data was analyzed using paired samples T tests. This effort was to determine if there was a significant difference in total heart rate variability, low frequency heart rate variability, high frequency heart rate variability and the low to high frequency heart rate variability ratio before and after a heel stick and before and after an axillary temperature measurement.
Summary

The design of the study was a repeated measures design with secondary analysis and paired samples. The setting in which the original study took place was a level III NICU at a Midwestern hospital. The subjects were a subset of ten infants who gestated less than 28 weeks. These infants had no CNS or cardiovascular abnormalities, no evidence of sepsis, no major surgery and no evidence of intraventricular hemorrhage. These infants had received no tranquilizers or neuromuscular blocking agents at the time of entry into the study. Furthermore, all infants had experienced the heel sticks and axillary temperature measurements as the first or only event in a cluster of care-giving procedures. All axillary temperature measurements and heel sticks for each infant occurred within a 14-day period. This minimized the effect of developmental changes. Materials, data collection methods and data analysis methods were described. Potential threats to validity were included and measures to compensate for them were included. The most significant threats were; threats to external validity related to the use of a convenience sample from a single hospital and threats to internal validity resulting from non-standardized treatment procedures.
CHAPTER IV

Results

This study examined whether or not total heart rate variability (the sum of very low, low and high frequency variability), high frequency heart rate variability and the ratio of low frequency to high frequency variability were useful in differentiating between procedures that were presumed to be painful and other routine care giving interventions that were presumed to be non-painful in pre-term, low birth weight infants. Heel sticks represented the painful procedures and axillary temperature measurements represented the non-painful procedures. Total heart rate variability, high frequency heart rate variability and the low/high frequency heart rate variability ratio before and after the heel sticks and axillary temperature measurements were compared using paired T tests. This discussion took place within the framework of the Roy Adaptation Model (Roy & Andrews, 1999). This study used paired sample T tests to answer three questions.

These questions were:

1) Was there a difference in total heart rate variability responses before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants?

2) Was there a difference in high frequency heart rate variability before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants?
3) Was there a difference in the low frequency/high frequency heart rate variability ratio before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants?

Sample

Ten infants were treated in this study’s sample. There were 4 females (40%) and 6 males (60%). The sample included 1 infant who was black/non-hispanic, 1 infant who was hispanic and eight infants who were white/non-hispanic. The mean post-conception age (PCA) was 27.9 weeks with a standard deviation of 2.3 weeks and a mean birth weight of 831.7 grams with a standard deviation of 171.6 grams.

Findings

Question 1: was there a difference in total heart rate variability (total HRV) responses before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants?

A paired samples t test was conducted. This was done to see if there was a difference in total heart rate variability before and after a heel stick and before and after what was considered an axillary temperature measurement in low birth weight, pre-term infants. The dependant variable was total heart rate variability. The means, standard deviations and p values for these total heart rate variability scores are presented in Table 1. The results for the paired samples t tests indicated a significant difference in total HRV after an axillary temperature measurement but no significant difference after a heel stick.
Table 1: Paired T Test results.

<table>
<thead>
<tr>
<th></th>
<th>HS</th>
<th>P-value</th>
<th>AX</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF HRV BEFORE</td>
<td>24.77+/44.59</td>
<td>.437</td>
<td>17.6 +/- 27.91</td>
<td>.323</td>
</tr>
<tr>
<td>HF HRV AFTER</td>
<td>17.36+/22.91</td>
<td></td>
<td>49.0 +/- 124.1</td>
<td></td>
</tr>
<tr>
<td>LF/HF BEFORE</td>
<td>25.22+/24.43</td>
<td>.453</td>
<td>39.34 +/- 56.88</td>
<td>.699</td>
</tr>
<tr>
<td>LF/HF AFTER</td>
<td>19.92+/12.72</td>
<td></td>
<td>39.0 +/- 32.43</td>
<td></td>
</tr>
<tr>
<td>TOTAL HRV BEFORE</td>
<td>1104.75+/896.72</td>
<td>.546</td>
<td>857.81 +/- 765.65</td>
<td>.032</td>
</tr>
<tr>
<td>TOTAL HRV AFTER</td>
<td>1249.86+/1179</td>
<td></td>
<td>2968.97+/3731.35</td>
<td></td>
</tr>
</tbody>
</table>

HS-heel stick; AX-axillary temperature measurement; HRV in milliseconds squared per Hz

Question 2: Was there a difference in high frequency heart rate variability (HF HRV) before and a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants?

A paired samples T test was conducted to see if there was a difference in high frequency heart rate variability before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants. The dependant variable was high frequency heart rate variability. The means, standard deviations and p values for these high frequency heart rate variability (HRV) scores were presented in table 1. The results for the paired samples T test indicated no significant differences in the mean high frequency HRV before and after a heel stick or before and after an axillary temperature. High frequency HRV(HF HRV) was measured before and after 13 heel sticks in 10 infants. There was a decrease in HF HRV after 8 of the heel sticks. HF HRV increased after 5 of these heel sticks. Four infants displayed large amounts of HF HRV after a heel stick. HF HRV was measured before and after 16 axillary temperature measurements involving 10 infants. HF HRV increased in 12 cases and decreased in 4 cases. Six infants displayed large amounts of HF HRV after an axillary temperature measurement.
measurement. Individual infants displayed very little consistency in measured HF HRV either before or after the heel stick and axillary temperature measurements.

Question 3: Was there a difference in the Low frequency/High frequency heart rate variability ratio (LF/HF HRV) before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants?

A paired samples t test was conducted to see if there was a difference in the low to high frequency heart rate variability ratio before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants. The dependant variable was the LF/HF HRV. The means, standard deviations and p values for the LF/HF HRV scores were presented in Table 1. The results for the paired samples T test indicated no significant difference in the mean LF/HF HRV before and after an axillary temperature measurement and before and after a heel stick. LF/HF HRV was measured 16 times before and after an axillary temperature. Eight infants displayed an increase in LF/HF HRV and 8 displayed a drop in LF/HF HRV. A similar outcome occurred before and after the heel stick.

The skewness of the total HRV before and after the heel stick was less than one. The skewness of the total HRV after the axillary temperature measurement was less than one. The skewness of the high frequency HRV and LF/HF HRV variables in the non-painful group were greater than one. The skewness of the high frequency HRV and LF/HF HRV variables in the painful group were greater than one.

Incidental findings indicated that heart rate was an indicator that distinguished between an axillary temperature measurement and a heel stick in this group of subjects.
Heart rate significantly increased following a heel stick but remained essentially unchanged following an axillary temperature measurement (Table 2).

Table 2: Comparison of Mean Heart Rate for Heel Stick and Axillary Temperature.

<table>
<thead>
<tr>
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<th>HS</th>
<th>P-value</th>
<th>AX</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Heart Rate Before</td>
<td>164.32 +/- 19.5</td>
<td>.002</td>
<td>155.87 +/- 14.97</td>
<td>.268</td>
</tr>
<tr>
<td>(beats/minute)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Heart Rate After</td>
<td>170.23 +/- 21.11</td>
<td></td>
<td>156.96 +/- 14.14</td>
<td></td>
</tr>
<tr>
<td>(beats/minute)</td>
<td></td>
<td></td>
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</tbody>
</table>

HS-heel stick; AX-axillary temperature measurement

Summary

Paired samples T tests answered three research questions. There were no significant differences in either the high frequency heart rate variability or the low to high frequency heart rate variability ratio before and after a heel stick or before and after an axillary temperature measurement. There was no significant change in total HRV after a heel stick. There was a significant difference in total heart rate variability after an axillary temperature measurement and total HRV was seen to increase.

There was a trend for total HRV to increase following a heel stick. There was a trend for the high frequency HRV to decrease following a heel stick and to increase following an axillary temperature measurement. There was also a trend for the low to high frequency HRV ratio to decrease following both the axillary temperature measurement and the heel stick. Although changes in heart rate were not a focus of this study, incidental findings indicated that heart rate increased significantly following a heelstick. Heart rate remained unchanged following an axillary temperature measurement.
CHAPTER V

Discussion

Pain was a common experience for the hospitalized, pre-term neonate. The pain often resulted from the various invasive procedures necessary to treat pre-term infants. This study examined changes in heart rate variability in response to what the investigator believed to be painful and non-painful interventions. This chapter provided a discussion of the findings of this study. Conclusions based on these findings were explored. The limitations of this study were identified. Implications for nursing theory, practice and education were debated. Finally, directions for future research in this method of pain measurement were mapped.

Findings

The results were unexpected. Total HRV, HFHRV and the LF/HF HRV were expected to remain unchanged in the axillary temperature group. It was expected that HF HRV and total HRV would decrease in the heel stick group. It was also expected that the LF/HF HRV would increase in the heel stick group. These expectations were not supported by the results.

One of the research questions asked whether or not there was a difference in HF HRV before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants. There were no significant differences in these two groups or events based on the results of paired samples T tests. Even though the differences were not significant, HF HRV increased after an axillary temperature
measurement and decreased after a heel stick. Also, there was large amount of variance between infants both before and after the heel stick and axillary temperature measurements. Parasympathetic nervous system influence on heart rate tended to decrease after a heel stick and increase after an axillary temperature measurement.

There were several possible explanations for these findings. All humans had weak linkages between afferent fibers and dorsal horn cells during the first post-natal week so that a single stimulus can elicit pain responses that last several minutes whereas other stimuli may not cause a reaction (Evans et al., 2001). Infants in this age group perceived and reacted to routine care giving procedures as if they were painful (Evans et al., 2001). Light touch was thought to be aversive to pre-term infants (Grunau, 2000). They may react in similar ways when experiencing either a heel stick or an axillary temperature measurement. Mazursky et al. (1998) found that autonomic influences on heart rate in pre-term infants were developmentally delayed until approximately 32 weeks post-conception and that autonomic control of the heart was impaired in infants less than 32 weeks post conception. Mazursky et al. (1998) stated that there was evidence that the sympathetic nervous system matured before the parasympathetic nervous system. Some of these infants in this study may not have had a mature parasympathetic nervous system. Evans et al. (2001) stated that pre-term infants had meager energy reserves and this may have altered how they responded to stimuli. The high frequency band reflects parasympathetic activity (Lindh et al., 1997; Mazursky et al., 1998).

Lindh et al. (1997) found no significant changes in high frequency HRV in pre-term infants after a heel stick. These findings supported the results of this study. Lindh et
al. (1997) used a small sample of infants who exhibited a wide range of gestational and post-conception ages. Their sample had a range of gestational ages equal to 24-33 weeks and was aged 27-35 weeks post-conception. An alternative possibility was that the device used by Lindh et al. (1997) was not perceived to be painful.

Lindh et al. (2000) reached similar conclusions regarding pain and high frequency HRV in a sample of full term infants. They examined changes in LF HRV, HF HRV and total HRV in 60 full term infants. One group received EMLA topical anesthetic prior to venipuncture and the other group received a placebo topical cream. The placebo group displayed decreased LF HRV and total HRV. There was no significant change in high frequency HRV. Their was no change in HF HRV after a painful stimulus in the current study. This result was supported by Lindh et al. (2000). There was a great deal of difficulty in drawing parallels between the full term infants used in Lindh et al. (2000) and the premature infants in the current study due to the significant developmental differences in the autonomic nervous system between term infants and pre-term infants less than 28 weeks gestational age (Grunau 2000, Mazursky et al. (1998).

Another research question asked if there was a difference in the LF/HF HRV before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants. A paired samples T test yielded no significant differences in either of these two groups or events. However, the mean LF/HF HRV decreased somewhat in both the painful and non-painful groups. None of the authors cited in the literature review have used the LF/HF HRV when studying the pain response in this population. The results of the current study indicated that the LF/HF HRV was not
a useful pain indicator. Mazursky et al (1998) examined responses to a presumably painful stimulus and found that pre-term infants did not display a significant change in the LF/HF HRV in response to head up tilting to 45 degrees until after 32 weeks post-conception. This supported the results of the current study. Mazursky et al. (1998) stated that the LF/HF HRV ratio reflected sympathetic/parasympathetic balance (Mazursky et al., 1998).

The final research question asked whether or not there was a difference in total heart rate variability before and after a heel stick and before and after an axillary temperature measurement in low birth weight, pre-term infants. A paired samples T test was performed and the results indicated a significant increase in total HRV in the axillary temperature group but no significant changes in total HRV in the heel stick group. The trend was for total heart rate variability to increase after either a heel stick or an axillary temperature measurement.

A possible explanation for no change in HRV following the heel stick and before squeezing could be that the heel stick device used by Lindh et al. (1999) was not perceived to be painful. Lindh et al. (1997) also saw a significant drop in total HRV in pre-term infants following a painful stimulus. This finding contradicted the results of this study.

Changes in heart rate were not considered as a focus of the original research questions posed and answered by this study. An incidental finding demonstrated that heart rate was a sensitive indicator of pain in this group of infants. Heart rate increased significantly following a heel stick. There was no significant change in heart rate
following an axillary temperature measurement. This indicated a significant increase in sympathetic nervous system activity following a heel stick compared to that following an axillary temperature in this group of infants.

It was difficult to make comparisons with results from other researchers that used the Standard Deviation or Standard Error methods to measure changes in heart rate variability. Comparisons made between results obtained using the Fast Fourier Transform and the Standard Deviation/Standard Error methods may only be possible when discussing total heart rate variability. The Fast Fourier Transform to created a graph of heart rate frequency power with units of milliseconds squared/Hertz along the y-axis and frequency along the x-axis. It was an algorithm that converted amplitude as a function of time to amplitude as a function of frequency. Heart rate variability (power) was the area under the resulting curve. This curve was then divided up into high, low and very low frequency ranges. Total heart rate variability was the sum of the high, low and very low frequency power and represented the entire area under the curve. As the area under a specific part of the curve became smaller, it was interpreted as a decrease in heart rate variability measured by that frequency band.

The Standard Deviation method was a strictly time based method. The instantaneous heart rate was typically recorded every three seconds. The standard deviation of the mean heart rate was calculated over a moving window that was 60 seconds in length. Variation in the size of this standard deviation was the measure of heart rate variability. As the standard deviation became larger, this was interpreted as an
increase in heart rate variability. As it became smaller, this was interpreted as a decrease in heart rate variability.

The baseline heart rate variability for both methods were those HRV measurements obtained when the infant was in an undisturbed resting state for a period of time. The necessary length of time required to establish a resting state varied from researcher to researcher and no one standard was adopted. Often the length of the resting period was restricted by the frequency of medical and nursing interventions performed by the staff caring for the infants participating in any particular study.

The groups who used the Standard Deviation method had mixed results. McIntosh et al. (1993) found that heart rate variability increased following a heel stick in pre-term infants. McIntosh et al. (1993) found no change in HRV following a sham heel stick. This result, if comparison can be allowed, did not agree with the current study where total HRV was seen to increase significantly after an axillary temperature measurement (a non-painful stimulus) and did not change after a heel stick (a painful event). McIntosh et al. (1993) are also the only group that found increased in heart rate variability after a painful stimulus. Johnston et al. (1995) and Stevens and Johnston (1994) saw no significant changes in heart rate variability after a painful stimulus and concluded it was not a useful measure of the pain response. These studies supported the results of this study. Gonsalves and Mercer (1993), Porges (1992), Porter et al. (1988) and Owens and Todt (1984) all found heart rate variability decreased during the pain response. Gonsalves and Mercer (1993), Porges et al. (1992) and Porter et al. (1988) measured HRV with the
Standard Deviation method. Owens and Todt (1984) just looked at the graph of instantaneous heart rate during pain and concluded that total HRV decreased during pain. Again, if comparison were allowed, Gonsalves and Mercer (1993), Porges et al. (1992), Porter et al. (1988) and Owens and Todt (1984) had results that supported the findings of Lindh et al. (1997) and Lindh et al. (1999,2000). Lindh et al. (1997) and Lindh et al. (1999, 2000) used the Wavelet Transform method and found decreased total HRV during pain. Gonsalves and Mercer (1993), Porges et al. (1992), Porter et al. (1988) and Owens and Todt (1984) had results that do not support the findings of this study.

The meanings of these findings are complex and at best inconclusive. HF HRV and the LF/HF HRV were not useful measures of pain in this population according to the results of the current study. In contrast, Lindh et al. (1999, 2000) concluded high frequency HRV decreased during the pain response. However, they used full term infants. On the other hand, Lindh et al. (1997) used premature infants and found no significant difference in high frequency HRV in pre-term infants following a painful stimulus. Their sample may have little in common from a developmental standpoint with the sample used in the current study. The infant sample that Lindh et al. (1997) used was considerably older and had a wide post-conception age range. The results of the current study demonstrated a trend for LF/HF HRV and the LF/HF HRV to decrease during pain.

The finding of a significant increase in total HRV after a non-painful event was in direct contrast to Lindh et al. (1997) and Lindh et al. (1999,2000), Gonsalves and Mercer (1993), Mcintosh et al. (1993), Porter et al. (1988), Porges et al. (1992) and Owens and
Todt (1984). This result was completely unexpected. Mcintosh et al. (1993) found that heart rate variability remained unchanged during the non-painful situation and increased only during a painful stimulus. However, Mcintosh et al. (1993) used a non-painful stimulus that was different than the one used in this study.

Conclusions

High frequency HRV and the LF/HF HRV ratio were not useful measures of pain in pre-term, low birth weight infants. Total HRV increased significantly after an axillary temperature measurement in this study but the meaning of this was unclear. Total HRV increased after a heel stick in this study, but it was not statistically significant. These results were very qualified. Total HRV decreased in Lindh et al. (1997) and Lindh et al. (1999, 2000).

Although it was not considered as part of the research questions this study sought to answer, heart rate was a sensitive pain indicator in this group of infants. There was a significant increase in heart rate following a heel stick and no significant change in heart rate following an axillary temperature measurement.

Limitations

Generalizations based on the results of this study were extremely limited if they exist at all. The data were unusual. Skewness greater than one indicated the HF HRV and the LF/HF HRV data were not normally distributed. The standard deviations of the total HRV, HF HRV and the LF/HF HRV were extremely large and in many cases nearly
equal or exceed the values of their means. This indicated unacceptable variation in the
distribution of the data. In comparison, Lindh et al. (1997) and Lindh et al. (1999, 2000)
used the Wavelet Transform method (a type of frequency domain analysis) and
consistently demonstrated standard deviation values for these same measures that were
much smaller and which indicated normal distribution of their data. Lindh et al. (1999,
2000) used principal component analysis (PCA) in addition to frequency domain
analysis. PCA is a method to display trends in frequency domain analysis and does not
alter mean and standard deviation values of total HRV, HF HRV and the LF/HF HRV.

Based on these problems with this study, the ability to draw any trustworthy
conclusions was extremely limited. Since no one person or group of persons performed
the heel sticks and axillary temperature measurements there may have been inconsistency
in how the procedures were executed. There was no control of extraneous stimuli such as
light, noise and temperature, although this particular NICU did an excellent job at
providing an optimal environment for the infants. There was no strict control on the time
of day that measurements were taken.

Implications

Total HRV, HF HRV and the LF/HF HRV were not helpful indicators of the pain
response in pre-term, low birth weight infants less than 28 weeks gestational age. Heart
rate was a sensitive indicator of pain in this age group. Also axillary temperature
measurements need to be examined to determine if they were interpreted as painful by
this age group.
Recommendations for Further Research

The usefulness of heart rate variability in measuring the pain response in low birth weight infants younger than 28 weeks post-conception remained in doubt. Continued research into the relationship between pain and heart rate variability needs to be performed to help clarify whether or not it is valid as a pain measurement method in infants less than 32 weeks post-conception. Efforts need to be made to determine at what age HRV may be predictive of pain.

Summary

The findings of the present research study indicated changes in total HRV, high frequency HRV and the LF/HF HRV in response to a heel sticks to axillary temperature measurements in pre-term, low birth weight infants less than 28 weeks gestational age were not useful in differentiating pain from stress. Changes in heart rate were useful in differentiating pain from stress in this group of infants. The results of the present study were inconclusive. The author believes that the measurement of heart rate variability will become established as a valid tool to objectively measure pain in the pre-term infant population that is older than 28 weeks post-conception. Findings were discussed in relationship to the current literature. Implications for nursing theory, practice and education were discussed and future research recommendations were provided.

This study found no support for the use of heart rate variability as a pain measure in this age group. Unfortunately, it shed little light on the relationship between heart rate variability and pain in low birth weight, pre-term infants. The statistical analysis revealed
no significant results regarding the effect of pain on high frequency HRV and the LF/HF HRV. Although there were significant changes in total HRV, the interpretation of results was puzzling since total HRV increased after both painful and non-painful stimuli and the greater magnitude and statistically significant increase was seen in the non-painful group. There was a downward trend in high frequency HRV after pain, corresponding to an upward trend in the non-painful treatment group. These changes were, however, not statistically significant. There was a significant increase in heart rate after a heel stick that did not occur following an axillary temperature measurement. Heart rate was shown to be a sensitive indicator of pain in this sample of infants.

This study does have several important limitations. There were large fluctuations in values for the HRV measurements in all frequency ranges even with the same infant. The data was not normally distributed and was heavily skewed in most situations. There may have been inconsistency in the heel stick and axillary temperature procedures due to different personnel performing these procedures. Sample measurements were obtained during different times of day and this may have affected the results. There was no control of environmental variables that may have occurred simultaneously with sample measurements. These may have included changes in temperature, light and noise.

Continued research into monitoring and measuring pain in pre-term, low birth weight infants is extremely important. Nursing and medicine need a reliable and accurate tool to objectively assess the amount of pain that these infants experience during the frequent procedures performed to provide their medical care. An accurate measurement
tool is needed so that health care professionals can monitor and minimize the pain that these infants have to endure.
REFERENCES


Academic Employee Disclosure of Potential Conflict of Interest Form for Sponsored Programs

This form must be completed by faculty and staff and submitted with each application for sponsored programs (including publicly-funded grants and privately supported projects).

<table>
<thead>
<tr>
<th>Name &amp; Telephone Extension*</th>
<th>Dept.</th>
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<tr>
<td>James McGray, RN</td>
<td>School of Nursing</td>
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<tr>
<th>Title and/or Position</th>
<th>School</th>
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<tbody>
<tr>
<td>Graduate Nursing Student</td>
<td>School of Nursing</td>
</tr>
</tbody>
</table>

* P.I./Program Director must list on Page 2 all Academic Employees associated with this project.

**PROJECT TITLE:**
Stability of Infant Responses to Painful Procedures

**SPONSOR:** NIH, NINR

**MCO Acct. #:** 94215003

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Page 1
Name of company involved: 

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_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ 

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Reviewed by: Department Chair 

Reviewed by: Associate Vice President for Research 

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ABSTRACT

This study sought to establish the utility of heart rate variability measurement as a tool to assess pain in low birth weight premature infants. It used a repeated measures design with secondary analysis and paired samples. Subjects were a subset of 10 infants who were less than 28 weeks gestational age. Heart rate increased significantly following a heel stick and remained unchanged following an axillary temperature measurement. There was a significant increase in heart rate during what is thought to be pain that did not occur following a presumably non-painful stimulus. Heart rate was shown to be a sensitive indicator of pain in this sample of infants. No support was found for the use of heart rate variability as a pain measure in this age group and post-conception age range.