NONNUTRITIVE SUCKING AND SUCROSE-INDUCED ANALGESIA: EFFECT ON HEART RATE, OXYGEN SATURATION, AND PAIN IN INTUBATED INFANTS

By

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– primum non nocere

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Critically ill neonates who require artificial airways are unable to vocalize due to the blocking of their vocal chords by the endotracheal tube. Pain assessment in this neonatal population is difficult due to the inability of the infants to self-report their pain with cries of distress. While pain is a common part of the hospital experience, nonnutritive sucking-induced analgesia with sucrose is offered less to intubated neonates. The purpose of this study was to determine the effect of nonnutritive sucking (NNS) combined with sucrose-induced analgesia on heart rate, oxygen saturation, and pain behaviors as measured by the Neonatal Infant Pain Scale (NIPS) in intubated infants. Using a repeated measures cross-over design, 14 infants between the ages of 32 and 42 weeks were sampled by convenience from a Neonatal Intensive Care Unit. Each infant served as it's own control, and were randomly assigned to participate first in one of two conditions resulting in 28 observations. In the treatment condition infants were offered NNS with sucrose, and in the control condition were not. Heart rate and oxygen saturation were measured in 30-second intervals during a 5-minute baseline period, a heel stick, and 5-minute follow-up period. Pain behaviors were measured in one minute intervals. Findings were analyzed using a within-subjects repeated measures analysis of variance. Significant differences were noted between the control and intervention conditions. Heart rate significantly increased

following the heel stick in the control condition; main effect F (df 1, 13) = 46.65, $p < .001$; phase effect F (df 3, 39) = 101.73, $p < .001$; interaction effect F (df 3, 39) = 24.69, $p < .001$. Oxygen saturation significantly decreased following the heel stick in the control condition; main effect F (df 1, 13) = 19.08, $p = .001$; phase effect F (df 3, 39) = $p < .001$; interaction effect F (df 3, 39) = $p < .001$. The NIPS Score significantly increased following the heel stick in the control condition; phase effect F (df 1, 13) = 697.88, $p < .001$. Findings will be used to further knowledge related to pain in intubated infants in the hospital setting.

CHAPTER 1
INTRODUCTION

Despite what is known about the harmful effects of pain during the early developmental period, pain in intubated infants often goes unrecognized. This is because the cries of intubated infants are silenced by the same endotracheal tube that supports their lives by supplying oxygen. The lack of an audible distress cry makes the assessment of pain difficult. Intubated infants are therefore seldom offered the pacifying effects of nonnutritive sucking (NNS) (Miller & Anderson, 1993). In order to effectively manage pain in intubated infants, health care professionals must learn to recognize the infant's physiologic and behavioral response to pain.

Along with establishment of the existence of pain in neonates, attention to the treatment of pain has not followed. It is estimated that between 1995 and 2003 neonates cared for within neonatal intensive care units (NICU) endured a total of 38,426 invasive and potentially painful procedures (D'Apolito, 2006). According to a study published in the Journal of the American Medical Association, each infant during the first 14 days after admission to the NICU undergoes an average of 16 stressful or painful procedures per day (Carbajal, et al., 2008). Attempts to reduce pain and the resulting negative outcomes without altering the stability of the infant with pharmacologic agents remain a challenge for the health care team. Nonnutritive sucking with sucrose is a nonpharmacologic option that may provide a beneficial reduction in both immediate and long term, physiological and behavioral responses to untreated sensations of pain.

Immediate Responses (Physiological and Behavioral)

Immediate physiologic responses to pain in infants include sympathetic nervous system involvement; notably increases in heart rate, respiratory rate, intracranial pressure, decreases in oxygen saturation, and changes in blood pressure (Stevens & Johnson, 1994). Additional autonomic nervous system involvement in infants yields alterations in skin color, nausea,

vomiting, and dilated pupils. Immediate behavioral responses to pain in infants include cries, body movement, and changes in facial expression (Stevens, Johnson, & Horton, 1994). Despite differences in gestational age, facial expressions (particularly brow bulge, eye squeeze, and nasolabial furrow) are considered valid indicators of infant pain (Stevens, 1993). Physiologic indicators, including heart rate and oxygen saturation, are easily accessible in the intensive care unit, but are sometimes unreliable due to data obtainment error and not specific to pain alone (Barr, Rotman, Yaremko, Leduc, & Francoeur, 1992). It has therefore been concluded that when measuring procedural pain such as heel sticks, physiologic indicators should be used in conjunction with behavioral indicators, including behavioral state scores based on cries, body movements, and changes in facial expression (Stevens & Johnson, 1994).

Long Term Responses to Pain (Physiological and Behavioral)

Management of neonatal and infant pain is important not only to provide comfort, but also to prevent long-lasting negative consequences related to painful experiences (Grunau, 2002). It is believed that neonates may experience pain from the moment of birth, even when born prematurely. By 20 weeks gestation neural pathways and sensory receptors are developed and intact. It is not until almost full gestation that the inhibitory pathways for pain modulation are mature (Anand, Phil, & Carr, 1989). The inability to modulate pain leads to a decreased pain threshold, and prolonged periods of hypersensitivity in premature infants (Fitzgerald, M., Millard, C., & MacIntosh, N., 1988). Even nonnoxious stimuli (such as a change in positioning or handling) may be perceived as painful (Evans, Vogelpohl, & Bourguignan, 1997). Repetitive pain and local injury to tissue, such as repeated heel sticks, may further reduce the pain threshold (Anand, 1998; Reynolds & Fitzgerald, 1995).

Pain has been found to have detrimental effects that compromise growth, development, and health (Boss, 2002). Repeated pain may lead to negative physiologic outcomes further

compromising the health of the infant. Some potential negative physiologic outcomes include increased peripheral vascular resistance, increased myocardial oxygen consumption, increased production of carbon dioxide, and decreased gastric immobility (Beacham, 2004). As a result, weight loss and fatigue may occur.

A major by-product of pain is stress. A cascade of biochemical reactions result from stress with in particular, the activation of the sympathetic nervous system which releases catabolic glucocorticoids (epinephrine, norepinephrine, and cortisol). The glucocorticoids retard protein synthesis, cell growth, and neuron myelinization. The result is a breakdown of protein, carbohydrate, and fats stores delaying the repair of injured tissues (Piano & Huether, 1998).

Increases in heart rate and blood pressure are evident with repeated episodes of untreated pain (Puchalski & Hummel, 2002). As a consequence, alterations may occur in venous, intracranial, and arterial oxygen saturation (Stevens, Johnson, & Gibbs, 2000). A direct correlation was found between the number of episodes of hypotension and hypoxia and intraventricular hemorrhage in preterm infants (Low, et al. 1992). Behavioral responses to pain have included cries, alteration in body movement from relaxed to flexed or extended, and changes in facial expression from relaxed muscles to grimace (Stevens & Johnson, 1994).

Application to Nursing

The participation of nurses in pain management is crucial to achieve short and long term positive health outcomes for infants who are positioned to experience repetitive or severe pain. Attention to comfort is a foundational element of nursing (Watson, 1979). Ethically, there is an obligation for nurses to look for an expression of pain and to alleviate pain in those who cannot advocate for themselves (Beauchamp & Childress, 2008), This applies to an intubated newborn who cannot verbalize pain through a cry.

Nurses are best positioned to assess, treat, and prevent pain in the hospital because they are nearest the patient. One frequently studied intervention nurses can employ to alleviate infant pain is nonnutritive sucking (NNS). Nonnutritive sucking is the placement of a pacifier into a neonate's mouth to promote sucking behaviors without breast milk or formula, hence the term nonnutritive (Blass & Hoffmeyer, 1991; Gibbens, Stevens, Hodnett, et al. 2002). The mechanical effect from the act of orotacile suckling is hypothesized to work by blocking the body's ability to transmit the sensation of a painful impulse back to the brain. This alteration of pain perception is commonly known as Gate Control Theory (Melzack & Wall, 1965). It has been hypothesized that if the pain is not recognized by the brain, or the transmission of the signal is blocked, the negative consequences of pain do not follow.

More recent studies show that the combination of sucrose and NNS is more effective in altering the perception of pain than NNS alone (Harrison, Johnston, & Loughnan, 2003). In addition to Gate Control, the two additional mechanisms of pain modulation offered by the addition of sucrose are thought to be the release of short-acting endogenous opioids and the attention-gaining response to the strong taste (Harrison et al., 2003). Sucrose is a disaccharide composed of fructose and glucose that combines for a strong, sweet taste (Blass & Hoffmeyer, 1991). The calming effects are from a mediated opioid response that is activated through the taste receptors located at the tip of the tongue (Blass & Watt, 1999). Taste-induced analgesia has been demonstrated in both human and nonhuman newborns and is dependent on the ability of the subject to detect a sweet taste--not merely through ingestion of the sucrose. This is important for the study reported here because sucrose was administered orally to the tongue. Sucrose administered to preterm neonates by a nasogastric tube (not orally) failed to produce an analgesic effect for heel sticks (Ramenghi & Levene, 1999). Thus, a simple intervention such as the

combination of NNS with the oral administration of sucrose shows promise for promoting the mediation of pain in intubated infants.

Nurse researchers have a duty to find nursing interventions that will work and to validate their use at the bedside, especially for patients who cannot advocate for themselves (American Academy of Pediatrics, 2000). This study was guided by the alteration of the perception of pain with the Gate Control Theory. Two bioethical considerations, nonmaleficence and beneficence, and the concept of caring, were also used to guide this research. The altering of pain perception with NNS in combination with sucrose can potentially improve the health and development of seriously ill infants by providing a nonpharmacologic treatment. The purpose of this study is to determine the effect of nonnutritive sucking (NNS) combined with sucrose-induced analgesia on heart rate, oxygen saturation, and pain behaviors (measured by the Neonatal Infant Pain Scale) in intubated infants between the ages of 32 weeks gestation to less than or equal to 42 weeks gestation.

Specific Aims

Specific Aim 1

Determine the effect of NNS and sucrose-induced analgesia (treatment condition) on heart rate in intubated infants during a painful event (heel stick).

Hypothesis 1

Infants will have lower mean heart rates in the NNS condition with sucrose (treatment condition) during a heel stick than those infants not offered NNS with sucrose (control condition).

Specific Aim 2

Determine the effect of NNS and sucrose-induced analgesia (treatment condition) on oxygen saturation in intubated infants during a painful event (heel stick).

Hypothesis 2

Infants will have higher mean oxygen saturations in the NNS condition with sucrose (treatment condition) as measured by noninvasive pulse oximetry during a heel stick than those infants not offered NNS with sucrose (control condition).

Specific Aim 3

Determine the NIPS scores in the NNS condition with sucrose (treatment condition) in intubated infants during a painful event (heel stick).

Hypothesis 3

Infants will have lower NIPS scores in the NNS condition with sucrose (treatment condition) during a heel stick than those infants not offered NNS with sucrose (control condition.

CHAPTER 2
REVIEW OF LITERATURE

A steadily increasing number of premature infants are being kept alive through the extraordinary efforts of neonatal intensive care units (Aslam, Panjvani, & Rajegowda, 2007). Often, these neonates require respiratory support in the form of artificial airways that is punctuated by daily painful procedures (including venous access and heel sticks).

This study is guided by two bioethical principles, beneficence and nonmaleficence (Beauchamp & Childress, 2008), the concept of caring, and the Gate Control Theory. The author will use the Gate Control Theory to conceptualize the alteration of the perception of pain with NNS and sucrose-induced analgesia. Melzack and Wall (1965) theorized a gating mechanism within the spinal cord and in the thalamus. These theoretical gates in the pain pathway can be opened or closed, allowing or not allowing pain to register in the brain. This results in the modulation of pain by closing the gate to the area of the brain that receives and reacts to the painful or noxious stimuli. For example, as in the study presented here, through the introduction of the intervention of NNS with sucrose analgesia.

Bioethical principles, such as beneficence and nonmaleficence, and concepts, such as caring, serve as guidelines for professional behavior. Healthcare agencies have attempted to address the issue of pain control through the creation of codes and position statements. What follows is a historical review of bioethical codes, pain, and bioethics and infant pain.

Bioethical Codes

The English physician Thomas Percival wrote the first code of bioethics in 1794 entitled "Medical Ethics; or a Code of Institutes and Precepts" to serve as a guide for physicians. The code asserted moral authority and independence of physicians to serve others. It was later revised and adopted by the American Medical Association (AMA) in 1847 to address health care

needs (Center for the Study of Ethics in the Professions [CSEP], 1999). The AMA Code of Medical Ethics included, "…when pestilence prevails, it is their (physician) duty to face danger, and to continue their labours for the alleviation of the suffering, even at the jeopardy of their own lives." This provision was deleted in 1977 (http://www.library.dal.ca/kellogg/Bioethics/codes/codes.htm).

Codes of bioethics are now the defining standard of professionalism for health care providers. They were put in place to shift decision-making amongst physicians from autonomous practice to a more standardized process of bioethical behavior. The most unique contribution of Percivalian ethics was the transition from individual physician duties to core collective responsibilities of the profession. Specifically, the role of the physician to serve others, and care for the sick was introduced. A moral consideration was also noted with the emphasis on individual honor for the physician (DePender & Ileda-Chandlere, 1990).

Later, specific guidelines for ethical behavior were developed. In 2003 Beauchamp suggested the use of specification (a method which reduces the vagueness of principles) to specify the ethical guidelines. Four principles were identified by Beauchamp as foundational to biomedical ethics: 1) respect for autonomy, 2) nonmaleficence, 3) beneficence, and 4) justice (Beauchamp, 2003; Macklin, 2003).

Four Principles of Bioethics

The first foundational principle of biomedical ethics is respect for autonomy. This principle encompasses freedom from controlling forces or self-rule. Two conditions essential for autonomy are liberty (the absence of controlling forces), and agency (the ability to act intentionally) (Beauchamp & Childress, 2008). The principle of respect for autonomy was not chosen as a guideline for this research because infants do not exhibit liberty, in addition to agency.

The second foundational principle of biomedical ethics is nonmaleficience. The principle of nonmaleficence involves the act of not inflicting or causing harm. It involves refraining purposely from actions that cause harm. The maxim *Primum non nocere* associated with medical ethics means first do no harm (Beauchamp & Childress, 2008). The principle of nonmaleficience was chosen because it closely related to this study of doing no harm in the infant population.

The third foundational principle of biomedical ethics is beneficence. The principle of beneficence involves obligation and moral duty. Examples include preventing harm, protecting and defending, and removing conditions that cause harm (Beauchamp & Childress, 2008). Beneficence would require nurses to identify and alleviate pain and suffering in patients. The principle of beneficence was chosen to guide this study because it was consistent with the concept of preventing both short and long term damage caused by untreated pain.

The fourth foundational principle of biomedical ethics is justice. Fair and equitable are terms that have been associated with the definition of justice. It was noted, however, that the principle of justice was not independent from other principles, notably beneficence and nonmaleficence (Beauchamp & Childress, 2008). It was for this reason that the principle of justice was not specifically chosen to guide this research.

Caring

In her major work entitled *Caring, a Feminine Approach to Ethics & Moral Education* (1984), Nel Noddings, the distinguished professor from Stanford University, explores a feminine approach to ethics. Her argument is that caring is basic in human life. She makes the distinction between being cared-for and caring-about. Caring-for comes first in life to be followed by extension to caring–about, or to care about others. Noddings argues that caring about others is

fundamental to a sense of justice. Natural caring comes before ethical caring and is similar to that of a mother for a child.

Caring is an extension of the positive duty of beneficence. A positive duty is the ethical obligation to act. A negative duty is the ethical obligation to withhold an action that would be harmful. This is consistent with nonmaleficence (Beauchamp & Childress, 2008). Kellogg (2006) states the Hippocratic Oath is foundational to western medicine and includes the concepts of beneficence and nonmaleficence. The Nuremberg Code addresses these concepts by requiring the avoidance of and protection from injury (Kellogg, 2006). Later, the Declaration of Helsinki in 1964 requires the protection of the well being of human subjects (Kellogg, 2006)

Despite this history of ethical obligations to do good and avoid harm, modern medical practices expose infants to pain that is repetitive, acute, and prolonged (Anand & Phil, 2001). One recommendation made is that clinical units should develop written guidelines for pain management in neonates. These guidelines are often expressed through the adoption of existing codes of ethics that address pain, either directly or indirectly. Conflicts regarding the need to perform necessary procedures that cause harmful pain and the medical benefits continue. Principles of medical ethics, such as nonmaleficence and beneficence, are relevant to the issues of infant pain. Given that infants are persons and entitled to moral regard, an understanding of the moral principles that guide medical care is important in this vulnerable population. Ethical principles can serve as guides in the treatment of pain.

Medical and Nursing Principles Related to Pain

Healthcare agencies and organizations have attempted to address the issue of pain control through the creation of standards, codes, and position statements. The following describes the many diverse efforts including the standard of pain management by the Joint Commission on Accreditation of Healthcare Organizations. Codes of ethics, such as those supported by the

American Nurses Association and the National Association of Neonatal Nurses are described. Position statements on infant pain, such as those created by the American Academy of Pediatrics, the American Pain Society, the National Association of Neonatal Nurses, and the American Nurses' Association are included.

The primary organization that accredits hospitals in the United States, the Joint Commission on Accreditation of Healthcare Organizations [JCAHO] (2001), released standard RI.1.2 that states patients must be involved in all aspects of their own care, including the effective management of pain (JCAHO, 2001). This means nurses must take cues from their patients to adequately interpret their indications of pain. In addition, the American Hospital Association (AHA) released the Patient's Bill of Rights in 1973 outlining the rights of a patient. Later in 1992 revisions were made to include the right of the patient to receive considerate and respectful care (AHA, 1992).

Application to Pediatrics

More specifically, the American Academy of Pediatrics and the American Pain Society (2001) found the issue of procedure-related pain in infants important, and comprised a joint statement that advocates for the alleviation pain when possible. For procedural pain, the statement says that anticipation of the patient's pain is the key to optimal management, and that adequate treatment is the humane approach. As a consequence, the measurement of pain is now considered the fifth vital sign and is common practice in hospitals and clinics. Unfortunately, in practice there is inconsistency on how to assess and measure pain in nonverbal populations. Taken together, this suggests that bedside nurses are practicing the assessment of pain without research evidence that shows consistency and efficacy of their techniques.

In response to the need for further guidance regarding the management of infant pain, the National Association of Neonatal Nurses (NANN) released the Position Statement Number 3019

on Pain Management in Infants in 1999. It states nurses must be diligent in the management of infant pain (Duhn & Medves, 2004). The NANN believes that infants do feel pain, and pain assessment should include both a physiologic and behavioral dimension. In the study reported here, pain was measured by observing a combination of behaviors utilizing the Neonatal Behavioral Pain Scale (NIPS), and physiological factors. The NIPS scores procedural pain behavior in both term and preterm infants (Duhn & Medves, 2004).

The National Association of Neonatal Nurses also released a code of ethics that mandated that the primary responsibility of the nurse is to the patient, including the protection of the patient's physical well being (NANN, 2006). The assessment, prevention, and alleviation of pain in an evidence-based manner fall within this ethical code.

One of the goals of neonatal caregivers according to the 2006 American Academy of Pediatrics Policy Statement is to prevent neonatal pain. It, however, further states major gaps remain in the knowledge of the best way to prevent and relieve pain. In the latest position statement for pain management of infants by the National Association of Neonatal Nurses (NANN), emphasis is placed on providing the most effective pain relief that can be given safely (National Association of Neonatal Nurses, 1999). Currently the National Association of Neonatal Nurses set the standards for the neonatal nursing profession. The organization further states it has a moral and ethical responsibility to include new knowledge and methods of infant pain assessment and treatment.

In general, the profession of Nursing is governed by the International Council of Nurses (ICN) and the American Nurses' Association (ANA). Both governing bodies have developed codes of ethics to guide nursing practice. The ICN (2006) released their code of ethics, the preamble of which states that nursing care is "respectful" and "unrestricted by considerations of

age." The professional association that represents all nurses, the ANA, also has a code of ethics that gives nurses the duty to both prevent illness, such as those caused by untreated procedural pain, and to alleviate suffering. The preface to the ANA code supports the principles of autonomy, beneficence, nonmaleficence, and justice (ANA, 2006). Through the creation of these codes and position statements, these governing bodies of nursing have attempted to guide and support ethical decision making in nursing practice.

In summary, diverse healthcare agencies have attempted to address the issue of pain control through the creation of some of the above mentioned codes and position statements. Painful procedures continue to exist in the hospital setting. Pain assessment is essential for practice, but the measurement of pain in the nonverbal population remains difficult and at best, an estimate. The nonverbal intubated infant is not able to verbally state the presence of pain, and physiologic indicators such as vital signs are often unreliable. Physiologic indicators may not be specific topics since they reflect a nonspecific response to stress (Barr, 1992). A more scientifically grounded, evidence-based approach to the assessment and treatment of neonatal pain is therefore necessary. The goal of this study was therefore to use an evidence-based approach to address the issue of infant pain control A functional theory, the Gate Control Theory, was identified and used to assist in the understanding of the alteration of the perception of pain through NNS in intubated infants.

Pain

Gate Control Theory

The Gate Control Theory is the theoretical framework identified for use in this study to illustrate the alteration of the perception of pain with NNS and sucrose-induced analgesia, and to further depict the effect on heart rate, oxygen saturation, and pain assessment. The Gate Control

Theory is a functional theory, which can be used to describe the phenomenon of NNS and its influence on pain.

The behavioral pain response to noxious stimuli is detected in infants as early as 24 weeks gestation (Coskun & Anand, 2000). Pain signals traveling to the brain can be interrupted by stimulating the periphery of the pain site, the appropriate signal-carrying nerves at the spinal cord, the corresponding areas in the brain stem, or the cerebral cortex. The ability of the nerve to detect the pain signal, or noxious stimuli, and transport that information to the cerebral cortex is known as nociception (McGrath, 1993). Activities that inhibit nociceptive transmission, and thereby close the "pain gate" include rubbing, massage, and cuddling (Hatfield, 2008). The pain gate to the brain can be closed by stimulating nerves responsible for carrying the touch signal, or mechanoreceptors, which enables the relief of pain. Painful stimuli may travel down the nerve pathways, but the sensation of pain would not be recognized because the theoretical gate would be closed (Melzack & Wall, 1965). Studied techniques illustrating this include massage, rubbing, and the application of heat and cold (Doody, Smith, & Webb, 1991). In a recent study by Jain, Kumar, & McMillan (2006), the rhythmic and continuous sucking action of NNS which is similar to massage or rubbing was found to act as a stimulus and alter the transmission of pain. Nonnutritive sucking provides a soothing relief before, during, and after a painful procedure by closing the pain gate and altering the pain transmission.

Nerve fibers which transport the transmission of pain come in two different sizes. The information that needs to travel to the brain fastest will use the large diameter myelinated fibers called A-fibers. Motor information regarding movement and proprioception, the sense of where body parts are located in space, utilize the large, faster fibers to travel from the periphery to the brain. Information that does not need to travel as fast uses smaller, slower, nonmyelinated fibers

called C-fibers. These fibers carry information regarding pain, temperature, and physical distortion such as bending and stretching (McGrath, 1990, Helms & Barone, 2008).

The physiologic mechanisms involved in the ability to detect noxious stimuli, and then transmit the painful stimuli to the brain take the slower route of the C-fibers. This is believed to be a primitive survival mechanism because although pain reception is important for health, it can be inhibiting in a dangerous or threatening situation, and thereby not the first priority for survival (Melzack et al., 1965). In some instances, flight is more important than pain relief. In order to do this one must be able to move quickly and freely. One must know where one's body parts are located in order to move successfully out of harm's way. In this instance, pain is not the priority. Drawing on this knowledge, the Gate Control Theory was built.

Since it is theorized that the stimulation of the periphery of the pain site, or the appropriate signal-carrying nerves at the spinal cord, diminish the experience of pain, studies have been conducted to test this theory. In a recent study by Jain, Kumar, & McMillan (2006), prior leg massage was noted to decrease pain responses to heel sticks in preterm infants. Harrison et al. (2003) stated that the rhythmic and continuous sucking action of NNS can alter the transmission of pain by providing soothing relief before, during, and after a painful procedure via the mechanism of closure of the "pain gate".

Level of Theory

The Gate Control Theory is an example of a middle-range theory. As described by Meleis (1997), middle-range theories consider a limited number of variables, have a particular substantive focus, and are more susceptible to empirical testing. A middle-range theory is appropriate to guide nursing research specifically because it is measurable.

The Gate Control Theory contains four key concepts. The first key concept is the painful stimulus, or a negative stressor such as the presence of noxious or painful stimuli. The second is

the interruption of the stimulus. The intervention to alter the perception of the stimulus is the closing of the "pain gate". The third key concept is the transmission of the painful stimulus whereby no intervention to alter the perception of the stimulus occurred, or no closing of the "pain gate". The last key concept is the pain response. This is the stage following the transmission of painful stimulus. Application of the key concepts of the Gate Control Theory is described below (see Concept Map Figure 2-1)

- Painful stimulus: The negative stressor such as the presence of noxious or painful stimuli. In the study reported here, a heel stick for a blood sample was employed to induce a negative stressor.
- Intervention: Nonnutritive sucking with sucrose-induced analgesia was the intervention used to alter the perception of the painful stimulus. This intervention was begun 2 minutes before the heel stick because the peak efficacy of the opioid effects is 2 minutes after administration (Harrison et al., 2003).
- No intervention: Absence of NNS (ONNS) with sucrose; the control condition.
- Pain response: Stage following the transmission of painful stimulus in the absence of NNS with sucrose-induced analgesia.
- Positive outcome: Improved respiratory function measured by increase in mean oxygen saturation levels, decrease in mean heart rate, and restful state as defined by decrease in NIPS score (Lawrence et al., 1993) following painful stimuli.
- Negative outcome: Increase in mean heart rate, decrease in mean oxygen saturation, or presence of pain state as defined by increased NIPS score (Lawrence et al., 1993).

Relational Statements of the Gate Control Theory

Concepts are ideas or constructs that are labeled by means of language (Walker & Avant, 1995). Concepts allow the classifying of experiences in a meaningful and often measurable way. They serve as fundamental elements essential for theory building. Before a theory can be predicted or explained, it must be formulated. When relationships are observed between one or more concepts, it is expressed as a statement. A relational statement identifies a relationship between one or more concepts (Peterson & Bredow, 2004).

Relational statements of the concepts of the Gate Control Theory include the following: a painful stimulus initiates the transmission of the stimulus. Transmission of the painful stimulus results in a pain response. Interruption of the stimulus decreases the transmission of the painful stimulus and decreases the pain response. A painful stimulus without intervention will lead to a pain response and negative outcome. This is a bidirectional relationship. A pain response would lead to a negative outcome, which could lead to heightened negative responses and outcomes in a cyclic pattern (Anand, 1998). A painful stimulus with intervention will result in a positive outcome. This is a unidirectional relationship.

Application of the relational statements to this study include the experience of a heel stick (painful stimulus) which can be altered to avoid a painful perception (closure of the "pain gate") with the intervention of NNS with sucrose (treatment group). No intervention of NNS with sucrose (control group) following a painful stimulus results in transmission of the painful stimulus (no closure of the "pain gate"), a pain response, and adverse outcomes (increased heart rate, decreased oxygen saturation, and lower NIPS scores). In order to better understand pain behavior and relationships, clear definitions of the concepts and statements were presented.

Theoretical Assumptions of the Gate Control Theory

Recognizing assumptions of a theoretical work is the first step in understanding the theory (Barnum, 1998). Theoretical assumptions are beliefs assumed to be true. Evidence exists of the validity or invalidity of the assumptions as a result of empirical testing (Walker & Avant, 1995). A theoretical assumption of the Gate Control Theory is the interruption of the transmission of the painful stimulus (closure of the "pain gate") is assumed to be not noxious, and therefore will result in no pain response (Melzack & Wall, 1965; Dickenson, 2002; Stojanovic & Abdi, 2002; Fletcher, 2004; Hatfield, 2008). Application of the theoretical assumption to this study is that the introduction of NNS with sucrose will not be a noxious stimulus. The studies reviewed here did

not reveal any instances of increased heart rates, decreased oxygen saturation, or increased NIPS scores in the presence of NNS with sucrose.

The Gate Control Theory serves as the basis for the explanation of the alteration of pain perception through NNS. Like pain itself, the Gate Control Theory is not age specific and can be modified for the population it is applied to. In a recent study by Hatfield (2008), the Gate Control Theory with oral sucrose analgesia provided the theoretical framework to examine infant pain. Forty infants ages 37 to 42 weeks gestation received oral sucrose with nonnutritive sucking prior to routine immunizations at their 2 and 4 months well-child visits. It was concluded that sucrose was effective for decreasing behavioral pain response after immunization. However, the infants in the study were all classified as healthy and not hospitalized.

Pain in Infants

While infant pain is discussed in contemporary nursing and medical literature, few studies address the specific concerns of infants who cannot vocalize their discomfort because of intubation. Infant pain itself is a recent concept in the literature. Swafford and Allen (1986) reported that pediatric patients seldom needed medication for the relief of pain because they tolerate discomfort well. Up until the mid-1980s, many infants did not receive anesthesia for surgery, and postoperative analgesia was the exception, rather than the norm (Franck, 2002).

It has been established that infants, full-term or preterm, can detect and respond to painful stimuli (Franck, 2002). Dunn and Medves (2004) stated that the anatomical structures necessary to process pain are mature from mid to late fetal gestation. This is compounded by the decreased inhibitory ability found in infants who were repeatedly exposed previously thereby causing increased sensitivity to pain—a condition that actually increases the vulnerability to pain of an already vulnerable population.

Though attempts to manage infant pain have improved, the inequities between adult and pediatric patients have continued and are well documented in the literature. Compared to adults, children continue to be poorly managed. Eland and Anderson (1977) compared 25 children, aged 4 to 18, with 18 adults postoperatively. The children received 24 doses of analgesic while the adults received 671. Beyer, DeGood, Ashley, and Russell (1983) compared children and adults who received open-heart surgery. In a single postoperative period twenty-five percent of the children received no analgesia postoperatively. In contrast, all of the adults received analgesics postoperatively. This disparity in treatment between those who are able to verbalize pain (those not intubated or with verbal cognition) and those who are not continues today (Gibbins et al., 2002). This is consistent with the inability of the intubated infant to advocate for itself due to age and intubation. These studies demonstrate respect for the principles of nonmaleficence and beneficence with adults who receive analgesia because of their ability to seek pain relief, but not with infants and children who are not able to seek relief.

The lack of attention to infant pain may be due to the lack of understanding by the healthcare provider of the ability of infants to perceive and respond to pain (Franck & Lefrak, 2002). Common myths regarding pediatric pain management include the following: infants do not feel pain because their nervous system is immature, children do not feel pain as intensely as adults, children do not remember pain, children who do not act like they are in pain are not in pain, children can say where it hurts, it is unsafe to administer narcotics to children because they may become addicted, and the child needs to experience pain (Burokas, 1985). This is in addition to the fear of possible side effects of anesthetics and analgesics in infants, including respiratory depression (Franck & Lefrek, 2002). Franck also found the fear of possible side effects of anesthetics and analgesics in infants may discourage the aggressive use of pain-relieving

medications in infants. Anand and colleagues (2005) stated that awake intubation occurs more often in young children, and that the procedure is associated with severe pain and stress, changes in vital signs, and increased difficulty of the procedure itself from failure to anesthetize.

According to the American Academy of Pediatrics (AAP), the need to relieve pain is significant due to the harmful effects of pain on the infant's developmental outcome (AAP, 2002). The pain response results in increased heart and respiratory rates, increased blood pressure, decreased oxygenation saturation, and a release of adrenal stress hormones. With chronic pain, precious energy resources required for growth, development, and healing are used instead to cope with pain. Disturbances of sleep cycles, feeding patterns, and self-regulation have also been associated with pain. As a result, growth patterns in regard to height and weight gain are interrupted (Mitchell & Boss, 2002).

The disturbed sleep cycle resulting from pain has been described as having immediate and long-term consequences. The neurological systems that control attention, emotion, and the sleep/wake states interact with one another. Pain and stress resulting in repeated disruptions can affect the infant's neurodevelopment, putting the child at risk for later emotional disturbances, learning disorders, poor adaptive behavior, and attention deficits (Grunau, 2000). Attempts to pacify infants may lead to reduced disturbances of these cycles (Miller & Anderson, 1993). One such mechanism of pacification is nonnutritive sucking.

Interventions to Treat Infant Pain

Sucking behavior has its origins in the early development of the infant. Ingelman-Sundberg and Wirson (1965) documented sucking behavior prior to birth—as early as 18 weeks gestation. Infants possess the ability to consistently suck by 32 weeks (Medoff-Cooper, Verklan, & Carlson, 1993). Nonnutritive sucking (NNS) is believed to be a pacifying mechanism with reports dating back to the 15th century (Cornelius, D'Auria, & Wise, 2008). The pacifying effects

of nonnutritive sucking were first noted in relationship and to newborn movement (Kessen & Leutzendorff, 1963; Kessen, Leutzendorff, & Stoutsenberger, 1967).

Only recently has the relationship between painful distress and the effect of nonnutritive sucking been under scientific study. In 1984 Field & Goldson studied behavioral state, heart rate, and respirations during heel stick procedures. Samples compared healthy, term infants (N = 48), preterm infants (N = 48), and subjects in intensive care nurseries (N = 48). Unequal and varying degrees of acquity were compared along with a limited sample size. Lack of clarity as to whether the subjects in the intensive care nursery were intubated, and the lack of sucrose were also identified. Because of the lack of sample and procedure description, the need for further investigation continues.

In 1989 Campos compared the effectiveness of swaddling and pacifiers in reducing pain-induced distress in 2 week old infants who received heel sticks and 2 month old infants who received injections. In the 2 week old group who received pacifiers, the heart rate levels and crying declined more rapidly than when in the swaddling condition. In addition to differing ages and varying interventions, the sample sizes were small (N= 32).

In 1994 DiPietro and associates examined the behavioral and physiologic effects of nonnutritive sucking during gavage feeding in preterm infants. It was noted that the decrease in heart rate and elevation of pain threshold were not sustained following discontinuation of the intervention (nonnutritive sucking). This suggests the intervention of NNS was causative of the favorable physiologic outcomes of decreased heart rate and increased pain threshold.

The continuous and rhythmic sucking action of nonnutritive sucking has potential correlation to improved respiratory and gastrointestinal function, and reduced energy expenditure and behavioral stress. Intubated infants are not usually offered NNS with sucrose due to the lack

of an audible cry, thus the absence of the perception of distress. Nonnutritive sucking with sucrose has been documented to have multiple benefits for infants.

Improved respiratory function can be related directly to increased transcutaneous oxygen tension (TcPaO2). A meta-analysis of the effects of NNS on TcPaO2 was conducted through a computer search on research over the past 30 years. The TcPaO2 levels were noted to be significantly increased with NNS (Shiao, Chang, Lannon, & Yarandi, 1997).

Another potential benefit of NNS may be improved gastrointestinal function. It has been shown that sucking initiates and assists in the completion of the gastrointestinal cycle. Gastric secretory and motor functions needed for digestion are increased during NNS (Widstom et al., 1988). Improved weight gain may result from improved gastrointestinal function, as well as decreased energy expenditure.

Nonnutritive sucking has also been correlated with cardiac functioning in infants. Energy expenditure and heart rate have been directly correlated. Woodson and Hamilton (1986) found that NNS decreased heart rate leading to the conclusion that NNS decreased energy expenditure. Although sample size was limited (N = 10), Miller and Anderson (1993) concluded that heart rates were lower for those intubated infants in the NNS condition than those receiving routine care during and following intravenous catheter insertion.

The analgesic effects of sucrose have been reported in both term and preterm infants (Herschel, Khoshnood, Ellman, Maydew & Mittendork, 1998). Blass and Hoffmeyer (1991) were the first to examine the combined effects of NNS with sucrose for relief of procedural pain in the neonatal population. The combination of sucrose and NNS was found to have a more synergistic effect than the use of sucrose or NNS alone (Cabajal, Chuvet, Couderc & Olivier-Martin, 1999). The analgesic effect of sucrose is reversed with the administration of naloxone

(Barr et al., 1995), an opioid antagonist, suggesting that the action of sucrose is similar to that of opioid analgesics. The analgesic action of sucrose may involve pain-modulating mechanisms that interfere with pain transmission (Barr et al., 1995).

Following a review of randomized controlled clinical trials, the International Evidenced-Based Group for Neonatal Pain published guidelines for the management of pain in infants. The recommended sucrose solution to be used with a pacifier as a pain relief measure for term infants was 24% sucrose with a maximum dose of 2 ml, and 12% to 24% sucrose with a maximum dose of 1 ml for preterm infants (Anand & Phil, 2001). Though pain and a lack of oral stimulation in the intubated infant have been found to have detrimental effects such as compromised growth, development, and health (Boss, 2002), no study was identified in this review that used NNS with sucrose in intubated infants. One explanation is that they are not offered the pacifying effects of NNS due to the presence of the endotracheal tube, which occupies the oral cavity and silences the cry. Research does not support withholding the intervention that is effective in other infant populations. According to the ethical principles of nonmaleficience, beneficence, and caring, nurses are ethically bound to assess and treat pain. The offer of a safe and effective method of pain reduction, such as NNS with sucrose, would fall in the purview of the nurse.

Bioethics and Infant Pain

Considerations in Nursing

Though physicians write (or withhold) the orders that allow the management of pain in the hospital setting, the primary responsibility for pain management in the hospital is assigned to nurses (Simons, Franck, & Roberson, 2001). One obvious moral conflict is that to provide medical benefit to patients, it is often necessary to perform treatments that cause harmful pain. One way to evaluate and balance this dilemma is through the guidance of bioethical principles. While physicians may evaluate what treatments are best and necessary to restore health, it

requires a level of paternalism and a compromise of self-determination or autonomy. It has traditionally been the role of nurses to advocate on behalf of patients to physicians. This is one way of minimizing potential harm and to promote the ability of the infant and parents to keep their voices.

Factors Impacting Nursing Assessment of Pain

The active and essential role nurses play in pain management is recognized in the literature. Because nurses are the caregivers at the bedside, they make judgments regarding the assessment of pain and implement pain-relieving interventions. Nurses' perception of pain is the primary precursor to symptom relief. In an attempt to explore factors that influence nurses' assessments of their patient's pain, Hamers, Abu-Saad, Halfens, and Schumacher (1994) directed a qualitative study exploring pain assessment and interventions. Data was collected using a semi-structured interview, observation of subjects, and examination of nursing records. The subjects were a convenience sample of 10 nurses working in a pediatric ward in both a general and university hospital in the Netherlands. Factors identified that influenced nurses' decisions were the following; medical diagnosis, child's facial expressions, age, parents, and the nurses' knowledge, experience, attitude, and workload, infant behavior, and physiology. Despite the limited number of participants and cultural differences, the findings were repeatedly observed in other studies. What follows is a review of studies identifying similar findings in relation to the nursing assessment of pain in infants.

Medical Diagnosis

The infant's medical diagnosis was identified as a component that influenced nurses' pain assessment. The more severe the medical diagnosis, the greater amount of pain anticipated by the nurses. This observation also held for the implementation of pain-relieving interventions (Hamers et al., 1994, Hamers et al., 1996).

Infant's Behavior, Expression, and Physiology

In a 1989 qualitative study examining nurses' perceptions of pain in the neonatal intensive care unit, infant behavior was categorized according to seven areas: facial expressions, facial color, limb movement, torso activity, breathing pattern, and cry state (Pigeon, McGrath, Lawrence, & MacMurray, 1989). Children in pain were more likely to be crying, to have marked changes in facial color, to have rigid limbs and torso, to have irregular breathing, and to have movement. However, there was no discernible relationship between specific procedures and severity of pain. For example, handling and changing a diaper were identified by some RNs as a cause of mild pain and by others as a source of severe pain.

In an attempt to describe behaviors of infants and toddlers when in acute pain, 32 children were observed following surgery, fractures, or burns (Mills, 1989). In this qualitative study using grounded theory methodology, data sources included child observations, parent interviews, and patient records. Three pain behavior categories were identified including motor movement, communication, and facial expressions (Mills, 1989). The children were observed on three separate occasions. Parent interviews were audio taped following the observations. Parents were able to describe behaviors that indicated pain in their child. Pain was communicated by infants (birth to 3 months of age) through crying. Some nurses stated that sustained crying was their cue to give analgesics to infants. Crying in infants from birth to 3 months of age was intermittent and less sustained than in older infants. The significance of Mills findings is that some nurses stated that sustained crying was their cue to give analgesics.

Infant Age

Certain characteristics of the child were noted to influence the nurses' pain assessment and intervention including the characteristics of the child's facial expressions and chronological age (Hamers et al., 1994). This was further supported in a study examining postoperative assessment

of pediatric pain, crying was identified as the major indicator of pain (Hultgren, 1990). In this qualitative study, 48 RNs from a convenient sample of pediatric and neonatal intensive care units were interviewed utilizing open-ended questions. Over 60% of the nurses in this study described the behaviors of crying and agitation as warranting pain medication administration.

Parental Participation

Parental participation and support was a factor in the nurses' perception of pain. A qualitative study was reviewed involving in-depth interviews of 24 parents of children hospitalized on a surgical ward and 11 members of the nursing staff. A parent suggested that health professionals could only respond to physical signs and could not recognize her assessment of subtle changes in her child (Calley, 1997).

In a study that combined qualitative and quantitative methods, 20 parent and 20 nurse interviews were conducted. The qualitative method of phenomenology was used to guide the interviews. Findings revealed that the nurses perceived that the parents were receiving more support than the parents reported. The parents reported being more satisfied with their children's pain management, and the children received more analgesics when they were cared for by a nurse with a lower educational grade (Simons, 2002).

Nurse Knowledge, Work Experience, and Attitude.

In Hultgren's 1990 study, the researcher cited prior work experience as the major influence on analgesic administration by nurses. Pain relief was the most common goal in administering narcotics in the immediate postoperative period. However, nurses with an associate Arts degree or hospital diploma education were much more likely to state that the goal of narcotic administration was keeping the patient quiet and calm. Nursing decisions to medicate and medication choices also differed. Nurses differed widely in how much pain the infant "should"

have by the second day. Seven out of 36 respondents felt acetaminophen should be "sufficient by the second postoperative day".

In 2005 Van Hulle collected data from nurses (N = 67) regarding nurses' knowledge and attitudes of children's pain. It was reported that most demonstrated knowledge and a positive attitude toward relieving pain, but lacked knowledge of the occurrence of respiratory depression and thought the children over reported their pain.

Common myths of pediatric pain exist. One common myth is the idea that children do not remember pain. It is of note that in this study after the first burn dressing change, an 8-month-old infant cried in anticipation of events. She cried when she saw masks on nurses and when she was physically moved to the treatment room. That behavior was perhaps indicative of remembering a painful event. Motor behaviors have been misinterpreted regarding pain. Efforts to self-console have been misrepresented as evidence of the absence of pain. Attempts by the child to self-distract by playing briefly with a toy may not indicate that the child is pain free and not in need of analgesics (Mills, 1989). The misinterpretations of pain may be due to the nurse's knowledge, work experience, or attitude regarding pain.

Another qualitative study utilizing grounded theory methodology was reviewed which described how parents and nurses respond to hospitalized young children experiencing pain from surgical interventions. Participant observation was used to identify care behaviors. Interviews with 22 parents, 24 nurses, and 11 children were also conducted. The children stated that their parent's presence was the major care practice useful in relieving the pain. Comforting the children was not noted as a major activity for the nursing staff. Nonpharmacologic nursing measures, such as teaching the child relaxation techniques, were rarely used by the nurses. Providing analgesic medication was the most frequent practice conducted by the nursing staff.

However, the degree of pain relief was not always adequate for the children (Woodgate & Kristjanson, 1996).

In review of the literature dealing with nurses' perceptions and attitudes of pain, the concept of comfort was also examined. Comfort has been contrasted with discomfort and viewed as a state of well being. Pain has been associated with discomfort. Using a phenomenological method, 36 patients who had experienced traumatic injuries or life-threatening illnesses were invited to tell their stories with minimal interruption from the researcher. The theme emerged that comfort was not an ultimate state of peace and serenity but rather the relief from discomfort (Morse, Bottorff, & Hutchinson, 1995). In a similar study conducted in 1994 by Morse, Butoroff, and Hutchinson, the phenomenology of comfort was again explored. The authors argued that the goal of providing total comfort was unattainable in patient care. The role of nursing is to enhance comfort, and to ease and relieve distress.

In an observational study involving nurses on 36 shifts, Twycross (2007) noted that pain administration practices did not conform to current recommendations. Pain assessment was not routinely performed, or non-drug methods for pain relief consistently used. Further investigation for practice reasons (lack of knowledge, attitude, or workload) was needed.

Nurses' Workload

In 2007 observational studies were reviewed to explore the relationship between nurse staffing and patient outcomes (Kane, 2007). Better patient outcomes in intensive care units and in surgical units were associated with higher nurse/patient ratios. Positive outcomes were associated with decreased mortality, pressure ulcer incidence, invasive line sepsis, and respiratory infection. However, the amount of nursing knowledge, or experience was not addressed. Also, pediatric units were not included.

Infant pain management involves not only the infant, but also the health professional and family. Factors impacting the nursing assessment of infant pain were discussed including the infant (diagnosis, behavior, expression, physiology, age), parent (parental participation), and nurse (knowledge, experience, attitude, workload).

Toward an Effective Assessment of Pain in Infants

In order to achieve effective pain management, an effective pain assessment tool is needed. Because infants can not self-report, physiological indicators (heart rate, respiratory rate, oxygen saturation, blood pressure, palmar sweating, vagal tone, plasma cortisol, catecholamine levels) have been measured to assess pain (American Academy of Pediatric Policy Statement, 2006). Physiological indicators, however, are sometimes unreliable due to data obtainment error and are not specific to pain alone (Barr, Rootman, Yaremko, Leduc, & Francoeur, 1992). Behavioral indicators (facial expressions, crying, movement) have also been used to assess pain, but may be absent or diminished if the infant is pharmacologically or neurologically impaired. Physiological and behavioral indicators are also further defined by chronologic age. For example, some pain assessment tools are age specific for preterm or term infants. Therefore, a multidimensional pain assessment tool appropriate for chronologic age measuring both physiologic and behavioral components is recommended (American Academy of Pediatric Policy Statement, 2006).

Multiple pain assessment tools have been developed to assess infant pain. Example of multidimensional pain assessment tools include the PIPP (Premature Infant Pain Profile), CRIES (Crying, Requires Oxygen Saturation, Increased Vital Signs, Expression, Sleeplessness), NIPS (Neonatal Infant Pain Scale), N-Pass (Neonatal Pain Agitation and Sedation Scale), PAT (Pain Assessment Tool), and the SUN (Scale for Use in Newborns) (American Academy of Pediatrics, 2009). The pain assessment tools measure different physiologic and behavioral indicators, such as blood pressure and sleep patterns for the PAT. The nature of pain assessed also differs. The

CRIES pain assessment tool is designed specifically for postoperative pain (American Academy of Pediatrics, 2009). The multidimensional pain assessment tool chosen for this study was the NIPS (Neonatal Infant Pain Scale) which measures respiratory patterns as a physiologic indicator, and facial expression, cry, movement of arms and legs, and state of arousal as behavioral indicators. Procedural pain, such as heel sticks, is the type of pain recommended to be assessed with the NIPS (Duhn, & Medves, 2004). The NIPS was chosen as the pain assessment tool for this study due to the multidimensional ability (physiologic and behavioral), age considerations (infant), type of pain recommendation (procedural), and ease of use.

With all that is now known about the detrimental effects of both acute and long-term untreated pain on the future health and development of infants, it is the right of infants and their parents to expect and to receive adequate pain management. It is important to note that infant pain is articulated in the literature only through the experiences of caregivers—whether nurses, physicians, or parents. As a concept, it is impossible to operationalize infant pain through the spoken experiences of infants because of the nonverbal nature of infants. Franck, Allen, Cox, and Winter (2005) found that parents attributed most infant pain to medical procedures, though Simons, Franck, and Roberson (2001) stated that parents had low expectations for the relief of their child's pain. Homer and colleagues (1999) found that the primary reason expressed for dissatisfaction on a hospital post-discharge survey was inadequate management of their child's pain. This prompted an editor's note positing that this may even be a form of child abuse worthy of investigation.

Perhaps this dissonance is one of the reasons that have motivated researchers to better understand infant pain. Only recently has there been any attempt to quantify the physiological measures that express infant pain. Parents in most societies serve as the other half of the

autonomous unit, the parent-child dyad. A respect for infant-parent autonomy would require that both parental satisfaction and actual measures of infant pain come together to provide a complete picture of infant well being.

Summary

Pain has been found to have detrimental effects compromising infant growth, development, and health (Boss, 2002). Nursing participation in pain management is crucial to achieve positive health outcomes for infants who experience repetitive or severe pain. Considerations in nursing and pain management were discussed including factors impacting nursing assessment of pain. Factors examined included the infant (medical diagnosis, age, behavior, expression, physiology), parent (parental participation), and nurse (knowledge, experience, attitude, workload) (Twycross, 2007; Kane, 2007). Further investigation for practice issues (lack of knowledge, attitude, and workload) is needed for the clinical setting. Pain assessment tools designed to assess infant pain were discussed including the PIPP, CRIES, NIPS, N-Pass, PAT, and SUN (American Academy of Pediatrics, 2009). A multidimensional pain assessment tool appropriate for chronologic age that measures both physiologic and behavioral components was recommended (American Academy of Pediatrics Policy Statement, 2006) The nature of different types of pain was also discussed, i.e., procedural versus postoperative (American Academy of Pediatrics, 2009). The multidimensional pain assessment tool chosen for this study was the NIPS (Neonatal Infant Pain Scale) which measures respiratory patterns as a physiologic indicator, and facial expression, cry, movement of arms and legs, and state of arousal as behavioral indicators. Procedural pain, such as heel sticks, is the type of pain recommended to be assessed with the NIPS (Duhn, & Medves, 2004). The NIPS was chosen as the pain assessment tool for this study due to the multidimensional ability (physiologic and behavioral), age considerations (infant), type of pain recommendation (procedural), and ease of use.

In summation, this strongly supports that the assessment and treatment of infant pain continues to be multifactorial, inconsistent, and at times insufficient for pain alleviation. Hospitalized infants continue to endure a multitude of invasive and potentially painful procedures ((D'Apolito, 2006; Carbajal, et. al., 2008). Management of neonatal and infant pain is important not only to provide comfort, but also to prevent long-lasting negative consequences related to painful experiences (Grunau, 2002). Pain has been found to have detrimental effects that compromise growth, development, and health (Boss, 2002). Repeated pain may lead to negative physiologic outcomes further compromising the health of the infant.

For intubated infants who routinely encounter painful conditions, the relief of pain can potentially improve the health and development of seriously ill infants. Given the lack of literature addressing the assessment and treatment of pain in intubated infants, nurse scientists must generate more evidence to fill this gap. Further study of nonnutritive sucking and sucrose in intubated infants on measurable clinical outcomes following painful episodes is needed.

The following chapter will discuss a repeated measures cross-over design study examining the effects of nonnutritive sucking combined with sucrose-induced analgesia on heart rate, oxygen saturation, and pain behaviors as measured by the Neonatal Infant Pain Scale in intubated infants. Nursing participation in the assessment and treatment of infant pain management is crucial to achieve positive health outcomes for infants who experience repetitive or severe pain. The following study outlines this work.

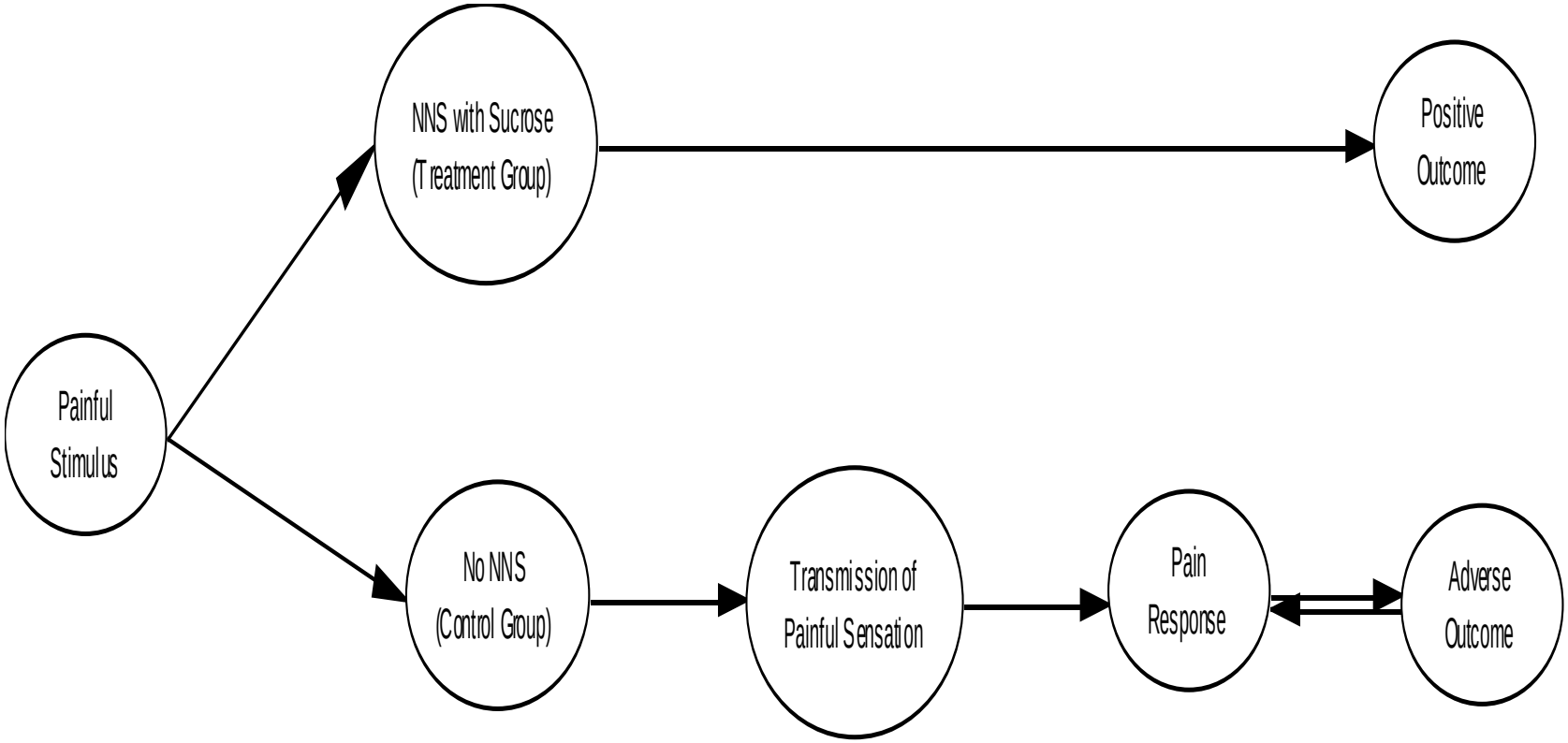

Figure 2-1. Concept Map

CHAPTER 3
METHODS

Design

The purpose of this study was to determine the effect of nonnutritive sucking (NNS) combined with sucrose-induced analgesia on heart rate, oxygen saturation, and pain behaviors (measured by the Neonatal Behavioral Pain Scale (NIPS)) in 32-to-42 week intubated infants.

Subjects and Setting

Using a repeated measures cross-over design (Maxwell & Delaney, 1990), 14 infants were chosen by convenience from a 112 bed (sixty bed level two, fifty-two bed level three) neonatal intensive care unit population located in central Florida. There were 14 infants, all of which were diagnosed with respiratory distress. It was a diverse sample in terms of ethnicity: 5 African-American (35.7%), 4 Caucasian (28.6%), 4 Hispanic (28.6%), and 1 Asian (7.1%). Nine infants were male (64.3%) and 5 were female (35.7%). The mean gestational age was 35.14 (SD = 2.85) with a mean age since birth of 4.79 days (SD = 5.58; Range: 19). Weight ranged from 1769 grams to 3642 grams. Mean birth weight was 2351.86 grams (SD = 805.35). Each subject served as their own control for a total of 28 observations. Each subject was monitored before, during, and after a required, routine heel stick.

Power Analysis

In order to achieve 80% power with an alpha of 0.05 using an effect size of 0.75 (based on the means 7.7 and 4.3, standard deviation 3.9 from Brovedani**,** Montico, Shadlow, Strajn, and Demarini (2007)), it was determined that a minimum of 14 subjects per observational condition were needed.

Inclusion criteria were as follows:

- Greater than or equal to 32 weeks gestation at birth and less than or equal to 42 weeks of gestational age

- Intubated
- Receiving assisted mechanical ventilation
- Clinically demonstrate a sustained suck reflex
- Require routine heel stick as part of medical care
- 30 minute uneventful period prior to the heel stick

Exclusion criteria were as follows:

- Medication for sedation administered within 2 hours prior to heel stick—to avoid the effect of additional opioid or decreased level of consciousness that blunts response to painful stimulus
- History of nondevelopmental neurological deficits—should have ability to suck and respond to stimulus
- Diabetes—unable to receive sucrose if susceptible to hyperglycemia
- Necrotizing enterocolitis—gut must remain empty; oral sucrose is contraindicated

This study was approved by the Internal Review Boards of Winnie Palmer Hospital for Women and Babies, Orlando Healthcare in Orlando, Florida, and the University of Florida, in Gainesville, Florida.

Variables

Independent Variable

Non-nutritive sucking (NNS) with the addition of sucrose was the independent variable. During the treatment condition (NNS with sucrose), the infant was given a pacifier with the nipple coated in 1ml of a 24% sucrose solution, Sweet-Ease©. The infant was given the coated nipple 2 minutes prior to the painful procedure (heel stick). The 2-minute time interval for optimal efficacy is thought to coincide with the endogenous opioid release triggered by taste (Gibbins & Stevens, 2001). The rubber shield siding of the pacifier was removed from one side to allow a more comfortable fit between the nipple and the endotracheal tube. The nipple was kept in the infant's mouth for the observation period even when the infant was not sucking.

Dependent Variable

The dependent variables were heart rate (recorded by a cardiac monitor), oxygen saturation (recorded by a peripherally attached transcutaneous oxygen saturation monitor), and the infant's behavioral response (as measured by the NIPS Behavioral Pain Scale).

Heart Rate. A change in heart rate represents an increase or decrease in agitation, energy expenditure, and/or pain (Woodson & Hamilton, 1986; Miller & Anderson, 1993) A mounted EKG Phillips Intellivue MP70 Neonatal Monitor was used by the researcher to obtain the heart rate when the audible beep on the prerecorded tape alarmed. The prerecorded tape alarmed with an audible beep every thirty seconds. The researcher wore an earpiece to hear the alarm.

Oxygen Saturation

A change in the oxygen saturation represents an increase or decrease in transcutaneous oxygen tension (TcPaO2) reflective of a change in respiratory function. The same Phillips Intellivue MP70 Neonatal Monitor was used by the researcher to obtain the oxygen saturation when the audible beep on the prerecorded tape alarmed.

NIPS Behavioral Pain Scale

The NIPS Behavioral Pain Scale (Appendix A) measures pain behavior in term and preterm infants who may not be able to verbalize the presence or severity of pain (Duhn & Medves, 2004). The multidimensional tool scores procedural pain by assessing five categories of behavior: facial expression, cry, breathing patterns, limb movement, and arousal. Each category is scored on a 0-1 scale, except cry which is scored 0-2. In the category facial expression, 0 = relaxed muscles (restful face, neutral expression), and 1= grimace (tight facial muscles, furrowed brow, chin, jaw). In the cry category, 0 = no cry (quiet, not crying), 1 = whimper (mild moaning intermittent), and 2 = vigorous cry (with the intubated infant noted as obvious mouth and facial movement). In the breathing patterns category, 0 = relaxed (usual pattern for this infant), and 1 =

change in breathing (retractions, irregular, faster than usual, gagging, holding breath). The limb movement category is divided into arms and legs. In the arms category 0 = relaxed or restrained (no muscular rigidity; occasional random movement of arms), and 1 = flexed or extended (tense straight arms, rigid and/or rapid extension, flexion). In the legs category 0 = relaxed or restrained (no muscular rigidity; occasional random leg movement) and 1 = flexed or extended (tense, straight legs; rigid and/or rapid extension, flexion). In the arousal state category, 0 = sleeping or awake (quiet, peaceful sleeping or alert random leg movement, and 1 = fussy (alert, restless, and thrashing). The total score is between 0-7. A score of 3 or greater indicates pain.

In previous studies the psychometric properties of the NIPS Behavioral Pain Scale revealed interrater reliability (Pearson's correlations 0.92 to 0.97), internal consistency (Cronbach's alphas 0.87 to 0.95), concurrent validity (correlations 0.53 to 0.84 when compared to visual analogue scale), and construct validity (change in pain scores over time was seen with main effect of time being statistically significant, $F = 18.97$, $P < 0.001$) (Duhn & Medves, 2004). These tests were performed in both preterm and full-term neonates (Franck, Greenberg, & Stevens, 2000).

In the present study, inter-rater reliability was conducted between the researcher and a second rater who was an experienced neonatal intensive care registered nurse well-versed in NIPS scoring. Inter-rater reliability was assessed by having the same second rater score 100% of the procedures (see Table 3-1). The researcher scored the heart rate, oxygen saturation, and the NIPS scores. The second rater scored the NIPS scores. The second rater stood across from the first rater, but within view of the infant. The proportion of agreements between the researcher and second rater was 98.2%.

Painful Event

The painful event was a scheduled heel stick for blood sample obtainment performed by the registered nurse. A total of six different registered nurses with greater than two years of neonatal intensive care unit nursing experience performed the heel stick. The steps of the heel stick included: 1) cleaning the heel with an antiseptic immediately prior to the heel stick (alcohol if greater than 2 weeks of age, or betadine swab followed with sterile water prep for infants less than 2 weeks of age (Folk, 2007)), 2) holding the extremity firmly, 3) puncturing the inner outside edge of the heel with a sterile heel stick lancet, and then 4) compressing the heel to facilitate blood collection. The heel stick was not in a cluster of other events. It occurred after a 30-minute uneventful period. In order to maintain equality between the two groups, no difference in the amount of investigator contact with the infants was noted between the two groups to maintain equality of treatment.

Procedure

Following informed consent, the infants was randomly assigned to receive first either the NNS with sucrose (treatment) condition (see Table 3-2) or the ONNS (control) condition (see Table 3-3). While the infant remained in their assigned incubator bed, the heart rate and oxygen saturation (TcPaO2) was measured in 30-second intervals during a 5-minute baseline period, during a heel stick, and during a 5-minute follow-up period. The behavioral state score (NIPS Behavioral Pain Scale) was measured in one minute intervals.

Heart rate and oxygen saturations were collected every 30 seconds from digital recordings at the bedside monitor. Using a tape recorder (Sony Corp., Japan, model 1C Recorder 1CD-325), an audible beep was produced every 30 seconds on a prerecorded tape prompting the time for data collection. The researcher wore earplugs to eliminate sound interference. The NIPS

scores were collected every minute. Data was collected and transcribed onto data collection sheets (Appendix B and C) by the same researcher and second rater.

Treatment Condition

In the treatment condition (NNS) with sucrose, following the 5-minute baseline period, the infant was given a pacifier coated by a maximum dose of 1ml of a 24% sucrose solution (Sweet-Ease©). The pacifier was prepared for administration by dipping the entire nipple in the cup of sucrose solution and then placing it into the infant's mouth on the top of the tongue. The pacifier was kept in the infant's mouth 2 minutes before the heel stick, during the heel stick, and during the 5-minute follow-up period even when the infant was not sucking.

Control Condition

In the control condition (ONNS) the heart rate and oxygen saturation (TcPaO2) were measured in thirty second intervals during a five-minute baseline period, during a heel stick, and during a five-minute follow-up period. The behavioral state (NIPS score) was measured in one minute intervals.

Risks and Benefits

There was no risk associated with this study for the treatment (NNS with sucrose) or control groups. The lack of use of this intervention may be due to the misinterpretations or attitude regarding pain, the nurse's knowledge, or work experience.

The risk for the control group (ONNS) was that they will not receive the potential comforting effect of NNS with sucrose.

Subjects could withdraw at any time due to parental or legal guardian wishes, or the infant's physical condition. No subjects withdrew from the study.

Each subject was assigned a code to assure anonymity. Demographic information of the subject included age, gender, ethnicity, diagnosis, birth weight, length of admission, and any

surgical history. Confidentiality was maintained throughout. Records were kept in a locked cabinet in the researcher's locked office.

Data Analysis

Data analysis was performed utilizing SPSS software. Data analysis included descriptive statistics on demographic data reporting mean and a standard deviation. For heart rate, oxygen saturation, and the Neonatal Infant Pain Scale (NIPS) the mean of each 30-second period was analyzed. These data points were divided into the following four phases. Phase 1 was defined as the baseline and was the mean of the first 10 observations. Phase 2 was defined as NNS (treatment condition) or continued baseline (control condition) and was the mean of the next 4 observations. Phase 3 was the mean of the first five post-heel stick observations. Phase 4 was the mean of the last five post-heel stick observations. A repeated-measures analysis of variance (ANOVA) was performed (using the means of each 30-second period of heart rate, oxygen saturation, and NIPS score) to answer each of the research hypotheses (Hair, Anderson, Tatham, & Black, 1998).

Hypothesis 1

Infants will have lower mean heart rates in the NNS condition with sucrose (treatment condition) during a heel stick than those infants not offered NNS with sucrose (control condition).

Hypothesis 2

Infants will have higher mean oxygen saturations in the NNS condition with sucrose (treatment condition) as measured by noninvasive pulse oximetry during a heel stick than those infants not offered NNS with sucrose (control condition).

Hypothesis 3

Infants will have lower NIPS scores in the NNS condition with sucrose (treatment condition) during a heel stick than those infants not offered NNS with sucrose (control condition).

Table 3-1. Inter-rater Reliability of Observations

NNS Data	GA	Age	Race	Sex	Weight	1st Obs.	2nd Obs.	IRR $1^{st}/2^{nd}$
1	41 wk	6 days	Black	Male	3030 gm	ONNS	NNS	100%
2	37 wk	13 days	Hispanic	Female	3298 gm	ONNS	NNS	100%
3	36 wk	9 days	White	Female	2240 gm	NNS	ONNS	100%
4	32 wk	1 day	Black	Male	769 gm	NNS	ONNS	91.70%
5	34 wk	19 days	Black	Male	1359 gm	ONNS	NNS	100%
6	38 wk	0 days	Black	Male	3191 gm	ONNS	NNS	100%
7	38 wk	2 days	Hispanic	Female	3642 gm	ONNS	NNS	91.70%
8	34 wk	1 day	White	Male	1814 gm	ONNS	NNS	100%
9	37 wk	1 day	Hispanic	Male	2612 gm	NNS	ONNS	100%
10	32 wk	1 day	Asian	Male	2286 gm	NNS	ONNS	100%
11	33 wk	5 days	White	Female	2275 gm	ONNS	NNS	91.70%
12	32 wk	5 days	Hispanic	Male	1604 gm	NNS	ONNS	100%
13	32 wk	1 day	Black	Female	2166 gm	NNS	ONNS	100%
14	36 wk	3 days	White	Male	2535 gm	NNS	ONNS	100%

Note. *1^{st} Obs*. = First Observation Condition (NNS or ONNS); *2^{nd} Obs.* = Second Observation Condition (NNS or ONNS); *IRR $1^{st}/2^{nd}$* = Mean percentage agreement of first inter-rater and second inter-rater of all heart rate readings, oxygen saturation readings, and NIPS scores

Table 3 -2. Treatment Condition Observation for NNS with Sucrose

Age in Days	Heart Rate (HR)	O2 Sats % (O2%)	NIPS
Baseline Phase			
1 minute	HR 1a 30 seconds	O2% 1a 30 seconds	
	HR 1b 60 seconds	O2% 1b 60 seconds	NIPS 1 minute
2 minute	HR 2a 30 seconds	O2% 2a 30 seconds	
	HR 2b 60 seconds	O2% 2b 60 seconds	NIPS 2 minute
3 minute	HR 3a 30 seconds	O2% 3a 30 seconds	
	HR 3b 60 seconds	O2% 3b 60 seconds	NIPS 3 minute
4 minute	HR 4a 30 seconds	O2% 4a 30 seconds	
	HR 4b 60 seconds	O2% 4b 60 seconds	NIPS 4 minute
5 minute	HR 5a 30 seconds	O2% 5a 30 seconds	
	HR 5b 60 seconds	O2% 5b 60 seconds	NIPS 5 minute
NNS Introduction Phase			
1 minute	HR 6a 30 seconds	O2% 6a 30 seconds	
	HR 6b 60 seconds	O2% 6b 60 seconds	NIPS 6 minute
2 minute	HR 7a 30 seconds	O2% 7a 30 seconds	
	HR 7b 60 seconds	O2% 7b 60 seconds	NIPS 7 minute
Heel Stick Phase			
After Heel Stick Phase			
1 minute	HR 8a 30 seconds	O2% 8a 30 seconds	
	HR 8b 60 seconds	O2% 8b 60 seconds	NIPS 8 minute
2 minute	HR 9a 30 seconds	O2% 9a 30 seconds	
	HR 9b 60 seconds	O2% 9b 60 seconds	NIPS 9 minute
3 minute	HR 10a 30 seconds	O2% 10a 30 seconds	
	HR 10b 60 seconds	O2% 10b 60 seconds	NIPS 10 minute
4 minute	HR 11a 30 seconds	O2% 11a 30 seconds	
	HR 11b 60 seconds	O2% 11b 60 seconds	NIPS 11 minute
5 minute	HR 12a 30 seconds	O2% 12a 30 seconds	
	HR 12b 60 seconds	O2% 12b 60 seconds	NIPS 12 minute

Table 3-3. Control Condition Observation for ONNS

Age in Days	Heart Rate	O2 Sats %	NIPS
Baseline Phase			
1 minute	HR 1a 30 seconds	O2% 1a 30 seconds	
	HR 1b 60 seconds	O2% 1b 60 seconds	NIPS 1 minute
2 minute	HR 2a 30 seconds	O2% 2a 30 seconds	
	HR 2b 60 seconds	O2% 2b 60 seconds	NIPS 2 minute
3 minute	HR 3a 30 seconds	O2% 3a 30 seconds	
	HR 3b 60 seconds	O2% 3b 60 seconds	NIPS 3 minute
4 minute	HR 4a 30 seconds	O2% 4a 30 seconds	
	HR 4b 60 seconds	O2% 4b 60 seconds	NIPS 4 minute
5 minute	HR 5a 30 seconds	O2% 5a 30 seconds	
	HR 5b 60 seconds	O2% 5b 60 seconds	NIPS 5 minute
ONNS Phase			
1 minute	HR 6a 30 seconds	O2% 6a 30 seconds	
	HR 6b 60 seconds	O2% 6b 60 seconds	NIPS 6 minute
2 minute	HR 7a 30 seconds	O2% 7a 30 seconds	
	HR 7b 60 seconds	O2% 7b 60 seconds	NIPS 7 minute
Heel Stick Phase			
After Heel Stick Phase			
1 minute	HR 8a 30 seconds	O2% 8a 30 seconds	
	HR 8b 60 seconds	O2% 8b 60 seconds	NIPS 8 minute
2 minute	HR 9a 30 seconds	O2% 9a 30 seconds	
	HR 9b 60 seconds	O2% 9b 60 seconds	NIPS 9 minute
3 minute	HR 10a 30 seconds	O2% 10a 30 seconds	
	HR 10b 60 seconds	O2% 10b 60 seconds	NIPS 10 minute
4 minute	HR 11a 30 seconds	O2% 11a 30 seconds	
	HR 11b 60 seconds	O2% 11b 60 seconds	NIPS 11 minute
5 minute	HR 12a 30 seconds	O2% 12a 30 seconds	
	HR 12b 60 seconds	O2% 12b 60 seconds	NIPS 12 minute

CHAPTER 4
RESULTS

This research was conducted with 14 hospitalized intubated infants who were 32 to 41 weeks gestational age at birth (mean 35.14 weeks gestational age, standard deviation 2.85) ranging from 0 to 19 days old (mean 4.79 days, standard deviation 5.58) at study onset. Each infant was intubated and receiving assisted mechanical ventilation. The purpose of this research was to determine the effect of nonnutritive sucking (NNS) combined with sucrose-induced analgesia on heart rate, oxygen saturation, and pain behaviors (measured by the Neonatal Infant Pain Scale) before, during, and after a painful event (heel stick) in this population.

The following hypotheses were tested in this research:

1. Infants will have lower mean heart rates in the NNS condition with sucrose (treatment condition) following a heel stick than infants not offered NNS with sucrose (control condition).
2. Infants will have higher mean oxygen saturations in the NNS condition with sucrose (treatment condition) as measured by noninvasive pulse oximetry following a heel stick than those infants not offered NNS with sucrose (control condition).
3. Infants will have lower NIPS scores in the NNS condition with sucrose (treatment condition) following a heel stick than those infants not offered NNS with sucrose (control condition).

Sample

Participant Demographics

There were 14 infants all of which were diagnosed with respiratory distress. It was a diverse sample in terms of ethnicity. Nine infants were males (64.3%) and 5 were female (35.7%).

The mean gestational age was 35.14 (SD = 2.85) with a mean age in days of 4.79 (SD = 5.58; Range: 19). Mean IMV was 23.79 (SD = 6.18). Mean PEEP was 4.64 (SD = 0.84). The mean APGAR ratings at 1 minute were 5.57 (SD = 2.65).

Thirteen of the infants were delivered by cesarean section (92.9%), and one was not (7.1%).

Observations

There were two periods when data was collected through observation sessions. They are referred to as "NNS" (treatment group) and "non-NNS" (control group). The only difference between the two conditions was the introduction of NNS with sucrose in the treatment group prior to the heel stick. Observation sessions were conducted, in average, within 24 hours of each other. The observation sessions were counterbalanced. For example, the NNS session was conducted first followed by the non-NNS session. In the analyses that follow, the "EXPCONDITION" variable differentiates the NNS and non-NNS conditions. There were three dependent variables: heart rate, oxygen saturation, and NIPS scores. In each observation session, there were twenty-four heart rate observation points, twenty-four oxygen saturation observation points, and twelve NIPS observation points.

Heart Rate

In both the NNS and non-NNS condition, there were 24 heart rate observation points (see Tables 3-2 and 3-3). In the non-NNS condition, the first 14 observation points were baseline observations of resting infant heart rate. The next 10 observations points were infant heart rate post-heel stick. In the NNS condition, the first 10 observation points were baseline observations of resting infant heart rate. The next 4 observation points were observations of heart rate when NNS with sucrose was introduced. The next 10 observation points were post-heel stick.

Oxygen Saturation

In both NNS and non-NNS sessions, there were 24 oxygen saturation observations (see Tables 3-2 and 3-3). Identical to the heart rate observation method, the first 14 observation points in the non-NNS condition provided baseline oxygen saturation measurements. The last 10

observations were post-heel stick measurements of oxygen saturation. In the NNS condition, the first 10 observations were baseline measurements of oxygen saturation, the next 4 observations measured oxygen saturation during NNS, and the final 10 data points represented oxygen saturation post-heel stick.

NIPS Scores

In contrast to the 24 heart rate and oxygen saturation measurements, there were only 12 NIPS score observations in each session (see Tables 3-2 and 3-3). In both the NNS and non-NNS conditions, the first five NIPS scores were baseline measurements while the last seven NIPS scores were post-heel stick measurements.

Results

Visual Analyses

Figures 4-1 through 4-14 depict heart rate and blood oxygenation for each infant pre- and post heel-stick across experimental and control conditions. The charts have dual y-axes displaying both heart rate and oxygen saturation observations. Figure 4-15 displays mean heart rates across control and NNS conditions. Figure 4-16 displays oxygen saturation levels across control and NNS conditions. Table 4-11 displays the mean phase differences in heart rate and oxygen saturation in the experimental and control conditions.

Aggregated Data Analyses

Two-factor within subjects ANOVA

For both the experimental and control conditions, there were 24 data points (see Tables 3-2 and 3-3).

- FACTOR 1 (EXPCONDITION). Each baby was exposed to a control and intervention condition (Factor 1). The treatment factor had 2 levels:
    - Control (non-NNS)
    - Experimental (NNS)

- FACTOR 2 (PHASE): These data points were divided into the following four phases;
    - Phase 1: Baseline
        - Defined as the mean of the first 10 observations
    - Phase 2: NNS (intervention condition) or Continued Baseline (control condition)
        - Defined as the mean of the next 4 observations
    - Phase 3: First five post-heel stick observations
        - Defined as the mean of the first five observations post-heel stick
    - Phase 4: Last five post-heel stick observations
        - Defined as the last five observations post-heel stick

For Factor 2 (PHASE), analyses were conducted on the means for each of the four phases identified above. By aggregating observations into means, and then running the ANOVA on the phase means, the problem of having an unacceptably small ratio of observations to subjects is avoided. Also, there is less concern about serial dependency of data, although this is always a concern in repeated measures ANOVA. This analysis permits examination of three different effects: main effect for TREATMENT, main effect for PHASE, and whether there is at TREATMENT*PHASE interaction.

Heart Rate

Heart rate means and standard deviations for each phase are displayed below. HRCPhase1 is the mean of the first ten heart rate observations in the "control" or non-NNS Phase1 condition. HRCPhase2 is the mean of the next four heart rate observations in the non-NNS condition (effectively, an extension of baseline). HRCPhase3 is the mean of the first 5 heart rate observations in the non-NNS condition. HRCPhase4 is the mean of the last 5 heart rate observations in the non-NNS condition. HRIPhase1 is the mean of the first 10 baseline observations in the NNS condition. HRIPhase2 is the mean of the 4 observations during introduction of NNS. HRIPhase3 is the mean of the first 5 observations post-heel stick.

HRIPhase4 is the mean of the last 5 observations post-heel stick. It is of note that the heart rates in Phases 1 and 2 of both the control and intervention phases are similar. However, the heart rates in Phases 3 and 4 of both the control and intervention phases are greater in comparison. The heart rate mean in the intervention Phase 4 (135.64) is less than the heart rate mean in the control Phase 4 (150.64) suggesting the return to baseline was occurring in the intervention phase.

ANOVA Results

This is a 2 x 4 within-subjects factorial ANOVA. There are two levels for EXPCONDITION (1 = Control or non-NNS; 2 = NNS). There are four levels for PHASE (defined above).

ANOVA Interpretation

1. The factor EXPCONDITION F (1, 13) = 46.65, p <.001, partial η^2 = .78. There is a strong main effect for the experimental condition with about 78% of the variation in mean scores due to the assignment to condition.

2. The factor PHASE F (3, 39) = 101.73, p < .001, partial η^2 = .89. There is a strong main effect for PHASE with about 89% of the variation in mean scores due to phase. It was expected that there would be differences in mean scores across phases when the NNS and non-NNS conditions were collapsed. The four phases were different from one another independent of the NNS and non-NNS condition.

3. The interaction effect EXPCONDITION*PHASE F (3.39) = 24.69, p <.001, partial η^2 = .66. There is a strong interaction effect with about 65% of the variation due to the interaction effect. The difference in mean scores for experimental condition (NNS vs. non-NNS) depends on the phase. Even with few subjects, the interaction effect was evident.

At this point there are statistically significant effects. The output below breaks those effects down with regard to EXPCONDITION, PHASE, and the INTERACTION EFFECT

Experimental Effects (Heart Rate)

Main Effect for EXPCONDITION (Heart Rate)

The mean and standard deviation for non-NNS (1) and NNS (2) conditions, collapsing across the phase is displayed below.

The pairwise comparisons are displayed below for the main effect of the two conditions using Bonferroni adjustment. This table indicates that the main effect for condition reflects a significant difference ($p < .001$) between the two conditions.

Main Effect for PHASE (Heart Rate)

The results for PHASE are displayed below. The first box shows the mean heart rate scores for PHASE irrespective of level of EXPCONDITION (i.e., non-NNS and NNS):

It was expected that heart rate would increase during Phase 3 observations (the phase immediately after the heel stick) irrespective of whether the infant was in the NNS or non-NNS condition. The pairwise comparisons are displayed below for the main effect of the four phases using Bonferroni adjustment.

Phases 3 and 4 were significantly different from Phases 1 and 2. In addition, Phase 3 and Phase 4 were significantly different from one another, suggesting recovery was occurring. This illustrates the importance of breaking down the first five post-heel stick observations from the last five post-heel stick observations.

Interaction Effect: EXPCONDITION*PHASE (Heart Rate)

The means for each experimental condition and phases are provided below:

The interaction effect can be seen visually. The phase means for Phases 3 and 4 are significantly different from one another. The phase means for Phases 1 and 2 are not.

Bonferroni-corrected paired sample t-tests contrasted the means for the phases and confirmed the interaction effect. Heart rate means for the NNS and non-NNS baseline sessions were not significantly different from each other. For the first baseline phase, $t(13) = .74$, *ns*. For the second baseline phase, $t(13) = 1.26$, *ns*. However, heart rate means for the NNS and non-NNS post-heel stick phases were significantly different. For the first post-heel stick phase, $t(13) = 8.49$, $p < .01$, $\eta^2 = .85$. For the second post-heel stick phase, $t(13) = 8.98$, $p < .001$, $\eta^2 = .86$. Thus, the effect is entirely found in the post-heel stick phases and is consistent with the experimental hypotheses.

The large effect sizes are interpreted as follows: In the first post-heel stick comparison, 85% of the variation in differences between heart rates is accounted for by condition (i.e., the manipulation of the independent variable, NNS). In the second post-heel stick comparison, 86% of the variation in differences between heart rates is accounted for by the independent variable. Both are very robust effects.

Latency to Heart Rate Recovery

Given that mean heart rate differences were robust, a second question is whether the infants differed across sessions in their recovery latencies. In other words, did the infants in the NNS condition recover to baseline heart rate faster than the infants in the control condition?

Table 4-12 shows latency to recovery for each infant. See the note at the bottom of the table for interpretation. The point of the analysis was to create a confidence interval around the observed heart rate mean during baseline and then identify the first heart rate observation post-heel stick that may be located within the baseline confidence interval. Note that none of the non-NNS heart rates fell within the confidence interval, whereas 10 of the 14 NNS infant heart rates did, suggesting a much shorter latency in recovery time. Figure 4-15 also displays shorter

latency to recovery times. Thus, there is a statistically significant interaction effect in the hypothesized direction for heart rate, and latency to recovery times are shorter.

Oxygen Saturation

Two Factor Within-Subjects ANOVA

Phases were arranged as per the heart rate data. Oxygen saturation means and standard deviations for each phase are displayed below. OXSATCPhase1 is the mean of the first ten oxygen saturation observations in the "control" or non-NNS Phase1 condition. OXSATCPhase2 is the mean of the next four oxygen saturations in the non-NNS condition (effectively, an extension of baseline). OXSATCPhase3 is the mean of the first 5 oxygen saturation observations in the non-NNS condition. OXSATCPhase4 is the mean of the last 5 oxygen saturation observations in the non-NNS condition. OXSATIPhase1 is the mean of the first 10 baseline observations in the NNS condition. OXSATIPhase2 is the mean of the 4 observations during the introduction of NNS. OXSATIPhase3 is the mean of the first 5 observations post-heel stick. OXSATIPhase4 is the mean of the last 5 observations post-heel stick. It is of note that the oxygen saturations in Phases 1 and 2 of both the control and intervention phases are similar. However, the oxygen saturations in Phases 3 and 4 of both the control and intervention phases are less in comparison. The oxygen saturation mean in the intervention Phase 4 (97.68) is greater then the oxygen saturation mean in the control Phase 4 (94.30) suggesting the return to baseline was occurring in the intervention phase.

ANOVA Interpretation

The factor EXPCONDITION $F(1,13) = 19.09$, $p = .001$, partial $\eta^2 = .59$. There is a strong main effect for the experimental condition with about 59% of the variation in mean scores due to the assignment to condition.

The factor PHASE F (3, 39) = 53.83, $p < .001$, partial $\eta^2 = .80$. There is a strong main effect for PHASE with about 80% of the variation in mean scores due to phase.

The interaction effect EXPCONDITION*PHASE F (3.39) = 22.28, $p < .001$, partial $\eta^2 = .63$. There is a strong interaction effect with about 63% of the variation due to the interaction effect. Even with low power (few subjects), the interaction effect was evident.

At this point there are statistically significant effects. Like the heart rate data, these results show a main effect for EXPCONDITION, PHASE, and the interaction effect EXPCONDITION * PHASE. Notice that the effect sizes (partial eta squared) are similarly large. The output below breaks those effects down with regard to EXPCONDITION, PHASE, and the INTERACTION EFFECT

Experimental Effects (Oxygen Saturation)

Main Effect for EXPCONDITION (Oxygen Saturation)

The mean and standard deviation for non-NNS (1) and NNS (2) conditions, for EXPCONDITION after collapsing across phases is displayed below:

The pairwise comparisons are displayed below for the main effect of the two conditions using Bonferroni adjustment. This table indicates that the main effect for condition reflects a significant difference ($p < .001$) between the two conditions.

Main Effect for PHASE (Oxygen Saturation).

The results for PHASE are displayed below. The first box shows the mean oxygen saturation scores for PHASE irrespective of level of EXPCONDITION (i.e., non-NNS and NNS). Notice that there is a change in Phase 3 in that oxygen saturation levels drop. In Phase 4, it appears the mean is beginning to return back to baseline levels (increase from 94.5 to 95.9).

The pairwise comparisons are displayed to follow for the main effect of the four phases using Bonferroni adjustment. Like heart rate, Phases 1 and 2 are significantly different from Phases 3 and 4. In addition, Phases 3 and 4 are significantly different from each other.

Interaction Effect: EXPCONDITION * PHASE (Oxygen Saturation)

The means for each experimental condition and phases are provided below.

As depicted earlier, the oxygen saturation means and plot show where the interaction effect occurs. Phase 3 and 4 means are significantly different from one another across experimental conditions. The phase means for Phases 1 and 2 are not.

Four Bonferroni-corrected paired-samples t-tests contrasted the means for the NNS and non-NNS conditions. As with the heart rate analysis, baselines oxygen saturation means for the NNS and non-NNS conditions were not significantly different from one another. For the first baseline phase, $t(13) = 1.69$, ns. For the second baseline phase, $t(13) = -.91$, ns. In contrast, paired sample t-tests for the post-heel stick means were statistically significant. For the first post-heel stick phase, $t(13) = 4.87$, $p < .001$, partial $\eta 2 = .65$. For the second post-heel stick phase, $t(13) = 5.36$, $p < .001$, partial $\eta 2 = .69$. Thus, the interaction effect is found in Phase 3 and Phase 4, suggesting a therapeutic advantage for the NNS condition with regard to oxygen saturation levels.

The effect sizes are interpreted as follows: In the first post-heel stick comparison, 65% of the variation in differences between oxygen saturations is accounted for by condition (i.e., the manipulation of the independent variable, NNS). In the second post-heel stick comparison, 69% of the variation in differences between oxygen saturation is accounted for by the independent variable. Both are very robust effects.

Latency to Oxygen Saturation Recovery

In many ways, the results for oxygen saturation recovery mimic results for heart rate recovery. Table 13 shows latency to recovery statistics for oxygen saturation for each infant. Note that in the NNS condition, 9 of the 12 infants achieved an oxygen saturation level during recovery that was greater than the lower limit of the 95% confidence level for the baseline mean. Conversely, none of the infants during the non-NNS (control) condition achieved an oxygen saturation level higher than the lower limit of the 95% confidence level for the baseline mean. Further, the delta value for the z-scores for the highest observed oxygen saturation level during NNS and non-NNS conditions was uniformly positive, meaning that the treatment effect was always in the therapeutic direction. In two cases, delta could not be calculated since there was no variation in oxygen saturation during non-NNS baseline (and the corresponding 95% confidence interval could not be calculated).

NIPS Scores

In contrast to the heart rate and oxygen saturation measurements, there were only 12 NIPS score observations. In both the NNS and non-NNS conditions, the first five scores were baseline measurements (pre-heel stick). The last seven NIPS scores were post-heel stick measurements. The pre-heel stick means and standard deviation NIPS scores in both the control (NIPSCPre) and intervention (NIPSIPre) conditions were less than the post-heel stick means and standard deviation NIPS scores. Figure 4-17 displays mean NIPS scores across control and NNS conditions.

ANOVA Interpretation

These results show a main effect for PHASE, but not for EXCONDITION or EXPCONDITION*PHASE.

1. The factor EXPCONDITION F (1, 13) = 2.46, p =.140 *ns*, partial η^2 = .16. There is a weak main effect for the experimental condition with about 16% of the variation in mean scores due to the assignment to condition.

2. The factor PHASE F (1, 13) = 697.88, $p < .001$, partial η^2 = .98. There is a strong main effect for PHASE with about 98% of the variation in mean scores due to phase.

3. The interaction effect EXPCONDITION*PHASE F (1.13) = 1.95, p =.186 *ns*, partial η^2 = .13. The p value is not significant. There is a weak interaction effect with about 13% of the variation due to the interaction effect.

Factors that May Mediate the Effect

Birth Weight

There was a relatively strong correlation between birth weight (in grams) and the size of the change effect reported in the far right column for both heart rate and oxygen saturation in Tables 12 and 13. For heart rate, recall that the value of delta is the z-score difference for lowest achieved heart rate in an infant across NNS and non-NNS conditions. Thus, a large negative delta value indicated a large standardized difference in heart rate recovery in the therapeutic direction. Birth weight correlated $r(12) = -0.62$, $p = 0.17$ with the delta value for heart rate recovery, meaning that higher birth weights were associated with greater therapeutic effect (i.e., lower heart rates relative to baseline in the NNS condition). The effect was not as large for oxygen saturation and the result was not statistically significant, $r(12) = .27$, *ns*.

FiO_2

The other variable that seems to be strongly related to treatment effect is FiO_2, fraction of inspired oxygen. FiO_2 had a borderline relationship to the heart rate effect, $r(12) = .511$, $p = .06$ and was significantly related to the oxygen saturation effect, $r(12) = .59$, $p = .05$.

Table 4-1. Descriptive Statistics of Heart Rate

	Mean	Std. Deviation	N
HRCPhase1	135.1214	9.28507	14
HRCPhase2	136.8750	10.12221	14
HRCPhase3	155.1429	7.55836	14
HRCPhase4	150.6429	7.53257	14
HRIPhase1	133.8786	7.65428	14
HRIPhase2	134.3750	6.59162	14
HRIPhase3	141.0857	8.27553	14
HRIPhase4	135.6429	7.71140	14

Table 4-2. Mauchly's Test of Sphericity of Measure: MEASURE 1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	Df	Sig	Greenhouse-Geisser	Epsilon* Huynh-Feldt	Lower-bound
ExpCondition	1.000	.000	0		1.000	1.000	1.000
Phase	.410	10.457	5	.064	.701	.839	.333
ExpCondition*Phase	.323	13.249	5	.022	.608	.703	.333

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

b. Design: Intercept

Within Subjects Design: ExpCondition + Phase + ExpCondition * Phase

The Mauchly's test was negative for Phase suggesting no violation of the sphericity assumption. The significance value is greater than .05, $W = .410$, $\chi^2(5) = 10.46$, $p > .05$.

Table 4-3. Within-Subjects Factors of Measure: MEASURE 1

Exp Cond.	Phase	Dependent Variable
1	1	HRCPhase1
	2	HRCPhase2
	3	HRCPhase3
	4	HRCPhase4
2	1	HRIPhase1
	2	HRIPhase2
	3	HRIPhase3
	4	HRIPhase4

Table 4-4. Tests of Within-Subjects Effects Measure: MEASURE 1

Source		Type III Sum of Squares	Df	Mean Square	F	Sig	Partial Eta Squared
ExpCondition	Sphericity Assumed	1882.720	1	1882.720	46.652	.000	.782
	Greenhouse-Geisser	1882.720	1.000	1882.720	46.652	.000	.782
	Huynh-Feldt	1882.720	1.000	1882.720	46.652	.000	.782
	Lower-bound	1882.720	1.000	1882.720	46.652	.000	.782
Error(ExpCondition)	Sphericity Assumed	524.637	13	40.357			
	Greenhouse-Geisser	524.637	13.000	40.357			
	Huynh-Feldt	524.637	13.000	40.357			
	Lower-bound	524.637	13.000	40.357			
Phase	Sphericity Assumed	3489.702	3	1163.234	101.732	.000	.887
	Greenhouse-Geisser	3489.702	2.103	1659.602	101.732	.000	.887
	Huynh-Feldt	3489.702	2.518	1385.954	101.732	.000	.887
	Lower-bound	3489.702	1.000	3489.702	101.732	.000	.887
Error(Phase)	Sphericity Assumed	445.937	39	11.434			
	Greenhouse-Geisser	445.937	27.336	16.313			
	Huynh-Feldt	445.937	32.733	13.624			
	Lower-bound	445.937	13.000	34.303			
ExpCondition*Phase	Sphericity Assumed	1130.066	3	376.689	24.692	.000	.655
	Greenhouse-Geisser	1130.066	1.825	619.046	24.692	.000	.655
	Huynh-Feldt	1130.066	2.108	536.060	24.692	.000	.655
	Lower-bound	1130.066	1.000	1130.066	24.692	.000	.655
Error (ExpCondition*Phase)	Sphericity Assumed	594.970	39	15.256			
	Greenhouse-Geisser	594.970	23.731	25.071			
	Huynh-Feldt	594.970	27.405	21.710			
	Lower-bound	594.970	13.000	45.767			

Table 4-5. Estimates of Measure: MEASURE 1

Exp Condition	Mean	Std. Error	Lower Bound	Upper Bound
1	144.446	2.095	139.919	148.972
2	136.246	1.921	132.096	140.395

Table 4-6. Pairwise Comparisons of Measure: MEASURE 1

(I) Exp Condition	(J) Exp Condition	Mean Difference (I-J)	Std. Error	Sig.*	Lower Bound	Upper Bound
1	2	8.200*	1.201	.000	5.606	10.794
2	1	-8.200*	1.201	.000	-10.794	-5.606

Based on estimated marginal means

*The mean difference is significant at the .05 level.

a. Adjustment for multiple comparisons: Bonferroni.

Table 4-7. Estimates of Measure: MEASURE 1

Phase	Mean	Std. Error	Lower Bound	Upper Bound
1	134.500	2.114	129.933	139.067
2	135.625	2.055	131.186	140.064
3	148.114	1.949	143.903	152.326
4	143.143	1.858	139.129	147.157

Table 4-8. Pairwise Comparisons

(I) Phase	(J) Phase	Mean Difference (I-J)	Std. Error	Sig.*	Lower Bound	Upper Bound
1	2	-1.125	.482	.219	-2.624	.374
	3	-13.614*	1.033	.000	-16.823	-10.406
	4	-8.643*	1.021	.000	-11.815	-5.471
2	1	1.125	.482	.219	-.374	2.624
	3	-12.489*	1.018	.000	-15.652	-9.327
	4	-7.518*	.887	.000	-10.275	-4.761
3	1	13.614*	1.033	.000	10.406	16.823
	2	12.489*	1.018	.000	9.327	15.652
	4	4.971*	.858	.000	2.307	7.636
4	1	8.643*	1.021	.000	5.471	11.815
	2	7.518*	.887	.000	4.761	10.275
	3	-4.971*	.858	.000	-7.636	-2.307

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni.

*The mean difference is significant at the .05 level.

Table 4-9. ExpCondition * Phase Measure: Oxygen Saturation

Exp Condition	Phase	Mean	Std. Error	Lower Bound	Upper Bound
1	1	98.400	.577	97.153	99.647
	2	97.821	.881	95.919	99.724
	3	92.886	1.205	90.283	95.488
	4	94.300	1.000	92.139	96.461
2	1	97.907	.691	96.414	99.400
	2	98.179	.686	96.697	99.660
	3	96.129	.804	94.391	97.866
	4	97.686	.644	96.295	99.076

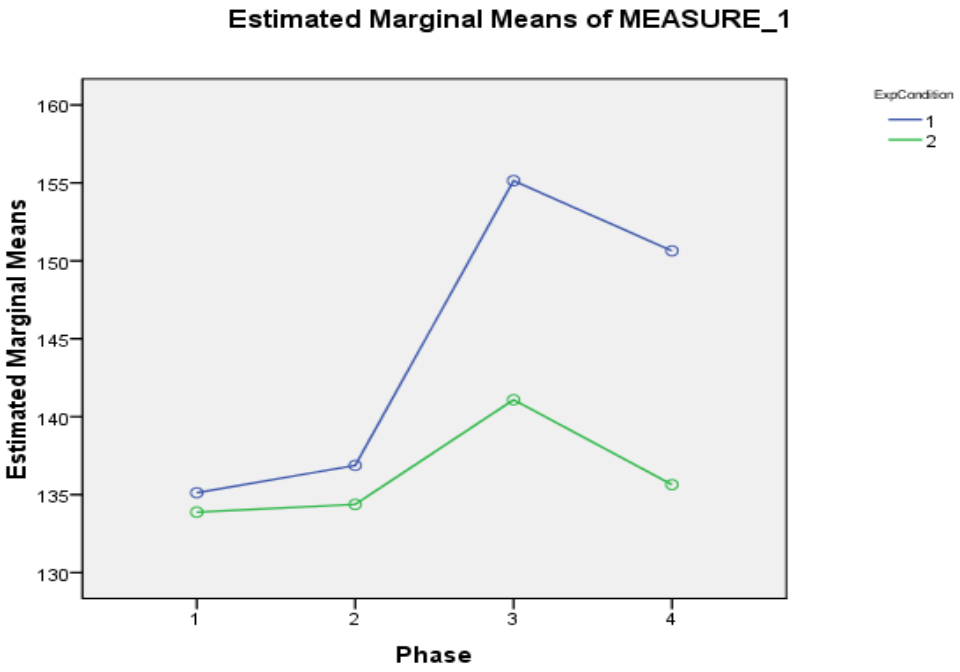

Figure 4-1. Estimated marginal means of measure 1

Table 4-10. Descriptive Statistics of Oxygen Saturation

	Mean	Std. Deviation	N
OXSATCPhase1	98.4000	2.16013	14
OXSATCPhase2	97.8214	3.29543	14
OXSATCPhase3	92.8857	4.50758	14
OXSATCPhase4	94.300	3.74227	14
OXSATIPhase1	97.9071	2.58560	14
OXSATIPhase2	98.1786	2.56535	14
OXSATIPhase3	96.1286	3.00933	14
OXSATIPhase4	97.6857	2.40859	14

Table 4-11. Mauchly's Test of Sphericity Measure: Oxygen Saturation

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	Df	Sig	Greenhouse-Geisser	Epsilon* Huynh-Feldt	Lower-bound
ExpCondition	1.000	.000	0		1.000	1.000	1.000
Phase	.191	19.405	5	.002	.530	.592	.333
ExpCondition*Phase	.335	12.827	5	.026	.636	.743	.333

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

b. Design: Intercept

Within Subjects Design: ExpCondition + Phase + ExpCondition*Phase

The Mauchly's test was significant for phase, W = .191, X2 (5) = 19.40, p = .002, and significant for the interaction effect, W = .335, X2 (5) = 12.8, p = .026.

Table 4-12. Tests of Within-Subjects Effects Measure: Oxygen Saturation

Source		Type III Sum of Squares	Df	Mean Square	F	Sig	Partial Eta Squared	Noncent parameter	Observed Power*
ExpCondition	Sphericity Assumed	73.775	1	73.775	19.082	.001	.595	19.082	.981
	Greenhouse-Geisser	73.775	1.000	73.775	19.082	.001	.595	19.082	.981
	Huynh-Feldt	73.775	1.000	73.775	19.082	.001	.595	19.082	.981
	Lower-bound	73.775	1.000	73.775	19.082	.001	.595	19.082	.981
Error(ExpCondition)	Sphericity Assumed	50.262	13	3.866					
	Greenhouse-Geisser	50.262	13.000	3.866					
	Huynh-Feldt	50.262	13.000	3.866					
	Lower-bound	50.262	13.000	3.866					
Phase	Sphericity Assumed	254.973	3	84.991	53.829	.000	.805	161.487	1.000
	Greenhouse-Geisser	254.973	1.591	160.227	53.829	.000	.805	85.659	1.000
	Huynh-Feldt	254.973	1.777	143.447	53.829	.000	.805	95.679	1.000
	Lower-bound	254.973	1.000	254.973	53.829	.000	.805	53.829	1.000
Error(Phase)	Sphericity Assumed	61.578	39	1.579					
	Greenhouse-Geisser	61.578	20.687	2.977					
	Huynh-Feldt	61.578	23.107	2.665					
	Lower-bound	61.578	13.000	4.737					
ExpCondition*Phase	Sphericity Assumed	82.672	3	27.557	22.282	.000	.632	66.847	1.000
	Greenhouse-Geisser	82.672	1.909	43.312	22.282	.000	.632	42.531	1.000
	Huynh-Feldt	82.672	2.229	37.089	22.282	.000	.632	49.667	1.000
	Lower-bound	82.672	1.000	82.672	22.282	.000	.632	22.282	.992
Error (ExpCondition*Phase)	Sphericity Assumed	48.233	39	1.237					
	Greenhouse-Geisser	48.233	24.814	1.944					
	Huynh-Feldt	48.233	28.977	1.665					
	Lower-bound	48.233	13.000	3.710					

a. Computed using alpha = .05

Table 4-13. Measure: Oxygen Saturation

Exp Condition	Mean	Std. Error	95% Confidence Interval Lower Bound	Upper Bound
1	95.852	.883	93.943	97.760
2	97.475	.679	96.008	98.942

Table 4-14. Pairwise Comparisons Measure: Oxygen Saturation

(I) Exp Condition	(J) Exp Condition	Mean Difference (I-J)	Std. Error	Sig.a	Lower Bound	Upper Bound
1	2	-1.623	.372	.001	-2.426	-.820
2	1	1.623	.372	.001	.820	2.426

Based on estimated marginal means.
*The mean difference is significant at the .05 level.
Adjustment for multiple comparisons: Bonferroni.

Table 4-15. Estimates Measure: Oxygen Saturation

Phase	Mean	Std. Error	Lower Bound	Upper Bound
1	98.154	.620	96.815	99.493
2	98.000	.764	96.349	99.651
3	94.507	.969	92.415	96.600
4	95.993	.780	94.309	97.677

Table 4-16. Pairwise Comparisons Measure: Oxygen Saturation

(I) Phase	(J) Phase	Mean Difference (I-J)	Std. Error	Sig.*	Lower Bound	Upper Bound
1	2	.154	.217	1.000	-5.222	.829
	3	3.646*	.502	.000	2.088	5.205
	4	2.161*	.276	.000	1.302	3.019
2	1	-.154	.217	1.000	-.829	.522
	3	3.493*	.354	.000	2.393	4.593
	4	2.007*	.242	.000	1.255	2.759
3	1	-3.646*	.502	.000	-5.205	-2.088
	2	-3.493*	.354	.000	-4.593	-2.393
	4	-1.486*	.343	.005	-2.551	-.421
4	1	-2.161*	.276	.000	-3.019	-1.302
	2	-2.007*	.242	.000	-2.759	-1.255
	3	1.486*	.343	.005	.421	2.551

Based on estimated marginal means
a. Adjustment for multiple comparisons: Bonferroni.
*The mean difference is significant at the .05 level.

Table 4-17. ExpCondition * Phase Measure: Oxygen Saturation

Exp Condition	Phase	Mean	Std. Error	Lower Bound	Upper Bound
1	1	98.400	.577	97.153	99.647
	2	97.821	.881	95.919	99.724
	3	92.886	1.205	90.283	95.488
	4	94.300	1.000	92.139	96.461
2	1	97.907	.691	96.414	99.400
	2	98.179	.686	96.697	99.660
	3	96.129	.804	94.391	97.866
	4	97.686	.644	96.295	99.076

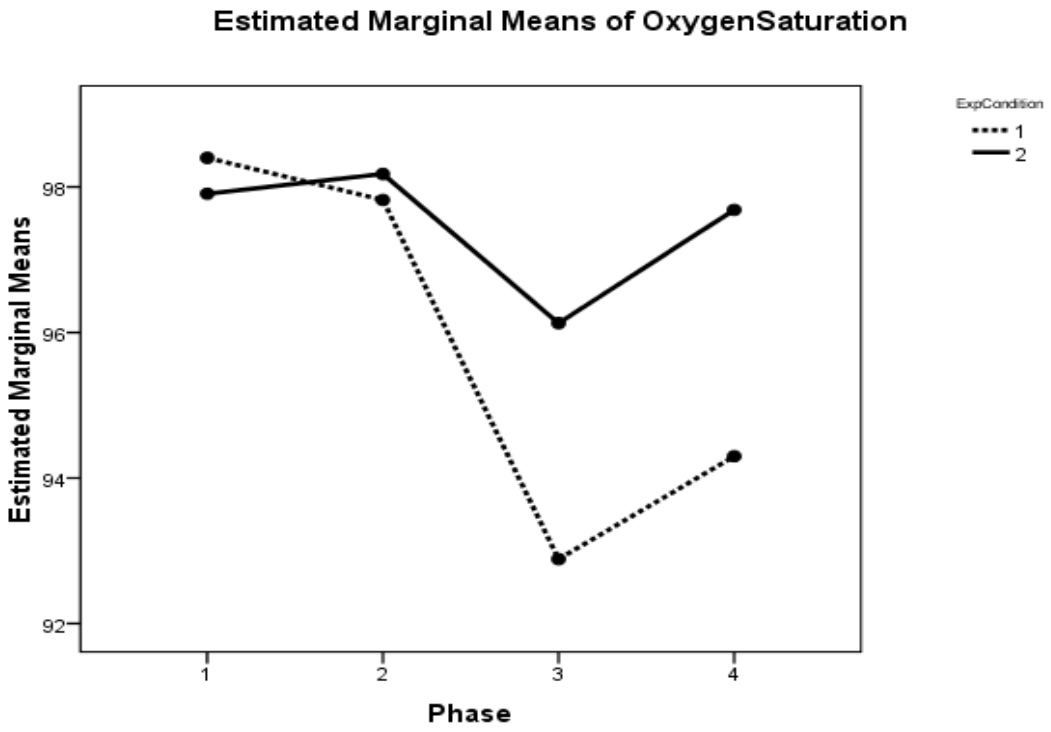

Figure 4-2. Estimated marginal means of oxygen saturation

Table 4-18. Descriptive Statistics of NIPS Scores

	Mean	Std. Deviation	N
NIPSCPre	.0204	.07636	14
NIPSCPost	5.0857	.85831	14
NIPSIPre	.0000	.00000	14
NIPSIPost	4.6286	.92439	14

Table 4-19. Mauchly's Test of Sphericity

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	Df	Sig	Greenhouse-Geisser	Epsilon* Huynh-Feldt	Lower-bound
ExpCondition	1.000	.000	0		1.000	1.000	1.000
Phase	1.000	.000	0		1.000	1.000	1.000
ExpCondition*Phase	1.000	.000	0		1.000	1.000	1.000

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent variables is proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests are displayed in the Tests of Within-Subjects Effects table.

b. Design:Intercept

Within Subjects Design: ExpCondition+Phase+ExpCondition*Phase. The test was not significant for condition, phase, or interaction effect.

Table 4-20. Tests of Within-Subjects Effects Measure: NIPS Score

Source		Type III Sum of Squares	Df	Mean Square	F	Sig	Partial Eta Squared	Noncent parameter	Observed Power*
ExpCondition	Sphericity Assumed	.798	1	.798	2.468	.140	.160	2.468	.307
	Greenhouse-Geisser	.798	1.000	.798	2.468	.140	.160	2.468	.307
	Huynh-Feldt	.798	1.000	.798	2.468	.140	.160	2.468	.307
	Lower-bound	.798	1.000	.798	2.468	.140	.160	2.468	.307
Error(ExpCondition)	Sphericity Assumed	4.205	13	.323					
	Greenhouse-Geisser	4.205	13.000	.323					
	Huynh-Feldt	4.205	13.000	.323					
	Lower-bound	4.205	13.000	.323					
Phase	Sphericity Assumed	328.899	1	328.899	697.878	.000	.982	697.878	1.000
	Greenhouse-Geisser	328.899	1.000	328.899	697.878	.000	.982	697.878	1.000
	Huynh-Feldt	328.899	1.000	328.899	697.878	.000	.982	697.878	1.000
	Lower-bound	328.899	1.000	328.899	697.878	.000	.982	697.878	1.000
Error(Phase)	Sphericity Assumed	6.127	13	.471					
	Greenhouse-Geisser	6.127	13.000	.471					
	Huynh-Feldt	6.127	13.000	.471					
	Lower-bound	6.127	13.000	.471					
ExpCondition*Phase	Sphericity Assumed	.668	1	.668	1.950	.186	.130	1.950	.253
	Greenhouse-Geisser	.668	1.000	.668	1.950	.186	.130	1.950	.253
	Huynh-Feldt	.668	1.000	.668	1.950	.186	.130	1.950	.253
	Lower-bound	.668	1.000	.668	1.950	.186	.130	1.950	.253
Error (ExpCondition*Phase)	Sphericity Assumed	4.450	13	.342					
	Greenhouse-Geisser	4.450	13.000	.342					
	Huynh-Feldt	4.450	13.000	.342					
	Lower-bound	4.450	13.000	.342					

a. Computed using alpha = .05

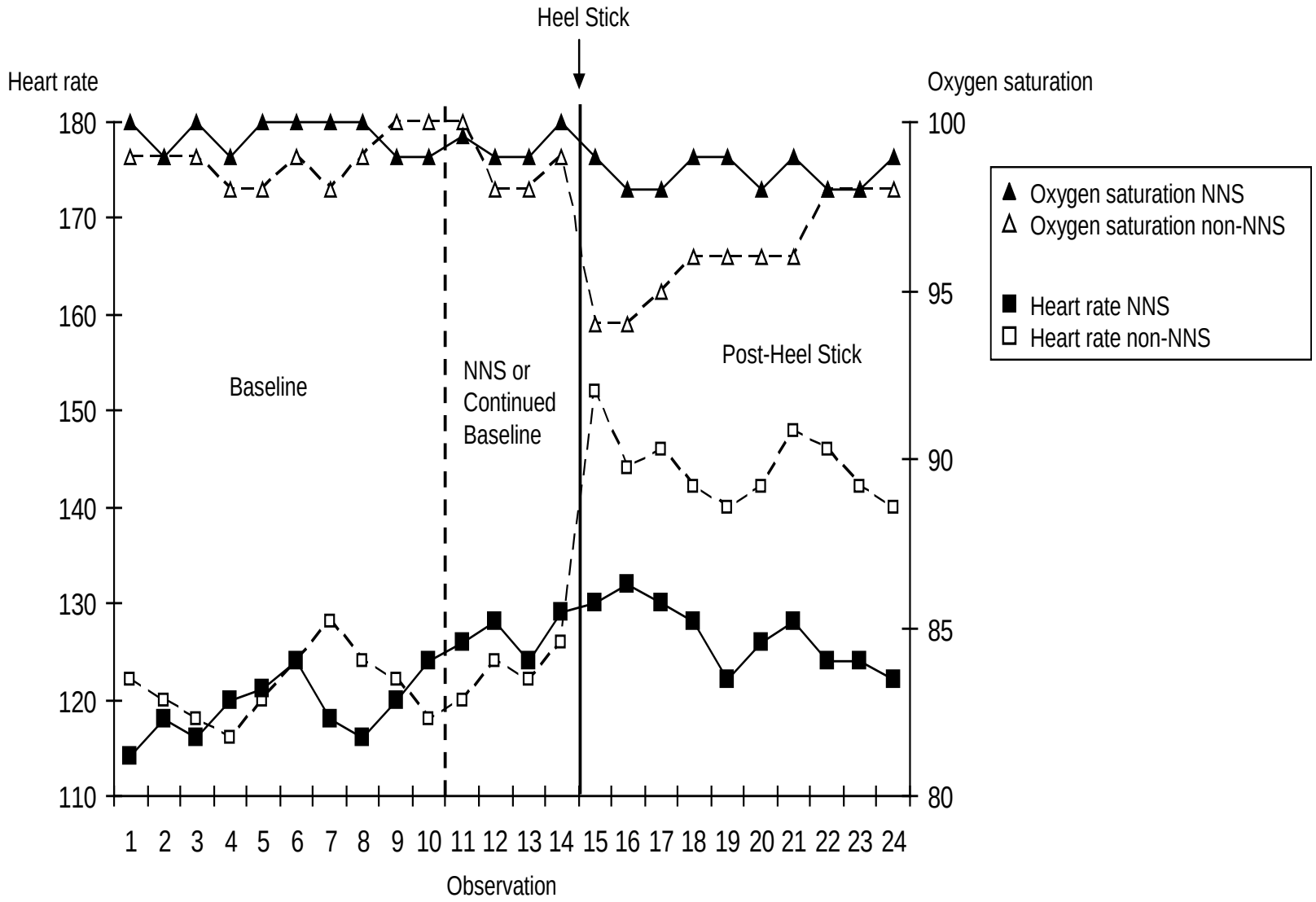

Figure 4-3. Heart rate and oxygen saturation levels for Infant 1 (African-American male, Gestational Age = 41 days; 6 days old).

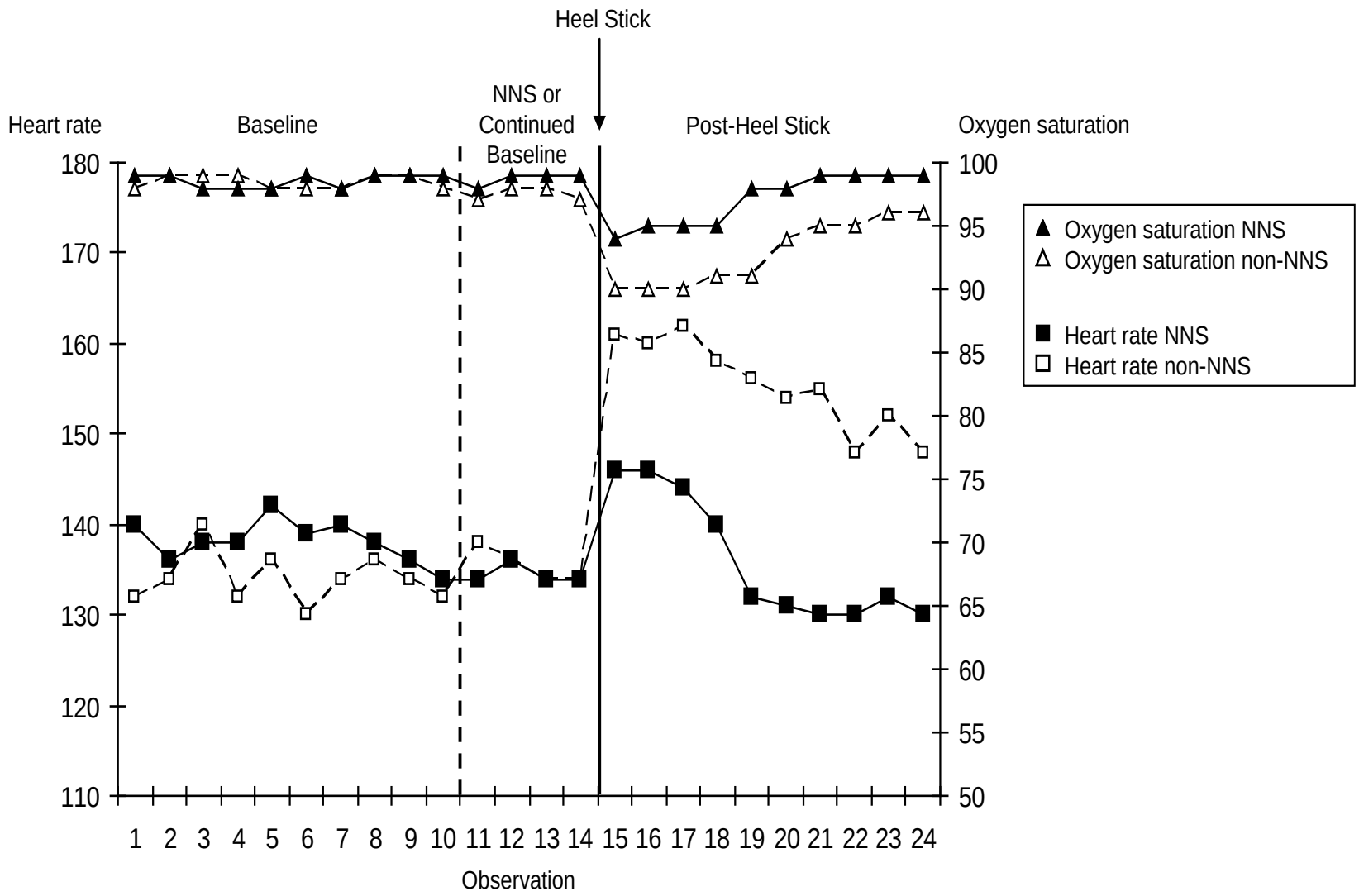

Figure 4-4. Heart rate and oxygen saturation levels for Infant 2 (Hispanic female, Gestational Age = 37 days, 13 days old).

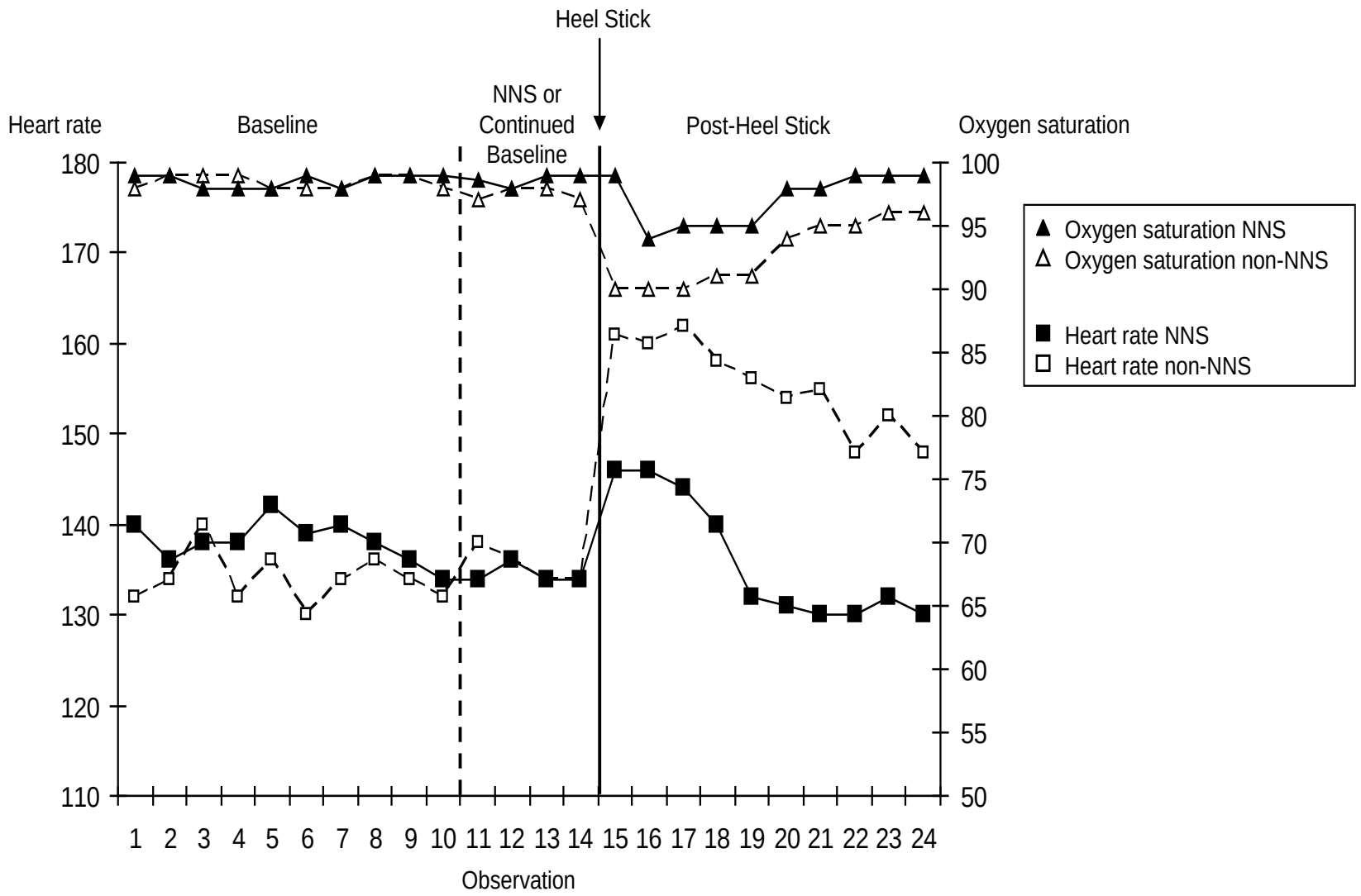

Figure 4-5. Heart rate and oxygen saturation levels for Infant 3 (Caucasian female, Gestational Age = 36 days; 9 days old)

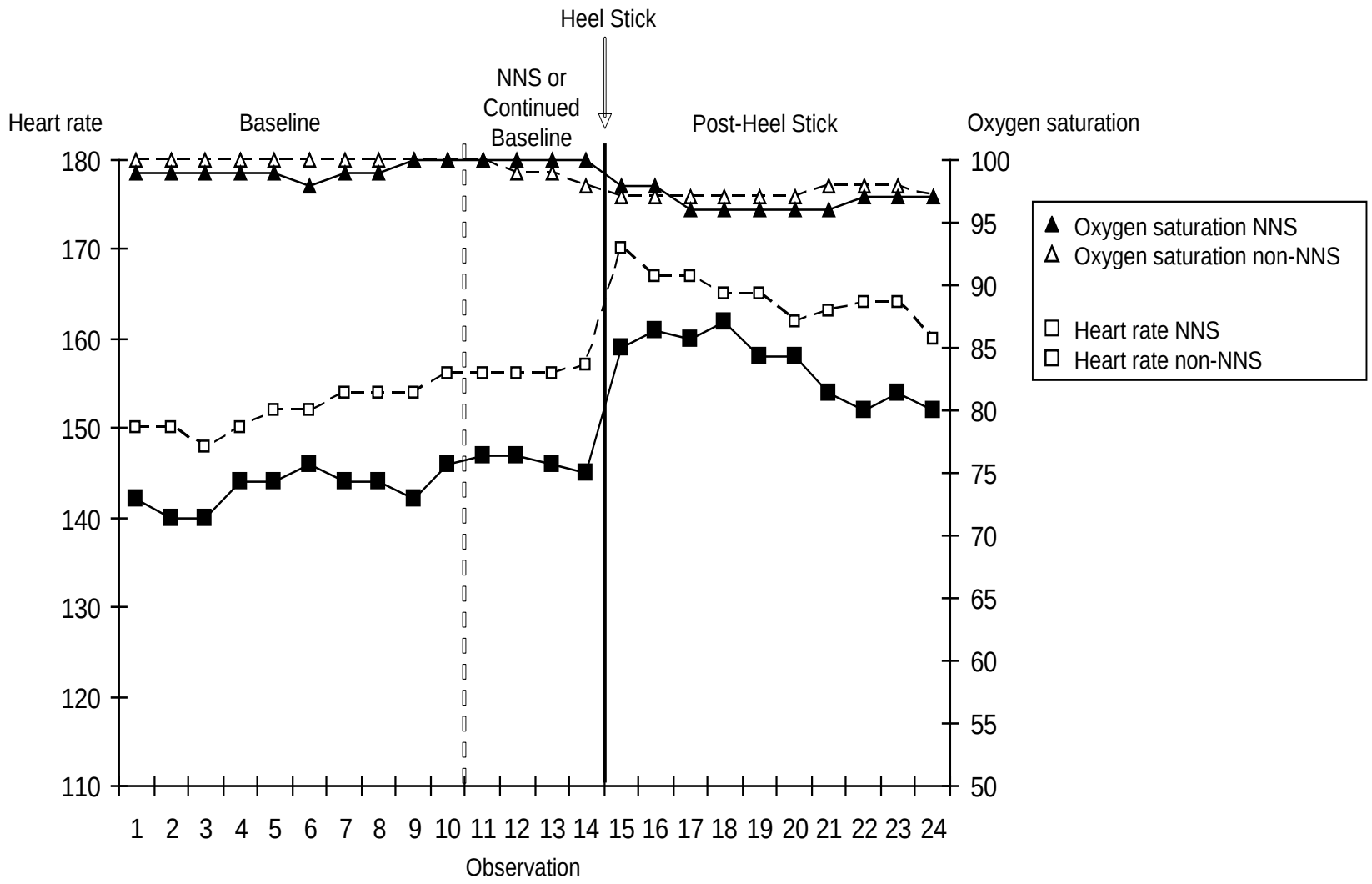

Figure 4-6. Heart rate and oxygen saturation levels for Infant 4 (African-American male, Gestational Age = 32 days; 1 day old).

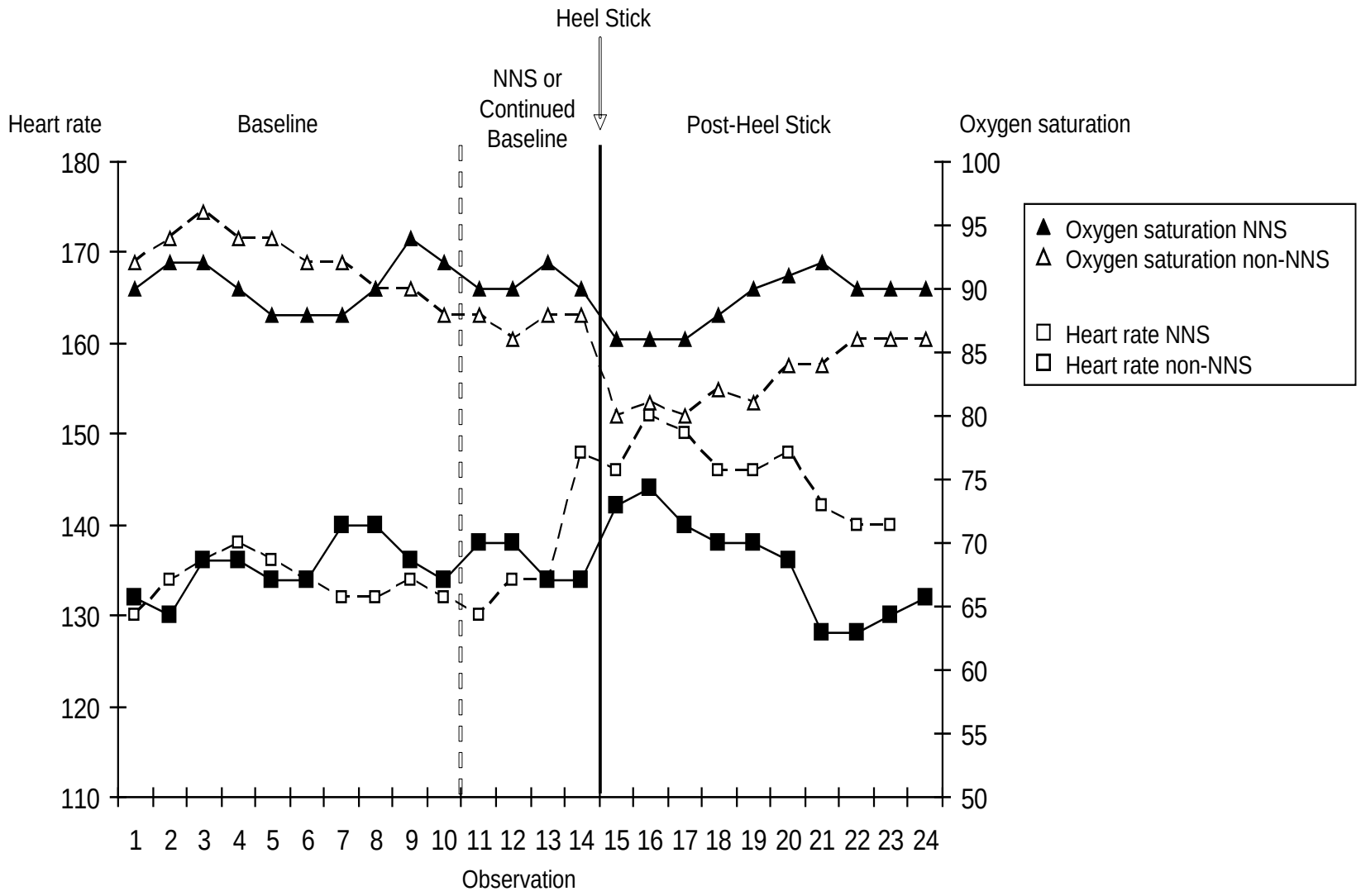

Figure 4-7. Heart rate and oxygen saturation levels for Infant 5 (African-American male, Gestational Age = 34 days; 19 days old).

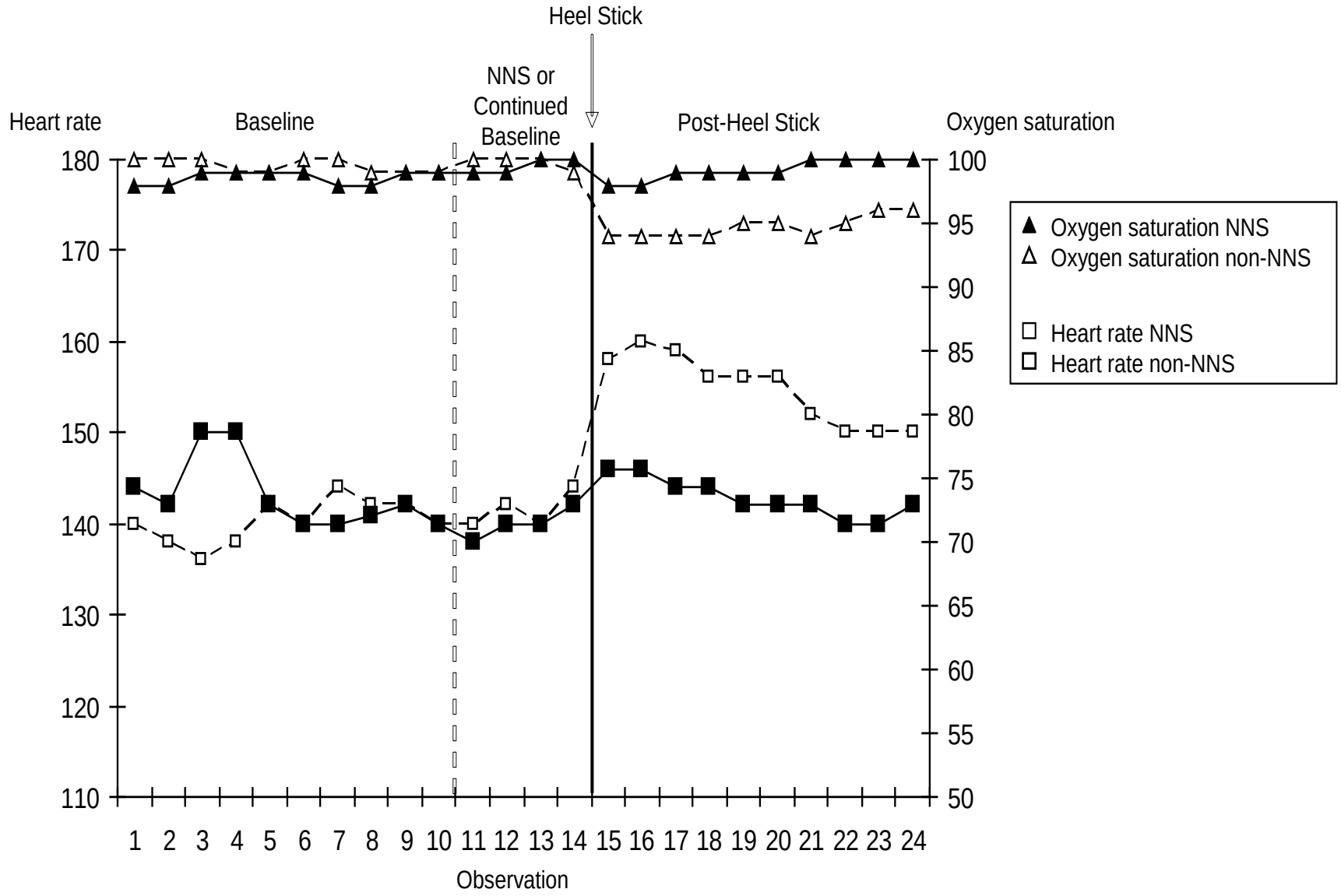

Figure 4-8. Heart rate and oxygen saturation levels for Infant 6 (African-American male, Gestational Age – 38 days; <1 day old).

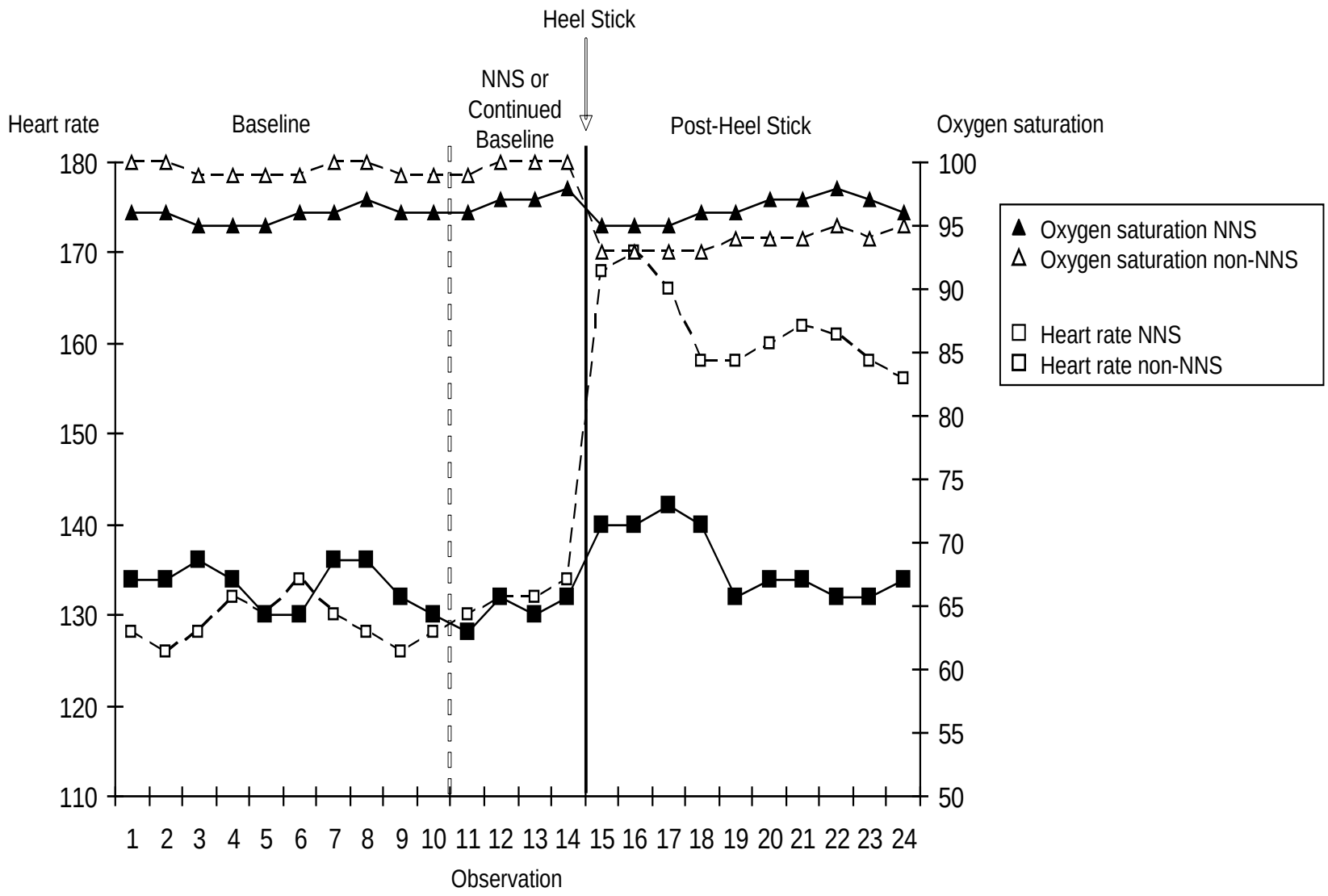

Figure 4-9. Heart rate and oxygen saturation levels for Infant 7 (Hispanic female, Gestational Age = 38 days; 2 days old).

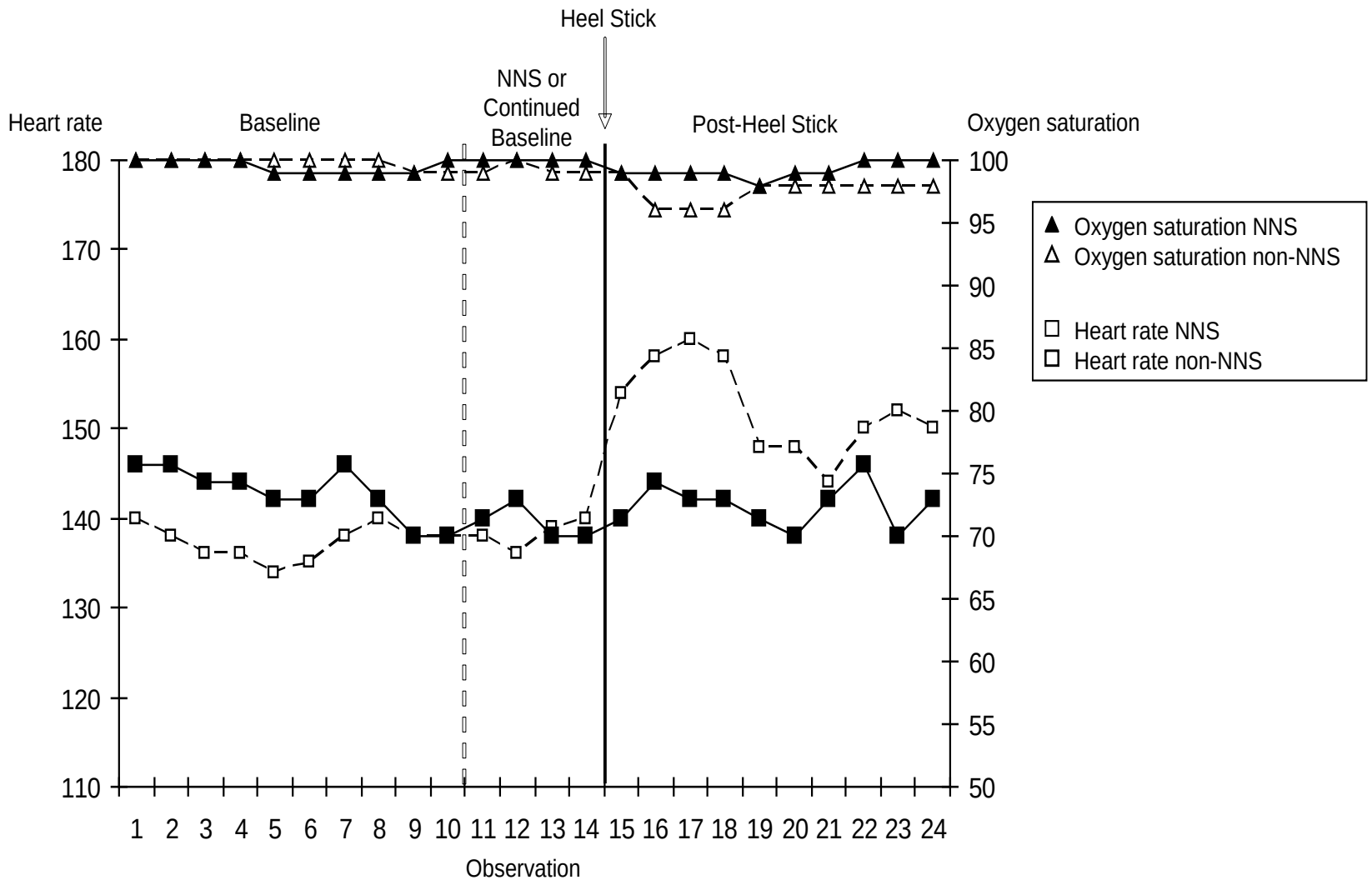

Figure 4-10. Heart rate and oxygen saturation levels for Infant 8 (Caucasian male, Gestational Age = 34 days; 1 day old).

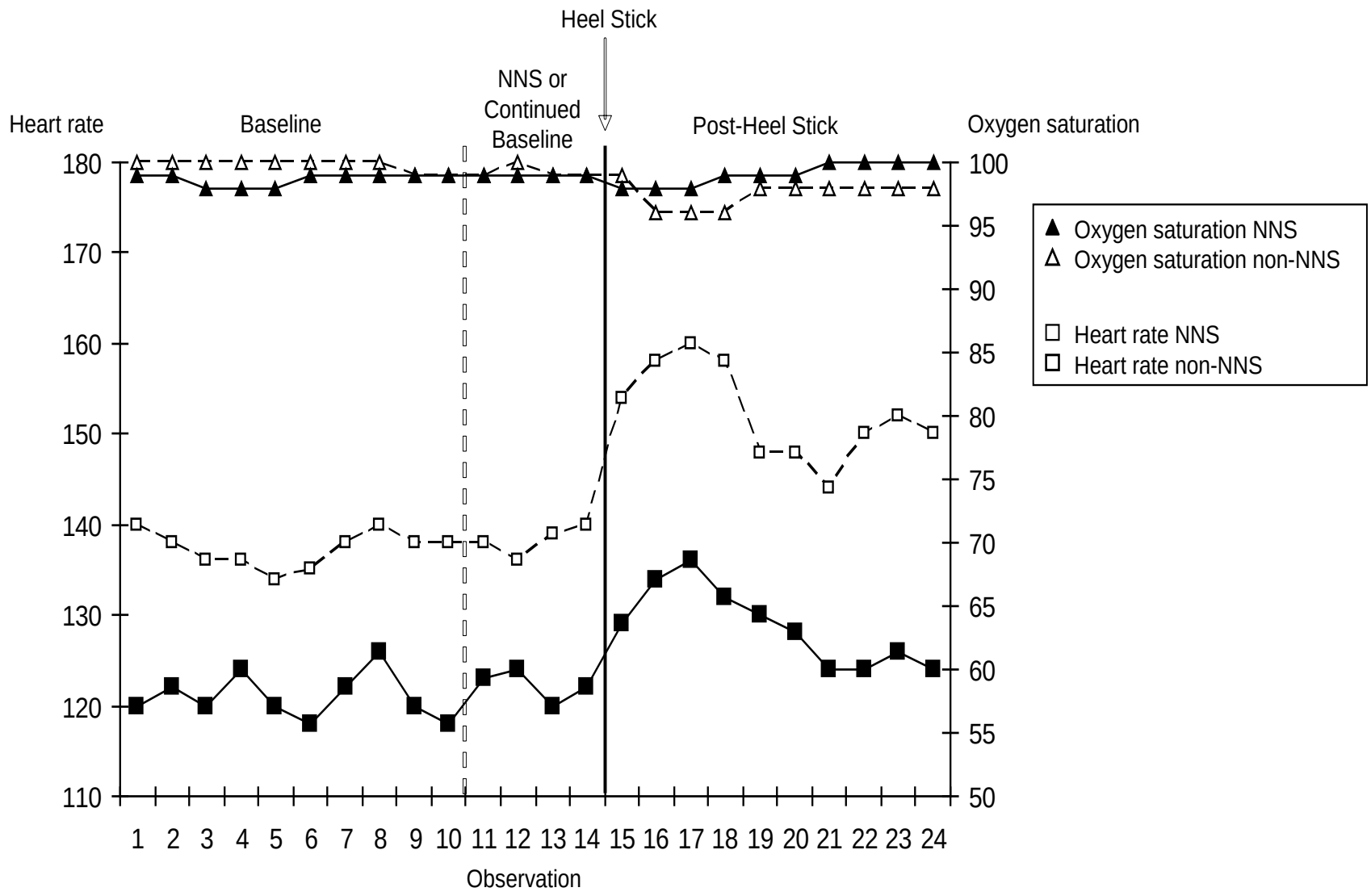

Figure 4-11. Heart rate and oxygen saturation levels for Infant 9 (Hispanic male, Gestational Age = 37 days, 1 day old).

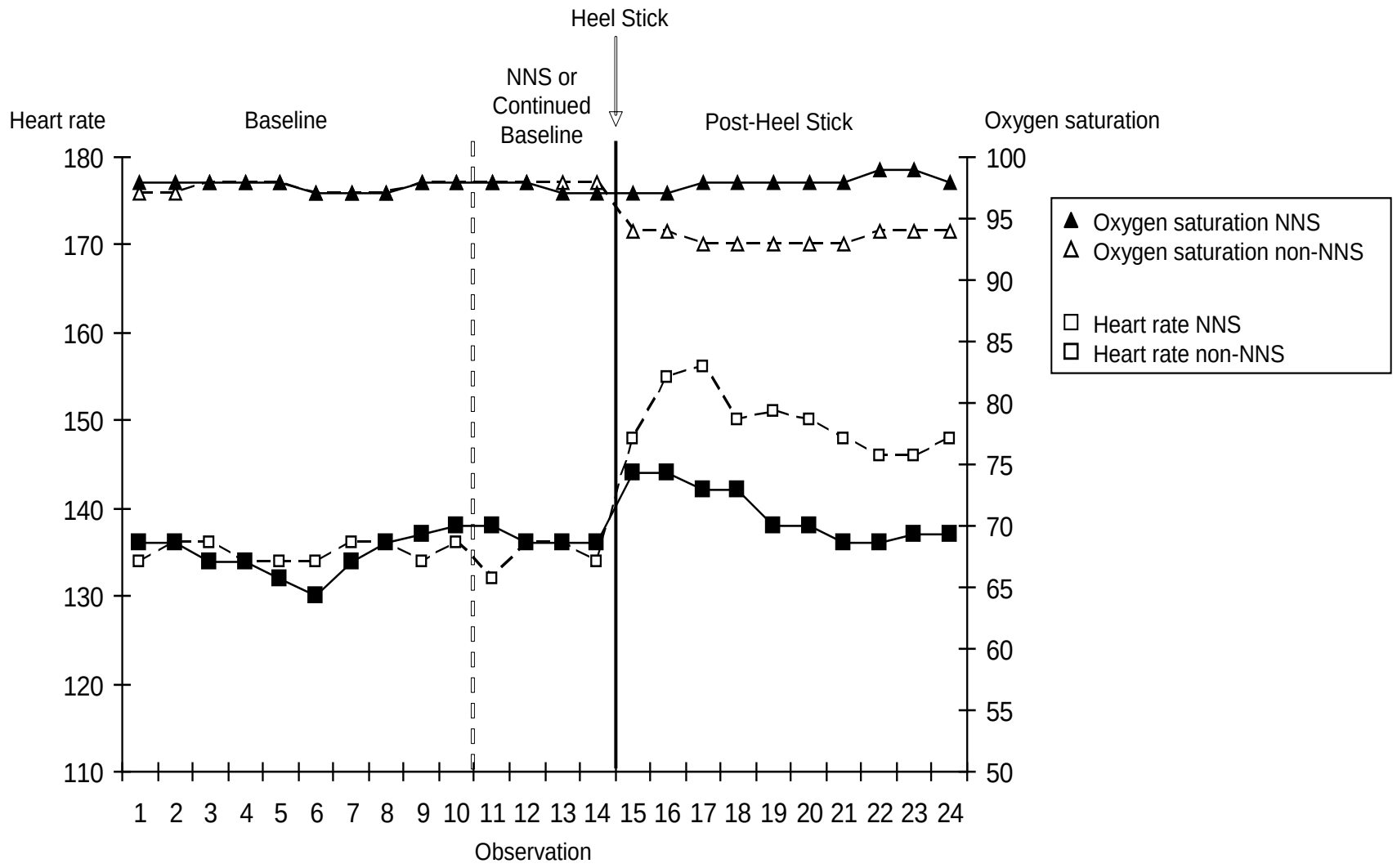

Figure 4-12. Heart rate and oxygen saturation levels for Infant 10 (Asian male, Gestational Age = 32 days; 1 day old)

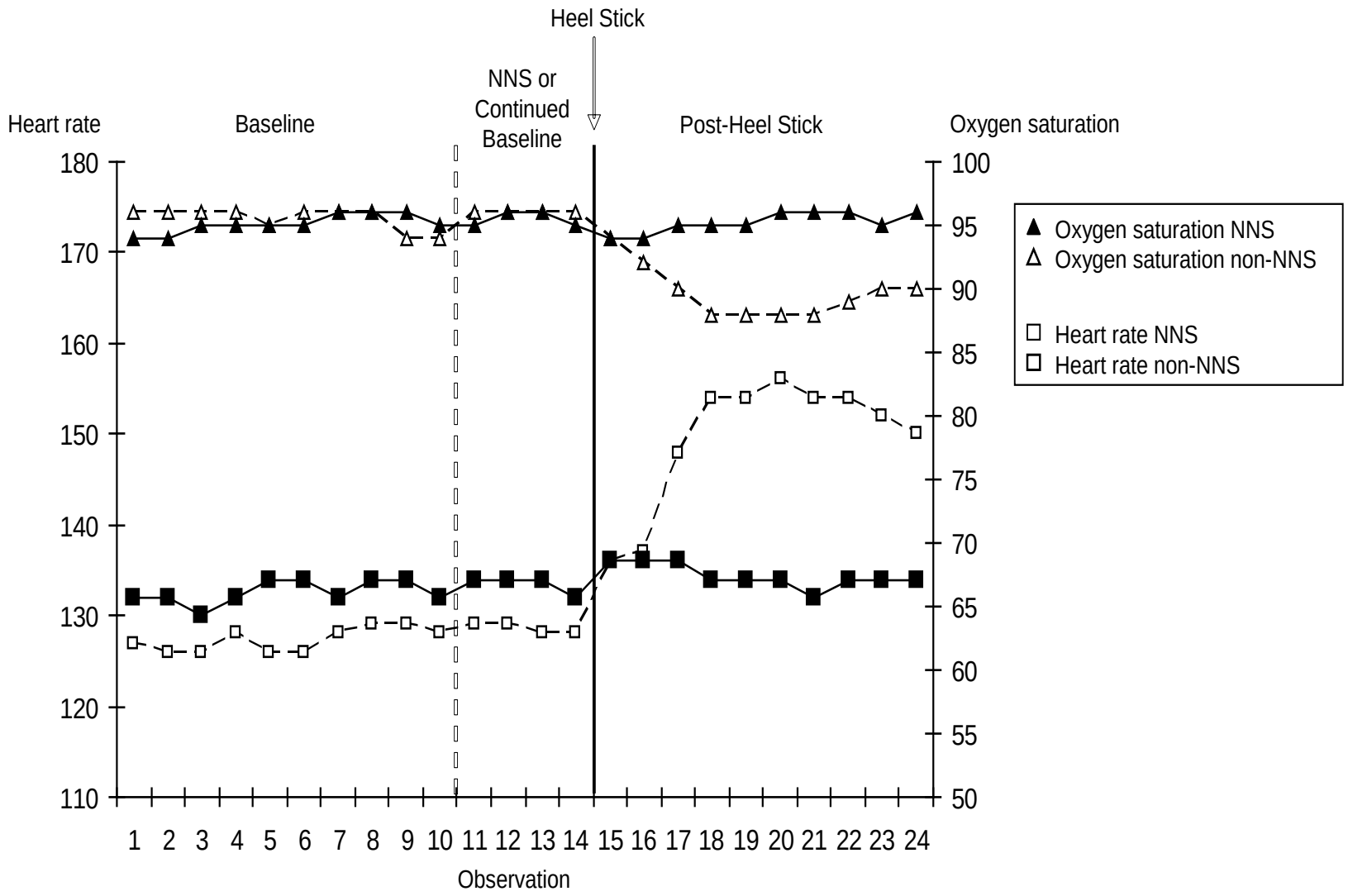

Figure 4-13. Heart rate and oxygen saturation levels for Infant 11 (Caucasian female, Gestational Age = 33 days; 5 days old).

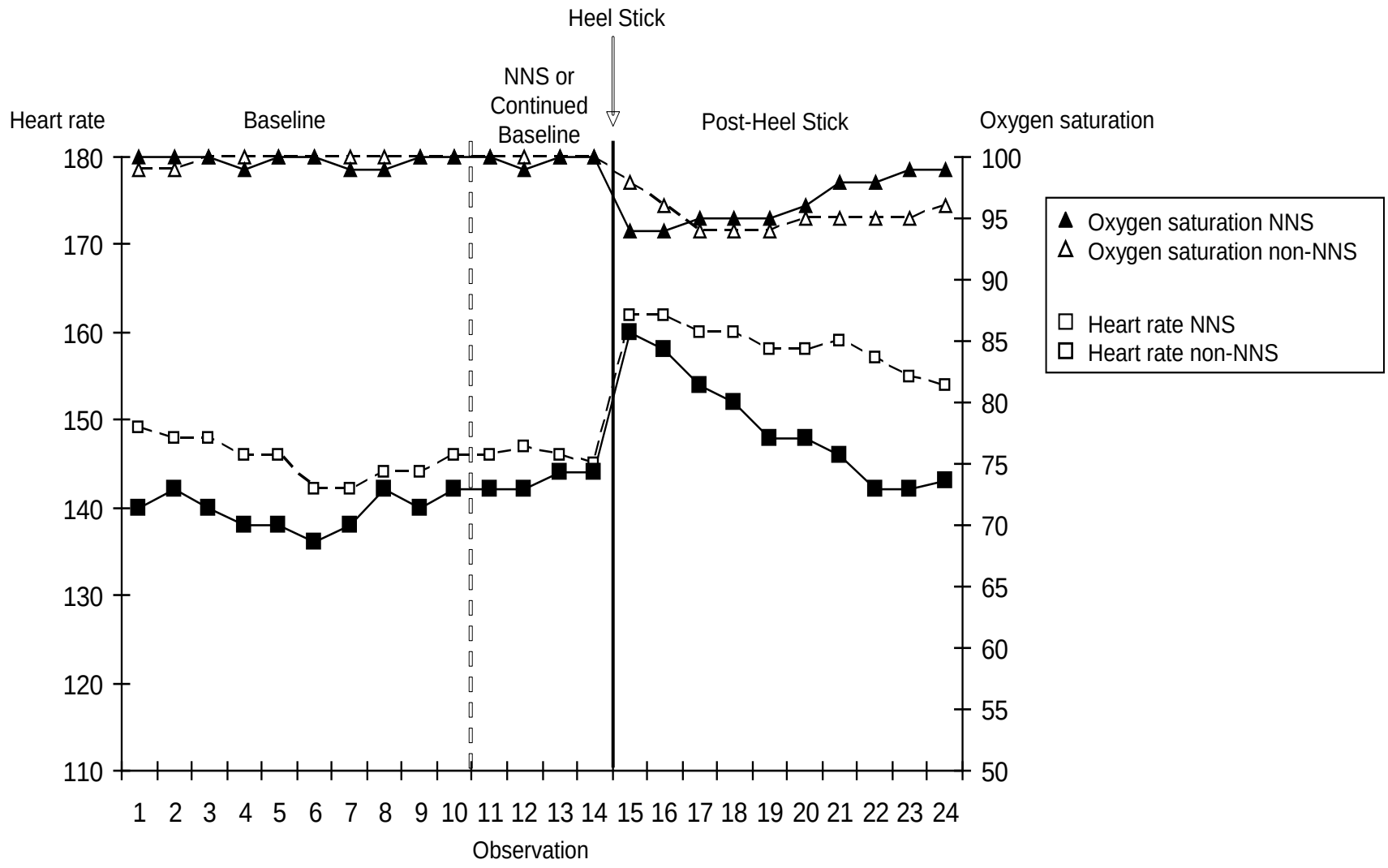

Figure 4-14. Heart rate and oxygen saturation levels for Infant 12 (Hispanic male, Gestational Age = 32 days; 5 days old).

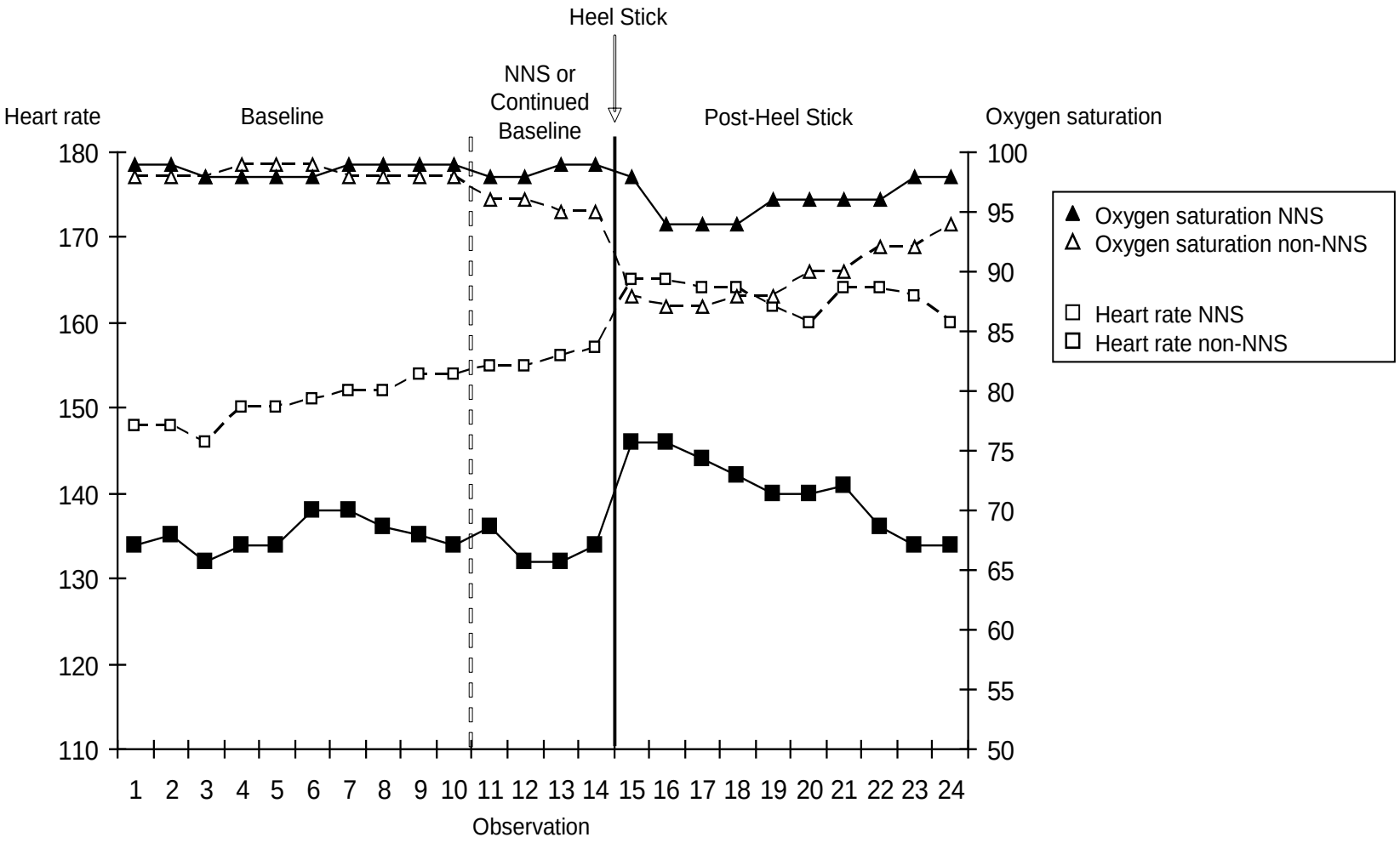

Figure 4-15. Heart rate and oxygen saturation levels for Infant 13 (African-American female, Gestational Age = 32 days; 1 day old).

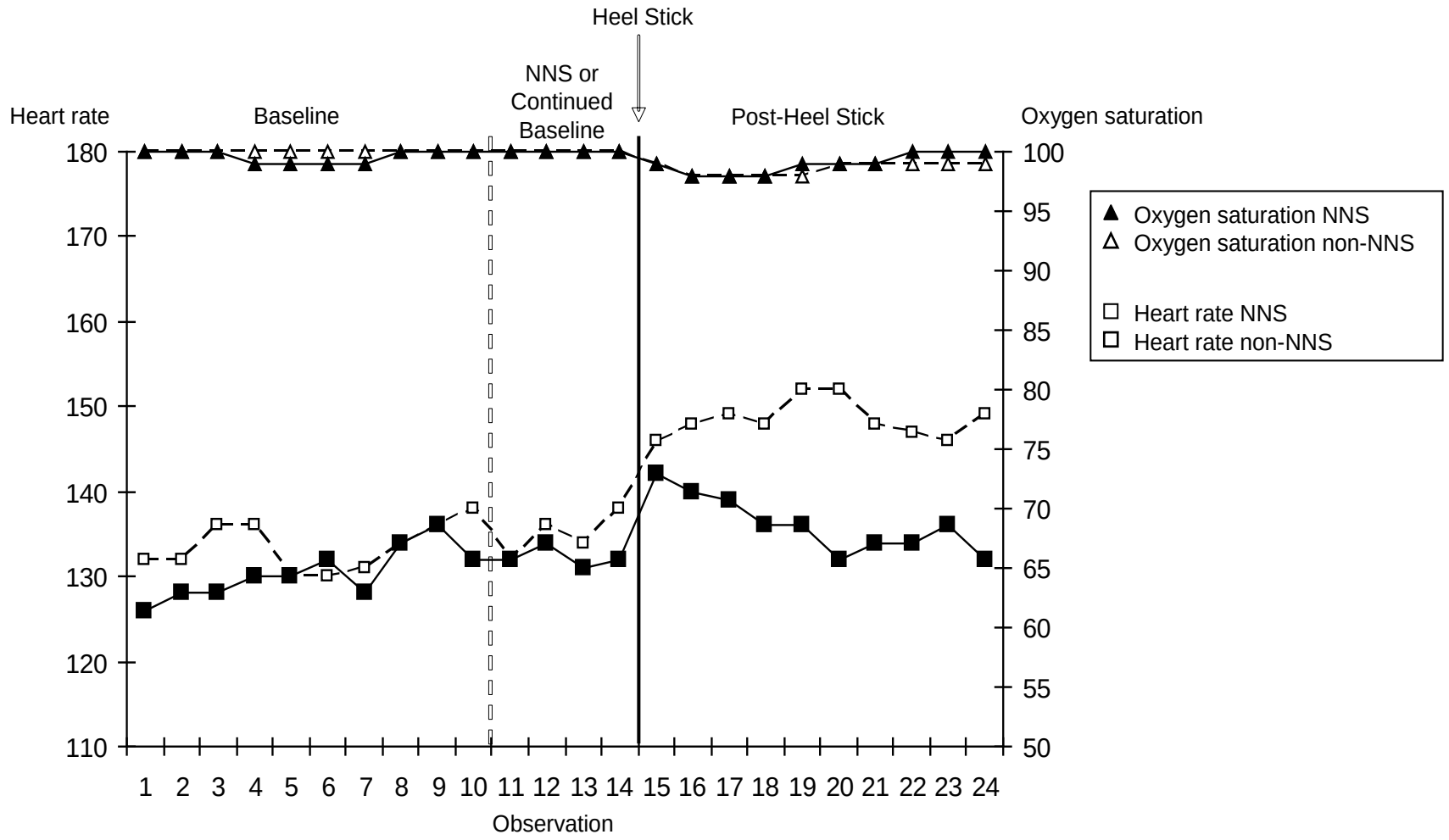

Figure 4-16. Heart rate and oxygen saturation levels for Infant 14 (Caucasian male, Gestational Age = 36 days; 3 days old).

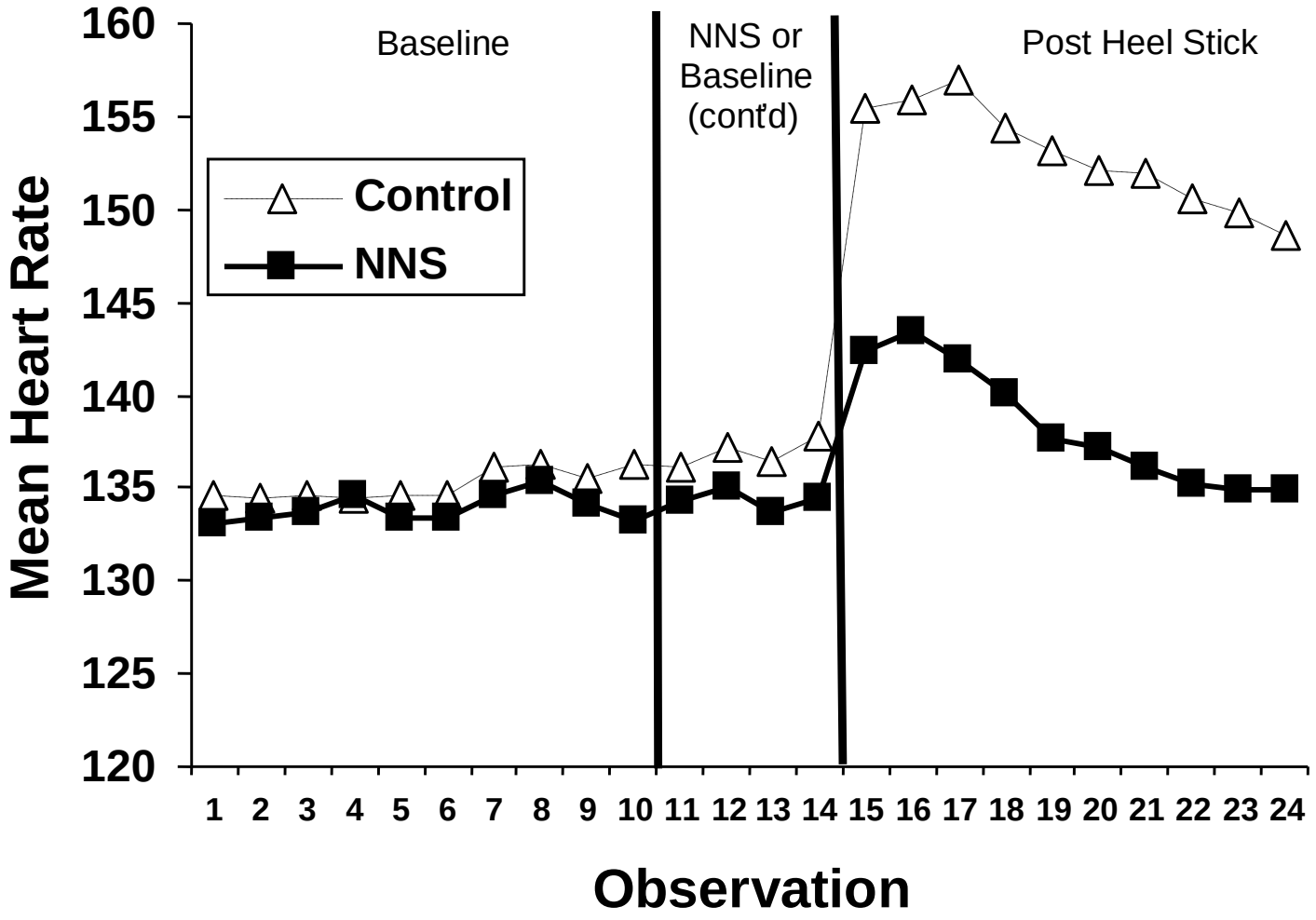

Figure 4-17. Mean heart rate across control and NNS conditions.

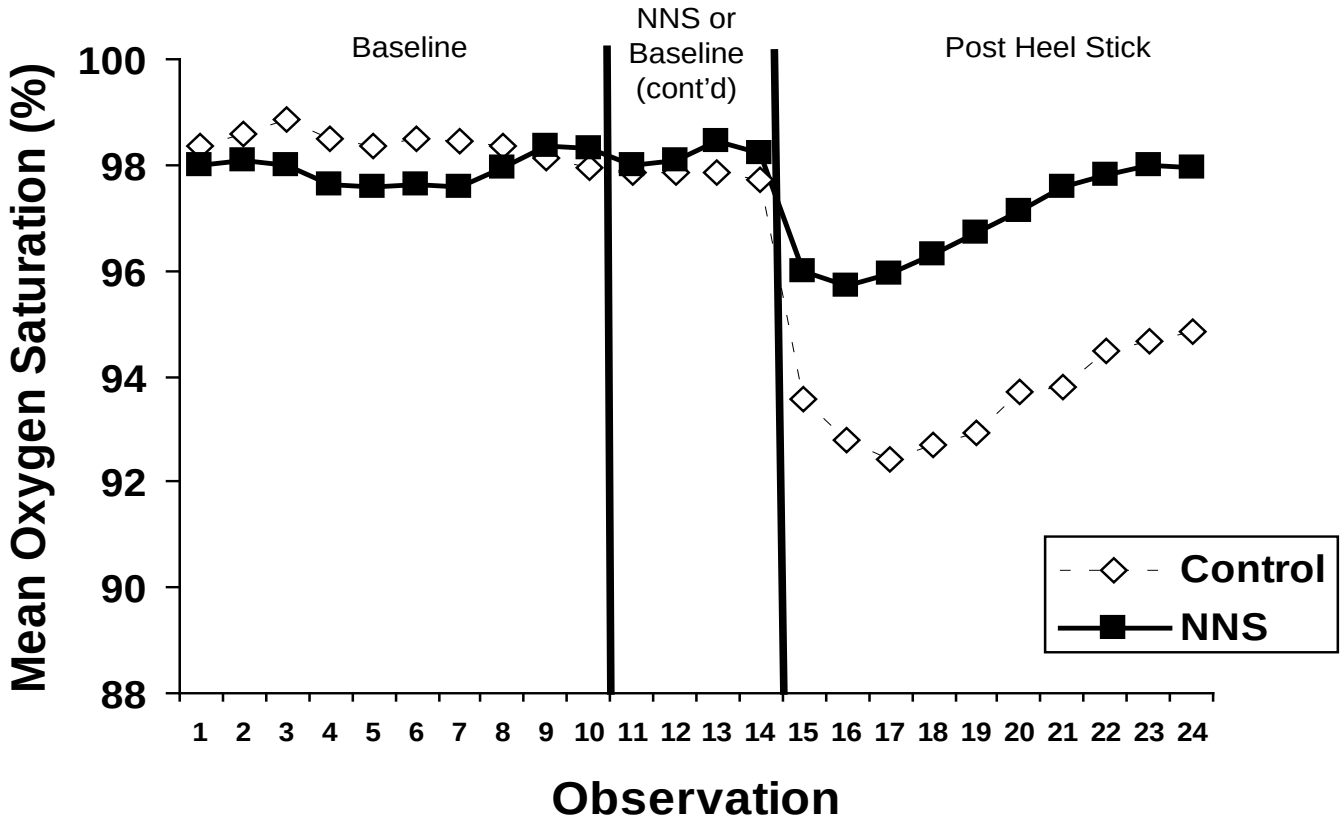

Figure 4-18. Mean oxygen saturation levels across control and NNS conditions.

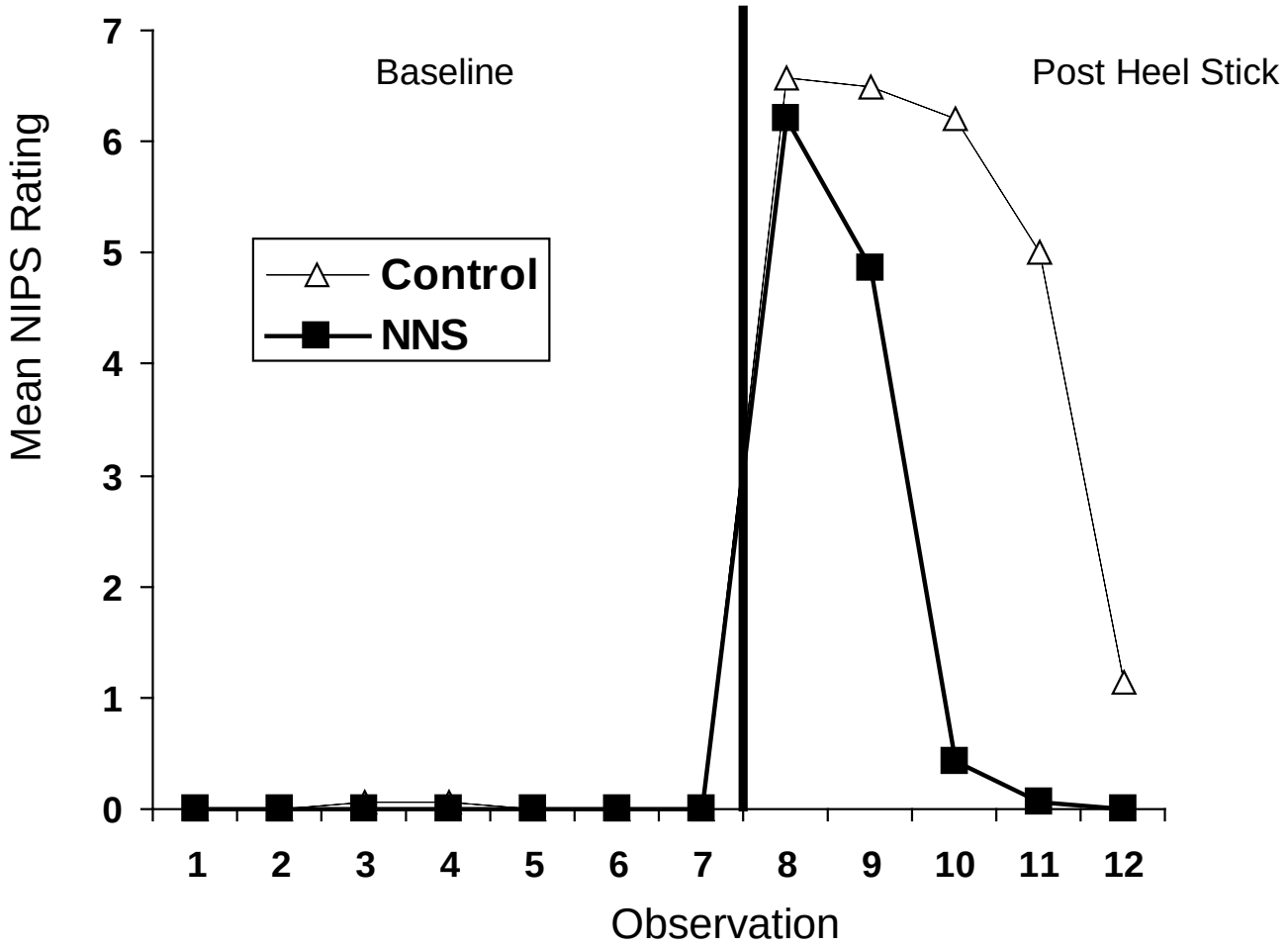

Figure 4-19. Mean NIP ratings across control and NNS conditions.

Table 4-21. Characteristics of Race

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Caucasian	4	28.6	28.6	28.6
	Black	5	35.7	35.7	64.3
	Hispanic	4	28.6	28.6	92.9
	Asian	1	7.1	7.1	100.0
	Total	14	100.0	100.0	

Table 4-22. Characteristics of Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	9	64.3	64.3	64.3
	Female	5	35.7	35.7	100.0
	Total	14	100.0	100.0	

Table 4-23. Characteristics of APGAR Scores at 1 minute

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	2	14.3	14.3	14.3
	3	2	14.3	14.3	28.6
	4	1	7.1	7.1	35.7
	6	2	14.3	14.3	50.0
	7	2	14.3	14.3	64.3
	8	5	35.7	35.7	100.0
	Total	14	100.0	100.0	

Table 4-24. Characteristics of APGAR Scores at 5 minutes

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	4	2	14.3	14.3	14.3
	6	2	14.3	14.3	28.6
	7	1	7.1	7.1	35.7
	8	5	35.7	35.7	71.4
	9	4	28.6	28.6	100.0
	Total	14	100.0	100.0	

Table 4-25. Characteristics of C Section Frequencies

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Yes	13	92.9	92.9	92.9
	No	1	7.1	7.1	100.0
	Total	14	100.0	100.0	

Table 4-26. Demographics of Birth Weight, APGAR Scores, and Ventilator Settings

		Birth weight GM	APGAR 1 min	APGAR 5 min	Fi02	IMV	PEEP
N	Valid	14	14	14	14	14	14
	Missing	0	0	0	0	0	0
	Mean	2351.86	5.57	7.36	27.14	23.79	4.64
	Median	2280.50	6.50	8.00	26.50	25.00	5.00
	Std. Deviation	805.353	2.652	1.737	5.362	6.179	.842
	Minimum	1769	1	4	21	8	3
	Maximum	3642	8	9	38	30	6

Table 4-27. Characteristics of Individual Birth Weights

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1769	1	7.1	7.1	7.1
	1359	1	7.1	7.1	14.3
	1604	1	7.1	7.1	21.4
	1814	1	7.1	7.1	28.6
	2166	1	7.1	7.1	35.7
	2240	1	7.1	7.1	42.9
	2275	1	7.1	7.1	50.0
	2286	1	7.1	7.1	57.1
	2535	1	7.1	7.1	64.3
	2612	1	7.1	7.1	71.4
	3030	1	7.1	7.1	78.6
	3191	1	7.1	7.1	85.7
	3403	1	7.1	7.1	92.9
	3642	1	7.1	7.1	100.0
	Total	14	100.0	100.0	

Table 4-28. Characteristics of FiO2 Frequencies

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	21	3	21.4	21.4	21.4
	23	1	7.1	7.1	28.6
	24	2	14.3	14.3	42.9
	25	1	7.1	7.1	50.0
	28	1	7.1	7.1	57.1
	29	2	14.3	14.3	71.4
	30	1	7.1	7.1	78.6
	32	1	7.1	7.1	85.7
	35	1	7.1	7.1	92.9
	38	1	7.1	7.1	100.0
	Total	14	100.0	100.0	

Table 4-29. Characteristics of IMV Frequencies

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	8	1	7.1	7.1	7.1
	18	1	7.1	7.1	14.3
	20	2	14.3	14.3	28.6
	21	1	7.1	7.1	35.7
	23	1	7.1	7.1	42.9
	25	3	21.4	21.4	64.3
	28	1	7.1	7.1	71.4
	30	4	28.6	28.6	100.0
	Total	14	100.0	100.0	

Table 4-30. Characteristics of PEEP Frequencies

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	3	1	7.1	7.1	7.1
	4	5	35.7	35.7	42.9
	5	6	42.9	42.9	85.7
	6	2	14.3	14.3	100.0
	Total	14	100.0	100.0	

Table 4-31. Mean Phase Differences in Infant Heart Rate and Oxygen Saturation in Experimental and Control Conditions

Phase	Heart Rate		Oxygen Saturation	
	Non-NNS (SD)	NNS (SD)	Non-NNS (SD)	NNS (SD)
Baseline (Phase1)	135.12 (9.29)	133.88 (7.65)	98.40 (2.16)	97.91 (2.59)
NNS/Baseline 2 (Phase 2)	136.88 (10.12)	134.38 (6.59)	97.82 (3.30)	98.18 (2.57)
Immediate Reaction (Phase 3)	155.14 (7.56)	141.09 (8.28)	92.89 (4.51)	96.13 (3.01)
Recovery (Phase 4)	150.64 (7.53)	135.64 (7.71)	94.30 (3.74)	97.69 (2.41)

Note. "Baseline": first ten resting measurements; "NNS/Baseline 2": Next four measurements (NNS was introduced in treatment condition, baseline was extended in non-NNS condition); "Immediate Reaction": first five measurements post-heel stick; "Recovery": last five measurements post-heel stick.

Table 4-32. Infant Heart Rate Recovery

					Recovery (HR Post Heel Stick)				
Infant	Condition	*M*	*SD*	95% CI Upper Limit	95%CI Lowest HR	HRCI	OBS	*z*	Δ
1	*Non-NNS*	*121.71*	*3.31*	*123.77*	*140*	*N/A*	*DNR*	*5.52*	
	NNS	121.29	4.66	124.18	122	122	5	.15	-5.36
2	*Non-NNS*	*134.43*	*2.62*	*136.05*	*148*	*N/A*	*DNR*	*5.17*	
	NNS	137.07	2.62	138.69	130	132	5	-2.70	-7.88
3	*Non-NNS*	*124.14*	*2.66*	*125.79*	*138*	*N/A*	*DNR*	*5.22*	
	NNS	126.43	2.21	127.80	130	130	DNR	1.62	-3.60
4	*Non-NNS*	*153.21*	*2.89*	*155.00*	*160*	*N/A*	*DNR*	*2.35*	
	NNS	144.07	2.34	145.52	152	152	DNR	3.39	1.04
5	*Non-NNS*	*133.14*	*2.68*	*134.81*	*140*	*N/A*	*DNR*	*2.55*	
	NNS	135.43	2.87	137.21	128	136	6	-2.58	-5.14
6	*Non-NNS*	*140.57*	*2.28*	*141.98*	*150*	*N/A*	*DNR*	*4.14*	
	NNS	142.21	3.60	144.44	140	144	3	-0.62	-4.76
7	*Non-NNS*	*129.86*	*2.66*	*131.50*	*156*	*N/A*	*DNR*	*9.84*	
	NNS	132.43	2.62	134.05	132	132	5	-0.16	-10.01
8	*Non-NNS*	*137.57*	*1.91*	*138.76*	*144*	*N/A*	*DNR*	*3.37*	
	NNS	141.86	3.08	143.77	138	140	1	-1.25	-4.62
9	*Non-NNS*	*130.00*	*3.68*	*132.28*	*140*	*N/A*	*DNR*	*2.72*	
	NNS	121.36	2.34	122.81	124	124	DNR	1.13	-1.59
10	*Non-NNS*	*134.86*	*1.29*	*135.66*	*146*	*N/A*	*DNR*	*8.62*	
	NNS	135.21	2.22	136.59	136	136	7	0.35	-8.27

Table 4-32. Continued

					Recovery (HR Post Heel Stick)				
Infant	Condition	*M*	*SD*	95% CI Upper Limit	95%CI Lowest HR	HRCI	OBS	*z*	Δ
11	*Non-NNS*	*127.64*	*1.22*	*128.40*	*137*	*N/A*	*DNR*	*7.70*	
	NNS	132.86	1.29	133.66	132	132	7	-0.66	-8.36
12	*Non-NNS*	*145.64*	*2.10*	*146.94*	*154*	*N/A*	*DNR*	*3.98*	
	NNS	140.57	2.41	142.06	142	142	DNR	0.59	-3.39
13	*Non-NNS*	*152.00*	*3.33*	*154.06*	*160*	*N/A*	*DNR*	*2.40*	
	NNS	134.57	1.95	135.78	134	134	9	-0.29	-2.70
14	*Non-NNS*	*133.93*	*2.79*	*135.66*	*146*	*N/A*	*DNR*	*4.33*	
	NNS	130.93	2.79	132.66	132	132	6	0.38	-3.95

Note. *M* = Mean heart rate (HR) for fourteen observation sessions prior to heel stick; *OBS* = Number of observations post-heel stick until heart rate was inside upper limit of 95% confidence interval; *HRCI* = value of first occurrence of infant recovery heart rate within 95% confidence interval for baseline mean; *LOWEST HR* = Lowest recorded heart rate during ten post-heel stick recovery observations. *DNR* = Heart rate did not recover to a value within 95% confidence interval of baseline heart rate during ten post- heel stick observations (scheduled 30 seconds apart). *z* = z-score for lowest heart rate post-heel stick referenced against baseline mean and standard deviation. Δ = change in *z*-score for lowest heart rate post-heel stick from control condition to NNS condition. Change is measured in standard deviation units. Negative sign indicates change in therapeutic direction.

Table 4-33. Infant Oxygen Saturation Recovery

					Recovery (HR Post Heel Stick)				
Infant	Condition	*M*	*SD*	95% CI Lower Limit	Highest OX	OXCI	OBS	*z*	Δ
1	*Non-NNS*	*98.90*	*0.74*	*98.44*	*98*	*N/A*	*DNR*	*-1.22*	
	NNS	99.60	0.52	99.28	99	N/A	DNR	-1.16	0.06
2	*Non-NNS*	*98.50*	*0.53*	*98.17*	*96*	*N/A*	*DNR*	*-4.74*	
	NNS	98.60	0.52	98.28	99	99	7	0.77	5.52
3	*Non-NNS*	*99.60*	*0.52*	*99.28*	*97*	*N/A*	*DNR*	*-5.03*	
	NNS	99.70	0.48	99.40	99	N/A	DNR	-1.45	3.59
4	*Non-NNS*	*100.00*	*0.00*	*100.00*	*98*	*N/A*	*DNR*	*N/A*	
	NNS	99.10	0.57	98.75	98	N/A	DNR	-1.94	N/A
5	*Non-NNS*	*92.20*	*2.39*	*90.72*	*86*	*N/A*	*DNR*	*-2.59*	
	NNS	90.40	2.07	89.12	90	92	5	0.77	3.36
6	*Non-NNS*	*99.50*	*0.53*	*99.17*	*96*	*N/A*	*DNR*	*-6.64*	
	NNS	98.60	0.52	98.28	99	100	3	2.71	9.35
7	*Non-NNS*	*99.40*	*0.52*	*99.08*	*95*	*N/A*	*DNR*	*-2.71*	
	NNS	95.80	0.63	95.41	98	96	4	3.48	6.19
8	*Non-NNS*	*99.80*	*0.42*	*99.54*	*94*	*N/A*	*DNR*	*-1.90*	
	NNS	99.50	0.53	99.17	100	100	8	0.95	2.85
9	*Non-NNS*	*98.60*	*0.52*	*98.28*	*94*	*N/A*	*DNR*	*-8.91*	
	NNS	98.70	0.48	98.40	99	100	4	2.69	11.60
10	*Non-NNS*	*97.50*	*0.53*	*97.17*	*94*	*N/A*	*DNR*	*-664*	
	NNS	97.70	0.48	97.40	98	99	3	2.69	9.33

Table 4-33. Continued

					Recovery (HR Post Heel Stick)				
Infant	Condition	*M*	*SD*	95% CI Lower Limit	Highest OX	OXCI	OBS	*z*	Δ
11	*Non-NNS*	*9550*	*0.85*	*94.97*	*94*	*N/A*	*DNR*	*-1.77*	
	NNS	95.10	0.74	94.64	95	96	3	1.22	2.98
12	*Non-NNS*	*99.80*	*0.42*	*99.54*	*98*	*N/A*	*DNR*	*-4.27*	
	NNS	99.70	0.48	99.40	99	N/A	DNR	-1.45	2.82
13	*Non-NNS*	*98.30*	*0.48*	*98.00*	*94*	*N/A*	*DNR*	*-8.90*	
	NNS	98.60	0.52	98.28	98	N/A	DNR	-1.16	7.74
14	*Non-NNS*	*100.00*	*0.00*	*100.00*	*99*	*N/A*	*DNR*	*N/A*	
	NNS	99.60	0.52	99.28	100	100	8	0.77	N/A

Note. *M* = Mean oxygen saturation level for fourteen observation sessions prior to heel stick; *OBS* = number of observations post-heel stick until oxygen saturation value was inside lower limit of 95% confidence interval; *OXCI* = oxygen saturation level when first within lower limit of 95% confidence interval; *HIGHEST OX* = Highest oxygen saturation level during ten post-heel stick recovery observations. *DNR* = Oxygen saturation level did not recover to a value within upper limit of 95% confidence interval of baseline; *z* = z-score for highest post heel stick oxygen saturation level referenced against baseline data; Δ = change in z-score for highest oxygen saturation level post heel-stick from control condition to NNS condition. Change is measured in standard deviation units. Positive value indicates change in therapeutic direction.

CHAPTER 5
DISCUSSION

Summary

The purpose of this study was to determine the effect of nonnutritive sucking (NNS) combined with sucrose-induced analgesia on heart rate, oxygen saturation, and pain behaviors (measured by the Neonatal Infant Pain Scale) in intubated infants between the ages of 32 weeks gestation to less than or equal to 42 weeks gestation. In order to determine the effect of NNS combined with sucrose-induced analgesia (treatment condition) on the dependent variables (heart rate, oxygen saturation, and pain behaviors), three specific aims were identified.

The first specific aim one was to determine the effect of NNS and sucrose-induced analgesia (treatment condition) on heart rate in intubated infants during a painful event (heel stick). It was determined as hypothesized that infants had lower mean heart rates in the NNS condition with sucrose (treatment condition) during a heel stick than those infants not offered NNS with sucrose (control condition).

The second specific aim was to determine the effect of NNS and sucrose-induced analgesia (treatment condition) on oxygen saturation in intubated infants during a painful event (heel stick). It was determined as hypothesized that infants had higher mean oxygen saturations in the NNS condition with sucrose (treatment condition) as measured by noninvasive pulse oximetry during a heel stick than those infants not offered NNS with sucrose (control condition).

The third specific aim was to determine the NIPS scores in the NNS condition with sucrose (treatment condition) in intubated infants during a painful event (heel stick). It was determined as hypothesized that infants had lower NIPS scores in the NNS condition with sucrose (treatment condition) during a heel stick than those infants not offered NNS with sucrose (control condition).

In the treatment condition the infants were offered NNS with sucrose and in the control condition were not. Heart rate and oxygen saturation were measured in 30-second intervals during a 5-minute baseline period, a heel stick, and a 5-minute follow-up period. Pain behaviors were measured in one minute intervals. In this study all heel sticks elicited a response even though different RNs performed the heel stick.

All dependent variables returned to baseline during or after the 5-minute follow-up period. However, the rate at which the variables stabilized was greater in the treatment condition as compared to the control. A visible depiction of the return to baseline of mean heart rates, oxygen saturations, and NIPS ratings in the control and treatment condition is illustrated in Figure 4-15, 4-16, ad 4-17. An explanation suggested for the faster rate of return to baseline is the treatment of NNS with sucrose-induced analgesia.

Comparable studies of infants not receiving oral or nasogastric nutrition, and examining ventilator data is unique in concept and study completion. For example, previous studies have been conducted with infants examining nonnutritive sucking (with or without sucrose) describing stability, or the pain response (Gibbens, et al., 2002; Pinelli, Symington, & Ciliska (2002). Many of those studies involve infants with NNS before or while tube/bottle feeding (DiPietro, 1994; Gill, 1992, McCain, 1995). However, those infants were not intubated and on mechanical ventilation.

Stevens and Ohlsson (2004) studied sucrose administered by oral syringe, nasogastric tube, or pacifier for analgesia in newborn infants undergoing heel sticks or venepunctures. Whether or not the infants were intubated on mechanical ventilation is unclear. Not all infants, either term or preterm, in the neonatal intensive care unit are intubated and on mechanical ventilation. Other studies (Gibbins, et. al., 2002; Stevens, et al., 2005) examined the effect of sucrose for

procedural pain in preterm and term infants. Although those studies did not exclude intubated infants as admission criteria, the ventilator settings (such as intermittent mechanical ventilation, continuous positive airway pressure, percentage of oxygenation) were not disclosed or even discussed. In this study the mean FiO2 was 27.14 (SD 5.3); mean IMV was 23.79 (SD = 6.18); mean PEEP was 4.64 (SD = 0.84). The demographics of ventilator settings in this study are depicted in Table 4-6. The characteristics of FiO2, IMV, and PEEP frequencies are depicted in Tables 4-8, 4-9, and 4-10.

Clearly the standard of care is for all infants to exist in a minimal pain, or pain free environment. Unfortunately, that has not been consistently achieved. There is no reason to think infants would not suffer from repeated painful procedures. This study clearly demonstrated that physiologic and behavioral changes occurred following a routine event.

Issues and Limitations

Despite the large census of the neonatal intensive care unit where the study was conducted (a daily census of greater than one hundred per day), infants who met the criteria were far fewer. A similar study examining physiologic and behavioral changes following a routine painful event with NNS sucrose-induced analgesia in the intubated neonatal population had not been done before at this facility, or reported in the literature.

There are several issues that need to be considered as mediating effects. These include gestational age and age in days, weight, infant acuity, and parental availability. The infants in this study not only had to be sick enough to require intubation and mechanical ventilation, but also functional enough to respond to stimuli and able to suck. Sucking behavior has been documented prior to birth as early as 18 weeks gestation (Wirson, 1965). Consistent sucking has been documented by 32 weeks gestation (Medoff-Cooper, Verklan, & Carlson, 1993).

Gestational age and age in days could therefore, alter the results of the study if the infant was too young. All infants in this study were at least 32 weeks gestational age. The mean gestational age was 35.14 (SD = 2.85) with a mean age in days of 4.79 (SD = 5.58; Range: 19). The demographics of gestational age and age in days at point of study are depicted in Table 3-1.

Another issue in regard to age is accumulated exposure to painful stimuli. The longer the infant remains hospitalized, particularly in the intensive care unit, theoretically the more painful events would be experienced. Frequency of painful exposures may alter the results, and thus present an issue. To avoid this in the study, a 30 minute uneventful period for the infant was required prior to the heel stick.

In addition to age, birth weight was a factor that mediated effect. Characteristics of individual birth weights are listed in Table 4-7. The mean birth weight in grams was 2351.86 (SD = 805.35). Demographics for birth weight are listed in Table 4-6. As noted earlier, there was a relatively strong correlation between birth weight (in grams) and the size of the change effect reported for both heart rate and oxygen saturation (see Tables 4-12 and 4-13). For heart rate, the value of delta is the z-score difference for lowest achieved heart rate in an infant across NNS and non-NNS conditions. Thus, a large negative delta value indicated a large standardized difference in heart rate recovery in the therapeutic direction. The higher birth weights were associated with greater therapeutic effect (i.e., lower heart rates relative to baseline in the NNS condition). Infant number 7 was the heaviest in the study (3642 grams) and had the largest negative delta value (-10.01). Birth weight correlated $r(12) = -0.62$, $p = 0.17$ with the delta value for heart rate recovery, meaning that higher birth weights were associated with greater therapeutic effect (i.e., lower heart rates relative to baseline in the NNS condition), but was not

statistically significant. The effect was not as large for oxygen saturation, and the result was not statistically significant, $r(12) = .27$, *ns*.

In addition to age, weight, and infant acuity, parental availability was also an issue. Many parents were not available for obtainment of consent, and therefore the infants could not be included in the study. Reasons for lack of parent availability included the recovering physical condition of the mother limiting her ability to consent. For example, a limitation was if the mother had just undergone a cesarean section and was not able to cognitively consent. The lack of parental presence was primarily the lack of the father's presence. The lack of parental availability was a limitation. It is feasible that some subjects could have been missed. Despite an almost daily review of existing potential subjects by the researcher, the time period for data collection of the 14 subjects was almost six months.

A limitation of this study was the routine and medically required heel sticks needed for measurement of the painful event. Heel sticks are often routine, but not necessarily frequent. With the possibility of arterial or umbilical lines in the intensive care unit, the frequency of drawing blood needed for laboratory measurement (such as for glucose values) from heel sticks was reduced or eliminated. The design of this study required the infants to serve as their own control, and thus required 2 separate heel sticks (one for the treatment and one for the control condition). If the infant did not require a heel stick for blood collection, or another method was chosen (such as by venipuncture, arterial stick, or umbilical line stick), the heel stick was not performed.

Another limitation of this study was during data collection the second observer collected data on the NIPS scores only and not heart rate or oxygen saturation. The primary researcher collected data on the NIPS scores, heart rate, and oxygen saturation. As a result there was no

inter-rater reliability for heart rate and oxygen saturation, only the NIPS scores. This could have affected the findings.

During the data collection process no videotaping of the subjects was allowed in the neonatal intensive care unit due to the increased lighting and noise. Continuous hard copy tracings of the heart rate and oxygen saturation were also not available. Videotaping and hard copy tracings are both measures that could have provided visual documentation. Lack of both presented a limitation to the study and were not anticipated during the planning.

Application

Painful procedures continue to exist in the hospital setting. Pain assessment is essential for nursing practice, but the measurement of pain in the nonverbal population remains difficult. The nonverbal intubated infant is not able to verbally state the presence of pain, and physiologic indicators such as vital signs are often unreliable. The participation of nurses in pain management is crucial to achieve positive health outcomes for infants who are positioned to experience repetitive or severe pain.

Nurse researchers have a duty to find nursing interventions that will work and to validate their use at the bedside, especially for patients who cannot advocate for themselves (American Academy of Pediatrics, 2000). Nurses are best positioned to assess, treat, and prevent pain in the hospitalized patient because they are nearest the patient. One frequently studied intervention nurses can employ to alleviate infant pain is nonnutritive sucking (NNS).

Attention to comfort is a foundational element of nursing (Watson, 1979). Ethically, there is an obligation for nurses to look for an expression of pain and to alleviate pain in those who cannot advocate for themselves (Beauchamp & Childress, 2008). This applies to an intubated newborn who cannot verbalize pain through a cry. This also applies to those unable to communicate pain regardless of age, such as those with dementia, or altered mental status. This

disparity in treatment between those who are able to verbalize pain (those not intubated or with verbal cognition) and those who are not continues today (Gibbins et al., 2002).

Ethical principles can serve as guides in the treatment of pain. Two bioethical considerations, nonmaleficence and beneficence, and the concept of caring, were used to guide this research. Conflicts regarding the need to perform necessary procedures that cause harmful pain and the medical benefits continue. Given that infants are persons and entitled to moral regard, an understanding of the moral principles that guide medical care is important in this vulnerable population. Ethical principles can serve as guides in the treatment of pain. This study demonstrated respect for the principles of nonmaleficence, beneficence and caring with infants who were not able to seek relief.

Recommendations

To increase generalizability to the neonatal population, a recommendation for future studies would be to consider examining infants with similar descriptive conditions such as APGAR scores and mode of delivery. The APGAR score was developed in 1952 by anesthesiologist Virginia Apgar and measures 5 factors (Activity, Pulse, Grimace, Appearance, Respiration) at 1 and 5 minutes post delivery. Each factor is scored on a scale of 0 to 2, with 2 being the best. The factors are added together for a score of 0 to 10, with 10 being the best possible (Apgar, 1952). In this study, 8 was the most frequent APGAR score at 1 minute (35.7%) and 5 minutes (35.7%). See Tables 4-3 and 4-4.

Another study could examine infants who were products of the same type of delivery. In this study, infants were born mostly by c-sections rather than vaginal deliveries. The frequency of c-sections (92.9%) was great in this study as compared to vaginal births (7.1%). See Table 4-5. Besides types of delivery, events that occurred during delivery could be examined. For

example, for future study infants who were products of epidurals receiving narcotics, or other anesthetic agents could be examined.

A recommendation for a future study would be obtainment of continuous hard copy printouts of the heart rate and oxygen saturations. Also, data collection by videotaping the subjects would increase inter-rater reliability for the NIPS scores and documentation of the behaviors.

Another recommendation would be for longer observation periods beyond the five-minute post heel stick period. Longitudinal data would be helpful in determining when complete and sustained return to baseline occurred. Although data were collected in this study for five minutes post heel stick, complete and sustained return to baseline had not occurred for every subject. Many studies observed behavior for a five-minute period (Gill, 1992; DiPietro, 1994). McCain in 1995 observed behavior of the experimental group with NNS for ten minutes.

Other studies reviewed lacked long-term outcomes (Pinelli, 2003). Long-term outcomes such as oral aversion, or the effect of NNS on breastfeeding could be explored. In addition, none of the subjects were followed after discharge from the hospital to measure outcomes (Pinelli, 2003).

Additional research to examine and moderate physiologic and pain responses in the intubated infant is needed. Intubated infants are already physiologically compromised, needing ventilator assistance either in the form of increased amounts of oxygen, mechanical breathes, or airway pressure. Specific interventions, such as NNS with sucrose described in this study, need to be further explored to decrease the stress and pain associated with routine procedures in the neonatal population. Other interventions include altering the environmental surroundings of light, sound, temperature, and touch. While conducting this study a notable difference in

behavior occurred when the infants were in the treatment condition of nonnutritive sucking and sucrose-induced analgesia in comparison to the control.

In addition, developmental outcomes related to procedural pain and stress need to be further explored. Completion of infantile milestones, such as recognition of familiar sound, could be assessed. The quality of the response to pain could be gauged related to stress intensity.

In previous studies nonnutritive sucking-induced analgesia with sucrose has been shown to decrease physiologic and behavioral pain responses. Yet, in practice it is offered less to intubated infants. This is possibly due to a lack of knowledge, experience or workload. Also, the addition of the pacifier with the endotracheal tube is unfamiliar. Increased education of nurses regarding neonatal pain assessment, intervention, and response is needed.

In summary, intubated critically ill infants are unable to vocalize a pain response in the form of a cry due to the blocking of the vocal chords by the endotracheal tube. Pain assessment in this neonatal population is thereby difficult due to the inability of the infants to self-report their pain with silent cries of distress. This study included the physiologic measures of heart rate and oxygen saturation, plus pain behaviors as measured by the Neonatal Infant Pain Scale. This study found that the infants had lower mean heart rates, higher mean oxygen saturations, and lower NIPS scores in the NNS condition with sucrose (treatment condition) during a heel stick than those infants not offered NNS with sucrose (control condition). There was a statistically significant interaction effect in the hypothesized direction for hear rate and oxygen saturation, and latency to recovery times were shorter. While pain continues to be a common part of the hospital experience, in this study nonnutritive sucking-induced analgesia with sucrose was effective in positively altering heart rate, oxygen saturation, and pain behavior.

APPENDIX A
NEONATAL INFANT PAIN SCALE (NIPS)

NNS and Sucrose-Induced Analgesia Study											
	Date	Diagnosis	Race	Sex	GA	Age in Days	Heart Rate	O2 Sats %	NIPS	Comments	
STAMP											
						1 min					
						2 min					
						3 min					
Notes						4 min					
						5 min					
						NNS					
						1 min					
						2 min					
						STICK					
						1 min					
						2 min					
						3 min					
						4 min					
						5 min					
Legend											
	Race	Sex									
	a=Caucasi	M=male									
	b=Black	F=female									
	c=Latin										
	d=Indian										
	e=Asian	f=other									

Table A-1 Neonatal Infant Pain Scale

Pain Assessment	Score
FACIAL EXPRESSION	
0 – Relaxed muscles	Restful face, neutral expression
1 – Grimace	Tight facial muscles; furrowed brow, chin, jaw, (negative facial expression – nose, mou
CRY	
0 – No Cry	Quiet, not crying
1 – Whimper	Mild moaning, intermittent
2 – Vigorous Cry	Loud scream; rising, shrill, continuous (Note: Silent cry may be scored if baby is intubated as evidenced by obvious mouth and facial movement.
BREATHING PATTERNS	
0 – Relaxed	Usual pattern for this infant
1 – Change in Breathing	Indrawing, irregular, faster than usual; gagging; breath holding
ARMS	
0 – Relaxed/Restrained	No muscular rigidity; occasional random movements of arms
1 – Flexed/Extended	Tense, straight arms; rigid and/or rapid extension, flexion
LEGS	
0 – Relaxed/Restrained	No muscular rigidity; occasional random leg movement
1 – Flexed/Extended	Tense, straight legs; rigid and/or rapid extension, flexion
STATE OF AROUSAL	
0 – Sleeping/Awake	Quiet, peaceful sleeping or alert random leg movement
1 – Fussy	Alert, restless, and thrashing

APPENDIX B
NEONATAL INFANT PAIN SCALE DATA COLLECTION SHEET

NEONATAL/INFANT PAIN SCALE	1 min	2 min	3 min	4 min	5 min	NNS	1 min	2 min		1 min	2 min	3 min	4 min	5 min
	SCORE	SCORE	SCORE	SCORE	SCORE	ONNS	SCORE	SCORE		SCORE	SCORE	SCORE	SCORE	SCORE
Facial Expression														
0=Relaxed Muscles														
1=Grimace														
Cry														
0=No Cry														
1= Whimper														
2=Silent Cry														
Breathing Patterns														
0=Relaxed														
1=Change in Breathing														
Arms														
0=Relaxed/Restrained														
1=Flexed/Extended														
Legs														
0=Relaxed/Restrained														
1=Flexed/Extended														
State of Arousal														

0=Sleeping/Awake														
1=Fussy														
	TOTAL	TOTAL	TOTAL	TOTAL	TOTAL		TOTAL	TOTAL		TOTAL	TOTAL	TOTAL	TOTAL	TOTAL

DATE

TIME

ID #

APPENDIX C
DATA COLLECTION SHEET

NNS and Sucrose-Induced Analgesia Study											
	Date	Diagnosis	Race	Sex	GA	Age in Days	Heart Rate	O2 Sats %	NIPS	Comments	
STAMP											
						1 min					
						2 min					
Notes						3 min					
						4 min					
						5 min					
						NNS					
						1 min					
						2 min					
						STICK					
						1 min					
						2 min					
						3 min					
						4 min					
Legend						5 min					
	Race	Sex									

	a=Caucasian	M=male									
	b=Black	F=female									
	c=Latin										
	d=Indian										
	e=Asian	f=other									

APPENDIX D
UNIVERSITY OF FLORIDA INFORMED CONSENT

UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

This is a research study of providing a pacifier (nonutritive sucking) and sweetner (sugar water) to your baby before, during, and after a routine heel stick ordered by a physician. Heart rate and oxygen saturation will be measured from the bedside monitors. The pain score will be determined by the Principle Investigator through observation of your baby.

Could participating in this study offer any direct benefits to you? Yes, as described on page 123.

Could participating cause you any discomforts or are there any risks to you? No, as described on page 122.

Please read this form which describes the study in some detail. I or one of my co-workers will also describe this study to you and answer all of your questions. Your participation is entirely voluntary. If you choose to participate you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 846-1494. If you decide to take part in this study, please sign this form on page **Error! Bookmark not defined.**.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study?

Nonnutritive Sucking and Sucrose-Induced Analgesia: Effect on Heart Rate, Oxygen Saturation, and Pain in Intubated Infants

3. Who do you call if you have questions about this research study?

Harriet D. Miller, PhD (c), ARNP; Principle Investigator; beeper: 407-980-5149, cell: 354-514-9100

4. Who is paying for this research study?

The sponsor of this study is no one

5. Why is this research study being done?

The purpose of this research study is to examine the effect of a pacifier (nonnutritive sucking) with sucrose (sweetner) on your baby's heart rate, oxygen saturation, and level of discomfort before, during, and after a routine, ordered heel stick. Two heel sticks will be observed, one with the pacifier and sweetner, and one without. The heel sticks are part of routine, standard care ordered by a physician for needed laboratory results. The heel sticks are not obtained only for the purpose of this research.

You are being asked to be in this research study because your infant in intubated and has routine heelsticks performed.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

Nothing different will be done as part of your normal clinical care.

7. What will be done only because you are in this research study?

Babies who are intubated are not usually offered a pacifier for comfort measures. If you give permission for your baby to be in this study, your baby will be offered a pacifier with sweetner before, during, and after a routine, ordered heel stick. Your baby's heart rate and oxygen saturation will be recorded by monitors that are already attached. Your baby's behavior will be recorded by the Principal Investigator. No heel sticks will be done for research purposes only, but rather are part of routine, standard care. Perhaps this information will help care givers in providing care.
If you have any questions now or at any time during the study, please contact Harriet Miller, PhD (c), ARNP in question 3 of this form.

8. How long will you be in this research study?

Each baby will be observed twice during a heel stick; once with a pacifier with sweetner, and once without a pacifier with sweetner. The time for observation for each heel stick will be 5 minutes before the heel stick, during the heel stick, and for 5 minutes after the heel stick. The heel sticks are part of routine, standard care ordered by a physician for needed laboratory results. The heel sticks are not obtained for the purposes of this research only.

9. How many people are expected to take part in this research study?

Up to 16 babies.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

10. What are the possible discomforts and risks from taking part in this research study?

There are no anticipated risks or possible discomforts to your baby for taking part in this study. The heel stick is used to provide standard care.

The researcher will take appropriate steps to protect any information collected. However, there is a slight risk that information about your baby could be revealed inappropriately or accidentally. Depending on the nature of the information such a release could upset or embarrass you, or possibly even affect your insurability or employability. Question 17 in this form discusses what information about your baby will be collected, used, protected, and shared.

Other possible risks to you may include: There are no anticipated risks to your baby for taking part in this study.
This study may include risks that are unknown at this time.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform Harriet Miller, PhD (c), ARNP (listed in question 3 of this consent form) or the person reviewing this consent with you before enrolling in this or any other research study or project.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call the name of PI or contact person listed on the front page of this form.

11a. What are the potential benefits to you for taking part in this research study ?

It is not known if your baby will benefit from this study. However, it is hoped that the use of a pacifier with sweetner will make your baby more comfortable.

11b. How could others possibly benefit from this study?

It is hoped that if pacifiers with sweetner help in painful situations, other babies will be provided with a sweetened pacifier to help alleviate distress in clinical practices.

11c. How could the researchers benefit from this study?

In general, presenting research results helps the career of a scientist. Therefore, Harriet Miller, PhD (c), ARNP may benefit if the results of this study are presented at scientific meetings or in scientific journals.

12. What other choices do you have if you do not want to be in this study?

You do not have to participate in this study and routine care will be provided for your infant.

13a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled.

If you decide to withdraw your consent to participate in this study for any reason, please contact Harriet Miller, PhD (c), ARNP at (cell) 352-514-9100, or (beeper)407-980-5149. They will tell you how to stop your participation safely.

If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office at (352) 846-1494.

13b. If you withdraw, can information about you still be used and/or collected?

No

13c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

If your baby's condition does not allow him or her to suck the pacifier.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

14. If you choose to take part in this research study, will it cost you anything?

No

15. Will you be paid for taking part in this study?

No

16. What if you are injured because of the study?

Please contact the Principal Investigator listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

17. How will your privacy and the confidentiality of your research records be protected?

Information collected about you will be stored in locked filing cabinets or in computers with security passwords. Only certain people have the legal right to review these research records, and they will protect the secrecy (confidentiality) of these records as much as the law allows. These people include the researchers for this study, certain University of Florida officials, the hospital or clinic (if any) involved in this research, and the Institutional Review Board (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research). Otherwise your research records will not be released without your permission unless required by law or a court order.

Researchers will take appropriate steps to protect any information they collect about you. However there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information such a release could upset or embarrass you, or possibly even affect your insurability or employability.

If the results of this research are published or presented at scientific meetings, your identity will not be disclosed.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternatives to being in the study; and how privacy will be protected:

Signature of Person Obtaining Consent Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your privacy will be protected. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

You voluntarily agree to participate in this study. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting Date

APPENDIX E
ORLANDO REGIONAL INFORMED CONSENT

Page 1 of 5

INFORMED CONSENT FORM

Nonnutritive Sucking and Sucrose-Induced Analgesia: Effect on Heart Rate, Oxygen Saturation, and Pain in Intubated Infants

Good medical care includes obtaining informed consent before beginning any experimental procedure. The patient or subject should be told the nature, purpose, alternative and possible side effects of the therapy. This experimental research study is being conducted by Harriet D. Miller, PhD (c), ARNP.

Principal Investigator(s): Harriet D. Miller, PhD (c), ARNP

Sub-Investigator(s): Charlene Krueger, PhD Robert Baum, PhD
Sandra Seymour, PhD Josephine Snider, EdD

Investigational Site(s): Winnie Palmer Hospital for Women and Babies

This consent form gives detailed information about the research study. Your doctor will discuss this information with you. Once you understand the study, you will be asked to sign this form if you wish to participate.

1. **PURPOSE OF RESEARCH STUDY:** The purpose of the research study is to examine the effect of a pacifier (nonnutritive sucking) with sucrose (sweetner) on your baby's heart rate, oxygen saturation, and level of discomfort before, during, and after a routine heel stick. Two heel sticks will be observed, one with the pacifier and sweetner, and one without. The heel sticks are part of routine, standard care ordered by a doctor for needed laboratory results. The heel sticks are not obtained only for the purpose of this research. Your baby is being asked to be in this research study because he or she is intubated and has routine heel sticks performed.

2. **EXPECTED DURATION:** Each baby will be observed twice during a heel stick; once with a pacifier with sweetner, and once without a pacifier with sweetner. The time for observation for each heel stick will be 5 minutes before the heel stick, during the heel stick, and for 5 minutes after the heel stick. The heel sticks are part of routine, standard care ordered by a physician for needed laboratory results. The heel sticks are not performed for the purposes of this research only.

3. **PROCEDURES TO BE FOLLOWED:** Information will be collected from the baby by the same researcher and transcribed onto data collection sheets. Information will include age, sex, race, diagnosis, weight, length of admission, and any surgical history.

Confidentiality will be maintained throughout. Following informed consent, and an order for a heelstick for a blood sample by the physician, the heart rate and oxygen saturations will be collected from printed recordings at the bedside monitor every 30 seconds before, during, and after the hee lstick. The Principle Investigator will record the Pain Score by observing the baby every minute before, during, and after the heel stick. A pacifier with a sweetner will be offered to the baby to see if the calming effects of the pacifier is helpful.

4. IDENTIFICATION OF EXPERIMENTAL PROCEDURES: Offering a pacifier with a sweetner to a baby on a breathing machine (ventilator) is not the usual standard of care.

5. POTENTIAL RISKS AND DISCOMFORTS: The treatment used in this program may cause some or none of the side effects listed. In addition, there is always the risk of very uncommon or unknown side effects occurring. The doctor may prescribe medication to keep the side effects under control. The use of medication could result in added costs. Neither Orlando Regional Healthcare System, Inc., nor the Investigator(s) are financially responsible for these costs).

6. POTENTIAL BENEFIT TO SUBJECT OR OTHERS:

It is hoped that you (your baby's) participation in this research study will lead to knowledge that may help others who have similar conditions.

7. ALTERNATIVE PROCEDURES OR TREATMENTS: There is no alternative treatment other than not offering a pacifier with sweetner during a heel stick.

8a. CONFIDENTIALITY OF RECORDS:

Your baby's study record will be kept in a confidential form at Winnie Palmer Hospital. The confidentiality of your baby's record is carefully guarded. No information by which your baby can be identified will be published in any publication. No information by which your baby can be identified will be released to any third party except as provided herein or as required by law. Representatives of the Food and Drug Administration (FDA) and the sponsor and their agents may have access to the study record, as well as your baby's medical record, which may contain your baby's name, and the FDA may be required by law in certain circumstances to release information in its possession.

8b. AUTHORIZATION TO USE OR DISCLOSE PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH:

The Federal Privacy Regulations explain how your baby's health information will be used and to whom it will be disclosed (given to) for this research study. You will be provided with a copy of the Notice of Privacy Practices, which describes the Orlando Regional Healthcare System,

Inc. privacy practices. Your baby's protected health information may be used or disclosed for research purposes.

The following protected health information will be collected during this study: Name, birth date, personal medical history, current and past medications, therapies, surgeries, procedures, information from current and past physical examinations.

<u>Who may Use or Disclose your Protected Health Information?</u>

The following individuals / organizations may use or disclose your baby's protected health information for this research study:

Study doctor and the study staff

Orlando Regional Healthcare Institutional Review Board

University of Florida Institutional Review Board

<u>To whom may your Protected Health Information be Disclosed?</u>

As part of the study, the study doctor and the study staff may disclose the results of study-related tests and procedures that may identify you to the following:

Orlando Regional Healthcare Institutional Review Board

Food and Drug Administration (FDA)

Office for Human Research Protection (OHRP)

In addition to the list of individuals and organizations to whom your Protected Health Information may be disclosed, others may receive the information that is not currently known. If information from your records is given to any of these people, they might give it to someone else. If this happens, the information will no longer be protected. Someone Orlando Regional Healthcare gives the information to is supposed to protect it, but Orlando Regional Healthcare cannot always keep that person from giving it to someone else. Your PHI may no longer be protected by the Federal Privacy Rule once it is disclosed by the study doctor to these other parties.

By agreeing to participate in this research study and signing this informed consent, you are authorizing Orlando Regional Healthcare System, Inc, Winnie Palmer Hospital for Women and Babies, and Harriet D. Miller, PhD (c), ARNP to use and disclose your protected health information for the purpose of research related to this study. Only the smallest amount of protected health information necessary will be used.

There is no expiration date for the use of your health information for this research study. It may be used until all follow-up procedures and all research/data collection has been completed. It may also be used

until the federal regulatory agency check that the data requirements have been met. Your baby's health information may be used in future additional re-checking of data accuracy (correctness). At the time that your baby's records no longer need to be checked, Orlando Regional Healthcare will destroy (shred) your baby's research records.

Additional information about confidentiality of and access to your baby's protected health information while your baby participates in this research study:

- If your doctor wishes to use your baby's identifiable information for any other reason than this research study, he/she must get your permission for that purpose.
- You may withdraw your permission to use your baby's protected health information by talking with your doctor or research staff and making a request in writing. Use and release of information that was already gathered may continue when necessary in checking and reporting important events (such as accounting for your withdrawal from the study, adverse events reported to the FDA to monitor safety of participants, or federal regulatory agency audits (reviews).
- If you withdraw your permission to use your baby's health information, neither Orlando Regional Healthcare System, Inc. nor Harriet D. Miller, PhD (c), ARNP, will release information collected after your withdrawal to any other third party.
- If you withdraw your permission to use and release your baby's health information, you will no longer be able to participate in the study. However, if you decide to withdraw from the study, you will not be penalized or lose benefits to which you are otherwise entitled.
- Your doctor may discuss other research projects with you if he/she thinks the other projects relate to your baby's condition. However, your baby's health information cannot be given to another doctor or sponsor for the reason of asking you to enroll your baby in another research study.

You have the right to inspect (look over) and obtain a copy of your baby's health information that is kept for research purposes for as long as this information is held by your study doctor or Orlando Regional Healthcare System, Inc. However, to ensure the integrity of the research, you will not be able to review some of the study information until the end of the study.

9. **COMPENSATION:** There is no financial compensation for participation in this study.

10. **RESEARCH RELATED INJURY:** In the event that injury occurs as a result of this research, treatment will be available. However, you will not be reimbursed by Orlando Regional Healthcare System Inc. or the investigator for these costs. For more information about your baby's rights as a research subject, you may call the Institutional

Review Board Office, at (321) 841-5895. The doctor involved in your baby's care is available to answer any questions you have concerning participation in this research program. You are free to ask the investigator Harriet D. Miller, PhD (c), ARNP at Ph # (321) 841-8332 any questions concerning this research study that you have now or in the future.

11. VOLUNTARY PARTICIPATION: You are free to refuse or stop participation in this research study at any time without penalty or loss of benefits to which you are otherwise entitled. You are free to seek care from a physician of your choice at any time. If you do not take part in or withdraw from the study, your baby may continue to receive care for which you will be financially responsible.

12. ADDITIONAL RISKS: Participation in this study may involve risks to the subject which are currently unforeseeable.

13. INVOLUNTARY TERMINATION: Your baby's participation in this study may be stopped by the investigator under the following circumstances: not able to suck on pacifier.

14. PROCEDURES FOR WITHDRAWAL: When your baby completes the study or should you for any reason stop your baby's participation in the study, your baby will not be followed after the completion of or withdrawal from the study.

15. NEW FINDINGS: Significant new findings developed during the course of the research which may relate to your willingness to continue your baby's participation will be provided to you.

16. NUMBER OF PARTICIPANTS: The approximate number of babies involved in the study at this site will be 14.

17. ADDITIONAL COST: No additional cost to the baby will result from participation in the research study.

18. FINANCIAL DISCLOSURE: This clinical research study is paid for by the investigator.

Nonnutritive Sucking and Sucrose-Induced Analgesia: Effect on Heart Rate,

Oxygen Saturation, and Pain in Intubated Infants

19. SIGNATURES: My signature indicates that I consent and authorize _____ _____ and whomever he (she) may designate as his (her) assistant(s) including Orlando Regional Healthcare System, Inc., its employees and its agents to perform upon _____ (name of patient or "myself") the research described above. If any unforeseen conditions arise in the course of the research calling in the Doctor's judgment for procedures in addition to or different from those planned, I (we) further request and authorize the Doctor to do whatever he (she) deems advisable.

I AM MAKING A DECISION WHETHER OR NOT TO PARTICIPATE (OR HAVE MY CHILD PARTICIPATE) IN THIS STUDY. I HAVE READ, OR HAD READ TO ME IN A LANGUAGE THAT I UNDERSTAND, ALL OF THE ABOVE, ASKED QUESTIONS, RECEIVED ANSWERS CONCERNING AREAS I DID NOT UNDERSTAND, AND WILLINGLY GIVE MY CONSENT TO PARTICIPATE IN THIS STUDY. UPON SIGNING THIS FORM I WILL BE GIVEN A COPY.

_____ _____
Signature of Subject, Parent or Legal Representative Date

_____ _____
Signature of Witness Date

I have explained and defined in detail the research procedure in which the patient has consented to participate.

_____ _____
Investigator's Signature Date

Translator/Interpreter

Name_____
Phone#_____

Address_____
_____

For Signatures by Parent, Guardian, or Legal Representative, please describe the authority to act on behalf of the participant below:

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BIOGRAPHICAL SKETCH

Harriet Miller was born in Spokane, Washington. She received her Bachelor of Science in Nursing from the University of Florida, and was inducted into the Alpha Theta Chapter of Sigma Theta Tau in 1982. She obtained a Master's of Science in Nursing in Critical Care as a Clinical Nurse Specialist, and later a post-master's degree as an Advanced Registered Nurse Practitioner in Pediatric Health from the University of Florida. She has worked in clinical and managerial roles in the acute and critical care areas of Pediatric and Neonatal Intensive Care. Currently she is a doctoral candidate in Nursing with a minor in Bioethics at the University of Florida. Her past research has focused primarily on infant pain in the critical care setting. Currently she is the Clinical Nurse Specialist in Neonatal Services at Winnie Palmer Hospital for Women and Babies in Orlando, Florida.