COMPLEMENTARY AND INTEGRATIVE METHODS OF PEDIATRIC ACUTE PAIN MANAGEMENT:

A RANDOMIZED CONTROLLED CLINICAL TRIAL

By

Nora E. Stinley

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Chair:

Laura M. Juliano, Ph.D.

Deborah O. Norris, Ph.D.

David N. Kearns, Ph.D.

Pamela S. Hinds, Ph.D.

Maureen E. Lyon, Ph.D.

Dean of the College of Arts and Sciences

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Thanks are not enough for the people who have supported me from the very beginning of my dreams to the fruition of this project and beyond! I am surrounded by a family I am thankful for every day, who loves me unconditionally. Jeff, Mom, Dad, Jimmy, Tommy, Kay Kay, Michael and Mark, it is a mutual love. My friends have bolstered me with laughter and needed fun, and I am looking forward to years and years more! And finally, without the willing and helpful participation of so many patients at Children's National, this research would have been impossible.

This was a labor of love dedicated to you all.

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ABSTRACT

Pain management is a critical aspect of patient care, and has become a nationwide standard of care. In particular, pediatric patients suffer from undertreated pain due to an inability to properly articulate and manage their pain experiences, which can have negative developmental consequences. Patients and parents frequently cite ineffective pain management as a primary source of dissatisfaction in pediatric patient care, and there has been a shift from a pain management approach to treating pediatric pain to a comfort management approach. This study examined the physiological and psychological outcomes of two fast-acting complementary and integrative interventions designed to provide comfort management to pediatric patients undergoing needle stick procedures.

Two experiments were conducted using a two-group randomized controlled clinical design, each with a sample size of forty participants between the ages of eight and 18 years. The physiological and psychological outcomes of a binaural beats intervention, and a mindfulness meditation intervention were compared with standard of care treatment during the needle sticks. Treatment Group participants in both experiments demonstrated clinically less physiological stress, psychological anxiety, and pain compared with the Control Groups, demonstrated by an effect size of 0.3 or higher. Furthermore, Treatment Group participants who practiced mindfulness meditation showed a statically significant decrease in heart rate compared to Control Group participants, p=0.02. These findings support the use of fast-acting integrative interventions with pediatric patients receiving needle sticks.

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CHAPTER 1

INTRODUCTION

Pain management is a critical aspect of pediatric patient care, and has become a nationwide standard of care issued by the Joint Commission on Accreditation for Healthcare Organizations (JCAHO, 1999). Health care facilities across the nation are implementing a systems approach to pain management based on recommendations set forth by the American Pain Society (American Society of Anesthesiologists Committee on Standards and Practice Parameters, 2011; Bellande et al., 2012; Gordon et al., 2005; Meghani et al., 2012; Murinson, Mezei, Kozachik, Buenaver, De Silva, 2012). However, patients and clinicians are still reporting undermanaged pain during hospital stays and outpatient procedures (Avansino, Peters, Stockfish, Walco, 2012; Kirsh, Passik, Rich, 2013; Pyati, Gan, 2007).

Undertreated pain can be the result of inadequate pain assessments, patients' inability to properly report pain, the lack of appropriate therapies to treat pain, the complexity of pain, and other factors (Breivik et al., 2008; Herr et al., 2006; Sinatra, 2010; Stalnikowicz, Mahamid, Kaspi, Brezis, 2005). In particular, pediatric patients suffer from undertreated pain due to an inability to properly articulate their pain experiences, which can have negative developmental consequences (Bartholomeusz, Callister, Hodgson, 2013; Cohen et. al, 2007). Children who do not receive adequate pain management interventions may experience residual physiological and psychological effects of pain-related trauma (Avansino et al., 2012; Cohen, 2008; Noel, McMurtry, Chambers, McGrath, 2010).

Patients and parents frequently cite ineffective pain management as a primary source of dissatisfaction in pediatric patient care, and a reason for changing care providers (Kennedy, Luhmann, Zempsky, 2008; Kozlowski et al., 2012; McNeill, Sherwood, Starck, 2004; Press Ganey, 2011). Children who are frequently hospitalized consider procedure-related pain the worst part of

being ill (Blount, Piira, Cohen, Cheng, 2006; Kennedy et al., 2008, McMurtry, Noel, Chambers, McGrath, 2011). Procedural pain is experienced both during major medical procedures, and during small procedures like blood draws or venipunctures. Interventions such as binaural beats, in which a different rhythm is played to each ear creating the auditory illusion of calming soundwaves, are easily accessible to staff and patients (Reedijk, Bolders, Hommel, 2013). Mindfulness meditation is another intervention that creates a sense of calm and relaxation through guided instruction on bring awareness to one's breathing (Mrazek et al., 2012). Providing patients with interventions such as these, may reduce pain and the fear that characterizes medical phobias.

Pediatric Acute Pain and Needle Phobias

Medical phobias, including and most prominently the fear of needle sticks, affect approximately 5% to 10% of children in the United States (American Psychiatric Association, 2013; Jenkins, 2014). Needle phobias develop in childhood, but can persist into adulthood, along with the problematic behavior of avoiding medical care (Bird & McMurtry, 2012; Jenkins, 2014; Noel, McMurtry, Chambers, McGrath, 2010; Noel, Chambers, McGrath, Klein, Stewart, 2012: Noel, Chambers, Petter, McGrath, Klein, Stewart, 2012; Taddio et al., 2012). Pediatric patients often site the acute pain of needle sticks as some of the worst pain experienced during hospitalization, resulting in anxiety, fear, and avoidance behaviors (McMurtry, Noel, Chambers, McGrath, 2011; Noel, Chambers, McGrath, et al., 2012; Noel, Chambers, Petter, et al., 2010). Pharmacological interventions like topical anesthetics are typically used to manage the physiological pain of a needle stick; however, needle phobia can still develop as a result of unaddressed pain and distress (Bird & McMurtry, 2012). Current methods of pain management are often under-used during needle stick procedures, and inadequately address the complex nature of the experience (Bird & McMurtry,

2012; Taddio et al., 2009).

Pain management is a critical aspect of patient care; however, the American Society for Pain Management Nursing has determined that "pain management" is an insufficient approach to patient care. The Society for Pain Management nursing instead encourages "comfort management" during painful medical procedures (Czarnecki et al., 2011). Comfort management refers to the "management of pain, anxiety, and any other discomforts that may occur with procedures." (Czarnecki et al., 2011). The comfort management approach to needle sticks not only reduces the immediate pain and of a procedure, but also helps to reduce the fear, anxiety, and negative memories associated with the procedure (Du et al., 2008; McMurtry et al., 2011; Noel, Chambers, McGrath, et al., 2012; Schwabe, Wolf, Oitzl, 2010). Integrative interventions such as expressive arts therapies, relaxation, and mindfulness techniques counteract the physiological stress response, and also mitigate psychological and emotional distress as well (Czarnecki et al., 2011; Grewal, Petter, Feinstein, 2012; Noel et al., 2010; Noel, Chambers, Petter, et al., 2012; Yoo, Kim, Hur, Kim, 2011). Hospitals are using complementary and integrative interventions with adult and pediatric populations; however there is little research on the validity and effectiveness of these interventions (Surette, Vanderjagt, Vohra, 2013). The current study examines the bio-psychosocial outcomes and clinical feasibility of using binaural beats, and guided mindfulness meditation as complementary and integrative interventions during pediatric needle stick procedures.

The Psychobiology of Acute Pain Procedures

Needle sticks are simple medical procedures that are typically short in duration. However, these procedures elicit a complex, and sometimes long-lasting reaction from pediatric patients. While children specifically list the physiological pain of a needle stick as one of the leading causes of hospital pain, the acute pain experience is designed to be short-lived and adaptive (Voscopoulos

& Lema, 2010; Walco, 2008). However, children begin to display signs of distress and discomfort long before the sensation of acute pain is even experienced. This distress is a direct result of anticipatory anxiety and fear of the pending acute pain experience (Bird & McMurtry, 2012; Noel et al., 2010).

Fear of pain is the most salient aspect of the needle stick procedure, and is a psychological event that activates the stress response (Bird & McMurtry, 2012). The stress response is a biological event involving a top-down cascade of cortical activity referred to as the hypothalamic-pituitary adrenal (HPA) axis (Schwabe, Wolf, Oitzl, 2010). Activation of the HPA-axis results in a variety of physiological responses, specifically including release of the stress hormone cortisol, as well as increased heart rate, respiration rate, and hyper-vigilance. Additionally, elevated cortisol interferes with hippocampal, amygdal, and other memory systems affecting accurate memory formation (Schwabe et al., 2010). The sympathetic nervous system (SNS) is also activated during the stress response, eliciting the release of norepinephrine and its salivary surrogate, alpha amylase (Mravec, 2011). Alpha amylase is an enzyme produced by the salivary glands and is used as a biomarker of norepinephrine (Granger et al., 2006; Mravec, 2011). The comfort management approach to care emphasizes the importance of adequately managing psychological fear and anxiety, and biological stress to diminish the negative impact of these events.

Inadequate management of stress and anxiety can exacerbate the negative experience of the needle stick procedure. Fear of the needle stick can intensify the psychological perception of acute pain, though the physiological stimulus remains the same (Bird & McMurtry, 2012). Children often struggle to isolate the sensation of experienced pain from the sensations of fear and stress, which results in the inaccurate report of severe pain (Bird & McMurtry, 2012). This inaccurate report explains why needle stick procedures receive some of the highest patient-reported pain scores

during hospitalization (Anson, Edmundson, Teasley, 2010; Bird & McMurtry, 2012; Noel, McMurtry, Chambers, McGrath, 2010; Press-Ganey, 2011).

Additionally, the increase in fear and stress, paired with the increase in perceived pain can lead to physical reactions from a child such as crying, screaming, and physical struggle. The combination of these physiological, behavioral, and psychological reactions impedes accurate recall of the needle stick procedure (Cohen et al., 2001; Noel, McMurtry, Chambers, McGrath, 2010; Bird & McMurtry, 2012). The child's inability to form an accurate memory of the procedure can lead to the formation of a traumatic memory (Noel, McMurtry, Chambers, McGrath, 2010; Schwabe et al., 2010). A traumatic memory of the needle stick reinforces the development of a needle phobia (Bird & McMurtry, 2012; Cohen, Blount, Jansevics Cohen, Ball, McClellan, Bernard, 2001; Noel, McMurtry, Chambers, McGrath, 2010).

Traumatic memories are more likely to form during needle stick procedures managed with the current standard of care treatment option. Standard of care refers to the treatment policies put in place by the governing entities within a hospital or healthcare facility (Baxter, Cohen, McElvery, Lawson, von Baeyer, 2011). The current standard of care treatment for needle stick procedures prioritizes pain management by pairing a topical anesthetic, such as numbing cream or vapocoolant cold spray, with the needle stick (Baxter et al., 2011). Patients who receive standard of care treatment during needle stick procedures are more likely to develop negative, exaggerated, or traumatic memories of the procedure (Noel et al., 2010). Children should be provided with interventions that prioritize the comfort management approach to care, minimizing pain, anxiety, stress, and other discomforts that occur during acute pain procedures (Craig, 2014).

Complementary and Integrative Interventions for Acute Pain Procedures

Reviews of complementary and integrative interventions with a pediatric population show the growing acceptance and use of these approaches to care (Pillai Riddell et al., 2011; Yip, Middleton, Cyna, Carlyle, 2011). Interventions that incorporate relaxation, mindfulness, and participant empowerment can also be classified as complementary and alternative mind-body therapies (NCCAM, 2012; Surrette, Vanderjagt, Vohra, 2013). The National Center for Complementary and Alternative Medicine (NCCAM) defines mind-body therapies as practices that "focus on the interactions among the brain, mind, body, and behavior with the intent to use the mind to affect physical functioning and promote health" (NCCAM, 2012). NCCAM also sites a need for research into mind-body therapies, specifically the need for randomized controlled trials looking at the outcomes of such practices (NCCAM, 2012). In an attempt to contribute to the area of mind-body research, this set of experiments independently examined the use of binaural beats (Study 1), and mindfulness meditation (Study 2) with pediatric patients undergoing needle stick procedures.

Binaural beats and mindfulness meditation were chosen for examination because they are both cost-effectiveness and fast-acting pain management solutions. Topical anesthetics are the current methods used to manage needle stick pain. The wait time necessary to ensure creams like liposomal 4% lidocaine achieve effectiveness is a minimum of 30 minutes (Brenner et al., 2013). This wait time serves as a barrier to effective care in a fast-paced medical setting, and therefore renders topical anesthetics ineffective in time-sensitive situations. The complementary and integrative methods described below have a wait time of five to fifteen minutes before they become effective, and therefore may be used in time-sensitive situations (Doherty, 2014; Thompson & Gauntlett-Gilbert, 2008; Zeidan, Gordon, Merchant, Goolkasian, 2010).

Binaural Beats

Binaural beats are an integrative mind-body therapy used to increase awareness and focus, and to induce relaxation. The binaural beat phenomenon occurs when two beats of different frequencies are played to a listener over headphones. A different beat frequency is projected to each ear, creating an auditory illusion. The brain perceives a third frequency, which is the difference between the two frequencies heard by the ears (Reedijk, Bolders, Hommel, 2013). This third frequency is known as the binaural beat (Filimon, 2010; Sun, Sung, 2013). The binaural beat stimulates the brain, inducing a frequency following response, or a FFR (Vernon, Peryer, Louch, Shaw, 2012). The FFR affects the "electrocortical activity of the brain" and is a "mechanism for potential behavior change" (Vernon et al., 2012). This FFR, or entrainment, affects "neural firing patterns" and brain stem activity to induce relaxation (Reedijk et al., 2013; Vernon et al., 2012). The cerebral brainwave shift stimulated by binaural beats is similar to the shift that occurs during meditation (Shapiro, 2014).

Like meditation, binaural beats can be used as a tool to induce calm and mindfulness during stressful situations. A study examining the impact of hypnotherapeutic techniques and binaural beats on perceived pain found that both techniques reduced perceived pain in an adult population (Balan, Cocoana, Gabor, Gabriel, Vas, 2014). In their study, Treatment Group One participants received hypnotherapy from a licensed psychotherapist prior to receiving a painful stimulus. Treatment Group Two participants listened to binaural beats for five minutes prior to receiving the painful stimulus. Control Group participants did not take part in an intervention; rather they received the painful stimulus. The pain stimulus in all conditions was squeezing the ring finger with a hemostatic clamp. The participants were then asked to rate their perceived pain on a ten-point Likert scale. Treatment Group One and Two reported significantly less perceived pain

compared to the Control Group (Balan et al., 2014). This study demonstrates the potential use of binaural beats to manage pain; however it was conducted with a non-clinical adult population.

Binaural beats can also be used to induce relaxation and counteract the stress response. Binaural beats can shift the brain's wave state. For example, this sound technology can shift the brain's waves from beta waves to alpha waves. Puzi (2013) studied the impact of binaural beats on college students who just completed a school exam. Thirty-three students listened to alpha frequency binaural beats immediately after the examination period. Subjects began the session with brainwave frequencies in the beta range. After listening to the binaural beats, nearly all subjects showed an increase in alpha brainwaves and a decrease in beta brainwaves (Puzi, 2013). Beta waves are associated with anxious and hyper vigilant physiological and psychological states, while alpha waves are associated with calm and relaxed physiological and psychological states (Filimon, 2010). The induction of an alpha brain wave state leads to the top-down initiation of the relaxation response through cortical signaling (Bagdasaryan, Le Van Quyen, 2013). Children undergoing stressful acute pain procedures may benefit from the reduction in perceived pain and decreased stress associated with binaural beat interventions.

Mindfulness Meditation

Mindfulness meditation is a type of breath-focused awareness that develops "increased awareness of the present… to reduce stress and control emotion" (National Center for Complementary and Alternative Medicine, 2010). Deep breathing has been used for decades to help pediatric patients manage painful procedures like needle sticks (Ellis, Sharp, Newhook, Cohen, 2004). However, deep breathing is categorized as a distraction technique, not meditation, and few randomized controlled outcomes studies have been conducted to examine this intervention (Koller, Goldman, 2012; Pederson, Harbaugh, 1995; Pringle et al., 2001). Breath-

focused awareness differs from deep breathing techniques, as it does not encourage deep breathing; rather it focuses on the sensation of the breath (National Center for Complementary and Alternative Medicine, 2010).

The concepts of focusing on a perceptible sensation, being present in the moment, and increasing awareness not only inform the practice of breathing awareness, but also the general practice of mindfulness (Hofmann, Grossman, Hinton, 2011). Introducing mindfulness practices early in a child's development can have long term effects by assisting with the management of anxiety, stress, and self-regulation (Greenberg, Harris, 2012). Breath-focused mindfulness meditation has been shown to reduce mind-wandering and increase participants' focus on the present moment (Mrazek et al., 2012). Participants' focus on the breath has been shown to reduce repetitive and negative thoughts of fear and anxiety (Feldman, Greeson, Senville, 2010).

Mindfulness meditation not only has psychological benefits, it has numerous physiological benefits as well including increased heart rate variability, reduce blood pressure, and physical relaxation (Burg, Wolf, Michalak, 2012; Busch, Magerl, Kern, Haas, Hajak, Eichhammer, 2012; Gregoski, Barnes, Tingen, Harshfield, Treiber, 2011; Jerath, Edry, Barnes, Jerath, 2006). The act of focusing on the breath subconsciously encourages deep, slow breathing, which "increases vagal activation leading to reduction in sympathetic activation" (Mason, Vandoni, deBarbieri, Codrons, Ugargol, Bernardi, 2013). Deep breathing done at a slow pace activates stretch receptors in the lungs (Kox, Vaneker, van der Hoeven, Scheffer, Hoedemaekers, Pickkers, 2012). The lung stretch receptors provide afferent information to the vagus nerve, stimulating its activation (Kox et al., 2012; Mason et al., 2013). The vagus continues these bottom-up signals through ascending projections to inhibit the sympathetic activation within the brainstem, as well as signal the limbic and cortical areas of the brain, decreasing hyper-vigilance (Taylor, Goehler,

Galper, Innes, Bourguignon, 2010). Increased vagal activation also slows the heartbeat, increasing the duration between each beat and therefore increasing heart rate variability (Taylor et al., 2010). Reduced sympathetic activation reduces blood pressure, and increases physical relaxation. This complex bottom-up reaction is the direct result of breath-focused mindfulness during stressful situations (Tharion, Samuel, Rajalakshmi, Gnanasenthil, Subramanian, 2012).

Feasibility and Outcomes of Complementary and Integrative Interventions for Acute Pain Procedures

The extant literature examining the use of complementary and integrative interventions to manage pain in a pediatric population is limited in scope and design (Pillai Riddell et al., 2011; Tan et al., 2014). This research team conducted a previous study in which an art therapy intervention was used as a pain management technique with pediatric patients undergoing needle stick procedures. Stinley, Norris and Hinds (2013) demonstrated the clinical feasibility and psychobiological outcomes of this complementary and integrative intervention. The results showed that participants who were engaged in the art therapy technique exhibited significantly fewer pain behaviors like crying and resistance. The participants who created art during the procedure also showed a significant decrease in subjective anxiety from pre-procedure measures to post-procedure measures, $p= 0.04$. The difference in heart rate between the group who received standard of care treatment, and the group who participated in art therapy, there was a trending decrease in heart rate in the art therapy Treatment Group, $p=0.06$. These preliminary findings indicate a need for complementary and integrative interventions during needle stick procedures, and prompted further research into additional interventions. This research team demonstrated the success of this paradigm, and realized a need for further research into additional interventions.

Two individual experiments were conducted to examine the psychobiological outcomes of

complementary and integrative interventions, and the feasibility of administering them with a pediatric population. The first experiment examined the use of binaural beats with this population, while the second experiment examined the use of mindfulness meditation. Physiological outcomes included the collection of the salivary biomarkers cortisol and alpha amylase. Change in participant heart rate was also examined in each experiment, to understand the impact these interventions have on the biological stress response. Pain behaviors such as crying, resistance, screaming, and the need for restraint were observed and the psychological outcomes of subjective pain and anxiety were assessed. Feasibility was determined by participant enrollment and retention. It was hypothesized that binaural beats and mindfulness meditation would be successfully administered to a pediatric population, and these participants would exhibit fewer physiological and psychological symptoms of acute pain than their Control Group counterparts who will be receiving standard of care treatment.

CHAPTER 2

METHODS

These experiments were reviewed and approved by the American University Institutional Review Board and the Institutional Review Board and Nursing Research Assistance Committee at Children's National Health System in Washington, D.C.

Participants

Participants for both experiments were recruited through the laboratory medicine unit at Children's National Health System. Participants were males and females between the ages of 8 and 18 years. Non-English-speaking patients were also excluded because all information sheets and intervention materials were presented in English. In Experiment One: Binaural Beats, 31 female patients between the ages of 8 and 18 years, and nine male patients between the ages of 8 and 18 years participated in the study. The mean age of the Treatment Group was 14.3 years (SD = 3.6), and the mean age of the Control Group was 12.95 years (SD = 3.3?). Patients were referred to the Laboratory Medicine Clinic from the following hospital outpatient clinics: Adolescent Health, Cardiology, Children's Health, Diabetes, Developmental Medicine, Endocrinology, Gastroenterology, Genetics, Hematology, Infectious Disease, Neurology/Neuroscience, Nephrology, Orthopedics, Psychiatry, Pulmonary, Special Immunology, General Medical. In Experiment Two: Mindful Breathing, 24 female patients between the ages of 8 and 18 years, and sixteen male patients between the ages of 8 and 18 years participated in the study. The mean age of Treatment Group participants in this experiment was 11.9 years (SD = 3.14), and the mean age of Control Group participants was 13.25 years (SD = 2.9). Patients were referred to the Laboratory Medicine Clinic from the following hospital outpatient clinics: Adolescent Health, Cardiology, Children's Health, Otorhinolaryngology, Gastroenterology, Heart and Kidney, Nephrology, Neurology/Neuroscience, Obesity, Orthopedics, Special Immunology, General Medical.

Materials

The sound/music directive used in Experiment One was a binaural beat in the alpha wavelength range of 8-12 Hz. Binaural beats are a mind-body therapy that occurs when a frequency is played in one ear, while a different but complementary frequency is played in the other ear. The brain perceives the difference between the two frequencies. In the case of alpha waves the difference is 8-12 Hz, which creates a phenomenon known as entrainment (Filimon, 2010). The alpha wavelength induces mental relaxation, which is incompatible with a state of stress or anxiety (Puzi, 2013; Sun & Sung, 2013). Participants were asked to listen to the binaural beats on sanitizable headphones connected to an Apple iPod mp3 player.

The mindfulness meditation directive used in Experiment Two was a five-minute voice recording instructing participants to be aware of their breath, and the present moment. The recording encouraged participants to feel safe and in control during stressful situations, and reminded participants that they are always in control of the breath. Participants were invited to listen to the mindfulness meditation directive on headphones connected to an Apple iPod mp3 player.

Design and Procedure

Experiment One: Binaural Beats took place in the Laboratory Medicine Clinic for three weeks. After the completion of Experiment One, Experiment Two: Mindful Breathing took place for three weeks with a different group of participants. Potential participants for both experiments were referred to the Laboratory Medicine Clinic of a major metropolitan area children's hospital. The Laboratory Medicine Clinic performs all blood draw needle stick procedures referred from the hospital's outpatient clinics. Laboratory Medicine staff were informed that a study was being conducted on the unit, but were blind to the conditions of the study. The study team conducted a

similar, but separate, experiment with the Laboratory Medicine team (Stinley et al., 2013), and was familiar with the unit procedures when enrollment phase began. Enrollment took place during the patient intake procedure conducted at the start of each patient's appointment with Laboratory Medicine.

During the enrollment phases of Experiments One and Two, the Principal Investigator acquired written informed consent and assent from potential participants and their parents before the needle stick procedure. Patients and parents typically waited for 20 minutes after delivering the blood draw order to the Laboratory Medicine Clinic and prior to receiving the needle stick. This wait period allowed the Principal Investigator to provide a thorough description of the study to the patients and parents and time for asking and answering questions. Subjects who decided to participate then signed the consent and assent forms. This method of study enrollment allowed parents to be present to provide consent and avoided any interruption to the needle stick procedure. All subjects were informed that they could withdraw from the study at any time. Participants were also informed that if they felt the need to speak with anyone after completion of the study, they could contact the Principal Investigator for a follow up discussion. The Principal Investigator made arrangements with the Laboratory Medicine Clinic's attending physician, fellow, and nursing staff, to be available for referral in case of any adverse physical or psychological effects of the study. Support from these team members was never necessary during the duration of either study. After enrollment in the study, the Principal Investigator used a random number generator to assign the Participant to the treatment or control condition of the study. Participants provided blood samples from a needle stick in the inner crook of their elbows, otherwise known as the antecubital area.

The procedures described here were followed in Experiment One and Experiment Two. Participants were connected to the Masimo Radical 7 pulse oximeter to record the Participant's

heart rate and blood oxygen saturation each minute. The pre-procedure anxiety questionnaire and anticipated pain scale were administered at this time. During the next five minutes, Treatment Group participants received the intervention. Treatment Group participants enrolled in Experiment One listened to the binaural beats intervention. Treatment Group participants enrolled in Experiment Two listened to the mindfulness meditation interventions. Both interventions were administered using an iPod Nano MP3 player and headphones. These headphones were removed after the five minute intervention, prior to entering the procedure room. In keeping with standard of care treatment, control subjects in both experiments waited in the Laboratory Medicine waiting room where a television is used as a distraction method. The recording of heart rate continued during the needle stick procedure, and for five minutes post-procedure. When the needle stick procedure was complete, the Principal Investigator administered the post-procedure anxiety questionnaire and subjective pain scale. Participants were asked to swab their mouths for salivary collection five minutes after the needle stick procedure. The time lapse between the stressful physiological stimulus of the needle stick and the saliva collection was ten minutes. This time lapse is sufficient for detecting changes in the salivary levels of alpha amylase (Ditzen et al., 2014). When subjects in the Control and Treatment Groups completed the study, the Principal Investigator ensured that the Participant was not in any physical danger. The Principal Investigator reminded each parent and Participant of the contact information on the Information Sheet in case of any additional questions. The study session was then considered complete and the Principal Investigator provided the Participant with a complementary pack of colored pencils and a mandala coloring sheets as compensation.

Measures

The measures described in this section were used in both studies.

Masimo Radical 7 Pulse Oximeter

This machine records heart rate. The Masimo brand machinery is used throughout Children's National. Heart rate is an easily recorded and valid physiological indicator of pain, stress, and anxiety (Fisher & Newman, 2013).

Salivette Saliva Collection

Participants in both experiments provided a salivary sample after the needle stick procedure. Salivary levels of the stress hormone cortisol and the enzyme alpha amylase were analyzed. The time lapse between the announcement of the stressful psychological stimulus and the sample collection was fifteen minutes. This time lapse is a sufficient amount of time for detection of change in salivary levels of cortisol (Kudielka et al., 2012). Salivary assays of hormones are considered a valid method of non-invasive hormone analysis (Carroll, Raff, Findling, 2008; Elamin, Murad, Mullan, et al., 2008; Rubin, Hotopf, Papdopoulos, Cleare, 2005).

Hospital Fears Rating Scale

This one-item anxiety questionnaire is a validated visual analogue scale from the which measures situational anxiety related specifically to the hospital experience. The reliability and validity of the Hospital Fears Rating Scale are both high; when visual analogue scales of anxiety were compared with fully recognized scales, the VAS version demonstrated a greater ability to "detect statistically important changes over time" (Bringuier, S., Dadure, C., Raux, O., Dubois, A., Picot, M-C., Capdevila, X., 2009).

10-Point Likert Scale/Wong-Baker Faces Scale

Participants were asked to complete a self-report visual analogue scale (VAS) before the needle

stick procedure to measure anticipated pain. The same VAS was administered after the needle stick procedure to measure subjective pain. The Wong-Baker Faces Scale VAS is a highly reliable self-report measure of acute patient pain (Garra, Singer, Taira, et al., 2010). This scale has a higher validity rating than the Verbal Rating Scale, as well as higher reliability and validity than simple numerical rating scales (Bijur, Silver, Gallagher, 2001; Ohnhaus, Adler, 1975; Price, Bush, Long, Harkins, 1994). Visual analogue scales like the VAS pain scale and the Hospital Fears Rating Scale have been found to be successfully and accurately completed by children age 6 years and older (Shields, Palermo, Powers, Grewe & Smith, 2003).

Statistical Analysis

A sample size of 40 participants per experiment was determined a priori based on the estimated number of participants needed to detect a moderate effect size difference of half a standard deviation in each physiological and psychological outcome between the two groups. This determination was based on the assumptions that there would be at least fifteen assessments of heart rate per participant in each experiment, that the correlation across multiple measurements per participant was 70%, that power was set to 90%, and the 2-tailed type I error was set to 1.25%.

The change in the physiological measure of heart rate was calculated by subtracting the earlier occurring value from the later occurring value. For instance, the change in heart rate during Minute One of the intervention was subtracted from Minute Five of the intervention to obtain the delta value. Calculating the change in heart rate over time removes the confounding variables of age and/or medical condition by showing the raw change in value. The changes in the psychological measures of subjective anxiety and pain were calculated by subtracting the baseline measure of each from the endpoint measure.

The Shapiro-Wilk test was conducted to determine the normality of data collected from Treatment and Control Groups in Experiment One and Experiment Two. Data collected during Experiment One showed a non-normal distribution for all measures, $p<0.05$. Data collected during Experiment Two showed a non-normal distribution for all measures, $p<0.05$, except heart rate measures from Minute 5 to Minute 15, $p>0.05$. Because the assumption of normality for parametric testing was not met for measures in Experiment One, non-parametric tests were used. Non-parametric tests were used in Experiment Two for all measures except for heart rate from Minute 5 to Minute 15; parametric testing was used on these normally distributed measures.

To compare outcome distributions between Treatment and Control Groups in Experiment One, a comparison of means was conducted. Between groups comparisons were made using the Mann-Whitney-Wilcoxon rank sum test. This statistical test is used when the assumption of normality is violated, rendering the Welch t-test unusable. The Mann-Whitney-Wilcoxon test compares outcomes of data sets that contain outliers, and is best suited to testing data from randomized studies (Wu, Han, Chen, Tu, 2014). Within group comparisons were made using the Wilcoxon signed rank test, also a non-parametric test. The Wilcoxon signed rank test is used to determine differences in paired data sets containing outliers, therefore violating the assumption of normality (LaVange & Koch, 2006).

A comparison of means was also conducted on the outcome distributions of Treatment and Control Groups in Experiment Two. For those outcomes that showed a considerable variability and violated the assumption of a normal distribution, the Mann-Whitney-Wilcoxon rank sum and Wilcoxon signed rank test were used. The outcome measures of heart rate from Minute 5 through Minute 15 were normally distributed, and so the unpaired Welch t-test was used for a between groups comparison (Wu et al., 2014).

The physiological and psychological outcomes measured in Experiments One and Two are considered health-related quality of life (HRQL) outcomes. Meaningful changes in these outcomes are not always best reflected by statistical significance, but rather by determining the minimally important difference (MID) (Norman, Sloan, Wyrwich, 2003). MID is defined as the "minimal level of real change" related to an intervention and measured by disease-specific physiological indicators, or patient-perceived differences indicated via psychological measures (Norman, Sloan, Wyrwich, 2003). This real level of change is considered clinically significant, as it considers the effects of the intervention from the participants' perspectives (Norman et al., 2003). Effect size is a standard indicator of MID, and Cohen's d is the most consistently used criterion for determining a small, moderate, or large effect size (ES). Small MID was set at an ES of 0.2, moderate MID was set at an ES of 0.5, and large MID was set at an ES of 0.8 (Norman, Sloan, Wyrwich, 2003).

CHAPTER 3

RESULTS

Experiment One: Binaural Beats

Demographic Characteristics

Forty-three patients were approached to enroll in this study. Forty participants between the ages of eight years and 18 years enrolled in Experiment One, demonstrating an enrollment rate of 93%. Each of the forty participants remained in the study through completion, demonstrating a retention rate of 100%. There were no statistically significant differences between the Treatment and Control Group demographic variables. Please refer to Table 1.

Significant Findings

Clinical significance was detected in the average decrease of heart rate experienced by Treatment Group participants as they entered the procedure room, after the binaural beat intervention, indicated by a moderate effect size, d=0.5. The average change in Treatment Group heart rate was 16.4 beats per minute (SD=11.9), while the average change in Control Group heart rate was 24.15 beat per minute (SD=15.5), *Mann-Whitney U*=142, 258 (Table 2).

The average change in heart rate from the baseline measure to the needle stick event was also significantly lower in the Treatment Group, an average increase of 7.5 beats per minute (SD=10), compared with the Control Group, an average increase of 16 beats per minute (SD=21.6), *Mann-Whitney U*=19, 381. An effect size of d=0.4 indicates Treatment Group participants experienced greater heart rate stability over time (Table 3).

A statistically significant difference exists in the incidence of tachycardia experienced by either the Treatment or Control Groups. Significantly fewer Treatment Group participants experienced the rapid increase of heart rate by 20 beats per minute followed by a rapid decrease of 20 beats per minute, p=0.05, *chi square*=3.95 (Table 4).

The average change in subjective anxiety in Treatment Group participants was zero (SD=0.79), while the average change in subjective anxiety in the Control Group was an increase of 0.4 (1.04), *Mann-Whitney U*=154, 246 (Table 6). These averages were clinically difference from one another indicated by the effect size, *d*=0.4. The perceptible decrease in subjective anxiety felt by some Treatment Group participants is further supported by the finding that significantly fewer Treatment Group participants displayed pain behaviors when compared with the Control Group. This comparison reached clinical significance, *d*=0.4, and near statistical significance, *p*=0.07, *Mann-Whitney U*=142, 255 (Table 8).

There were no other statistically or clinically significant findings in Experiment One, please refer to Tables 1-10, and figures 1-4 below for further details.

Table 1. Experiment One: Binaural Beats Demographic Characteristics

	Treatment Group	SD	Control Group	SD	Total	SD	P-value
Mean Age: years	14.3	3.6	12.95	3.3	13.93	3.5	0.51†
Gender:							
Male	5		4		9		0.72†
Female	15		16		31		

Note: †Mann-Whitney-Wilcoxon rank sum

Table 2. Experiment One Average Change in Heart Rate

Event	Avg. Δ H.R. Treatment Group	SD	Avg. Δ H.R. Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Baseline to Minute 5	-2.15	8	-1	4.9	-2, 4	0.62†	-0.51	181, 219	-0.23♦
Entering Procedure Room	16.4	11.9	24.15	15.5	-2, 15	0.12†	-.16	142, 258	**-0.5♦♦**
Needle Stick	-6.45	12	-7.15	14.8	-12, 7	0.65†	0.46	183, 217	0.05
Needle Removal	-9.45	8.4	-13.95	13.2	-10, 4	0.37†	0.89	167, 233	0.35♦
5 minutes post-procedure	-0.95	6.9	-0.8	11.4	-6, 5	0.92†	0.09	196, 204	-0.004

Note: Heart rate indicated in beats per minute, †Mann-Whitney-Wilcoxon rank sum, ♦MID≥0.2, ♦♦MID≥0.5

Table 3. Experiment One Average Change in Heart Rate from baseline to Needle Stick

Event	Avg. Δ H.R. Treatment Group	SD	Avg. Δ H.R. Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Baseline to Needle Stick	7.5	10	16	21.6	-6,7	0.79†	0.81	19, 381	**-0.4♦**

Note: Heart rate indicated in beats per minute, †Mann-Whitney-Wilcoxon rank sum, ♦MID≥0.2

Table 4. Experiment One Tachycardia between Groups Comparison

Tachycardia	Treatment Group N (%)	Control Group N (%)	Chi-Square Statistic	P-value
Increase and decrease of 20 bpm or more	4 of 20 participants 20%	10 of 20 participants 50%	3.95	**0.05***

*p≤ 0.05

Table 5. Experiment One Salivary Analyte Levels

Salivary Analyte	Treatment Group	SD	Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Cortisol (µg/dL)	0.572	0.84	0.287	0.51	-0.17, 0.01	0.17†	1.38	149, 251	0.6♦♦
Alpha-Amylase (U/mL)	158.38	144.28	107.09	77.29	-53.1,23.3	0.56†	0.58	178, 222	0.6♦♦

Note: †Mann-Whitney-Wilcoxon rank sum, ♦♦ MID≥0.5

Table 6. Experiment One Average Change in Anxiety between Groups Comparison

Event	Treatment Group	SD	Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Avg. Change in Anxiety	0	0.79	0.4	1.04	0,2	0.18†	-0.91	154, 246	**-0.4**♦

Note: †Mann-Whitney-Wilcoxon rank sum, ♦ MID≥0.2

Table 7. Experiment One Average Change in Anxiety within Group Comparison

	Avg. Pre-Procedure Anxiety	Avg. Post-Procedure Anxiety	Confidence Intervals (95%)	P-value	Z-score	U
Treatment Group	1.75	1.75	-1, 1	1∞	Inf.	23
Control Group	2.05	2.45	-1.5, 0	0.11∞	-1.21	20

Note: ∞Wilcoxon signed rank

Table 8. Experiment One Distribution of Pain Behaviors between Groups Comparison

Number of Pain behaviors Shown	Treatment Group	Control Group	Confidence Interval (95%)	P-value	Z-score	U	Effect Size
			0,1	0.07†	-1.43	145,255	**-0.5♦♦**
0	16	11					
1	2	4					
2	2	1					
3	0	2					
4	0	1					
5	0	1					

Note: †Mann-Whitney-Wilcoxon rank sum, ♦♦MID≥0.5

Table 9. Experiment One Average Change in Pain between Groups Comparison

Event	Treatment Group	SD	Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Avg. Change in Pain	-0.6	1.93	-0.3	1.41	-0.94,2.14	0.4†	-0.34	187, 213	-0.21♦

Note: †Manny-Whitney-Wilcoxon rank sum, ♦MID≥0.2

Table 10. Experiment One Average Change in Pain within Group Comparison

	Avg. Anticipated Pain	Avg. Experienced Pain	Confidence Intervals (95%)	P-value	Z-score	U
Treatment Group	3.55	2.95	-0.5, 2	0.23∞	-0.74	34
Control Group	2.05	2.45	-1, 2	0.3∞	-0.53	26

Note: ∞Wilcoxon signed rank

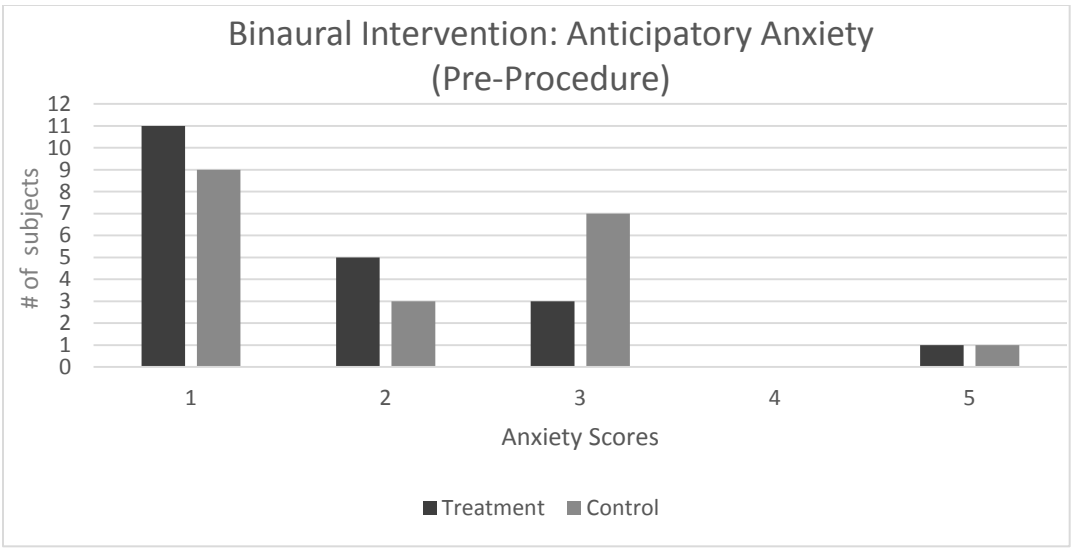


Figure 1. Distribution of pre-procedure subjective anxiety scores in Experiment One.

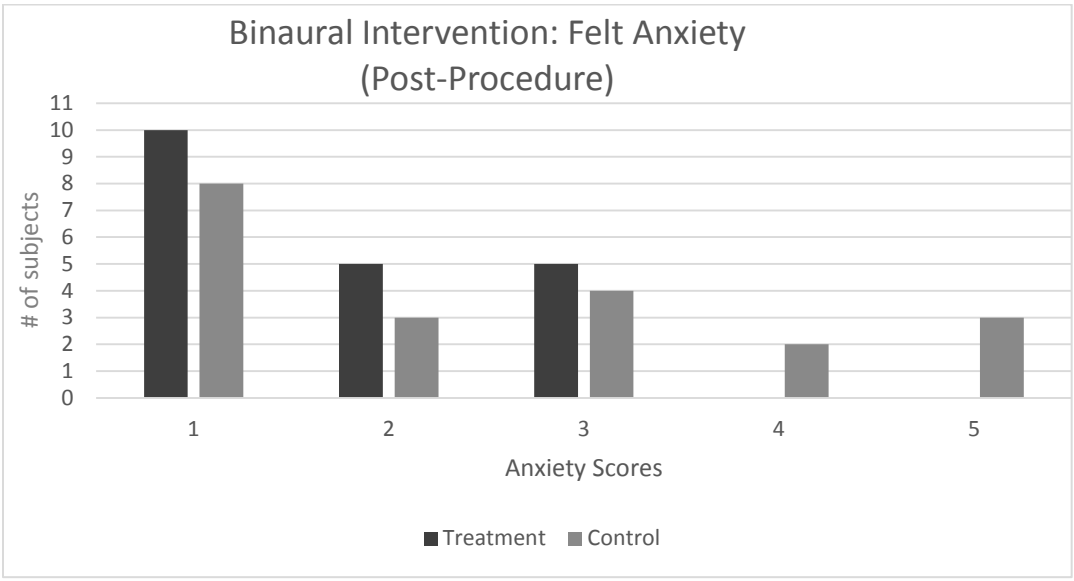


Figure 2. Distribution of post-procedure subjective anxiety scores in Experiment One.

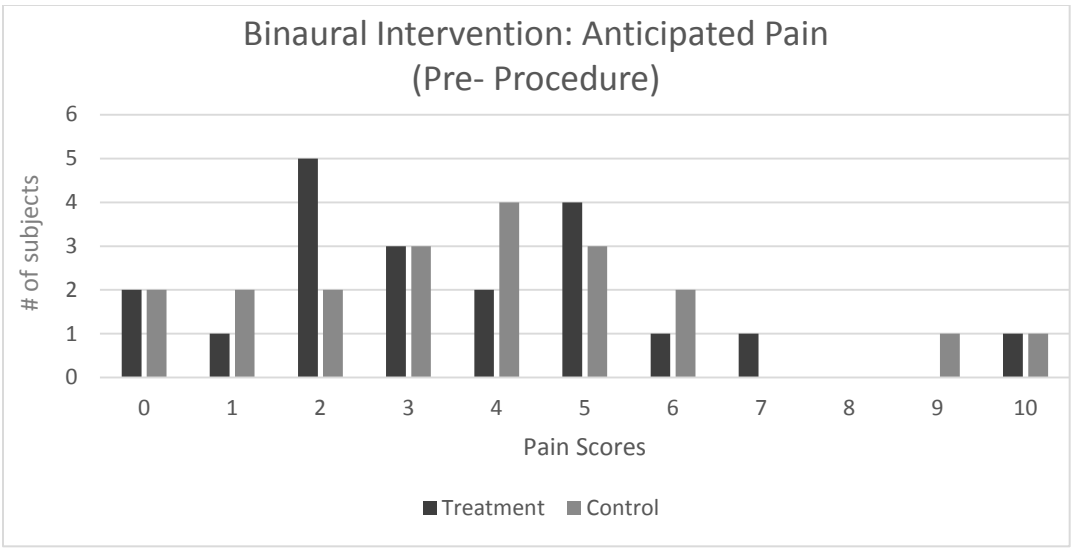


Figure 3. Distribution of anticipated pain scores in Experiment One.

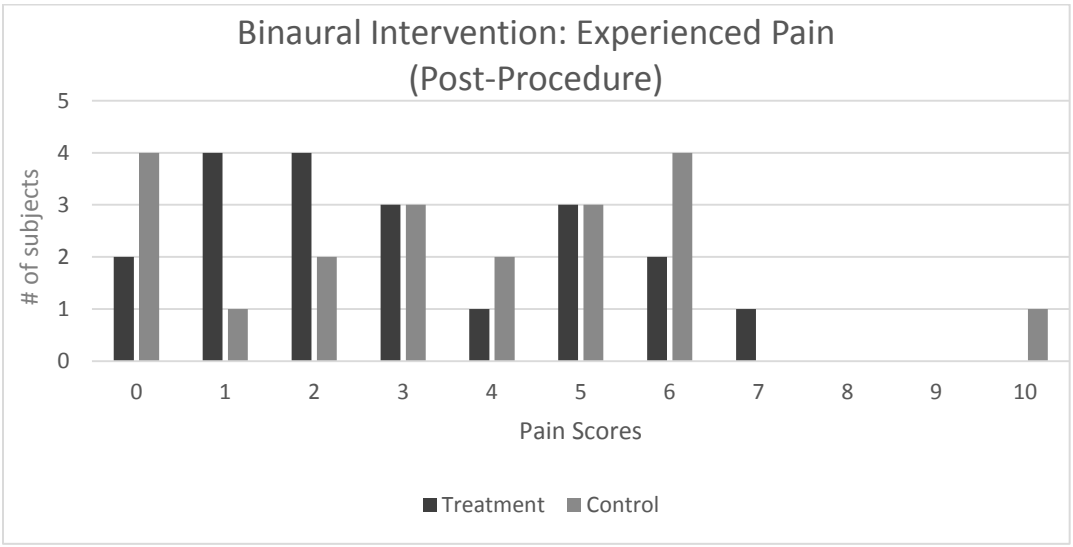


Figure 4. Distribution of experienced pain scores in Experiment One.

Experiment Two: Mindfulness Meditation

Demographic Characteristics

Forty-six patients were approached to enroll in this study. Forty participants between the age of eight and 18 years enrolled in Experiment Two. The enrollment rate for this experiment was 87%, while the retention rate was 100% as all forty participants remained in the study through completion. There were no significant differences in demographic characteristics between Treatment and Control Groups. Please refer to Table 11.

Significant Findings

The change in Treatment Group heart rate was an average decrease of 3.75 beats per minute (SD=7.2) during the mindfulness intervention. Control Group participants experienced an average increase in heart rate of 0.5 (SD=5.4) beats per minute during the same time. This difference in averages is statistically significant, p=0.02, *Mann-Whitney U*=114, 286). The decrease in Treatment Group heart rate compared to the increase in Control Group heart rate during the intervention time frame was also clinically significant, showing a moderate effect size d=0.7. Please refer to Table 12 for these findings.

There was a statistically significant difference between the Treatment and Control Groups in regard to displayed pain behaviors. Treatment Group participants displayed significantly fewer pain behaviors when compared with the Control Group, p=0.005, *Mann-Whitney U*=130, 270. This observed difference in pain behaviors also reached clinical significance, with a moderate effect size of d=0.6 (Table 18). A clinically significant decrease in subjective pain was also found in the Mindfulness Meditation Treatment Group, whose average pain score decreased by 1.1 points (SD=2.42) from pre-procedure measures to post-procedure measures. Control Group participants reported an average decrease of 0.15 points (SD=1.98). The *Mann-Whitney U*

values for this measure were 150, 250. Clinical significance was determined by a moderate effect size of d=0.5 (Table 19).

There were no other significant differences between the Treatment and Control Groups in Experiment Two: Mindfulness Meditation. Please refer to Tables 11-20, and figures 5-8 below.

Table 11. Experiment Two Demographic Characteristics

	Treatment Group	SD	Control Group	SD	Total	SD	P-value
Mean Age: normal years	11.9	3.14	13.25	2.9	13.18	3.1	0.16†
Gender:							0.53†
Male	9		7		16		
Female	11		13		24		

Note: †Mann-Whitney-Wilcoxon rank sum

Table 12. Experiment Two Average Change in Heart Rate

Event	Avg. Δ H.R. Treatment Group	SD	Avg. Δ H.R. Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Baseline to Minute 5	-3.75	7.2	0.5	5.4	0.99,6.99	**0.02**†*	-2.05	114, 286	**-0.7**♦♦
Entering Procedure Room	29.95	11.9	25	8.3	-11.52, 1.62	0.13¤	-1.13		0.6♦♦
Needle Stick	-12.75	15.5	-14.65	18.4	-12.8, 9	0.72¤	0.58		0.1
Needle Removal	-15.4	13.2	-12.1	9.3	-4.1, 10.5	0.382¤	-0.31		-0.3♦
5 minutes post-procedure	0.35	10.1	-2.85	9.3	-9.4, 3	0.3¤	-0.52		0.3♦

Note: Heart rate indicated in beats per minute, †Mann-Whitney-Wilcoxon rank sum, ¤Welch un-paired t-test, *p<0.05, ♦MID≥0.2, ♦♦MID≥0.5

Table 13. Experiment Two Average Change in Heart Rate from Baseline to Needle Stick

Event	Avg. Δ H.R. Treatment Group	SD	Avg. Δ H.R. Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	Effect Size
Baseline to Needle Stick	13.45	17.5	10.6	15.2	-13.3, 7.62	0.58¤	0.2	0.2♦

Note: Heart rate indicated in beats per minute, ¤Welch un-paired t-test, ♦small MID

Table 14. Experiment Two Tachycardia Symptoms between Groups

Tachycardia	Treatment Group N (%)	Control Group N (%)	Chi-Square Statistic	P-value
Increase and decrease of 20 bpm or more	10 of 20 participants 50%	13 of 20 participants 65%	0.92	0.33

Table 15. Experiment Two Salivary Analyte Levels

Salivary Analyte	Treatment Group	SD	Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Cortisol (μg/dL)	0.241	0.3	0.222	0.2	-0.03, 0.07	0.28†	-1.09	159, 241	-0.05
Alpha-Amylase (U/mL)	143.3	73.3	148.8	122.3	-63.7,49.2	0.6†	0.47	182, 218	0.09

Note: †Mann-Whitney-Wilcoxon rank sum

Table 16. Experiment Two Average Change in Anxiety between Groups

Event	Treatment Group	SD	Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Avg. Change in Anxiety	0.2	1.3	0.3	0.9	-1,1	0.38†	-1.88	270, 130	-0.3♦

Note: †Mann-Whitney-Wilcoxon rank sum, ♦ MID≥0.2

Table 17. Experiment Two Average Change in Anxiety within Groups

	Avg. Pre-Procedure Anxiety	Avg. Post-Procedure Anxiety	Confidence Intervals (95%)	P-value	Z-score	U
Treatment Group	2.7	2.5	-1, 0.5	0.52∞	0.05	42
Control Group	2.45	2.9	-2, 0	0.04∞	-1.75	3.5

Note: ∞Wilcoxon signed rank, *p<0.05

Table 18. Experiment Two Distribution of Pain Behaviors between Groups

Number of Pain behaviors Shown	Treatment Group	Control Group	Confidence Interval (95%)	P-value	Z-score	U	Effect Size
			1,3	0.005†**	-1.88	130, 270	-0.6♦♦
0	16	10					
1	4	5					
2	0	1					
3	0	1					
4	0	2					
5	0	1					

Note: †Mann-Whitney-Wilcoxon rank sum, **p<0.01, ♦♦MID≥0.5

Table 19. Experiment Two Average Change in Pain between Groups

Event	Treatment Group	SD	Control Group	SD	Confidence Intervals (95%)	P-value	Z-score	U	Effect Size
Avg. Change in Pain	-1.1	2.42	-0.15	1.98	-1, 2	0.85†	-1.35	150, 250	-0.5♦♦

Note: †Manny-Whitney-Wilcoxon rank sum, ♦♦MID≥0.5

Table 20. Experiment Two Average Change in Pain within Groups

	Avg. Anticipated Pain	Avg. Experienced Pain	Confidence Intervals (95%)	P-value	Z-score	U
Treatment Group	4	2.95	0, 3	0.07∞	-1.46	81
Control Group	3.55	3.4	-1.5, 2.5	0.93∞	1.46	4.5

Note: ∞Wilcoxon signed rank

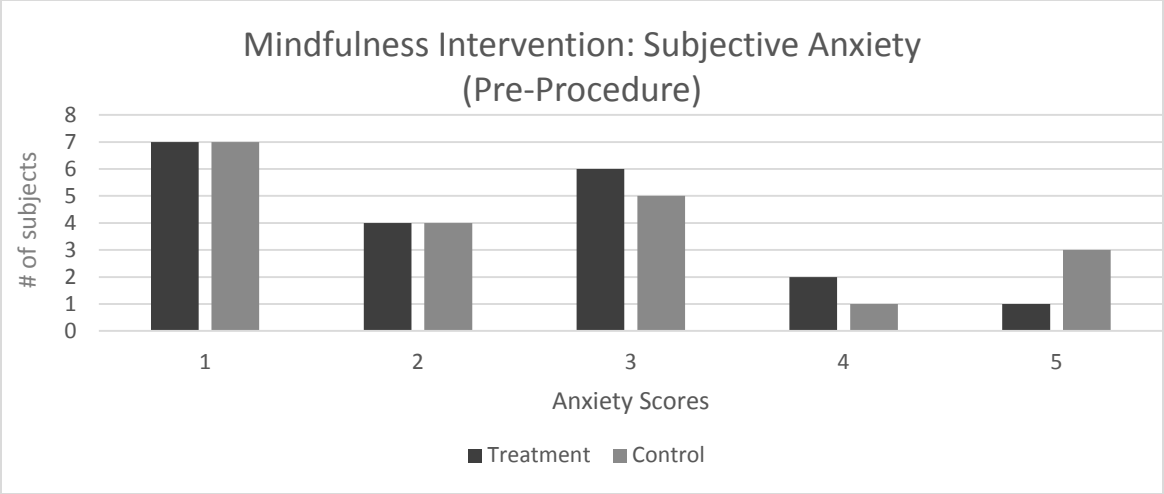


Figure 5. Distribution of pre-procedure subjective anxiety scores in Experiment Two.

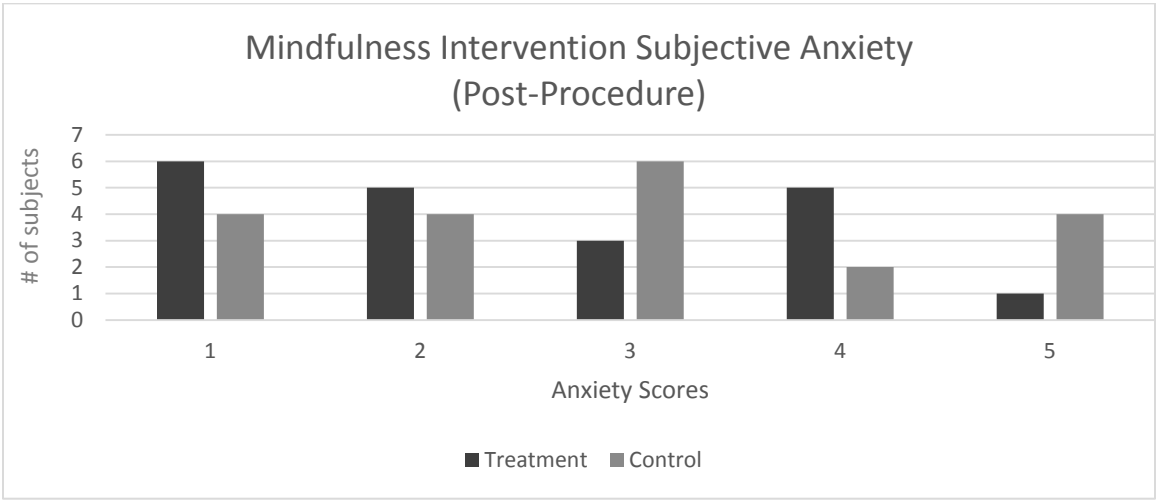


Figure 6. Distribution of post-procedure subjective anxiety scores in Experiment Two.

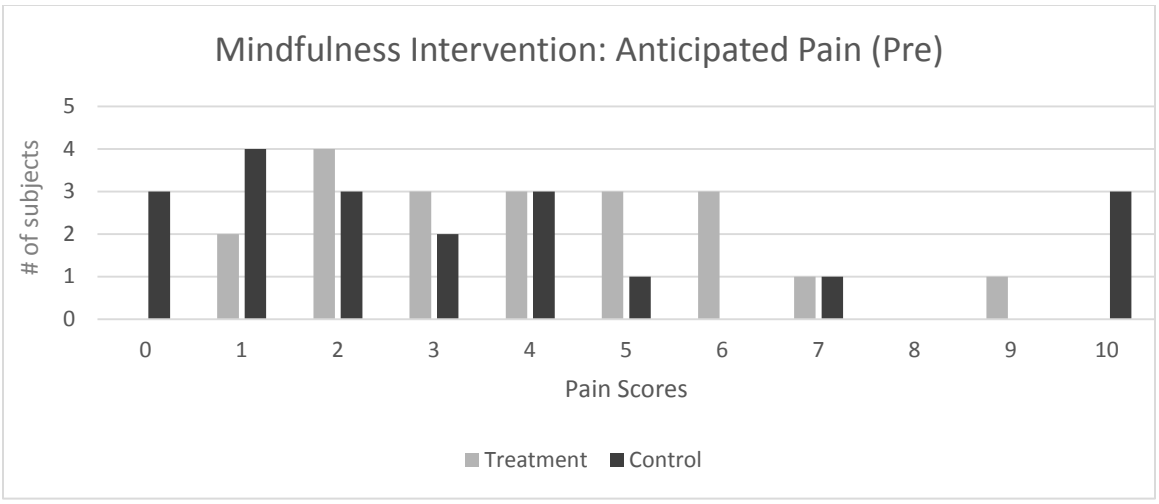


Figure 7. Distribution of anticipated pain scores in Experiment Two.

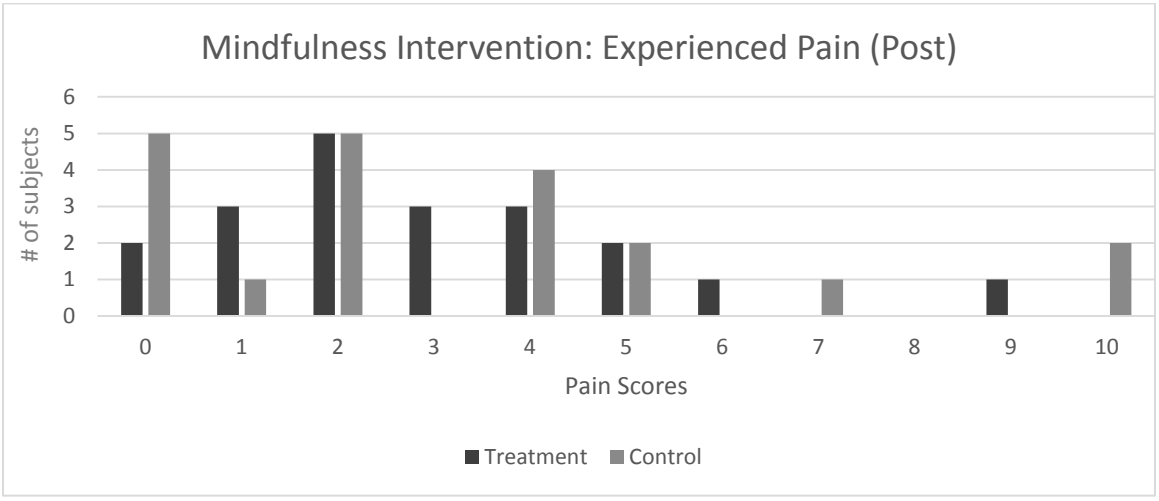


Figure 8. Distribution of experienced pain scores in Experiment Two.

CHAPTER 4

DISCUSSION

The results of this study provide preliminary support for the use of complementary and integrative interventions with a pediatric population undergoing acute pain procedures. The results of Experiment One: Binaural Beats indicated there were several small and moderate Minimally Important Differences detected in the Treatment Group, specifically the change in heart rate, change in anxiety, change in pain, and display of pain behaviors. Experiment Two: Mindfulness Meditation also yielded important findings in the detection of small and moderate clinically significant differences in the areas of change in heart rate, change in anxiety, change in pain, and display of pain behaviors. Additionally, there were statistically significant findings in Experiment Two, notably a decrease in heart rate during participants' practice of mindfulness meditation, as well as fewer pain behaviors displayed by those same participants. These supportive findings specifically address the use of binaural beats and mindfulness meditation to ameliorate the psychobiological symptoms of acute pain.

Change in Heart Rate

Change in heart rate was an important measure in this study, as it is the predominant physiological symptom of needle phobia, and a symptom of acute pain (Fazalbhoy, Birznieks, Macefield, 2012; Ritz, Meuret, Ayala, 2010; Schwabe et al., 2010). Tachycardia is the drastic rise and fall in heart rate experienced by many who fear needle sticks, and can have a detrimental effect for a variety of reasons, the foremost being the threat of syncope. Syncope is the medical term for fainting, and is often experienced immediately following a needle stick procedure (Ritz, Meuret, Ayala, 2010). The threat of syncope exists when a quick increase in heart rate of 20 beats per minute or more is followed by a quick decrease in heart rate of 20 beats per minute or

more (Ritz, Meuret, Ayala, 2010). This condition can also lead to severe headaches, a dramatic increase in blood pressure, and nausea (Fazalbhoy et al., 2012). The dramatic increase in heart rate, followed by an equally dramatic decrease is thought to be caused by the stimulation of the sympathetic nervous system immediately followed by the inhibition of the same system, causing a severe disruption to autonomic homeostasis (Ritz, Meuret, Ayala, 2010). Preventing tachycardia and syncope is important to maintain the safety and comfort of patients undergoing needle stick procedures.

The results of Experiments One and Two provide compelling evidence supporting the use of binaural beats and mindfulness meditation to reduce the occurrence of tachycardia, syncope, and other negative physiological side effects of needle phobia. While Treatment Group participants were listening to the binaural beats intervention or the mindfulness meditation intervention, their average heart rates decreased to a level indicating relaxation and calm. There was a small minimally important difference between the Treatment and Control Groups in Experiment One, indicating a causal relationship between decreased heart rate and listening to binaural beats. Treatment Group participants in Experiment Two also experienced a decrease in heart rate during mindfulness meditation, however this decrease in heart rate was statistically significant when compared with the Control Group. This statistically significant difference is supported by a moderate minimally important difference, which indicates the practice of mindfulness meditation reduces heart rate. The findings of Experiment Two support previous studies that show mindfulness meditation reduces heart rate and increased relaxation (Burg, Wolf, Michalak, 2012; Tharion et al., 2012).

Treatment Group participants in Experiment One: Binaural Beats not only showed a decrease in heart rate while listening to the intervention, they also showed a more stable heart

rate during entry into the procedure room. These same participants showed more stable heart rates overtime as well, from the baseline time point to the time of the needle stick. In fact, only 20% (n=4) of Treatment Group participants in Experiment One experienced tachycardic symptoms, compared to 50% (n=10) of Control Group participants. These findings support the use of binaural beats during needle stick procedures as a means of reducing tachycardia and eliminating the threat of syncope during needle stick procedures.

Treatment Group participants in Experiment Two: Mindfulness Meditation experienced a decrease in heart rate during the intervention period; however, they experienced less stability in heart rate during all other time points except needle removal. One possible explanation for these results is the cessation of the mindfulness meditation intervention prior to the needle stick procedure. It is possible that Treatment Group participants experienced less heart rate stability when compared with Control Group participants because they entered a state of relaxation, only to be exposed to an external stressor immediately after. These findings suggest the need to continue the mindfulness intervention during the needle stick procedure to maintain a lower, more stable heart rate over time.

Salivary Biomarkers

The psychological anticipation and/or experience of a frightening or painful stimulus activates the physiological stress response via the hypothalamic-pituitary adrenal (HPA) axis (Schwabe, Wolf, Oitzl, 2010). The resulting release of cortisol is an important indicator of the level of stress experienced during trying situations, and it impacts other experiences such as memory formation (Schwabe et al., 2010). Additionally, the sympathetic nervous system (SNS) is activated during the stress response, resulting in the release of norepinephrine and its salivary surrogate, alpha amylase (Mravec, 2011). The salivary analytes cortisol and alpha amylase were collected during

Experiments One and Two to gather information about the extent of HPA and SNS activation, and participants' physiological and psychological stress.

The results of Experiment One: Binaural Beats indicate salivary cortisol and alpha amylase levels were nearly double in the Treatment Group when compared with the Control Group. The moderate to large effect size indicates a clinically significant causal relationship between the use of binaural beats and an increase in the salivary analytes. This difference between the Treatment and Control conditions in Experiment One may be due to the incompatibility of the specific binaural beat pattern used with this sample population. In some instances, binaural beats can alter cortical arousal by heightening it, especially in a child and adolescent population (Atwater, 2009). Heightened cortical arousal can occur in younger children who are not exposed to the binaural beats for a sufficient period of time, approximately 20 minutes or more (Duric, Assmus, Gundersen, Elgen, 2012). Children and adolescents typically require a longer exposure to experience a shift in brainwaves, as the cortical networks supporting alpha and theta waves and are still developing, as are synchronized oscillations that support the alpha wave state (Konrad, Firk, Uhlhaas, 2013). A solution to eliminate the potential heightening of cortical arousal is to design age-specific binaural beat patterns, and to elicit them for longer than five minutes at a time.

The salivary analyte results in Experiment Two: Mindfulness Meditation indicate a slightly higher average level of cortisol in the Treatment Group, and a slightly lower average level of alpha amylase. There are a few explanations for these negligible differences in the salivary analytes collected for this study. The first is that participants did not engage in mindfulness meditation for a sufficient amount of time. If participants had been exposed to mindfulness meditation throughout the needle stick procedure, perhaps HPA axis and SNS activation would have decreased more significantly. Another potential explanation is that though mindfulness meditation reduces the

impact of psychological and psychological stress, it does not eliminate it. Again, if mindfulness meditation is practiced throughout the needle stick procedure, perhaps the psychological and physiological stress will continue to lessen.

Subjective Anxiety

Subjective anxiety was measured before and after the needle stick procedures to reflect participants' anticipatory anxiety, and the anxiety caused by the actual needle stick event. The binaural beats and mindfulness meditation interventions were provided prior to the needle stick in an attempt to mitigate the psychological distress that arises before the stimulus of the needle is presented. Previous studies have shown that reducing and managing anticipatory anxiety can reduce anxiety caused by the actual stressor (Bird & McMurtry, 2012; Noel, McMurtry, Chambers, et al., 2010). Additionally, managing anticipatory anxiety can reduce experienced pain, and the inaccurate reporting of pain (Anson, Edmundson, Teasley, 2010; Bird & McMurtry, 2012; Noel, McMurtry, Chambers, et al., 2010).

The results of Experiment One indicate there was no statistically significant difference between the average change in anxiety between Treatment and Control groups. However, the small to moderate effect size indicates that Treatment Group participants experienced a clinically perceptible decrease in anxiety over time. Additionally, fewer Treatment Group participants (n=5) experienced an increase in anxiety over time compared to participants in the Control Group (n=9). The Treatment and Control Groups each had one participant who reported the highest level of pre-procedure anxiety possible, a score of 5 out of 5. While the participant in the Control Group maintained that high level of anxiety throughout the procedure, the Treatment Group participant reported a decrease in anxiety over time. These findings indicate the use of

binaural beats cause a perceptible decline in participant anxiety, and could have a positive impact on experienced anxiety and pain during the actual needle stick procedure.

Experiment Two yielded results that were similar to Experiment One, showing the average change in anxiety was statistically insignificant between the Treatment and Control Groups. Again, a small to moderate effect size was detected in the Treatment Group indicating a perceptible clinical difference in anxiety in these participants. Yet another similarity between the two experiments exists in the number of Treatment Group participants who experienced a decrease in anxiety over time (n=4). However, only one member of the Control Group reported a decrease in subjective anxiety. Additionally only one Treatment Group participant reported feeling the maximum amount of anxiety during the needle stick procedure, while four Control Group participants reported feeling the greatest amount of anxiety during the needle stick. These findings suggest the practice of mindfulness meditation causes a reduction in subjective anxiety in children.

It should be considered that while four Treatment Group participants reported a decrease in anxiety, ten participants reported an increase in this measure. In fact, fewer Control Group participants (n=7) reported an increase in anxiety over time compared to the Treatment Group. The increase in subjective anxiety felt by half the Treatment Group participants in Experiment Two may be a result of the extreme sense of relaxation experienced during the mindfulness intervention followed by the stressful experience of the needle stick without the mindfulness prompt. Each of the twenty Treatment Group participants reported feeling relaxed or calm immediately after listening to the mindfulness meditation intervention. Further studies should be conducted to determine if the continued use of the mindfulness prompt throughout the needle stick procedure continues to provoke feelings of calm and relaxation in participants. The

increases in anxiety reported by Treatment Group participants in Experiment Two were still lower than those reported by the Control Group. The increase in anxiety from pre-procedure to post-procedure was statistically insignificant in the Treatment Group, however the Control Group reported a statistically significant increase in anxiety over time. These findings suggest lower anxiety levels are caused by the use of mindfulness meditation prior to needle stick procedures.

Pain Behaviors

Pain behaviors are exhibited in an attempt to escape and avoid pain or, when pain is unavoidable, to communicate the experienced discomfort (Hadjistavropoulos et al., 2011). These behaviors are acted out in facial expressions such as grimacing, vocal exclamations, emotional expressions like crying, resistant behavior, and attempt to escape the situation. Pain behaviors can occur as a part of the anticipatory stress response in an attempt to protect oneself or to communicate one's needs to observers (Hadjistavropoulos et al., 2011). Children are accustomed to parental assistance as a result of the displayed pain behaviors (Hadjistavropoulos et al, 2011). Because needle sticks are medical protocol, it is rare for parents to interfere and remove their children from the perceived danger. This break from typical parental behavior can bring up feelings of disempowerment and lack of control in pediatric patients (Du et al., 2008). Pain behaviors tend to escalate, and drastic measures such as physical restraint are used to ensure the needle stick is completed.

Pain behaviors were observed in Experiments One and Two, to provide additional information regarding participants' states of anxiety. Experiment One: Binaural Beats showed no statistically significant difference between the number of pain behaviors displayed by the Treatment and Control Groups. However, at $p=0.07$, there is a trend toward significance

indicating more pain behaviors were displayed by the Control Group. Additionally, a moderate effect size further supports these findings, and previous studies that indicate more pain behaviors are displayed when patients receive standard of care treatment during needle sticks (Baxter et al., 2011; Noel et al., 2010).

The results of Experiment Two: Mindfulness Meditation not only indicate more pain behaviors were displayed by Control Group participants, but that this difference is statistically significant, $p=0.005$. The moderate to large effect size confirms these findings, and supports the use of mindfulness meditation to reduce pain behaviors during needle stick procedures. These findings support previous studies that showed children who practiced mindfulness experienced the redirection of attention to the breath, and a sense of control and self-regulation through calming behaviors (Greenberg, Harris, 2012; Rush, in press).

Anticipated Pain vs. Experienced Pain

Anticipated pain is an amalgamation of anxiety, reflex, memory, and learned behavior (Du et al., 2008; Noel, Chambers, McGrath, et al., 2012; Noel, McMurtry, et al., 2010). Anticipated pain is different from experienced pain, as it is the level of pain patients expect to feel and is often exaggerated (Bird & McMurtry, 2012; Noel, Chambers, et al., 2012). Experienced pain refers to the physical sensation of the needle stick. While experienced pain is meant to be a truer reflection of the pain felt during needle stick procedures, it is also often overestimated (Noel, Chambers, et al., 2012). Overestimation of pain is a result of patients' anticipatory anxiety turning to fear when the needle is presented. This fear further spurs the physiological stress response, and heightens skin sensitivity (Hall et al., 2012). This study measured anticipated and experienced pain to better understand the pain experience.

The results of Experiment One indicate there was little correlation between the use of binaural beats and a change in pain scores. This study examined the difference between participants' anticipated pain and experienced pain. The results showed no significant difference in pain score changes between the Treatment and Control Groups. While there was a minimally important difference between the Treatment Group scores, it was very small, ES=0.2. Forty percent of Treatment Group participants reported less experienced pain than had been anticipated. However, thirty percent reported more experienced pain than was anticipated, and thirty percent reported no change from anticipated pain to experienced pain. Only thirty percent of Control Group participants reported less experienced pain than anticipated; however, only fifteen percent reported higher levels of experienced pain than was anticipated. Thirty-five percent of Control Group participants reported no change from anticipated pain to experienced pain. While there are some small differences between the Treatment and Control Groups in Experiment One, the differences were not significant enough to imply a correlation between less experienced pain and the use of binaural beats before an acute procedure. These findings indicate a need for further research, perhaps with a larger sample population, or a longer exposure to the binaural beat intervention.

The results of Experiment Two show the practice of mindfulness meditation decreases experienced pain. While there was no statistically significant difference between the Treatment and Control Groups' change in pain, there was a moderate minimally important difference, ES=0.5. This result indicates Treatment Group participants experienced perceptibly less pain than had been anticipated. Fifty percent of Treatment Group participants experienced less pain than was anticipated. Only 25% of Control Groups experienced less pain. While 20% of Treatment Group participants felt more pain than anticipated, 30% of Control Group participants

felt more pain than expected. Additionally, the difference between anticipated pain and experienced pain within the Treatment Group is trending towards statistical significance, p=0.07. This result is consistent with the clinically significant findings, and the causal relationship between mindfulness practice and the reduced impact of anticipated pain and anxiety on experienced pain.

Pain Management to Comfort Management: A Shift in Perspective

Pain management is a vital part of patient care, as inadequate pain management is linked to susceptibility to chronic pain, economic burden, and even increased mortality (Baratta, Schwenk, Viscusi, 2014; McNeill, Sherwood, Starck, 2004; Noel, McMurtry, et al., 2010). While the nationwide efforts to improve pain management are an important step in patient care, even those efforts are not enough to provide optimal care. Most acute pain management efforts focus on the physiological experience of pain, providing topical anesthetics to mask the sensation of the needle stick. In a recent randomized controlled study, 114 pediatric patients aged five to 18 years received a needle stick after half the participants had a fifteen minute application of liposomal 4% lidocaine numbing cream, and the other half had a placebo cream (Brenner et al., 2013). The study results showed there was no significant difference in experienced pain between the Treatment and Control Groups, and the topical anesthetic was not effective after only a fifteen minute wait period (Brenner et al., 2013). Additionally, Brenner at al. found that the use of topical anesthetic did nothing to alleviate anticipatory or procedural anxiety. The findings indicated that the factor having the greatest impact on patient pain was anxiety; patients with higher anxiety scores also had higher pain scores (Brenner et al., 2013). The results of Brenner et al.'s study support the shift from a pain management approach to care to a more comfort-centered approach.

The findings of this study support the comfort management approach to needle stick procedures, as the binaural beats and mindfulness meditation interventions demonstrated the "management of pain, anxiety, and any other discomforts that may occur with procedures." (Czarnecki et al., 2011). These complementary and integrative methods provided relief for participants not only in the area of experienced pain, but also experienced tachycardia, anxiety, and the demonstration of pain behaviors in as little as five minutes. The promising trends described here are not only beneficial for the participants during the immediate needle stick experience, but they also have the potential to benefit these participants during future needle sticks and other medical procedures.

Previous sections of this study discussed the importance of reducing stress and anxiety during a needle stick experience to prevent the potential for current and future traumatization. High levels of stress and anxiety during medical procedures create cognitive conditions ideal for the formation of traumatic memories (Schwabe et al., 2010). While this study found no effect on the stress hormone cortisol after a five minute application of the binaural beats and mindfulness interventions, it should be noted that the potential for traumatic memory formation is still reduced. Traumatic memory formation is also likely to occur when a patient's affect is unstable, and the contextual factors of the procedure are unstable (Noel, McMurtry et al., 2010). Reducing anxiety, and the likelihood for crying and other pain behaviors stabilizes the patient's affect, and many of the contextual factors of the needle stick procedure. For instance if a patient is less anxious, s/he is able to pay more attention to what the nurse is instructing her/him to do. This patient is also less likely to present any physical struggling, and therefore feels more in control of what is happening during the procedure (Noel, McMurtry et al., 2010). Patients are more likely to have an accurate recall of their experienced pain under these stable conditions. Parents and medical staff are also more able to

positively reframe the experience in the immediate aftermath of the procedure, removing the potential for traumatic recall (Bird & McMurtry, 2012; Noel, McMurtry et al., 2010). Providing interventions, like binaural beats and mindfulness, to stabilize affect and contextual factors fits within the comfort management approach to care.

Study Limitations

The results of this study show promising trends supporting the use of complementary and integrative methods for pediatric acute pain; however, there were several limitations. The first limitation encountered in this study was sample size. The sample size n=40 was based on the estimated number of participants needed to detect a moderate effect size difference of half a standard deviation in each outcome for both groups. While the sample size was sufficient to detect ES, it may have been too small to detect statistically significant effects. A post-hoc power analysis will be conducted to determine the sample size necessary to detect statistical significance. Increasing the sample size of this study may have also ensured a normal distribution of data, which would have allowed for the use of more robust parametric statistical analyses. Given that this study was intended to be a feasibility and outcomes study, the sample size of 20 participants per group was sufficient, and several moderate ES were detected.

Several limitations can be found in the study design. The most prevalent of these limitations was the inability to truly blind participants and clinic staff to the treatment and control conditions of the study. While the information provided to participants and staff did not reveal the intended effects of the interventions, it was clear which group participants were assigned to because they were required to wear headphones. In the future, placebo recordings could be provided to prevent participants and staff from determining which study condition is they are participating in or witnessing, respectively. Another limitation of the study design was the cessation of the

intervention prior to the needle stick procedure. Participants may have benefited more from a longer intervention period prior to the needle stick. However, it is more likely that experiencing the intervention during the stressful event would have been of more benefit to the participants. This claim is further evidenced by the verbal feedback from seven participants in Experiment One, and 11 participants in Experiment Two. The verbal feedback generally expressed a desire to continue listening to the interventions throughout the needle stick procedure. Future studies should consider adjusting the design to implement the interventions prior to, and during, the needle stick.

Self-report measures are valuable for providing data on the perceptible effects of an intervention from the participants' perspective; however these measures are susceptible to demand characteristics. The study team received extensive training on the masking of demand characteristics through allowable deception, reduced interaction with the participant, and intervention fidelity. Laboratory Medicine staff also received a brief training on proper conduct during study session. Despite providing the proper training to those outside the study team, study team members could not control participant interactions. It is possible that study participants were influenced by remarks made by staff members during the needle stick interventions. It is likely that participants determined which group was receiving active treatment and which group was receiving standard of care treatment. Both of these potential confounds could be remedied by a double blind study design.

Finally, the study location may have been a limitation, as it was a working medical clinic. Participants in both groups remained in the clinic waiting room during the pre-procedure period, subjected to the busy environment characteristic of the clinic. The Laboratory Medicine Clinic is a very high volume clinic, seeing an average of 80-120 patients per day. This high volume of patients and families leads to overcrowding in the seating area, and a high noise level. The noises of the

clinic waiting area consist of the television, patient names being called, conversation, anxious discussions from patients, and the crying of patients receiving their blood draws. The floor plan of the Laboratory Medicine Clinic is open, meaning procedure rooms are located right off the waiting area with no hall or corridor to separate the two areas. The waiting area of the clinic is also a thoroughfare from the hospital floors to the laboratory testing area, with a great deal of foot traffic and transport cart traffic. These factors all contribute to an inherently frenetic environment, which may have had confounding effects on the outcomes of this study.

Future Directions

Though the limitations mentioned above exist, the results of this study are promising and encourage the use of complementary and integrative methods to provide a more complete approach to managing acute pain symptoms. While the outcomes of this study indicate a trend towards reduced pain and anxiety, further research should be conducted to verify these findings. Efficacy studies with larger sample sizes are needed to provide normally distributed data and greater statistical power. Perhaps homogenizing the sample population according to medical diagnosis during efficacy studies could provide richer information about diagnosis-specific benefits of complementary and integrative interventions. Redesigning the interventions to continue throughout the needle stick procedure may also provide vital information about the optimal application of these interventions.

As mentioned in the above sections, several participants expressed the desire to continue listening to the interventions during their needle stick procedures. While these interventions have proven to be fast acting, future studies may examine the optimal length of time needed to administer these interventions. Finally, additional research should be conducted to determine the impact these complementary and integrative methods have on memory formation. In a study

conducted by Noel, McMurtry, Chambers and McGrath, the researchers found that undermanaged needle stick pain was more likely to lead to the formation of traumatic memories (2010). These researchers followed up with study participants by phone two weeks post-needle stick procedure. Participants were asked to recall the pain and fear they experienced during the needle stick. Participants who received standard of care treatment were more likely to recall the needle stick experience in a traumatic way, and over-estimate the pain and anxiety they had experienced. A similar follow-up could be conducted in future studies examining the use of binaural beats and mindfulness meditation during painful needle stick procedures.

These future studies are necessary to ensure patients do not have to endure undermanaged procedural pain. Complementary and integrative interventions not only have the potential to reduce acute pain symptoms, they also provide patients with a sense of empowerment in an inherently powerless setting. This sense of empowerment is a result of the proper management of pediatric acute pain, and can prevent a lifetime of medical trauma.

APPENDIX A:

PARTICIPANT RESPONSES TO MINDFULNESS MEDITATION

	Comments Made by Individual Treatment Groups Participants after Mindfulness Meditation
1	I feel really good, relaxed.
2	That was so relaxing, I could have fallen asleep.
3	I'm feeling calm and relaxed.
4	I am totally relaxed.
5	I feel very safe.
6	I'm relaxed.
7	I feel better, I'm definitely not as scared.
8	I feel really concentrated and I also feel really relaxed.
9	I felt like it was helping me.
10	That was relaxing, it felt like therapy.
11	It was relaxing.
12	I feel relaxed.
13	I am feeling more relaxed.
14	That felt good.
15	It was nice.
16	I am feeling calm.
17	I feel relaxed.
18	That was relaxing and now I have a good feeling.
19	I'm relaxed.
20	I'm not nervous at all, I feel very calm and relaxed.

APPENDIX B:

BINAURAL BEATS CONSENT AND ASSENT FORMS

CHILDREN'S HOSPITAL

Department of Creative & Therapeutic Arts Services

111 Michigan Avenue, NW

Washington, DC 20010

(202) 476-5000

CONSENT TO PARTICIPATE

IN A CLINICAL RESEARCH STUDY

TITLE OF STUDY: Feasibility and Outcomes of Complementary and Alternative Pain Management Interventions for Children Experiencing Acute Pain

PRINCIPAL INVESTIGATOR: Nora Stinley, MA, Creative & Therapeutic Arts Services

INTRODUCTION: We would like to invite your child to be part of a research study at Children's National Health Systems, which is looking at different ways to lessen patient pain during medical procedures. Below is information about the study, including contact information if you have any questions later. If you have questions now, you may ask the research staff, the person who handed you this form.

We will ask you to sign this form to show that you understand the study. If your child is seven years old or older, we will talk to your child about the study. We will give you a copy of this form to keep. It is important that you know:

You do not have to join the study; it is voluntary.

You may change your mind and drop out of the study any time you want.

If we make any important change to the study we will tell you about it and make sure you still want to be in the study.

A. PURPOSE OF STUDY

The purpose of this research study is to see if a new kind of approach to dealing with patient pain can be used to help lessen the pain for our patients. This study is testing to see what a child's heart rate, body chemistry, pain, and worry are when children are listening to binaural beats when getting a needle stick, or when children are getting a needle stick alone. Your child is being asked to be in this study because your child is between the ages of 8 and 18, and your child is getting a needle stick.

B. PROCEDURE

The research staff will be looking at your child's pain scores, how nervous your child is, and how vital signs, like heart rate, have changed. We'll also be taking some cotton swabs of your child's spit to help us look at some of the chemicals in the body that are there during stressful times. At Children's National, our laboratory technicians are trained to take blood as quickly and painlessly as possible. This study will be using recorded sound and beats as an additional type of pain management. The types of recorded sounds being used are binaural beats. The patterns of the beats played through the earphones help to relax the person who is listening. For this study, your child will either be invited to listen to the binaural beats on a pair of headphones before her/his needle stick, or your child will receive the standard of care treatment before her/his needle stick.

Your child's heart rate will be recorded to measure her/his level of pain during the needle stick. To record these vital signs, your child will be connected to a machine using a finger cuff.

Your child's mouth will be swabbed to collect spit before, during and after the needle stick procedure.

Your child will be asked to show her/his level of pain and anxiety two ways before and after the needle stick. Anxiety will be measured before and after the needle stick by circling a number from 1-5 to show how nervous your child is. Pain will be measured after the needle stick by circling a number and face from 1-10 to show how much pain your child felt, and circling a number from 1-5 on a different sheet to show how much pain s/he felt. If your child is uncomfortable at any time during the study, your child may withdraw from the study.

This study is testing to see what a child's heart rate, body chemistry, pain, and worry are when children are listening to binaural beats when getting a needle stick, or when children are getting a needle stick alone. The finger cuff will measure your child's heart rate. The cotton swabs will collect your child's spit to help measure the body chemistry. The questions you child answers before and after the needle stick will help measure your child's pain and worry about the needle stick.

This needle stick is the only time your child will need to be involved in the study. There are no additional commitments.

Your child will be randomly placed in either the group that listens to the binaural beats while getting a needle stick, or the group that gets the needle stick as usual. Your child will be placed in either group using a machine that gives out a number 1 or 2 to your child. This is called a random assignment. Random assignment works a lot like flipping a coin; if the computer flips a heads your child will be assigned to the first group which listens to the beats during the needle stick, and if the computer flips a tails your child will be assigned to the second group which just gets the needle stick as usual. This "coin flip" method makes sure that your child has an equal chance of being in either group. There is little to no risk to your child if s/he listens to the sounds and beats. Your child will be receiving a needle stick no matter what group s/he is in. Regardless of the group

your child is assigned to, your child will receive standard of care treatment during her/his needle stick.

C. POTENTIAL RISKS/DISCOMFORT

If your child is in the group that listens to the binaural beats, there is a chance that your child might uncomfortable wearing the headphones used to listen. This risk probably will not happen, but if your child does feel uncomfortable wearing the headphones, s/he should let the research staff know that s/he is uncomfortable. Your child may withdraw from the study at any time.

D. POTENTIAL BENEFITS

The children who are part of this study will help us find out if it is possible to use treatments, like binaural beats, while patients get needle sticks. Children who are part of this study can also help us see if listening to binaural beats helps calm their bodies down before, during, and after needle sticks. The research staff will be able to tell if your child's body is calming down by recording their heart rate, and body chemistry. Telling us how much pain and fear they had right before and after the needle stick will let us know if the needle stick was more or less painful and/or frightening. If patients can listen to calming beats before and during needle sticks, we can start other studies to see if this treatment is more helpful to children getting needle sticks than just getting a needle stick as usual.

E. ALTERNATIVES TO PARTICIPATION

Participation in this study is voluntary. If you or your child chooses not to be in this study, your child will still receive the standard of care treatment during her/his needle stick.

F. QUESTIONS – WHO TO CALL

We want you to ask questions about any part of this study or consent form either now or at any time in the future. If you have research or medical questions about this study, call the research staff member Nora Stinley at 202-476-6519. If you believe your child is having discomfort as a result of being in this study, you should call Nora Stinley at 202-476-6519. If you have any questions or concerns about your rights in this research study at any time, please call Children's National's Manager of Customer Relations, at (202) 476-5000 or call the Chief Academic Officer of the Children's National Health Systems at (202) 476-5000.

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY

In 1996 the government passed a law known as The Health Insurance Portability and Accountability Act (HIPAA). This privacy law protects your individually identifiable health information (Protected Health Information or PHI). The privacy law requires you to sign an agreement so researchers can use or share your PHI for research purposes. This describes to you how information about you may be used or shared if you are in a research study. It is important that you read this carefully and ask a member of the research team to explain anything you do not understand.

I authorize, Nora Stinley and her research staff to create, access, use, and disclose my PHI for the purposes described below.

Protected Health Information that may be used and shared includes:

☐ Information that identifies you such as name, address, telephone number, date of birth, Social Security number, and other details about you

☐ Information that relates to your health or medical condition from your medical records

☒ Information obtained from the study procedures outlined in this consent form, for example: things done to see if you can join the study such as physical exams, blood and urine tests, x-rays and other tests, and any other medical information we learn from you about your health history and family history

☒ Laboratory results obtained on specimens collected from you (blood, urine, tissue)

☒ Questionnaires or surveys you complete

☐ Interviews conducted with you by members of the research team

☐ Audio/ video recordings

☐ Other *[please specify]:

*Example: *list any additional information that may be obtained from participants that is listed above such as information about financial and social circumstances, or educational level.*

The Researchers may use and share my Protected Health Information with:

- The Principal Investigator, other Investigators, Study Coordinators, and all administrative staff in charge of doing work for the study;
- Government agencies that have the right to see or review your PHI, including but not limited to the Office of Human Research Protections and the Food and Drug Administration;
- Children's National Medical Center Institutional Review Board;
- Audit Committee of the Children's National Medical Center Institutional Review Board;

♦ Quality Improvement Program Coordinator and other staff in the Office for the Protection of Human Subjects at Children's National Medical Center.

In addition to the above people and organizations, the Researchers may also use and share my Protected Health Information with:

☐ Doctors and staff at other places that are participating in the study. The name(s) of the other place(s) that are participating in this study are

☒ Laboratories and other people or organizations that look at your health information in connection with this study. The name(s) of the laboratory(ies) being used in this study is (are) American University in Washington, DC.

☐ The Sponsor of the study and people that the Sponsor may contract with for the study. The name of the Sponsor is

☐ The Contract Research Organization (an organization that helps the Sponsor run the study). The name of the Contract Research Organization is

☐ The Data Safety Monitoring Board (a group of people who examine the medical information during the study)

☐ The Medical Monitor for the Study (a person who reviews medical information during the study)

☐ The Patient Advocate or Research Ombudsman (person who watches out for your best interest)

☐ Any other outside entity who will receive health information

Please list:

Also, your primary physician will be contacted if during the course of the study the researcher learns of a medical condition that needs immediate attention.

Should your health information be disclosed to anyone outside of the study, your information may no longer be protected by HIPAA and this Authorization. However, the use of your health information will still be regulated by applicable federal and state laws.

<u>Storage of PHI in a Database:</u>

We would like to store personal health information collected from you in this study in a database for future research. The database is maintained by Creative & Therapeutic Arts Services.

Please indicate your approval of any or all of the following by initialing next to the statement:

My personal health information may be stored in the above named database for future analysis related to this study. ☐ Yes ☐ No _____ initials

My personal health information may be stored in the above named database for future analysis related to Feasibility and Outcomes of Complementary and Alternative Pain Management Interventions for Children Experiencing Acute Pain. ☐ Yes ☐ No _____initials

My personal health information may be stored in the above named database. Researchers may contact me to request my authorization for future studies that are not related to this study or the disease named above.

☐ Yes ☐ No _____ initials

My personal health information may be stored without any of my identifying information for use in other studies of other diseases. ☐ Yes ☐ No _____ initials

If you agree to participate in this research study, the research team, the research sponsor (when applicable) and the sponsor's representatives, may use Personally Unidentified Study Data. The Personally Unidentified Study Data does not include your name, address, telephone, or social security number. Instead, the researcher assigns a code to the Personally Unidentified Study Data. Personally Unidentified Study Data may include your date of birth, initials, and dates you received medical care. Personally Unidentified Study Data may also include the health information used, created, or collected in the research study. The research team or the research sponsor may share the Personally Unidentified Study Data with others to perform additional research, place it into research databases, share it with researchers in the U.S. or other countries, or use it to improve the design of future studies. They may also publish it in scientific journals, or share it with business partners of the sponsor and to file applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

You do not have to sign this Consent/Authorization. If you decide not to sign the Authorization, you will not be allowed to participate in the research study.

After signing the Consent/Authorization, you can change your mind and:

♦ Revoke this Authorization. If you revoke the Authorization, you will send a written letter

to: Nora Stinley to inform him/her of your decision.

You will be allowed to review the information collected for this research study.

This Authorization expires on 9/15/14.

If you have not already received a Notice of Privacy Practices from Children's National Medical Center, you may request a copy and will be given one. If you have any questions or concerns about your privacy rights, you may contact the Children's Hospital Privacy Officer at 301-572-6348.

G. CONFIDENTIALITY

We will keep the records of this study confidential. We will not tell anyone your child was in the study. Your child's name will not be used on any of the forms used in this study other than the consent and assent forms. The assent and consent forms will be kept separate from the other forms used in this study so no connection can be made. Only the research staff will be able to access the forms collected during this study. The forms will be kept in a locked office in a locked cabinet. The federal government can review the study records and medical records to make sure we are following the law and protecting the children in the study and to make sure our results are correct. Your child's medical record is confidential, but just like any medical record; there are some exceptions under state and federal law.

H. COMPENSATION

Your child will receive a packet of relaxation activities for participating in this study for future use.

I. ADDITIONAL ELEMENTS

Children's National will give you the services used in this study for free. You will not be charged for anything else we do that is part of the study. You will still have to pay for any medical care that is not part of the study.

You may contact Nora Stinley at any time. This can be before you decide to take part in the research by asking questions, or even after you finish the study. You can call Nora Stinley at 202-476-6519, located at 111 Michigan Ave NW, Suite 2801, Washington, DC, if you have any questions.

CONSENT:

By signing this form, you agree that you have talked to the Principal Investigator about the study and understand it, and want your child to be in the study. You agree that we have talked to you about the risks and benefits of the study, and about other choices. You may take your child out of the study at any time and no one will mind and nothing will change about your child's medical care other than not being in the study. Copies of this form will be:

(1) kept in the study file by the Principal Investigator and;

(2) given to you to keep.

Please call the Principal Investigator, Nora Stinley, at 202-476-6519 if you have any questions.

Printed Name of Participant: _____

Printed Name of Parent(s)/Guardian(s): _____

Signature of Participant: _____ Date: _____

(Participant must be 18 years of age or older)

Signature of Parent(s)/Guardian(s): _____ Date: _____

Witness (to signatures): _____ Date: _____

(may be investigator)

Translator's Signature (if, applicable): _____

Language: _____

CHILDREN'S NATIONAL MEDICAL CENTER

Department of Creative & Therapeutic Arts Services

111 Michigan Avenue, NW

Washington, DC 20010

(202) 476-5000

ASSENT TO PARTICIPATE

IN A CLINICAL RESEARCH STUDY

TITLE OF STUDY: Feasibility and Outcomes of Complementary and Alternative Pain Management Interventions for Children Experiencing Acute Pain

PRINCIPAL INVESTIGATOR: Nora Stinley, MA, *Creative & Therapeutic Arts Services*

INTRODUCTION: We would like to invite you to be part of a research study at Children's National Health System. Before you decide if you would like to participate, we want you to know why we are doing the study. We also want you to know about any risks (anything unexpected that might happen) and what you will be expected to do in the study. You can only be in the study if your parent(s) agree(s).

This form gives you information about the study. A research staff member will talk to you about the study and answer any questions you have. We encourage you to discuss this study with your family before making your decision. We will ask you to sign this form to show that you understand the study. We will give you a copy of this form to keep. It is important that you know:

You do not have to join the study;

You may change your mind and stop being in the study any time you want and no one will mind.

A. WHAT IS THE REASON FOR THE STUDY?

The purpose of this research study is to look for different types of treatments that can help you feel less scared and have less pain during needle sticks. This study is testing to see how fast your heart is beating, what chemicals are in your body, and what you're feeling and thinking when you're getting a needle stick. The treatment we're looking at in this study is a special type of music that can be played over headphones. You might be in a group that listens to the special music while you get your needle stick, or you might be in a group that gets the needle stick without any music. The reason you're being asked to participate in this study is because you are between the ages of 8 and 18 and because you are getting a needle stick.

B. WHAT WILL HAPPEN IN THE STUDY?

We'll look at how fast your heart is beating and how your body feels while listening to the music. We'll also ask you to swab the inside of your mouth with a cotton swab to see if the chemicals in your spit change or stay the same when you listen to this music. We'll ask you to answer some questions about how nervous you are, and how much pain you feel before and after your needle stick. At Children's National our laboratory medicine technicians are specially trained to make needle sticks go as fast and pain-free as possible. Other studies have tested things like making art to help patients who are getting blood draws. The special music used in this study has been used at other times and helps people feel relaxed, that's why we're trying it out her at Children's National.

Your heart rate will be recorded with a finger cuff to measure any changes happening in your body during the needle stick.

We'll ask you to swab the inside of your mouth with a special cotton swab before, during, and after the needle stick. This is how we'll collect your spit to see if the chemicals in your body change during the study.

You'll be asked to circle a number from 1 to 5 that shows how nervous you are about the needle stick before and after the needle stick. Afterwards, we'll ask you to circle a number from 1 to 10 to show how much pain you felt, and also to circle a number from 1 to 5 to show your pain level.

This study is testing to see if it's possible to let patients listen to this special music before and during a needle stick. We're also looking at how your body reacts to the music by looking at your heart rate, and body chemicals.

This needle stick procedure is the only time you will need to be involved in the study. There are no additional commitments.

There are two groups in this study. There's a group that will listen to music before and during the needle stick, with the questions before and after, the spit collection, and the finger cuff monitor. The other group you might be in is the one that gets a needle stick like it's usually done without music, plus answering the questions, collecting spit, and wearing the finger cuff. A computer will choose which group you're in by showing a number 1 or 2. This is called a random assignment and works a lot like flipping a coin; if the computer flips a heads you will be assigned to the first group which listens to music and if the computer flips a tails you will be assigned to the second group which doesn't listen to music. This "coin flip" method makes sure that you have the same chances of being in either group. Regardless of the group you are assigned to, you will be getting your scheduled needle stick. There is very little risk to you if you choose to participate in this study. You might feel a little uncomfortable wearing the headphones to listen to the music. Just let the research staff know and we'll help you with that. If you are uncomfortable at any time, you may withdraw from the study.

C. WHAT POSSIBLE UNEXPECTED THINGS COULD HAPPEN?

If you are in the group that listens to music, there is a chance that you might feel a little uncomfortable wearing the headphones to listen to the sounds, or you may feel uncomfortable swabbing your mouth for spit. This probably will not happen, but if you do feel uncomfortable, you should let the research team know. If you think something is wrong or you're not feeling good because of something you think is a part of the study, tell the research staff or your doctor or nurse right away. You can withdraw from this study at any time.

D. WHAT POSSIBLE GOOD THINGS COULD HAPPEN?

The children who are part of this study will help us find out if it is possible to use this special music with patients who receive needle sticks. Children who are part of this study can also help us see if listening to the special music helps to calm their body down when they feel nervous or scared about the needle stick. We'll be able to figure out if your body is calming down by recording heart rate, and body chemicals in spit. Telling us what your pain level and fear level are before and after the needle stick will let us know if listening to the music made the needle stick more or less painful and/or frightening. After we find out if it's possible to the special music during needle sticks, we can do future studies to see if it's helpful to let patients listen to the special music during needle sticks.

Finding out if there is a better way to help you while you get a needle stick could be helpful to you in the future.

WHAT OTHER CHOICES DO YOU HAVE IF YOU DO NOT WANT TO BE IN THE STUDY

Your participation in this study is voluntary. If you choose not to be in this study, you will still receive your scheduled needle stick like you normally would.

F. HOW WILL WE KEEP YOUR RECORDS PRIVATE?

We will keep the records of this study confidential. We will not tell anyone you were in the study. Your name will not be used on any of the forms used in this study other than the consent and assent forms, which will be kept separate from the other forms used in this study so no connection can be made. Only the Principal Investigator will be able to access the forms collected during this study. The forms will be kept in a locked office in a locked cabinet. The federal government can review the study records and medical records to make sure we are following the law and protecting the children in the study and to make sure our results are correct. Your medical record is confidential, but just like any medical record; there are some exceptions under state and federal law.

ASSENT

By signing this form, you agree that you have talked to the researcher about the study and understand it, and want to be in the study. You also agree that you have been told about the risks (unexpected things) and benefits (good things) of the study, and about other choices. You

may stop being in the study at any time and no one will mind and nothing will change about your medical care other than not being in the study. Please call the Principal Investigator, Nora Stinley, at 202-476-6519, located at 111 Michigan Ave NW, Washington, DC, if you have any questions.

Printed Name of Participant: _____

Signature of Participant: _____

Witness (to signature): _____ Date: _____
(may be investigator)

Translator's Signature (if, applicable): _____ Date: _____

Language: _____

AFFIDAVIT OF PERSON OBTAINING ASSENT: I certify that I have explained to the above individual(s) the nature and purpose of the study, potential benefits, and possible risks associated with participation in this study. I have answered any questions that have been raised.

Printed Name of Individual Obtaining Consent: _____

Title: _____ Signature: _____ Date: _____

APPENDIX C:

MINDFULNESS MEDITATION CONSENT AND ASSENT FORMS

CHILDREN'S HOSPITAL
Department of Creative & Therapeutic Arts Services
111 Michigan Avenue, NW
Washington, DC 20010
(202) 476-5000

CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

TITLE OF STUDY: Feasibility and Outcomes of Complementary and Alternative Pain Management Interventions for Children Experiencing Acute Pain
PRINCIPAL INVESTIGATOR: Nora Stinley, MA, Creative & Therapeutic Arts Services

INTRODUCTION: We would like to invite your child to be part of a research study at Children's National Health Systems, which is looking at different ways to lessen patient pain during medical procedures. Below is information about the study, including contact information if you have any questions later. If you have questions now, you may ask the research staff, the person who handed you this form.

We will ask you to sign this form to show that you understand the study. If your child is seven years old or older, we will talk to your child about the study. We will give you a copy of this form to keep. It is important that you know:
You do not have to join the study; it is voluntary.
You may change your mind and drop out of the study any time you want.
If we make any important change to the study we will tell you about it and make sure you still want to be in the study.

A. PURPOSE OF STUDY

The purpose of this research study is to see if a new kind of approach to dealing with patient pain can be used to help lessen the pain for our patients. This study is testing to see what a child's heart rate, body chemistry, pain, and worry are when children are listening to breathing instruction when getting a needle stick, or when children are getting a needle stick alone. Your child is being asked to be in this study because your child is between the ages of 8 and 18, and your child is getting a needle stick.

B. PROCEDURE

The research staff will be looking at your child's pain scores, how nervous your child is, and how vital signs, like heart rate, have changed. We'll also be taking some cotton swabs of your child's spit to help us look at some of the chemicals in the body that are there during stressful times. At Children's National, our laboratory technicians are trained to take blood as quickly and painlessly as possible. This study will be using recorded breathing instructions as an additional type of pain management. The types of recorded sounds being used are breathing instruction. The

instructions played through the earphones help to relax the person who is listening. For this study, your child will either be invited to listen to the breathing instruction on a pair of headphones before her/his needle stick, or your child will receive the standard of care treatment before her/his needle stick.

Your child's heart rate will be recorded to measure her/his level of pain during the needle stick. To record these vital signs, your child will be connected to a machine using a finger cuff.

Your child's mouth will be swabbed to collect spit after the needle stick procedure.

Your child will be asked to show her/his level of pain and anxiety two ways before and after the needle stick. Anxiety will be measured before and after the needle stick by circling a number from 1-5 to show how nervous your child is. Pain will be measured after the needle stick by circling a number and face from 1-10 to show how much pain your child felt, and circling a number from 1-5 on a different sheet to show how much pain s/he felt. If your child is uncomfortable at any time during the study, your child may withdraw from the study.

This study is testing to see what a child's heart rate, body chemistry, pain, and worry are when children are listening to breathing instruction when getting a needle stick, or when children are getting a needle stick alone. The finger cuff will measure your child's heart rate. The cotton swabs will collect your child's spit to help measure the body chemistry. The questions you child answers before and after the needle stick will help measure your child's pain and worry about the needle stick.

This needle stick is the only time your child will need to be involved in the study. There are no additional commitments.

Your child will be randomly placed in either the group that listens to the breathing instruction while getting a needle stick, or the group that gets the needle stick as usual. Your child will be placed in either group using a machine that gives out a number 1 or 2 to your child. This is called a random assignment. Random assignment works a lot like flipping a coin; if the computer flips a heads your child will be assigned to the first group which listens to the breathing instructions during the needle stick, and if the computer flips a tails your child will be assigned to the second group which just gets the needle stick as usual. This "coin flip" method makes sure that your child has an equal chance of being in either group. There is little to no risk to your child if s/he listens to the instructions. Your child will be receiving a needle stick no matter what group s/he is in. Regardless of the group your child is assigned to, your child will receive standard of care treatment during her/his needle stick.

C. POTENTIAL RISKS/DISCOMFORT

If your child is in the group that listens to the breathing instruction, there is a chance that your child might uncomfortable wearing the headphones used to listen. This risk probably will not happen, but if your child does feel uncomfortable wearing the headphones, s/he should let the

research staff know that s/he is uncomfortable. Your child may withdraw from the study at any time.

D. POTENTIAL BENEFITS

The children who are part of this study will help us find out if it is possible to use treatments, like breathing instruction, while patients get needle sticks. Children who are part of this study can also help us see if listening to breathing instruction helps calm their bodies down before, during, and after needle sticks. The research staff will be able to tell if your child's body is calming down by recording their heart rate, and body chemistry. Telling us how much pain and fear they had right before and after the needle stick will let us know if the needle stick was more or less painful and/or frightening. If patients can listen to breathing instructions before and during needle sticks, we can start other studies to see if this treatment is more helpful to children getting needle sticks than just getting a needle stick as usual.

E. ALTERNATIVES TO PARTICIPATION

Participation in this study is voluntary. If you or your child chooses not to be in this study, your child will still receive the standard of care treatment during her/his needle stick.

F. QUESTIONS – WHO TO CALL

We want you to ask questions about any part of this study or consent form either now or at any time in the future. If you have research or medical questions about this study, call the research staff member Nora Stinley at 202-476-6519. If you believe your child is having discomfort as a result of being in this study, you should call Nora Stinley at 202-476-6519. If you have any questions or concerns about your rights in this research study at any time, please call Children's National's Manager of Customer Relations, at (202) 476-5000 or call the Chief Academic Officer of the Children's National Health Systems at (202) 476-5000.

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY

In 1996 the government passed a law known as The Health Insurance Portability and Accountability Act (HIPAA). This privacy law protects your individually identifiable health information (Protected Health Information or PHI). The privacy law requires you to sign an agreement so researchers can use or share your PHI for research purposes. This describes to you how information about you may be used or shared if you are in a research study. It is important that you read this carefully and ask a member of the research team to explain anything you do not understand.

I authorize, Nora Stinley and her research staff to create, access, use, and disclose my PHI for the purposes described below.

Protected Health Information that may be used and shared includes:

☐ Information that identifies you such as name, address, telephone number, date of

birth, Social Security number, and other details about you
☐ Information that relates to your health or medical condition from your medical records
☒ Information obtained from the study procedures outlined in this consent form, for example: things done to see if you can join the study such as physical exams, blood and urine tests, x-rays and other tests, and any other medical information we learn from you about your health history and family history
☒ Laboratory results obtained on specimens collected from you (blood, urine, tissue)
☒ Questionnaires or surveys you complete
☐ Interviews conducted with you by members of the research team
☐ Audio/ video recordings
☐ Other *[please specify]:

*Example: *list any additional information that may be obtained from participants that is listed above such as information about financial and social circumstances, or educational level.*

The Researchers may use and share my Protected Health Information with:

- The Principal Investigator, other Investigators, Study Coordinators, and all administrative staff in charge of doing work for the study;
- Government agencies that have the right to see or review your PHI, including but not limited to the Office of Human Research Protections and the Food and Drug Administration;
- Children's National Medical Center Institutional Review Board;
- Audit Committee of the Children's National Medical Center Institutional Review Board;
- Quality Improvement Program Coordinator and other staff in the Office for the Protection of Human Subjects at Children's National Medical Center.

In addition to the above people and organizations, the Researchers may also use and share my Protected Health Information with:

☐ Doctors and staff at other places that are participating in the study. The name(s) of the other place(s) that are participating in this study are
☒ Laboratories and other people or organizations that look at your health information in connection with this study. The name(s) of the laboratory(ies) being used in this study is (are) American University in Washington, DC.
☐ The Sponsor of the study and people that the Sponsor may contract with for the study. The name of the Sponsor is
☐ The Contract Research Organization (an organization that helps the Sponsor run the study). The name of the Contract Research Organization is
☐ The Data Safety Monitoring Board (a group of people who examine the medical information during the study)
☐ The Medical Monitor for the Study (a person who reviews medical information during the study)
☐ The Patient Advocate or Research Ombudsman (person who watches out for your

best interest)

☐ Any other outside entity who will receive health information
Please list:

Also, your primary physician will be contacted if during the course of the study the researcher learns of a medical condition that needs immediate attention.

Should your health information be disclosed to anyone outside of the study, your information may no longer be protected by HIPAA and this Authorization. However, the use of your health information will still be regulated by applicable federal and state laws.

Storage of PHI in a Database:

We would like to store personal health information collected from you in this study in a database for future research. The database is maintained by Creative & Therapeutic Arts Services.

Please indicate your approval of any or all of the following by initialing next to the statement:

My personal health information may be stored in the above named database for future analysis related to this study. ☐ Yes ☐ No _____ initials

My personal health information may be stored in the above named database for future analysis related to Feasibility and Outcomes of Complementary and Alternative Pain Management Interventions for Children Experiencing Acute Pain. ☐ Yes ☐ No _____initials

My personal health information may be stored in the above named database. Researchers may contact me to request my authorization for future studies that are not related to this study or the disease named above.
☐ Yes ☐ No _____ initials

My personal health information may be stored without any of my identifying information for use in other studies of other diseases. ☐ Yes ☐ No _____ initials

If you agree to participate in this research study, the research team, the research sponsor (when applicable) and the sponsor's representatives, may use Personally Unidentified Study Data. The Personally Unidentified Study Data does not include your name, address, telephone, or social security number. Instead, the researcher assigns a code to the Personally Unidentified Study Data. Personally Unidentified Study Data may include your date of birth, initials, and dates you received medical care. Personally Unidentified Study Data may also include the health information used, created, or collected in the research study. The research team or the research sponsor may share the Personally Unidentified Study Data with others to perform additional research, place it into research databases, share it with researchers in the U.S. or other countries, or use it to improve the design of future studies. They may also publish it in scientific journals, or share it with business

partners of the sponsor and to file applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

You do not have to sign this Consent/Authorization. If you decide not to sign the Authorization, you will not be allowed to participate in the research study.

After signing the Consent/Authorization, you can change your mind and:

- Revoke this Authorization. If you revoke the Authorization, you will send a written letter to: Nora Stinley to inform him/her of your decision.

You will be allowed to review the information collected for this research study.

This Authorization expires on 9/15/14.

If you have not already received a Notice of Privacy Practices from Children's National Medical Center, you may request a copy and will be given one. If you have any questions or concerns about your privacy rights, you may contact the Children's Hospital Privacy Officer at 301-572-6348.

G. CONFIDENTIALITY

We will keep the records of this study confidential. We will not tell anyone your child was in the study. Your child's name will not be used on any of the forms used in this study other than the consent and assent forms. The assent and consent forms will be kept separate from the other forms used in this study so no connection can be made. Only the research staff will be able to access the forms collected during this study. The forms will be kept in a locked office in a locked cabinet. The federal government can review the study records and medical records to make sure we are following the law and protecting the children in the study and to make sure our results are correct. Your child's medical record is confidential, but just like any medical record; there are some exceptions under state and federal law.

H. COMPENSATION

Your child will receive a packet of relaxation activities for participating in this study for future use.

I. ADDITIONAL ELEMENTS

Children's National will give you the services used in this study for free. You will not be charged for anything else we do that is part of the study. You will still have to pay for any medical care that is not part of the study.

You may contact Nora Stinley at any time. This can be before you decide to take part in the research by asking questions, or even after you finish the study. You can call Nora Stinley at 202-476-6519, located at 111 Michigan Ave NW, Suite 2801, Washington, DC, if you have any questions.

CONSENT:

By signing this form, you agree that you have talked to the Principal Investigator about the study and understand it, and want your child to be in the study. You agree that we have talked to you about the risks and benefits of the study, and about other choices. You may take your child out of the study at any time and no one will mind and nothing will change about your child's medical care other than not being in the study. Copies of this form will be:

(1) kept in the study file by the Principal Investigator and;

(2) given to you to keep.

Please call the Principal Investigator, Nora Stinley, at 202-476-6519 if you have any questions.

Printed Name of Participant: _____

Printed Name of Parent(s)/Guardian(s): _____

Signature of Participant: _____ Date: _____

(Participant must be 18 years of age or older)

Signature of Parent(s)/Guardian(s): _____ Date: _____

Witness (to signatures): _____ Date: _____
(may be investigator)

Translator's Signature (if, applicable): _____

Language: _____

CHILDREN'S NATIONAL MEDICAL CENTER
Department of Creative & Therapeutic Arts Services
111 Michigan Avenue, NW
Washington, DC 20010
(202) 476-5000

ASSENT TO PARTICIPATE
IN A CLINICAL RESEARCH STUDY

TITLE OF STUDY: Feasibility and Outcomes of Complementary and Alternative Pain Management Interventions for Children Experiencing Acute Pain
PRINCIPAL INVESTIGATOR: Nora Stinley, MA, *Creative & Therapeutic Arts Services*

INTRODUCTION: We would like to invite you to be part of a research study at Children's National Health System. Before you decide if you would like to participate, we want you to know why we are doing the study. We also want you to know about any risks (anything unexpected that might happen) and what you will be expected to do in the study. You can only be in the study if your parent(s) agree(s).

This form gives you information about the study. A research staff member will talk to you about the study and answer any questions you have. We encourage you to discuss this study with your family before making your decision. We will ask you to sign this form to show that you understand the study. We will give you a copy of this form to keep. It is important that you know:
You do not have to join the study;
You may change your mind and stop being in the study any time you want and no one will mind.

A. WHAT IS THE REASON FOR THE STUDY?

The purpose of this research study is to look for different types of treatments that can help you feel less scared and have less pain during needle sticks. This study is testing to see how fast your heart is beating, how much oxygen is in your blood, what chemicals are in your body, and what you're feeling and thinking when you're getting a needle stick. The treatment we're looking at in this study is breathing instructions that can be played over headphones. You might be in a group that listens to the breathing instructions while you get your needle stick, or you might be in a group that gets the needle stick without any breathing instructions. The reason you're being asked to participate in this study is because you are between the ages of 8 and 18 and because you are getting a needle stick.

B. WHAT WILL HAPPEN IN THE STUDY?

We'll look at how fast your heart is beating and how much oxygen your blood is carrying to your body to see how your body feels while listening to the breathing instructions. We'll also ask you to swab the inside of your mouth with a cotton swab to see if the chemicals in your spit change or stay the same when you listen to these instructions. We'll ask you to answer some questions about how nervous you are, and how much pain you feel before and after your needle stick. At Children's National our laboratory medicine technicians are specially trained to make needle

sticks go as fast and pain-free as possible. Other studies have tested things like making art to help patients who are getting blood draws. The breathing instructions used in this study have been used at other times and help people feel relaxed, that's why we're trying it out here at Children's National.

Your heart rate and blood oxygen level will be recorded with a finger cuff to measure any changes happening in your body during the needle stick.

We'll ask you to swab the inside of your mouth with a special cotton swab after the needle stick. This is how we'll collect your spit to see if the chemicals in your body change during the study.

You'll be asked to circle a number from 1 to 5 that shows how nervous you are about the needle stick before and after the needle stick. Afterwards, we'll ask you to circle a number from 1 to 10 to show how much pain you felt, and also to circle a number from 1 to 5 to show your pain level.

This study is testing to see if it's possible to let patients listen to these breathing instructions before and during a needle stick. We're also looking at how your body reacts to the breathing instructions by looking at your heart rate, blood oxygen level, and body chemicals.

This needle stick procedure is the only time you will need to be involved in the study. There are no additional commitments.

There are two groups in this study. There's a group that will listen to breathing instructions before and during the needle stick, with the questions before and after, the spit collection, and the finger cuff monitor. The other group you might be in is the one that gets a needle stick like it's usually done without breathing instructions, plus answering the questions, collecting spit, and wearing the finger cuff. A computer will choose which group you're in by showing a number 1 or 2. This is called a random assignment and works a lot like flipping a coin; if the computer flips a heads you will be assigned to the first group which listens to breathing instructions and if the computer flips a tails you will be assigned to the second group which doesn't listen to breathing instructions. This "coin flip" method makes sure that you have the same chances of being in either group. Regardless of the group you are assigned to, you will be getting your scheduled needle stick. There is very little risk to you if you choose to participate in this study. You might feel a little uncomfortable wearing the headphones to listen to breathing instructions. Just let the research staff know and we'll help you with that. If you are uncomfortable at any time, you may withdraw from the study.

C. WHAT POSSIBLE UNEXPECTED THINGS COULD HAPPEN?

If you are in the group that listens to breathing instructions, there is a chance that you might feel a little uncomfortable wearing the headphones to listen to the instructions, or you may feel uncomfortable swabbing your mouth for spit. This probably will not happen, but if you do feel uncomfortable, you should let the research team know. If you think something is wrong or you're

not feeling good because of something you think is a part of the study, tell the research staff or your doctor or nurse right away. You can withdraw from this study at any time.

D. WHAT POSSIBLE GOOD THINGS COULD HAPPEN?

The children who are part of this study will help us find out if it is possible to use these breathing instructions with patients who receive needle sticks. Children who are part of this study can also help us see if listening to breathing instructions help to calm their body down when they feel nervous or scared about the needle stick. We'll be able to figure out if your body is calming down by recording heart rate, blood oxygen levels, and body chemicals in spit. Telling us what your pain level and fear level are after the needle stick will let us know if listening to the breathing instructions made the needle stick more or less painful and/or frightening. After we find out if it's possible to listen to the breathing instructions during needle sticks, we can do future studies to see if it's helpful to let patients listen to these instructions during needle sticks.

Finding out if there is a better way to help you while you get a needle stick could be helpful to you in the future.

WHAT OTHER CHOICES DO YOU HAVE IF YOU DO NOT WANT TO BE IN THE STUDY

Your participation in this study is voluntary. If you choose not to be in this study, you will still receive your scheduled needle stick like you normally would.

F. HOW WILL WE KEEP YOUR RECORDS PRIVATE?

We will keep the records of this study confidential. We will not tell anyone you were in the study. Your name will not be used on any of the forms used in this study other than the consent and assent forms, which will be kept separate from the other forms used in this study so no connection can be made. Only the Principal Investigator will be able to access the forms collected during this study. The forms will be kept in a locked office in a locked cabinet. The federal government can review the study records and medical records to make sure we are following the law and protecting the children in the study and to make sure our results are correct. Your medical record is confidential, but just like any medical record; there are some exceptions under state and federal law.

ASSENT

By signing this form, you agree that you have talked to the researcher about the study and understand it, and want to be in the study. You also agree that you have been told about the risks (unexpected things) and benefits (good things) of the study, and about other choices. You may stop being in the study at any time and no one will mind and nothing will change about your medical care other than not being in the study. Please call the Principal Investigator, Nora Stinley, at 202-476-6519, located at 111 Michigan Ave NW, Washington, DC, if you have any questions.

Printed Name of Participant: _____

Signature of Participant: _____

Witness (to signature): _____ Date: _____
(may be investigator)

Translator's Signature (if, applicable): _____ Date: _____
Language: _____

AFFIDAVIT OF PERSON OBTAINING ASSENT: I certify that I have explained to the above individual(s) the nature and purpose of the study, potential benefits, and possible risks associated with participation in this study. I have answered any questions that have been raised.

Printed Name of Individual Obtaining Consent: _____

Title: _____ Signature: _____ Date: _____

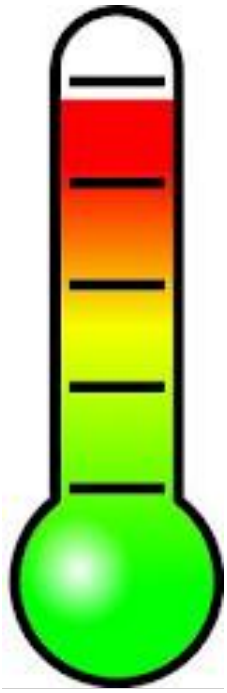
APPENDIX D:

SUBJECTIVE ANXIETY MEASURE

Pre-Procedure Anticipatory Anxiety Measure:

The Hospital Fears Rating Scale

Pretend the thermometer below will measure how scared or nervous you feel about your needle stick. Circle the temperature your fear thermometer would show.



(5)_____This is really scary! I am really scared about this.

(4) I am between scared but ok, and really scared.

(3)_____This is scary, but I'm ok.

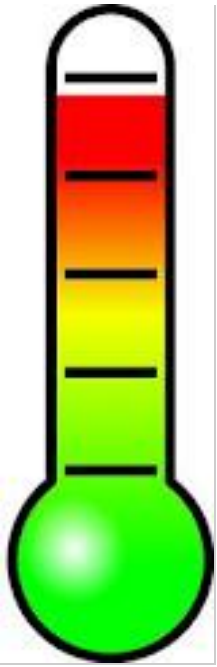
(2) I am between not being scared at all and scared but ok.

(1)_____I'm not scared. No problem at all.

Post-Procedure Felt Anxiety Measure:

The Hospital Fears Rating Scale

Pretend the thermometer below measured how scared or nervous you felt about your needle stick. Circle the temperature your fear thermometer would show.



(5)_____This was really scary! I was really scared about this.

(4) I was between scared but ok, and really scared.

(3)_____This was scary, but I'm ok.

(2) I was between not being scared at all and scared but ok.

(1)_____I wasn't scared. No problem at all.

APPENDIX E:

SUBJECTIVE PAIN MEASURES

Pre-Procedure Expected Pain Measure:

Circle the number that matches how much pain you think you'll feel during the needle stick.

|0--------1--------2--------3--------4--------5--------6--------7--------8--------9--------10|

No Pain **Worst Pain**



Post-Procedure Experienced Pain Measure:

Circle the number that matches how much pain you think you'll feel during the needle stick.

|0--------1--------2--------3--------4--------5--------6--------7--------8--------9--------10|

No Pain **Worst Pain**



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