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The Effect of Music-Reinforced Nonnutritive Sucking on State of Preterm, Low Birthweight Infants Experiencing Heelstick

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This study examined the physiologic and behavioral effects of music-reinforced nonnutritive sucking (NNS) for preterm, low birthweight (LBW) infants experiencing heelstick. Subjects were 60 infants, age 32 to 37 weeks post conceptional age in a neonatal intensive care unit. Infants were randomly assigned to one of three treatment groups: pacifier-activated lullaby (PAL), pacifier-only, and no-contact. Experimental infants were provided the Sondrex® PAL System®, which plays music contingent on infant sucking. Pacifier-only infants did not receive music reinforcement for sucking, and no-contact infants were not provided a pacifier or music at any point during the procedure. Stress level and behavior state were assessed continuously and heart, respiratory, and oxygen saturation rates were recorded at 15-second intervals for all infants. Most physiologic data results were inconclusive. However, analysis of behavior state and stress level revealed the following significant differences for the PAL and pacifier-only groups compared to the no-contact group, all of which were greatest between the PAL and no-contact groups: lower during-heelstick behavior state means, less time in undesirable behavior states, lower during- and post-heelstick stress level means, and smaller behavior state and stress level differences between intervals. In addition, the PAL group had a significantly lower pre-heelstick stress level mean than the no-contact group. Behavior state and stress level were also more stable across time for the PAL group than the other groups, and patterns

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This manuscript is based on the author's dissertation completed at the Florida State University (Whipple, 2004). The full dissertation includes gender analysis as well as additional pre, during, and postprocedure interval divisions with similar results that may provide some guidance for designing future studies.

of changes in oxygen saturation, behavior state, and stress level indicate that music-reinforced NNS may facilitate return to homeostasis.

Review of Literature

Neonatal Intensive Care

Preterm infants are known to be at high-risk for manifestation of sensory, motor, and cognitive deficits later in childhood, as they exhibit greater incidence of all disabilities than the general population of fullterm infants (Parmelee, Beckwith, Cohen, & Sigman, 1983), whether directly caused by premature birth or related to inappropriate stimulation during the newborn period (Duffy, Als, & McAnulty, 1990). The first goal of neonatal intensive care is infant survival. Consequently, medical intervention is the primary initial focus. As a result, the environment of the Neonatal Intensive Care Unit (NICU) may interfere with the maturation and organization of the infant's central nervous system and fail to meet the infant's developmental needs (White-Traut, Nelson, Burns, & Cunningham, 1994). Infant neurologic development is cephalocaudal and proximodistal, manifested in initially more fully developed receptors of tactile and vestibular stimulation than those of hearing and vision (Owens, 2001). The nature of the NICU can overstimulate the lesser developed distance receptors through continual presence of bright lights and noxious sounds, and neglect the more mature tactile and vestibular pathways (White-Traut et al., 1994). Also potentially disrupting to the infant's growth and development are the necessary caregiving and medical procedures (Duffy et al., 1990).

Barker and Rutter (1995) studied the pattern of invasive procedures performed from admission to discharge for 54 infants, 76% of which were born preterm, admitted consecutively to an NICU over a period of three months. A total of 3283 procedures were recorded, with 74% of those performed for infants born before 31 weeks gestation. The most procedures performed for a single infant numbered 488 for a female born at 23 weeks gestation. The most frequently performed procedure was blood collection via heelstick, accounting for 56% of the procedures. The next most commonly performed procedure was endotracheal suctioning (26%), followed by peripheral venous cannula insertion (8%). Other procedures performed were venous blood sample; intubation; intramuscular injection; insertion of venous long line, peripheral arterial line, and umbilical catheter; arterial stab; lumbar puncture; chest drainage; and suprapubic aspiration.

Investigations suggest that preterm neonates have increased sensitivity to pain and that acute painful stimuli lead to development of prolonged periods of increased pain sensitivity. In addition, acute physiologic changes caused by painful or stressful stimuli have been implicated as factors in the development or extension of intraventricular hemorrhage (IVH), and ischemic changes leading to periventricular leukomalacia (PVL), while therapeutic interventions that provide comfort or analgesia in preterm infants have been correlated with decreased incidence of severe IVH (Anand, 1998). Further, while infants may not consciously remember events, they may develop procedural memory that can lead to abnormal behavioral patterns or altered sensory processing in later life. Early damage can lead to prolonged structural and functional alterations in pain pathways that can last into adult life (Anand, 2000) and such changes can promote increased anxiety, altered pain sensitivity, stress disorders, and hyperactivity and attention disorders, leading to impaired social skills and patterns of self-destructive behavior (Anand & Scalzo, 2000).

Neonatal Pain Assessment

Because pain responses are multidimensional, it seems that pain measurement in preterm infants should also be multidimensional. Researchers generally evaluate pain responses using chemical, behavioral, and physiologic means (Dyke, 1993). While most infants display concordant reactions between behavioral and autonomic responses, some show opposite responses with one measure high and another measure low (Morison, Grunau, Oberlander & Whitfield, 2001). In term newborns, the pain stimulus response tends to mimic the stress response of adults, though there is insufficient research regarding chemical responses (e.g., alterations in salivary cortisol) in preterm infants (Dyke, 1993).

Behavioral responses. Regularly assessed behaviors include motor responses, facial expressions, crying, disruptions in state, and alterations in sleep-wake cycles (Dyke, 1993). For example, Grunau, Holsti, Whitfield, and Ling (2000) observed in very low birthweight (VLBW), preterm infants that changes in sleep/waking state, facial brow raising, finger splay, and leg extension, as well as the physiologic measure of heart rate (HR) were significantly related to experience of procedures that would be considered to cause distress (i.e., endotracheal suctioning, chest physiotherapy, diapering, and gavage feeding). Further, Johnston, Sherrard, et al. (1999) positively correlated cry duration with pain scores of preterm infants experiencing heelstick procedures.

Physiologic responses. Physiologic responses can include increased HR and blood pressure (BP), the presence of palmar sweating, increased intracranial pressure, varying transcutaneous oxygen tension ($TcPO_2$), increased respiratory rate (RR), decreased vagal tone, decreased oxygen saturation (SaO_2), and the presence of a galvanic skin response. For example, HR, RR, and SaO_2 of preterm infants experiencing routine painful procedures (i.e., injection, heelstick, squeezing of the heel to induce blood flow, and tape removal) and nonpainful procedures that could still induce stress in a high-risk infant (i.e., handling, temperature measurement, alcohol swabbing, patting, taping a tube, feeding, and pacifier insertion) have been measured to be significantly different between pre-, during-, and post-procedure intervals, with HR and RR significantly higher and SaO_2 significantly lower during painful procedures than during those considered to be nonpainful (Gonsalves & Mercer, 1993).

Measuring variability in physiologic variables is another, and possibly more effective, method of evaluating pain. Historically, studies have considered HR reactivity as a unidimensional measure that increases with a painful stimulus, typically increasing immediately following the noxious stimulus, and declining during the recovery period. Like all homeostatic functions, greater increases and decreases in HR are considered to indicate health and maturity, since organized patterns of physiologic measures can denote increased capacity of the infant to respond to changing environmental demands. Consequently, quantification of variability in HR patterns may provide a measure of changes in autonomic and CNS activity that reflect behavior responses of the infant (Dyke, 1993) and should be regarded as an index of reactivity rather than a specific measure of infant pain or stress.

The comparison of low and high frequencies is considered the preferred method for obtaining measures of HR variability (HRV), yet this method is complex and standard deviations instead can provide some HRV information (Oberlander & Saul, 2002).

Regardless, all physiologic indicators of pain and distress should be considered in light of normal parameters. Infant HR should be between 100 and 200 beats per minute or not greater than 20% over baseline. Changes in HR paired with irritability should also be monitored as should changes in HR that occur along with SaO_2 below 86%. Respiratory rate should not exceed 20 over baseline and episodes of apnea paired with bradycardia or oxygen desaturation are considered to be outside of normal parameters. Finally, SaO_2 of 86% or greater is within normal limits, though all gradual, consistent desaturation should be monitored (Burns, Cunningham, White-Traut, Silvestri, & Nelson, 1994).

Factors Influencing Neonatal Pain Responses

Several factors may influence physiologic pain responses, including behavior state (Oberlander, Grunau, Fitzgerald, & Whitfield, 2002; Oberlander & Saul, 2002), gestational age at birth and time of intervention (Johnston, Stevens, Yang, et al., 1996; Oberlander & Saul, 2002), and frequency and intensity of medical or caregiving procedures (Oberlander et al., 2002). Infants close to term age display smaller HR increases in response to invasive procedures than those born prematurely (Oberlander & Saul, 2002) and also demonstrate smaller HR increases even when studied at the same post conceptional age (PCA) (Johnston, Stevens, Yang, et al., 1996). It also seems that behavioral immaturity may be associated with greater frequency of invasive procedures, while birth factors are associated with physiologic immaturity (Johnston & Stevens, 1996). Based on behavioral responses to heelstick procedures, preterm infants who spend PCA weeks 28 through 32 in an NICU are less mature in pain responses than newborn premature infants born at 32 weeks. Further, based on observed changes across time, it appears that infants who experience frequent heelstick procedures may learn to anticipate the painful stimulus (Goubet, Clifton, & Shah, 2001). Also, the magnitude of behavioral and physiologic responses of term and preterm infants born as early as 28 weeks gestation to nursing and medical procedures tends to increase with rising level of procedural invasiveness, demonstrating that intensity of procedure may also influence infant pain responses (Porter, Wolf, & Miller, 1999). Also, some behavioral and physiologic pain responses may be more evident during painful procedures when infants have been handled not long before the procedure. Porter, Wolf, and Miller (1998) found that infants who were handled prior to a baseline period as if they were being prepared for a lumbar puncture procedure displayed higher mean HR, greater behavioral arousal, and more facial activity during a subsequent heelstick procedure than did the non-handled infants. In addition, Grunau et al. (2000) found facial brow raising to be significantly related to the number of invasive procedures an infant had experienced within the previous 24 hours.

Pharmacologic Neonatal Pain Management

Untreated pain in infants is associated with increased major morbidity and mortality (Anand, 1998, 2000; Menon, Anand, & McIntosh, 1998). Choice of pharmacologic intervention to manage pain in neonates is based largely on the type of pain. Antipyretic analgesics like acetaminophen (Tylenol®) may assist in managing inflammatory pain, though intravenous (IV) opiates tend to be the primary pharmacologic form of analgesia used with neonates (Menon et al., 1998). Sedatives including benzodiazipines and barbituates may also be used (Mainous, 1995).

Analgesics. While necessary, the use of analgesia during the first few days of life is complicated by prematurity and critical illnesses (van Lingen, Simons, Anderson, & Tibboel, 2002). Accuracy in dosing is challenging since many drugs are not recommended by the manufacturer or have not been tested for neonates and the toxic dose for some infants may be the desirable dose for others. In addition, the use of opioid analgesics (e.g., morphine & fentanyl) in neonates may present dangers such as negative cardiovascular effects and convulsions (Mainous, 1995). Further, use of pharmacologic pain management may inhibit some pain indicators, as behavioral and physiologic responses are more difficult to assess in the presence of mechanical ventilation, pharmacologic interventions, and physical restraints (Dyke, 1993). However, opiates have benefits such as promotion of stability, decreased incidence of advanced IVH in preterm infants receiving ventilator assistance, and better behavioral and cognitive outcomes at long-term follow-up (van Lingen et al., 2002).

Sedatives. Sedative agents can facilitate physiologic stability in the presence of less acutely painful stimuli or when opiates would produce adverse effects (Menon et al., 1998). However, sedatives also present dangers, such as dependence; possible increased risk of IVH; and gastric mucosa irritation, which is a challenge for premature infants already at risk for feeding intolerance. Further, sedation for relief of pain without analgesia is rarely acceptable; however, certain analgesics and sedatives are interactive and addictive and require close monitoring of infant respiration (Mainous, 1995).

Local anesthesia and topical treatment. Local anesthesia of skin and mucous membranes, such as with Eutectic Mixture of Local Anesthetic (EMLA), can be beneficial for infants experiencing invasive procedures (Menon et al., 1998), with diminished physiologic and behavioral responses during circumcision documented for infants who received EMLA compared to those who did not. Such treatment may also diminish pain responses during venipuncture, arterial puncture, and percutaneous venous catheter placement (Taddio, Ohlsson, Einarson, Stevens, & Koren, 1998). However, EMLA has not been shown to diminish heelstick pain (McIntosh, van Veen, & Brameyer, 1994; Taddio et al., 1998), likely because the components of the mixture cause vasoconstriction that reduce blood flow and lead to more painful squeezing of the heel to obtain adequate blood samples (McIntosh et al., 1994).

Role of Developmental Intervention

A variety of interventions for premature infants, often from opposing theoretical bases, yield similar results (Feldman & Eidelman, 1998), and the type of intervention may be less important than its influence in promoting homeostasis (Dieter & Emory, 1997). The NICU should not only assure survival but also support infant developmental progression (Blickman, Brown, Als, Lawhon, & Gibes, 1990) through environmental, caregiving, and pain reduction practices. Environmental adaptations include shielding from overhead lights and noise (Als & Duffy, 1989; Modrein-McCarthy, McCue, & Walker, 1997) and adjustment of ambient temperature (Modrein-McCarthy, McCue, & Walker, 1997). Since reduction of noxious stimuli can improve oxygenation of blood and thereby reduce need for supplemental oxygen and ventilator support, method and timing of all sensory input, including medical and caregiving procedures, must be considered (Blickman et al., 1990). Caregiving practices of staff and parents to reduce infant pain and stress responses can include positioning, sleep state regulation protection (Als & Duffy, 1989), soothing music or touch, containment or rocking, spring-loaded lances for heelsticks, analgesics during stressful procedures (Modrein-McCarthy et al., 1997), and nonnutritive sucking (NNS) (Als & Duffy, 1989; Modrein-McCarthy et al., 1997). Intervention should be tailored to the infant's autonomic, motor, and state behaviors, and stability should be monitored so that continual modifications to care may be made (Modrein-McCarthy et al., 1997).

The use of such adaptations has resulted in documentation of the following medical and neurodevelopmental benefits for premature, VLBW infants:

- earlier normalization of feeding behaviors;
- reduction in duration of mechanical ventilation and supplemental oxygen support (Als & Duffy, 1989; Als et al., 1986; Als et al., 1994; Blickman et al., 1990) and incidence of IVH, bronchopulmonary dysplasia (BPD), and pneumothorax (Als & Duffy, 1989; Als et al., 1994);
- increase in daily weight gain (Als et al., 1994) and decrease in length of hospitalization and related expenses; (Als et al., 1994; Als & Duffy, 1989); and
- better psychomotor, motor, verbal, memory, and cognition capabilities throughout childhood (Als et al., 1986; Als et al., 1994; Als & Gilkerson, 1997; Blickman et al., 1990).

Nonnutritive sucking. A form of neonatal intervention often incorporated into individualized caregiving is provision of NNS. The earliest components of sucking behaviors have been observed in the fetus beginning around 7 or 8 weeks PCA. Oral and gag reflexes first appear between 12 and 16 weeks and sucking appears by 24 weeks. Sucking and swallowing are present by 28 weeks, but are not fully coordinated until around 32 to 34 weeks PCA (Pinelli & Symington, 2003). The following benefits of NNS have been documented for preterm infants, regardless of the presence of painful stimuli:

- increased $TcPO_2$ (Shiao, Chang, Lannon, & Yarandi, 1997) and relationships in $TcPO_2$ levels among pre-sucking, sucking, and post-sucking intervals, indicating that NNS may facilitate optimal oxygenation (Burroughs, Asonye, Anderson-Shanklin, & Vidyasagar, 1978);
- decreased HR, suggesting that NNS reduces energy expenditure and possibly explaining why NNS has been shown to enhance preterm infant growth (Shiao et al., 1997; Woodson & Hamilton, 1988); and
- reduced length of hospitalization (Pinelli & Symington, 2000, 2003).

Nonpharmacologic Neonatal Pain Management

Sensory stimulation. Given the cumulative nature of stimulation and hypersensitivity of preterm infants, touch in the form of stroking during painful procedures can increase infant stress rather than serve as a soothing intervention. Beaver (1987) found that stroking the infant's leg during a heelstick procedure was more aversive to preterm infants than the painful procedure alone, as evidenced by a greater change in physiologic measures from the baseline period.

Yet music may be beneficial for preterm infants during noxious procedures. Burke, Walsh, Oehler, and Gingras (1995) reported results from four case studies of preterm infants with BPD undergoing suctioning, which has been shown to be a stress-producing intervention for neonates. For these infants, the presentation of music in the form of recorded intrauterine sounds blended with synthesized female voices for 15 minutes following suctioning resulted in reduced level of arousal compared to no intervention, and more time spent sleeping than without music or with vibrotactile stimulation. Also, Butt and Kisilevsky (2000) demonstrated that, in preterm infants older than 31 weeks PCA, the presentation of piano and a cappella voice recordings of a lullaby affected more rapid return of HR, behavioral state, and facial expressions of pain to baseline levels following heelstick procedures.

Nonnutritive sucking and sucrose. Field and Goldson (1984) investigated the effects of NNS on behavior state and cardiac responses of healthy term and preterm infants, and preterm infants in an NICU, all experiencing heelsticks. Regardless of gestational age and clinical stability, those infants who were given pacifiers spent significantly more time in alert and quiescent states and less time in fussing and crying states during and after heelsticks. Results suggested that NNS during heelstick procedures may diminish behavioral distress in all neonates regardless of gestational age. Similarly, Miller and Anderson (1994) discovered that infants receiving assisted mechanical ventilation cried significantly less, had lower HRs during IV catheter insertion, and had significantly smaller HR increases from baseline to post-cry when provided opportunities for NNS.

Another method of nonpharmacologic pain management for neonates is the use of sucrose with and without NNS. The calming and pain-relieving effects of sucrose are thought to be mediated by endogenous opioid pathways activated by sweet taste (Gibbins & Stevens, 2001). Stevens, Yamada, and Ohlsson (2003) completed a review of the use of orally administered sucrose as analgesia in hospitalized term and preterm neonates, finding that sucrose decreased HR, crying, facial activity, and pain scores in infants experiencing heelstick or venipuncture.

Opposite of sucrose, the analgesic effects of NNS are thought to be activated through nonopioid pathways by stimulation of orotactile and mechanoreceptor mechanisms. Because combining NNS and sucrose involves opioid and nonopioid pathways as well as orogustatory- and orotactile-induced analgesia, the combination offers the most potent nonpharmacologic intervention. This combination is still not sufficient for managing severe pain, but it can be incorporated with other pharmacologic and nonpharmacologic interventions to create multi-faceted pain-relieving strategies (Ramenghi, Evans, & Levene, 1999)

Music Therapy Intervention for Preterm Infants

Results of a meta-analysis of the efficacy of music in intervention for premature infants completed by Standley (2002) revealed an effect size of 0.83, indicating benefits of almost a full standard deviation greater than had no intervention been implemented. Results were not differentiated based on PCA at time of intervention, birthweight, or method of music presentation. The use of music alone or combined with other types of stimulation has resulted in consistent benefits for hospitalized, premature, LBW infants, including decreased length of hospitalization;

increased rates of NNS and feeding, weight gain, and SaO_2; decreased HR; and behavior state modulation.

Music listening. Music listening alone by hospitalized premature infants has resulted in decreased initial weight loss and observed stress behaviors (Caine, 1991), increased weight gain (Malloy, 1979), improved SaO_2 (Cassidy & Standley, 1995; Standley & Moore, 1995), decreased HR and RR (Cassidy & Standley, 1995), and less crying at 6 months after hospital discharge (Standley, 1991). In fact, Cassidy and Standley (1995) found no contraindications for music during the first week of life as early as 24 weeks gestation, though sensory stimulation, including auditory stimulation, is often restricted for those very young and clinically unstable infants, such as those with chest tubes or receiving certain types of assisted ventilation. In some situations, music listening may provide the most beneficial type of stimulation, yet, depending on infant age and stability, implementation of modified auditory, tactile, visual, and vestibular stimulation procedures, whether simplified for younger infants or with greater complexity to encourage interaction for more mature infants, could be developmentally appropriate (Abromeit, 2003; Whipple, 2005).

Music-reinforced nonnutritive sucking. A meta-analysis of studies regarding the effects of music as reinforcement for subjects ranging in age from 2 days to 24 years revealed that the use of contingent music alone or when paired with nonmusic stimuli was more effective than non-contingent music and contingent nonmusic stimuli (Standley, 1996). A separate meta-analysis of studies utilizing contingent music specifically for infant learning, with infants ranging from 34 weeks PCA to 8 months of age, indicated that contingent music had a positive and significant impact (Standley, 2001).

Supported by these results, Standley (2000) developed the pacifier-activated lullaby system to reinforce NNS. The system was found to significantly increase sucking frequency of preterm infants as young as 32 weeks PCA, with mean PCA of 35.5 weeks, when reinforced with 10-second intervals of a recording of a woman singing lullabies. In an average of 2.5 minutes, infants learned to suck frequently enough for music to be played continuously, and sucking rates during contingent music were 2.43 times greater than those during no-music conditions. In addition, infants may have improved sucking pacing as well as sucking rate, an important aspect of the suck-swallow-breathe coordination necessary for independent feeding. The same system was used by Standley (1999) to assess transfer of increased sucking rates to feeding behaviors. Baseline evening bottle-feeding rates were lower than morning bottle-feeding rates for preterm infants aged approximately 36 weeks PCA who were referred for services due to delays in independent feeding. For infants who received an opportunity for approximately 15 minutes of music-reinforced NNS from 30 minutes to one hour prior to evening bottle-feeding, mean evening feeding rate was significantly increased from morning rate, while evening rate mean for control infants was somewhat decreased from the morning rate.

Documentation of these benefits led to development by Healing Health Systems of the Sondrex® Pacifier Activated Lullaby (PAL) System®. The PAL system, designed to teach pacing and endurance of sucking necessary for nipple feeding, plays music contingent on infant sucking. A wired or wireless transmitter connected to a pacifier sends a signal to the Sondrex® Sound CD System and the infant is rewarded with music, provided he or she generates a certain threshold of sucking pressure. The PAL system also has the capability to play continuous music with or without the use of the pacifier and transmitter. The device has received approval as a mechanism to facilitate poor feeding behaviors from the United States Food and Drug Administration.

The purpose of this study was to examine the effects of music-reinforced NNS using the Sondrex® PAL System® on pain responses of preterm, LBW infants experiencing a painful procedure, specifically blood collection via heelstick. Physiologic and behavioral measures for infants provided the PAL were compared to those for infants provided only a pacifier and those who received no intervention beyond standard care.

Method

Subjects and Setting

Subjects (N = 60) were preterm (born prior to 37 weeks gestation, based on estimated date of confinement), LBW (born weighing less than 2500 g) infants, hospitalized in an NICU, experiencing a heelstick for the purpose of blood collection. Infants were excluded from the study based on the following:

- < 32 weeks PCA at the time of study participation;
- $\geq$ 37 weeks PCA at the time of study participation;
- cleft palate, cleft lip, or other oral anomalies;
- diagnosed grade 3 or 4 IVH, hydrocephalus, or PVL;
- size too small or too large for the Wee Soothie® (recommended weight of 3 to 5 pounds) or Soothie® ($\geq$ 5 pounds) pacifier as determined by nursing staff;
- ventilator assistance at the time of study participation.

Subject identification and group assignment did not control for gestational age or clinical stability of infants beyond the above listed inclusion and exclusion criteria. Infants were randomly divided into one experimental and two control groups totaling 20 infants each, evenly divided between males and females. Information was recorded from infant medical charts regarding weight and gestational age at birth and at the time of study participation, medical and developmental assessments, diagnoses, and interventions. Birthweight was not recorded for one male in the no-contact group. Acuity Score, a measure of infant clinical stability, was recorded on the day of study participation; an Acuity Score was not available for 3 infants (pacifier-only: 1 male, 1 female; no-contact: 1 male). The Acuity Score incorporates the following factors: feeding behaviors; bedding (i.e., open warmer, incubator, or open crib); requirement for oxygen, cardiorespiratory monitor, and pulse oximetry; use of heat lamp or phototherapy; medications and tubing, including IV lines; additional care requirements, such as suctioning, circumcision, or ostomy care; and behavior state and responses to caregiving. Higher Acuity Scores indicate lower infant clinical stability.

All demographic and treatment variables were analyzed using a One-way Analysis of Variance (ANOVA) test with an alpha level of .05. Also compared were the duration of the heelstick procedure and, for the experimental and pacifier-only control groups, the duration of sucking before the heelstick procedure began and for the pre-, during-, and post-heelstick intervals combined. Sucking duration was defined as the length of time during which an infant was offered a pacifier, regardless of the presence of actual sucking, measured from the time the pacifier was initially placed in the infant's mouth. No significant differences were found among groups based on these demographics.

The same demographic variables were examined for a subset of 40 infants for whom an additional physiologic variable of SaO_2 was available for analysis. The SaO_2 sample included 14 infants (7 male, 7 female) in the experimental group, 13 pacifier-only infants (7 male, 6 female), and 13 no-contact infants (4 male, 9 female). Of the infants mentioned above for whom Acuity Score was not available, the pacifier-only female and the no-contact male were SaO_2 Subjects. Using a one-way ANOVA, a significant difference was found among treatment groups for Acuity Score, $F(2, 35)$, $p = .04$. Examination of group means revealed that the experimental group had the lowest Acuity Score (or highest clinical stability); however, post hoc analysis using Tukey's honestly significant difference (HSD) showed that the contrast indicated does not appear to be for any of the three pairs. Therefore, contrast tests were completed to isolate the difference. Results revealed that the largest difference occurred between the PAL group and the combined pacifier-only and no-contact control groups ($T = 2.56$, $p = .01$). No other significant differences were found among treatment groups for the SaO_2 subsample.

Factors potentially affecting pain responses but not analyzed with demographic variables include medications, multiple heel-sticks during the observed heelstick procedure, and administration of sucrose before or during the heelstick procedure. Within the sample of 40 infants for whom SaO_2 data were available, 18 (45%) were receiving caffeine citrate to decrease incidences of apnea (Mainous, 1995). These subjects were divided fairly evenly among the three groups, with 7 infants (50%) of the experimental, 6 infants (46.15%) of the pacifier-only, and 5 infants (38.46%) of the no-contact groups. In addition, one female infant in the pacifier-only group was receiving dobutamine and epinephrine, which could affect cardiac functioning, and one male in the pacifier-only group was receiving pentobarbital, a barbituate sedative, which can depress cardiorespiratory functioning (Mainous, 1995). No other infants were receiving any medications likely to affect pain responses. Of the total sample of 60 infants, 3 (2 pacifier-only & 1 no-contact) required two needle sticks to satisfy the necessary volume of blood collection. Sucrose was administered to 16 infants (26.67%), distributed as 6 (30%) of the experimental, 3 (15%) of the pacifier-only, and 7 (35%) of the no-contact groups.

This study was performed in a Level III, 110-bed NICU in the southeastern United States. The researcher identified subjects by daily reviewing the NICU patient summary book, which included the specified inclusion and exclusion criteria. The nurse and medical chart of infants deemed eligible for study inclusion were then consulted to ensure that exclusion criteria were not omitted from the shift report book. Parents were approached regarding the study once the researcher identified their infants as having met the study inclusion criteria. The procedure and rationale for the study were explained at that time and parents who agreed to enroll their infants in the study signed an Informed Consent. At that point, the infant was randomly assigned to one of the three groups. The researcher reviewed lab orders daily to determine when infants whose parents had given study inclusion consent were scheduled to experience heelsticks.

Equipment

Two identical digital video cameras were used. One camera was placed on a tripod beside the infant's bed in order to allow videotaping of the entire procedure and the infant's responses at close range. The other camera, also on an adjustable tripod, was focused on the infant's monitor(s).

The Sondrex® PAL System® is manufactured by Healing HealthCare Systems; the Wee Soothie® and Soothie® pacifiers are distributed by Children's Medical Ventures. The Sondrex® PAL sensor is self-calibrating, adjusting the suck pressure threshold required for music activation based on each infant's first suck. The default setting for sound duration is 10 seconds, meaning that music will play for 10 seconds following each suck and then cease until the infant sucks again. It is possible for infants to suck frequently enough to receive continuous music. This 10-second sound duration setting has been used successfully in previous studies (Standley, 1999, 2000) and was used in this study as well. The level of music was maintained not to exceed 65dB, based on American Academy of Pediatrics (1997) recommendations and guidelines from previous music therapy studies with the NICU population (Cassidy & Ditty, 1998; Standley, 2003). The Sondrex® speakers default at 65 dB when kept 6 inches from the infant's head, placed bilaterally. Music used was from the Sondrex® PAL Custom Compact Disc, Volume I, which includes traditional lullabies sung by a single female child's voice with piano accompaniment. This music selection was consistent with research regarding optimal auditory stimulation for premature infants, as lullabies focus on vowels, which is optimal for language development, and have relatively stepwise melodies that are often sung softly, steadily, and continuously, which reduces risk of overstimulation (Whipple, 2005). Also, mother's voice, followed by other female voices, is the auditory stimulus most preferred by infants (Standley & Madsen, 1990), and simple instrumentation, preferably with only one accompanying instrument (e.g., piano or guitar), limits the potential for overstimulation (Standley, 2003).

The Continuous Response Digital Interface (CRDI) system incorporates a software program and a box that connects to a personal computer via a USB cable. A maximum of eight dials can be connected to the CRDI box. Moving from left to right, data potential ranges from 0 to 255 for each dial (Center for Music Research, 2003). The device and software were developed in the late 1980s at the Center for Music Research at the Florida State University, with the goal of creating an inexpensive, nonverbal system, designed to be multipurpose, easily adapted for various types of measurement (Geringer, Madsen, & Gregory, 2004).

For this study, two CRDI dials were used, with one assigned to behavior state and one assigned to stress level, and two additional identical dials connected for reliability observation. For behavior state, the following data ranges were determined: deep sleep, 15–54 (35); light sleep, 55–94 (75); drowsy, 95–134 (115); alert 135–174, (155); active, 175–214 (195); and crying, 215–255 (235); and an additional range of 0–14 to represent any point when view of the infant was obstructed. Values in parentheses represent the target value for each behavior state, which was marked with a red dot on the dial to increase reliability and consistency of data recording among subjects. These determinations were based on the six standard infant behavior states defined in the Assessment of Preterm Infants' Behavior (Als, Lester, Tronick, & Brazelton, 1982a). For the stress level dial, a line was drawn at the point corresponding to a value of 15, so that all space to the left of that line and all values below 15 represented an obstructed view of the infant and undeterminable stress level. The following corresponding values were marked for the stress behaviors listed from minimal to maximal on the stress level continuum dial, not for the purpose of target points, but for guidance to aid in increased reliability and consistency among subjects: sucking or sleeping without signs of distress, 17; finger splay, leg or foot extension, or grimace, 35; startle or tremor, 55; whimper, sneeze, yawn, or hiccough, 75; grunting, 95; fussing or halt hand, 120; struggling movements, crying, or cry face, 155; intense crying, 195; and intense crying with change of body position in bed, 245. These stress behaviors and signs of overstimulation considered during stress level analysis are samples of those defined by Burns et al. (1994) and Als, Lester, Tronick, and Brazelton (1982b). Engagement cues as defined by Burns et al. (1994) were also considered as reference points when classifying infant behaviors.

Research Design

This study employed a multiple sample, posttest only design. Groups included the Sondrex® PAL System®, pacifier-only, and no-contact control. Data collection occurred over a period of 5.5 months. A one-trial design was used for each subject.

Dependent Measures

Pain and distress are not clearly differentiated in literature, nor are effects of noxious versus painful procedures. However, accepted behavioral and physiologic indicators of both from both types of experiences include changes in HR, RR, SaO_2, and behavior state, and demonstration of specific overt stress behaviors. Therefore, for this study, the following dependent measures were selected for measurement and are considered to be responses to both painful and otherwise noxious aspects of the heelstick procedure.

Heart and respiratory rates were recorded at 15-second intervals throughout the pre, during, and postprocedure intervals from the videotape of each infant's monitor. In cases where the monitor was blocked (e.g., the phlebotomist or nurse stood between the camera and monitor) or the monitor displayed a noisy signal for HR or RR, the next available data within 5 seconds were recorded for that particular data point for both variables. If information was not available within 5 seconds for one of the variables, the value available for the other variable at the actual 15-second point was recorded and the cell for the other variable left empty. If data were not available for either variable within 5 seconds, both cells were left empty for that 15-second data point. Thirteen data points for each variable were possible for each baby during the 3-minute pre and postintervals. The during-procedure interval was a different duration for each infant (range: 54 seconds - 13 minutes, 57 seconds) and therefore, there were 16 to 56 potential data points for each variable. For all 60 subjects, at least 50% of all data points were complete for each variable for all three intervals. Percentages of collected data ranged from 76.92% to 100% for HR for both pre and postintervals, 84.62% to 100% for RR for both pre and postintervals, 55.56% to 100% for HR for the during-procedure interval, and 77.78% to 100% for RR for the during-procedure interval.

Data were also available for SaO_2 for 40 infants. This variable was recorded from the monitor videotape at 15-second intervals. If HR and RR for a particular interval were recorded at a time other than the 15-second data point, that same alternate point was also used for the SaO_2 level. However, if SaO_2 was not available within 5 seconds for any data point, the first SaO_2 level within the subsequent 5 seconds was recorded. For the 40 subjects with SaO_2 data, 100% of all data points were complete for the postinterval; at least 50% of all data points were complete for the pre and during intervals, with percentage ranges from 84.62% to 100% and 55.56% to 100% for the pre and during intervals, respectively.

A reliability observer recorded the physiologic data of HR, RR, and SaO_2 for six of the monitor videotapes (10% of the sample). Interrater reliability was calculated as the percentage of identical agreement on the sample of data points for each variable for the six subjects' videotapes. The combined sample resulted in a total of 242 data points with interrater agreement of 97.93% (range: 91.18%–100%) for HR, 97.11% (range: 82.35%–100%) for RR, and 95.04% (range: 83.33%–100%) for SaO_2. The interrater reliability for all physiologic variables for all subjects combined was 96.69%.

For infants in both control groups and the experimental group, infant behavior state and stress level were simultaneously and continuously recorded for the pre, during, and postprocedure intervals using the CRDI system while watching a videotape recording of the heelstick procedure. The CRDI dials were both set to capture data once per second, resulting in 180 data points each for behavior state and stress level for both the pre and post intervals, and from 54 to 837 data points for the during interval. Data points below 15 and 17 for behavior state and stress level, respectively, were eliminated, leaving empty cells, as they indicated an obstructed view of the infant during videotape review.

A reliability observer watched and recorded data for the two behavior variables for 10% of the sample by watching six infant videotapes simultaneously with the researcher, recording behavior state and stress level using two additional, identical CRDI dials. Interrater reliability was calculated using Pearson product-moment correlation. Results for individual subject videotape analysis ranged from $r = 0.88$ to $r = 0.99$ ($p < .001$) for behavior state and $r = 0.81$ to $r = 0.98$ ($p < .001$) for stress level. For the six subjects combined, reliability measures were $r = 0.95$ and $r = 0.97$ for behavior state ($p < .001$) and stress level ($p < .001$), respectively.

Procedures

The researcher was present in the NICU when infants whose parents had given consent for study participation were scheduled to have blood collected. The researcher was responsible for providing all PAL intervention and recording all data for control and experimental infants. A team of phlebotomists and in some cases, the infant's nurse conducted the blood collection heelstick procedure. A separate spring-loaded heelstick device was used for all infants.

For experimental infants, intervention began approximately 3 minutes prior to the heelstick and continued throughout the duration of and approximately 3 minutes following the blood collection procedure. Infants were provided the Sondrex® PAL System®, which played music contingent on infant sucking on a Wee Soothie® or Soothie® pacifier. A separate pacifier and transmitter were used for each infant and the transmitter was disposed of following intervention, though the pacifier was left for the infant's future use. Continuous light, gentle pressure from the researcher's finger was kept on the pacifier to prevent its slipping or falling out of the infant's mouth. If necessary to initiate a sucking response, the researcher gently stroked the infant's cheek with one finger to generate a suck. This was discontinued following initial pacifier placement and initial suck from an infant or 30 seconds, whichever came first. If an infant spit out or used his or her tongue to thrust out the pacifier, the researcher waited 5 seconds, then reinserted the pacifier each time this occurred. Additional standard care and pain management procedures, such as swaddling, cuddling, and sucrose (Als et al., 1986; Als et al., 1996; Bellieni et al., 2001; Gibbins & Stevens, 2001; VandenBerg, 1995) were not limited for infants in the PAL experimental group.

Infants in the first control group, pacifier-only, were provided either the Wee Soothie® or Soothie® pacifier, but did not receive music reinforcement for sucking. Otherwise, procedures were the same as described for the experimental condition.

For these two conditions, each infant received PAL or pacifier-only intervention on only one occasion. The combined pre, during, and postprocedure intervals were planned to be limited to 15 minutes or less, in order to avoid the potentially contaminating factor of infant fatigue. While many published pain measurement scales employ a 2-minute observation period prior to and following noxious procedures (Lawrence et al., 1993), 3 minutes was selected as the length of time for pre and postprocedure intervals in this study because infants receiving PAL intervention in previous studies learned to suck with the frequency necessary to elicit continuous music in an average of 2.5 minutes (Standley, 1999, 2000). This 3-minute interval allowed time for infant learning to occur prior to painful intervention, but in most cases, did not extend the PAL or pacifier-only intervention to a length that would increase the likelihood of fatigue, as previous use has demonstrated a decrease in sucking near the 14-minute point (Standley, 2000). Only 10 infants (5 PAL, 4 pacifier-only, and 1 no-contact control) had sessions exceeding 15 minutes. Extended sessions occurred either because the heelstick did not begin as quickly as expected, causing the pre-sucking interval to be extended, or because the infant was scheduled to have a large sample of blood collected or was not bleeding well, both factors which can cause the actual heelstick procedure to last for an extended period of time.

A final no-contact control group was also included. Infants in this group were not provided pacifier or music listening opportunities during the pre, during, and postheelstick procedure intervals. However, as for the PAL and pacifier-only groups, other previously described standard care and pain management procedures were not limited for infants in this control group.

Data Collection

Pre, during, and post intervals were determined during videotape review based on the audible click of the heelstick needle signaling the beginning of the during-procedure interval. The pre interval ended 1 second before that and was considered to have begun 3 minutes and 1 second before the heelstick click. The end of the during-procedure interval was considered to be the second at which the application of the adhesive bandage was completed or the end of the gauze strip bandage was placed, depending which type of bandage was used. The post interval began 1 second later and ended 3 minutes after that. Regardless of the actual length of pacifier-sucking and videotaping in the pre and post intervals, only the 3 minutes immediately prior to the heelstick and the 3 minutes immediately following the conclusion of the blood collection procedure were used for data collection; the entire during-procedure interval was used.

Results

Data were subjected to a variety of statistical computations, with all p values acquired via two-tailed tests.

Physiologic Variables

Heart rate. Means of HR data were calculated for each infant for pre, during, and post-heelstick intervals, from which group means were achieved for the same intervals. All group means were compared for the three treatment groups using Multivariate Analysis of Variance (MANOVA) with an alpha level of .05. Results indicated no significant differences among groups for the three intervals. To examine changes in infant HR from one interval to the next, differences between the three intervals were calculated for each infant using the following formulas: during interval minus pre interval, during interval minus post interval, and post interval minus pre interval. Group mean interval differences were then calculated (see Table 1). Again, no significant differences among groups were found for the three mean interval mean differences.

In order to evaluate and compare HRV in this study, the mean of each data point was calculated for each group, from which the

TABLE 1
Heart Rate, Respiratory Rate, and Oxygen Saturation Interval Means and Standard Deviations

	PAL (n = 14)		Pacifier-only (n = 13)		No-contact (n = 13)	
	M	SD	M	SD	M	SD
1st data point						
HR	158.85	16.14	154.15	19.13	157.45	14.04
RR	62.50*	24.88	62.50*	19.34	42.45	30.17
SaO_2	94.36	13.87	95.00	4.53	96.54	3.28
Pre interval						
HR	162.25	8.93	157.39	12.18	160.93	11.79
RR	52.89	17.73	58.05	15.11	49.68	10.21
SaO_2	95.46	6.19	95.45	4.25	96.23	2.70
During interval						
HR	179.87	13.41	170.64	16.86	178.94	15.24
RR	48.14	16.81	56.40 *	18.24	45.06	8.57
SaO_2	95.08	4.99	93.44	7.52	94.56	3.86
Post interval						
HR	167.88	12.21	161.83	13.47	167.38	15.95
RR	56.18	17.48	62.31	21.75	53.32	15.70
SaO_2	97.81	1.95	96.83	2.57	97.43	2.36
During - Pre						
HR	17.63	10.84	13.25	9.31	18.01	15.47
RR	−4.75	8.61	−1.65	10.11	−4.63	9.53
SaO_2 (Pre – During)	0.38	8.06	2.01	7.57	1.67	3.44
Post – Pre						
HR	5.63	10.54	4.43	9.40	6.45	12.96
RR	3.29	12.39	4.25	11.17	3.65	13.61
SaO_2 (Pre – Post)	−2.36	6.46	−1.38	3.31	−1.19	1.43
During – Post						
HR	11.99	10.50	8.82	10.43	11.56	17.73
RR	8.04	11.61	−5.90	13.46	−8.27	16.21
SaO_2 (Post – During)	2.74	4.27	3.38	6.34	2.87	3.58
Post point $SaO_2 \geq 95\%$	1.64	1.49	2.15	2.03	1.92	2.47
Post point SaO_2 stays $\geq 95\%$	3.79	4.51	4.85	5.55	5.08	5.29
% Pre < 86% SaO_2	4.94	12.29	3.54	7.42	1.18	2.89
% During SaO_2 < 86%	8.49	17.39	15.45	27.64	4.84	11.75
% Post SaO_2 < 86%	0.55	206	2.37	4.85	0.59	2.13
% Total SaO_2 < 86%	4.78	7.39	6.85	10.79	2.66	6.04

*$p < .05$, with statistically significant difference(s) between group(s) indicated and no-contact control group.

TABLE 2
Means and Standard Deviations of 15-Second Data Point Heart Rate, Respiratory Rate, and Oxygen Saturation Means

	PAL		Pacifier-only		No-contact	
	M	*SD*	*M*	*SD*	*M*	*SD*
Combined intervals (n = 82)						
HR	181.06	14.62	160.60	7.06	174.81	10.67
RR	46.77	12.09	62.08	10.95	46.61	11.60
SaO_2	95.57	2.18	95.76	2.12	95.54	2.09
Pre Interval (n = 13)						
HR	176.62	4.15	157.38	3.78	161.00	2.79
RR	52.89	5.26	58.11	4.10	49.68	6.05
SaO_2	95.46	1.62	95.39	.87	96.21	.73
During (n = 56)						
HR	188.72	11.40	161.21	8.03	182.24	5.89
RR	43.16	12.74	63.24	13.28	43.18	13.45
SaO_2	94.78	2.16	95.53	2.49	94.54	2.15
Post (n = 13)						
HR	167.38	4.15	161.85	5.41	167.46	6.39
RR	56.18	4.36	62.31	5.33	53.33	4.57
SaO_2	97.82	.69	96.83	1.27	97.43	1.09

Note. n refers to the sample of mean data points.

means and standard deviations for the combined and separate intervals were found. Means and standard deviations for HR 15-second interval means are listed in Table 2.

To further explain the significant interactions, Pearson product-moment correlations were completed for all interval means and interval mean differences, with the following variables: age in days at time of study participation, Acuity Score, duration of during-heelstick interval, duration of sucking prior to heelstick, and behavior state at the first second of the pre-heelstick interval (see Table 3).

Respiratory rate. Respiratory rate means and mean differences were calculated for the same intervals as for HR. All means and mean differences were compared for the three treatment groups using a MANOVA (see Table 1). Results indicated a significant difference among treatment groups for the first data point, $F(2, 57) = 4.36, p = .01$, and for the during interval mean, $F(2, 57) = 3.20, p = .04$. Tukey's HSD post hoc analysis revealed that the

TABLE 3

Significant Pearson's Product-Moment Correlations of Selected Demographic Variables with Heart Rate, Respiratory Rate, and Oxygen Saturation Means

	Physiologic Variable	Demographic Variable	Interval	*r*	*p*
All Subjects	HR	Initial behavior state	Post – Pre	−.41	.001
		Acuity Score	During	−.30	.02
			Post	−.30	.02
		Heelstick duration	During	−.51	.02
		Pre sucking duration	Post – During	−.57	.009
			Post – Pre	.49	.02
	RR	Heelstick duration	During – Post	.29	.02
	SaO_2	Acuity Score	During	−.41	.01
			During – Post	−.32	.04
			% Combined < 86%	.37	.02
Within PAL group	RR	Acuity Score	Pre	.49	.02
	SaO_2	Initial behavior state	During	.55	.04
			Post point ≥ 95%	−.64	.01
Within pacifier-only group	RR	Initial behavior state	Pre	.53	.01
		Acuity Score	During – Post	.62	.006
		Heelstick duration	During – Post	.66	.001
Within no-contact group	HR	Initial behavior state	Pre	.45	.04
			Post – Pre	−.55	.01
		Heelstick duration	During – Post	.49	.02
	SaO_2	Initial behavior state	% Post < 86%	.64	.01
		Age	% Post < 86%	.56	.04
		Acuity Score	During	−.77	.003
			% Post < 86%	.59	.04

statistically significant difference for the first data point occurred between the no-contact group and both the pacifier-only and PAL groups (*M* difference = −20.05, standard error = 7.96, p = .03), with the latter groups displaying a higher initial RR. The during-heelstick interval difference occurred between the pacifier-only and no-contact control groups (*M* difference = −11.35, standard error = 4.64, p = .04), with pacifier-only group infants displaying a higher mean RR.

Comparisons of RR variability in the forms of means and standard deviations of each 15-second data point for the combined and separate intervals are listed in Table 2.

To further explain the significant differences, Pearson product-moment correlations were completed for the interval means and interval mean differences, with the same variables as for HR (see Table 3).

Oxygen saturation. Means and mean differences were calculated for SaO_2 for the same intervals as for HR and RR. However, since SaO_2 would be expected to be higher when HR and RR were lower, the formulas for determining mean differences were reversed. Interval means and mean differences were compared for the three treatment groups using MANOVA. The following measures were also computed and compared: percent of cells for separate and combined pre-, during-, and post-procedure intervals in which SaO_2 was below 86%; post interval data point (each data point represented the passing of 15 seconds) at which the infant's SaO_2 first reached 95% or higher; and the post interval data point at which the infant's SaO_2 remained at 95% or higher. For some infants, this was the same data point; however, for infants whose SaO_2 continued to fluctuate below 95% throughout the post interval, a value of 14 was used for the second measure, indicating a point in time beyond the post interval, since only 13 data points were possible for the 3-min post interval. No significant differences were revealed among treatment groups (see Table 1).

Comparisons of SaO_2 variability in the forms of means and standard deviations of each 15-s data point for the combined and separate intervals are listed in Table 2.

Using the same variables as for HR and RR, Pearson product-moment correlations were completed and indicated significant correlations for all subjects combined and within the three separate treatment groups (see Table 3).

Mean interval difference patterns. There were some consistent patterns in mean interval differences. For the variable of HR, there was an increase for all treatment groups from the pre to the during-heelstick interval, as was anticipated when designing formulas to determine mean interval differences. However, RR mean interval differences occurred in the opposite direction than expected for the pre to during and during to post intervals in all three groups, indicated by negative values in Table 1, which could indicate apnea, another signal of distress (Burns et al., 1994). In all three groups, the expected RR increase occurred from the pre to post interval.

For the variable of SaO_2 for the PAL group, the mean differences between pre and post intervals occurred in the opposite direction expected, evidenced by negative values in Table 1, as SaO_2 was higher in the post than pre interval and during than pre interval. The pacifier-only and no-contact control groups displayed mean interval differences as expected in all but one calculation: an increase from pre to post interval mean. While not significant, the PAL group first reached 95% or higher SaO_2 and remained at or higher than 95% SaO_2 at earlier points in the post interval than the other two groups, and the no-contact group had the lowest percentages of intervals in which SaO_2 was less than 86% for the combined and separate intervals, except for the post interval during which the PAL group's percentage of non-optimal SaO_2 data points was lowest.

Variability over time. Based on standard deviations of the three physiologic variables across the entire heelstick procedure and for the separate pre, during, and postheelstick intervals, SaO_2 appears to be much less variable than HR and RR.

Correlations. As shown in Table 3, more significant correlations with physiologic measures occurred for the variables of Acuity Score and initial behavior state than for other variables, followed by heelstick duration, though heelstick duration correlations were inconsistent. Few correlations were evident for age and length of sucking prior to heelstick.

Results of Pearson's product-moment correlations indicated that Acuity Score is negatively correlated with HR and positively correlated with RR, meaning that as Acuity Score increased (or infant's clinical stability decreased), HR decreased within the during and post intervals and RR increased for pre interval mean within the PAL group and mean difference in during and post interval means for the pacifier-only group. As expected, negative correlations of Acuity Score with SaO_2 indicate that as Acuity Score increased, SaO_2 decreased for the during interval, as well as for the mean difference between during and post interval means. Results also indicated that as Acuity Score increased, percent of time in which SaO_2 was less than 86% increased.

Correlations of initial behavior state with HR and RR measures indicate that the higher initial behavior state was assessed to be, the higher pre interval no-contact HR and pacifier-only RR means were. In addition, as initial behavior state increased, during interval SaO_2 means increased and mean differences in pre and post interval HR means decreased within the no-contact group. Also expected, a higher initial behavior state score was associated with an earlier point at which SaO_2 reached 95% or greater within the post interval for the PAL group, yet was associated with a higher percentage of time in which SaO_2 was below 86% within the no-contact group.

Consistent with age effects seen in previous studies (Johnston & Stevens, 1996; Johnston, Stevens, Yang, et al., 1996), correlation analysis revealed that as age increased, the mean difference in pre and post interval behavior state means increased for the PAL group, and the percent of time in which SaO_2 was less than 86% during the post interval increased for the no-contact control group.

Behavioral Variables

Behavior state. Means and mean differences were calculated for behavior state for the same intervals, using the same formulas as for HR and RR, and again were compared for the three treatment groups using MANOVA. Also compared was the percent of data points for separate and combined pre-, during-, and post-procedure intervals in which the behavior state CRDI value was above 174, which would correspond to the undesirable Active and Crying behavior states. Results indicated significant group differences for the following measures:

- during interval behavior state mean,
- mean difference in pre and during interval means,
- mean difference in during and post interval means,

- percent of during interval data points indicating Active and Crying states, and
- percent of combined interval data points indicating Active and Crying states.

In all cases Tukey's HSD post hoc analysis indicated that the statistically significant differences occurred between the pacifier-only and no-contact control groups as well as between the PAL and no-contact groups. In the case of mean difference in pre and during interval means, the largest difference was between the pacifier-only and no-contact control groups, but in all other cases, the larger difference was between the PAL and no-contact groups. Means and standard deviations are listed in Table 4, significant F values in Table 5 and Tukey's HSD post hoc analysis results in Table 6.

In order to evaluate and compare variability of behavior state over time, the mean of each 1-second data point was calculated and then the mean for the combined and separate intervals divided by group was found. Means and standard deviations for behavior state 1-second interval means are listed in Table 7 and a graph of behavior state for all groups over time is found in Figure 1

Using the same variables as for the physiologic data analysis, Pearson product-moment correlations indicated significant correlations for all subjects combined as well as within the three treatment groups. Significant correlations are listed in Table 8.

Stress level. Stress level means and mean differences were calculated for the same intervals, using the same formulas as for HR and RR, and again were compared for the three treatment groups using MANOVA. Results indicated significant group differences for the following measures:

- pre interval stress level mean,
- during interval stress level mean,
- post interval stress level mean,
- mean difference in pre and during interval means, and
- mean difference in during and post interval means.

Post hoc analysis using Tukey's HSD indicated that the statistically significant difference for pre interval mean occurred between the PAL experimental and no-contact groups. For all other measures

TABLE 4
Behavior State and Stress Level CRDI Value Interval Means and Standard Deviations

	PAL (n = 20)		Pacifier-only (n = 20)		No-contact (n = 20)	
	M	*SD*	*M*	*SD*	*M*	*SD*
Behavior State						
1st data point	92.00 (n = 20)	28.17	88.68 (n = 19)	27.89	91.90 (n = 20)	33.22
Pre Interval	96.45	17.79	103.38	14.96	100.92	27.94
During	127.35*	32.94	128.51*	29.03	176.15	40.14
Post	91.71	16.07	99.31	19.99	105.35	23.89
During – Pre	28.27*	46.71	33.70*	45.14	92.96	47.97
Post – Pre	69.98	14.94	73.65	21.49	73.24	30.29
During – Post	35.64*	39.57	29.19*	26.12	70.80	48.16
% Pre > 174	0.00	0.00	0.78	3.49	16.68	29.37
% During > 174	12.99*	28.87	15.91*	27.69	55.64	35.16
% Post > 174	0.00	0.00	2.42	9.46	4.94	8.92
% Total > 174	4.33*	9.62	6.37*	12.24	21.26	13.93
Stress Level						
1st data point	19.65* (n = 20)	315	18.74 (n = 19)	2.35	27.35 (n = 20)	23.62
Pre Interval	21.73	3.13	25.67	8.77	32.12	17.09
During	50.00*	46.85	59.37*	47.75	125.08	50.56
Post	21.33*	41.78	25.51*	12.75	39.29	19.41
During – Pre	28.27*	46.71	33.70*	45.14	92.99	47.97
Post – Pre	−0.39	5.00	−0.16	15.07	7.17	29.37
During – Post	28.67*	47.18	33.86*	39.68	85.79	53.38

* $p < .05$, with statistically significant difference(s) between group(s) indicated and no-contact control group.

TABLE 5
F Values for Significant Behavior State and Stress Level Group Differences

	Sum of Squares	*df*	Mean Square	*F*	*p*
Behavior State					
During	31,023.55	2	15,511.78	12.75	< .001
During – Pre	51,498.94	2	25,749.47	11.72	< .001
During – Post	20,059.65	2	10,029.82	6.59	.003
% During > 174	22,700.74	2	11,350.37	11.79	< .001
% Combined > 174	3416.10	2	1708.05	11.62	< .001
Stress Level					
Pre	1099.95	2	549.8	4.16	.02
During	66,938.88	2	33,469.440	14.08	< .001
Post	3531.01	2	1765.51	9.72	< .001
During – Pre	51,498.94	2	25,749.47	11.72	< .001
During – Post	39,905.23	2	19,952.61	8.79	< .001

TABLE 6
Tukey's HSD for Behavior State and Stress Level Group Differences

	Groups		*M* Difference	Standard Error	*p*
Behavior State					
During	No-contact	PAL	48.81	11.03	< .001
		Pacifier-only	47.64		< .001
During – Pre	No-contact	PAL	64.68	14.82	< .001
		Pacifier-only	59.26		.001
Post – During	No-contact	PAL	35.17	12.34	.01
		Pacifier-only	41.60		.004
% During > 174	No-contact	PAL	42.64	9.81	< .001
		Pacifier-only	39.73		< .001
% Total > 174	No-contact	PAL	16.93	3.83	< .001
		Pacifier-only	14.89		.001
Stress Level					
Pre	No-contact	PAL	10.39	3.64	.01
During	No-contact	PAL	75.07	15.42	< .001
		Pacifier-only	65.71		< .001
Post	No-contact	PAL	17.95	4.26	< .001
		Pacifier-only	13.78		.006
During – Pre	No-contact	PAL	64.68	14.82	< .001
		Pacifier-only	59.26		.001
During – Post	No-contact	PAL	57.12	15.06	.001
		Pacifier-only	51.93		.003

TABLE 7
Means and Standard Deviations of 1-Second Behavior State and Stress Level Means

	PAL		Pacifier-only		No-contact	
	M	*SD*	*M*	*SD*	*M*	*SD*
Combined intervals (n = 1197)						
Behavior State	111.25	13.47	110.92	12.21	146.25	40.53
Stress Level	29.16	12.75	32.39	15.61	85.17	48.89
Pre interval (n = 180)						
Behavior State	96.47	3.55	103.37	5.99	100.41	5.36
Stress Level	21.69	1.34	25.68	3.29	32.17	5.53
During interval (n = 837)						
Behavior State	118.62	8.08	116.44	10.49	174.79	24.85
Stress Level	32.45	13.98	36.33	18.11	117.72	35.01
Post interval (n = 180)						
Behavior State	91.77	6.39	99.37	10.06	10536	10.94
Stress Level	21.33	2.13	25.51	6.26	39.29	12.22

Note. n refers to sample of mean data points.

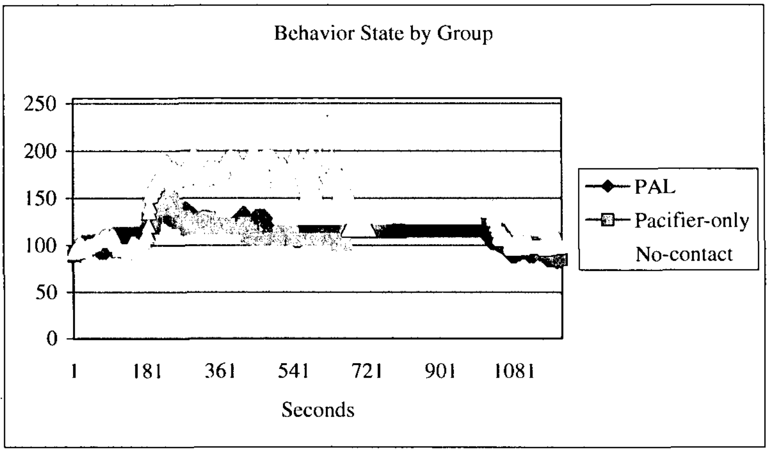

FIGURE 1.
Behavior state by group.
Note. Interval data point ranges follow: pre, 1–180; during 181–1017; and post, 1018–1197. Sample size decreased following data point 234 and resumed to full size at data point 1018. Line breaks indicate that data were not recorded for any subjects in that treatment group for those data points.

TABLE 8
Significant Pearson's Product-Moment Correlations of Selected Demographic Variables with Behavior State and Stress Level Means

	Behavioral variable	Demographic variable	Interval	r	p
All subjects	Behavior state	Initial behavior state	Pre	.74	<.001
			During	.29	.02
				−.30	.02
	Stress level	Initial behavior state	Post	−.29	.02
			Post − Pre	−.34	.008
Within PAL group	Behavior state	Initial behavior state	Pre	.84	<.001
	Stress level	Age	During − Post	−.46	.03
Within pacifier-only group	Behavior state	Initial behavior state	Pre	.77	<.001
		Age	Post	−.46	.04
		Acuity Score	During	−.49	.03
			During − Pre	−.51	.03
	Stress level	Acuity Score	During − Pre	−.51	.03
			During − Post	−.48	.04
		Heelstick duration	During − Post	−.46	.04
Within no-contact group	Behavior state	Initial behavior state	Pre	.72	<.001
		Heelstick duration	% Pre > 174	.50	.02
	Stress level	Initial behavior state	Post	−.51	.02
			Post − Pre	−.56	.01

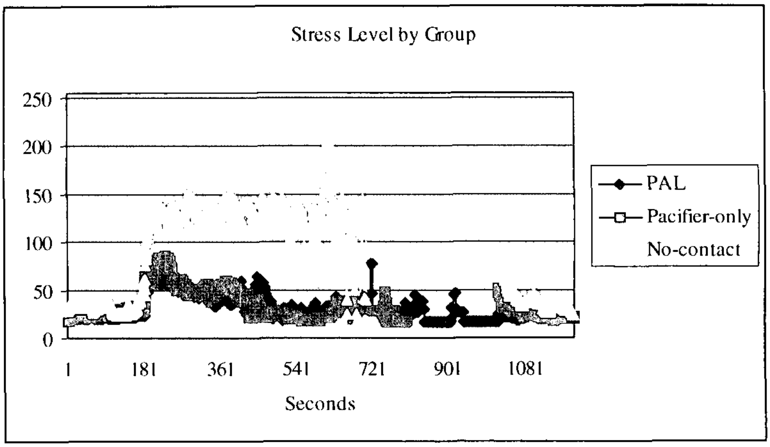

FIGURE 2.
Stress level by group.
Note. Interval data point ranges follow: pre, 1–180; during 181–1017; and post, 1018–1197. Sample size decreased following data point 234 and resumed to full size at data point 1018. Line breaks indicate that data were not recorded for any subjects in that treatment group for those data points.

the significant differences occurred both between the pacifier-only and no-contact control groups and between the PAL and no-contact groups, though the differences were greatest between the PAL and no-contact groups. Means and standard deviations are listed in Table 4, significant F values in Table 5, and post hoc analysis results in Table 6.

Comparisons of stress level variability in the forms of means and standard deviations of each 1-second data point for the combined and separate intervals are listed in Table 7 and a graph of stress level for all groups over time is found in Figure 2.

Using the same variables as for the physiologic data and behavior state analysis, Pearson product-moment correlations indicated significant correlations for all subjects combined and within the three treatment groups (see Table 8).

Mean interval difference patterns. There are some consistent patterns in mean interval differences. For the variables of behavior state and stress level, there were increases as anticipated for all treatment groups from the preheelstick to during-heelstick interval. However, opposite the anticipated result, post interval mean was less than pre interval mean for stress level for PAL and pacifier-only groups, indicating that decreases throughout the post interval led to behavior state and stress level means less than baseline measures.

For the measure of behavior state, the percent of time spent in Active and Crying behavior states for combined and separate intervals was lowest for PAL group infants, followed by pacifier-only group infants. These differences were significant for the PAL and pacifier-only groups compared to the no-contact group.

Variability over time. Based on standard deviations of the two behavioral variables across the entire heelstick procedure and for the separate pre, during, and postheelstick intervals, behavior state and especially stress level appear to be more stable for the PAL group than for the other two groups. For behavior state, standard deviations were smallest for the PAL group for the pre-, during-, and post-heelstick means, though the pacifier-only group displayed the smallest standard deviation for all intervals combined. The largest standard deviations in the combined, during, and post intervals occurred for the no-contact group. For stress level, standard deviations were smallest for the PAL group and largest for the no-contact group for all separate and combined intervals.

Graphic analysis of the behavioral variables supports the standard deviation comparisons for the three treatment groups. There was an observable initial increase in behavior state and stress level at the beginning of the during interval for all three treatment groups. This initial increase was greater for the no-contact group than for the PAL and pacifier-only groups and remained at the higher level, while stress level for the PAL and pacifier-only groups began to decrease slightly. The PAL and pacifier-only groups showed some variability during the remainder of the during interval, more for stress level than behavior state, while the no-contact group displayed several observable spikes in stress level and behavior state. Toward the end of the during interval, however, no-contact group behavior state and stress level dropped to levels close to those of the PAL and pacifier-only groups. At the beginning of the post interval, there was a drop in behavior state and stress level for all three groups that continued to decrease then stabilize.

Correlations. As shown in Table 8, more significant correlations with behavioral measures occurred for the variable of initial behavior state than other variables, followed by Acuity Score, then age and heelstick duration. No correlations were evident for length of sucking prior to heelstick. It should be noted that the initial behavior state measure is included in the pre interval, as four of the nine significant correlations for initial behavior state were within the pre interval and two were for a comparison of the pre and post intervals. Results of Pearson product-moment correlations indicated that as initial behavior state increased, during and pre interval behavior state means increased, post interval stress level means decreased, and mean differences between pre and post interval stress level means were reduced, demonstrating potential influence of this variable beyond the pre interval.

Acuity Score was negatively correlated with during interval behavior state means and mean differences between pre and during interval behavior state and stress level means, and during and post interval stress level means within the pacifier-only group, meaning that as Acuity Score increased, those values for pacifier-only infants decreased. Other negative correlations indicated that as age increased, post behavior state means within the pacifier-only group decreased, as did the difference between during and post interval stress level means for the PAL group, both consistent with age effects found in previous studies (Johnston & Stevens, 1996; Johnston, Stevens, Yang, et al., 1996). In addition, as heelstick duration increased, mean differences between during and post interval stress level means decreased within the pacifier-only group. Finally, longer heelstick durations were associated with higher percentages of time spent in Active and Crying behavior states within the no-contact group only.

Discussion

Greater treatment group differences were evident for behavioral than physiologic measures. Examination of means and standard deviations revealed that much more variability existed across time within all groupings for the HR and RR measures than for SaO_2, behavior state, and stress level. Potential causes for the lack of significance within physiologic results are numerous.

First, the variable of RR was inherently flawed because the cardiorespiratory monitor and sensors used actually recorded infant movement, including respiration, more than assessed RR specifically. Still, the measure of RR was included in this study since changes in movement could indicate distress. Further, the mean first RR data point was significantly higher for the PAL and pacifier-only groups than for the no-contact group. This could have been related to initial pacifier placement that, in many cases, had just occurred. On the other hand, this difference could have been a baseline difference caused by unknown factors. Also supporting inconsistencies within the RR measure is the fact that fewer significant correlations were found for demographic variables with RR than with any other physiologic or behavioral measure. The relatively inconsistent pattern of RR may indicate that it is not a reliable measure. Smaller standard deviations may signal SaO_2 as a more reliable indicator of pain and distress than HR and RR for the population in this study.

Also, while much research regarding NNS and HR has indicated a calming effect of NNS manifested in lower HR, the fact that both of the groups with larger HR increases were provided with opportunities for NNS may also indicate that their increase in HR between the pre and during intervals was due to self-regulatory sucking on the pacifier, as Woodson and Hamilton (1986) found a significant positive correlation for HR with motor activity in preterm infants due to their common association with energy expenditure. Further, since the PAL is designed and has been shown to increase pacifier sucking (Standley, 2000), this effect could explain why the PAL group had the highest during interval HR mean.

Further, while changes in HR, RR, and SaO_2 coincided with the introduction and withdrawal of noxious stimuli, group interval means remained within normal limits (Burns et al., 1994), possibly reducing the chance for significant physiologic differences among groups.

Still, there seems to be some physiologic evidence that the PAL is beneficial for facilitating return to homeostasis within the postheelstick period. The standard deviations for HR and RR over time were smallest for the PAL group for the post interval, though they had been larger than the other two groups for the combined and pre intervals for HR and RR and had been the largest for the during interval for HR. In addition, the PAL group first reached 95% or higher SaO_2 and remained at or higher than 95% SaO_2 at earlier points in the post interval than the other two groups. Also, for the PAL group, there were mean increases in SaO_2 and from pre to post intervals, larger than the other group increases. This pattern is important because it is opposite expected outcomes, with SaO_2 higher in the post-procedure interval than in the pre-procedure interval, which functioned as the baseline period. Still, this should be considered cautiously since Acuity Score was found to be significantly higher for PAL SaO_2 subjects than for the other two groups combined, and some negative correlations for Acuity Score with SaO_2 for during and mean interval differences were found, though not for the specific measures discussed.

Unlike the physiologic measures, behavioral measures in this study revealed many significant group differences. Behavioral observation is important within this study. First, interrater reliability was high for behavior state and stress level assessment. In addition, a meta-analysis completed by Standley and Whipple (2003) regarding music therapy treatment with pediatric patients, though not including the NICU population, indicated that behavioral observations tend to be more conservative than physiologic measures. Further, in the current study, the initial assessment measure of behavior state was significantly correlated with multiple physiologic as well as behavioral measures. Finally, DiPietro, Cusson, Caughy, and Fox (1994) found that NNS may lessen behavioral distress for preterm infants without altering physiologic responsiveness.

Supporting the use of music-reinforced NNS for preterm, LBW infants experiencing heelstick, results of this study indicate that the PAL group had significantly lower during interval behavior state means, smaller mean differences in pre and during interval and during and post interval behavior state means, and spent less time in Active and Crying states for the combined and during intervals than the no-contact group. Competent development is represented by smoothness in modulation, regulation, and differentiation of five observable behavioral subsystems of functioning: autonomic, motor, state regulatory, attention/interactive, and self-regulatory. Aroused states are characterized by high levels of motor activity and disorganized behavior patterns, and may be counterproductive to energy conservation (Als & Duffy, 1989). In addition, the PAL group had significantly lower pre, during, and post interval stress level means, and smaller mean differences for pre to during interval and during to post interval stress level means. Except for the pre interval mean difference which was significant only between the PAL and no-contact groups, these differences also occurred for the pacifier-only control group compared to the no-contact control group, though the differences were greatest between the PAL and no-contact groups. Also, as with changes in SaO_2 that signaled return to homeostasis, the post interval stress level mean was less than the pre interval mean for the PAL and pacifier-only groups, as decreases throughout the post interval led to behavior state and stress level means less than baseline measures, though group differences were not significant.

Behavior state and stress level also appear to be more stable for PAL than for the other two treatment groups. Standard deviations for behavior state were smallest for the PAL group for the three separate intervals, and for stress level, PAL group standard deviations were smallest for the combined and separate intervals. The largest standard deviations, and therefore most variation, were found in the no-contact group for combined, during, and post intervals for behavior state and for all combined and separate intervals for stress level.

Interestingly, a higher initial behavior state score was associated with an earlier point at which SaO_2 reached 95% or greater within the post interval for the PAL group only, yet was also associated with a higher percentage of time in which SaO_2 was below 86% within the no-contact group. These seemingly opposite significant correlations seem to further support the use of music-reinforced NNS in pain management.

This study has some limitations, as many variables of the heelstick procedure itself were beyond the control of the researcher. Procedural changes could include the addition of a separate baseline measurement prior to the period of time when preparation for the heelstick procedure occurs. In this study, preparation for the heelstick occurred at any point in time during the pre interval. For all infants, heelstick preparation progressed as follows: removal of blankets and clothing from the infant's foot, placement of a heel-warmer on the infant's foot, and cleansing of the heelstick site, followed by the actual heelstick using a spring-loaded heelstick device. However, for some infants these steps occurred in close succession and for others, they were generously spaced, sometimes with heel-warmer placement occurring prior to the official pre interval period. This variability meant that some infants were handled more frequently than others and eliminated the possibility for an actual baseline measurement. Much variation also existed within the method used for blood collection, as phlebotomists and nurses used different techniques for encouraging blood flow. Some squeezed, while other flexed the infant's foot; some scraped the vial along the infant's heel, while others allowed the blood to drop into the vial. Reduction in this process variation could be achieved by enlisting only one phlebotomist or nurse to collect blood for the heelstick procedures used for data collection, or by enlisting cooperation from the team of phlebotomists and nurses in use of a specific, consistent technique. In addition, separate intervals for bandaging the heelstick site following blood collection and for post procedure recovery could also be beneficial and could help in future analysis to determine if decrease in physiologic and behavioral indicators of distress observed in graphic analysis occurred during the bandaging period, were due to a shut-down effect caused by overstimulation or pain saturation with longer periods of painful stimulation, or were caused by outliers since the sample became smaller as time passed within the during interval.

Duration of sucking prior to the heelstick was also affected by lack of control over the heelstick procedure itself. Fatigue is a potential concern of extended length of NNS. Therefore, the procedure was designed to include 3 minutes of NNS for PAL and pacifier-only infants prior to the heelstick. However, this time period actually ranged from 3 min, 15 s to 10 min, 40 s, as it was not possible for the researcher to know exactly when the phlebotomist would begin the heelstick for each infant. Each phlebotomist had multiple infants from which to collect blood each day, all with varying heelstick procedure time requirements, and could not always accurately anticipate the amount of time until he or she would arrive at an infant's bedside. Few correlations were found for sucking duration prior to heelstick, which can be interpreted to mean that longer NNS periods did not seem to limit effectiveness of the PAL or pacifier-only interventions. In a meta-analysis of studies involving NNS for neonates, Shiao et al. (1997) found larger effects on reducing HR increases when infants experiencing painful procedures sucked for longer periods of time. However, the duration of NNS in the studies reviewed ranged from 2 to 5 min, compared to 6 min, 18 s to 27 min, 33 s of total NNS in this study. Therefore, it may be still advisable to attempt greater control of this variable in future research.

Since so many significant correlations were revealed for initial behavior state, age, Acuity Score, sucking duration prior to heelstick, and heelstick duration variables with physiologic and behavior measures, greater control over these factors may need to be established. To reduce variability in heelstick duration, data collection could be limited to heelstick procedures in which a set amount of blood (e.g., one vial) is to be collected. This would also likely reduce incidences of multiple heelsticks being necessary during a single heelstick procedure. Criteria could also be set for infant age and Acuity Score. However, excluding infants based on these factors could limit the opportunity to document pain management benefits for younger, less stable infants who are likely to experience more heelsticks (Barker & Rutter, 1995). In light of evidence of long-term detrimental effects of neonatal pain (Anand, 1998, 2000; Oberlander et al., 2000), it may instead be beneficial to employ Analysis of Covariance (ANCOVA) procedures including these variables in future study. Of course, all of the suggested procedure adaptations require greater control over the heelstick procedure and are only possible with facility cooperation. Further, highly controlled studies may yield less "real" results, as clinical application of these procedures will necessarily have the variability that was evident in this study.

Initially, physiologic data was to be downloaded from cardiorespiratory and SaO_2 monitors, providing continuous data that could be correlated with continuous behavior state and stress level data obtained using the CRDI system. Since this option was not available within the Sondrex® PAL System® at the time of study implementation, the format of tables and graphs allowed for comparison of those variables. The data point at which the actual heelstick occurred was not included in analysis due to the delayed display of its effect on the monitor, which caused this point to be difficult to determine. In future study, especially with continuous data, it might be possible to capture that information. The ability to download frequency and strength of infant sucking for the PAL and pacifier-only group infants from the Sondrex® PAL System® could provide insight into causes of HR, RR, and SaO_2 changes during the pre interval, as those variables could be affected by NNS as well as heelstick preparation procedures. In addition, sucking data could be compared to peaks and valleys in physiologic and behavioral changes. Future research should include this option once it is made available by the manufacturer.

Additional study may also support use of music-reinforced NNS during other painful and stressful procedures frequently experienced by premature infants, to include intubation, endotracheal suctioning, peripheral venous cannula and line insertion, umbilical catheter placement, intramuscular injection, lumbar puncture, and chest drainage (Barker & Rutter, 1995), as well as during dressing changes and eye exams. During suctioning for ventilator-dependent infants, the continuous music function of the Sondrex® PAL System® could be used for infants unable to consistently produce adequate sucking strength and frequency to activate the contingent music function. In addition, music-reinforced NNS might be beneficial for term or older preterm infants during circumcision. Some insight could also be gained by observing PAL effects on HR, RR, SaO2, behavior state, and stress level under non-painful conditions. Since NICU infants frequently experience distress, regardless of the presence of an actual painful event, such investigation could potentially provide support for use of the Sondrex® PAL System® for modulating preterm, LBW infant behavior in non-painful situations. One such use could be facilitation of Alert states optimal for feeding, as preterm neonates have limited periods of alertness and those periods are ideal for interactions that may tax their limited ability to maintain behavioral organization (Pickler, Frankel, Walsh, & Thompson, 1996). Finally, it is possible that the combination of music and NNS in this study became overstimulating once the painful stimulus of the heelstick was introduced. Beaver (1987) found that stroking the infant's leg during a heelstick procedure appeared to be more aversive to preterm infants than the heelstick alone, based on changes in physiologic measures from the baseline period. That same effect may have occurred in this study for the PAL group within the during-heelstick interval. If that is the case and this population of infants would be better served with only one additional input during noxious or painful procedures, use of the music-reinforcement for NNS function of the Sondrex® PAL System® may be beneficial for the pre and postprocedure intervals, with use of the pacifier alone once the painful or noxious procedure begins.

This study provides much evidence to support benefits of music-reinforced NNS for attenuating behavior state and stress level increases for preterm, LBW infants experiencing heelstick. Such information documents another method of nonpharmacologic pain management for the population of premature infants, and identifies an additional benefit of the Sondrex® PAL System®.

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