Development of a New Pain Assessment Instrument: Pain Assessment and Care for the Extremely Low Gestational Age Infant Focused Instrument (PACEFI)

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DEVELOPMENT OF A NEW PAIN ASSESSMENT INSTRUMENT: PAIN ASSESSMENT AND CARE FOR THE EXTREMELY LOW GESTATIONAL AGE INFANT FOCUSED INSTRUMENT (PACEFI)

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Abstract

Pain in extremely low gestational age (ELGA) infants remains under-assessed and poorly managed despite the fact that pain may have profound consequences with regard to infants' neuro-development (Als, 1982). Pain prevention is a critical goal of pain assessment, yet barriers exist. Most critical is the lack of valid, reliable, and clinically useful pain tools. This observational descriptive study focused on the development of a gestational age appropriate instrument for 24–29 6/7 week infants and evaluation of the new instrument, Pain Assessment and Care for the Extremely Low Gestational Age Infant Focused Instrument (PACEFI). Additionally, differences in behavioral cues and physiologic indicators were evaluated for ELGA infants and very low gestational age (VLGA) infants for non-invasive and invasive procedures. Nurse raters used the PACEFI to rate these infants during both procedures at baseline, during, and recovery to assess variation in expected pain. The PACEFI demonstrated a high internal consistency (.879) and appeared to be contributing to the measurement of pain. A RANOVA found a significant difference in rating scores ($p < .001$) for both procedures. Baseline and recovery scores were lower than during scores. ELGA infants demonstrated a dampened response ($p < .023$) as compared to the VLGA infants during the invasive procedure. Alternatively, ELGA infants demonstrated a more vigorous response for non-invasive procedure and dropped below baseline scores at recovery. The whole care experience during the non-invasive procedure may have led to sensitization for the VLGA infant and overwhelming energy expenditure for the ELGA infant. Furthermore, physiologic indicators

and behavioral cues were inconsistent arguing for independent assessment of these parameters. Knowledge gained from this study: 1) provides information regarding gestational age differences in pain behaviors; and (2) clarifies if the measurement of these behaviors addresses the immediate need for pain assessment for this vulnerable population.

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Chapter 1

Problem of the Study

Pain in ELGA and VLGA Infants

According to the U.S. Centers for Disease Control and Prevention (CDC), preterm births have increased in the United States by 21% since 1981, with the occurrence of very low gestational age births (weights < 1500 g) reaching 63,983 per year (CDC, 2009). Advances in technology since the 1980s have improved the likelihood of survival of the extremely low gestational age (ELGA) infant, but this survival comes at a neuro-developmental cost. A study of infants by Carbajal, Rousset, and Danan (2008) (m = 33 weeks, n = 430) in a level three neonatal intensive care unit (NICU) noted that, during their first 14 days of life, these infants experienced 60,969 procedures, including 42,413 (69.6%) painful and 18,556 (30.4%) stressful procedures, during their hospital stay. The number of painful procedures ranged from 4–613 per infant (m = 115) during the study period, with 0–62 such procedures (m = 16) per day (Carbajal et al., 2008). Of note, infants with a low gestational age experienced a higher amount of painful procedures (Carbajal et al.). The majority of the 42,413 procedures categorized as painful were performed without pharmacological therapy or nonpharmacological interventions (Carbajal et al.). These statistics are alarming due to a growing fear that untreated pain and suffering may directly contribute to poor long-term developmental consequences later in life (Anand, 2000b; Grunau, Whitfield, Petrie & Fryer, 1994).

Pain was defined by the International Association for the Study of Pain (IASP) (1979) as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” (p. 250). This definition implied that pain was subjective and that self-reporting is necessary. In 2003, the definition was amended to include nonverbal populations (IASP, 2003). The revised definition acknowledged the significance of nonverbal indicators of pain for infants (Sternberg, Al Chaer, 2007). Assessment of infant pain is a complex task for nurses, due to the disparity in gestational ages of infants and the infants' limited ability to express pain. Preterm infants, especially ELGA infants, are reliant on health care professionals to recognize, assess, and treat their pain.

Infants who are extremely premature are typically the most ill among newborns, and commonly require care that involves invasive procedures (Page, 2004; Johnston, Stevens, Yang & Horton 1995). Preterm infants can demonstrate the following negative physiological effects in response to potentially painful stimuli: (a) increase or decrease in heart rate (HR), and or blood pressure (BP) and respiratory rate (RR); (b) increased intracranial pressure; and (c) long-term alterations in neuro-pathway development (Beacham, 2004; Mitchell & Boss, 2002; Mitchell, Brooks, Roane, 2000). Of particular concern is the effect of pain response on energy conservation in the preterm population, as energy conservation is of the utmost importance for both growth and healing. The multiple painful procedures premature infants experience on a daily basis deplete energy and limit growth and healing processes (Mitchell et al). Furthermore, pain triggers a stress response which destabilizes physiologic parameters and increases intracranial pressure (Mitchell & Boss). There is a decline in oxygen supply and production of stress hormones, which transfers energy from growth and healing to physiologic stabilization and impairs the functioning of the immune system (Mitchell & Boss; Mitchell et al; Walden, 2010). These factors, in turn, can increase morbidity and mortality for the preterm infant (American Academy of Pediatrics & Canadian Paediatric Society, 2006; Anand & Hickey, 1987; Anand, Phil, Hickey, 1992; Grunau & Tu, 2007; Mitchell & Boss, 2002).

High Level Processing of Pain

Prior to the 1980s it was thought that infants lacked the capability of experiencing pain (Byers & Thornley, 2004; McGraw, 1941; Zisk, 2003). However, it is now known that fetuses at 20 weeks' gestational age have the appropriate pain receptors to sense pain (Evans, 2001; Glover & Fisk, 2007; Zisk, 2003). Even as recently as 2004, it was thought that the preterm infant was unaware of pain (Zelazo, 2004). By utilizing near infrared spectroscopy (NIRS), Bartocci, Bergqvist, Lagercrantz & Anand (2006) demonstrated lateralization of pain processing of venipuncture across gestational ages (28–36 weeks) and identified the neuro-anatomical location of these pain responses. These pain responses indicate that preterm infants may be consciously processing the painful stimuli in the higher centers of the brain (Bartocci et al.). In addition, Slater et al., (2006) used NIRS to demonstrate that infants (25–45 weeks postnatal age) processed pain in the cortex and thus provided support for the possibility for pain-induced plasticity.

Acute pain is processed by the nociceptive pathways in the dorsal horn of the spinal cord (Pattinson & Fitzgerald, 2004). It has been established that ELGA infants have a beginning complement of nociceptive neurons at 24–25 weeks' gestation (Glover & Fisk, 2007). These dorsal horn neurons and their fiber connections are noted to develop continually up to 40 weeks' gestation and beyond (Pattinson & Fitzgerald). Thus, the ELGA infant's connective fibers are immature causing an ineffective modulation of pain (Evans, 2001). Descending pain pathways in the ELGA infant are present, but they lack collateral connections into the dorsal horn (Beggs & Fitzgerald, 2007). In addition, inhibitory synaptic transmissions are also immature (Beggs & Fitzgerald). It has been noted that infants at lower gestational ages have a longer latency from the time of noxious stimulus to response to the stimuli (Slater et al., 2006). Although, these infants (25–45 weeks' gestation) were noted to have a long latency from stimulus to response, they were noted to have a clear onset of response implying that pain was being processed at a cortical level (Slater, et al.).

Memory and Pain

There is growing evidence that fetuses may recollect painful experiences. Fetuses at 30 weeks' gestation were found to habituate sounds and recall these sounds for up to 10 minutes (Dirix, Nijhuis, Jongsma, & Hornstra, 2009). These same fetuses at 34 weeks' gestation were able to retain the sounds they heard 4 weeks earlier (Dirix, et al.). These findings imply that fetuses are able to recognize and possibly retain sounds as early as 30 week gestation. In addition, Grunau, et al., (1994) identified that ELGA infants who experienced repeated painful procedures may be at risk for developing somatization symptoms (unexplained stomachaches and headaches) as early as age four years. Furthermore, Taddio, Katz, Ilersich, & Koren (1997) noted that unanasthetized male infants who underwent circumcisions were more apt to demonstrate increased behavioral responses at their 4-month immunizations. Also, Peters, et al., (2003) found that toddlers who underwent negative hospital experiences (longer stays in the NICU) early in life were more apt to have increased behavioral expressions at their 14-month immunizations. These findings imply that infants who have experienced previous untreated pain may express their memories of pain through psychosomatic symptoms and atypical behavioral responses later in life. Further investigation is needed to determine if memory is possible so early in life.

Vulnerability of Brain Development

Acute or chronic pain caused by painful procedures during early neonatal life may induce alterations in anatomic, neurochemical, and physiologic features of neural pathways (Beggs & Fitzgerald, 2007). At the time of birth, underlying neurobiological mechanisms of the ELGA infant are developing. This neural growth includes building a foundation of subplate neurons, configuration, arrangement and accumulation of cortical neurons, expansion of dendrites and axons, construction of synapses, selective reduction of neurons and synapses, as well as the creation and separation of glial cells (Grunau, Holsti, & Peters, 2006). Due to neural activity and brain plasticity any maladaptive processes have the potential to cause alterations in sensory connections (Beggs & Fitzgerald, 2007). Thus, noxious stimuli in ELGA infants may cause long-term changes as a result of the extensive postnatal development of an ELGA infant's brain.

Results from studies completed on animal models show that negative effects from pain can alter both structure and function of the brain. (Grunau et al.,2006; Sternberg & Al Chaer, 2007). Repeated noxious stimulation of fibers can lead to hyperexcitability with sensitization of the dorsal horn extending well beyond the period of stimulation (Grunau & Tu, 2007). Although speculative, it is thought that the direct effects of recurrent pain over long periods of time may reprogram stress-sensitive systems which in turn may create a chronic stress state of disregulation affecting the hippocampus (Anand, Al-Chaer, Bhutta, Whit Hall, 2007). Thus, this disregulation may lead to poor self regulatory behaviors (Grunau, 2003), that may affect high order executive function in childhood (Grunau & Tu, 2007). Moreover, there is growing evidence that pain exposure can alter brain development more generally, causing a variety of long-term consequences such as: cognitive deficits, behavioral problems, poor motor performance and attention deficits (Grunau, 2002; Mitchell & Boss 2002).

Economic Cost of Pain in ELGA infants

Quantifying pain and suffering in the ELGA infant is complicated and assigning an economic cost to these concepts is difficult (Lee, 2007). It is known that care of the ELGA infant can be exorbitant. The Institute of Medicine (2006) stated that the societal economic burdens of preterm birth are estimated at a minimum of $26.2 billion or $51,600 per infant born preterm. Nearly two thirds of this cost is for medical care ($16.9 billion or $33,200 per preterm infant) (IOM, 2006). However, costs extend beyond discharge for ELGA infants due to their need for early intervention ($611 million or $1,200 per infant), special education requirements ($1.1 billion or $2200 per infant) and rehospitalization (IOM, 2006). Consequently, the cost of not attending to neonatal pain can be acknowledged in the ELGA infant's adverse long-term consequences along with the decreased quality of life from untreated pain (Lee).

Pain is a universal concern which has been extensively researched in adults and children. However, there remains a gap in the literature for the prevalence and assessment of pain in infants. Despite this fact, it can be inferred that ELGA infants have a high incidence of pain based on the number of painful procedures that they typically experience while in the NICU (Carbajal et al., 2008). This lack of assessment, intervention, and treatment of neonatal pain has implications for the physiological and psychological health of future generations.

Purpose of the Study

The purpose of this study focused on development of a psychometrically robust, reliable, valid, and clinically useful pain assessment measure for the ELGA infant population as a critical first step towards improved pain evaluation and management for these infants. The components of this project included: (1) integrating the information from a preliminary study to ascertain registered nurses perceptions of the most accurate pain cues in ELGA infants, a literature review, views of expert consultants, review of preexisting pain instruments, and the investigators' own experience; and (2) using these data and existing research findings to develop a quick, reliable, and valid pain assessment instrument with clinical utility to be used in the ELGA (24–29 6/7 week gestation) infant patient population. In sum, this study evaluated similarities and differences in pain behaviors for different gestational ages (24–33 6/7 weeks' gestation) while undergoing any invasive and non-invasive (diaper change) procedure during three conditions: baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling), using a newly developed pain assessment instrument the Pain Assessment for Care of the Extremely Low Gestational Age Infants Focused Instrument (PACEFI).

Aims

Specifically, the present study was designed to achieve the following aims:

1. To establish preliminary reliability and validity for the PACEFI instrument during an invasive procedure.

2. To evaluate whether or not 24–29 6/7 week infants exhibit the same behavioral cues as their 30–33 6/7 week counterparts during any invasive procedure baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling).

3. To evaluate whether or not 24–33 6/7 week infants exhibit different behavioral cues during a non-invasive procedure versus an invasive procedure at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling).

4. To evaluate whether or not there is a significant relationship between physiologic indicators and behavioral cues at baseline (5 minutes prior to handling), during and recovery (5 minutes after handling) for a non-invasive and invasive procedure.

Hypothesis

The study tested the following hypotheses:

Hypothesis 1. The PACEFI instrument will demonstrate preliminary reliability and validity during an invasive procedure.

Hypothesis 2. Infants 24 –29 6/7 weeks' gestation will exhibit different behavioral cues for any invasive procedure at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling) versus their 30–33 6/7 week counterparts.

Hypothesis 3. Infants 24–33 6/7 weeks' gestation will not exhibit behavioral pain cues during a non-invasive procedure at baseline (5 minutes prior to handling), during and recovery (5 minutes after handling).

Hypothesis 4. Physiologic and behavioral pain indicators for ELGA infants 24–29 6/7 weeks' gestation and VLGA infants 30-33 6/7 weeks gestation will not correlate at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling).

Operational Definition of Terms

Extremely Low Gestational Age Infant: Any infant less than 30 weeks gestation.

Very Low Gestational Age Infant: Any infant 30–33 6/7 weeks gestation.

Pain: Pain is a dynamic response to a stressor which elicits specific stress behaviors. The behavioral response to pain is a subset of behavioral stress responses and varies as a function of neuro-development. ELGA infants are nonverbal; thus; pain expression is indicated through behavioral responses such as facial expressions and extremity movements.

Painful Procedures: Painful procedures are identified as procedures that include actual or potential tissue damage (IASP, 2003).

Snap II Illness Severity Score: The Snap II instrument is a 6-item measurement instrument that determines illness severity in infants (Richardson, Corcoran, Escobar, 2001).

Behavioral cues: Behavioral cues are cues exhibited by infants to express pain. The behavioral cues included in this study are: crying, grimace, nasolabial bulge, furrowing, eye squeeze, mouthing, lips pursed, stretch mouth, Taut Tongue, Push away arms, push away legs, pull away arms, pull away legs, full body pull away, pull extremities midline, hands on face, fisting, finger splay, curling toes, and sit on air. (Appendix D).

Physiologic cues: Physiologic indicators included in this study are heart rate, respiratory rate and oxygen saturation.

Assumptions

This study assumes that nurse raters will be able to identify behavioral cues in infants less than 34 weeks' during all invasive and non-invasive procedures. Furthermore, it is assumed that the behavioral cues for infants 24–29 6/7 weeks' will be different than their 30–33 6/7 week counterparts.

Significance of the Study

Over the past 10 years, there has been an initiative for change in practice resulting in a dramatic improvement of pain assessment in infants. Despite these advances, pain assessment for the ELGA infant remains challenging for clinicians. It has been established that ELGA infants continue to be under assessed, poorly managed, and under-treated for pain relief (Sinno et al., 2003; Stevens, Pillai, Riddell, Oberlander, Gibbins, 2007c). Although one goal of nursing is prevention and/or alleviation of pain, there remains a gap between knowledge and practice related to pain assessment for ELGA infants (Stevens et al). Currently, there is a need for a better understanding of pain and pain behaviors as well as improved assessment, prevention, and management strategies for the ELGA infant.

Many of the challenges in pain assessment for ELGA infants can be attributed to their neurological immaturity (Stevens et al., 2007c). The ELGA infant's neurologic immaturity can lead to nurses misunderstanding infant pain, further complicating what nurses consider as evidence in expression of pain for these infants. Additionally, existing pain measures have excluded the ELGA infant thus limiting clinicians and researchers' assessment of infant pain (Stevens et al., 2007c). Development of nursing knowledge relevant to pain assessment for the

ELGA infant is essential given that it will decrease pain and suffering while promoting the ELGA infants' well being. Development of a theoretically derived, developmentally appropriate, reliable and valid clinically useful pain assessment instrument with demonstrated reliability and validity that can guide nurses with their pain assessment specific to the ELGA infant is essential. Pain prevention and/or alleviation remain the primary goal for nursing care of these infants (Francis, 2011). Chapter 2 will provide a review of the salient challenges to assessment of ELGA infant pain.

Chapter 2

Review of the Literature

This chapter reviews existing research that examines pain assessment and measurement related to 24–29 6/7 week infants' physiologic and behavioral predictors, current pain assessment for these infants, and the challenges that influence pain assessment in ELGA infants. The specific area of concern for this study is the inadequacy of existing pain assessment instruments and the need to develop and test a new measure.

Four Major Limitations to Pain Assessment in the ELGA Infant

A review of the literature regarding existing pain assessment instruments found four major limitations for pain assessment for the ELGA infant including: (1) challenges to nurses assessment of pain for the ELGA infant; (2) difficulty in recognizing behavioral indicators of the pain response for ELGA infants; (3) lack of reliable, valid, and clinically useful pain assessment instruments for the ELGA infant; and (4) unreliability of multidimensional pain assessment instruments for the ELGA infant.

1. Challenges to nurses' assessment of pain for the ELGA infant. First, no single pain assessment instrument is universally used in the NICU (Stevens Anand, McGrath., 2007b; Beacham, 2003; Blauer & Gertsman, 1998; Spence, Gillies, Harrison, Johnston, & Nagy, 2003), and nurses do not use cues incorporated into existing assessment instruments (Fuller, 1998; Reyes, 2003). To date, neonatal pain remains inconsistent with regards to assessment and documentation (Gallo, 2003; Polkki, Korhonen, Saarela, Vehvilainen-Julkunen, Pietila, 2010; Reyes, 2003). Both a lack of understanding of neonatal pain and the difficulty of performing assessments in the ELGA population contribute to the problem (Brown & Timmins, 2005; Fuller, Neu, & Smith, 1999; Gallo, 2003; Page, 2004). The ability of nurses to identify pain in neonates is crucial for pain management. However, there is little agreement among nurses as to what behavioral and/or physiologic cues indicate pain for the preterm population (Brown & Timmins, 2005; Fuller et al., 1999; Halimaa et al., 2001; Reyes; Rouzan 2001). Bradshaw & Zeanah (1986) noted that pediatric nurses use different types of cues based on nine categories (physiologic, affect, body language, oral sounds, withdrawal, anxiety, irritability, depression, and parental judgment) some of which are not captured in current pain assessment instruments. In addition, Reyes (2003) noted nurses (*n*=24) agreed that pain was often unrecognized, ratings were inconsistent, and pain instruments were unclear as to rating pain intensity. Jacob & Puntillo (1999) reported that cues most frequently used by nurses for pain assessment included facial expression, body language and physiological signs. Although, some evidence suggests that nurses may not rely on infant behavioral cues for pain assessment and subsequent decisions about medication administration (Hudson-Barr, Duffey, Holditch-Davis, Funk, & Frauman, 1998). There are a number of possible explanations for the lack of assessment of behavioral cues including a lack of knowledge as to what constitutes pain symptoms in infants and a lack of education in the use of existing tools (Halimaa et al.; Rouzan; Salantera, 1999).

There remains an ongoing conflict regarding what type of painful stimulus merits treatments with analgesia for pain versus comfort measures for agitation (Dick, 1993). This confusion concerning pain treatment versus comfort measures may contribute to the under-treatment of pain in infants (American Academy of Pediatrics & Canadian Paediatric Society, 2006). Reluctance to use analgesia may be due to concern regarding potential side effects, and a lack of awareness of clinical situations that may inflict pain (Mathew & Mathew 2003). However, a key contributing factor to under-treatment is the lack of developmentally appropriate, brief, and valid pain assessment measures that can be readily incorporated into nursing practice for the ELGA population (Holsti & Grunau, 2007; Reyes, 2003).

2. Difficulty in recognizing behavioral cues of the pain response for ELGA infants. Second, many pain instruments do not take into consideration gestational age. The lack of consideration for gestational age differences is a contributing factor to the first limitation regarding challenges for nursing pain assessment in the ELGA population. The need for gestational age-specific assessment tools is supported by numerous studies showing that physiologic and behavioral responses to pain in infants differ across gestational age groups (Gibbins et al., 2008b; Johnston et al., 1995; Morison, Grunau, Oberlander, & Whitfield, 2001). Neurologic immaturity in ELGA infants contributes to the lack of specific pain response that can be seen in their VLGA infant and full-term counterparts. Fitzgerald, Shaw, & MacIntosh (1988) found that cutaneous reflexes are established in infants less than 27 weeks' gestation. The less mature infant had a more diffuse response, while the more mature infant could isolate the pain and elicit a specific response (Fitzgerald et al.). The diffuse response suggests that at younger ages infants may be unable to distinguish and direct a specific response. In addition, Andrews, Desai, Dhillion, Wilcox and Fitzgerald (2002) found that unilateral abdominal stimulus performed on neonates (30–41.2 weeks' gestation) induced bilateral hip flexion in younger infants. It was noted that as the infants matured, limb flexion decreased to unilateral flexion leading eventually to no movement of either hip (Fitzgerald et al., 1988). This maturation is indicative of increasing neuronal organization with older post-conceptual ages. Physiologic parameters such as heart rate (HR) and oxygen saturation are easily available parameters for infant pain assessment. However, alone these parameters may be non-specific to pain as they increase or decrease based on many other factors influencing infants (Ranger, Johnston, &

Anand, 2007). Gestational age, prior painful experience, and illness severity all contribute to an infant's response to pain (Grunau, Oberlander, Fitzgerald, Lee, 2001; Morrison et al., 2001; Pineles, 2007). Pineles (2007) found that preterm infants (28–32 weeks' gestation) developed a decreased pain threshold or sensitization with additive painful procedures for HR but not for behavioral responses. Additionally, Walden et al. (2001) noted that heart rate increased during a heel stick procedure and remained elevated at the recovery phase for the less than 27 week infant group, while infants above 27 weeks returned to baseline, indicating that the less mature infants may remain in a hypersensitive state. Furthermore, Luca-Thompson et al. (2008) compared younger born infants (28-31 weeks gestation) to older born infants (32-34 weeks gestation). The older born infant group demonstrated better regulation of their physiologic response. In addition, both groups demonstrated increased behavioral cues for the heel stick procedure. However the younger born infant group demonstrated less self soothing behaviors as compared to their older born infant counterparts at 3-5 weeks after birth. These studies suggest that ELGA and full-term infants have differing behavioral and physiologic responses to pain related to their neuro-development

In general, full-term infants have a more robust reaction to pain whereas preterm infants can have a dampened response, which may in turn mask the fact that they are in pain (Barr, 1998; Shapiro, 1993; Stevens et al., 2007c). For example, ELGA infants often become lethargic and listless when coping with overstimulation that may result in pain leading to an artificially lower pain score (Boyd, 2003; Grunau, 2002). The Neonatal Pain, Agitation, Sedation Scale (NPASS) (Hummel, & Pulchalski, 2003); and the Neonatal Infant Pain Scale (NIPS) (Lawrence, Alcock, McGrath, Kay, MacMurray, Dulber, 1993) are scales developed for infants that do not appropriately capture the lack of response from ELGA infants after repeated exposure to painful stimuli (Boyd, 2003).

A combination of illness severity and a high number of treatment procedures (Beacham, 2003; Oberlander & Saul, 2002; van Dijk, Peters, Bouwmeester, Tibboel, 2002) may cause the infant either to “shut down” (Als, 1982) or to become hypersensitive to painful stimuli. Infants undergoing painful procedures may deplete their energy reserve which triggers them to “shut down” in order to conserve energy (Als). It is not clear whether the “shut down” (Als) response constitutes a chronic pain response or an acute procedural pain response in a fatigued infant. In addition, the current state of the science regarding pain in ELGA infants is so underdeveloped that it provides no distinction between acute and chronic pain responses (Stevens et al., 2007c), and does not even support that such a distinction can be made given the early stage of ELGA infants’ neurodevelopment. While it is known that early and cumulative pain experiences in ELGA infants are associated with a decrease in the intensity of behavioral responses over time (Grunau, 2002). This diminished response does not necessarily mean that there is a decrease in the immediate experience of pain because, as previously noted, these infants have not developed the nerve fibers that can inhibit pain. Without the proper inhibitive neural circuitry infants will not be to able modulate or even stop the pain (Evans, 2001).

Although ELGA infants may have a less robust reaction to pain than full-term infants or even their VLGA infant counterparts, there is clear evidence in the literature that behavioral cues can be identified in these infants. For example, Gibbins et al. (2008b) found that although infants less than 27 weeks’ gestation did not have a significant increase in baseline heart rate after heel stick, they did demonstrate a number of behavioral responses to painful procedures including brow bulge and eye squeeze. Holsti, Grunau, Oberlander, & Whitfield (2004) found that eight behavioral pain cues (fisting, finger splay, hands on face, frowning, and flexion of arms and legs, extension of arms and legs) were identified in infants less than 30 weeks' gestation, including ELGA infants. Johnston et al. (1995) noted that 26-week gestation infants responded differentially to a sham heel stick versus a true heel stick. This indicates that ELGA infants are capable of differentiating acute sharp pain and exhibiting signs of pain specifically through behavioral cues. In contrast to behavioral responses, variability of heart rate (HR) in pain response in the ELGA infant has been shown to be dependent on previous pain experience. ELGA infants can have heightened HR reactivity when handled prior to painful procedures (Grunau et al., 2001). The heightened heart rate implies that previous painful experience may sensitize infant physiology that promotes a negative feedback loop in which an infant may have HR increases with both painful and non-painful stimuli (Grunau et al.; Holsti, Grunau, Oberlander, Whitfield, 2005). While physiologic cues such as heart rate and respiratory rate may augment the nurse's assessment of pain, both heart rate and respiratory rate may not be specific to pain in the ELGA population (Stevens et al., 2007c).

3. Lack of reliable, valid, and clinically useful pain assessment instruments for the ELGA infant. Challenges the nurse encounters in pain assessment and the lack of gestational age specific instruments contribute to the third limitation concerning pain instruments' lack of reliability, validity, and clinical utility for the ELGA population (Boyd, 2003; Stevens et al., 2007c). Although there are an abundance of pain instruments in the literature that have been evaluated for preterm infants and many of these instruments state that they are appropriate for the ELGA infant, this premise remains insufficiently tested.

Instruments developed for preterm infants include: the Behavioral Indicators of Infant Pain (BIIP) (Holsti & Grunau, 2007b); the Echelle Douleur Inconfort Nouveau-ne, Neonatal Pain and Discomfort Scale (EDIN) (Debillon et al., 2001); the Neonatal Facial Coding System (NFCS) (Grunau & Craig, 1987); the Neonatal Infant Pain Scale (NIPS) (Lawrence et al.,1993); the Neonatal Pain Agitation and Sedation Scale (NPASS) (Hummel & Pulchaski, 2003); Pain Assessment in Neonates (PAIN) (Hudson-Barr et al., 2002); and the Premature Infant Profile (PIPP) (Stevens, Johnston, Petryshen & Taddio,, 1996). All instruments demonstrate limitations (See Appendix A). These limitations include lack of supportive data for reliability and exclusion of 24–26 week infants from the sample (i.e., the PIPP, PAIN, NPASS, BIIP) along with complexity of these instrument (i.e., the NFCS, PIPP) (Boyd, 2003; Koeppel, 2002). In addition, many of these existing instruments address pain assessment for older infants by incorporating behaviors that are not readily seen in the ELGA infant. Items chosen for existing pain scales include robust cry (NIPS, NPASS, PAIN), behavioral state (BIIP, NIPS, NPASS, PAIN, PIPP), physical activity (restlessness, squirming) (EDIN, NIPS, NPASS, PAIN), and consolability (EDIN, NPASS) (Boyd, 2003; Duhn & Medves, 2004).

Reliability and validity testing generally has been done with infants 32 weeks and above (Stevens et al., 2007c). The BIIP which is a pain measure for preterm infants was validated on 23–32 week infants. However, 88 infant assessments were completed at 32 weeks and an additional 12 assessments were completed; and of those assessments only four were for ELGA infants (Holsti, Grunau, Oberlander & Osiovich, 2008). The NIPS was validated on infants with a mean gestational age of 33.5 weeks; the PIPP was validated on infants above 28 weeks; the NPASS validated 13 infants less than 28 weeks, the PAIN scale was validated with 15 infants less than 28 weeks with a mean gestation age of 33 weeks; and the EDIN was validated on infants with a mean gestational age of 31.5 weeks (Hummel, Puchalski, Creech, & Weiss, 2008; Debillon et al., 2001; Hudson-Barr et al., 2002; Stevens et al., 1996; Lawrence et al., 1993). The fact that the majority of the validation studies were done on older gestational-aged infants brings into question the generalizability of the results to the ELGA population.

Many instruments, which have reliability and validity, have little evidence of clinical utility. This lack of clinically useful instruments may be due either to the length of time required to complete the test with the instrument and/or the complexity of scoring (Marceau, 2003). For example, the Premature Infant Pain Instrument (PIPP) and the Neonatal Facial Coding System (NFCS) are cumbersome tools in terms of scoring and length of time for completion (Boyd, 2003; Koeppel, 2002). The PIPP was developed for use in both the clinical and research arenas. Components of the PIPP include gestational age, heart rate, oxygen saturation, behavioral state, and three components of the cry face. (See Appendix A.) This tool can be challenging to use because it requires a 10-step process whereby the nurse assesses pain prior to the painful procedure (baseline), during and 30 seconds after the procedure, with subsequent mathematical calculations to establish a score (Koeppel, 2002). The Neonatal Facial Coding System (NFCS) has behavioral indices and is also quite complex to apply. (See Appendix A.) It requires extensive training and is considered to be time consuming (Boyd, 2003), and for that reason use is primarily limited to research (Stevens et al., 1996). Like the PIPP the NFCS has established reliability and validity but requires multiple training sessions for reinforcement of scoring reliability (Boyd, 2003).

4. Unreliability of multidimensional pain assessment instruments for the ELGA infant. As discussed earlier, challenges in nursing pain assessment, the lack of a gestational age-specific instrument, and the paucity of a reliable, valid, and clinically useful instrument factor into the fourth major limitation regarding multidimensional instruments. Multidimensional instruments incorporate both physiologic and behavioral pain cues, while unidimensional instruments incorporate behavioral pain cues. The ELGA infant's physiologic variability presents a dilemma for multidimensional pain instruments. For example, variability of heart rate in response to painful stimuli has been shown to be dependent on previous pain experience in the ELGA infant (Grunau et al, 2001; Holsti et al, 2005; Morison et al., 2003). Holsti et al. (2005) found that 29-week infants assessed at a post-conceptual age of 32 weeks had heightened heart rate reactivity when handled prior to painful procedures. These results imply that previous painful experience may sensitize infant physiology and promote the "windup phenomenon" (Anand, 2000; Sternberg & Al Chaer, 2007; Woolf, 1996). This phenomenon involves purposeful stimulation causing sensitization of the dorsal horn which extends beyond the painful procedure and causes a state of increased and prolonged stress in the infant (Anand; Morison et al.; Jennings & Fitzgerald, 1998; Sternberg & Al Chaer; Woolf).

A literature review conducted by Franck and Miakowski (1997) noted that heart rate increases with both painful and non-painful stimuli. Furthermore, Gibbins et al. (2008b) noted that ELGA and full-term infants (*n*=149) did not have a significant change from their baseline HR during the heel stick phase. Due to the inconsistencies in physiologic responses, these responses should not be used alone to verify presence or absence of pain, as they are not specific to pain (Gibbins et al., 2008). The variability in infants with regard to physiologic response creates complexity in nursing assessment of pain. The variation in physiologic response suggests that combining physiologic and behavioral scores into one pain score may cloud assessment of an infant's true pain response due to the lack of specificity for heart rate (Holsti, et al, 2007b; Johnston et al., 1995; Morison et al., 2001). The blurring of an infant's true pain score indicates that multidimensional instruments may under or overestimate pain in the ELGA population. In addition, as previously stated, differences in state can alter pain response which argues for assessing physiologic and behavioral pain cues independently. Scores which are confounded by items that are not consistently measuring the same constructs are not reliable. In other words, the boundaries of the construct should be clear so that the items in the scale do not unintentionally drift into unintended domains (i.e., pain versus stress) (DeVellis, 2003). The unreliable instrument in turn could promote systematic errors in the scores that may be a factor in under- or over-medicating for pain due to inaccurate pain scores which is of great concern with regards to the ELGA infant neurodevelopment. Presently, there is no single pain assessment measure that is universally accepted in the NICU (Stevens et al., 2007c). There have been many attempts to place pain items in an instrument based on general pain behaviors for all gestational ages. Yet, current neonatal pain assessment instruments cannot distinguish pain behaviors for the ELGA infant along a continuum for low versus high pain. ELGA infants may be classified on a scale that does not capture their identifiable behaviors to pain without proper identification of developmentally appropriate pain behaviors.

Theoretical Framework

The Synactive Theory of Development was selected as the theoretical framework to guide this study due to its fit with the conceptualization of pain in ELGA infants used in this study. It is well established in the literature that ELGA and VLGA infants are able to demonstrate behaviors associated with pain (Fitzgerald, Shaw & Macintosh, 1988; Gibbins et al., 2008; Holsti et al., 2004). As previously stated, expression of pain behaviors directly correlates to an infant's neurodevelopmental maturity hence their gestational age (Fitzgerald et al., 1988; Gibbins et al., 2008b). Different gestational age infants (younger gestational age to older gestational age) exhibits pain behaviors along a neurodevelopmental continuum. Pain is conceptualized as a stressor impacting development and eliciting stress behaviors. Hence the behavioral response to pain is viewed as a subset of behavioral stress responses and varies as a function of neurodevelopment.

Als (1982) Synactive Theory of Development (STD) provides a useful framework for anticipating pain expression as a function of neurodevelopment. The STD framework identifies the individuality and specificity with which an infant navigates the developmental process (Als). Infant development focuses on how an individual infant appears to handle their environment (Als). The synactive component of the theory assesses the capacity of an infant to adapt, adjust and differentiate the five subsystems including autonomic, motor, state regulatory, attentional/interactional, and self regulatory which are interrelated with each other and the environment (Als).

The STD allows clinicians to recognize both stress and pain in infants and appropriately intervene with organizational strategies for that individual infant (Holsti et al., 2004). The five various subsystems discussed exist together, constantly interacting and regulated by the infant based on the infant's ability to maintain a balance with each subsystem (Als, 1982). Each subsystem is responsible for a set of self-regulatory behaviors (See Table 1).

Table 1

Self Regulatory Behaviors of the Infant

Autonomic Stability	Motoric Stability	State Stability and Attentional Regulation
Even respiration Appropriate color Feeding well/gaining weight	Normal posture Normal tone Coordinated movements	Differentiated sleep states Balanced crying Self calming Active alertness

Adapted from: Als, H. (1982). Toward a Synative Theory of Development: Promise for the Assessment and Support of Infant Individuality. Infant Mental Health Journal, 3 (4), 229-243.

As described by Als (1982), while in utero the uterus provided a protective environment allowing soft subtle movements for the infant, while the amniotic fluid provides muffled sensory inputs (Als). After birth the ELGA infant is unable to regulate many of the subsystems due to the infant's neurodevelopmental immaturity (Als). Often medical technology must take over regulation of the autonomic system, while the preterm infant is left to adjust to extrauterine life (Als). Frequently, the ELGA infant will "shut down" to try and regain strength (Als). If the infant is unable to adapt to the new environment disorganization of the subsystems may occur (Als). Dysregulation of the subsystems may cause extended pain, which may affect developmental processes such as regulation of attention, arousal and emotion (Grunau & Tu, 2007). Hence, an ELGA infant in pain without proper strategies to organize may be at risk for neurodevelopmental disturbances. If this disorganization continues, it can lead to a cycle of increasing stress and maladaptive behavior (Grunau & Tu, 2007). This in turn may place the infant at future risk for organizational and attention deficits (Grunau, 2002; Mitchell & Boss 2002).

The preterm infant and full-term infant have different developmental timetables (Als, 1982). The full term infant is organizing and working towards increasing their alert state, while the preterm infant may not be capable of that task and spends the majority of the time in a quiet sleep state (Als). The full term infant responds robustly to noxious stimuli, while the preterm infant has a dampened response (Gibbins et al., 2008b; Stevens et al., 2007c). Infants express behaviors along a continuum running parallel to their neuro-development. According to Als (1982), infants at 13–16 weeks' gestation in utero are opening and moving their eyes, at 17–20 weeks' gestation they have coordinated hand to face actions, 21–24 weeks' gestation they have fast eye movements, and at 28–31 weeks' gestation they have complex extremity movement. Additionally, the sensory and stress response of the fetus includes: reacts if touched on the lips at 8 weeks; reacts if touched on face at 12 weeks; places hand on mouth and may suck thumb at 13 weeks; reacts if the body is touched at 14 weeks; reallocates blood to the brain at16 weeks; produces norepinephrine and endorphin at 18 weeks; responds to sounds and external light stimulus, can produce a cortisol response at 20–26 weeks; and heart rate can react to sound at 28 weeks (Glover & Fisk, 2007). Current literature demonstrates that it is likely infants have the necessary anatomical pathways for pain awareness at 26 weeks with immature pathways in place at 20 weeks, indicating that infants feel pain (Glover & Fisk).

There is clear evidence that ELGA infants can react to pain (Stevens et al., 2007c; Gibbins et al., 2008; Johnston et al., 1995). Gibbins et al (2008b) demonstrated similarities in pain response for ELGA infants (23–28 weeks' gestation) during a painful procedure. Although, all infants showed the same responses to the painful procedure, the least mature infants showed less of a response (Gibbins et al., 2008b). Facial activity represents the most specific indicator for pain response in neonates across gestational ages (Stevens et al., 2007; Walden, 2010). In addition preterm infants display more generalized motor extensions of their extremities along with fingersplay, fisting, hands on face, and sit on air (Holsti et al., 2004; Walden, 2010). However, if repeated behavioral or physiologic cues go unanswered the infant may become energy depleted and shut down their response (Barr, 1998; Ranger et al., 2007). Alternatively, full term infants have a more robust response with crying and swiping movement from the unaffected limb to push noxious stimuli away (Walden, 2010). In general preterm infants albeit diminished can mount a response to pain (Gibbins et al., 2008b).

Als (1982) developed The Newborn Individualized Developmental Care and Assessment Program (NIDCAP) based on the Synactive Theory of Development Model. This developmentally sensitive program provides a detailed behavioral catalog of 85 infant stress behaviors. While it is clear that pain is associated with stress behaviors, not all stress behaviors are a response to pain (Craig, Whitfield, Grunau, Linton, Hadjistavropoulos, 1993). Holsti et al.

(2004) have identified stress behaviors uniquely related to acute pain including: finger splay, fisting, hand on face, frowning (brow lowering), flexing of arms and legs, and extension of arms and legs, sleep/wake state, and change in heart rate. These stress behaviors are reflected in the STD (See Table 2). Unfortunately, it is not clear if any of these eight behaviors correspond to the cues nurses look for or rely on in their intuitive assessment of neonatal pain, or whether these eight behaviors can be placed along a neurodevelopmental continuum.

Table 2 includes behaviors that Als (1982) has identified as stress and are indicated with a (♦). Behaviors that Holsti et al. (2004) have identified as uniquely related to acute pain are indicated with an asterisk (*). All of these behaviors have been incorporated into the initial draft of the PACEFI (See Appendix B) along with behaviors itemized in pain instruments as indicators of pain i.e. Neonatal Facial Coding System (○), Neonatal Pain Agitation and Sedation Scale (♠), and The Premature Infant Pain Profile (●) (Boyd 2003). All other behaviors are based on the applicant's clinical experience and insights.

Table 2

Pain Behaviors Incorporated into the PACEFI

Autonomic	Motoric	State-Related
Full Body Pull Away ♦	Eye Squeeze ● ○ Frown ● ○ Grimace ♦ ○ Nasolabial Bulge * ● ○ Lips pursed ○ Mouthing Stretched Mouth ○ Taut Tongue ♦ ○ Flexion Arm, Leg * ♦ Extension Arm, Leg * ♦ ♠ Extremities to Midline Fingersplay * ♦ ♠ Fisting * ♠ Salute Hands on Face * ♦ Sit on Air ♦ Toe Curl ♠	Crying ♦ ♠

Summary

ELGA infants experience hundreds of painful procedures as part of the life saving care they need to survive (Carbajal et al., 2008). Unfortunately their neurodevelopment renders them highly vulnerable to pain and its long-term effects. They are both unable to regulate the painful experience and may be most at risk for long-term consequences such as cognitive deficits, behavioral problems, poor motor performance and attention deficits due to the effects of painful stimuli on their developing neurological system (Grunau, 2002; Grunau & Tu, 2007).

Performing accurate pain assessment is a prerequisite to preventing long-term consequences in the ELGA infant (Stevens et al., 2007b). Yet, nursing assessment of pain remains a challenge for many reasons including: the neurological immaturity of the ELGA infant, a lack of reliable, valid pain measures for use with ELGA infants, confusion with existing pain measures for differences in physiologic versus behavioral pain cues, and a lack of clinical usefulness of instruments. To date the state of the science prevents nurses from quickly and validly assessing pain in ELGA infants. Neonatal pain is detrimental for infant development (Grunau, 2002; Mitchell & Boss 2002). Nurses' quick and accurate assessment of pain is essential for an infant's well-being. Until a developmentally appropriate reliable, valid, and rapid assessment instrument is developed for this population, nurses will not be able to accomplish their goal at preventing and/or alleviating pain.

This project addressed the need for a theoretically based, developmentally appropriate, rapid pain assessment instrument for the ELGA population through a three step process. First, the information from a preliminary study to ascertain registered nurses perceptions of the most accurate pain cues in ELGA infants, a literature review, views of expert consultants, review of preexisting pain instruments, and the investigators own experience was incorporated into development of the new instrument for ELGA infants. Second, these data were combined with existing research findings to develop a reliable and valid pain instrument which focused on the ELGA infant. Third, data were collected to determine frequency of pain behaviors for different gestational; ages (24–33 6/7 week infants) during any invasive a non-invasive procedure under three different pain conditions (i.e. 5 minutes prior handling, during, and 5 minutes after handling).

Chapter 3

Methods

Overview

This study addressed the following specific aims (1) to establish preliminary reliability for the PACEFI instrument; (2) to evaluate whether or not 24–33 6/7 week infants exhibit the same behavioral pain cues for an invasive procedure (3) to evaluate whether or not 24–33 6/7 week infants exhibit the same behavioral cues for a non-invasive procedure; and (4) to evaluate whether or not physiological pain indicators correlate with behavioral pain cues on the PACEFI.

Design

An observational descriptive design was utilized to evaluate beginning reliability for the PACEFI for the ELGA and VLGA infant population. Nurse raters completed a preliminary version of the new pain assessment instrument, the PACEFI (see Appendix D) to measure pain exhibited by ELGA and VLGA infants who underwent any invasive procedure (i.e., heel stick) or a non-invasive procedure (i.e., diaper change) for three pain conditions (i.e., at 5 minutes prior to baseline, during, and 5 minutes after handling). This preliminary version of the PACEFI incorporated cues from current pain instruments developed for preterm infants, nurses' perceptions of the most reliable pain cues in the ELGA infants (preliminary study), infant observations based on clinical experience of the principal investigator (PI), and the literature.

This study was conducted at an 18-bed, level III neonatal intensive care unit (NICU) and a 13-bed, level II nursery in a large metropolitan hospital in Massachusetts. Research approval was obtained from Boston College Institutional Review Board and the Partners Human Research Committee prior to conducting the proposed investigations. A waiver for written, informed consent was granted in accordance with the Partners Human Research Committee and Boston College Institutional Review Board.

Sample

A purposive sample was drawn from a population of ELGA and VLGA infants who were 24–33 6/7 weeks gestation in a large metropolitan level III NICU and level II nursery. The most recent center specific statistics available for very low birth weight infants (< 1500 grams) indicate there were a total of 66 admissions to the Massachusetts General Hospital NICU in 2008 (Vermont Oxford, 2008). Center specific statistics by birth weight in 2008 include: 4.5% infants < 501 grams, 1.5% infants 501–600 grams, 4.5% infants 601–700 grams, 4.5% infants 701-800 grams, 9% infants 801–900 grams, 6% infants 901–1000 grams, 12% infants 1001–1100 grams, 9% infants 1101-–1200 grams, 11% infants 1201-–1300 grams, 20% infants 1301-–1400 grams, 18% > 1400 grams (Vermont Oxford, 2008).

This NICU afforded a sufficient pool of ELGA infants (approximately 50 in an 8-month period) from which to collect data. The pool of ELGA infants was estimated using the weekly census for 1 month and projecting admissions of ELGA infants over a 6-month period for the study site.

Inclusion Criteria. ELGA infants between 24–33 6/7 weeks during the first 14 days of postnatal age were included.

Exclusion Criteria. Infants were excluded if they had any of the following conditions: congenital heart disease, chromosomal syndromes or genetic anomalies (e.g., anacephalic, spina bifida, mylomenigecele, hydrocephalus), or significant central nervous system abnormalities (e.g., congenital or acquired, including greater than a grade III intraventricular hemorrhage). Infants who were withdrawing from maternal drug use were also excluded due to the side effects of the medications (e.g., Ativan, Phenobarbital) required to treat these infants.

An a priori power analysis was conducted to determine sample size to ensure protection from Type I and II statistical errors for the proposed research. The software program G-Power, version 3.1.3, was utilized to determine an appropriate sample size for a repeated measures ANOVA and Pearson Product-Moment correlations (Faul, Erdfield, Lang & Buchner, 2007). A sample size of 28 infants was determined sufficient for the RANOVA analysis based on a small effect size of .25, a power of .80 and an alpha of .05. However, a sample size of 80 infants was needed based on a correlation of .3, a power of 80 and an alpha of .05 for a two tailed test. Although, this study analysis was under-powered (n = 31) the results are discussed due to the exploratory nature of the study.

Gestational age groups were collected and placed into two groups: the ELGA group (24–29 6/7 weeks gestation) and the VLGA group (30–33 6/7 weeks gestation). Two separate PACEFI pain ratings (non-invasive, invasive) were required for each ELGA and VLGA infant during the three different pain conditions (i.e., 5 minutes prior baseline, during, and 5 minutes after handling) to capture any differences in non-invasive and invasive behaviors present for the three pain conditions.

Materials

Demographic Characteristics of Infants (See also Appendix B). Demographic data of infants was collected by the nurse rater using a demographic questionnaire to guide chart review (see Appendix B). The demographic data identified through chart review included the following variables: gestational age at birth, birth weight, gender, Score of Neonatal Acute Physiology-II (SNAP-II), number of painful procedures preceding the observation window (birth to observation) for PACEFI scoring, cranial ultrasound results, narcotic or other analgesic exposure, and respiratory support (Holsti et al., 2007b). Total intravenous morphine from birth was calculated using the average daily dose of IV morphine multiplied by the number of days on IV morphine (adjusted for daily weight) as recommended by Holsti et al. (2007b). Painful procedures preceding the observation window for PACEFI scoring are defined as any of the following: intubation, heel stick, venous stick, tape removal, umbilical catheter placement, percutaneous line placement, arterial stick, suctioning (ETT and nasopharyngeal), nasogastric tube placement, lumbar puncture, extubation, intramuscular injection, and intravenous line placement. These painful procedures were included given that multiple studies have shown that an accumulation of painful procedures correlate to a dampened pain response in the ELGA infant (Gibbins et al., 2008b; Grunau, 2002; Grunau et al., 2001).

Physiologic data (heart rate, respiratory rate, and oxygen saturation) was collected at one time point during each rating (5 minutes prior baseline, during, 5 minutes after recovery). Although physiologic and behavioral pain indicators should not correlate for pain expression in ELGA infants, the current state of the science regarding pain in ELGA infants is underdeveloped and further inquiry is needed.

Demographic Characteristics of Nurse Raters (See also Appendix C). Demographic characteristics of nurse raters were assessed using a self-administered demographic questionnaire. The demographic data included the following: gender, age, degree earned, certifications, years of experience as a registered nurse, and years of experience in the NICU. This information was collected to identify if differences exist among ratings using, experienced expert nurses (greater than 5 years experience in a NICU or Level II nursery).

Procedure

Development of the Pain Assessment and Care of Extremely Low Gestational Age Infants Focused Instrument (PACEFI) (See also Appendix D). The PACEFI is a new instrument that is designed to assess pain in the ELGA infant. The PACEFI instrument was developed using the information from a preliminary study to ascertain the registered nurses perceptions of the most accurate pain cues in ELGA infants, a literature review, views of expert consultants, review of preexisting pain instruments, and the investigator's own experience. The PACEFI is a 20-item dichotomous (yes/no) procedural pain assessment instrument that assesses behavioral cues an ELGA infant may exhibit during a painful procedure (see Appendix D). ELGA infants (24–29 6/7 weeks) were observed at two separate times (invasive, non-invasive) and each item was scored for frequency (i.e. no, it was not observed (0); yes, it was observed (1)). Infants are scored as "no pain" (0) if they do not exhibit any behaviors described by PACEFI items. Demographic data collected on the PACEFI include: hospital pain instrument in use, hospital pain score before and after the painful procedure, nonpharmacological interventions, last type of handling, last time of handling, and infant position. For the purpose of this study preliminary reliability was determined. Further investigation for goodness of fit of the items will be determined in future studies.

The Score of Neonatal Acute Physiology II (SNAP-II Score). The Snap-II score is a standardized score predicting illness severity and mortality risk for preterm infants. Six physiologic variables (temperature, blood pressure, PaO_2/fraction of inspired oxygen ratio, serum pH, seizures, and urine output) are collected within the first 12 hours of life (Richardson, Corcoran, Escobar, 2001). Scores can range from 0–115; higher scores reflect sicker infants (Richardson et al.). The SNAP-II score was determined to have a high predictive (0.91) and criterion (0.90) validity (Richardson et al.). Scores below 30 signify low illness; severity scores above 30 signify high illness (Dammann et al., 2009).

Piloting of the PACEFI

The PACEFI was trialed by two nurse raters. The nurse raters observed videotapes of 28-week gestational age infants. Ratings were completed on four different infants. The preliminary ratings were completed to determine if the PACEFI was easy to understand and complete within the time frame of 5 minutes specified in the study. The PACEFI was well understood and easy to complete.

Raters & Rater Training

The Principal Investigator, a clinical nurse specialist (CNS), a nursing director (ND) and two level II staff nurses were asked to serve as raters. Of the four raters, only the two staff nurses actually rated infants due to time constraints of the CNS and ND. These raters were registered nurses and had a minimum of 5 years of practice in a level II nursery. The form used to collect PACEFI rating data also identified which nurse rater completed the PACEFI.

All nurse raters attended an orientation session provided by the PI which included a guide for the PACEFI. As part of this training, nurse raters were taught how to observe for pain cues using pictures of infants exhibiting behaviors associated with pain in a PowerPoint presentation. Once the pictures were rated by the nurse raters individually, these ratings were then compared and discussed. In addition the PI scheduled drop in sessions where both the PI and nurse raters observed the same infant and independently rated the PACEFI, ratings were then compared and discussed. This technique is usual practice in teaching pain assessment to nurses (Gallo, 2003; Ista, van dijk, Tibboel, & de Hoog, 2005). The explanation and practice session lasted approximately 30 minutes.

Infant Identification and Observation of ELGA Infants

Infants were identified by the PI rounding in the NICU and level II nursery every morning and afternoon. Infants who met inclusion criteria were independently rated by the nurse rater with the PACEFI during observation of routine invasive and non-invasive patient care procedures. Invasive procedures are identified as procedures that include actual or potential tissue damage (i.e., heel stick or endotracheal tube (ETT) suctioning) (IASP, 2003; Evans, McCartney, Lawhon, & Galloway, 2005). Heel stick, ETT suctioning, oropharyngeal suctioning, lumbar puncture, venipuncture, intubation and nasogastric tube insertion are all classified as "painful" procedures (Cignacco et al., 2008). The non-invasive procedure included a diaper change. Demographic data for the observed infant was collected by the nurse rater from the infant's medical record from birth to the day of testing (see Appendix B).

Once an ELGA infant was identified for observation, the nurse rater approached the nurse caring for this infant and the study was discussed to determine if the ELGA infant was eligible for observation. A plan was made with direction from the infant's nurse for collection of data without interruption of patient care. This study was solely observational and for this reason usual care for the ELGA infant was maintained and not interrupted. Once the schedule was known for the routine invasive or non-invasive patient care procedures the nurse rater met the nurse at the infant's bedside 5 minutes prior to the procedure.

Infants at 24–33 6/7 weeks' gestation were observed by a nurse rater during routine invasive and non-invasive procedures. The nurse rater rated the ELGA infant using the PACEFI under three different conditions: Baseline (5 minutes prior to any type of handling), During (during the invasive procedure), and Recovery (5 minutes after the last contact with the infant). The ratings for three conditions (baseline, during, recovery) for the non-invasive and invasive procedures are needed to evaluate the difference in behavioral pain cues for each individual infant in their gestational age group. The time frame for observation was chosen based on previous infant pain studies (Lucas-Thompson et al., 2008). Each infant was rated by a nurse rater using the PACEFI at two different time points (non-invasive, invasive).

For descriptive purposes, physiologic data (i.e., heart rate, respiratory rate, and oxygen saturation) were collected in real time from the cardiac monitor by the nurse rater during the rating period (baseline, during, recovery).

Data Analysis Plan

Descriptive Statistics. The mean, median, range, and standard deviation percentages and frequencies were used to summarize infant and nurse demographic characteristics. Categorical variables were summarized with percentages and frequencies. Continuous variables were summarized with mean, median, range, and standard deviation. PACEFI data were also examined for the presence of random and/or systemic missing data, significant skewness, and outliers.

Descriptive statistics (mean, median, range, standard deviation) were used to determine the number of previous painful procedures ELGA and VLGA infants experienced prior to the observations (non-invasive, invasive). The number of invasive procedures preceding the observation window were summed for the non-invasive and invasive procedure for each infant group (ELGA, VLGA). Item scores were summed to give a PACEFI total score for each pain condition. The summed PACEFI score for each pain condition observed (baseline, during, recovery) for the invasive and non-invasive procedure was then correlated with the summed total number of painful procedures an infant experienced prior to the observation window to determine if the effect of these prior procedures needed to be controlled for in the tests of study hypotheses.

Descriptive statistics (frequencies, percentages) were used to determine the amount of ventilatory support the ELGA and VLGA infants experienced prior to the two procedures (non-invasive, invasive). The amount of ventilatory support (room air, nasal cannula, nasal continuous positive pressure, mechanical ventilation) preceding the observation window was determined for the invasive and non-invasive procedure for each infant group (ELGA, VLGA). Item scores were summed to give a PACEFI total score for each pain condition. The summed PACEFI score for each pain condition observed (baseline, during, recovery) for the invasive and non-invasive procedure was then correlated with the amount of ventilatory support an infant experienced prior to the observation window to determine if the effect of increased ventilatory requirements needed to be controlled for in tests of study hypotheses.

A Fisher's exact test was undertaken to compare nurse raters on each PACEFI item for each pain condition. The Fisher's exact is used to calculate the significance of difference for categorical data and allows for a small sample size and cell frequencies of 5 or fewer (Polit & Tatano-Beck, 2012).

Principal Analysis of Hypotheses.

Hypothesis 1. The PACEFI instrument will demonstrate preliminary reliability and validity during an invasive procedure. The Kuder-Richardson Formula 20 (KR-20) was used to determine beginning reliability for the PACEFI at baseline, during, and recovery for an invasive procedure. The KR-20 was chosen to evaluate the internal consistency of the PACEFI instrument. The KR-20 is a specific version of the coefficient alpha used to analyze instruments that are scored dichotomously for yes and no answers (Polit & Hungler, 1999). The KR-20 generates a reliability coefficient that has a normal range .00 ± 1.00, with higher values indicating a higher level of internal consistency (Polit & Tatano-Beck, 2012). The KR-20 alpha, corrected item to total statistics, inter-item correlations, and item score if deleted were calculated to determine if the items in the PACEFI contributed to the measurement of pain.

Hypothesis 2. Infants 24–29 6/7 weeks' gestation will exhibit different behavioral indicators during any invasive procedure at baseline (5 minutes prior to handling), during and recovery (5 minutes after handling) versus their 30–33 6/7 week counterparts. A repeated-measures ANOVA was undertaken to determine the difference for with-in subjects (group differences across time points), between subject (differences between groups across all time) and an interaction effect (group differences varied across time) (Polit & Tatano-Beck, 2012). Each

PACEFI item score for each pain condition (baseline, during, recovery) were summed for a total score for the invasive rating for each infant. Once item scores were totaled, a repeated measures ANOVA was undertaken to compare the two gestational age groups (ELGA = 24–29 6/7, VLGA = 30–33 6/7 week infants) to total PACEFI scores for each pain condition (baseline, during, recovery).

Hypothesis 3. Infants 24–33 6/7 weeks gestation will not exhibit behavioral pain cues during a non-invasive procedure at baseline (5 minutes prior to handling), during and recovery (5 minutes after handling). A repeated-measures ANOVA was undertaken to determine the difference for with-in subjects (group differences across time points), between subject (differences between groups across all time) and an interaction effect (group differences varied across time) (Polit & Tatano-Beck, 2012). Each PACEFI item score for each pain condition (baseline, during, recovery) was summed for a total score for the non-invasive rating for each infant. Once item scores were totaled, a repeated measures ANOVA was undertaken to compare the two gestational age (ELGA = 24–29 6/7, VLGA = 30–33 6/7 week infants) to total PACEFI scores for each pain condition.

Hypothesis 4. Physiologic and behavioral pain indicators for ELGA infants (24–29 6/7 weeks' gestation) and VLGA infants (30-33 6/7 weeks gestation) will not correlate at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling). Pearson Product-Moment correlations were use to determine the relationship between physiologic indicators and behavioral cues for ELGA and VLGA infants. All scores above (r = .3) were considered. Due to the exploratory nature of the study a statistical correction was not utilized due to the small sample size and the risk of type II error (Polit & Tatano-Beck, 2012). Item scores were summed to give a PACEFI total score for each pain condition. The summed PACEFI scores for each situation observed (baseline, during, recovery) during an invasive and non-invasive procedure were then correlated with physiologic indicators (heart rate, respiratory rate, oxygen saturation) to determine the relationship for physiologic indicators and behavioral cues.

Limitations and Threats to Validity

There are three identified or acknowledged limitations or threats to validity in this study. First, this study utilized demographic information found in the infant's medical records. A potential limiting factor originated from incomplete documentation and missing data. When possible, this effect was minimized by speaking with the nurse caring for the infant to obtain missing data.

Second, there are specific threats to validity primarily related to the sample bias. The 25–33 6/7 week infant population is small. It is not possible to sample randomly from this population or to sample in such a way as to ensure good gender and racial representation. The small ELGA infant population located in Massachusetts may cause an uneven sample with regard to gender and race, which may limit generalizability of the findings to the subjects included in the study groups. However, there is no clear evidence regarding gender and racial differences in pain responses for this population, and the existence of gender and racial differences in pain scores can be explored in future research.

Third, there was a potential for behavioral observations of infant pain to drift. However, this threat to validity was minimized by the nurse raters' initial training and the inter-rater reliability meetings scheduled throughout the data collection period, during which raters rated infants along with the PI and discussed ratings and any inconsistency in the ratings.

Protection of Human Subjects

Protection of the rights of human subjects was rigorously enforced using the criteria as identified by the Office for Human Resource Protections and by the policy listed under 45 CFR 46, Protection of Human Subjects, Section §46.205, Research Involving Neonates. The proposed study was conducted at an 18-bed, large metropolitan hospital in Massachusetts. Human Subject Research Committee approval was obtained from Boston College and the Massachusetts General Hospital prior to conducting the proposed investigations.

All ELGA infants routinely undergo these procedures multiple times during the day. The pain ratings on the PACEFI were done to coincide with these routine invasive procedures. The infant's environment was not altered and only the nurse caring for the infant had direct contact with the infant. No procedures, invasive or otherwise, were added for the observations. Usual care for pain prevention and alleviation of infant pain was continued.

Participation in the study was open to infants regardless of gender and ethnicity. Estimation for minority recruitment is difficult for this population. The Massachusetts study site population (unit specific) for VLBW infants (<1500 grams) with regards to ethnicity in 2008 was 19.7% Hispanic, 57.6% White, 16.7% Black, 0% Native American, 3% Asian, and 3% other race (percent of live births) (Vermont Oxford, 2008). The proposed project included both male and female infants (24–33 6/7 weeks) in the observations.

Anonymity was maintained for all study observations. No names were used. Confidentiality was strictly maintained and observations were identified by the use of consecutive numbers. The demographic information sheets and completed PACEFI are stored in a locked file at the PI's home office. No harmful procedures, situations, or materials that would be hazardous to the infants were anticipated.

Summary

In summary, an observational study was conducted to describe similarities and differences for pain assessment between ELGA and VLGA infants. The data were collected by nurse raters and analyzed utilizing repeated measures ANOVA, Pearson's Product-Moment correlations, and the KR-20. The findings of this study are described in Chapter 4 and provide information regarding preliminary reliability and validity of the PACEFI, similarities and differences between ELGA and VLGA infants in their pain response for invasive and non-invasive procedures, along with the relationship between physiological indicators and behavioral cues during invasive and non-invasive procedures.

Chapter 4

Findings

This chapter reports the statistical analysis evaluating similarities and differences in pain behaviors for different gestational ages (24–33 6/7 weeks' gestation) while undergoing any invasive and non-invasive (i.e., diaper change) procedure during three conditions—baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling)—using a newly developed pain assessment instrument: the PACEFI. Physiologic indicators and behavioral cues were also evaluated at baseline, during, and recovery for the invasive and non-invasive procedures to determine if a relationship exists for the measurement of pain. In addition, a preliminary analysis to examine internal consistency is reported for the PACEFI instrument. The implications for nursing practice are discussed in Chapter 5.

Data Analysis Procedures

Data were collected by infant observations and medical record reviews for 48 infants between 25–33 6/7 weeks' gestational age admitted to the NICU or Level II Nurseries at the Massachusetts General Hospital between the years 2010 and 2011. Data collection was conducted as described in the previous methodology chapter. The data were entered into a Microsoft Excel spreadsheet program, Version 2007. They were reviewed for accuracy and then imported into an analysis software program: SPSS, Version 19.0. Descriptive statistics were computed and examined for systematic and random missing data and marked skewness. No systematic missing data were found using the missing value analysis for SPSS, Version 19. Variables with random missing data above five percent were handled with listwise deletion procedure (Tabachnik & Fidell, 2007). Listwise deletion excludes cases with incomplete data (Munro, 2005). Skewness was a problem for several continuous variables. Fisher's measure of skewness—which is calculated by dividing the measure of skewness by the standard error of skew—was used to evaluate the study variables (Munro, 2005). Ninety-five percent of normal distributions fall between -1.96 and +1.96, the standard deviation from the mean; therefore any outliers are considered significantly skewed (Munro). Table 3 lists skewness values for continuous variables.

Table 3

Skewness for continuous study variables

Variable	Skewness
Prior Painful Procedures (non-invasive)	2.38
Prior Painful Procedures (invasive)	5.01
Day of Life (non-invasive)	2.73
Day of Life (invasive)	4.31
Snap Score	3.82

Note. Values +/- 1.96 are significantly skewed at the 0.05 level. (*N*=31)

One variable was recoded because of limited variability and low rates of occurrence as determined below. Gestational age was recoded from a continuous data point into two groups. Gestational age was collapsed in the ELGA infant group 25–29 6/7 week infants and the VLGA infant group 30–33 6/7 week infants as defined in the operational definitions (Chapter 2) for ELGA and VLGA infants. Table 2 shows the recoding of the gestational age variable for analysis purposes.

Table 4

Recoded Variable for Gestational Age

Variable name	Initial measurement groups with descriptive statistics	Recoded measurement groups with descriptive statistics
Gestational age	Continuous measurement	(0) 25–29 6/7 weeks (n = 16, 51.6%) (1) 30–33 6/7 weeks (n = 15, 48.4%)
25 weeks 3 (9.7%) 26 weeks 7 (22.6%) 27 weeks 1 (3.2%) 28 weeks 1 (3.2%) 29 weeks 4 (12.9%) 30 weeks 2 (6.5%) 31 weeks 4 (12.9%) 32 weeks 2 (6.5%) 33 weeks 7 (22.6%)		
	Mean = 29.2 weeks gestation Range = 25–33 weeks gestation *SD* = 2.9	

Note. Continuous measurement includes frequency, percents, mean, range and standard deviation (*SD*). Recoded variables include frequency and percents.

Sample

The population identified included all infants 24–33 6/7 weeks admitted to the level II nursery and level III NICU at the Massachusetts General Hospital. Out of the 48 infants included in the study only 31 infants had complete data (1 non-invasive and 1 invasive observational rating) for the analyses. Table 5 includes categorical data for the total sample (n = 31): *Gender, Gestational Age, Race, Procedure (non-invasive, invasive), Intraventricular Hemorrhage (non-invasive, invasive), Analgesia (non-invasive, invasive), Respiratory Support (non-invasive, invasive)* and *Non-pharmacological Interventions (non-invasive, invasive)* as seen in Table 5. Out of the total sample seventy-four percent of the total population was male infants. *Race* included Asian (12.9%), Black/AA (3.2%), Hispanic (19.4%), Pacific Islander (6.5%), White (9.7%), and

Unavailable/Missing (48%). The high rate of unavailable response may be due to the response options regarding race as well as missing data at the study site. The variables *Intraventricular Hemorrhage* and *Analgesia* were compressed into two dichotomized categories. The variable *Intraventricular Hemorrhage* (IVH) was dichotomized into none or grade I because 96% of the infants did not experience an intraventricular hemorrhage prior to the non-invasive observation rating. Ninety percent of the infants did not experience an intraventricular hemorrhage prior to the invasive observation rating. The variable *Analgesia* was dichotomized into none or *Fentanyl* because 93% of the infants did not receive any type of analgesia prior to both the non-invasive and invasive observational rating. *Respiratory Support* was collapsed into four categories based on observable conditions: *Room Air, Nasal Cannula, Nasal CPAP, and Ventilator*. ELGA and VLGA infants required *Room Air* (38%), *Nasal Cannula* (3.2%), *Nasal CPAP* (32%), and *Ventilator* (26%) during the non-invasive observation ratings. However, ELGA and VLGA infants required *Room Air* (35%), *Nasal Cannula* (3%), *Nasal CPAP* (25%), and *Ventilator* (35%) during the invasive observation rating. The variable *Non-pharmacological Interventions* was collapsed into five categories: *None*, *Containment, Containment with Sucrose, Containment with Pacifier* and *Pacifier.* Ninety five percent of infants received some kind of containment during the invasive procedure with an additional (18%) of the infants also receiving sucrose and/or a pacifier. Eighty nine percent of infants received some kind of containment during the non-invasive procedure with an additional (12%) of the infants also received sucrose and/or a pacifier.

Birth Weight, Gestational Age, Day of Life, Number of Painful Procedures, and *Snap Score* are displayed as continuous data (mean, median, standard deviation, range) as seen in Table 6. Infants had a mean birth weight of 1372 grams (*SD* = 515, *Range* = 730–2475), with a mean gestational age of 29.2 weeks (*SD* = 2.9, *Range* = 25–33). The results show that non-invasive procedures were rated on day of life (*m* = 4.1 days, *SD* = 3.0, *Range* = 0–13) and invasive procedures were rated on day of life (*m* = 3.4 days, *SD*= 4.1, *Range* = 0–14). The results also show the amount of prior painful procedures performed on infants leading up to and including the rating for non-invasive procedures (*m* = 22.3, *SD* 13.8, *Range* 2-58) and the amount of prior painful procedures for invasive procedures (*m* = 19.7, *SD* 14.3, *Range* 1–63). The mean Snap-II Score for illness severity was 10.89 (*SD* 10.3, *Range* 0–43).

Table 5

Infant Characteristics Categorical Variables

Variable	Frequency	Percent
Gender		
Male	23	74
Female	8	26
Gestational Age		
ELGA	16	51.6
VLGA	15	48.4
Race		
Asian	4	12.9
Black/AA	1	3.2
Hispanic	6	19.4
Pacific Islander	2	6.5
White	3	9.7
Unavailable	10	32.3
Missing	5	16.1
Procedure (non-invasive)		
Diaper Change	31	100.0
Intraventricular Hemorrhage (prior to non-invasive procedure)		
None	30	96.8
Grade I	1	3.2
Analgesia (prior to non-invasive procedure)		
None	29	93.5
Fentanyl	2	6.5

Continued: Infant Characteristics Categorical Variables

Variable	Frequency	Percent
Respiratory Support (during non-invasive procedure)		
Room Air	12	38.7
Nasal Cannula	1	3.2
CPAP	10	32.3
Ventilator	8	25.8
Non-pharmacological Interventions (during non-invasive procedure)		
None	1	3.2
Containment	25	80.6
Containment with Sucrose	1	3.2
Containment with Pacifier	2	6.5
Pacifier	3	3.2
Missing	1	3.2
Procedure		
Heel Stick	16	51.6
Nasogastric Tube	3	9.7
Endotracheal Suction	7	22.6
Oropharyngeal Suction	2	6.5
Intubation	1	3.2
Venipuncture	1	3.2
Lumbar Puncture	1	3.2
Intraventricular Hemorrhage (prior to invasive procedure)		
None	28	90.3
Grade I	2	6.5
Missing	1	3.2
Analgesia (prior to invasive procedure)		
None	29	93.5
Fentanyl	2	6.5
Respiratory Support (during to invasive procedure)		
RA	11	35.5
Nasal Cannula	1	3.2
NCPAP	8	25.8
Ventilator	11	35.5

Continued: Infant Characteristics Categorical Variables

Variable	Frequency	Percent
Non-pharmacological Interventions (during invasive procedure)		
Containment	25	80.6
Containment with Sucrose	1	3.2
Containment with Pacifier	4	12.9
Pacifier	1	3.2

Note. RA = room air, NCPAP = nasal continuous positive airway pressure, Respiratory Support = mode of ventilation, (*n*=31)

Table 6

Infant Characteristics Continuous Variables

Variable	Mean	Median	*SD*	Range
Birth Weight (grams)	1372	1305	515	730-2475
Gestational Age (weeks)	29.2	29	2.9	25-33
Day of Life (non-invasive)	4.1	3.5	3.1	0-13
Day of Life (Invasive)	3.4	3	4.1	0-14
Number of Prior Painful Procedures (non-invasive)	22.3	18	13.8	2-58
Number of Prior Painful Procedures (invasive)	19.7	16	14.3	1-63
Snap-II-Score	10.89	9	10.3	0-43

Note. Number of invasive procedures are counted from birth up until the procedure being rated. The Snap-II Score of < 30 denotes low illness severity. (*n* = 31).

Reliability Analysis for the PACEFI

A reliability analysis was conducted to answer the first aim establishing preliminary reliability for the PACEFI instrument. The Kuder Richardson Formula 20 (KR-20) was chosen to evaluate the internal consistency of the PACEFI instrument. The KR-20 is a specific version of the coefficient alpha used to analyze instruments that are scored dichotomously for yes and no answers (Polit & Hungler, 1999). The KR-20 generates a reliability coefficient that has a normal range .00–+1.00, with higher values indicating a higher level of internal consistency (Polit & Tatano-Beck, 2012).

The PACEFI Instrument

The PACEFI is a new instrument that is designed to assess pain in the ELGA infant. The PACEFI instrument was developed using the information from a preliminary study to ascertain registered nurses' perceptions of the most accurate pain cues in ELGA infants, a literature review, views of expert consultants, a review of pre-existing pain instruments, and the investigators' own experience. The PACEFI is a 20-item dichotomous (yes/no) procedural pain assessment instrument that assesses behavioral cues that the ELGA infant may exhibit during a painful procedure (see Appendix D). ELGA infants (25–33 6/7weeks) were observed for two different procedures (invasive, non-invasive) and each item was scored for frequency (i.e., no, it was not observed (0); yes, it was observed (1)). Infants are scored as "no pain" (0) if they do not exhibit any behaviors described by PACEFI items. Tables 7 and 8 include the endorsed items on the PACEFI instrument for the total sample of infants (n = 31) during the invasive procedure at baseline, during, and recovery and a non-invasive procedure at baseline, during, and recovery.

Table 7

PACEFI Endorsed Items for Each Item During Each Time Point for an Invasive Procedure

	Frequency of Endorsed Items (n = 31)		
Items	Baseline	During	Recovery
Eye Squeeze	1	10	3
Hands on Face	0	6	2
Cry	2	13	2
Furrow	1	18	4
Grimace	1	16	2
Nasolabial Bulge	1	18	3
Lips Pursed	0	2	0
Stretched Mouth	1	5	1
Taut Tongue	0	4	5
Push Arms	1	17	2
Push Legs	1	20	1
Pull Arms	1	12	2
Pull Legs	1	13	1
Full Body Pull Away	0	2	1
Sit on Air	1	5	2
Fisting	7	18	13
Mouthing	3	6	2
Fingersplay	4	18	3
Pull Body Midline	1	2	1
Toe Curl	0	6	3

Note. See Appendix D for item definitions.

Table 8

PACEFI Endorsed Items for Each Item During Each Time Point for a Non-invasive Procedure

	Frequency of Endorsed Items (*n* = 31)		
Items	Baseline	During	Recovery
Eye Squeeze	1	8	0
Hands on Face	4	6	5
Cry	0	15	0
Furrow	1	17	5
Grimace	1	14	0
Nasolabial Bulge	2	17	1
Lips Pursed	0	0	2
Stretched Mouth	3	6	2
Taut Tongue	4	4	0
Push Arm	1	20	1
Push Leg	2	22	1
Pull Arm	1	20	1
Pull Leg	2	22	1
Full Body Pull Away	1	1	1
Sit on Air	2	9	4
Fisting	3	25	13
Mouthing	1	1	1
Fingersplay	6	24	6
Pull Body Midline	2	3	3
Toe Curl	3	8	11

Note. See Appendix D for item definitions.

Reliability Analysis for the PACEFI Instrument at Baseline for the Invasive Procedure

The KR-20 is estimated for internal consistency at .140 for baseline, 5 minutes prior to handling before the invasive procedure. The PACEFI instrument included 20 items. However 17 items were removed due to zero variance (i.e., infants did not demonstrate behaviors). These items include: eye squeeze, hands on face, cry, furrow, grimace, nasolabial bulge, lips pursed, stretch mouth, taut tongue, push arms, push legs, pull arms, pull legs, full body pull away, sit on air, pull extremities midline, and toe curl. The KR-20 increases to .476 if the item fingersplay is deleted (Table 9). Inter-item correlations (Table 10) were also conducted; no significant correlations at the .05 level were noted. Fisting and mouthing showed a low positive correlation (r = .378). Corrected Item to Total Correlations (Table 9) were conducted for fisting (r =.139), mouthing (r = 327), and fingersplay (r = -.175). The items demonstrated little if any correlation for the PACEFI instrument at a baseline rating five minutes before handling prior to the invasive procedure. The low KR-20 at baseline is an expected finding as infants should not exhibit behaviors associated with pain at rest. The fact that no clear behaviors associated with pain were noted at the baseline ratings five minutes before handling prior to the invasive procedure is an encouraging finding.

Table 9

Item Analysis for the PACEFI Instrument (Baseline)

	n = Items	Mean	Variance	*SD*
Statistics for Scale	3	.47	.410	.640

	Alpha	Standardized Alpha
Reliability Coefficients	.140	.109

	Mean	Minimum Variance	Maximum	Range	Min/Max	Variance
Item Means	.156	.067	.333	.267	5.000	.024
Item Variance	.124	.067	.238	.171	3.571	.010
Inter-item Correlations	.039	-.189	.378	.567	-2.000	.072

	Scale Mean If KR-20 Deleted	Scale Variance If Item Deleted	Corrected Item Total Correlation	Squared Multiple Correlation	Alpha
Fisting	.13	.124	.139	.169	-.154
Mouthing	.40	.257	.327	.143	-.370
Finger Splay	.40	.400	-.175	.036	.476

Note. *n* = sample size, *SD* = standard deviation

Table 10

Inter-item Correlations for the PACEFI Instrument (Baseline)

	Fisting	Mouthing	Fingersplay
Fisting	1.00		
Mouthing	.378	1.00	
Fingersplay	-.189	-.071	1.00

Reliability Analysis for the PACEFI Instrument During the Invasive Procedure

The KR-20 was estimated at .879 during an invasive procedure. However, two items were excluded due to zero variance (i.e., infants did not demonstrate behaviors). These items include: lips pursed and full body pull away. The KR-20 increases if four items are deleted: sit on air .882, mouthing .888, fingersplay .886, and pull extremities midline .883. Inter-item correlation analyses (Table 11) were conducted for PACEFI items during an invasive procedure. The Inter-item Correlations (Table 12) indicate stronger relationships at .4–.9 for facial expressions such as eye squeeze, cry, furrow, grimace, nasolabial bulge, stretched mouth and taut tongue. There was a weaker relationship noted for motor activity at .3–.6 which included push arm, push leg, pull arm, pull leg, fisting, and sit on air. It is also noted that motor activity (push arm, push leg, pull arm, pull leg, fisting) were low to moderately correlated at .3-.5 with facial expression (eye squeeze, cry, furrow, grimace, nasolabial bulge, stretched mouth, and taut tongue). Further testing and analysis is needed to ascertain if these items form cohesive subscales.

Corrected Item to Total Correlations were computed for the 18 items (Table 11). Eye squeeze (r = .703), hands on face (r = .482), cry (r = .422), furrow (r = .876), grimace (r = .839), nasolabial bulge (r = .876), stretch mouth (r = .438), taut tongue (r = .476), push arm (r = .624), push leg (r =.574), pull arm (r = .706), pull leg (r = .518), fisting (r = .492), and toe curl (r = .380) indicate correlations above .38 with varying strengths of relationships between items suggesting these items are measuring pain. Sit on air (r = .211), mouthing (r = -.067), fingersplay (r = .148), and pull midline (r = .065) indicate little if any correlation and may not be contributing to the measurement of pain. The possibility of removing these items from the PACEFI instrument would need to be further explored.

Table 11

Item Analysis for the PACEFI Instrument (During)

	n = Items	Mean	Variance	*SD*
Statistics for Scale	18	6.93	23.495	4.847

	Alpha	Standardized Alpha
Reliability Coefficients	.879	.865

	Mean	Minimum	Maximum	Range	Min/Max	Variance
Item Means	.385	.067	.600	.533	9.000	.031
Item Variance	.222	.067	.267	.200	4.000	.003
Inter-item Correlations	.263	-.480	1.000	1.480	-2.082	.084

	Scale Mean If KR-20 Deleted	Scale Variance If Item Deleted	Corrected Item Total Correlation	Squared Multiple Correlation	KR-20 If Item Deleted
Eye Squeeze	6.67	20.381	.703	.	.865
Hands on Face	6.53	20.981	.486	.	.873
Cry	6.53	21.267	.422	.	.876
Furrow	6.40	19.257	.876	.	.857
Grimace	6.47	19.410	.839	.	.858
Nasolabial Bulge	6.40	19.257	.876	.	.857
Stretched Mouth	6.73	21.638	.438	.	.875
Taut Tongue	6.73	21.495	.476	.	.873
Push Arm	6.33	20.381	.624	.	.867
Push Leg	6.40	20.543	.574	.	.869
Pull Arm	6.40	19.971	.706	.	.864
Pull Leg	6.53	20.838	.518	.	.872
Sit on Air	6.73	22.495	.211	.	.882
Fisting	6.33	20.952	.492	.	.873
Mouthing	6.80	23.600	-.067	.	.888
Fingersplay	6.33	22.524	.148	.	.886
Pull Body Midline	6.87	23.267	.065	.	.883
Toe curl	6.67	21.667	.380	.	.877

Note. *n* = sample size, *SD* = standard deviation. It is possible that squared multiple correlations were not calculated due to high correlations and low variance.

Table 12

Inter-item Correlations for PACEFI Instrument (During)

	Eye	Hand	Cry	Fur	Grim	Bulge	Lip	Mouth	Tongue	Push Arm	Push Leg	Pull Arm	Splay
Eye	1.00												
Hand		1.00											
Cry	.425	1.00											
Fur	.451		.409	1.00									
Grim	.555		.649	.743	1.00								
Bulge	.506	.326	.503	.940	.809	1.00							
Lip			.401				1.00						
Mouth			.435				.402	1.00					
Tongue				.419	.369		.542	1.00					
Push A	.476		.390	.542	.461	.367	.354			1.00			
Push L				.383	.430	.657				.560	1.00		
Pull A			.552	.361	.442	.390				.689	.387	1.00	
Pull L			.439			.486		.375		.362	.721	.559	
Body								.364					
Sit Air								.679	.679	.333			
Fisting	.371			.426	.461					.420			
Splay											1.00		
Midline							.364						
Toe Curl												.482	

Note. All items are significant < .05 level. The table has been reduced to include only significant items.
Eye = Eye Squeeze, Hand = Hands on Face, Fur = Furrow, Grim = Grimace, Bulge = Nasolabial Bulge, Lip = Lips Pursed, Mouth = Stretched Mouth, Tongue = Taut Tongue, Splay = Fingersplay.

Reliability Analysis for the PACEFI Instrument at Recovery for an Invasive Procedure

The KR-20 was estimated at .792 at recovery five minutes after the invasive procedure was completed. However, six items were excluded due to zero variance (i.e., infants did not demonstrate behaviors). These items include: lips pursed, taut tongue, full body pull away, sit on air, mouthing, and pull extremities midline. The KR-20 increases if these items are deleted: mouthing .816 and toe curl .804. Inter-item Correlation (Table 13) analyses were conducted for

PACEFI items at the recovery rating for an invasive procedure. The Inter-item Correlations (Table 14) indicate a low to moderate relationship at .4–.6 for facial expressions such as eye squeeze, cry, furrow, grimace, nasolabial bulge, and stretched mouth. There was moderate to high relationship at .6–.9 for motor activity including push arm, push leg, pull arm, pull leg, hands on face and fingersplay. It is also noted that the facial expressions and motor activity are low to moderately correlated at .3–.5 with furrow and cry.

Corrected Item to Total Correlations (Table 13) were computed for the 14 items. Eye squeeze (r = .369), cry (r = .593), furrow (r = .841), grimace (r = .471), nasolabial bulge (r = .369), push arm (r = .593), push leg (r = .369), pull arm (r = .593), (r = .369), fisting (r = .378), and fingersplay (r = .342) indicating correlations above .34 with varying strengths of relationships between items, these items seem to be measuring pain. Hands on face (r = .281), toe curl (r = .112) and stretch mouth (r = -.200) have low to negative correlations which indicate these items may not be contributing to the measurement of pain.

Table 13

Item Analysis for the PACEFI Instrument (Recovery)

	N	Mean	Variance	*SD*
Statistics for Scale	14	1.94	6.062	2.462

	Alpha	Standardized Alpha
Reliability Coefficients	.792	.800

	Mean	Minimum	Maximum	Range	Min/Max	Variance
Item Means	.138	.063	.500	.438	8.000	.013
Item Variance	.115	.063	.267	.204	4.267	.003
Inter-item Correlations	.222	-.258	1.000	1.258	-3.873	.127

	Scale Mean if KR-20 Deleted	Scale Variance If Item Deleted	Corrected Item Total Correlation	Squared Multiple Correlation	KR-20 If Item Deleted
Eye Squeeze	1.81	5.362	.369	.	.783
Hand on Face	1.81	5.496	.281	.	.790
Cry	1.88	5.317	.593	.	.769
Furrow	1.75	4.467	.841	.	.734
Grimace	1.88	5.450	.471	.	.777
Nasolabial Bulge	1.81	5.362	.369	.	.740
Stretched Mouth	1.88	6.250	-.200	.	.816
Push Arm	1.81	5.362	.593	.	.783
Push Leg	1.88	5.317	.369	.	.769
Pull Arm	1.81	5.362	.593	.	.783
Pull Leg	1.88	5.317	.369	.	.769
Fisting	1.44	4.929	.378	.	.789
Finger Splay	1.75	5.267	.342	.	.787
Toe curl	1.81	5.762	.112	.	.804

Note. *n* = sample size, *SD* = standard deviation. It is possible that squared multiple correlations were not calculated due to high correlations and low variance.

Table 14

Inter-item Correlations for PACEFI Instrument (Recovery)

	Eye	Hand	Cry	Fur	Grim	Bulge		Push Arm	Push Leg	Pull Arm	Pull Leg	Finger Splay
Eye	1.00											
Hand		1.00										
Cry			1.00									
Fur			.537	1.00								
Grim	.683	.683		.537	1.00							
Bulge			.683	.787	.683	1.00						
Mouth							1.00					
Push A			.683			.683		1.00				
Push L			1.00	.537				.683	1.00			
Pull A			.683					.999	.683	1.00		
Pull L			1.00	.537		.683		.683	.999	.683	1.00	
Splay		.787		.590	.537							1.00

Note. All items are significant < .05 level. The table has been reduced to only include significant items.
Eye = Eye Squeeze, Hand = Hand on Face, Fur = Furrow, Grim = Grimace, Bulge = Nasolabial Bulge, Splay = Fingersplay.

Summary

The PACEFI instrument appears to be contributing to the measurement of pain. The KR-20 at baseline was .140 which indicates items on the PACEFI were not observed while infants were at rest. During the invasive procedure, the KR-20 was .879 which is considered good, indicating that most items were contributing to the measurement of pain. The KR-20 remained elevated at recovery .792 which is an expected finding for this gestational age group due to prior sensitization and neuro-developmental immaturity. Chapter 5 will focus on a more in-depth discussion for reliability, specifically internal consistency.

Rating Differences Between Nurse Raters Using the PACEFI

The PACEFI instrument was rated by two different nurse raters (Table 15) for four individual infants at baseline, during, and recovery for both invasive and non-invasive procedures. Each rater was blinded to the other raters' observational rating. The four ratings included two non-invasive procedures (diaper change) and two invasive procedures (heel stick). The infant's gestational ages were as follows: 26 weeks (heel stick), 27 weeks (diaper change), 30 weeks (diaper change) and 31 weeks (heel stick). A Fisher's exact analysis was conducted to determine if there were any significant differences between nurse raters and rating observations using the PACEFI instrument. Although the sample is very small, it is thought that pilot data to examine differences between nurse raters for the use of the PACEFI would be valuable preliminary findings. There were no significant differences noted between the ratings.

Table 15

Demographic Data for Registered Nurse Raters

	Raters
Gender	
Female	3 (100)
Degree	
Bachelors	2 (66.7)
Masters	1 (33.3)
Years of Experience	Mean = 17.67
	Range = 14–21
	SD = 3.50

Note. Frequencies and percents are reported for categorical variables.
Mean, Range, and Standard Deviation are reported for continuous variables.

ELGA & VLGA Infant Differences for PACEFI Scores for the Invasive Procedure

Preparation of Data for RANOVA Analysis

A repeated measures analysis of variance (RANOVA) was conducted to answer the question for the second aim of whether or not 24–29 6/7 week ELGA infants exhibit the same behavioral cues as their 30–33 6/7 week VLGA infant counterparts for any invasive procedure at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling).

Prior to conducting the RANOVA the sample was split into two groups: ELGA infants (25–29 6/7 weeks' gestation) and VLGA infants (30–34 6/7 weeks' gestation).

Infant Characteristics

Seventy-four percent of the total population were male infants, and out of those 74%, ELGA infants accounted for 68.8% and VLGA infants accounted for 80% of the male population. *Race* included 64.6% responses either unavailable or missing. This may be due to the response options regarding race at the study site and missing demographic data in the medical records. The variable *Procedure* (non-invasive) was performed on 100% of the infants. The variable *Intraventricular Hemorrhage* (IVH) was dichotomized into none or grade I. Ninety-three percent of the ELGA infants and 100% of the VLGA infants for the non-invasive rating and 81% ELGA and 100% VLGA infants for the invasive rating did not experience an intraventricular hemorrhage. The variable *Analgesia* was dichotomized into none or Fentanyl. Eighty-seven percent of the ELGA and 100% of the VLGA infants during the non-invasive rating and 94% of ELGA and 93% of VLGA infants during the invasive rating did not receive any type of analgesia during this study. Respiratory Support was collapsed into four categories: *Room Air, Nasal Cannula, Nasal CPAP,* and *Ventilator.* Ninety-four percent of the ELGA infants required either NCPAP or ventilator support, while the VLGA population had the highest rate of infants on room air 73.3% during the non-invasive rating. The invasive rating included the same amount of ELGA infants' 94% requiring NCPAP or ventilator support, while 66% of the VLGA infants were in room air. The variable *Non-pharmacological Interventions* was collapsed into five categories: *None, Containment, Containment with Sucrose, Containment with Pacifier* and *Pacifier*. Over 80% of infants received some kind of containment during the non-invasive and invasive procedure. An additional 6% of the ELGA infants also received a pacifier during the non-invasive, while an additional 13% of the VLGA infants received sucrose and a pacifier. An additional 12% ELGA infants and 26% of VLGA infant received sucrose and and/or a pacifier during the invasive procedure. The variable *Procedure* (invasive) includes all invasive procedures performed on 100% of the infants during an observation.

To evaluate the difference between the groups, a *t*-test analysis was conducted for continuous variables and a chi square analysis was conducted for categorical variables (Table 16) to make group comparisons for ELGA and VLGA infants on the 16 demographic variables. Five variables were noted to be significant ($p < 0.05$) for group differences. The difference included: gestational age ($p < .001$), birth weight ($p < .001$), respiratory support for both the non-invasive ($p < .001$) and invasive rating ($p < .024$) and *Race* ($p < 0.36$). Gestational age and birth weight were expected differences as ELGA infants are younger in gestational weeks and weigh less due to the difference in age. Respiratory support was also expected to be different as ELGA infants were expected to require more ventilatory support than VLGA infants due to their lung immaturity at the time of birth. The invasive procedures between the two groups were significantly different. The largest difference noted between the two groups was ETT suctioning for the ELGA infants; this is expected as most infants were intubated at the time of the rating. Race appeared to be significantly different between groups. However, this may be due to the unavailable data (31% for ELGA infants) and unavailable and missing data (66% VLGA infants).

Table 16

Study Sample Descriptive Data ELGA versus VLGA infants

Variable	Frequency/Percent (%) ELGA (n = 16)	Frequency/Percent (%) VLGA (n = 15)	p*
Gestational Age	25 3 (18.8) 26 7 (43.8) 27 1 (6.3) 28 1 (6.3) 29 4 (25) Mean = 26.75 Range = 24-29 *SD*= 1.528	30 2 (13.3) 31 4 (26.7) 32 2 (13.3) 33 7 (46.7) Mean = 30.93 Range = 30-33 *SD*= 1.163	.001*
Gender	Male 11 (68.8) Female 5 (31.3)	Male 12 (80) Female 3 (20)	.474
Birth weight	Mean = 989.33 Range = 730-1500 *SD*= 220.66	Mean = 1754 Range = 1180-2475 *SD* = 433.59	.001*
Race	White 3 (18.8) Black A/A 1 (6.3) Hispanic 5 (31.3) Pacific Islander 2 (12.5) Unavailable 5 (31.3)	Asian 4 (26.7) Hispanic 1 (6.7) Unavailable 5 (33.3) Missing 5 (33.3)	.036*
Snap-II Score	< 30 low risk 14 (87.5) >30 High Risk 1 (6.3) Missing 1 (6.3)	< 30 low risk 12 (80) >30 High Risk 3 (20)	.362
Day of Life (non-invasive)	Mean = 4.40 Range = 0-10 *SD* = 2.92	Mean = 3.93 Range = 0-13 *SD* = 3.45	.877
Day of Life (invasive)	Mean = 3.44 Range = 0-12 *SD* = 3.46	Mean = 3.42 Range = 0-14 *SD* = 4.89	.918

Continued: Study Sample Descriptive Data ELGA versus VLGA infants

Variable	Frequency/Percent (%) ELGA (*n* = 16)	Frequency/Percent (%) VLGA (*n* = 15)	p*
Prior Procedures (non-invasive)	Mean = 26.25 Range = 2.58 SD = 17.47	Mean = 18.20 Range = 2.31 SD = 7.09	.415
Prior Procedures (invasive)	Mean = 26.06 Range = 11-63 *SD* = 16.34	Mean = 13.07 Range = 1-29 *SD* = 8.00	.359
IVH (non-invasive)	None 14 (87.5) grade I 2 (12.5)	None 15 (100)	.325
IVH (invasive)	None 13 (81.3) grade I 2 (12.5) Missing 1 (6.3)	None 15 (100)	.143
Analgesia (non-invasive)	None 14 (87.5) Fentanyl 2 (12.5)	None 15 (100)	.157
Analgesia (invasive)	None 15 (93.8) Fentanyl 6 (6.3)	None 14 (93.3) Fentanyl 1 (6.7)	.962
Respiratory Support (non-invasive)	RA 1 (6.3) NCPAP 7 (43.8) Vent 8 (50)	RA 11 (73.3) Nasal Cannula1 1 (6.7) NCPAP 3 (20)	.000*
Respiratory Support (invasive)	RA 1 (6.3) NCPAP 6 (37.5) Vent 9 (56.3)	RA 10 (66.7) Nasal Cannula 1 (6.7) NCPAP 2 (13.3) Vent 2 (13.3)	.002*
Nonpharmacological (non-invasive)	None 1 (6.3) Containment 13 (81.3) Contain/Sucrose 0 (0) Contain/Pacifier 1 (6.3) Missing 1 (6.3)	Containment 13 (80) Contain /Sucrose 1 (6.7) Contain/Pacifier 1 (6.7) Pacifier 1 (6.7)	.551
Nonpharmacological (invasive)	Containment 14 (87.5) Contain/ Sucrose 1 (6.3) Contain/Pacifier 2 (6.3)	Containment 14 (73.3) Contain/Pacifier 3 (20) Pacifier 1 (6.7)	.343

Continued: Study Sample Descriptive Data ELGA versus VLGA infants

Variable	Frequency/Percent (%) ELGA (n = 16)	Frequency/Percent (%) VLGA (n = 15)	p*
Procedure (invasive)	Heel Stick 8 (50) ETT Suction 7 (43.8) Lumbar Puncture 1 (6.3)	Heel Stick 8 (53.3) NG Placement 3 (20) Oral Suction 2 (13.3) Intubation 1 (6.7) Venipuncture 1 (6.7)	.020*
Procedure (non-invasive)	Non-invasive 16 (100%)	Non-invasive 15 (100%)	

Note. *t*-tests were completed for continuous data. Chi square was completed for categorical variables. Snap-II Score = illness severity, Prior procedures = all painful procedures counted up to and including the observational rating, Respiratory support= mode of ventilation, RA = room air, NCPAP = nasal continuous positive airway pressure, Contain/sucrose = containment/sucrose, contain/pacifier = containment/pacifier.
**p* values are significant at the .05 level.

Correlations for Possible Confounding Variables

Prior to conducting the RANOVA, a correlation matrix, was assessed to determine if any relationships exist between *Prior Painful Procedures (Count Pain)* and *Ventilation (Respiratory Support)* with the *Baseline, During, and Recovery* ratings. These variables were examined for Pearson's Product-Moment correlations above .30. Correlations at .30 are considered moderate (Polit & Tatano-Beck, 2012). For the purpose of this study the relationships will be discussed. *Prior Painful Procedures (Count Pain),* and *Ventilation (Respiratory Support)* were chosen as possible confounding variables with the non-invasive and invasive pain ratings at (baseline, during, and recovery) based on current evidence in the literature.

The group was split into ELGA and VLGA infants and the five variables (Ventilatory support, prior painful procedure, PACEFI total score baseline, PACEFI total score during, PACEFI total score recovery) were examined using Pearson's Product-Moment correlations to determine the relationship between total PACEFI scores at baseline, during, and recovery with prior painful procedures and ventilatory support. The ELGA group correlations are presented in Table 17. There were no significant correlations ($p < .05$) noted for the total PACEFI score and prior painful procedure or ventilatory support. Painful procedures include all invasive procedures up to and including rating for the non-invasive and invasive procedure. Ventilatory support includes four categories ranging from no ventilatory support (RA), to an infant requiring oxygen, (Nasal Cannula), to an infant requiring oxygen and positive pressure (NCPAP), to the highest support possible an infant requiring assisted ventilatory support by machine (Vent). Prior Painful Procedures (Count Pain) and Ventilation showed little if any correlation to the ratings Baseline, During, and Recovery.

Table 17

ELGA Infant Correlations for Possible Confounding Variables (n = 16)

	Count Pain	Ventilation	Baseline	During	Recovery
Count Pain	1.00				
Ventilation	.193	1.00			
Baseline	.037	-.038	1.00		
During	-.155	-.184	.371	1.00	
Recovery	.022	.006	-.160	.354	1.00

Note. Count Pain = all painful procedures prior to the rating, Ventilation = respiratory support which is portrayed from lowest to highest support required by an infant (RA, Nasal Cannula, NCPAP, Vent). Baseline, During, Recovery = Behavior Total Score

Pearson's Product-Moment correlations were conducted for the same five variables for VLGA infants. There were no significant correlations ($p < .05$) noted for VLGA infants (Table 18). *Prior Painful Procedures (Count Pain)* and the rating *During* showed a low positive correlation (r =

.327) indicating VLGA infants with high number of painful procedures prior to the rating demonstrated more behavioral cues during the invasive procedure (Figure 1).

Ventilation and the rating *Recovery* showed a low positive correlation (r = .339) indicating infant's requiring increased ventilatory support demonstrated more behavioral cues at recovery five minutes after handling (Figure 2).

Table 18

VLGA Infant Correlations for Possible Confounding Variables (*n* = 15)

	Count Pain	Ventilation	Baseline	During	Recovery
Count Pain	1.00				
Ventilation	-.228	1.00			
Baseline	-.223	-.151	1.00		
During	.327	.027	-.216	1.00	
Recovery	-.093	.339	-.189	.410	1.00

Note. Count Pain = all painful procedures prior to the rating, Ventilation = respiratory support which is portrayed from lowest to highest support required by an infant (RA, Nasal Cannula, NCPAP, Vent). Baseline, During, Recovery = Behavior Total Score

Figure 1. VLGA Age Infant Correlations for Prior Painful Procedures & Total PACEFI Scores During an Invasive Procedure

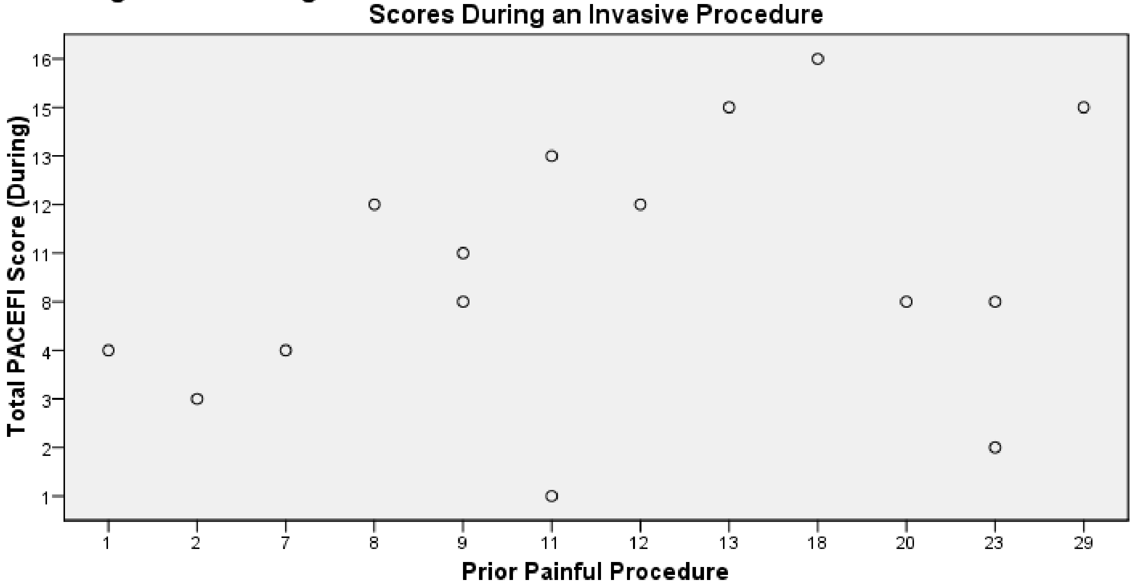
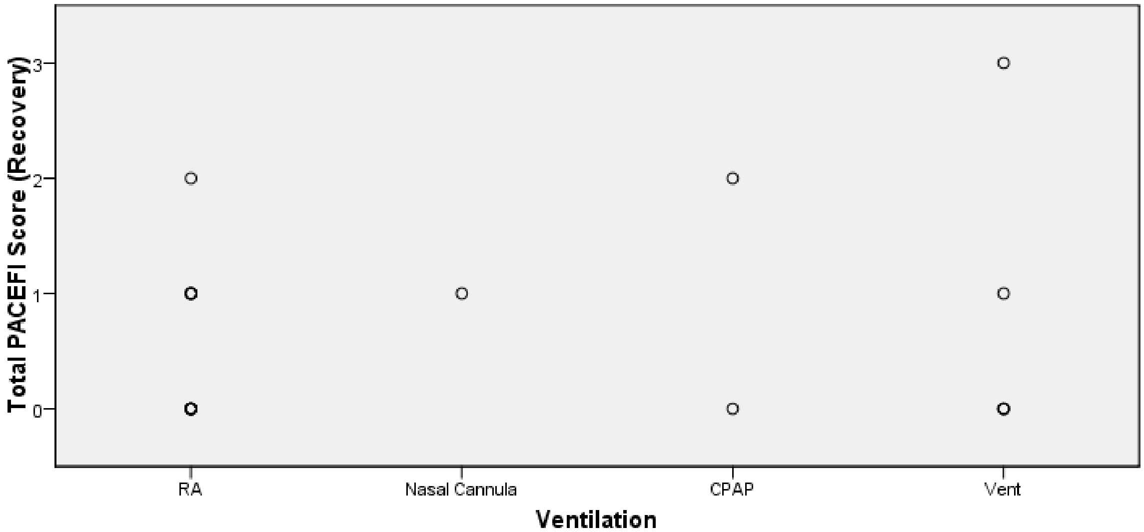


Figure 2. VLGA Infant Correlations for Ventilation & Total PACEFI Scores at Recovery for an Invasive Procedure



Summary

There were no significant relationships noted for ventilation and prior painful procedures with the total PACEFI scores. Ventilation and prior painful procedures were not included in the RANOVA analysis.

RANOVA Analysis

A repeated measures analysis of variance (RANOVA) was conducted to evaluate differences within subjects and between subjects. The RANOVA examined the effect of gestational age on baseline, during, and recovery ratings for an invasive procedure (*n* =31). There was one within subjects factor with three levels—Invasive baseline total score, Invasive during total score, Invasive recovery total score—and one between subjects factor with two levels—Gestational Age: ELGA *n* = 16, VLGA *n* = 15).

The assumption of compound symmetry was not met ($p < .009$). Due to the fact that the assumption of compound symmetry was not met for normally distributed ratings (baseline, during, recovery) an epsilon correction was used to decrease the likelihood of type I error (Munro, 2005). The univariate test with epsilon correction, the Greenhouse-Geisser, will be reported for the within subjects factors. There was a significant difference (Table 19) in rating scores ($F(1.553, 58) = 42.32$, $p < .001$) . The ratings for baseline and during ($p < .001$) and during and recovery ($p < .001$) were significant. During ($m = 7.025$) had significantly higher scores than baseline ($m = .879$) and recovery ($m = 1.244$) (Figure 3).

There was a significant ordinal interaction (Table 19) with the ELGA and VLGA groups for the ratings (baseline, during, recovery) ($F(1.535, 58) = 51.34$, $p < .023$) (Figure 4). The ELGA group had significantly lower scores at baseline ($m = .625$), and recovery ($m = 1.688$) and significantly higher scores at during ($m = 5.250$). The VLGA group had significantly lower scores at baseline ($m = 1.133$), and recovery ($m = .800$) and significantly higher scores at during ($m = 8.800$). The ELGA showed the least amount of change overall in ratings from baseline to during and during to recovery (Figure 5). Although both the ELGA and VLGA infants showed an increase from baseline to during and a decrease from during to recovery, the ELGA infants ($m = 5.252$) demonstrated a blunted response during the invasive procedure as compared to their VLGA counterparts ($m = 8.800$). The ELGA infants ($m = 1.688$) also demonstrated a slower recovery five minutes after the procedure was completed as compared to their VLGA counterparts ($m = .800$). There was no significant group difference (Table 19) noted for the ratings at baseline, during, and recovery between the ELGA and VLGA infants.

Summary

ELGA and VLGA infants demonstrated a similar response to the invasive procedure. Baseline and recovery were noted to be lower scores than during the invasive procedure. However, ELGA infants demonstrated less of a response than their VLGA counterparts. This may be due to neurodevelopmental immaturity. It was also noted that ELGA infants' recovery scores remained increased as compared to the VLGA infants. This too may be due to neuro-developmental immaturity related to an altered response to prior procedures causing sensitization for the infant. Further discussion is included in Chapter 5.

Table 19

Repeated Measures ANOVA for the PACEFI (During)

Source	df	MS	F	*p*
Between Subjects				
Gestational age	1	25.946	2.665	.113
Error	29	9.734		
Within Subjects				
Rating	1.5	474.164	42.329	.001
Rating x Gestational Age	1.5	51.340	4.583	.023
Error	45	11.202		

Note. df = degrees of freedom, MS = mean squared, F = F value, *p* = significance. (*n* = 31)

Figure 3. ELGA & VLGA Infants' PACEFI Scores for an Invasive Procedure (n = 31)

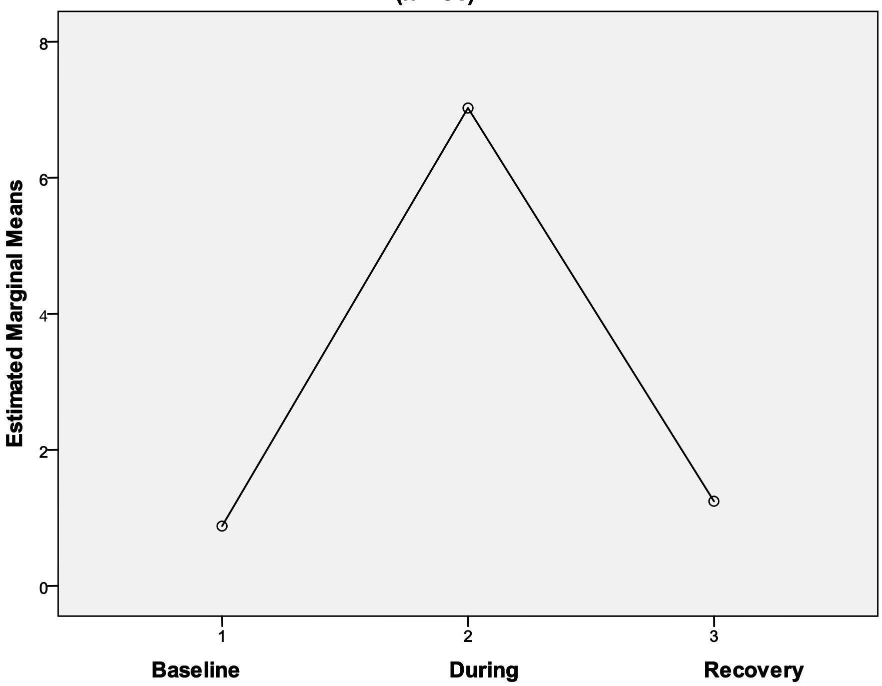


Figure 4. ELGA & VLGA Infants' PACEFI Scores for an Invasive Procedure

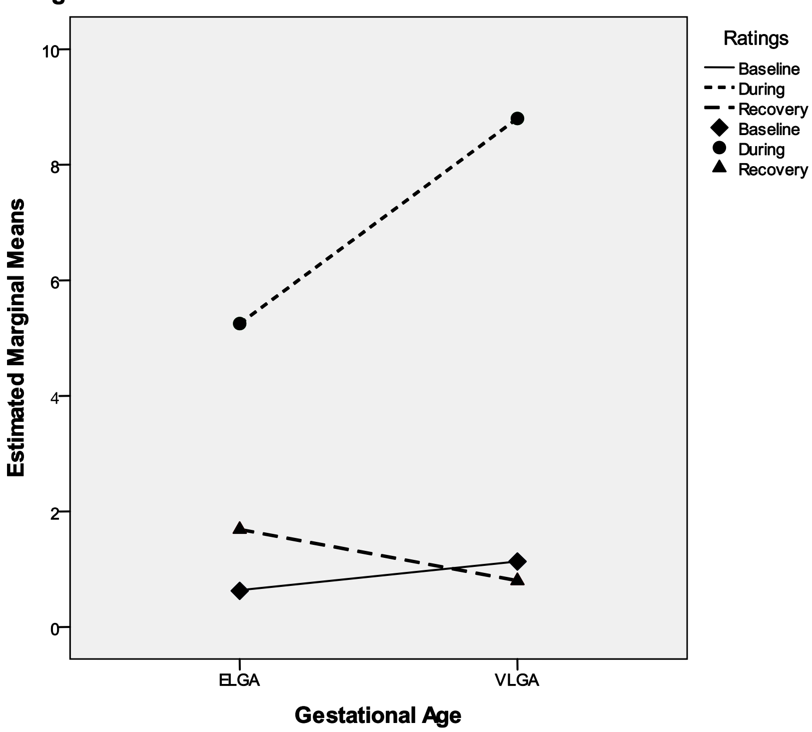
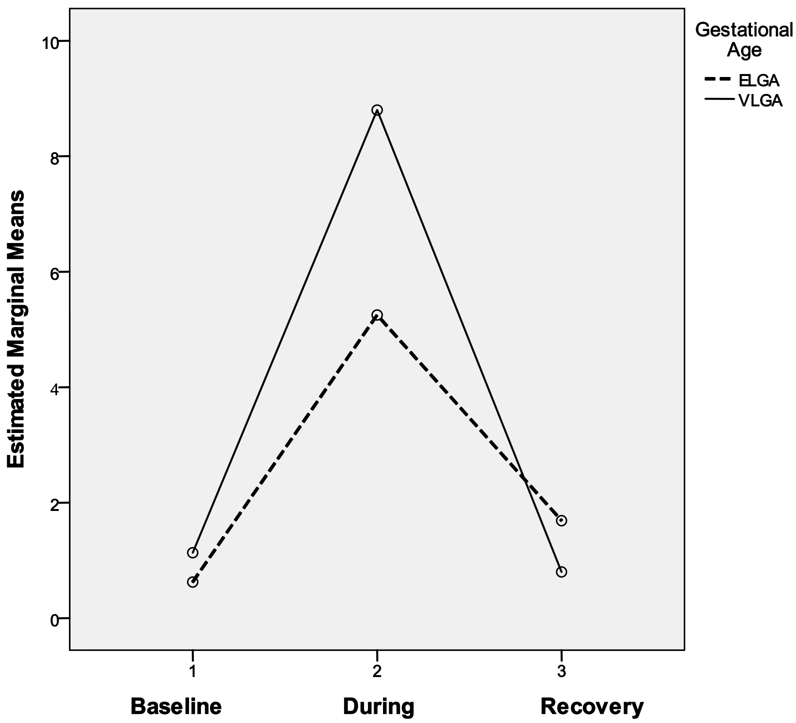


Figure 5. ELGA & VLGA Infants' PACEFI Scores for an Invasive Procedure



ELGA & VLGA Infant Differences for PACEFI Scores for the Non-invasive Procedure

A RANOVA was conducted to answer the question for the third aim whether or not 24–29 6/7 versus 30–33 6/7 week infants exhibit different behavioral cues during a non-invasive procedure versus a invasive procedure at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling). The same sample of infants is used for both Aims 2 and 3

Correlations for Possible Confounding Variables

Prior to conducting the RANOVA, a correlation matrix, was assessed to determine if any relationships exist between *Prior Painful Procedures (Count Pain), Respiratory Support* and the *Baseline, During, and Recovery* ratings for a non-invasive procedure. These variables were examined for Pearson's Product-Moment correlations above .30. *Prior Painful Procedure (Count*

Pain), and *Ventilation* were chosen as possible confounding variables with the non-invasive ratings (baseline, during, and recovery) based on current evidence in the literature.

The group was split into ELGA and VLGA infants and the five variables were examined using Pearson's Product-Moment correlations to determine the relationship between total PACEFI scores at baseline, during, and recovery with prior painful procedures and ventilatory support. The ELGA group correlations are presented in Table 20. There was a significant moderate negative correlation between *Prior Painful Procedures (Count Pain)* and the rating *During* (r = -.618, $p < .05$) ELGA infants who endured a high number of painful procedures prior to the rating demonstrated less behavioral cues during a non-invasive procedure (Figure 6). *Prior Painful Procedure (Count Pain)* and the rating *Recovery* showed a low negative correlation (r = -.480), while ELGA infants with a high number of prior painful procedures demonstrated less behavioral cues at the recovery five minutes after handling was completed (Figure 7). There were significant negative correlations between *Ventilation* and the rating *Baseline* (behaviors) (r = -.532, $p < .05$), and *Ventilation* and the *rating Recovery* (behaviors) (r = -.545, $p < .05$) ELGA infants requiring higher ventilatory support showed less behavioral cues at baseline 5 minutes prior to handling and recovery five minutes after handling was completed (Figure 8, 9).

Table 20

ELGA Infant Correlations for Non-invasive Ratings & Confounding Variables (*n*=16)

	Count Pain	Ventilation	Baseline	During	Recovery
Count Pain	1.00				
Ventilation	.334	1.00			
Baseline	-.193	-.532*	1.00		
During	-.618*	-.146	.519*	1.00	
Recovery	-.480	-.545*	.564*	.172	.100

Note. Count Pain = all painful procedures prior to the rating, Ventilation = respiratory support.
Baseline, During, and Recovery = Behavior Total Score
*Correlations significant at the 0.05 level (2 tailed)

Figure 6. ELGA Infant Correlations for Prior Painful Procedures & Total PACEFI Scores During a Non-invasive Procedure

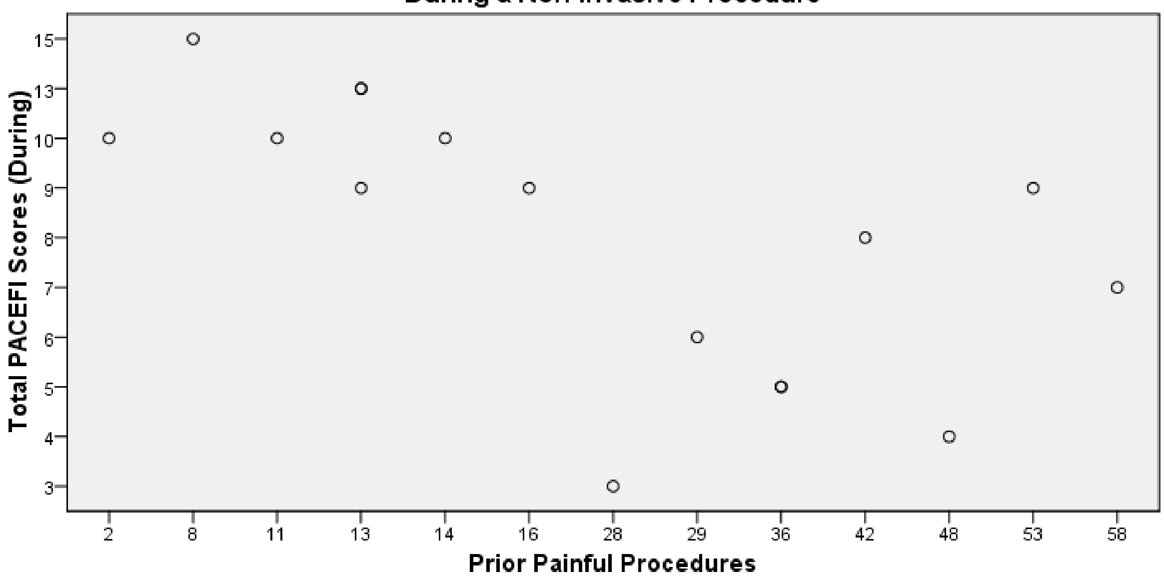


Figure 7. ELGA Infant Correlations for Prior Painful Procedures & Total PACEFI Score at Recovery for a Non-invasive Procedure

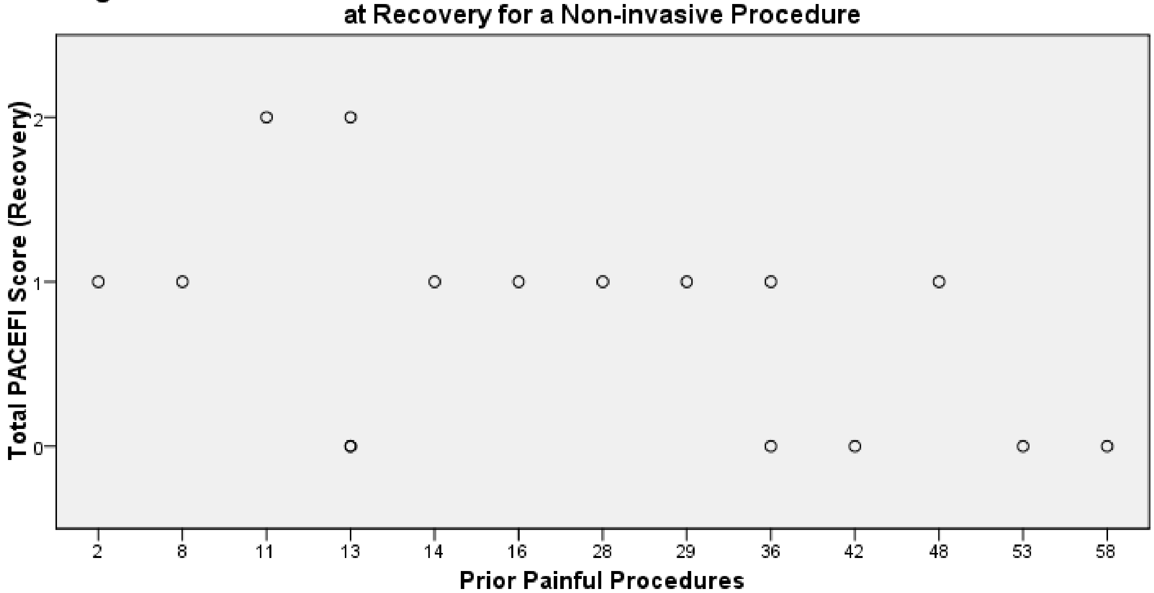


Figure 8. ELGA Infant Correlations for Ventilation & Total PACEFI Score at Baseline for a Non-invasive Procedure

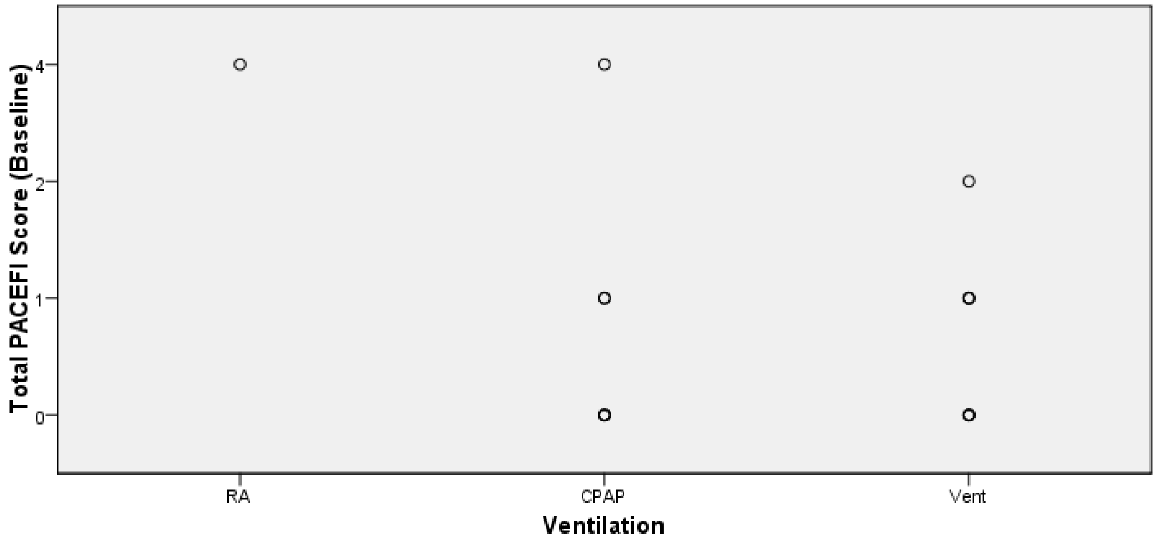
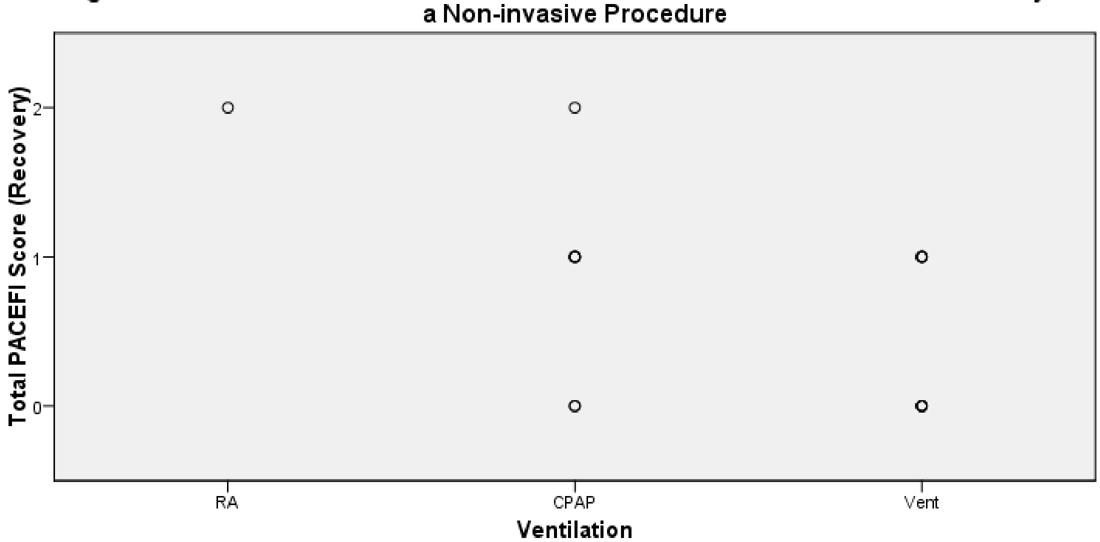


Figure 9. VLGA Infant Correlations for Ventilation & Total PACEFI Score at Recovery for a Non-invasive Procedure



VLGA infants' correlations are as follows (Table 21). *Prior Painful Procedures* and the rating *During* showed a significant moderate positive correlation (r = .520, $p < .05$). Previous painful procedures prior to the rating were related to increased behavioral cues during the non-invasive procedure (Figure 10). *Prior Painful Procedures* and the rating *Recovery* showed a small negative correlation (r = -.321). Prior painful procedures previous to the rating were associated with increased behavioral cues at recovery five minutes after handling was completed (Figure 11).

Table 21

VLGA Correlations for Confounding Variables (*n* = 16)

	Count Pain	Ventilation	Baseline	During	Recovery
Count Pain	1.00				
Ventilation	.297	1.00			
Baseline	.007	-.077	1.00		
During	.520*	-.230	.177	1.00	
Recovery	-.321	-.105	.517*	-.206	.100

Note. Count Pain = all painful procedures prior to the rating, Ventilation = respiratory support.
Baseline, During, and Recovery = Behaviors Total Score
*Correlations significant at the 0.05 level (2 tailed)

Figure 10. VLGA Infant Correlations for Prior Painful Procedures & Total PACEFI Score During a Non-invasive Procedure

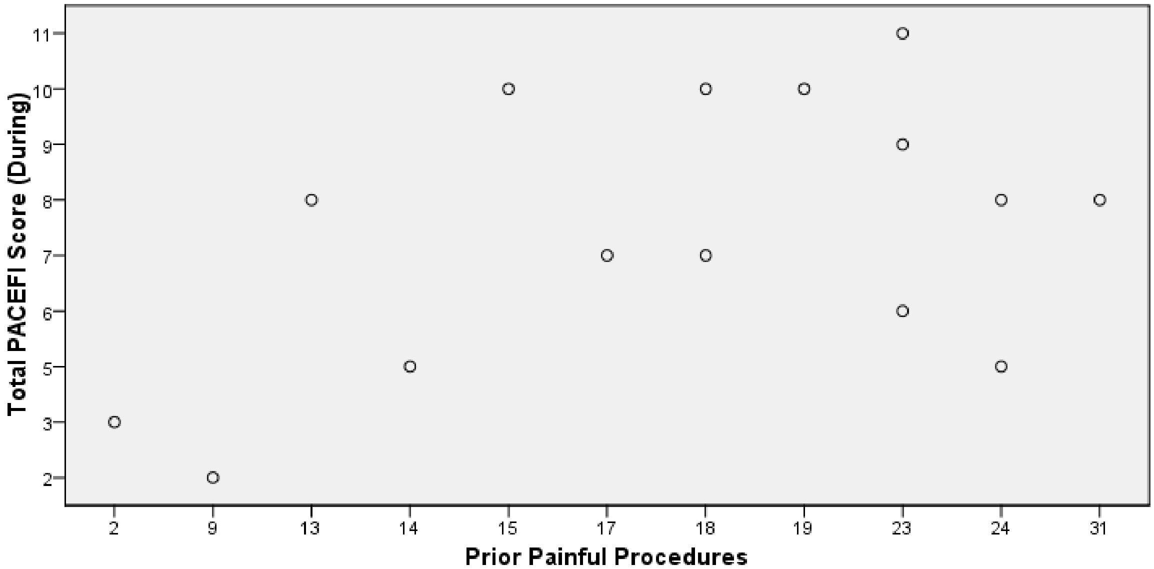
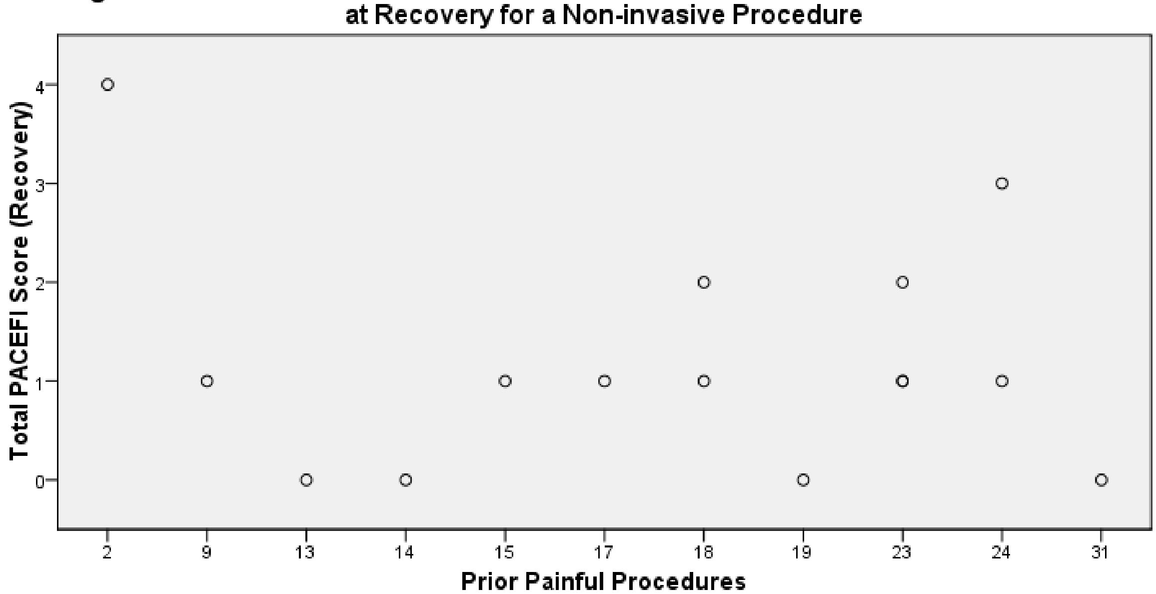


Figure 11. VLGA Infant Correlations for Prior Painful Procedures & Total PACEFI Score at Recovery for a Non-invasive Procedure



Summary

Significant relationships were found for prior painful procedures for both during and recovery during the non-invasive procedure. This finding indicates that infants were more likely to demonstrate increased behavioral cues during the non-invasive procedure if they endured a high number of previous invasive procedures prior to the rating. Prior painful procedures were included in a preliminary RANOVA analysis and were not significant. Due to the sample size of ELGA and VLGA infants, prior painful procedures were left out of the final analysis.

RANOVA Analysis

A RANOVA was conducted to examine the effect of gestational age on baseline, during, and recovery ratings for a non-painful procedure ($n = 31$). There was one within subjects factor with three levels: Non-invasive baseline total score, Non-invasive during total score, Non-invasive recovery total score; and one between subjects factor with two levels: gestational age (ELGA $n = 16$, VLGA $n = 15$).

The assumption of compound symmetry was not met ($p < .001$), therefore the univariate test with epsilon correction, Greenhouse-Geisser is reported (Table 21). There was a significant difference between the rating scores ($F(2,58) = 143.553$ $p <.001$). The ratings for baseline and during ($p < .001$) and during and recovery ($p < .001$) were significant. During ($m = 7.883$) had significantly higher scores than baseline ($m = .935$) and recovery ($m = .975$) (Figure 12). There was no interaction effect noted between ELGA and VLGA infants (Figures 13 and14). There was no significant group difference (Table 22) noted for the ratings baseline, during, and recovery between the ELGA and VLGA infants.

Summary

ELGA and VLGA infants demonstrated a similar response to the non-invasive procedure. Baseline and recovery scores were noted to be lower than during the invasive procedure. However, ELGA infants demonstrated a more robust response than their VLGA infant counterparts. This may be due to neurodevelopmental immaturity. It was also noted that ELGA infants' recovery score dropped lower than their baseline, which may indicate total exhaustion. This, too, may be due to neuro-developmental immaturity or it may be a response to sensitization prior to the procedure. Although diaper change is considered a non-invasive procedure, it may be that infants at this developmental age find this procedure painful. In addition due to the observational nature of the study, diaper change was part of a care experience and the prior sensitization may cause the ELGA infants to shut down and conserve energy (Als, 1982). Further discussion is included in Chapter 5.

Table 22

Repeated Measures ANOVA for the PACEFI Instrument (During)

Source	df	MS	F	*p*
Between Subjects				
Gestational age	1	1.600	.280	.601
Error	29	5.725		
Within Subjects				
Rating	1.2	78.946	143.553	.001
Error	36	5.503		

Note. df = degrees of freedom, MS = mean squared, f = F score, *p* = significance. (n=31)

Figure 12. ELGA & VLGA Infants' PACEFI Score for a Non-invasive Procedure (n = 31)

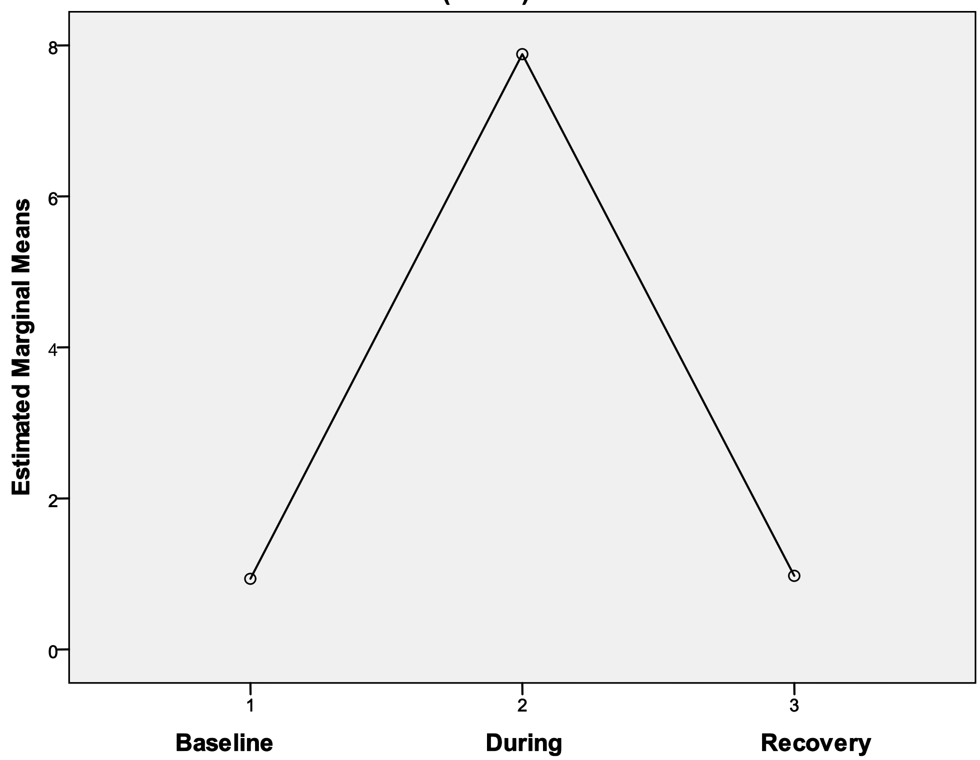


Figure 13. ELGA & VLGA Infants' PACEFI Scores for a Non-invasive Procedure

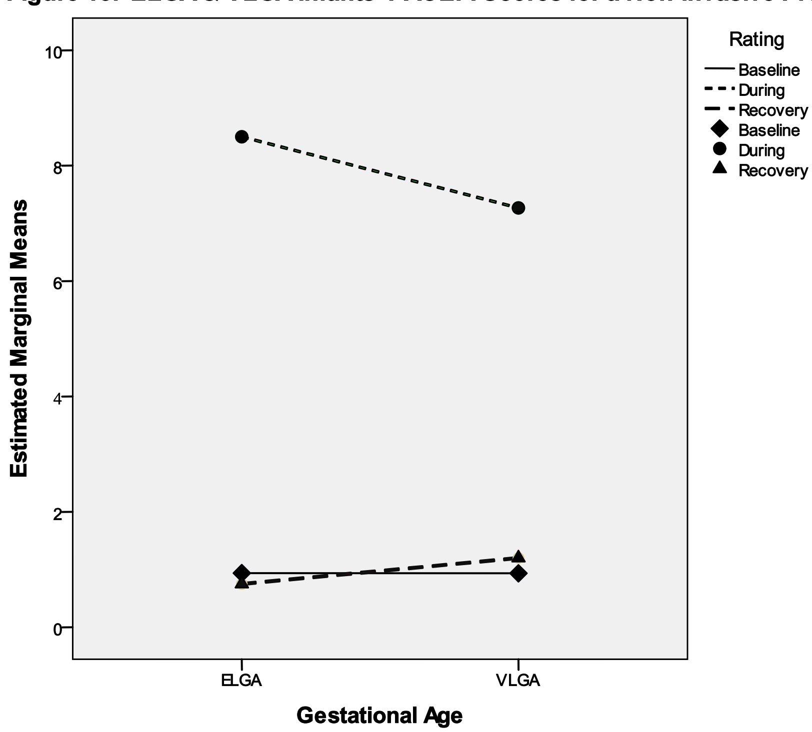
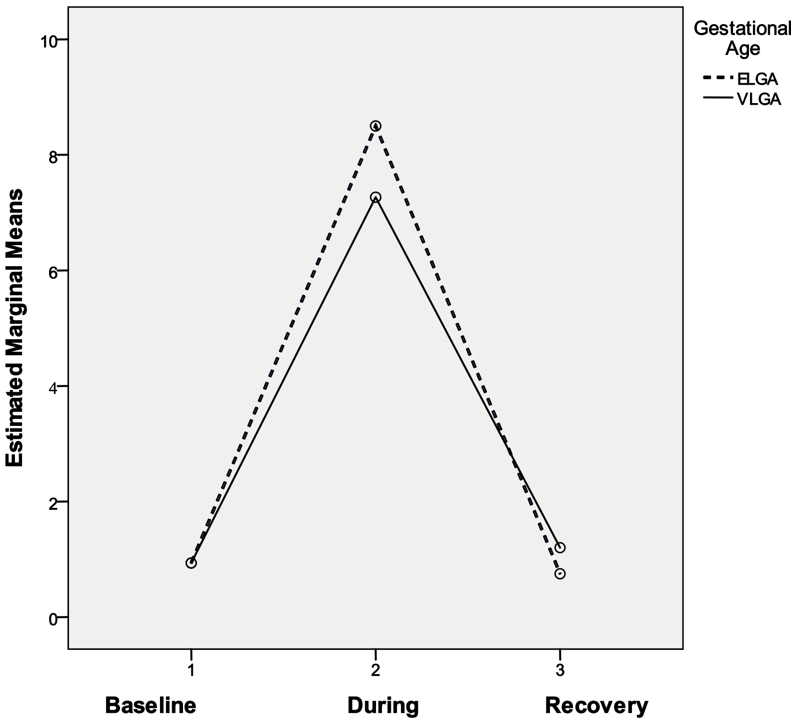


Figure 14. ELGA & VLGA Infants' PACEFI Scores for a Non-invasive Procedure



Relationships Between Physiologic Indicators and Behavioral Cues

Pearson Product–Moment correlations were conducted to evaluate whether or not there is a significant relationship between physiologic indicators and behavioral indicators for 24–33 6/7 week infants during an invasive and non-invasive procedure. The same sample used for Aims 2 and 3 will be used for this analysis: ELGA infants (n = 16) and VLGA infants (n = 15). All correlations above .30 will be reported for exploratory purposes due to the small sample size and the risk for a type II error.

Pearson's Product-Moment correlations were conducted for ELGA infants at baseline five minutes prior to handling before a non-invasive procedure (Table 23). There was low negative correlation between *Heart Rate* and *Oxygen Saturation* (r = -.362). Lower oxygen saturations were related to higher heart rates during the non-invasive procedure at baseline (Figure 15). *Heart*

Rate and the rating *Baseline* (behaviors) showed a significant moderate negative correlation (r = -.585, $p < .022$) with each other. Decreased behavioral cues at the baseline five minutes prior to handling were related to higher heart rates during the non-invasive procedure (Figure 16). *Oxygen Saturation* and the rating *Baseline* (behaviors) demonstrated a low positive correlation (r = .391) with each other. Increased behavioral cues at the baseline five minutes prior to handling were related to higher oxygen saturations during the non-invasive procedure (Figure 17).

Table 23

ELGA Infant Correlations Non-invasive Physiologic & Behavioral Variables at Baseline

	HR	RR	O2 Saturation	Behaviors
HR	1.00			
RR	-.264	1.00		
O2 Saturation	-.362	-.145	1.00	
Behaviors	-.585*	-.238	.391	1.00

Note. (n = 16). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O2 Saturation)
Behaviors = totaled summed item scores for Baseline
*Correlations significant at the 0.05 level (2 tailed)

Figure 15. ELGA Infant Correlations for Heart Rate & Oxygen Saturation at Baseline for a Non-invasive Procedure

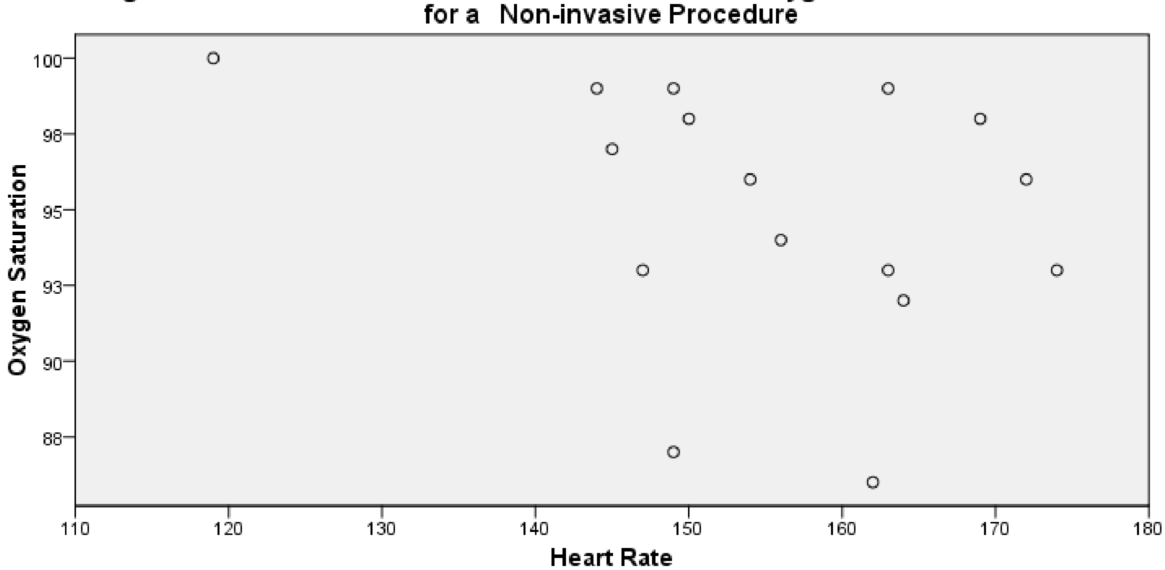


Figure 16. ELGA Infant Correlations for Heart Rate & Total PACEFI Score at Baseline for a Non-invasive Procedure

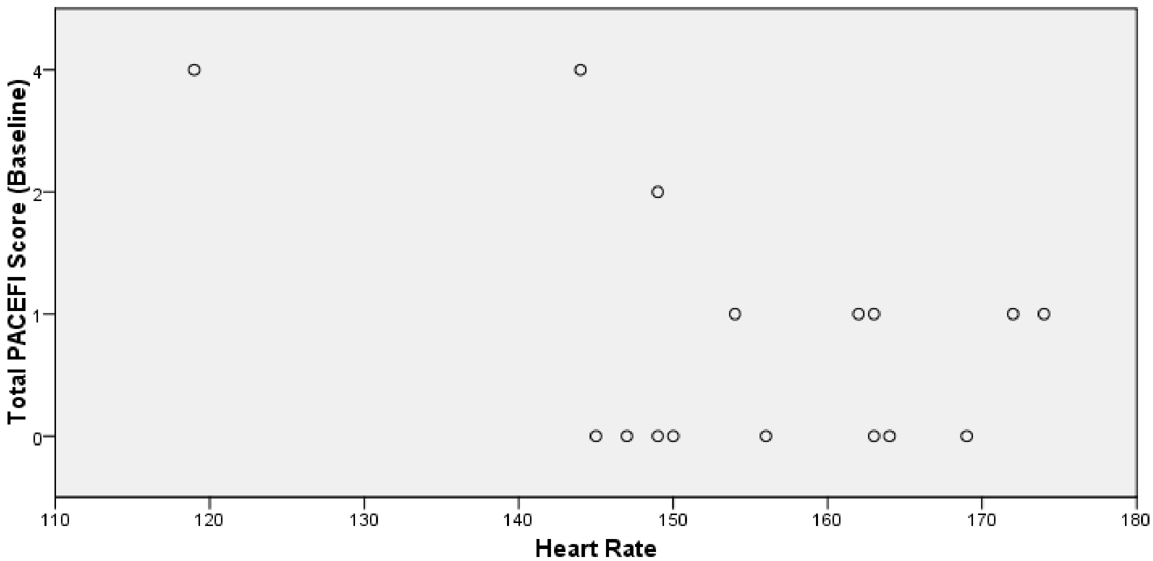
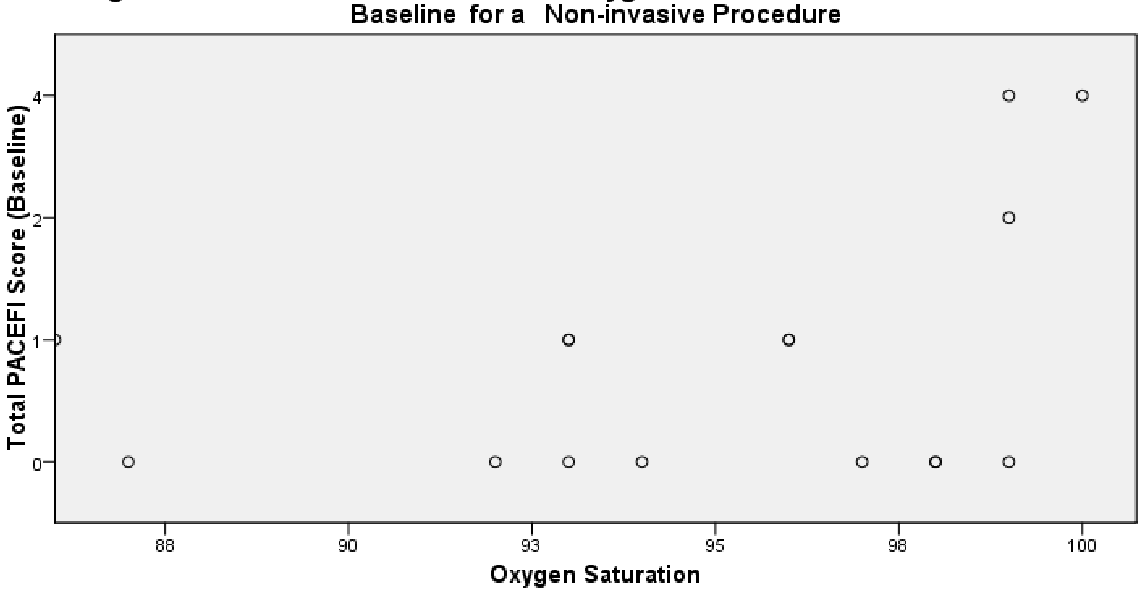


Figure 17. ELGA Infant Correlations for Oxygen Saturation & Total PACEFI Score at Baseline for a Non-invasive Procedure



Pearson's Product-Moment correlations were conducted for ELGA infants during a non-invasive procedure (Table 24). *Heart Rate* and *Respiratory Rate* demonstrated a low negative correlation (*r* = -.377) with each other. Higher heart rates were associated with lower respiratory rates (Figure 18).

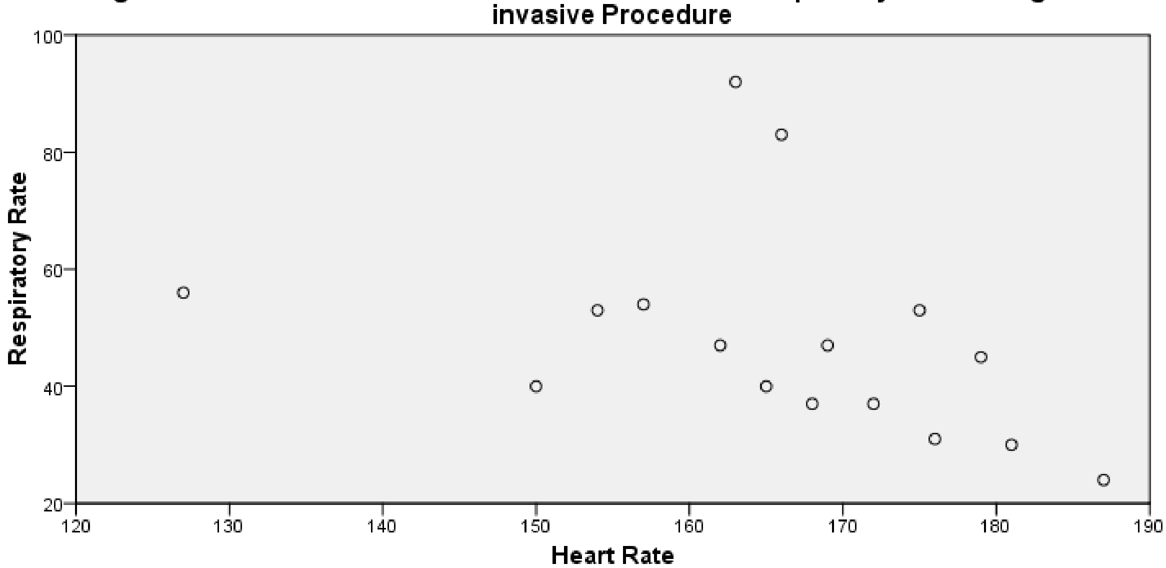
Table 24

ELGA Infant Correlations for Non-invasive Physiologic & Behavioral Variables at During

	HR	RR	O2 Saturation	Behaviors
HR	1.00			
RR	-.377	1.00		
O2 Saturation	-.255	-.290	1.00	
Behaviors	-.076	.213	.080	1.00

Note. (*n* = 16) Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O2 Saturation)
Behaviors = totaled summed item scores for During

Figure 18. ELGA Infant Correlations for Heart Rate & Respiratory Rate During a Non-invasive Procedure



Pearson's Product-Moment correlations were conducted for ELGA infants at recovery five minutes after handling was completed following a non-invasive procedure (Table 25). *Heart Rate* and *Oxygen Saturation* showed a significant moderate negative correlation (r = -.506, p < .045) with each other. High heart rates were associated with lower oxygen saturation at recovery five minutes after handling (Figure 19). *Oxygen Saturation* and the rating *Recovery* (behaviors) showed a moderate positive correlation *(r* = .444) with each other. Higher oxygen saturations were related to increased behavioral cues at recovery five minutes after handling (Figure 20).

Table 25

ELGA Infant Correlations Non-invasive Physiologic & Behavioral Variables at Recovery

	HR	RR	O2 Saturation	Behaviors
HR	1.00			
RR	.005	1.00		
O2 Saturation	-.506*	.136	1.00	
Behaviors	-.253	.196	.444	1.00

Note. (n = 16) Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O2 Saturation), Behaviors = totaled summed item scores for Recovery

Figure 19. ELGA Infant Correlations for Oxygen Saturation & Heart Rate at Recovery for a Non-invasive Procedure

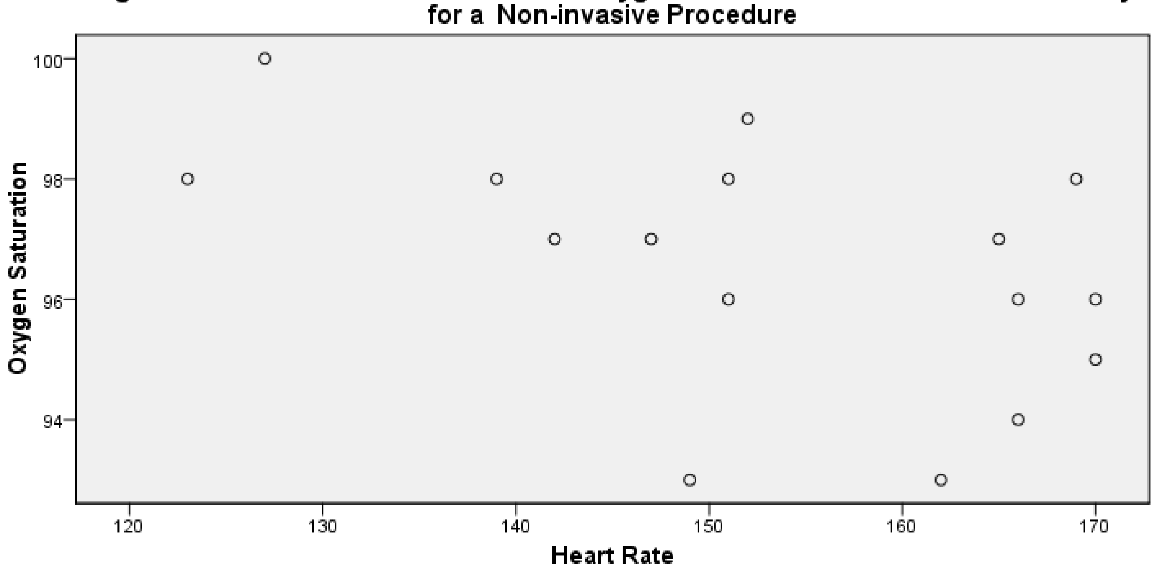
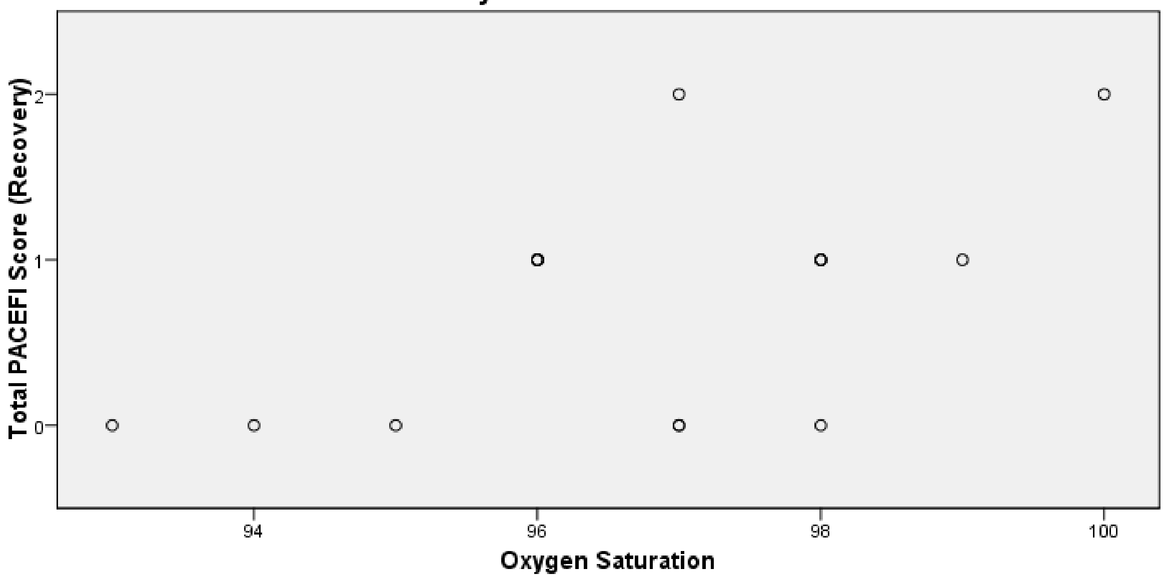


Figure 20. ELGA Age Infant Correlations for Oxygen Saturation & Total PACEFI Score at Recovery for a Non-invasive Procedure



Pearson's Product-Moment correlations were conducted for ELGA infants at baseline five minutes prior to handling before an invasive procedure (Table 26). *Heart Rate* and the rating *Baseline* (behaviors) for an invasive procedure showed a moderate significant positive correlation (r = -.570, p < .021) with each other. Increased behavioral cues at the baseline five minutes before handling were associated to higher heart rates. (Figure 21).

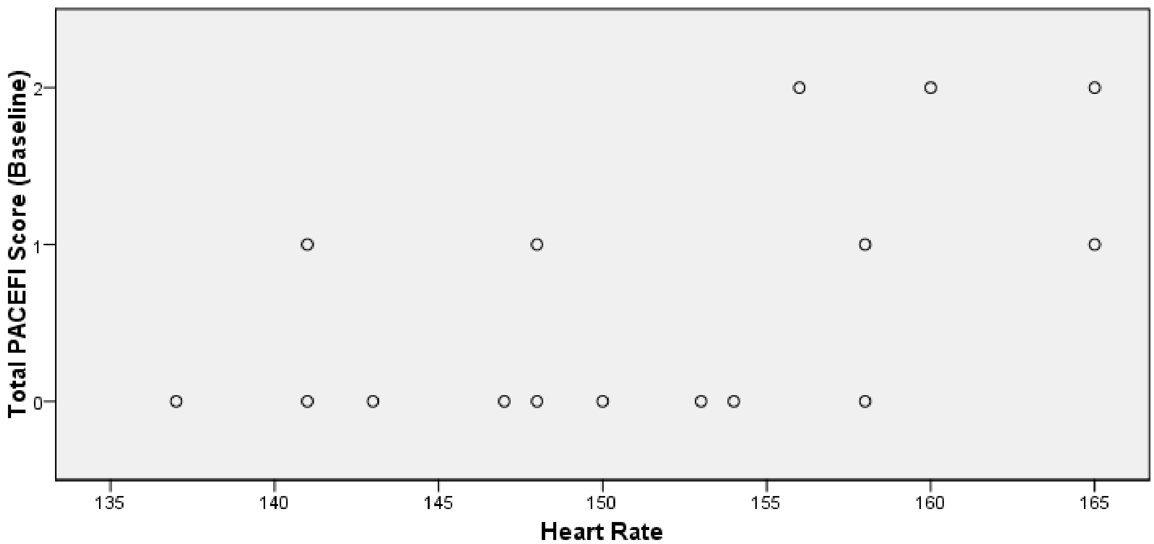
Table 26

ELGA Correlations for Invasive Physiologic and Behavioral Variables (Baseline)

	HR	RR	O2 Saturation	Behaviors
HR	1.00			
RR	-.019	1.00		
O2 Saturation	-.287	-.283	1.00	
Behaviors	.570*	-.264	.122	1.00

Note. Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O2 Saturation)
Behaviors = totaled summed item scores for Baseline
*Correlations significant at the 0.05 level (2 tailed)

Figure 21. ELGA Infant Correlations for Heart Rate & Total PACEFI Score at Baseline for an Invasive Procedure



Pearson's Product-Moment correlations were conducted for ELGA infants during an invasive procedure (Table 27). *Heart Rate* and *Respiratory Rate* showed a low negative correlation (r = -.419) with each other. Higher heart rates were associated with lower respiratory rates during an invasive procedure (Figure 22). *Heart Rate* and the rating *During* (behaviors) showed a low positive correlation (r = .447) with each other. Increased behavioral cues were associated with higher heart rates during an invasive procedure (Figure 23). *Respiratory Rate* and *Oxygen Saturation* showed a low positive correlation (r = .373) with each other. Lower respiratory rates were related to lower oxygen saturation (Figure 24). *Respiratory Rate* and the rating *During* (behaviors) showed a low negative correlation (r = -.350) with each other. Less behavioral cues were associated with high respiratory rates during an invasive procedure (Figure 25).

Table 27

ELGA Infant Correlations for Invasive Physiologic & Behavioral Variables at During

	HR	RR	O2 Saturation	Behaviors
HR	1.00			
RR	-.419	1.00		
O2 Saturation	-.279	-.373	1.00	
Behaviors	.447	-.350	-.290	1.00

Note. (*n* = 16). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O2 Saturation)
Behaviors = totaled summed item scores for During

Figure 22. ELGA Infant Correlations for Heart Rate & Respiratory rate During an Invasive Procedure

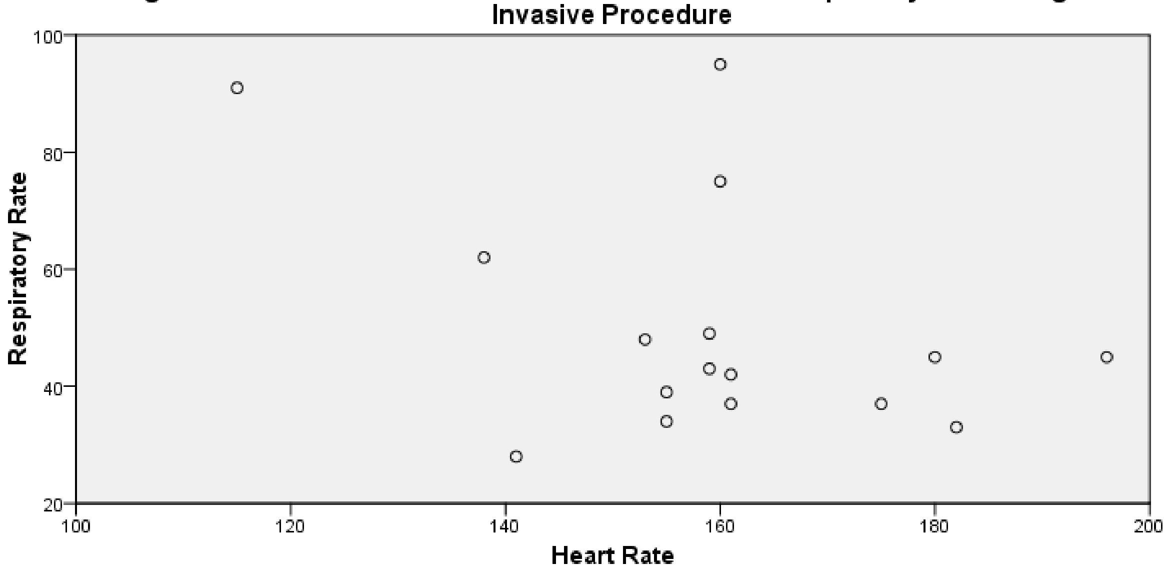
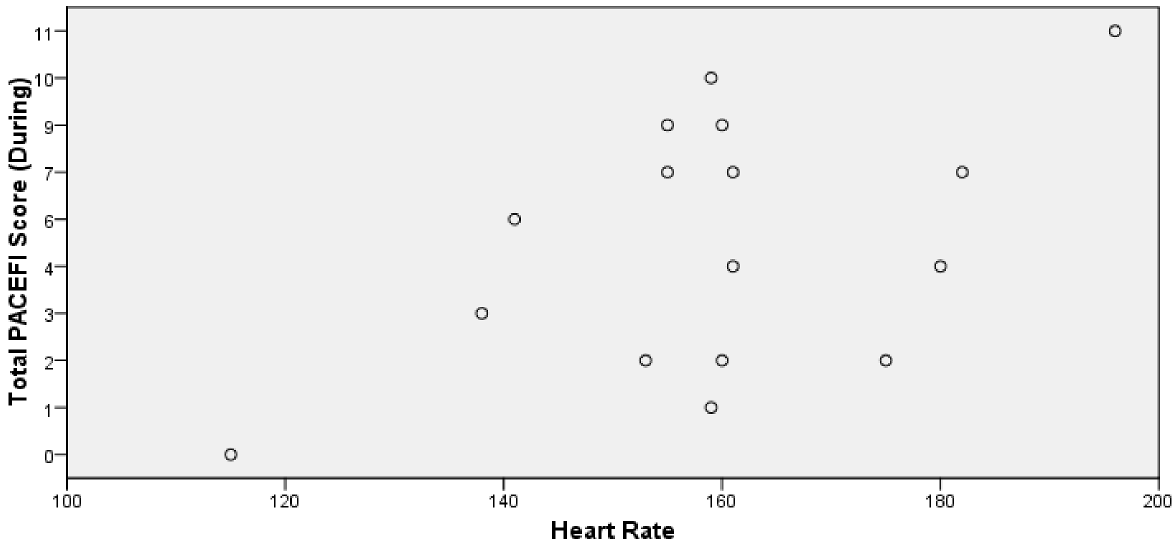


Figure 23. ELGA Age Infant Correlations for Heart Rate & Total PACEFI Score During an Invasive Procedure



Firgure 24. ELGA Infant Correlations for Respiratory Rate & Oxygen Saturation During and Invasive Procedure

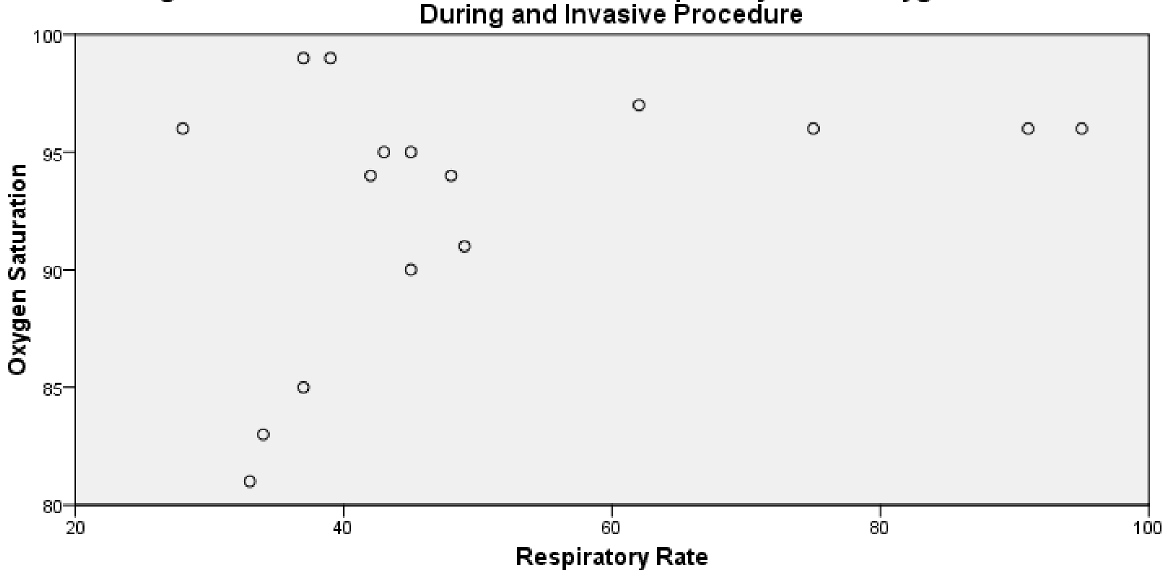
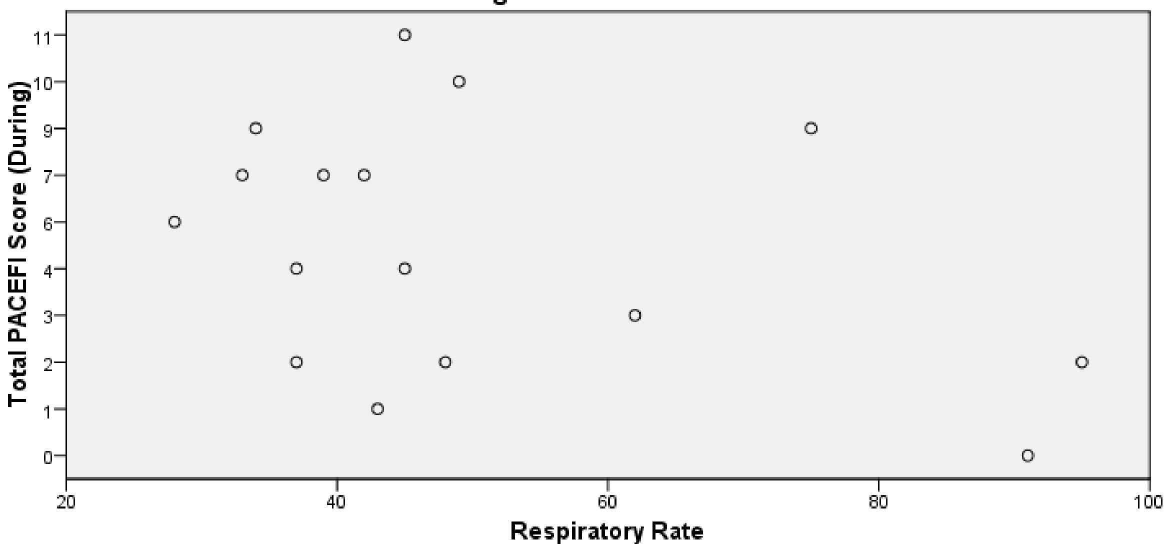


Figure 25. ELGA Infant Correlations for Respiratory Rate & Total PACEFI Score During an Invasive Procedure



Pearson's Product-Moment correlations were conducted for ELGA infants at recovery five minutes after handling was completed following an invasive procedure (Table 28). *Respiratory Rate* and the rating *Recovery* showed a low positive correlation (*r* = .348) with each other. Higher respiratory rates were associated with increased behavioral cues at recovery five minutes after handling was completed following an invasive procedure. (Figure 26).

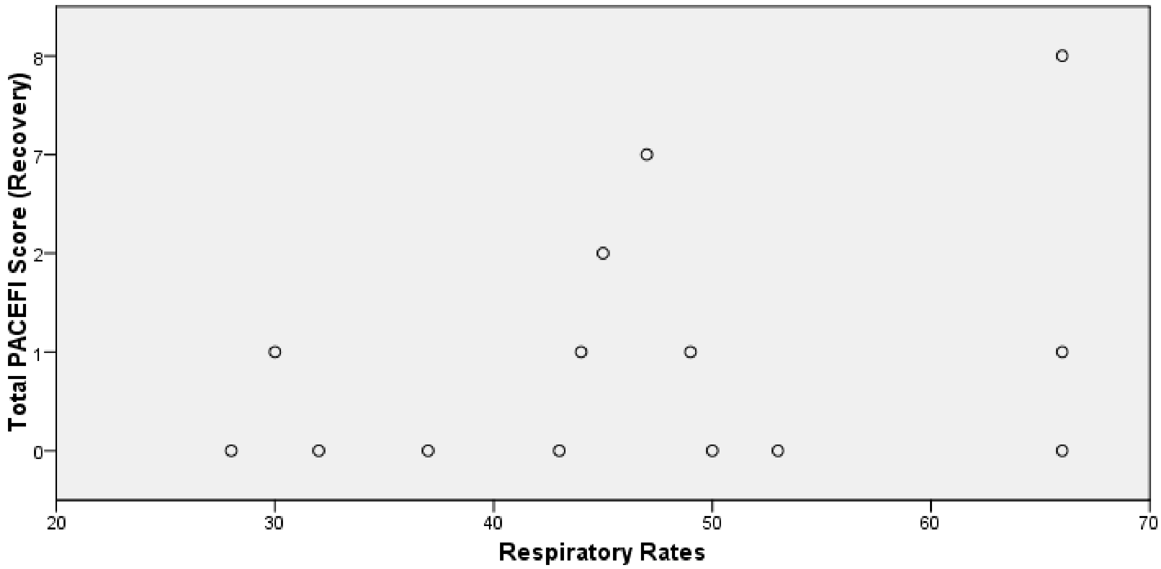
Table 28

ELGA Infant Correlations for Invasive Physiologic and Behavioral Variables at Recovery

	HR	RR	O2 Saturation	Behaviors
HR	1.00			
RR	-.194	1.00		
O2 Saturation	-.048	.220	1.00	
Behaviors	.049	.348	.090	1.00

Note. (*n* = 16). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O2 Saturation)
Behaviors = Totaled summed item scores for Recovery

Figure 26. ELGA Infant Correlations for Respiratory Rate & Total PACEFI Score at Recovery for an Invasive Procedure



Pearson's Product-Moment correlations were conducted for VLGA infants at baseline five minutes before handling prior to a non-invasive procedure (Table 29). *Heart Rate* and *Oxygen Saturation* showed a low negative correlation (*r* = -.437) with each other. Higher heart rates were related to lower oxygen saturations at baseline five minutes before handling prior to a non-invasive procedure (Figure 27). *Respiratory Rate* and the rating *Baseline* (behaviors) showed a low negative correlation (*r* = -.390) with each other. Lower respiratory rates were associated with increased behavioral cues at the baseline rating 5 minutes before handling prior to the non-invasive procedure (Figure 28).

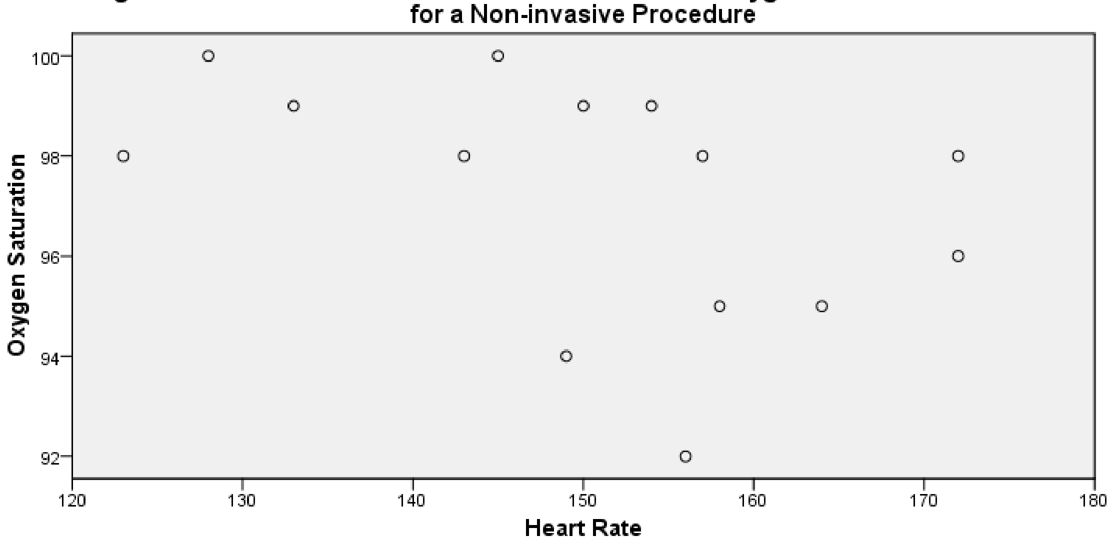
Table 29

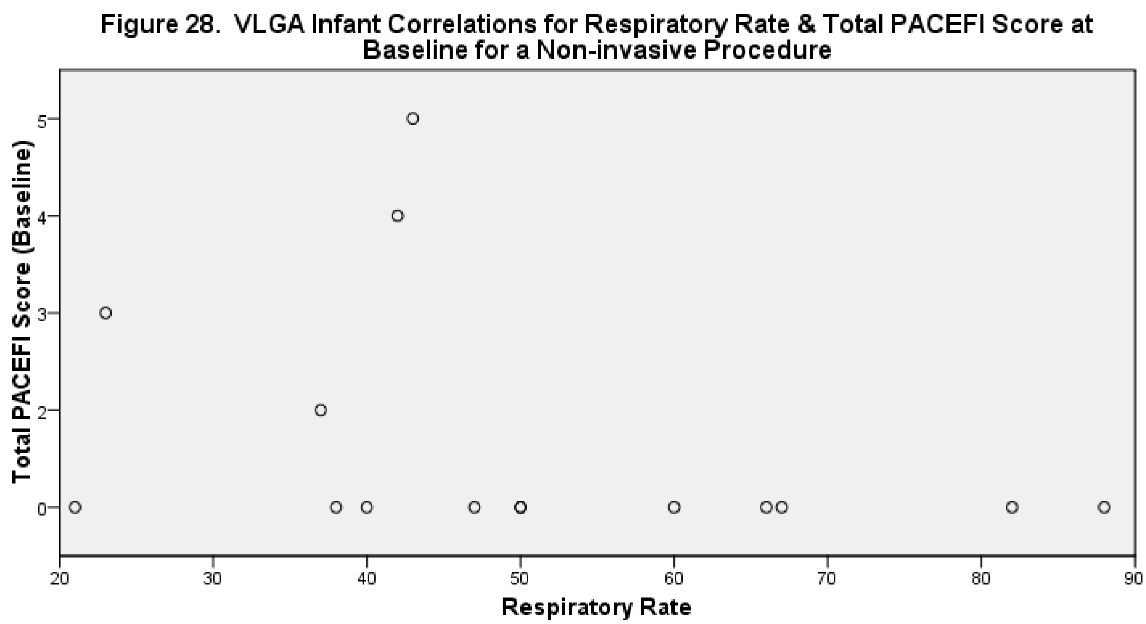
VLGA Infant Correlations for Non-invasive Physiologic and Behavioral Variables at Baseline

	HR	RR	O_2 Saturation	Behaviors
HR	1.00			
RR	-.252	1.00		
O_2 Saturation	-.437	-.174	1.00	
Behaviors	-.120	-.390	.290	1.00

Note. (n=15). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O_2 Saturation)
Behaviors = Totaled summed item scores for Baseline

Figure 27. VLGA Infant Correlations for Heart Rate & Oxygen Saturation at Baseline for a Non-invasive Procedure





Pearson's Product-Moment correlations were completed for VLGA infants during a non-invasive procedure (Table 30). *Heart Rate* and *Respiratory Rate* showed a moderate significant positive correlation (r = .641, p < .010) with each other. Lower heart rates were related to lower respiratory rates during a non-invasive procedure (Figure 29). *Heart Rate* and *Oxygen Saturation* showed a low negative correlation (r = -.417) with each other. Higher heart rates were associated with lower oxygen saturations during a non-invasive procedure (Figure 30). *Heart Rate* and the rating *Baseline* showed a low positive correlation (r = .438) with each other. Higher hearts were related to increased behavioral cues during a non-invasive procedure (Figure 31).

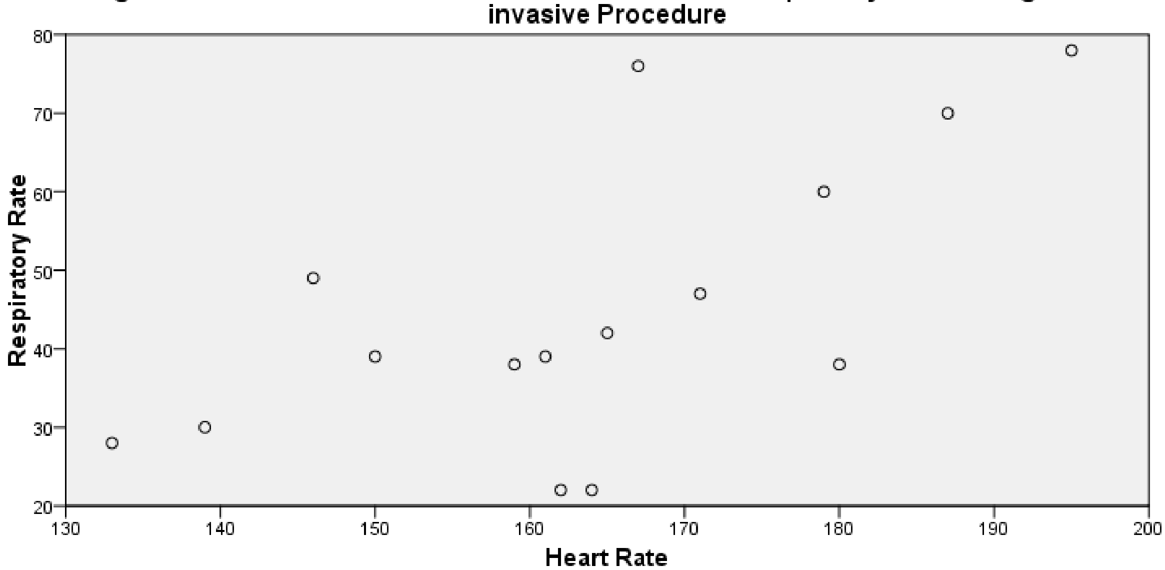
Table 30

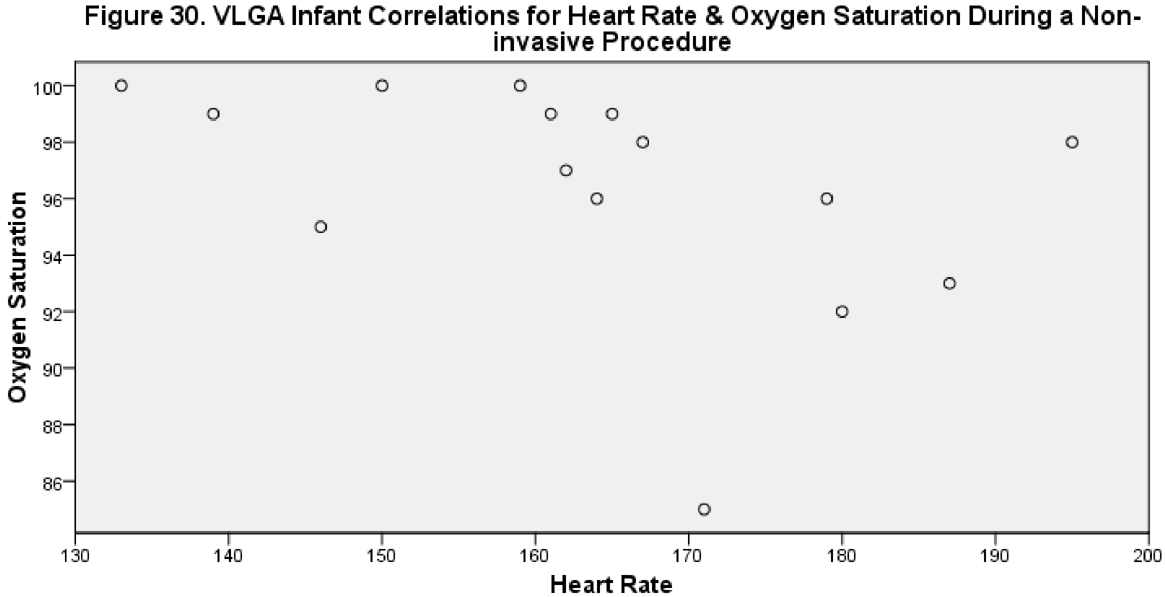
VLGA Infant Correlations for Non-invasive Physiologic and Behavioral Variables at During

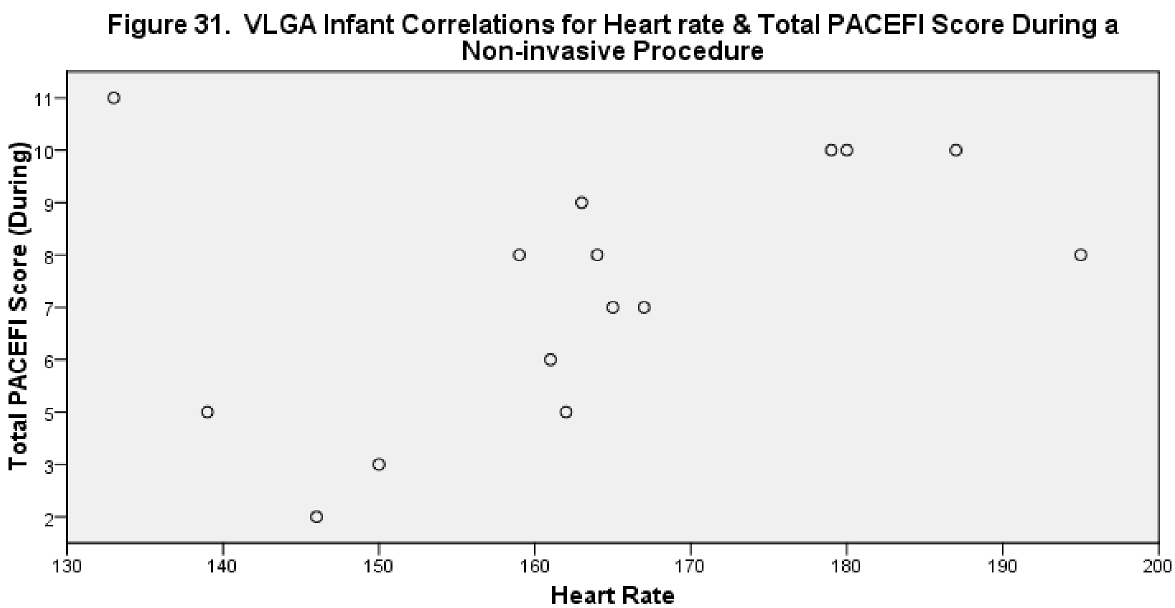
	HR	RR	O_2 Saturation	Behaviors
HR	1.00			
RR	.641*	1.00		
O_2 Saturation	-.417	-.156	1.00	
Behaviors	-.438	.181	-.299	1.00

Note. (*n* = 15). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O_2 Saturation) Behaviors = total summed item scores for During
*Correlations significant at the 0.01 level (2 tailed)

Figure 29. VLGA Infant Correlations for Heart Rate & Respiratory Rate During a Non-invasive Procedure







Pearson's Product-Moment correlations were completed for VLGA infants at recovery five minutes after handling was completed following a non-invasive procedure (Table 31). *Heart Rate* and *Respiratory Rate* showed a low positive correlation (r = .431) with each other. Lower heart rates were related to lower respiratory rates at recovery five minutes after handling was completed following a non-invasive procedure (Figure 32).

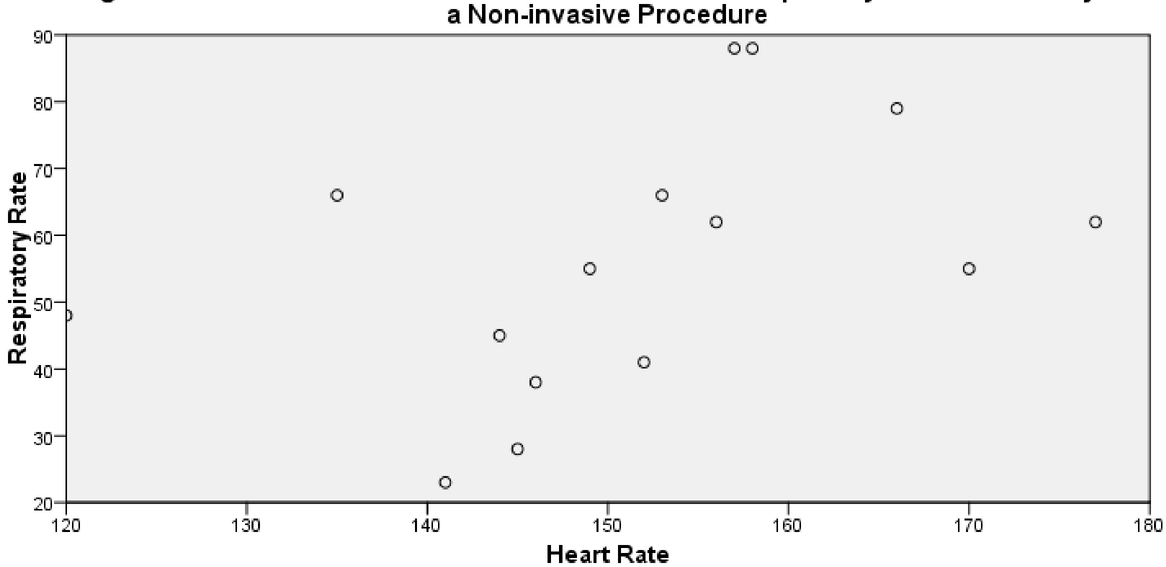
Table 31

VLGA Infant Correlations for Non-invasive Physiologic and Behavioral Variables at Recovery (*n*=15)

	HR	RR	O_2 Saturation	Behaviors
HR	1.00			
RR	.431	1.00		
O_2 Saturation	-.285	-.203	1.00	
Behaviors	.150	-.044	.146	1.00

Note. (*n* = 15). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O_2 Saturation)
Behaviors = Total summed item scores for Recovery

Figure 32. VLGA Infant Correlations for Heart Rate & Respiratory Rate at Recovery for a Non-invasive Procedure



Pearson's Product-Moment correlations were completed for VLGA infants at baseline five minutes before handling prior to an invasive procedure (Table 32). *Heart Rate* and *Oxygen*

Saturation showed a low positive correlation (*r* = .420) with each other. Lower heart rates were associated with lower oxygen saturations at baseline five minutes before handling prior to an invasive procedure (Figure 33). *Respiratory Rate* and the rating *Baseline* (behaviors) showed a low negative correlation (*r* = -.388) with each other. Although it appears that low respiratory rates were associated with increased behavioral cues at baseline during an invasive procedure, this finding may be spurious due to the outlier rating of 12 at baseline (Figure 34). The correlation without the outlier rating decreases to (*r* = .275). The outlier rating was completed on an infant who was crying at baseline from hunger. The infant was given sucrose, a non-pharmacologic intervention, and PACEFI scores decreased at during and recovery.

Table 32

VLGA Infant Correlations for Invasive Physiologic and Behavioral Variables at Baseline

	HR	RR	O_2 Saturation	Behaviors
HR	1.00			
RR	.236	1.00		
O_2 Saturation	.420	-.236	1.00	
Behaviors	.140	-.388	-.103	1.00

Note. (*n* = 15). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O_2 Saturation)
Behaviors = total summed scores for Baseline

Figure 33. VLGA Infant Correlations for Heart Rate & Oxygen Saturation at Baseline for an Invasive Procedure

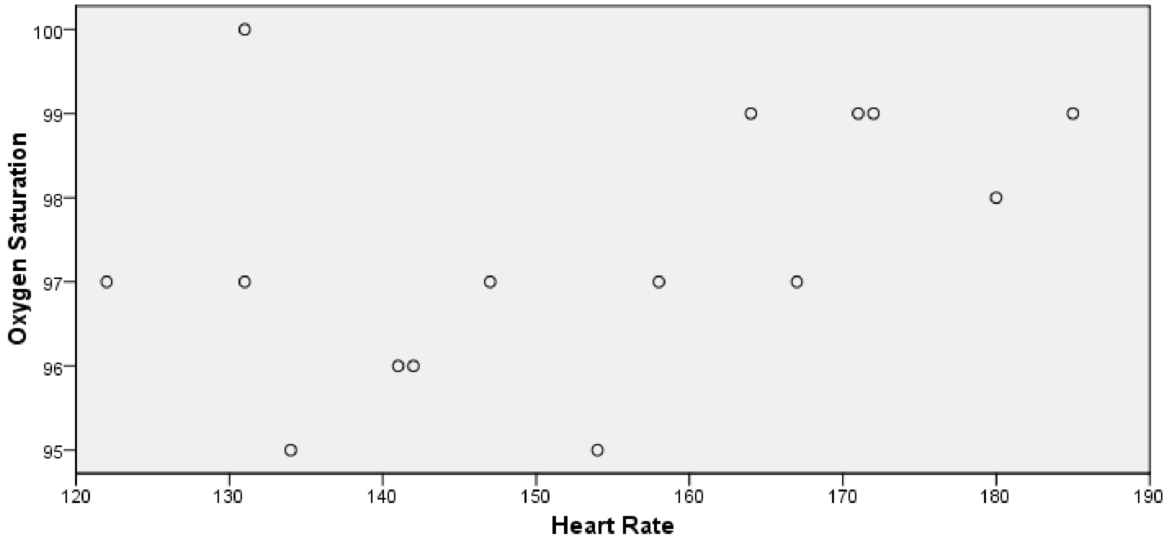
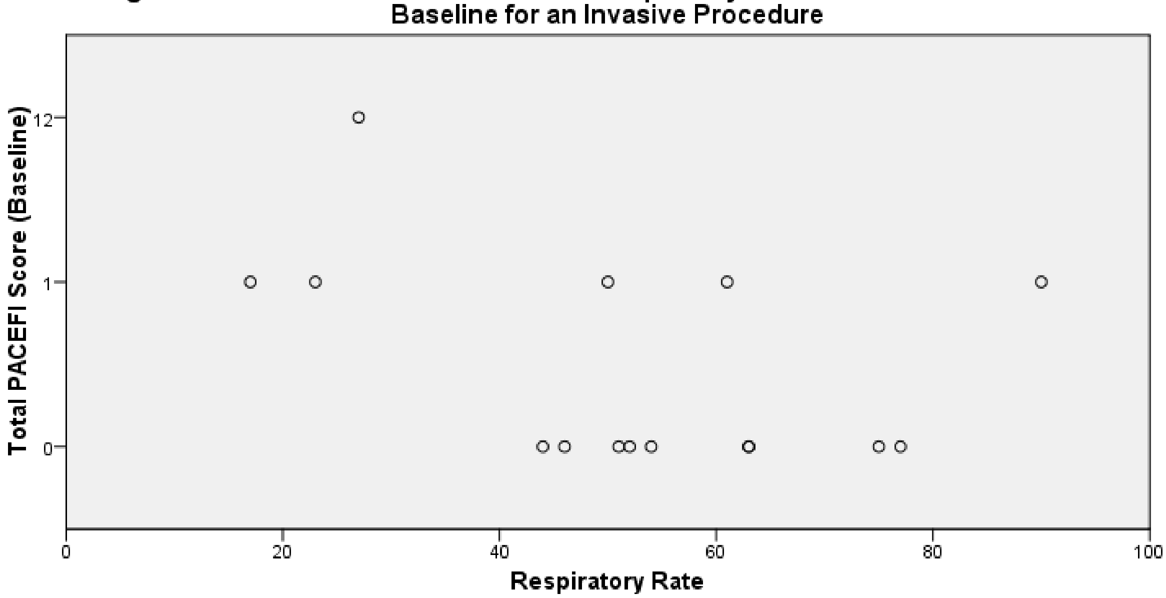


Figure 34. VLGA Infant Correlations for Respiratory Rate & Total PACEFI Score at Baseline for an Invasive Procedure



Pearson's Product-Moment correlations were completed for VLGA infants during an invasive procedure (Table 33). *Respiratory Rate* and the rating *During* (behaviors) showed a low negative correlation (r = -.307) with each other. Lower respiratory rates were related to increased behavioral cues during an invasive procedure (Figure 35). *Oxygen Saturation* and the rating *During* (behaviors) showed a low positive correlation (*r* = .390) with each other. Lower oxygen saturations were associated with less behavioral cues during an invasive procedure (Figure 36).

Table 33

VLGA Infant Correlations for Invasive Physiologic and Behavioral Variables at During (n=15)

	HR	RR	O_2 Saturation	Behaviors
HR	1.00			
RR	.265	1.00		
O_2 Saturation	.025	-.013	1.00	
Behaviors	-.033	-.307	.390	1.00

Note. (*n*=15). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O_2 Saturation)
Behaviors = totaled summed scores for During

Figure 35. VLGA Infant Correlations for Respiratory Rate & Total PACEFI Score During an Invasive Procedure

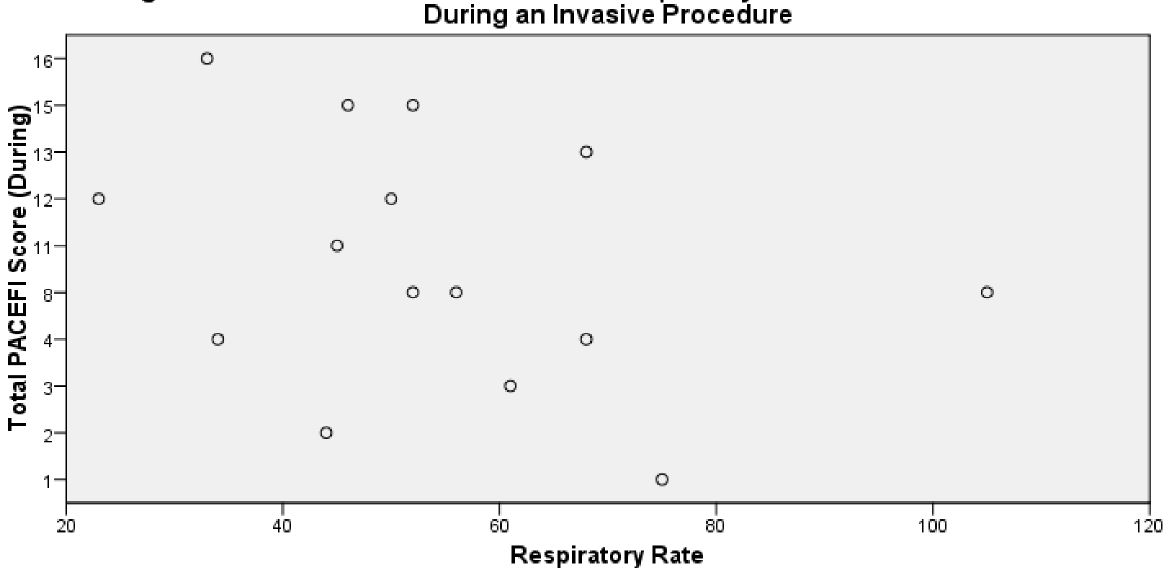
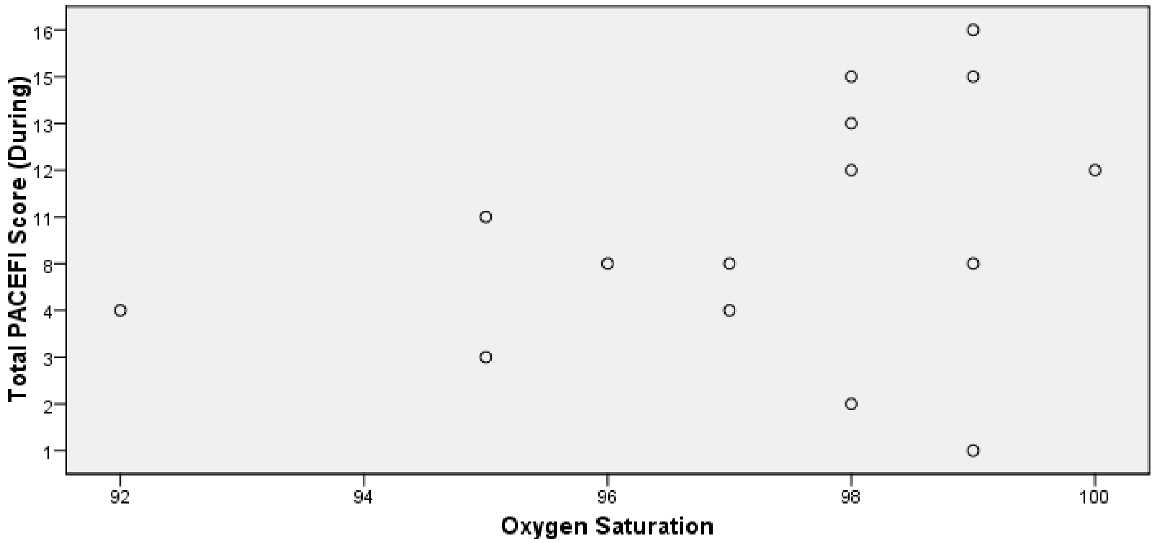


Figure 36. VLGA Infant Correlations for Oxygen Saturation & Total PACEFI Score During an Invasive Procedure



Pearson's Product-Moment correlations were completed for VLGA infants at recovery, five minutes after handling was completed following an invasive procedure (Table 34). *Heart Rate* and *Respiratory Rate* showed a low positive correlation (r = .328) with each other. Lower heart rates were related to lower respiratory rates after recovery five minutes after handling was completed following an invasive procedure (Figure 37). *Heart Rate* and the rating *Recovery* (behaviors) showed a low negative correlation (r = -.449) with each other. Higher heart rates were associated with less behavioral cues at recovery five minutes after handling was completed following an invasive procedure (Figure 38). *Respiratory Rate* and the rating *Recovery* (behaviors) showed a significant moderate negative correlation (r = -.550, p < .034) with each other. Lower respiratory rates were related to increased behavioral cues at recovery five minutes after handling was completed following an invasive procedure (Figure 39). *Oxygen Saturation* and the rating *Recovery* (behaviors) showed a low positive correlation (r = .447) with each other.

Higher oxygen saturations were associated with increased behavioral cues at recovery five minutes after handling was completed following an invasive procedure (Figure 40).

Table 34

VLGA Infant Correlations for Invasive Physiologic and Behavioral Variables at Recovery

	HR	RR	O2 Saturation	Behaviors
HR	1.00			
RR	.328	1.00		
O2 Saturation	-.283	-.194	1.00	
Behaviors	-.449	-.550*	.447	1.00

Note. (n=15). Heart Rate (HR), Respiratory Rate (RR), Oxygen Saturation (O2 Saturation)
Behaviors = totaled summed item scores for Recovery
*Correlations significant at the 0.5 level (2 tailed)

Figure 37. VLGA Infant Correlations for Heart Rate & Respiratory Rate at Recovery for an Invasive Procedure

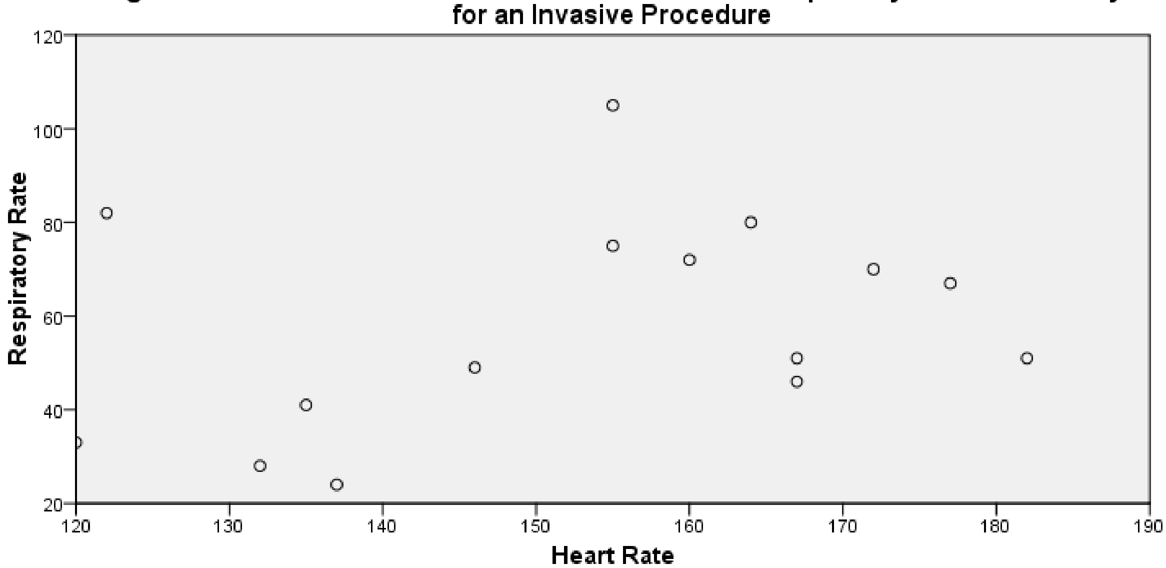


Figure 38. VLGA Infant Correlations for Heart Rate & Total PACEFI Score at Recovery for an Invasive Procedure

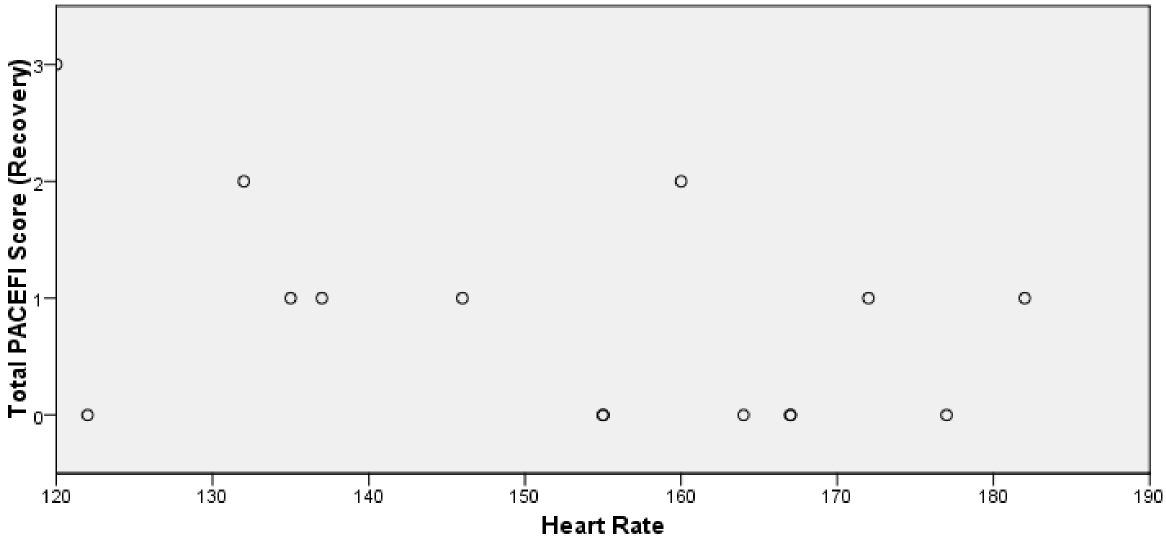


Figure 39. VLGA Infant Correlations for Respiratory Rate & Total PACEFI Score at Recovery for an Invasive Procedure

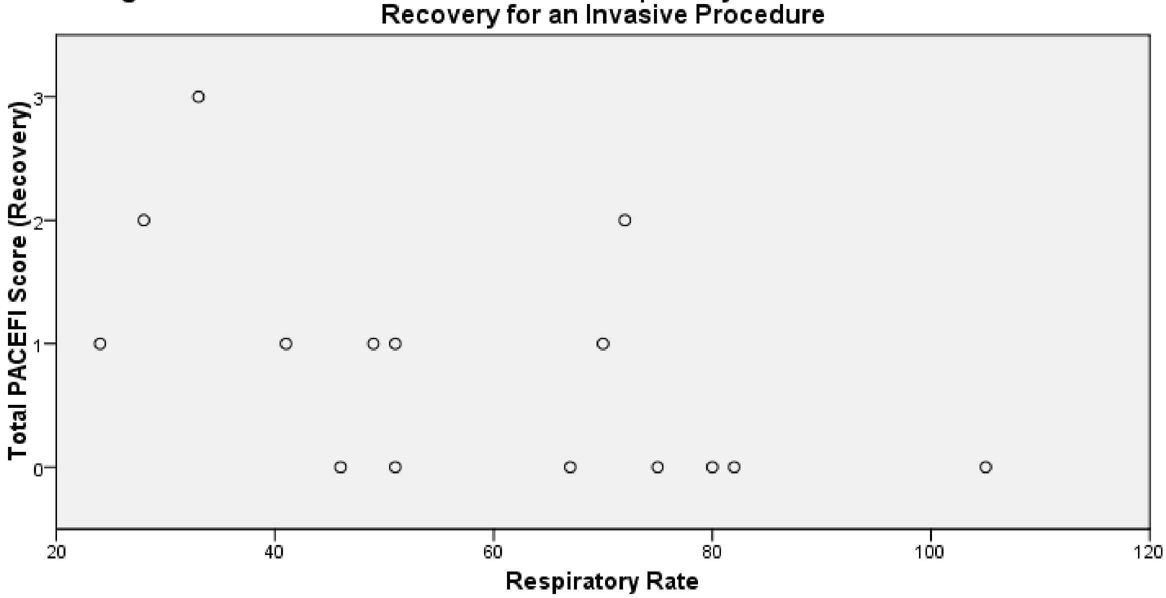
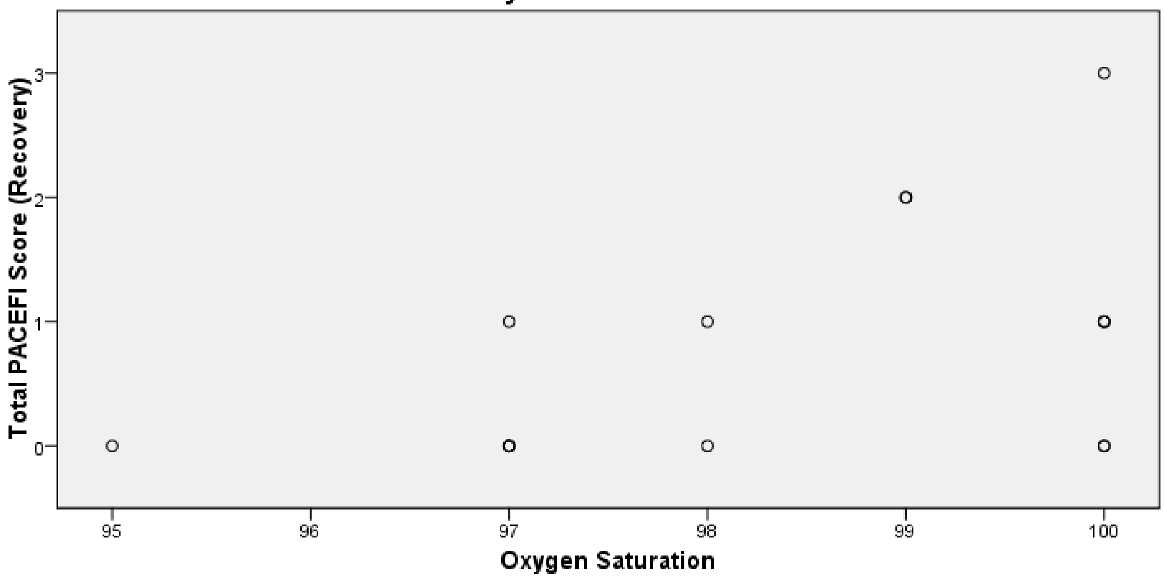


Figure 40. VLGA Age Infant Correlations for Oxygen Saturation & Total PACEFI Score at Recovery for an Invasive Procedure



Summary

Significant Correlations for ELGA & VLGA Infants for Invasive and Non-invasive Procedures. There were several significant relationships at the .05 level noted for both ELGA and VLGA infants during a non-invasive procedure. ELGA infants demonstrated higher PACEFI scores with increased heart rates at baseline for the invasive procedure. In addition, when ELGA infants had lower oxygen saturations at baseline and lower respiratory rates at recovery they demonstrated higher heart rates for the non-invasive procedure. Furthermore, VLGA infants demonstrated lower respiratory rates with decreased heart rates during a non-invasive procedure. Although there were significant correlations noted, the results should be viewed with caution as this is a small sample size and a statistical correction was not used due to the exploratory nature of this study. Further investigation is needed with larger sample sizes.

ELGA Infant Correlations for the Non-invasive Procedure. ELGA infants demonstrated increased heart rates at baseline, during and recovery for the non-invasive procedure. When the ELGA infants heart rate was increased it was noted that their respiratory rates and oxygen saturations decrease. ELGA infants also demonstrated lower PACEFI scores when their heart rates were increased at baseline. An increase in PACEFI scores was noted when these infants' oxygen saturations remained high at baseline and recovery.

ELGA Infant Correlations for the Invasive Procedure. ELGA infants demonstrated high heart rates at baseline and during for the invasive procedure. When the ELGA infant's heart rate remained high it was noted that their respiratory and oxygen saturations decrease. ELGA infants also demonstrated an increase in PACEFI scores when their heart rates remained high at baseline and during. Additionally, these infants demonstrated more cues when their respiratory rate remained increased at recovery.

VLGA Infant Correlations for the Non-invasive Procedure. VLGA infants demonstrated at increased heart rates at baseline and during. When the VLGA infant's heart rate remained increased it was noted that their respiratory rate and oxygen saturation decreased. These infants demonstrated a higher PACEFI score with and increased heart rate during the procedure. VLGA infants demonstrated a lower heart rate and respiratory rate at recovery.

VLGA infant Correlations for the Invasive Procedure. VLGA infants demonstrated decreased heart rates at baseline and recovery. When the VLGA infant's heart rates decreased their respiratory rate and oxygen saturation also decreased. VLGA infants demonstrated more cues when their respiratory rates and oxygen saturations were higher during and at recovery. They demonstrated lower PACEFI scores with lower oxygen saturations and higher heart rates during and at recovery.

Differences in Physiologic Indicators and Behavioral Cues for ELGA & VLGA Infants. It appears that physiologic indicators and behavioral cues demonstrated inconsistent relationships for ELGA and VLGA infants for all ratings. Higher heart rates were associated with low respiratory rates, low oxygen saturations and decreased behavioral cues for ELGA infants undergoing a non-invasive procedure. While, higher heart rates were associated with low respiratory rates, low oxygen saturations and increased behavioral cues for ELGA infants undergoing an invasive procedure. Alternatively for the VLGA infant higher hearts rates were associated with low respiratory rates, low oxygen saturation, and increased behavioral cues for a non-invasive procedure. Yet, higher heart rates were associated with lower respiratory rates, low oxygen saturation, and decreased behavioral cues for the invasive procedure. Further discussion is included in Chapter 5.

Conclusions

This chapter presented findings for the psychometric evaluation of the PACEFI instrument. In addition, similarities and differences for behavioral cues and physiological indicators specified on the PACEFI instrument were evaluated for ELGA and VLGA infants undergoing non-invasive and invasive procedures.

The results indicate that the PACEFI instrument demonstrated a low internal consistency for measuring pain at baseline (KR-20 = .140) five minutes prior to handling before the invasive procedure. There was a high internal consistency (KR-20 = .879) for measuring pain during invasive procedures. There was also a high internal consistency noted at recovery (KR-20 = .792) five minutes after handling following the invasive procedure.

There were no significant relationships noted at the .05 level between prior painful procedures and an infant's ventilatory requirements with the baseline, during, and recovery ratings for an invasive procedure. Alternatively, VLGA infants demonstrated more behavioral cues at the ratings during and recovery when they had an increased number of prior painful procedures and they required more invasive ventilatory support.

The ELGA and VLGA infant groups both had significantly lower scores for the PACEFI instrument at baseline and recovery and significantly higher behavioral scores during the invasive procedure. The ELGA infants showed the least amount of change overall in ratings from baseline to during and during to recovery. Although both the ELGA and VLGA infants showed an increase in scores from baseline to during and a decrease in scores from during to recovery it was noted that the ELGA infants demonstrated a blunted response during the invasive procedure as compared to their VLGA infant counterparts. The ELGA infants also demonstrated a slower recovery five minutes after the procedure was completed as compared to their VLGA infant counterparts. There was no significant group difference observed for the ratings baseline, during, and recovery between the ELGA and VLGA infants.

There were several significant relationships noted at the .05 level between prior painful procedures and an infant's ventilatory requirements with the baseline, during, and recovery ratings for a non-invasive procedure. An inverse relationship was noted for prior painful procedures and behavioral cues exhibited by the ELGA infants for the baseline and recovery ratings. ELGA infants who had an increased number of painful procedures performed prior to the observational rating demonstrated lower PACEFI scores for the ratings at during and recovery. ELGA infants also demonstrated decreased behavioral cues at the baseline and recovery ratings when they required more invasive ventilatory support. Alternatively, VLGA infants who also had an increased number of painful procedures performed prior to the observational rating demonstrated increased behavioral cues at the baseline and recovery ratings.

The ELGA and VLGA infants both had significantly lower scores for the PACEFI instrument at baseline and recovery and significantly higher behavioral scores during the non-invasive procedure. Although, there was no interaction effect observed between the infant groups it was noted that the VLGA infants demonstrated the least amount of changes from baseline to during than their ELGA counterparts. The VLGA infants also demonstrated a slower recovery five minutes after the procedure was completed as compared to their ELGA counterparts. This finding is contrary to what was demonstrated for the invasive procedure since the ELGA infants demonstrated a blunted response for the invasive procedure and the VLGA infants demonstrated less response for the non-invasive procedure.

Pearson's Product-Moment correlations were evaluated to determine the relationship between physiologic indicators and behavioral cues at baseline, during and recovery for both an invasive and non-invasive procedure. There were relationships noted between physiologic and behavioral cues for both ELGA and VLGA infants. However, these relationships were variable and not consistent for each infant, time point (baseline, during, recovery), or procedure.

The following chapter provides the reader with a detailed discussion regarding the outcomes of this study along with implications for nursing practice, education, and research.

Chapter 5

Discussion

A discussion of the study findings will address five main areas. First, evidence for the reliability of the PACEFI is summarized. Second, the similarities and differences in behavioral cues between ELGA and VLGA infants during an invasive procedure are discussed. Third, similarities and differences in behavioral cues for these same infants during a non-invasive procedure are summarized. Fourth, evidence for a relationship between physiologic indicators and behavioral cues for ELGA and VLGA infants during invasive and non-invasive procedures is reviewed. Lastly, study limitations are described, clinical implications are discussed, and recommendations for future research endeavors are reviewed.

The purpose of this study was to evaluate the reliability and validity of the PACEFI instrument as well as the similarities and differences between behavioral cues and physiologic indicators of ELGA and VLGA infants during both an invasive and non-invasive procedure. The study included a total of 31 infants—ELGA (n = 16) and VLGA (n = 15)—in a large metropolitan hospital in Boston. The mean gestational age was 29 weeks, the majority of infants were male (67%), and the mean birth weight was 1442 grams. The observational ratings were completed on average at day 3 of life for an invasive procedure and day 4 of life for a non-invasive procedure. The infants received 18–22 painful procedures prior to the observational ratings. Sixty-four percent of infants required some type of ventilatory support. Most infants (80%) were provided nonpharmacological interventions. The majority of infants were not considered severely ill (86%) did not have IVH (90%) and did not receive analgesia (96%) prior to the observational ratings.

The PACEFI Instrument

Neonatal pain behaviors were measured using the PACEFI, which was developed to assess ELGA infant pain. The PACEFI includes 20 behavioral items thought to be indicative of neonatal pain. The PACEFI is a 20-item dichotomous (yes/no) procedural pain assessment instrument that assesses behavioral cues that the ELGA infant may exhibit during an invasive procedure (see Appendix D). Infants were scored on each item for frequency (i.e., no it was not observed (0); yes it was observed (1)). Infants were scored as "no pain" (0) if they did not exhibit any behaviors described by PACEFI items.

Reliability Analysis for the PACEFI

Hypothesis 1. The PACEFI instrument will demonstrate preliminary validity and reliability during the invasive procedure.

Baseline (5 Minutes Before Handling)

The PACEFI instrument did not detect any clear behaviors at baseline associated with pain. This argues for validity because behavioral cues associated with pain should not be exhibited by infants prior to being handled or given an invasive procedure. However, it also resulted in the PACEFI demonstrating a low internal consistency (KR-20 = .140) at baseline.

Three behaviors fisting, mouthing and fingersplay were noted at baseline (Table 10). Fisting and fingersplay have been identified as stress behaviors (Als, 1982) as well as behaviors associated with pain (Holsti et al., 2004). Most infants in this study who exhibited fisting, fingersplay and mouthing were handled close to the time of the rating or at the time of the rating. Although approximately 93% of baseline ratings were done 5 minutes prior to any handling there were three ratings where this was not the case. It may be that infants rated on these three occasions were displaying stress cues. This would be consistent with Taddio, Shah, Gilbert, Macleod, & Katz (2002) finding that infants who are handled near to the time of the procedure may show increased cues due to their anticipation of the painful procedure. Alternatively, these infants may have been exhibiting cues related to hyperalgesia or allodynia because they were handled so close to the painful procedure. Hyperalgesia refers to a decreased pain tolerance and/or increased reaction to a painful event (Ghosh & Barr, 2007). Allodynia refers to experiencing pain from a non-painful event (Ghosh & Barr). The PACEFI instrument did not detect any clear behaviors at baseline associated with pain. The lack of painful behaviors scored on the PACEFI at baseline for these infants demonstrates preliminary validity.

During the Invasive Procedure

The PACEFI exhibited a high internal consistency (KR-20 = .879) during the invasive procedure. Facial expressions were highly correlated with each other (Table 12). Motor activity was also found to be low to moderately correlated with each other (Table 12). In addition facial expression and motor activity were low to moderately correlated with each other and appeared to be contributing to the measurement of pain (Table 12). Two of the 20 items were not used for any infant ratings: lips pursed and full body pull away. There could be several reasons these two behaviors were not consistently exhibited. First, pursing of the lips and pulling away all extremities might be behaviors of a more mature infant as greater developmental maturity and increased musculature may be required to exhibit these behaviors (Gibbins et al., 2008). Second, mechanical ventilation for some infants may have made it difficult to distinguish lips pursed. Lastly, these behaviors may not be behaviors this gestational age group uses to express pain.

Facial expression (eye squeeze, cry, furrow, grimace, nasolabial bulge, stretched mouth, and taut tongue) were highly correlated with each other during an invasive procedure (Table 12). Facial expressions are consistently utilized in current pain assessment instruments and considered a widely accepted indicator for pain in all neonatal populations (Stevens et al., 2007b). Gibbins et al. (2008) noted that 23–28 weeks' gestational age infants consistently demonstrated brow bulge, eye squeeze, nasolabial bulge, furrow, and vertical stretched mouth during a heel stick. Facial expression (open lips, stretched mouth, taut tongue, nasolabial furrow, brow bulge, and eye squeeze) were also noticed to increase in frequency when infants greater than 32 weeks gestational age underwent an acute painful procedure (Johnston, Stevens, Craig, & Grunau, 1993).

Hands on face, cry, stretched mouth and taut tongue all showed low correlation with each other (Table 12). Yet, these behaviors may contribute to the measurement of pain because the alpha did not increase if these behaviors were deleted from this analysis. For example, stretched mouth and taut tongue may be difficult to reliably assess in ELGA and VLGA infants experiencing pain. Additionally, these infants may be unable to move the required facial muscles due to the medical equipment secured to their cheeks along with the immaturity of their facial muscles (Gibbins et al., 2008). Further evaluation of these behaviors is needed to determine if they are: (a) specific to pain; and (b) able to be reliably assessed.

Motor activity (push arm, push leg, pull arm, pull leg, fisting, sit on air) were low to moderately correlated (Table 12). Yet, extremity movement was demonstrated by both ELGA and VLGA infants in this study during the invasive and non-invasive procedures. Movement of the extremities (push, pull) during a painful procedure is well documented in the literature and included in several pain instruments (Hudson-Barr et al., 2002; Hummel & Pulchalski, 2003; Lawrence et al., 1993). However, some researchers have chosen not to include body movements as a part of pain assessment because developmental care may obscure the nurse's assessment of this potential pain response (Stevens et al., 1996). Additionally, extremity movement seems to increase for both invasive and non-invasive procedures creating a concern that these movements are not specific to pain (Gibbins et al., 2008; Grunau, Holsti, Whitfield, Ling, 2000; Holsti et al., 2005b; Williams Khattack, Garza, & Lasky, 2009). Yet, Shasfoort et al., (2008) found that older infants (*m* = 84 days of age) demonstrated arm extension that was associated with pain using electromyographic sensors. This finding, albeit in older infants, begs the question: At what gestational age do extremity extensions become synchronous with pain? Meanwhile motor activities such as fisting and sit on air have been associated with both stress and pain in infants. (Als, 1982, Holsti et al., 2004; Holsti & Grunau, 2007; Morrison et al., 2003). Hence future studies are warranted to determine if certain types of motor activity are specific to pain in this infant population.

Facial expression (eye squeeze, cry, furrow, grimace, nasolabial bulge, stretched mouth, taut tongue) and motor activity (push arm, push leg, pull arm, pull leg, fisting) were low to moderately correlated with each other (Table 12). This was an interesting finding because the evidence supports facial cues being specific to pain (Stevens et al., 2007c), while the evidence for motor cues is variable (Gibbins et al., 2008; Grunau et al., 2000; Holsti et al., 2005b; Williams et al., 2009). However, relationships between body movements and facial expression for preterm infants are supported in the literature (Lucas-Thompson et al., 2008; Morrison et al., 2003). Morrison et al. (2003) found that preterm infants demonstrated marked facial cues along with increased body movements with a physiologic response. The body movements Morrison et al (2003) most commonly observed during and after the painful procedure included: limb extensions, fingersplay, hands on face and sit on air. Although body movements seemed to contribute to the assessment of pain in the present study, further research is needed to validate whether or not facial expression and motor cues together are contributing to the measurement of pain in these earlier born infants. Facial cues are sometimes difficult to observe in preterm infants due to medical technology. For this reason it is suggested that body movements be incorporated into the pain assessment for preterm infants (Morrison et al.). There are still questions regarding whether or not motor activity is specific to pain. Nevertheless, it is essential to incorporate an array of behaviors to decrease the likelihood of underestimating pain in this infant population given the state of the science (Holsti, Grunau, Oberlander, Whitfield, Weinberg, 2005b; Holsti & Grunau, 2007b; Morrison et al.).

Recovery (5 Minutes After Handling)

The PACEFI exhibited a high internal consistency at recovery (KR-20 = .792) after handling following the invasive procedure. Eye squeeze, hands on face, cry, furrow, grimace, nasolabial bulge, stretched mouth, taut tongue, push arm, push leg, pull arm, pull leg, fisting, and toe curl indicate low to moderate correlations with varying strengths signifying a pain response after the procedure had ended (Table 14). Current evidence suggests that ELGA and VLGA infants may experience hyperalgesia or allodynia from previous pain experiences due to their developmental immaturity. Furthermore, the sustained recovery response exhibited by the ELGA infant group may well be due to the short observation time of 5 minutes after handling. These infants might require a longer recovery phase than what this study allowed.

ELGA and VLGA infants did not return to baseline behaviors in this study, instead these infants maintained an increased number of stress cues well into the 5-minute recovery period. ELGA infants showed the slowest recovery as indicated by the PACEFI scores not returning to baseline. VLGA infants had a quicker recovery with PACEFI scores trending closer to baseline by 5 minutes after handling than their ELGA counterparts. Several investigators have shown that previous painful experiences contribute to altered pain perception in both the preterm and full-term population (Grunau et al., 2001; Johnston & Stevens, 1996; Taddio et al., 2002). Grunau et al. (2001) found that in comparison to infants above 2500 grams, infants less than 1500 grams were more likely to demonstrate fewer behavioral cues if they were exposed to an increased number of painful procedures. Alternatively, Morrison et al. (2003) found that earlier born infants (m = 30 weeks gestation) demonstrated an increase in stress behaviors during the procedure as well as at baseline and rest. Taddio et al. (2002) also found that full term infants who experienced repeated heel sticks in the first 24–36 hours could anticipate painful procedures and display increased pain behaviors pointing to more intense pain. This altered pain response may extend beyond the neonatal period into childhood (Abdulkader, Freer, Garry, Fleetwood-Walker, & McIntosh, 2008; Grunau et al., 1994; Taddio et al., 1997). PACEFI scores remained elevated into recovery for ELGA infants in this study for the invasive procedure. Although, pain scores were expected to drop to baseline after the noxious stimulus was removed for this age group, this finding is well documented and expected.

Certain behavioral cues were not exhibited by the infants for the invasive procedure. These cues include: sit on air, taut tongue, lips pursed, mouthing, full body pull away, and pull extremities. There could be a couple of reasons for this finding. First, these items may be specific to pain and the infants did not demonstrate them as they were not enduring the invasive procedure at rest. Second, mouthing and pull extremities midline may be self-soothing behaviors which would not be displayed during an invasive procedure. In addition, preterm infants may not be able to perform these behaviors due to their developmental immaturity (Als, 1982).

Summary

The PACEFI demonstrated low internal consistency (KR-20 = .140) at baseline validating that the items on the PACEFI were not measuring behaviors associated with pain. This finding supports that the PACEFI is measuring only pain and may contribute to the predictive validity of the instrument. There was a high internal consistency (KR-20 = .879) noted during an invasive procedure which suggests that most items included in the PACEFI were contributing to the measurement of pain. There was also a high internal consistency (KR-20 = .792) noted for recovery. Although the PACEFI scores should return to baseline after the procedure, previous research findings suggest that infants may demonstrate hyperalgesia or allodynia well into recovery, which corroborates the findings of this study. This reliability analysis was a first step in understanding if the PACEFI is a meaningful instrument for the measurement of pain for ELGA and VLGA infants. While the PACEFI instrument demonstrated a high internal consistency during the invasive procedure, additional reliability and validity testing is needed to determine if the problematic items are specific to the measurement of pain for this infant population.

Comparison of PACEFI Scores for ELGA and VLGA Infants for an Invasive Procedure

Hypothesis 2. Infants 24–29 6/7 weeks' gestation will exhibit different behavioral cues for any invasive procedure at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling) versus their 30–33 6/7 week counterparts.

This investigation explored the similarities and differences in observational ratings between ELGA and VLGA infants for an invasive procedure. The ELGA and VLGA infants demonstrated significantly lower scores at baseline and recovery and significantly higher scores during the invasive procedure. However, the ELGA infants showed the least amount of change overall in ratings from baseline to during and during to recovery. Although both the ELGA and

VLGA infants showed an increase in scores from baseline to during and a decrease in scores from during to recovery it was noted that the ELGA infants demonstrated a blunted response during the invasive procedure as compared to their VLGA counterparts. This is supported in the literature for some studies (Evans et al., 2005; Steven et al., 2007) but not for others (Badr et al., 2010). Stevens et al. (2007) reported a similar dampened response during an invasive procedure for infants less than 28 weeks as compared to infants greater than 31 weeks' gestational age (Stevens et al.). Evans et al. (2005) reported lower PIPP scores for infants less than 30 weeks during an invasive procedure. Alternatively, Badr et al. (2010) observed higher PIPP scores in the lowest gestational ages 27 to 32 weeks and lower scores for 32–35 weeks' gestation. An explanation for these lower PACEFI scores seen in ELGA infants may be due to developmental immaturity and their inability to regulate a response to prior painful procedures (Stevens et al., 2007c; Badr et al.; Grunau et al., 2001). Carbajal et al. (2008) reported that, on average, infants undergo 16 painful procedures per day. Of note infants with lower gestational ages experienced a higher amount of painful procedures (Carbajal et al., 2008). It was observed for this study that ELGA infants had an average of 26 prior painful procedures (invasive and non-invasive) up to the third or fourth day of life, and VLGA infants had an average of 13 prior painful procedures per day up to day of life 3 for the invasive procedure, and 18 prior painful procedures per day up to day of life 4 for the non-invasive procedures. A significant relationship between previous painful procedures and PACEFI scores was not observed for this study. The small sample size may have contributed to the lack of significance between prior painful procedures and the PACEFI scores. However, other researchers have reported dampened responses with previous painful experience (Johnston et al., 2007; Grunau et al., 2001). The dampened response for the ELGA infant group could be due to previous painful procedures which may have contributed to the lower scores for these infants during the invasive procedure (Johnston et al., 2007; Grunau et al., 2001; Johnston & Stevens, 1996). Additionally, it could be that the scores reflect the true score of these infants or it may well be both factors influencing the pain response for this infant population. It is important to note that although the ELGA infants exhibited a dampened response for this study these infants were clearly able to exhibit a definitive behavioral response during the invasive procedure.

The ELGA infants also demonstrated a slower recovery 5 minutes after handling as compared to their VLGA counterparts. This finding may be indicative of hyperalgesia or a hyperexcitable state in which the infant cannot turn off the pain response or sensation even once the painful stimulus has stopped (Ghosh & Barr, 2007; Fitzgerald, 2005). Repeated noxious stimulation of fibers may lead to hyperexcitability with sensitization of the dorsal horn extending past the period of stimulation (Beggs & Fitzgerald, 2007). Non-noxious stimuli such as handling prior to invasive procedures can also increase pain response scores for infants as well (Ahn & Jun, 2007; Cameron, Raingangar, & Khoori, 2007). This may be due to altered excitability in the spinal tract which may cause non-noxious stimuli to be perceived as painful (Evans, 2001; Grunau et al., 2001). ELGA infants were handled on average 54 minutes prior to the invasive procedure and 1 hour and 40 minutes prior to the non-invasive procedure. The fact that these infants were handled so close to the observational rating may have contributed to the elevated recovery scores demonstrated by the ELGA infants in this study.

VLGA infants demonstrated a higher amount of behavioral cues from baseline to during than did ELGA infants. This is an expected finding; as the neurodevelopmental system matures, infants are able to exhibit a more robust response to pain (Evans, 2001; Johnston & Stevens, 1996; Johnston et al., 1993). Additionally, the increased PACEFI scores during the invasive procedure may also be related to previous painful experience. VLGA infants were handled on average 1 hour 40 minutes prior to the invasive procedure and 2 hours prior to the non-invasive procedure. This frequent handling may have also contributed to the higher PACEFI scores. In addition, a small relationship between higher PACEFI scores during the invasive procedure and an increased number of prior painful procedures was noted for VLGA infants. There was also a small relationship noted for VLGA infants between lower PACEFI scores at recovery when they required more invasive ventilatory support for an invasive procedure. Mechanical ventilation has been shown to cause sensitization in ELGA and VLGA infants (Grunau et al., 2001). This sensitization may translate into an altered pain response (Grunau et al., 2001, Williams et al., 2009). However, 73% of VLGA infants did not require any ventilatory assistance which may have contributed to the lower recovery scores demonstrated in this study.

Summary

The response between ELGA and VLGA infants differed in the robustness of the response but not in the response itself. During the procedure, both infant groups demonstrated lower scores at baseline and recovery and higher scores during the procedure. ELGA infants tended to have higher scores at baseline and recovery signifying a sensitization from prior invasive or even non-invasive procedures. Infants in an excitable state may demonstrate more behavioral cues at baseline and recovery as their developmental immaturity inhibits modulation of their pain response (Evans, 2001; Fitzgerald, 2005). The fact that VLGA infants showed less behavioral cues at baseline and recovery supports the explanation that developmental maturity comes with advancing gestational age (Evans, 2001) and is reflected in observable behaviors. VLGA infants seemed to be able to modulate their pain response better than their ELGA counterparts.

Comparison of PACEFI Scores for ELGA and VLGA Infants for a Non-invasive Procedure

Hypothesis 3. Infants 24–33 6/7 weeks' gestation will not exhibit behavioral cues associated with pain for a non-invasive procedure at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling).

The ELGA and VLGA infants both had significantly lower scores for the PACEFI instrument at baseline and recovery and significantly higher behavioral scores during the non-invasive procedure. Although there was no significant interaction effect observed between the ELGA and VLGA infants it was noted that these infants demonstrated greater change from baseline to during than did their VLGA infant counterparts. Although the ELGA infant group had the greatest amount of change, the VLGA infant group also demonstrated a pain response. In addition, the ELGA infants demonstrated fewer behavioral cues at recovery than baseline as compared to their VLGA infant counterparts. Alternatively, VLGA infants' recovery scores stayed slightly elevated 5 minutes after handling. These findings are contrary to what was demonstrated for the invasive procedure.

While diaper change is not considered an invasive or even a painful procedure by RNs or physicians (Cignacco et al., 2008), both infant groups had a significant change in scores during this procedure. Diaper change for late preterm and full term infants may not be considered painful (Cignacco et al., 2008). However, for earlier born infants with translucent skin and the inability to modulate pain a diaper change may be perceived as painful (Evans, 2001; Gibbins et al., 2008; Morelius, Hellstrom-Westas, Carlen, Norman, Nelson, 2006). Increased pain scores for infants during diaper change are supported in the literature (Gibbins et al., 2008; Morelius et al., 2006). Morelius et al. (2006) found that preterm and full term infants both increased their pain scores during the diaper change. Additionally, ELGA infants (< 28 weeks' gestation) responded consistently for heel lance and diaper change with increased facial activity and elevated heart rates during both procedures (Gibbins et al.). For this study the younger gestational age infants demonstrated higher pain scores. Some evidence points to the fact that diaper change may produce a more severe response than even a heel lance generates in preterm infants (Hellerud, & Storm, 2002). Alternatively some studies have demonstrated less change in pain scores during diaper change, though the infant's average score was still considered mild to moderate pain as measured by the PIPP (Ballantyne, Stevens, McAllister, Dionne, & Jack, 1999).

The diaper change for this study was preceded by usual care activities such as repositioning, vital signs and physical assessment. This is due to the fact that the study was purely observational and the care experience for the infant was not altered. The higher scores noted during the diaper change may be related to prior sensitization due to cumulative exposures during the care experience (Holsti et al., 2005; Grunau et al., 2001). Routine procedures have been found to cause stress and pain for infants (Bellieni et al., 2009; Cameron et al., 2007; Morelius et al., 2006). Evidence has emerged regarding the possible detrimental effects that cluster care—providing all aspects of care at one time—may have for preterm infants (Ahn & Jun, 2007; Holsti et al., 2005b). Initially it was believed that providing care all at once allowed the infants to rest for longer periods of time, thereby decreasing the infant's stress and promoting growth and healing. However, several studies have found that cluster care produces an intense response by preterm infants that lasts well beyond the care experience (Ahn & Jun; Holsti et al., 2005; Holsti et al., 2005b). Cameron et al.(2007) noted that preterm infants were handled on average 53 times in a 24-hour period, mostly by nurses, with more than half of these handling episodes performed in a developmentally inappropriate manner. In addition more than half of the handling episodes demonstrated an increase in pain scores (Cameron et al.). Increased pain scores during diaper change have been demonstrated in several studies and may signify that diaper change may be more detrimental than previously thought (Gibbins et al., 2008; Morelius et al., 2006). ELGA and VLGA infants appear to react to the whole care experience (vital signs, physical assessment, repositioning, suctioning, abdominal girth, and assessment of nasogastric tube) prior to the diaper change. This reaction to previous experiences causes these infants to become agitated, thereby increasing their behavioral scores during the actual diaper change procedure. Furthermore, this sensitization may alter their neuro-pathways causing them to feel non-painful procedures as painful (Holsti et al., 2005). The findings from the present study add to this evidence of likely but unexpected adverse effects of cluster care.

A difference between the infant groups was demonstrated with regards to the PACEFI recovery scores. The fact the ELGA infants exhibited less behavioral cues at recovery than even baseline may be indicative of the lack of energy reserve and/or immature musculature (Als, 1982; Walden et al., 2001). ELGA infants who remain in a sensitized state, or experience non-painful procedures as painful deplete their energy reserve, begin to shut down, and consequently demonstrate a dampened or no behavioral response to both routine and painful procedures (Johnston et al., 1999). Als (1982) described ELGA infants as being unable to regulate stress which causes disorganization and eventually collapse. The recovery scores for the invasive procedure in this study remained above baseline. Yet, the recovery scores dropped below baseline for the non-invasive procedure which may indicate a lack of energy reserve and subsequent infant collapse in an attempt by the infant to conserve energy and regain physiologic stability (Als).The difference in scores between the invasive and non-invasive procedures may be due to the total care experience the infants experienced for the non-invasive procedure leading to increased energy demands on the infants.

Summary

Consistent with the ELGA and VLGA response to the invasive procedure, the robustness of the response differed but not the response itself. ELGA infants demonstrated a more vigorous response during the diaper change and dropped below baseline scores at recovery. The fact that the ELGA infants dropped below baseline scores at recovery suggests an overwhelming expenditure of energy. The quick decrease in behavioral cues may indicate “shut down” which is demonstrated by a decrease in or lack of response to conserve energy (Als, 1982). VLGA infants showed fewer behaviors during the diaper change and did not return to baseline at recovery. The VLGA infants appeared to demonstrate a somewhat more organized response during the diaper change procedure. This finding may be due to increasing developmental maturity contributing to these infants being better equipped to differentiate between stress and pain which translates to lower pain scores. Although VLGA infants did not appear to “shut down” (Als), these infants did exhibit higher scores at recovery. The higher recovery scores are in contrast to the findings for the invasive procedure. The slow recovery back to baseline may indicate some sensitization and excitability due to the handling throughout the whole care experience. This sensitization may place the VLGA infant in a hyperexcitable state leading to increased recovery scores well after the diaper change was completed.

Relationships Between Physiologic & Behavioral Indicators

Hypothesis 4. Physiologic and behavioral pain indicators for ELGA infants 24–29 6/7 weeks’ gestation and VLGA infants 30-33 6/7 weeks gestation will not correlate at baseline (5 minutes prior to handling), during, and recovery (5 minutes after handling).

Pearson Product–Moment correlations were calculated to evaluate whether or not there was a significant relationship between physiologic indicators and behavioral indicators for ELGA infants (24–29 6/7 weeks' gestation) and VLGA infants (30–33 6/7 weeks' gestation) during an invasive and non-invasive procedure. All correlations above (r = .30) were reported for exploratory purposes due to the small sample size and the risk for a type II error.

Variability between physiologic indicators and behavioral cues were noted for both ELGA and VLGA infants for invasive and non-invasive procedures. The following discussion highlights key relationships between physiological indicators and behavioral cues for both infant groups.

ELGA Infant Correlations

ELGA infants demonstrated increased heart rates at baseline along with decreased respiratory rates and decreased oxygen saturation at during and recovery for both invasive and non-invasive procedures. There is clear evidence that earlier-born infants demonstrate increased heart rates at baseline and maximum heart rate at heel lance along with decreased oxygen saturation during and at recovery for both non-invasive and invasive procedures (Gibbins et al., 2008b; Grunau et al., 2001; Johnston, Stevens, 1996; Stevens et al., 2007; Luca-Thompson et al., 2008; Walden et al., 2001). Higher heart rates (140–190 bpm) at baseline may be indicative of a hyperexcitable state prior to beginning both procedures. As previously stated, ELGA infants were handled close to the baseline ratings for both procedures placing them at risk for sensitization. It may be that previous experience causes these ELGA infants to become sensitized to handling due to their immaturity, which may increase vital signs making it difficult to distinguish a pain response.

ELGA infants also demonstrated less behavioral cues with lower oxygen saturation (80–91%) during the non-invasive procedure. Decreased behavioral cues with lower oxygen saturation may be attributed to these infants' inability to mount a response from a lack of oxygen due to the stress of the invasive procedure. Lower oxygen saturations during an invasive procedure are supported in the literature (Craig et al., 1993; Stevens et al., 2007). However, further investigation is required to determine the relationship between oxygen saturation and behavioral cues for this infant population.

ELGA infants for this study demonstrated increased behavioral cues at recovery 5 minutes after handling. The increased behavioral cues at recovery may be indicators of allodynia or hyperalgesia which causes infants to remain in a hyperexcitable state well after the procedure has ended (Holsti Grunau Whitfield, Oberlander & Lindh, 2006; Morrison et al., 2003). Walden et al. (2001) found that infants 27 to 32 weeks' gestation had a sustained heart rate for up to eight minutes after the heel stick procedure ended. In addition, Gaspardo, Chimello, Cugler, Martinez, and Linhares (2008) noted that heart rates of infants 25–33 weeks' gestation remained increased during the 10 minutes post heel stick. Additionally, Johnston et al. (1995) found that infants (32–34 weeks' gestation) had higher heart rates during both a heel stick and sham heel stick indicating a physiological response to a non-invasive procedure. The present study indicated that ELGA infants heart rates remained elevated possibly indicating a hyperexcitable state from previous handling. Higher heart rates were associated with low respiratory rates, low oxygen saturation and decreased behavioral cues for ELGA infants undergoing a non-invasive procedure. Higher heart rates were also associated with low respiratory rates, low oxygen saturation and increased behavioral cues for ELGA infants undergoing an invasive procedure. The inconsistent relationships between physiologic indicators and behavioral cues in this study have been duplicated in other research. Morrison et al. (2003) found an increase in mean heart rate along with a decrease in oxygen saturation when infants demonstrated more body movements. In addition, Morrison et al. (2001) reported a modest correlation between facial activity and change in heart rate between 26–32 week infants. Further research is needed with a larger samples size to further explore the relationship between physiologic indicators and behavioral cues for this infant population.

VLGA Infant Correlations

VLGA infants demonstrated increased heart rates at baseline along with decreased respiratory rates and decreased oxygen saturation at during and recovery for both invasive and non-invasive procedures. These infants did show an increased heart rate at baseline. However, it was in relation to a decreased oxygen saturation possibly causing cardiopulmonary compromise rather than the infant demonstrating a hyperexcitable state.

VLGA infants demonstrated increased behavioral cues with a higher heart rate during the non-invasive procedure which is suggestive of a pain response. They also demonstrated an increased heart rate with decreased behavioral cues at recovery for the invasive procedure possibly indicating better modulation of the pain response. Behavioral cues and physiologic indicators have been shown to correlate more strongly with advancing gestational age (Lucas-Thompson et al., 2008; Johnston & Stevens, 1996). However, for this study it is difficult to distinguish an association between physiologic indicators and behavioral cues related to advancing gestational age.

VLGA infants appeared to demonstrate more behavioral cues with lower respiratory rates for both the invasive and non-invasive procedure. The decreased respiratory rate may be attributed to these infants having difficulty regulating their breathing due to the stress of both procedures. Twenty-six percent of the VLGA infants required NCPAP or nasal cannula during the non-invasive procedure and 33% required NCPAP or nasal cannula during the invasive procedure indicating that these infants were already experiencing respiratory compromise. Alternatively, these infants may have had no trouble breathing and therefore could exhibit more behavioral cues as they were not energy depleted. This lack of energy depletion may be indicated when the infants exhibited more behavioral cues with higher oxygen saturations. Further investigation is required to determine the effect that respiratory rate has on the infant's ability to display behavioral pain cues during both an invasive and non-invasive procedure.

ELGA & VLGA Infant Correlations Summary

Overall, both groups of infants demonstrated inconsistencies among physiologic indicators and behavioral cues as well as between the physiologic indicators themselves. These findings highlight the variability between behavioral cues and physiologic indicators for ELGA and VLGA infants. The fact that there was a difference between the infant groups for vital signs with regard to the infants' response to pain may be due to maturational changes with increasing gestational age (Evans, 2001; Morrison et al., 2001). In general, physiologic parameters such as heart rate, respiratory rate, and oxygen saturation are reported to have variability across studies for infants and procedures, corroborating the belief that these parameters are not specific to pain (Beacham, 2004; Johnson et al., 1995; Stevens, Johnston & Grunau, 1995; Stevens et al., 1996) Although there is variability in vital signs, specifically heart rate, these parameters have been shown to increase or decrease during a painful procedure, illustrating that the infant can mount a response (Stevens et al., 2007c). In this context vital signs may be used as an indicator of pain reaction and response but not as a direct estimate of pain (Stevens et al., 2007c). Vital signs play an important part in pain assessment as they are readily accessible and at times contribute to the measurement of pain (Stevens et al., 2007c). However, based on this study's findings, it is recommended that vital signs should be evaluated independently and not be combined in a composite score with behavioral cues due to their lack of specificity regarding pain response.

Summary

The PACEFI demonstrated a high internal consistency and appeared to be contributing to the measurement of pain during the invasive procedure. The low internal consistency at baseline supports preliminary validity for the instrument. Although the internal consistency was high at recovery, there is evidence that supports this finding for the ELGA and VLGA infant population (Grunau et al., 2001; Morrison et al., 2003, Taddio et al., 2002). While the PACEFI instrument demonstrated a high internal consistency during the invasive procedure, additional reliability and validity testing is needed to determine if the problematic items are specific to the measurement of pain for this infant population.

The response between ELGA and VLGA infants differed in the robustness of the response but not in the response itself for both the invasive and non-invasive procedure. ELGA infants tended to have higher scores at baseline and recovery for the invasive procedure signifying a sensitization from prior invasive or even non-invasive procedures (Holsti et al., 2005; Morrison et al., 2003; Walden, 2001), while VLGA age infants showed less behavioral cues at baseline and recovery supporting the explanation that developmental maturity comes with advancing gestational age and is reflected in observable behaviors (Evans, 2001).

ELGA infants demonstrated a more vigorous response during the diaper change and dropped below baseline scores at recovery. VLGA infants showed fewer behaviors during the diaper change and did not return to baseline at recovery. The difference in response may be due to the difference between the invasive and non-invasive procedure. The non-invasive procedure encompassed an entire care experience. This care experience could lead to sensitization (Holsti et al., 2005; Holsti et al., 2005b; Morrison et al., 2003) for the VLGA infant and overwhelming energy expenditure (Als, 1982) for the ELGA infant producing the differences in PACEFI scores.

In general ELGA and VLGA infants demonstrated inconsistencies among physiologic indicators and behavioral cues as well as between the physiologic indicators themselves. This finding for the present study argues to keep behavioral cues and physiologic indicators independent of each other during infant pain assessment.

Limitations and Threats to Validity

There are six limitations or threats to validity in this study. First, this study utilized demographic information found in the infants' medical records. A potential limiting factor may originate from incomplete documentation contributing to missing data. This limitation was minimized by speaking with the nurse caring for the infant to obtain missing data.

Second, there are limitations related to sampling method and sample size. It was not possible to sample randomly from this population or to sample in such a way as to ensure adequate gender and racial representation. This small ELGA infant population located in Massachusetts may cause an uneven sample with regard to gender and race, which may limit the findings of this study with regard to generalization. However, there is no clear evidence regarding gender and racial differences in pain responses for this population, and the existence of gender and racial differences in pain scores can be explored in future research. A strength of this study was that PACEFI ratings were completed by day of life 3 and 4 for most infants enrolled in the study. Many researchers report results for ELGA infants but have collected data at an older post-conceptual age, such as 32 weeks gestation (Grunau et al., 2000; Holsti et al., 2004, Stevens et al., 2007c). In addition to sample bias, the small sample size may have reduced the ability to detect significant changes. This potential result was minimized by discussing low to moderate correlations and not utilizing a statistical correction to protect against type I error in the statistical analysis. Although not using a statistical correction increases the chance of false positives it was determined that a less conservative approach should be used so all results could be explored and interpreted with caution.

Third, there was potential for ratings to drift. In addition, raters were not blinded to the procedure creating the potential for observer bias. However, these limitations were minimized by the two nurse rater's initial training and the inter-rater meetings scheduled throughout the data collection period. Data analysis found no significant difference in ratings between nurse raters.

Fourth, physiologic data such as heart rate, respiratory rate, and oxygen saturation were collected at baseline, during, and recovery for both the non-invasive and invasive procedures. These data revealed the relationship between vital signs, oxygen saturation, and the total PACEFI scores (baseline, during, recovery). However, only one set of vital signs was obtained by observing the monitor one time for baseline, during, and recovery ratings. Vital signs were not collected for the duration of each time point (baseline, during, and recovery) which did not allow for calculation of the mean vital signs and oxygen saturation for each infant. In addition the Masimo pulse oximeter settings were set for a 16-second delay for the oxygen readings due to an institutional policy. This delay could cause a discrepancy in observed vital signs because a change may not be reflected on the screen during the observation of the cardiac monitor due to the delay. Future studies should focus on a continuous measurement of these parameters to obtain a comprehensive, synchronized account of the relationship between physiologic indicators and behavioral cues.

Fifth, this study included observations of different types of invasive procedures performed on infants. However, restricting observations to a single painful procedure would have greatly limited the number of observations. Furthermore, given the limited number of premature infants available at this study site, the population is limited, so allowing different types of painful procedures was a necessary strategy to carry out this study. The procedures in this study included: heel stick, ETT suctioning, oropharyngeal suctioning, lumbar puncture, venipuncture, intubation, and nasogastric tube insertion. Although these procedures differ, there is support in the literature that these procedures are all considered to be painful for infants (Cignacco et al., 2008).

Lastly, the variable sleep state was not included in this study. It is well documented that sleep state can influence an infant's response to pain. This study was purely observational in nature and due to the developmental care procedures used during baseline ratings; it would have been difficult to assess an infant's sleep state prior to care. Further research for sleep state is needed using the PACEFI.

Implications of Findings for Clinical Practice and Future Research

Clinical Implications

The findings in the present study outlined in Chapter 4 have several direct implications to clinical practice. This study will serve to guide clinical practice by informing providers of the pain response for both ELGA and VLGA infants. Behavioral cues, specifically facial cues, showed the most promise as indicators of pain assessment in ELGA and VLGA infants. In addition, motor cues also appeared to contribute to the measurement of pain. ELGA and VLGA infants in this study demonstrated a clear response to pain for both the invasive and non-invasive procedures. ELGA showed a dampened response to the invasive procedure, possibly signifying neuro-developmental immaturity, while VLGA infants demonstrated a more robust response to pain for the invasive procedure indicating an increasing pain response with developmental maturity. There was a notable increase in behavioral cues for both ELGA and VLGA infants during the noninvasive procedure, possibly related to the whole care experience. These findings add to the current knowledge that infants as young as 25 weeks can exhibit a clear pain response and this pain response will become more robust with advancing gestational age.

Additionally both ELGA and VLGA infants demonstrated variability of vital signs in comparison to behavioral cues during the invasive and non-invasive procedures. Vital signs are readily accessible parameters that clinical providers assess during routine care of infants (Stevens et al., 2007c). Most providers may infer that vital signs will change throughout a painful procedure. However, this may not be the case as vital signs are not considered specific to pain and they can increase or decrease during any type of care (Ranger et al., 2007). Furthermore, infants may have been sensitized from previous handling which, in turn, can increase their vital signs even after the painful stimulus is removed (Ghosh & Barr, 2007, Holsti et al., 2006). This study demonstrated that vital signs and behavioral cues did not have a consistent relationship across infants and across procedures. Several pain assessment instruments, such as the PIPP and NPASS, are frequently used in NICUs to assess pain (American Academy of Pediatrics & Canadian Paediatric Society, 2006; Boyd, 2003). These instruments are composite scores combining both physiologic indicators and behavioral cues (Boyd, 2003; Duhn & Medves, 2004; Stevens et al., 2007b). Combining these scores may cloud an infant's true pain and over- or underestimate the pain response (Johnston et al, 1995; Morrison et al., 2003; Holsti & Grunau., 2007b). Care should be taken when using these instruments to interpret if both the behavioral cues and physiologic indicators are mutually contributing to the measurement of pain (Stevens et al., 2007c).

A key factor measured for this study was the pain response of ELGA and VLGA infants demonstrated during the non-invasive procedures. ELGA infants generated higher pain scores during a diaper change, with recovery scores dropping below baseline. VLGA infants generated pain scores for the diaper change which remained slightly elevated at recovery. The fact that a diaper change produced the same response as an invasive procedure has significant implications in the delivery of routine care for these infants. Currently, best practice for routine care in the NICU is clustered care at the bedside, meaning that all care is given at prescribed points in time. For example, an infant may be due for routine care 6 times within a 24-hour period, with rest periods in between. Furthermore, RNs may group additional procedures into a care time to prevent waking the infant during the rest period, thereby increasing the total number of interventions that will be performed on that infant. For this study there were between 5–20 interventions being performed after the baseline rating was completed for each non-invasive procedure. The additional amount of handling during the non-invasive procedure may have caused the infant significant pain and stress. It appeared that this pain and stress caused the ELGA infants to collapse after the RN provided care because infants' recovery scores were close to zero, suggesting an inability to respond due to exhaustion. This finding is in direct contrast to findings related to the invasive procedure, during which the ELGA infants may have remained in a hyperexcitable state with higher recovery scores well after the procedure had ended. In addition, feedings were included usually after the diaper change was completed during a high stress time. Als (1982) described autonomic stress signals such as spitting up and hiccoughing which can contribute to feeding intolerance. Routine procedures are known to cause pain and stress for these infants (Zahr & Sossi, 1995; Morelius et al., 2006). Thus, clustering these procedures seems to elicit a sensitized state that may lead to increased energy expenditure and exhaustion (Holsti et al., 2005b; Morelius et al.). Cluster care may be too overwhelming for these infants and a new strategy for care delivery should be explored.

In summary this study demonstrated preliminary reliability and validity indicating that the PACEFI shows promise for use with ELGA and VLGA infants. In addition, this study showed that ELGA infants could mount a response to both the non-invasive and invasive procedures. VLGA infants demonstrated a more robust response than their ELGA counterparts, likely indicating a greater level of developmental maturity. Physiologic indicators were loosely related to behavioral cues and these relationships varied from infant to infant. ELGA and VLGA infants demonstrated a clear pain response to the non-invasive procedure indicating that routine care along with clustering care may not be as benign as typically believed. These findings have clinical implications for all care providers regarding pain assessment for these vulnerable infants. The knowledge gained from this study will influence practice patterns by illuminating the differences in the pain response for behavioral cues and physiologic indicators between ELGA and VLGA infants for both invasive and routine care procedures. This study contributes to the expanding knowledge of the pain response for ELGA and VLGA infants for both invasive and non-invasive procedures. Further investigation is needed to determine additional reliability and validity for the PACEFI.

Future Research

Further analysis of study data collected. The study data analyzed and reported represent a small portion of data analysis that could be done using the data from this study. This researcher plans to continue work with this data to further evaluate the pain response for the ELGA and VLGA infant population. Future analyses include evaluating differences in vital signs across data points (baseline, during, recovery), evaluating the effect of nonpharmacologic interventions and ventilatory support on the pain response, and examining the difference in pain scores between invasive procedures. Further data analysis will contribute to expanding the understanding of the pain response for these earlier born infants.

Further analysis of the PACEFI. This was a first step to validate the PACEFI for a specific infant population. However, future research for the PACEFI should focus on a larger sample to determine if there is hierarchical ordering of the behavioral cues as a next step in measuring and understanding pain in the ELGA and VLGA infants. Item response theory (IRT), specifically the Rasch Model, should be further explored as a way to capture the infant pain response along a hierarchical continuum.

The Rasch (1960) Model is an operationalization of IRT (i.e., an IRT measurement model) which estimates the location of persons and items on an underlying variable (traits, skills, abilities, attitudes, perceptions, and behaviors) of the person or items being measured (Wright & Stone, 1979). Consistent with the conceptualization of pain used here, the Rasch Model assumes that variables are unidimensional (Andrich, 1988). The IRT measurement model evaluates the relationship between the person's response to an item and the underlying construct being measured by the instrument (Wright, 1967; Wright & Stone). When one construct is held constant, such as pain then the person's responses are independent (Andrich; Wright). These independent personal responses imply that the specific construct being measured in the instrument is the only aspect producing the person's responses, which illustrates local independence (Andrich; Wright; Wright & Stone). Regardless of items used for calibration (no, low, moderate, high pain) or ELGA infants used to determine pain level, the same results should be achieved regardless of sample and items resulting in the property of invariance (Andrich; Wright). Hence using the IRT Rasch Model, pain can be operationally hypothesized as existing in a continuous hierarchical manner ranging from low to moderate to high pain (Wright &

Stone). Therefore, additional testing of the PACEFI with larger samples could allow for testing it using IRT. If a hierarchy of behavioral indicators could be demonstrated, then clinicians could better assess infants' response to care and possibly adjust care accordingly.

The findings for the current study suggest that the Rasch Model may provide a good conceptual fit for the measurement of pain in infants. A key feature of a fully developed IRT measurement system is that not all items in such a system need to be completed to derive a rating score (Ludlow, Haley, 1996). The IRT measurement model is likely to yield measures which can be completed quickly, lending themselves well to fast-paced clinical settings such as the NICU. Further testing is needed to determine if all the PACEFI items are contributing to pain measurement in addition to determining if the behavioral cues contributing to the pain response can be ordered along a hierarchical continuum from lowest pain measurement to highest.

Future research for novel care practices. In addition further research is needed to investigate a new care delivery method that would be beneficial for ELGA and VLGA infants. The practice of clustering care has been acculturated throughout NICUs. However, evidence from this study suggests that clustering care for routine procedures throughout the day may have a detrimental effect and possibly long-term, adverse consequences for these infants. There have been several studies that have quantified the fact that frequent routine handling may be detrimental to an infants' neurodevelopment (Zahr & Balian, 1995; Cameron et al., 2007; Morelius et al., 2006). Further research should focus on developing innovative interventions to determine novel care practices. This approach would generate a more developmentally sound care for these infants.

Future research for sleep state using the PACEFI. This study did not examine sleep state differences and the effect it may have on pain response. Evidence suggests that both differences in sleep organization and the amount of time spent in sleep may affect infants' expression of responses to pain (Grunau & Craig, 1987; Johnston et al., 1999; Stevens et al., 1996; Walden et al., 2001). Gestational age differences in sleep state organization further complicate pain assessment and argue for studying both ELGA and VLGA infants. Hence, further research is needed to determine if the PACEFI can capture pain during different types of sleep states.

Conclusions

To this researcher's knowledge, based on the current review of available literature, this is one of the few studies that compared pain response shortly after birth between ELGA and VLGA infants for both an invasive and non-invasive procedure. This study indicated that infants as young as 25 weeks' gestation can mount and exhibit a response to pain. A key finding of the study was the response that both ELGA and VLGA infants demonstrated for the non-invasive procedure emphasizing the need to rethink the way care is currently delivered to these infants. The implications for nursing research include evaluating and developing innovative strategies to deliver routine care that affects an infant's neurodevelopmental growth in a positive way. In addition, the PACEFI showed promise as a pain assessment instrument for the ELGA infant population. Additional testing of the PACEFI will be continued to determine further reliability and validity and whether or not behavioral cues can be ordered along a hierarchical continuum as a next step in providing developmentally specific pain assessment for these infants.

Prevention and management of pain are critical for the care of ELGA and VLGA infants. Recognition of pain response by clinical care providers is a key factor in providing superior pain management. The findings of this study will assist clinical providers in recognizing a greater array of behavioral cues, promoting understanding of the relationship between physiologic indicators and behavioral cues for both ELGA and VLGA infants, and assessing pain more accurately. In addition, the findings may contribute to an expanded awareness that these infants are extremely vulnerable to all caregiving activities and the simplest interventions may cause harm to an already compromised infant.

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Appendix A Pain Assessment Tools for Neonates

Pain Scale/Year	Population/ Type of Pain	Indicators	Validity/Reliability	Clinical Utility	Limitations
Behavioral Indicators of Infant Pain (Holsti & Grunau, 2007)	Procedural (23-32 weeks gestation)	Behavioral State, brow bulge, eye squeeze, and nasolabial furrow, horizontal stretch mouth, taut tongue, fingersplay, fisting	Tested on 92 infants ages 23-32 weeks. Internal consistency (0.82) Interrater reliability (r = 0.80-0.92) Construct validity (p < 0.0001) Concurrent validity (p < 0.0001)	Not established	Small sample of infants < 29 weeks .
EDIN Echelle Douleur IN confort Nouveau-ne, Neonatal Pain and Discomfort Scale (Debillon et al., 2001)	Prolonged (26-36 weeks gestation)	Behavioral facial activity, body movements, quality of sleep, and quality of contact with nurses and consolability	Tested on 76 pre-term infants, mean gestational age 31.5 weeks. Construct validity Interrater reliability (r=0.59-0.74). Internal consistency (0.86-0.94)	Has not been established (Boyd, 2003)	The authors note limitations including: establishing criterion validity, discriminate validity, sensitivity and specificity along with clinical utility
Neonatal Facial Coding System (NFCS) (Grunau & Craig,1987)	Procedural (38-42 weeks gestation)	Facial expressions: brow bulge, eye squeeze, nasolabial furrow and stretch vertical mouth, horizontal mouth, lips pursed, taut tongue, chin quiver, taut tongue	Tested on 140 well newborn infants (Duhn & Medves, 2004) Face/content validity Interrater reliability (r = 0.88) Intra-rater validity (r = 0.88) Concurrent validity(r=0.53-0.83)	Developed for research and requires extensive training (Boyd, 2003)	A complex tool. Sample: > 32 weeks, the lower facial actions may not be seen in ELGA infants due mechanical ventilation. (Boyd, 2003)
NIPS The Neonatal Infant Pain Scale (Lawrence et al., 1993)	Procedural (Boyd, 2003) (32-40 week gestation)	Physiologic breathing patterns Behavioral facial expression, crying, arm and leg posture, and state of arousal	Tested on 38 preterm and term infants and 90 procedures observed Interrater reliability (r=0.92-0.97) Internal consistency (0.87-0.95) Content validity (survey) Concurrent validity (r=0.53-0.84) Construct validity (p < 0.001)	Adapted from Children's Hospital of Eastern Ontario which is a post-operative pain tool	Sample: > 32 weeks

Pain Scale/Year	Population/ Type of Pain	Indicators	Validity/Reliability	Clinical Utility	Limitations
NPASS Neonatal Pain, Agitation and Sedation Scale (Hummel et al., 2003)	Prolonged (mechanical ventilation or postoperative pain) (< 28-35 weeks' gestation) (Stevens et al., 2007)	Behavioral crying, irritability, behavioral state, facial expression, extremities tone Physiologic vital signs, oxygen saturation	Tested on 72 subjects Interrater pain (r = 0.95) sedation (r = 0.95) Internal consistency Low pain (0.31) High pain (0.82) Discriminate validity (p < 0. 0001) Concurrent validity (r = 0.61-0.83)	Preliminary evidence (Hummel et al., 2008).	May underestimate pain with confounding items between pain/agitation and sedation. (Boyd, 2003) Correction for gestational age confounds pain rating.
PAIN (The Pain Assessment in Neonates) (Hudson-Barr et al., 2002)	Procedural (26-47 weeks' gestation)	Behavioral facial expression, cry, extremity movement, state of arousal Physiologic O_2 requirement, heart rate, breathing pattern	Tested on 196 neonate's gestational ages 26-47 weeks. (Duhn & Medves, 2004) Construct (p <0.001) Criterion validity (p <0.001)	Has not been established (Duhn & Medves, 2004)	Little difference was noted between basal and stimulus response scores Oxygen saturation remains a confounding variable with 95% oxygen saturation expected. However, ELGA infants when in O_2 never should reach this level of saturation due to retinopathy of prematurity. Exclusion of 24-26 week infants from validation studies
PIPP (Premature Infant Pain Profile (Stevens et al., 1996)	Procedural (28-40 weeks' gestation)	Behavioral brow bulge, eye squeeze and nasolabial furrow Physiologic heart rate and oxygen saturation Contextual gestational age and behavioral state	Tested on 4 data sets n=27, 39, 48,124 ranging in gestational age 28-40 weeks. Internal consistency (alpha=0.59 to 0.76) Construct validity Preterm (p < 0.16, 0.02) Term (p < 0.02) Construct validity in clinical setting (p < 0.0001) Interater reliability (ICC= 0.93-0.96) Intrarater reliability (ICC= 0.94-0.98) (Balantyne, 1999)	Complex instrument (Boyd, 2003)	Combining physiologic and behavioral data may be confounding scores due to the variability in physiologic indices. (Holsti & Grunau, 2007b) It has been reported cumbersome to use in clinical setting. (Koeppel, 2002) Exclusion of infants < 28 weeks from validation studies.

Appendix B
Infant Demographic Information Form

Nurse Rater ID_______________ Observation ID_____________

Please fill in 1-9 No item should be left blank.

#	**Infant Demographic Data**	
1	Gender	☐ Female ☐ Male
2	Gestational Age	______________weeks/days
3	Birth Weight	_____________grams
4	Race	white, non-Hispanic_______ white, Hispanic________ black, non-Hispanic_______ black, Hispanic___________ Asian or Pacific Islander___________ Native American___________ Mixed specify________________ Other______________
5	Snap-II Score	Score_____________
6	Count Painful Procedures up to Current Procedure	Number_______________
7	Cranial Ultrasound Report	Intraventricular Hemorrhage ☐Yes ☐ No Type_____________________________
8	Narcotic Exposure	☐ Yes ☐ No Medication____________________
9	Respiratory Support	☐ Yes ☐ No Type____________________

Appendix C

Registered Nurses Demographic Information Form

Nurse Rater ID______________ Date___________________________

Please mark the answer or answers that are true for you and fill in the blanks and boxes.

Are you?
☐ Female
☐ Male

What is your age? _____________________________

What degrees and certifications have you earned? (**Check all that apply**)

☐Associate's Degree
☐Diploma
☐Bachelor's Degree
☐Master's Degree
☐Doctoral Degree
☐ Nurse Practitioner
☐Associate's Degree in Other Field
☐Bachelor's Degree in Other Field
☐Master's Degree in Other Field
☐Doctoral Degree in Other field
☐Clinical Nurse Specialist
☐Clinical Educator
☐ Other (**Please describe in space below)**

Comment:____

How long have you been a Neonatal Intensive Care Nurse?__________________________

Thank you. Your answers will help me describe the people who participated in this study.

Attachment D

Pain Assessment and Care for Extremely Low Gestational Age Infants Focused Instrument (PACEFI)

Nurse Rater ID_____________________ Observation ID_____ Date_____________ Time________

Procedure___________________ Baseline_____ During_____ Diaper Change______ Recovery_____

Please observe the infant and mark yes or no for every item that you observe or do not observe. No item should be left blank. Record information in text box.

Eye Squeeze	Yes__________	No___________
Hands on Face	Yes__________	No___________
Crying	Yes__________	No___________
Furrow	Yes__________	No___________
Grimace	Yes__________	No___________
Nasolabial Bulge	Yes__________	No___________
Lips Pursed	Yes__________	No___________
Stretched Mouth	Yes__________	No___________
Taut Tongue	Yes__________	No___________
Push Away Arms	Yes__________	No___________
Push Away Legs	Yes__________	No___________
Pull Away Arms	Yes__________	No___________
Pull Away Legs	Yes__________	No___________
Full Body Pull Away	Yes__________	No___________
Sit on Air	Yes__________	No__________
Fisting	Yes__________	No___________
Mouthing	Yes__________	No___________
Finger Splay	Yes__________	No___________
Pull Extremities Midline	Yes__________	No___________
Curling Toes	Yes__________	No___________

Vital Signs

HR_____________

RR_____________

O2 SAT_____________

1. Hospital Pain Instrument

____

2. Hospital Pain Score

Before ______ After________

3. Non-pharmacologic interventions________________

____

3. Type of Handling Prior to Ratings___________________

____

4. Last Time of Handling____________________
(Hours/Minutes)

5. Infant Position____________

6. Handling During Observation

____

____

____

Description of Pain Cues

***Eye Squeeze:** Scrunching and closing of the eyelids.

Hands on Face: infant brings a hand to the forehead and then brings the hand back down again.

Crying: This cue can be heard or silent if the infant is intubated.

***Furrow**: Scrunching between eye brows.

Grimace: Simultaneously scrunching the cheeks, squeezing the eyes, and furrowing.

***Nasolabial Bulge:** Pulling up the cheeks and broaden the nasolabial furrow.

***Lips Pursed:** Lips are shaped as if the baby is pouting.

Stretched Mouth: Mouth is pulled open and appears wider than normal.

***Taut Tongue**: lowered in mouth with edges curled upward. Can be seen a wide open mouth.

Push Away Arms: The infant tries to push away the painful stimulus with hands or arms.

Push Away Legs: The infant tries to push away the painful stimulus with legs or feet.

Pull Away Arms: The infant pulls away from the painful stimulus with hands or arms.

Pull Away Legs: The infant pulls away from the painful stimulus with legs or feet

Full Body Pull Away: The pulls all four extremities away from midline.

Sit on Air: The infant lifts legs straight up in the air.

○**Fisting:** closes hand into a fist.

Mouthing: Open and closing mouth.

○**Finger Splay:** hands are open with fingers spread apart.

Pull Extremities Midline: The infant draws in all four extremities to midline.

Curling Toes: Tight closing and flexing of the toes to form curled toes.

Adapted from * Grunau, R., Craig K. (1987). Pain expression in neonates: facial action and cry. Pain, 28, 395-410;
○Holsti, L. Grunau, R. (2007). Initial validation of the Behavioral Indicators of Infant Pain (BIIP). Pain, 132 (3), 264-272.

Appendix F

PARTNERS HEALTHCARE SYSTEM

Partners Human Research Committee
Partners Human Research Office
116 Huntington Avenue, Suite 1002
Boston, MA 02116
Tel: (617) 424-4100
Fax: (617) 424-4199

Application: Notification of IRB Approval/Activation

Protocol #: 2010-P-001044/1; MGH

Date: 06/22/2010

To: Kim Francis, MS, APRN,BC
Nursing
15 Fruit St.

From: Fausta M. Figueroa
PHS Research Management
116 Huntington Ave Suite 1002

Title of Protocol:	Development of a New Pain Assessment Instrument: Pain Assessment and Care for the Extremely Low Gestational Age Infant Focused Instrument (PACEFI).
Version Date:	05/07/2010
Sponsor:	Foundation for Neonatal Research and Education
IRB Review Type:	Expedited
Minimal Risk:	45 CFR46.110 and 21 CFR56.110
Expedited Category/ies:	(7) Research on individual or group characteristics or behavior, or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or QA methodologies.
IRB Approval Date:	06/10/2010
Approval Effective Date:	06/22/2010
IRB Expiration Date:	06/10/2011

This Project has been reviewed and approved by the MGH IRB, Assurance # FWA00003136. During the review of this Project, the IRB specifically considered (i) the risks and anticipated benefits, if any, to subjects; (ii) the selection of subjects; (iii) the procedures for securing and documenting informed consent; (iv) the safety of subjects; and (v) the privacy of subjects and confidentiality of the data.

NOTES: The following documents have been reviewed and approved by the IRB:

Protocol Summary version 03/10
Questionnaires (1)
Letter (1)

As Principal Investigator you are responsible for the following:

1. Submission in writing of any and all changes to this project (e.g., protocol, recruitment materials, consent form, study completion, etc.) to the IRB for review and approval prior to initiation of the change(s), except where necessary to eliminate apparent immediate hazards to the subject(s). Changes made to eliminate apparent immediate hazards to subjects must be reported to the IRB within 24 hours.

Appendix F

BOSTON COLLEGE
Institutional Review Board
Office for Research Protections
Waul House, 3rd Floor
Phone: (617) 552-4778, fax: (617) 552-0498

IRB Protocol Number: 11.024.01

DATE: July 23, 2010

TO: Kim Francis

CC: June Horowitz

FROM: Institutional Review Board – Office for Research Protections

RE: Development of a New Pain Assessment Instrument: Pain Assessment and Care for the Extremely Low Gestational Age Infant Focused Instrument (PACEFI)

Notice of IRB Review and Approval
Expedited Review as per Title 45 CFR Part 46.110, FR 60366, FR, # 5 & 7
Waiver of Informed Consent [Title 45 CFR 46.116 (d)]

The project identified above has been reviewed by the Boston College Institutional Review Board (IRB) for the Protection of Human Subjects in Research using an expedited review procedure. This is a minimal risk study. This approval is based on the assumption that the materials, including changes/clarifications that you submitted to the IRB contain a complete and accurate description of all the ways in which human subjects are involved in your research.

This approval is given with the following standard conditions:

1. You are approved to conduct this research only during the period of approval cited below;
2. You will conduct the research according to the plans and protocol submitted (approved copy enclosed);
3. You will immediately inform the Office for Research Protections (ORP) of any injuries or adverse research events involving subjects;
4. You will immediately request approval from the IRB of any proposed changes in your research, and you will not initiate any changes until they have been reviewed and approved by the IRB;
5. The IRB has waived the requirement of obtaining informed consent under 45CFR 46.116 (d). The research involves no more than minimal risk; the alteration will not adversely affect the rights and welfare of subjects and the research could not

Appendix F

practicably be carried out without an alteration.

6. You will give each research subject a copy of the informed consent document;
7. You may enroll up to 48 participants.
8. If your research is anticipated to continue beyond the IRB approval dates, you must submit a Continuing Review Request to the IRB approximately 60 days prior to the IRB approval expiration date. Without continuing approval the Protocol will automatically expire on July 22, 2011.

Additional Conditions: Any *research personnel that have not completed an acceptable education/training program should be removed from the project until they have completed the training. When they have completed the training, you must submit a Protocol Revision and Amendment Form to add their names to the protocol, along with a copy of their education/ training certificate.*

Approval Period: **July 23, 2010-July 22, 2011.**

Boston College and the Office for Research Protections appreciate your efforts to conduct research in compliance with Boston College Policy and the federal regulations that have been established to ensure the protection of human subjects in research. Thank you for your cooperation and patience with the IRB process.

Sincerely,

Stephen Erickson
Director
Office for Research Protections

TSL