

IMPACT OF A NOVEL RELAXATION METHOD OF TOUCH ON NEONATAL
NEUROBEHAVIORAL DEVELOPMENT AMONG VERY PRETERM INFANTS

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DOCTOR OF PHILOSOPHY

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University of Missouri - Kansas City, 2012

ABSTRACT

Infants born very preterm (≤ 30 weeks estimated gestational age [EGA]) annually and are at greatest risk to develop significant neurodevelopmental abnormalities. These neurodevelopmental abnormalities are the result of complex conditions involving the interaction between multiple biological, genetic, and environmental risks. In an effort to manipulate and support the extra-uterine environment, infant massage has been aimed at decreasing stress and optimizing the infant's sensory experience. However, the majority of existing infant massage studies has varying protocols, are limited to healthy or convalescing preterm infants greater than 32 weeks postmenstrual age (PMA), and are seldom contingent on infant behavioral cues.

The M Technique is a gentle, structured, comforting touch method aimed at limiting stress and anxiety in fragile intensive care patients who are unable to tolerate conventional massage. Little is known about the effects of this technique on infants born very preterm. Therefore, the purpose of this matched case-control pilot study was to systematically test the cumulative effect of the M Technique on infant neurodevelopment, growth velocity, and physiologic and behavioral state in hospitalized very preterm infants in a Midwestern academic level IV neonatal intensive care unit (NICU).

Results indicate that very preterm infants who received the M Technique over a 5-week period did not differ significantly in neurobehavioral developmental and growth velocity compared to control infants. However, very preterm infants who received the M Technique had improved physiologic stability and more quiet sleep states from baseline to 10 minutes post the M Technique intervention over all three time points, suggesting improved physiologic stability and more quiet sleep state over time.

Research regarding the type, timing, and duration of comforting touch in infants born very preterm starting at 30 weeks' PMA is lacking. Preliminary findings from this study support an infant-driven (e.g., where the protocol is based on each infant response or cues) M Technique intervention to promote comfort and relaxation in high-risk infants born very preterm. A longitudinal research design with a larger sample size is needed to confirm and expand on the effects and potential mechanisms of the M Technique on neurobehavior and growth velocity.

The faculty listed below, appointed by the Dean of the School of Nursing, have examined a dissertation titled " Impact of a Novel Relaxation Method of Touch on Neonatal Neurobehavioral Development Among Very Preterm Infants", presented by Joan Renaud Smith, candidate for the Doctor of Philosophy degree, and hereby certify that in their opinion it is worthy of acceptance.

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CHAPTER 1

INTRODUCTION

Infants born very preterm (≤ 30 weeks estimated gestational age [EGA]) are at greatest risk to develop significant neurodevelopmental abnormalities (Aarnoudse-Moens, Duivenvoorden, Weislgas-Kuperus, Van Goudoever, & Oosterlaan, 2012; Aarnoudse-Moens, Oosterlaan, Duivenvoorden, Van Goudoever, Weislgas-Kuperus, 2011; Delobel-Ayoub et al., 2009). Noxious environmental factors, such as multiple painful procedures and excessive noise and lighting in the neonatal intensive care unit (NICU) result in increased infant stress, altered brain maturation, and negative neurodevelopmental outcomes (Rangon et al., 2007; Smith et al., 2011). In an effort to manipulate and support the extra-uterine environment, infant massage has been aimed at decreasing stress and optimizing the infant's sensory experience. However, the majority of existing infant massage studies has varying protocols. In addition, they are limited to healthy or convalescing preterm infants greater than 32 weeks' postmenstrual age (PMA), and are seldom contingent on infant behavioral cues (Smith, 2012). Out of concern for the physiological fragility of very preterm infants, few systematic, infant-driven comforting touch studies exist which have reported limited or inconsistent findings.

Recently, a novel alternative to providing infant massage to hospitalized high-risk infants was introduced, called the M Technique (Smith et al., 2012). The M Technique is a gentle, structured, comforting touch, relaxation method aimed at limiting stress and anxiety in fragile intensive care patients who are unable to tolerate conventional massage. Until recently, no studies have systematically examined the impact of the M Technique

on very preterm infants. A very promising feasibility study conducted by our research team revealed improved physiological and behavioral effects of the M Technique on infants born very preterm (Smith et al., 2012).

Background

Two-thirds of children born very preterm (≤ 30 EGA) develop cognitive impairments, a wide variety of learning disabilities, worsened executive function, along with social and emotional difficulties (Aarnoudse-Moens et al., 2012; Aarnoudse-Moens, 2011; Delobel-Ayoub et al., 2009). The cause of these adverse neurodevelopmental outcomes is multifactorial and includes existing medical conditions, genetics, poor postnatal growth, and noxious environmental factors. Environmental factors in the NICU result in increased infant stress, altered brain maturation, and negative neurodevelopmental outcomes (Rangon et al., 2007; Smith et al., 2011).

Neurodevelopmental supportive care strategies decrease stress and reduce the gap between the in utero and NICU environments (Als et al., 2004; Als, 2009; Vandenberg, 2007). Infant massage is a neurodevelopmental supportive care strategy aimed at decreasing stress, but the majority of existing infant massage studies have varying protocols, are limited to healthy or convalescing preterm infants greater than 32 weeks' postmenstrual age (PMA), and are seldom contingent on infant behavioral cues.

Study Purpose and Working Hypotheses

The purpose of this case-control pilot study was to systematically test the cumulative effect of the M Technique on infant neurodevelopment in hospitalized very preterm infants. To achieve our goals we proposed the following two Specific Aims:

Specific Aim 1

Examine the neurobehavioral and growth velocity impact of the M Technique for hospitalized very preterm infants. Our working hypothesis: Very preterm infants (≤ 30 weeks gestation) who receive the M Technique intervention will have improved (1) neurobehavioral development [NICU Network Neurobehavioral Scale (NNNS)]; (2) higher growth velocity (difference in infant weight at the beginning and end of protocol), compared to the control group.

Specific Aim 2

Examine the physiological and behavioral state impact of the M Technique for hospitalized very preterm infants. Our working hypothesis: Very preterm infants who receive the M Technique intervention (experimental group only) will have improved physiologic stability (heart rate [HR], respiratory rate [RR], oxygen saturations) and behavioral state (e.g., ABSS) changes from baseline at 3 different time points over the course of the 5 week intervention.

Significance

Findings from this study build upon the science of touch for very preterm infants and identifies the type, timing, and duration of a systematic comforting touch technique aimed at optimizing the infant's sensory experience and decreasing stress. This study bolsters the investigative team's previous application of this method that showed improved physiological and infant behavioral state outcomes (Smith et al., 2012). Results from this study also provides a framework to design larger, longitudinal outcomes studies including the effects of the M Technique on neurobehavioral and neurodevelopmental from term equivalent to school age. In addition, the preliminary

findings of this study assist the investigative team in achieving the long-term goal of studying the effectiveness of a parent-delivered M Technique intervention that will have infant, parent, and infant-parent dyad implications.

CHAPTER 2

INTEGRATIVE REVIEW OF THE LITERATURE

The following section was prepared in partial fulfillment of the requirements for a manuscript-format dissertation. This paper was published in 2012 in the journal *Advances in Neonatal Care*.

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Abstract

Infants born prematurely lose the protection of the uterus at a time of fetal development when the brain is growing and organizing exponentially. Environmental factors, such as stress in the newborn intensive care unit (NICU), may play a role in altered brain maturation and neurobehavioral outcomes. Strategies aimed at reducing stress and promoting infant well-being are essential to improve neurological and behavioral outcomes. Infant massage is a developmentally supported strategy aimed at promoting relaxation. However, despite the well documented benefits of infant massage, infants born very preterm (≤ 30 weeks gestation) are often excluded from these studies, leaving neonatal clinicians and families without guidance in how to provide a stress-reducing supplemental touch. Much of the touch in the NICU is procedural touch and infants born very preterm often miss out on *comforting* touch stimulation. A systematic review of the literature is presented with an aim to explore the research that examines the various *comforting* touch therapies used on hospitalized NICU infants born very preterm within the first few days of postnatal life. The purpose of the review is to identify appropriate stress-reducing *comforting* touch techniques for physiologically fragile very preterm infants that can inform and provide guidance to neonatal clinicians and families.

Keywords: touch, tactile stimulation, preterm, neonatal intensive care, comfort, massage

Comforting Touch in the Very Preterm Hospitalized Infant: An Integrative Review

Preterm infants (<37 weeks estimated gestational age [EGA]) are at increased risk for significant neurobehavioral and cognitive impairments, including academic underachievement, behavioral problems, and poor executive function.¹⁻³ Up to 60% of children born very preterm (\leq 30 weeks EGA) experience cognitive impairments, a wide variety of learning disabilities, and social and emotional difficulties.⁴⁻⁷ Infants born prematurely lose the protection of the uterus at a time of fetal development when the brain is growing and organizing exponentially. Environmental factors, such as stress in the newborn intensive care unit (NICU), may play a role in altered brain maturation and neurobehavioral outcomes.⁸⁻⁹ Discordance exists between the normal expectation of the brain of a preterm infant's brain's expectation for a protected uterine environment and the characteristics of a highly technical and stressful NICU environment.

In an effort to decrease the disparity between the immature human brain's expectation and the infant's environmental experience, a developmentally supportive environment is needed.¹⁰ Specific interventions aimed at decreasing stress by individually modifying the NICU micro- and macro-environments are essential to improve neurological and behavioral outcomes.¹¹⁻¹² These developmentally supportive interventions require continuous perceptive observations by caregivers to interpret and respond to physiologic and behavioral responses or cues of each infant.¹³ Infant massage, when contingent on infant cues, is a developmentally supportive intervention aimed at decreasing infant stress. Despite the well-documented benefits of a unimodal

delivery of preterm infant massage (increased weight gain,¹⁴⁻²³ decreased pain,²⁴ improved digestion,¹⁵ decreased hospitalization length of stay,²⁵ decreased stress,^{26,28,37} and improved neurological, motor, and behavioral development²⁹⁻³²), many of the existing studies have varying protocols, are limited to healthy or convalescing preterm infants greater than or equal to 32 weeks postmenstrual age (PMA), and are not provided contingent on infant cues. Additionally, a consensus is lacking on the type of tactile stimulation that is appropriate for high-risk very preterm infants in a level III NICU.

Touch is one of the first senses to develop, at approximately 7 weeks gestation, and lays the foundation for the development of verbal communication, learning, regulation, and social interaction.³³⁻³⁴ However, not all types of touch in the NICU result in positive effects. Different types of touch can result in various types of infant responses. In fact, much of the touch that occurs in the NICU is related to procedural tasks and is often over-stimulating and/or unpleasant for very preterm infants, resulting in adverse physiologic and behavioral state responses.³⁵⁻⁴² Therefore, in an effort to minimize unpleasant or procedural touch, some NICUs have implemented a *minimal handling/touch* policy.⁴²⁻⁴³ These restrictive policies allow very preterm infants to continue to receive the necessary lifesaving procedural touch while missing out on *comforting* touch.⁴² This limited exposure of *comforting* touch inhibits at-risk very preterm infants from positive touch that could decrease stress and promote a fundamental foundation for future experiences. These vulnerable very preterm infants are at highest risk of developing adverse neurological outcomes and would likely benefit most from stress reducing touch methods.

In an effort to reduce stress and promote comfort, researchers have spent more than 30 years examining different types of *comforting* touch in hospitalized preterm infants that include a wide range of infant gestational and post-menstrual ages, various levels of acuity (with the majority being stable, healthy), and varying protocols. These *comforting* touch techniques include *massage*, both with and without kinesthetic activity (unimodal),^{19,26} or with a combined additional stimulation⁴⁴ (auditory, visual, and vestibular stimulation, also known as multimodal stimulation); *therapeutic touch*⁴⁵ (a non-touch, energy balancing therapy), *acupressure and Meridian massage*¹⁴ (an Eastern vital energy therapy using specific points for pressure, kneading, and rubbing); *gentle human touch*⁴⁶ (GHT, a still touch without stroking or massage) or *Yakson*⁴⁷ (a Korean touch method similar to GHT but includes some caressing); and *Touch and caressing-tender in caring TAC-TIC therapy*⁴⁸ (*gentle/light systematic stroking and caressing*). The aim of this review is to explore the research that examines the various *comforting* touch therapies used on hospitalized (e.g., level III NICU) infants born very preterm (≤ 30 weeks gestation) whose average PMA, at the time touch therapy commences, is no greater than 31 completed weeks gestation. The purpose of this review is to identify appropriate stress-reducing *comforting touch* techniques for physiologically fragile very preterm infants that can inform and provide guidance to neonatal clinicians and families.

Methods

A literature search was performed using electronic databases. Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Database, and Google Scholar were all searched using the keywords, *massage*, *touch*, or *tactile stimulation*, with *preterm infants*. The search was limited to articles of the English

language and humans from the year 1980 to present in each database. The initial search yielded 247 abstracts, including some duplication.

Selection of Eligible Studies

Initially the titles of each article were reviewed and abstracts were selected. Abstracts were then evaluated and selected based on their relevance to the aim of this review; specifically touch therapy studies including hospitalized very preterm infants that reported infant outcomes (as opposed to parent outcomes). A number of articles were excluded after an initial review of titles and abstracts. Out of the remaining 225 abstracts reviewed, 78 articles were chosen to evaluate for use. The reference lists of the articles were also considered as a mechanism for increasing the depth and breadth of the discussion. After initial review of the articles, detailed exclusion criteria were established in order to meet the aim of the review (Table1).

Eleven published studies (Table 2) evaluated *comforting* touch and supplemental stimulation in infants whose average GA was equal to or less than 30 weeks and whose average PMA at the time of post-natal touch delivery was equal to or less than 31 weeks and were in a level III NICU. The term supplemental stimulation is used to describe the study⁵⁴ whose purpose was to observe infant responses to tactile stimulation rather than providing touch with the intention of promoting comfort. The study selection process is outlined in Figure 1.

Of the eleven studies, two studies evaluated infant massage,^{25,31} five studies evaluated GHT,^{46,49-52} two studies evaluated *Touch and caressing-tender in caring* (TAC-TIC) therapy,^{48,53} one study evaluated social stimulation including touch,⁵⁴ and one study evaluated therapeutic touch.⁴⁵ A range of study methodologies were reviewed,

including randomized controlled trials (RCT),^{25,45,49-50,52} follow-up outcomes of these RCT,^{31,51} pre-test/post-test time series interrupted design,^{48,53} a quasi-experimental,⁴⁶ and an observational, counter-balanced across session and infants design.⁵⁴ Of the eleven studies, two were reported as pilot designs.^{45,49} Included studies are summarized in Table 2.

FINDINGS

Various types of touch have been explored in infants born very preterm. The methodologies of the existing studies differ in their type of touch, frequency, duration, timing, pressure, sequence, and contingency on infant cues. Nevertheless, many of the existing touch studies suggest that these high-risk very preterm infants have positive stress-reducing effects. For the purpose of this review, four different types of *comforting* touch and one type of supplemental stimulation have been selected and examined.

Infant Massage

Studies examining the effectiveness of preterm infant massage have been reported for more than 35 years. Unfortunately, the results of the existing infant massage studies are inconsistent and difficult to compare because of a general lack of a consistent operational definition, varying protocols (the types of pressures, amounts, timing of the interventions, kinesthetic component, unimodal or multimodal) and the inclusion of subjects of varying GAs, levels of acuity (morbidity) and PMA at timing of the massage intervention. The majority of preterm infant massage literature has been conducted in healthy or convalescing preterm patients who no longer require intensive care services. For the purpose of this review, massage studies were included if the infants were in a

level III NICU and their average GA (≤ 30 weeks) and PMA at the time of post-natal touch delivery (≤ 31 weeks) met the inclusion criteria.

While multiple infant massage studies have included infants born at less than 32 weeks gestation, only two massage studies met the inclusion criteria of this review for early postnatal touch commencement (PMA equal to or less than of 31 weeks gestation). Both studies used the same patient population. Mendes and Procianoy²⁵ examined short-term benefits of infant massage, while Procianoy and colleagues³¹ examined long-term neurodevelopmental outcomes at two years of age. Mendes and Procianoy²⁵ conducted a RCT in a Brazilian NICU to examine the effects of a maternal delivered tactile-kinesthetic massage therapy on very preterm infants within 48 hours of life and until hospital discharge. Mothers from both groups provided skin-to-skin care. There were no demographic differences between the two groups, including GA, PMA, birth weight, and severity of illness. Mendes and Procianoy²⁵ examined the combined effects of stroking with kinesthetic (passive movement or range or motion) stimulation that lasted 15 minutes and was delivered 4 times per day. The intervention group went home 7 days sooner; and experienced significantly less late-onset sepsis. No difference in growth parameters between the two groups were observed, possibly due to the fact that all infants were held skin-to-skin.

Mendes and Procianoy²⁵ instructed mothers to perform one stage at a time and to observe the cues from her babies (tolerance or excessive stimulation), keep the babies in supine position, with stretched limbs close to the body and perform the kinesthetic stimulation to one limb at a time. Tactile stimulation was provided to specified areas of the face and descended to the external side of the upper and lower limbs using moderate

pressure. The kinesthetic stimulation consisted of passive exercise (flexion and extension) of upper and lower limbs, one limb at a time and up to three times at each articulation (wrist, elbow, ankle and knee). This protocol is different from many of the infant massage studies conducted in older and healthier infants that require frequent repositioning (moving from prone to supine back to prone) during the kinesthetic (passive range of motion) activity phase.²⁰ Findings from this study suggest that some infants born very preterm can tolerate a modified tactile-kinesthetic maternal delivered massage within the first few days of life. However, it is unclear whether or not the investigators phased in the various strokes and kinesthetic activity over time or whether the infant was able to tolerate it from the beginning and throughout their hospitalization.

Studies examining long-term effects of infant massage on infants born very preterm are lacking. Therefore, using the same patient population as Mendes and Procianoy,²⁵ a follow-up study was conducted by Procianoy and colleagues³¹ to examine the effects of a maternal-delivered massage therapy on neurodevelopmental outcomes at two years corrected age on very preterm infants. Findings at two years corrected age showed no difference between groups in respect to weight, length, head circumference, and overall growth rate. However, there were differences between groups in mean Mental Development Index (MDI) as reported on the Bayley Scales of Infant Development second edition (BSID-II). The authors concluded that continuous physical contact of tactile and kinesthetic stimuli plus skin-to-skin care improves cognition in infants born very preterm.

Out of the eleven studies examined in this review, these infant massage studies^{25,31} were the only studies that evaluated the effects of a maternal-delivered

comforting touch technique, resulting in a different person delivering the technique throughout the intervention. In order to protect the fidelity or the compliance of the intervention, one of the investigators met regularly with the mothers in the intervention group every 48 hours to assure that they were performing the intervention as instructed. Another distinguishing feature of these two infant massage studies^{25,31} is that participants in both groups also received skin-to-skin care, possibly explaining why there were no more differences in outcomes between the two groups.

Unlike the other studies in this review, Mendes and colleagues were able to demonstrate both short-²⁵ and long-term³¹ beneficial outcomes; however there was a lack of information regarding a specific infant-driven massage protocol. Mothers were taught to observe for over-stimulating stress signs but there is no description of whether or not the mothers stopped or modified the massage based on each infant's physiological or behavioral cues. No specific criteria are listed as to whether or not the massage was modified or terminated based on infant response cues, both physiological and behavioral. By these reports, it is unclear whether any infants did not tolerate the massage intervention. In an effort to replicate these infant massage studies, it would be useful for future investigators to know whether the infants displayed sustained tachycardia, persistent apnea, or persistent behavioral stress cues. In addition, it would also be helpful to know the infant's behavioral state prior to commencing massage, during, and post massage intervention; specifically whether the infants were in a quiet sleep, active sleep, alert, fussy, or crying state. It is also unclear whether the massage was solely delivered based on timing (at the convenience of the person delivering the massage) or based on the infant's behavioral state and cues.

Gentle Human Touch

Gentle human touch (GHT) is still, or contained, gentle touch without stroking, rubbing, or passive movement.^{46,49-52} GHT is a skin-to-skin touch contact technique designed specifically for physiologically fragile infants. Jay⁴⁶ conducted a quasi-experimental and observational study examining the physiological and behavioral effects of GHT in one of the first studies to evaluate GHT in medically fragile very preterm infants who were intubated and mechanically ventilated. Jay⁴⁶ provided GHT to thirteen very preterm infants by placing one hand on the head of the infant and the other on its abdomen for 12 minutes, 4 times per day, for 10 days, commencing when the infants were less than 96 hours of age. Each of the 13 infants received a total of 48 minutes of GHT per day. Infants who received GHT had higher hematocrit levels, resulting in fewer blood transfusions, and lower oxygen requirement over time, which appeared to be clinically significant compared to infants in a matched control group. However, there were no differences between groups for temperature range, weight gain, tolerance of feedings, or complications. More positive behavioral outcomes were reported in the experimental group, including fewer startle responses, decreased overall activity with observable quieting during GHT, and open hand positioning suggesting a more relaxed infant state over time.

Jay's⁴⁶ study described a fairly detailed method of GHT delivery and provided descriptive infant behavioral responses, however a detailed protocol describing a plan to modify or terminate the GHT intervention based on infant physiological or behavioral cues was not presented. Behavioral cues were measured during the intervention but there is no baseline behavioral state reported prior to the initiation of GHT. Therefore, it is

difficult to determine whether or not GHT delivery was based on infant cues, even though infant behaviors were observed.

Additional GHT studies have been conducted by Harrison and colleagues.⁴⁹⁻⁵² Preterm infants enrolled in these studies⁴⁹⁻⁵² ranged from 27 – 33 weeks GA, with the touch intervention commencing 6 to 9 days post birth. Similar to Jay's⁴⁶ study, these GHT studies⁴⁹⁻⁵² used a trained research nurse or occupational therapist who placed one hand on the infant's head and one hand on the lower back and buttocks for 10 to 20 minutes, ranging from 1 to 3 times per day, for 5 to 10 days.

Gentle human touch studies conducted by Harrison and colleagues used an infant-driven detailed protocol based on each infant's physiologic distress response (HR <100 BPM or >200 BPM for 12 seconds or more, or arterial OS levels <90% for longer than 30 seconds).⁴⁹⁻⁵¹ In the largest study of 84 PT infants (42 in the GHT group), 19% of the infants in the GHT group had to have one or more GHT sessions terminated early because of decreased heart rate or oxygen saturations values.⁵⁰ The investigators noted that these infants were of lower GAs and birth weight and had higher morbidity levels compared to infants who did not require early termination of the GHT sessions. Suggesting the need for continuous and systematic assessment of the type, amount, and timing of the touch intervention based on the physiologic stability and behavioral responses of each very preterm infant. Findings from these GHT studies^{49-50,52} revealed no significant differences in mean heart rate levels when investigators compared baseline (B), touch (T), and post-touch (PT) phases. Although significant decreases in oxygen saturations were observed from B to PT and T to PT, the differences in the means during these phases were not clinically significant.⁵⁰ Levels of motor activity, behavioral

distress, and modified behavioral distress all decreased when compared with B and PT.⁴⁹⁻
^{50,52} No differences between infants in both groups were noted for weight gain, morbidity scores, or hospital lengths of stay in infants who received GHT when compared to controls.^{49,52}

Harrison and colleagues⁵¹ conducted a separate regression analyses on 42 infants who received GHT to examine the level of change from baseline to touch. The purpose of the analyses was to identify potential factors related to physiological and behavioral responses to individual GHT session that could help predict when infants may have problems tolerating GHT. The findings from these regression analyses suggest that baseline behavioral state and baseline levels of motor activity, no movement, and behavioral distress were the most significant predictors of change from B to T phases on the nine dependent variables that were examined. However, the amount of variation in the dependent variables that was explained by the independent variables in the analyses was relatively small, ranging from 1.2% to 8.6%. For instance, very preterm infants who were more active or distressed at baseline had increased levels of REM sleep and a decreased heart rate suggesting that GHT had a relaxing or calming effect. On the contrary, very preterm infants with higher baseline levels of quiet sleep were associated with increased levels of REM sleep, active sleep, motor activity, and heart rate, and with decreased levels of modified behavioral distress suggesting that GHT may have aroused infants who were already in a quiet state. Infants with higher morbidity scores were associated with decreased levels of REM sleep and increased levels of motor activity suggesting that sicker infants became more agitated during the touch intervention.⁵¹

Unlike many of the other touch studies examined in this review, these GHT studies⁴⁹⁻⁵² provided a detailed infant-driven protocol based on infant cues. Harrison and colleagues⁵¹ findings suggest that very preterm infants in a distressed or awakened state prior to GHT delivery appear to have more comforting benefits as defined by a decrease in heart rate, more REM sleep, less motor activity, and less behavioral stress signs. Findings from these existing GHT studies^{46, 49-52} suggest that GHT may have a relaxing or calming effect on high-risk very preterm infants' physiologic and behavioral responses and reiterates the importance of continuous individualized assessment prior to, during, and post touch intervention. These GHT findings support the belief that *comforting* touch should not be commenced on a timed schedule, but rather infant-driven, when the infant demonstrates distress or arousing cues.

Touch and Caressing-tender in Caring (TAC-TIC) Therapy

Touch and caressing-tender in caring (TAC-TIC) therapy is a unimodal stimulation approach employing systematic stroking to preterm infants in intensive care.⁴⁸ TAC-TIC therapy is a *gentle/light* systematic and rhythmic stroking cutaneous stimulation that follows a cephalocaudal (head to toe) pattern. Each movement and stroke are given at the same speed with equal proportions of time allowed between each maneuver. One hand is always in contact with the infant's body to maintain continuity.⁴⁸

Adamson-Macedo and colleagues⁴⁸ and de Roiste and Bushnell⁵³ conducted interrupted pre-test/post-test time series studies to evaluate the effects of TAC-TIC therapy on 24 high-risk ventilated very preterm infants in a level III NICU in London. All participants received a maximum of two TAC-TIC sessions daily. TAC-TIC therapy started within the 3rd day of life. Investigators used a systematic sequence of stroking

movements, lasting 3 to 4 minutes, covering the whole of the head and body using gentleness, rhythm, equilibrium, and continuity of touch. Infants were not repositioned during the intervention. Heart rate,⁵³ respiratory rate,⁵³ and transcutaneous arterial oxygen tension (TcPO₂)^{48,53} were measured before, during, and after TAC-TIC therapy delivery. Findings supported the hypothesis that TAC-TIC therapy does not cause a fall in TcPO₂ during or after TAC-TIC therapy delivery.^{48,53} Results also demonstrated a decreased heart rate and an increased respiratory rate from the “during to after” stroking phases.⁵³ The investigators concluded that these high-risk ventilated infants who received TAC-TIC therapy appeared to have no harmful effects as reflected in the absence of a significant heart rate increase or TcPO₂ drop. The investigators also concluded that the post-stroking respiratory rate rise (possibly indicating stress) was accompanied by a decrease in heart rate (indicating less distress), limiting the ability to draw a definitive conclusion. However, the rise of respiratory rate and decline in heart rate are likely reflective of these infants’ extreme immature central nervous system and their inability to organize and regulate state and physiologic behaviors.⁵³

These investigators employed a *comforting* touch technique, TAC-TIC therapy, during the first week of postnatal life in a small convenience sample of high-risk ventilated very preterm infants without adverse effects physiologic effects. The investigators did not report infant behavioral states prior to, during, or post TAC-TIC therapy delivery. Again, these studies lack a description of a detailed infant-driven protocol so it’s unclear as to whether the TAC-TIC therapy needed to be modified or terminated in any of the participants. Only immediate physiologic outcomes were

evaluated and no long-term effects have been studied using this technique in this population of infants.

Social Stimulation

In an effort to further understand very preterm infants' response to sensory stimulation, specifically talking and touching, Oehler⁵⁴ conducted a counter-balanced across session study in 15 very preterm NICU patients. This study is different from other touch studies discussed in this review because the intent was not to provide a *comforting* or soothing touch but rather describe the development of the individual preterm infant's responsiveness to sensory stimulation, specifically talking, touching, and a combination of talking and touching. A female nurse (10 different nurses provided the stimulation) delivered the talking stimulation and spoke in a low, soft, "soothing" voice. The same female nurse successively stroked with one hand the infant's legs, arms, chest or back (depending on whether the infant was prone or supine), and head for 10 seconds, repeating the sequence for a total of 80 seconds. The study period began when participants were on average 28 weeks PMA and continued until 37 weeks PMA. In an effort to control for severity of illness and under nutrition (as defined by head growth), subjects were divided into three groups based on their degree of illness and head growth during the stay in the intensive care nursery. Body movement, eye movement, and a miscellaneous category (yawn, grimace, tongue protrusion, cry, smile, hand-to-mouth activity, and suck) were assessed simultaneously at 10-second intervals. Infant heart rate was measured as the fourth dependent variable.

Repeated measures analyses of variance were performed to assess the effects of illness, age, and stimulus comparing the pre-stimulus period to the stimulus condition.

Findings showed that infants as young as 30 weeks PMA displayed different response patterns to being talked to compared to being touched. Infants, who received auditory stimulation through periods of talking, opened and moved their eyes more than during the pre-stimulus period. These same very preterm infants responded differently to being touched by demonstrating more body movement. Additionally, the combination of talking and touching produced responses similar to touching alone, more body movement. Infants with higher severity of illness scores showed more avoidance behaviors during all stimulus conditions and the most avoidance during the combination of talking and touching, suggesting that stimulation can be aversive in these vulnerable infants. Interestingly, there was no significant change in infant heart rate for any stimulus condition.

Oehler's⁵⁴ study is the only one within this review that stratified infants based on their severity of illness scores and head circumference. Stratifying based on the infant's degree of illness is important because very preterm infants with major medical factors and a high severity of illness will likely be limited in their ability to regulate incoming sensory stimulation. Likewise, infants with restricted head growth are more likely to have poorer neurodevelopmental outcomes.⁵⁴ The investigator concluded that infants with higher severity of illness scores and more restricted head growth demonstrated more avoidance behaviors, especially during the combination of talking and touching, suggesting only one mode of stimulation should be delivered at a time. The investigator also concluded that appropriate or enriching stimulation still needs to be identified or defined in this group of very preterm ill infants and that nurses should exercise caution in touching and talking until further scientific research is done.

Similar to the very preterm infant massage studies,^{25,31} multiple people delivered the stimulation which may have affected the uniformity of the stimulation delivered. Like many of the studies in this review,^{45-46,48-49,52-53} the sample is small and the need for additional research to further substantiate the findings are needed. Additionally, the study did not address the infant's pre-stimulus behavioral state nor was there an attempt to control for infant behavioral state during the procedure.

Therapeutic Touch

Therapeutic Touch is a complementary therapy that does not require physical contact; it's a method of balancing and increasing the body's energy to promote healing.⁵⁵ Therapeutic Touch is intended for infants who are more physiologically fragile and not capable of integrating and organizing behavior.

Whitely and Rich⁴⁵ conducted a double blinded RCT pilot to explore whether or not Therapeutic Touch can be safely employed in hospitalized preterm infants to reduce stress. Ten infants were enrolled and randomly assigned to an intervention or control group. Each group of infants received either Therapeutic Touch or no Therapeutic Touch for 5 minutes on 3 consecutive days at the same time of day. Infants in the intervention group were positioned on the right side, nested for comfort, and Therapeutic Touch was modified by time and intensity to suit the sensitivity of each infant. Heart period variability (HPV) was measured 5 minutes before, during, and after the treatment phase. Results revealed a significant greater variability in the low-to-high-frequency ratio in the Therapeutic Touch group than in the No Therapeutic Touch group suggesting a more relaxed response in infants who received Therapeutic Touch. Additional findings indicated no adverse events (e.g., decreased oxygen saturations and increase in apneic

episodes) in the Therapeutic Touch group compared to the control group. These findings suggest that Therapeutic Touch can be tolerated in physiologically fragile very preterm infants and may promote infant stability.

This Therapeutic Touch study⁴⁵ is different from many of the studies examined in this review in that it provided a non-physical touch method to decrease stress and foster homeostasis. The investigators' main purpose was to demonstrate that Therapeutic Touch could be delivered without adverse effects and could reduce stress in physiologically fragile very preterm infants. Therapeutic Touch is infant-driven as the investigators report that the time and intensity of the intervention was modified based on each infant's physiological cues. However, the investigators did not report if the intervention needed to be modified or terminated. Since both physiological and behavioral indices are needed to best describe preterm infants' stress response,⁵⁶ the authors did not comment on behavioral states prior to, during, or post Therapeutic Touch.

Discussion

Similar to the massage studies in older and healthier preterm infants, many of the studies in this review have employed varying types of *comforting* and supplemental touch including noncontact touch,⁴⁵ still touch,^{46,49-52} light stroking touch,^{48,53} and moderate stroking with kinesthetic activity.^{25,31} The duration of each touch session (ranging from 3 minutes to 20 minutes per session), the number of times per day (1 to 4 times/day), the number of total days (3 days through total hospital stay), and the amount of pressure (moderate versus light) all varied. A systematic, infant-driven (contingent on both physiologic and behavioral cues) *comforting* touch method is needed that is reproducible for practice and research and provides direction to clinicians, families, and researchers on

the quality, quantity, timing, pressure, and use of strokes. These studies are also needed as the foundation to future studies designed to reveal the cellular mechanisms underlying either the negative or positive effects of massage techniques in preterm infants, since such knowledge might lead into new therapeutic approaches beneficial to not only preterm but any infant.

In general, the majority of the existing studies in this review lack adequate sample size to reliably predict whether or not *comforting* touch is stress reducing in very preterm infants within a level III NICU.^{45-46,48-49,52-53} Only two^{25,31} of the 11 studies in this review examined both short- and long-term effects of *comforting* touch with the remaining studies examining immediate behavioral and physiological outcomes. Of these two studies, only one examined the neurodevelopmental impact of *comforting* touch.³¹ Evidence from this review is inadequate to predict both short- and long-term effects of *comforting* touch. However, based on this review, very preterm infants within a level III NICU are able to display physiological and/or behavioral responses to *comforting* touch^{45,48-49,50-53} and supplemental stimulation.⁵⁴ Within this review, multiple touch^{25,31,,46,49,50,51,52,,48,53} and non-touch⁴⁵ methods have been employed without adverse effects in these at-risk infants. Nevertheless, only one⁵⁰ study demonstrated that infants of lower GA were less likely to tolerate *comforting* touch and two^{50,54} studies showed that infants with higher morbidity levels were less likely to tolerate *comforting*⁵⁰ or supplemental⁵⁴ touch strategies. Importantly, based on this review, physiologic stability and infant behavioral state should be astutely assessed prior to^{45,50-52}, during⁴⁵⁻⁵⁰⁻⁵², and post touch delivery.^{45-46,50-52}

Based on this review, neonatal caregivers and families can conclude that these types of *comforting* touch strategies can be employed without adverse effects in some physiologically fragile very preterm infants (without high morbidity levels) within the first few days of post-natal life.^{25,31,45-46,48-53} Additionally, the evidence from this review suggests that these *comforting* touch strategies may have soothing, immediate effects as evidenced by improved physiological and/or behavioral responses.^{45-46,48-53} Furthermore, the findings from this review support that physiologically fragile very preterm infants should not *only* be limited to non-contact Therapeutic Touch. The act of physical skin contact, with the intent of reducing stress, appears to promote well-being by improving physiologic stability and decreasing behavioral distress.^{46, 48-50,52-53} Based on this review, stroking even appears to be tolerated in a select population of very preterm infants and appears to provide both short-^{25,48,53} and long-term beneficial effects.³¹ However, not all very preterm ill infants can tolerate all types of tactile stimulation within the first two weeks of life.⁵⁴ Especially those infants with higher morbidity levels^{50,54} and possibly some infants of lower GA.⁵⁰

Still, caution should be used in extrapolating findings from this review to all very preterm infants within the NICU. Many of these studies have methodological limitations including small sample sizes, convenience sampling, retrospective controls, and the lack of a control group. It's important for neonatal caregivers to recognize that all very preterm infants within a level III NICU cannot tolerate all types of touch and each infant should be astutely observed based on his severity of illness, GA, physiologic stability, and behavioral state prior to, during, and post touch delivery. Further research is needed to provide specific recommendations on the type of very preterm infants that would most

likely benefit from *comforting* touch, specifically in relation to each infant's gestational and post-menstrual ages and levels of morbidity.

Thoughtful administration of the type (quality), the timing, and the amount (quantity) of *comforting* touch should be considered and should not be administered based on a timed interval but rather contingent on infant cues. Based on this review, very preterm infants in an active or distress state will likely benefit more than infants who are resting quietly and should otherwise not be disturbed.⁵¹ Hence, *comforting* touch delivery to at-risk infants needs to be individualized, mindful, and infant-driven. Neonatal care providers and parents need to be trained to astutely observe each infant's cues to determine the most appropriate quality and quantity of *comforting* touch while respecting the potential for providing sensory overstimulation.

Conclusion

This review indicates that the current evidence on *comforting* touch for very preterm infants is limited and the published studies have utilized small sample sizes. Caution should be taken in generalizing the findings presented in this review. Nonetheless, these findings do indicate that further *comforting* touch investigations in hospitalized very preterm infants are needed. More rigorous *comforting* touch research is needed with larger, randomized; systematic methodological designs to determine its short- and long-term effects. Specifically, the use of *comforting* touch as an intervention to reduce stress and promote comfort during painful procedures and its effect on preterm infant brain growth and neurobehavioral development. Research should not only focus on infant outcomes but should also evaluate the effectiveness of parent-delivered *comforting*

touch and the potential impact on parent mental/emotional health and parent-infant synchrony.

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Figure 2.1: Flowchart of Study Selection

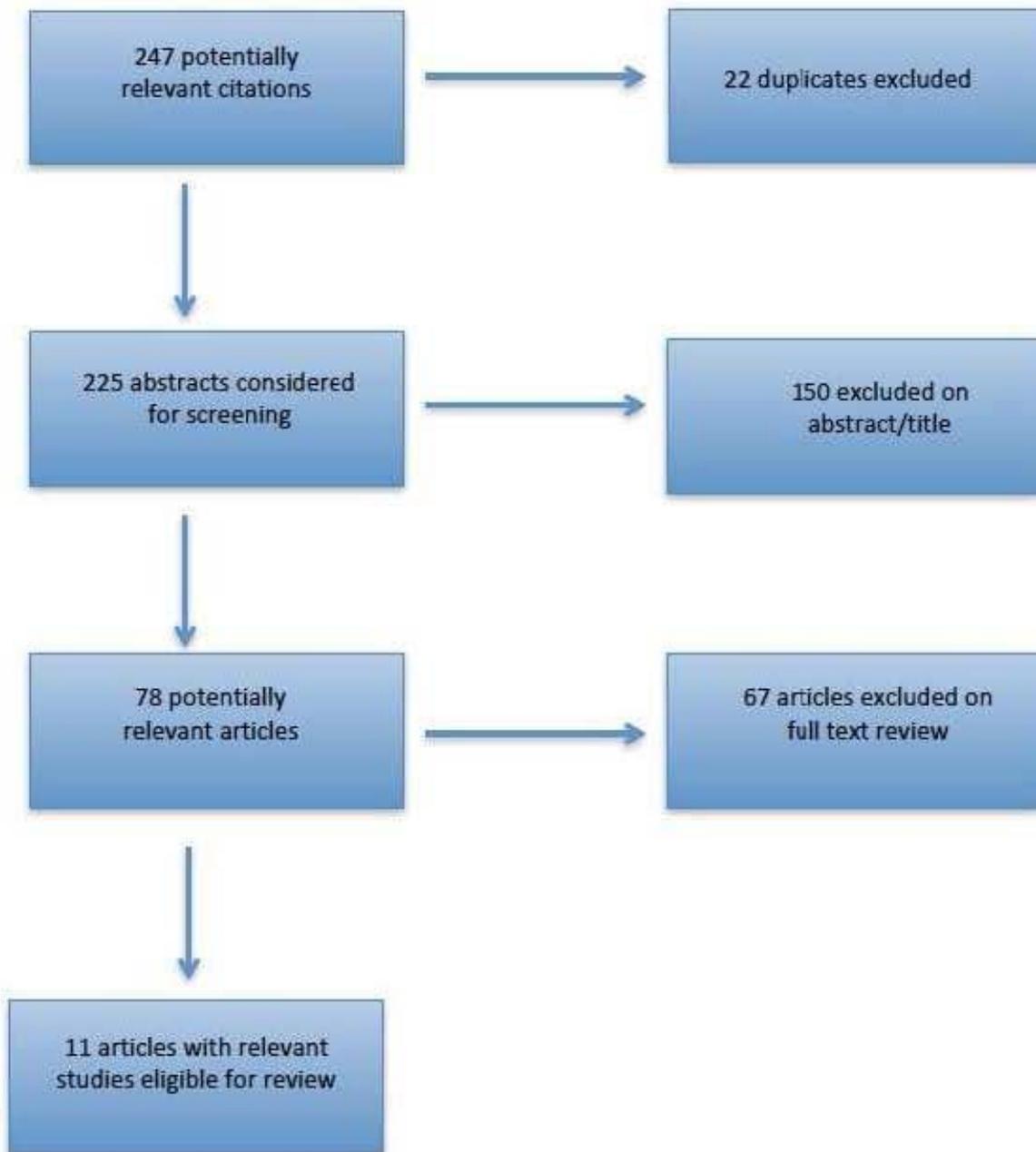


Table 2.1:

<i>Exclusion Criteria for Articles Deemed Ineligible for Review</i>
<p>Non-relevant Types of Touch Therapies:</p> <ul style="list-style-type: none">• Kangaroo care• Facilitated tuck• Multi-modal stimulation• Oral-motor stimulation• Mechanical vibration• Limited touch targeted to only one area of the body (e.g., arm only, leg only, etc.) <p>Population Not Relevant:</p> <ul style="list-style-type: none">• Participants whose average gestational age (GA) was greater than 30 weeks• Participants whose average post-menstrual age (PMA) was greater than 31 weeks at time of touch commencement <i>or</i> whose PMA was not adequately described or reported• Participants who were deemed <i>healthy or convalescing</i> (e.g., not requiring additional interventions other than heat source and nutrition) <p>Primary Outcome Measures Not Relevant:</p> <ul style="list-style-type: none">• Primary outcome not relevant to infant physiological or behavioral outcomes (e.g., parent responses or effects of different types of emollients) <p>No Intervention:</p> <ul style="list-style-type: none">• Single case study reports• Review articles

Table 2.2: Characteristics of Included Studies

Author/Year Published/Location	Purpose	Design/Setting	Participants' GA and PMA (at time of touch delivery)	Measurement	Results
Mendes and Procianoy ²⁵ (2008) <i>Location: Brazil</i>	To study the effect of maternal massage therapy on hospital stay in very-low-birth-weight infants who were already submitted to skin-to-skin care.	Blinded RCT All infants also received Skin-to-skin care.	104 infants (52/group) <=32 weeks Mean GA 29.7 weeks. Mean PMA: 30 weeks.	Primary outcome: Hospital Length of Stay Secondary outcomes: Growth <ul style="list-style-type: none"> • Weight • Head circumference • Length • Growth rate • Rohrer's Ponderal Index Age at partial/total oral feedings started Occurrence of late onset sepsis--> blood and/or CSF cultures, presence of NEC and BPD	IG discharged earlier—VLBW with higher probability of earlier hospital discharge, 1.85 (CI 95%: 1.09 to 3.13; $p=0.023$) times higher than the CG. Incidence of late-onset sepsis was significantly lower in the IG (IG: 10.8%, n=5; CG: 38.3%, n=18; $p=0.005$). No significant difference between groups for all other variables.
Procianoy et al. ³¹ (2010) <i>Location: Brazil</i>	To examine the effects of a mother-delivered massage therapy on neurodevelopment outcomes at two years corrected age.	Same as Mendes and Procianoy ²⁵ (2008). Follow-up was conducted at a University-based Hospital	Same as Mendes and Procianoy ²⁵ (2008) Follow-up performed at 2 years corrected age.	BSID-II Anthropometric measures: <ul style="list-style-type: none"> • Weight • Head circumference • Length • Weight grams/month • Head circumference (cm/month) • Length (cm/month) 	BSID-II at 2 years corrected age: <ul style="list-style-type: none"> • PDI—no differences between both groups • MDI-higher in intervention group compared to control ($p=0.035$) No significant difference between groups for anthropomorphic variables.
Jay ⁴⁶ (1982) <i>Location: United States</i>	Primary: To test the effects of GHT on the clinical improvement of mechanically ventilated very-short-gestation infants. Secondary: To examine the behavioral responses of very-short-gestation	Quasi-experimental Design. Retrospectively selected and matched CG. Observational data from IG only.	26 mechanically ventilated very PT infants Mean GA 29.53 weeks Mean PMA: <31 weeks* <i>*PMA not reported.</i> <i>GHT commenced within 96 hours of life resulting</i>	Physiological/Clinical data: Daily weight Daily temperature range Daily oxygen requirement Frequency of apnea and bradycardia Daily laboratory blood studies Daily fluid intake (advancement to and tolerance of oral nutrients)	Physiologic Outcomes: IG: higher hematocrit levels, ($p=0.05$) resulting in fewer blood transfusions and a lower oxygen requirement over time, although only marginally statistically significant ($p=0.06$) but appeared to be clinically significant. Behavioral outcomes: Observational

	infants to GHT.		<i>in infants averaging 31 weeks PMA or less.</i> IG: (n = 13) CG: (n = 13)	Total length of hospital stay Behavioral data (only for IG): Startle responses Non-startle responses Fine hand movements	assessment of IG only, supported a more relaxed state over time.
Harrison et al. ⁴⁹ (1996) <i>Location:</i> United States	To evaluate the effects of GHT on very preterm infants from day 7 to day 12 of life	RCT, pilot study.	30 very PT infants Mean GA 30.07 weeks. Mean PMA: 27-28 weeks (n = 2) 29-31 weeks (n = 5) 32-33 weeks (n = 8)	HR O2 Sats Activity levels Behavioral signs of distress Behavioral state Morbidity status (Neonatal Morbidity Scale—NMS) Behavioral organization	Significantly less: <ul style="list-style-type: none"> • Active sleep (p=0.008) • Motor activity (p=0.003) • Behavioral distress (p=0.033) during GHT sessions compared to baseline or post-GHT periods. Infants in the IG received more days of phototherapy (p=0.03) than CG infants.
Harrison et al. ⁵⁰ (2000) <i>Location:</i> United States	To evaluate the effects of a gentle human touch (GHT) intervention on preterm infants at 1 to 3 weeks of age	RCT	84 infants IG: (n=42) CG: (n=42) Mean GA: 30.7 weeks Sample stratified to 3 GA groups 27-28 weeks (n = 20) 29-31 weeks (n = 24) 32-33 weeks (n = 40) **Data not analyzed separately Mean PMA: 31.8 weeks* *Specific PMA not reported but since GHT delivery commenced within the 1 st week of life, the PMA averages approximately 31.8	HR Oxygen saturations Activity levels Behavioral signs of distress Behavioral state Morbidity status (Neonatal Morbidity Scale (NMS) Behavioral organization (Brazelton Neonatal Behavioral Assessment Scale) The following were measured at baseline, during GHT and post GHT: Physiologic Behavioral signs of distress Motor activity Behavioral state	A slight decrease in O2 sats across the 3 phases—baseline, treatment and post-treatment (p<0.001), although not clinically significant because they were not abnormal values. Significantly lower levels of: <ul style="list-style-type: none"> • Active sleep, (p =0.002), • Motor activity (p =0.001) • Behavioral distress (p =0.001) during GHT compared to baseline and post-touch phases.

			weeks.		
Harrison et al. ⁵¹ (2000) <i>Location:</i> United States	To identify the relationship between preterm infants' physiological and behavioral responses to a gentle human touch (GHT) intervention and developmental, health status, behavioral, and environmental variables.	Same as Harrison et al. ⁵⁰ (2000) (follow-up analyses)	Same as Harrison et al. ⁵⁰ (2000)	<p>Separate regression analyses were conducted for the level of change (GHT intervention minus Baseline values) on the following:</p> <p>Dependent Variables:</p> <ul style="list-style-type: none"> • O₂ Sats • HR • Motor Activity • Behavioral Distress • Quiet Sleep • Active Sleep • REM Sleep <p>Independent variables (possible predictors of responses to the GHT):</p> <ul style="list-style-type: none"> • GA • Birthweight • Health Status Indicators • Behavioral Variables • Environmental Variables 	<p>The strongest predictors of Change in Levels of Quiet Sleep during baseline include:</p> <ul style="list-style-type: none"> • Levels of REM sleep (*.49) • Levels of no movement during baseline (*-.38) <p>The highest predictive power of Changes in Levels of REM Sleep were baseline levels of:</p> <ul style="list-style-type: none"> • Quiet Sleep (.73) • No Movement (.36) • Motor Activity (.35) • Behavioral Distress (.31). <p>Significant predictors of Changes in Active Sleep were baseline levels of:</p> <ul style="list-style-type: none"> • REM Sleep (.79) • Quiet Sleep (.62) <p>Highest predictive power of Changes in Levels of Motor Activity were baseline level of:</p> <ul style="list-style-type: none"> • No Movement (.49) • REM sleep (.35) <p>The largest predictive power of Changes in Levels of Behavioral Distress were baseline levels of:</p> <ul style="list-style-type: none"> • Modified Behavioral Distress (-.40) • No Movement (.37) <p>The most significant predictor of Changes in Levels of Modified Behavioral Distress were baseline levels of:</p> <ul style="list-style-type: none"> • Behavioral Distress (-.66) <p>The most significant predictor of Changes in Levels of No Movement were baseline levels of:</p> <ul style="list-style-type: none"> • Motor Activity (.28)

					<p>The most significant predictor of Changes in Levels of Heart Rate were baseline level of:</p> <ul style="list-style-type: none"> • Quiet Sleep (1.14) • REM Sleep (.11) • Higher GA <p>Changes in Levels of O₂ Saturation (significant factor was the baseline of):</p> <ul style="list-style-type: none"> • Motor Activity (.16).
<p>Modrcin-Talbott et al.⁵² (2003)</p> <p><i>Location:</i> United States</p>	<p>Examine the physiological and behavioral effects of a gentle human touch nursing intervention on medically fragile preterm infants</p>	RCT	<p>20 infants between 27-32 weeks gestation were randomly assigned to each group IG: (n = 10) CG: (n = 10)</p> <p>Mean GA: 30.4 weeks Mean PMA: 31.4 weeks</p>	<p>Sleep states Behavioral activity (Neonatal Assessment Coding Sheet) HR O2 Sats</p>	<p>IG showed significantly less time in active sleep ($p = <0.05$) and the frequency of motor activity was less for the IG, which was approaching statistical significance ($p= 0.065$).</p>
<p>Adamson-Macedo et al.⁴⁸ (1994)</p> <p><i>Location:</i> England</p>	<p>To test the hypothesis that TAC-TIC therapy does not cause a fall in TcP02</p>	<p>A pre-test/post-test time series interrupted design, in three phases (before, during, and after touch therapy)</p>	<p>11 participants Mean GA 29.8 weeks Mean PMA 30 weeks</p> <p>Ventilated infants ranging from 2 to 8 days of age (M = 3rd day of life) when TAC-TIC therapy commenced.</p>	TcP02	<p>No significant falls in TcP02 ($p=0.32$) during or after application of the TAC-TIC therapy.</p>
<p>De Roiste and Bushnell⁵³ (2000)</p> <p><i>Location:</i> England</p>	<p>Purpose to examine the immediate physiological effects of systematic stroking on a sample of high-risk ventilated</p>	<p>A pre-test/post-test time series interrupted design, in three phases (before, during</p>	<p>13 very PT infants Mean GA: 29. 23 weeks Mean PMA: 30 weeks*</p>	<p>HR RR TcP02</p>	<p>HR: Decrease in heart rate from the “during to after” stroking phases ($p\leq 0.04$), but no changes from “before to during” phases or over the whole</p>

	preterms.	touch therapy, after touch therapy)	*Not reported but estimated at 30 weeks. Since intervention started within 3 to 9 days of birth.		“before to after” phases. RR: Increased from the “during to after” phases ($p<0.02$) there were no differences from “before to during” phases and “before to after” phases. TcP02: No changes seen in any phases.
Oehler ⁵⁴ (1985) <i>Location:</i> United States	To trace and describe the development of the preterm infant’s responsiveness to sensory stimuli, specifically talking and touching.	Observational, counter-balanced across sessions and infants design	15 participants Mean GA: 28 weeks Mean PMA: 29.5 *Not reported but estimated at 29.5 since the intervention occurred no later than 2 weeks after birth. Subjects separated by severity illness scores and head circumference: <ul style="list-style-type: none"> • Sickness index <60 and head circumference of at least 2.9 cm in 6 weeks ($n = 5$) • Sickness index >150 and head growth < 2.9 cm in 6 weeks ($n = 5$) • Sickness index > 60 but head growth of 2.9 cm or greater. ($n = 4$) **1 subject failed to fit	HR 3 sets of infant behaviors assessed simultaneously at 10-second intervals: <ul style="list-style-type: none"> • Body movement • Eye movement • Miscellaneous category (yawn, grimace, tongue protrusion, cry, smile, hand-to-mouth, and suck) 	Talking alone: More eye movement compared to pre-stimulus group ($p<0.001$) Touching alone: More body movement ($p<0.001$) Combined Talking and Touching: More body movement ($p<0.001$) Post-Hoc analysis revealed that the well group had significantly ($p<0.05$) more smiles and hand to mouth activity than the other 2 more groups with higher sickness indexes during touching, talk, and the combination of tactile touching and talking ($p<0.05$) Infants with higher illness scores had significantly more avoidance behaviors during talking ($p<0.05$) and twice as many avoidance behaviors during talking and touching than the well infants. The only effect of age was for infants with higher sickness indexes, increased smiles and hand-to-mouth activity with increasing age

			<i>in any of the groups and was dropped from analyses.</i>		No significant HR changes for any stimulus condition.
Whitely and Rich ⁴⁵ (2008) <i>Location:</i> Canada	To explore the hypothesis that non-touch therapy such as TT reduces stress to a clinically important degree and is safe to use in preterm infants.	A double-blinded, RCT, pilot study.	20 infants IG (<i>n</i> = 10) CG (<i>n</i> = 10) Mean GA: 27.33 weeks Mean PMA: 28.6 weeks	Primary Outcome: Physiologic stress: HPV (5 minutes before, during, and after the treatment phase). Secondary Outcome: Mean frequency of apnea and hypoxia (e.g. decreased O2 sats) to determine adverse events.	No difference in O2 sat levels and frequency of apneic episodes demonstrated in IG compared CG. Repeated-measures multivariate analysis of variance of HPV revealed differences in the interaction of group assignment with low-frequency, high-frequency, and low-to-high frequency ratio interaction ($F_{2,143}=8.076$, $p=0.000$) and for group, day, and low-to-high frequency ratio ($F_{2,288}=3.146$, $p=0.015$), and in the post-treatment time period ($F_{1,16}=6.259$, $p=0.024$), reflective of greater parasympathetic activity in IG.

Abbreviations: RCT, Randomized Controlled Trial; IG, Intervention Group; CG, Control Group; GA, Gestational Age; PMA, Post-Menstrual Age; CSF, Cerebral Spinal Fluid; NEC, Necrotizing Enterocolitis; BPD, Bronchopulmonary Dysplasia; BSID-II, Bayley Scales of Infant Development Second Edition; PDI, Psychomotor Developmental Index; MDI, Mental Developmental Index; VLBW, Very Low Birthweight; GHT, Gentle Human Touch; PT, Preterm; HR, Heart Rate; RR, Respiratory Rate; O2 Sats, Oxygen Saturations; TcP02, Transcutaneous Arterial Oxygen Tension; TT, Therapeutic Touch; HPV, Heart Period Variability

CHAPTER 3

THEORETICAL FRAMEWORK AND METHODS

This chapter is organized with a statement of the study design, the study's theoretical framework, a description of the subjects (the sample/setting, description of the protocol, human subject protection description and informed consent), the measures used to address the study's specific aims, the data management, and a description of the data analysis. This study began as a prospective pilot randomized controlled trial (RCT) with experimental and control groups to systematically test the cumulative effect of the M Technique in hospitalized very preterm infants. However, due to a dramatic decrease in admissions and census in the study's neonatal intensive care unit (NICU), retrospective cases were matched and a case-control design was used for the analysis.

Theoretical Framework

Developed from the discipline of psychology, the *Synactive Theory* of infant development is deductively derived from the systems, adaptation, and stress theory models (Als, 1982). Als' *Synactive Theory* is built upon Brazelton's earlier work and based on neurobehavioral and electrophysiological studies; the focus is on the dynamic, continuous interplay of hierarchically organized subsystems within the organism (Als & Gilkerson, 1997). The infant's behavior is seen as a continuous expression of brain function available for observation (Als, 1986). Preterm infants develop in an extra-uterine setting at a time when their brains are growing exponentially, more rapidly than at any other time throughout their life span. Their preterm brains are expecting a

protective *in utero* environment but instead are exposed to a noxious NICU environment that may lead to altered pathway development due to unexpected and overwhelming sensory experiences. The *Synactive Theory* of development has been used as a framework to decrease the disparity between the immature human brain's expectation and the infant's environmental experience (Als, 1986, 2009). Based on the *Synactive Theory*, each infant is astutely assessed for physiological and behavioral cues and then their individual environment is modified in an effort to mitigate stress.

Modification of the NICU environment is done through the application of neurodevelopmental supportive care strategies essential to improving neurological and behavioral outcomes. These supportive care strategies for very preterm infants include reducing exposure to noxious environmental stimulation while providing positive stimulation aimed at decreasing stress and reducing the gap between the *in utero* and NICU environments (Als et al., 2004; Als, 1986, 2009; Vandenberg, 2007). Therefore, the *Synactive Theory* provides a testable framework for the M Technique research in very preterm infants because it aims to ameliorate some of the negative neurological impact associated with prematurity (Als, 2009). Infants born very preterm have a wide range of complex conditions involving the interaction between multiple biological, genetic, epigenetic, and environmental risks. Figure 3.2 provides the visual constructs of the conceptual model that guides the investigation of this research project.

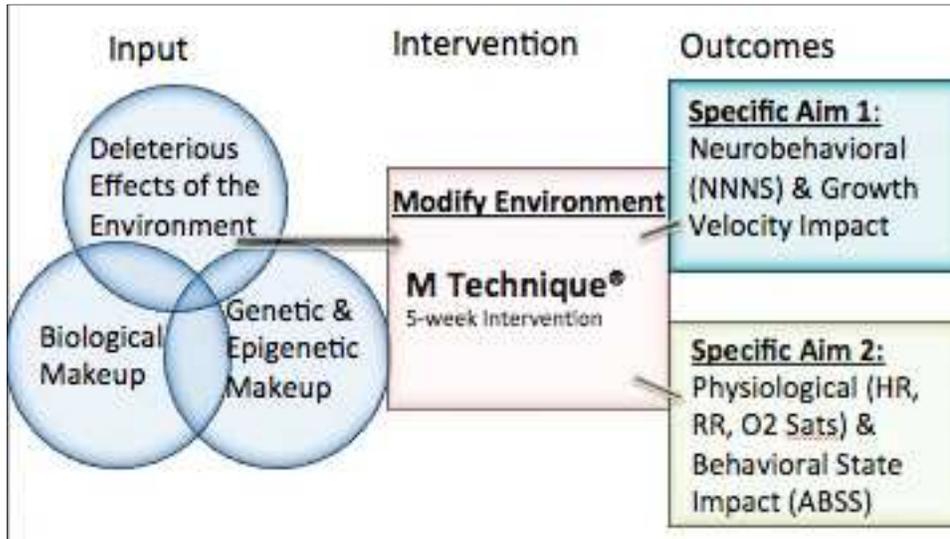


Figure 3.2. Conceptual Model

Methodology

Research Design

The study was conducted from September 2012 to January 2013 in the neonatal intensive care unit (NICU) of a 250-bed tertiary care academic pediatric setting. Ten very preterm infants (≥ 26 and < 30 weeks estimated gestational age [GA]) who received the M Technique were matched with 10 control infants for gestational age, race, and gender. Infants were prospectively randomly assigned to the intervention group to examine the effects of the M Technique on very preterm infants over 5 consecutive weeks. The study protocol began once the infants reached 30 weeks' postmenstrual age (PMA). Infant characteristics of interest were collected at enrollment and after the 5-week intervention.

Setting and Sample

St. Louis Children's Hospital is a 250-bed tertiary care academic pediatric hospital in the Midwest with a 75-bed NICU that admits approximately 750 babies annually. During 2010 and 2011, approximately 40 very preterm infants who met the inclusion criteria between ≥ 26 and < 30 weeks estimated GA were admitted to the NICU during a 2 month period. An attempt to recruit a sample of 20 male and female very preterm infants was made from September 2012 to January 2013. Following parental consent, eligible infants were randomized to the treatment or control groups. The randomization process used sequentially numbered, opaque sealed envelopes (SNOSE) that contained an index card with the word treatment or control (Doig & Simpson, 2005; Viera & Bangdiwala, 2007). Parents were provided the opportunity to select one of the envelopes that determined the infant's allocation. However, due to a dramatic decrease in the NICU admissions and census, only 13 very preterm infants were recruited and enrolled of which 10 were assigned to the intervention group. To properly control for this two-group comparison design, 10 matched very preterm infants were identified from a neurodevelopmental positioning study that was conducted the previous year, and this group served as the control group. This aforementioned neurodevelopmental study was a randomized study. Thus, this control group derived from a randomized study and properly matched to our intervention group provides a statistically robust control group to our study.

Typical power calculations were not applied because of the pilot design. This study provides the data to calculate an effect size for a future larger study. Twenty subjects were selected based on our previous M Technique feasibility study where 10

very preterm infants were recruited within a similar timeframe in an intervention group only. Potential subjects were identified within the first 5 to 7 days of age after consulting with the attending physician. A member of the research team approached the parents of eligible infants when the infants were nearing 30 weeks' PMA to provide informed consent. Parents were approached for informed consent together in a private setting. Inclusion criteria are (1) infants born ≥ 26 and < 30 weeks EGA (determined by Ballard), (2) 30 weeks PMA or less at time of M Technique delivery (appropriate for gestational age), and (3) no evidence of moderate to major brain injury (e.g. Grade II-IV intraventricular hemorrhage). Infants with septic shock, non-intact skin, respiratory failure (e.g., supplemental FiO₂ requirement $> 75\%$), moderate to severe brain injury (e.g. Grade II-IV intraventricular hemorrhage), persistent tachycardia, bradycardia or those deemed unstable as determined clinically by the attending physician, were excluded.

Procedure

Following institutional review board (IRB) approval from both institutions (Appendix A) and informed consent (Appendix B), infants were randomly assigned to the experimental. Control infants received routine NICU nursing care and were matched for age, gender, and race in order to control for confounding variables. Infants in the experimental group received routine NICU care and 7 minutes of the M Technique 6 times per week, no closer than 6 hour intervals, for 5 weeks, for a total of 30 M Technique applications. The delivery of the M Technique started once the infant reached 30 weeks PMA. In order to ensure consistency, the primary investigator and one of the trained members of the research delivered the technique.

Implementing the M Technique

The M Technique is a method of structured touch that follows a systematic set structure and pattern. Each movement and sequence follows a distinctive pattern. Planned modification or termination of the stroke was only done if the infant demonstrated signs of physical or behavioral distress. The M Technique was provided according to a published detailed protocol from the investigative team's feasibility study (Smith et al., 2012). Each stroke within each movement was repeated three times. The rationale for this set repetition was to decrease anxiety in the individual receiving the technique. The M Technique uses a set pressure of 3 (more than a tickle) where 0 is no pressure and 10 is crushing pressure. The speed of the M Technique is slow, constant, rhythmical and repetitive. The M Technique can be provided to any part of the body but for this study the technique was delivered to the infant's back while in a prone position. The duration and intensity of all aspects of the intervention are based on the infant's responses and did not exceed a total of 7 minutes. The primary investigator and another member of the research team have been trained extensively by Dr. Jane Buckle, the M Technique developer, and delivered the intervention. To ensure fidelity of the intervention performance, as part of the training, multiple return demonstrations were conducted on Dr. Buckle to achieve consistency and reduce variability between the M Technique givers. In addition, both trained givers met weekly to review and observed one another's technique to ensure the intervention was being delivered as planned.

Protection of Human Subjects

Permissions to conduct the study were obtained from the University of Missouri-Kansas City Social Sciences Institutional Review Board (SSIRB) and The Washington University in St. Louis Institutional Review Board prior to beginning study procedures. The IRB authorization agreement between UMKC and WUSTL IRB approval letter is attached in Appendix A

The potential risks to the research subjects were minimal. In order to protect against potential risks, the delivery of the M Technique was administered based on infant cue readiness (once in the morning and once in the afternoon/evening). Therefore, the M Technique was only delivered if the infant's physiological and behavioral state cues demonstrate readiness for the intervention (e.g., awake state, pink, relaxed breathing, arterial oxygen saturations >85%). If the infant displayed distress signs, the intervention was modified or stopped based on each infant's physiological (e.g., persistent HR >200 or <100 bpm; persistent apnea, or an increase of >.10 supplemental FiO₂ requirement) and behavioral (e.g., 3 or more persistent distress signs such as facial grimacing, finger splaying and crying) cues. Regardless of whether or not the infant was in the control or experimental group, all infants received standard nursing/medical care. It was possible that some infants may not have tolerated the M Technique at every session, therefore, a member of the research team conferred with the infant's primary attending physician to determine whether or not the infant was stable enough to receive the intervention. If the infant was not stable enough, the M Technique was not delivered at that time and future reassessment occurred. In order to reduce risk to the infant, the M Technique was administered by a trained member of the research team who was an experienced neonatal nurse practitioner trained in

recognizing infant stress signs. This infant-driven cue based readiness plan assisted in reducing the risk to each infant. Potential direct benefits to the experimental participants included decreasing stress, promoting relaxation and improving long-term neurodevelopment.

Consent Process

Potential subjects born very preterm were identified within 5-7 days of age after consulting with the attending physician. A member of the research team approached the parents of eligible subjects when they were approaching 30 weeks' PMA to provide informed consent. The member of the research team who approached the parents was not a member of the current clinical team involved in the care of the infant. On the initial meeting with the parents, general introductions to the research and the research team were discussed in a private setting (either in a single patient room or a closed-door private conference room on the unit (depending on the parent preference). A time convenient to the parents was identified to discuss the study in detail. The consent form was read through with the parents from start to finish with any questions relating to the research answered. At that time, the parents were informed that they had 1-2 days to consider the research opportunity for their infant. The research team member provided follow-up with the parents within 24 hours to answer any further questions. If the parents wished they could arrange a time to meet with the researcher and sign the informed consent forms. Members of the research team did not initiate the consent procedure during the most vulnerable postnatal period, the first 72 hours of life. In order to promote transparency, the parents were invited to attend the M Technique sessions given to their child. The research team did everything they could to protect

the patient's privacy. All personal information was de-identified and maintained in the strictest confidence and was only available to members of the research team. No identifiers will be collected per HIPAA regulations.

Measures

Data Collection

A simple form to collect the demographic and descriptive variables data for each infant was developed by the primary investigator (Appendix C). In order to examine specific aim one, neurobehavioral outcomes and growth velocity, infant neurobehavior was measured using the Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS) and infant weight was measured using pre- and post-intervention weights for between group comparisons. Specific aim two, physiological and behavioral state responses of the M Technique over time, was addressed by measuring heart rate, respiratory rate, and arterial oxygen saturation as well as the Anderson Behavioral State Scale (ABSS).

Infant neurobehavior. The Neonatal Intensive Care Unit Network Neurobehavioral Scale (NNNS) is a comprehensive assessment of neurological integrity and behavioral function used specifically in at-risk, drug exposed and preterm, infants (Lester & Tronick, 2004). Research supports the validity and reliability of the NNNS in very preterm infants (Brown, Doyle, Bear, & Inder, 2006; Stephens et al., 2010) and it has shown long-term predictive ability (Liu et al., 2010). The NNNS was administered at the end of the 5-week intervention period, once the infants reached 35 weeks' PMA. All evaluations were performed by a single trained occupational therapist with expertise in evaluating very preterm infant neurobehavior and who was blinded to

the allocation. The evaluator is certified in the use of the neurobehavioral measures being used and has evaluated infants in the NICU, for other research studies, using the same measures. Each NNNS evaluation started approximately 45 minutes to 1 hour prior to a scheduled feeding or hands-on care. The evaluations took approximately 25 to 30 minutes to complete.

The 115 NNNS items were scored manually and entered into a SPSS syntax (SPSS Inc, Chicago, Illinois) which gave a weight to each item and generated 13 summary scores including: habituation, orientation, tolerance of handling, quality of movement, self-regulation, nonoptimal reflexes, stress signs, arousal, hypertonia, hypotonia, asymmetry, excitability, and lethargy. Summary score ranged from 0 to 13. Higher summary scores signified more of the function observed during the evaluation; lower scores, represented less of the function. It's important to note that because some of the infants were in an open-bay environment, they could not be protected from other noise in the environment during the evaluation; therefore, habituation (which requires the environment to be noise free) could not be assessed. Hence, 12 summary scores are report.

Infant weight. Infant daily weights were collected at 30 weeks' PMA and 35 weeks' PMA. Weight data were extracted from the infant's electronic medical record (EMR) and compared to assess a difference in growth velocity between the two groups.

Infant physiological measures. Heart rate (HR), respiratory rate (RR), and oxygen saturations (SaO₂) were measured continuously beginning 5 minutes before, during, and up to 10 minutes after the intervention. The HR, RR, and SaO₂ measures were obtained via a Philip's monitoring system and Nellcor pulse oximeter and

confirmed by a member of the research team who separately tracked each autonomic response. This research team member, a neonatal occupational therapist, documented autonomic responses at baseline and every minute throughout the data collection period. The same individual collected these data throughout the study.

Infant behavioral state (IBS). Twelve categories of infant behavioral state (e.g., quiet sleep, irregular sleep, active sleep, very active sleep, drowsy, alert inactivity, quiet awake, active, very active, fussing, crying, and hard crying) were measured using the Anderson Behavioral State Scale (Gill, Behnke, Conlon, McNeely, & Anderson, 1988). The ABSS allows for classification of behavior into states from sleep to awake to crying. Rules for scoring as outlined by the originators are summarized with instrument in Appendix E. Infant behavioral state was assessed and documented at baseline and every minute throughout the entire data collection period by a member of the research team, trained to reliability. This trained research team member is a neonatal physical therapist with more than 15 years experience in neurodevelopmental supportive care. Prior to data collection, a second member of the research team independently judged behavioral states to ensure reliability. Inter-rater reliability was assured at a level >90% throughout the study. However, to ensure consistency, the same member of the research team recorded each infant's behavioral state throughout the study. State scores were recorded directly onto the ABSS and scores were entered into SPSS 18 software.

Data Management

The primary investigator (PI) directed and maintained oversight of all data related operations. To help protect confidentiality, hard copy of data records were

identified only by study number and stored in a locked file cabinet. All electronic data were stored in a secure format using password-protected computer records. Data quality was monitored by inspection of the data for patterns of missing values or outliers. In a separate locked file cabinet, the PI kept a log of de-identified health information stored by study numbers only. All file cabinets containing data were inside a locked badge-accessed only office in a badge-accessed corridor. Access to locked files was restricted to the research team members. Participants' identification codes were simply their numerical enrollment in the study and did not lend themselves to inadvertent or unauthorized identification of participants. The anonymous codes assigned to participants were verified and maintained by the PI throughout the study.

Data Analysis

Data were analyzed using the Statistical Packet for the Social Sciences (SPSS) 18.0. Descriptive statistics were used to describe infant characteristics, NNNS summary scores, and physiologic and behavioral state scores. Inferential statistics were used to address the following specific aims:

Specific Aim 1

Examine the neurobehavioral and growth velocity impact of the M Technique for hospitalized very preterm infants. Our working hypothesis: Very preterm infants (≤ 30 weeks gestation) who receive the M Technique intervention will have improved (1) neurobehavioral development [NICU Network Neurobehavioral Scale (NNNS)]; (2) higher growth velocity (infant weight at the beginning and end of protocol), compared to the control group.

- A Mann-Whitney U test was used to determine the differences in NNNS summary scores between the experimental and control groups.
- Infant growth velocity was collected as daily weight at baseline at 30 weeks' PMA (prior to the intervention) and at 35 weeks' PMA (post-intervention). A Mann-Whitney U test was conducted to evaluate differences between weights.

Specific Aim 2

Examine the physiological and behavioral state impact of the M Technique for hospitalized very preterm infants. Our working hypothesis: Very preterm who receive the M Technique intervention (experimental group only) will have improved physiologic stability (HR, RR, oxygen saturations) and behavioral state (e.g., ABSS) changes from baseline at 3 different time points over the course of the 5 week intervention.

- Physiologic (HR, RR, O2 Saturations) and behavioral state (ABSS) data were collected continuously on the experimental group only and the data were averaged at baseline and during the M Technique at 1-minute intervals and then at 5 minutes and 10 minutes following the intervention at 3 different time points (beginning, midway and at the end of 5 weeks) to examine the cumulative effect of the M Technique over time. Repeated measures analysis of variance (RMANOVA) was performed combining data points and these results were confirmed by SAS mixed model statistical analysis. Additional descriptive statistics were performed and graphs and figures were developed to provide visual illustration of trends over time.

CHAPTER 4
FEASIBILITY STUDY

The following section was prepared in partial fulfillment of the requirements for a manuscript-format dissertation. This paper was published in 2012 in the journal *Advances in Neonatal Care*.

Smith, J. R., Raney, M., Conner, S., Coffelt, P., McGrath, J., Brotto, M., Inder, T.
(2012). Application of the M Technique[®] in hospitalized very preterm infants: A
feasibility study. *Advances in Neonatal Care*, 12(Suppl.5), S10-7. PubMed PMID:
22968000.

Abstract

Purpose: To explore the application of a novel relaxation method (the M Technique) in hospitalized very preterm infants in a level IIIC NICU.

Design: A feasibility, observational intervention study.

Subjects: 10 very preterm infants were enrolled to receive the treatment intervention. Eligible infants born less than 30 weeks' gestation received the intervention at 30 weeks' postmenstrual age (PMA).

Methods: Based on infant readiness, each infant received the M Technique for 5 minutes. Physiologic parameters (heart rate, respiratory rate, and oxygen saturations), behavioral variables (stress and relaxation cues) and infant behavioral state were measured 5 minutes before, during, and up to 10 minutes after the intervention, continuously.

Results: Descriptive analysis revealed that baseline physiologic, behavioral state, and behavioral cue parameters changed during and after the M Technique. A decrease in HR and RR occurred during the M Technique ($p=0.006$, $p>0.001$ respectively) and a decrease in HR occurred at the end of the M Technique session ($p=0.02$). Additionally, an increase in SaO₂ occurred during and at 5 minutes following the M Technique session ($p=0.04$, $p=0.02$, respectively). State scores decreased from baseline (*mean* 5.1, range 3-9) to after the intervention (*mean* 2.0, range 1-4). As the intervention was delivered, more positive than negative behavioral cues were observed throughout, at the end, and after the M Technique session.

Conclusion: In this feasibility study, the M Technique can be delivered without adverse effects to very preterm infants who are 30 weeks' PMA. Additional research is

needed with a larger, randomized design to determine short and long-term effects specifically related to neurological outcomes.

Background

Up to two-thirds of children born very preterm (≤ 30 weeks' estimated gestational age [EGA]) experience cognitive impairments, a wide variety of learning disabilities, impaired executive function, and social and emotional difficulties.¹⁻⁵ These high-risk very preterm infants often begin their lives in an unprotected and over stimulating newborn intensive care unit (NICU) during a critical period of rapid brain growth and organization. Environmental factors in the NICU, many resulting in increased stress, may play a role in altered brain maturation and developmental outcomes.⁶⁻⁷ Neurodevelopmental supportive care strategies for very preterm infants include reducing exposure to noxious environmental stimulation and positive stimulation aimed at decreasing stress and reducing the gap between the *in utero* and NICU environments.⁸⁻¹⁰

Infant massage (IM) is recognized as a developmentally supportive intervention aimed at decreasing infant stress and optimizing the infant's sensory experience to improve long-term development. Although preterm (< 37 weeks' EGA) IM benefits are well-documented, the majority of existing studies have varying protocols, are limited to healthy or convalescing preterm infants greater than or equal to 32 weeks' postmenstrual age (PMA) and are not consistently contingent on infant cues.¹¹⁻¹⁷ Additionally, IM studies traditionally incorporate kinesthetic stimulation (e.g. passive range of motion of the lower and upper extremities), requiring frequent repositioning of the infant between supine and prone.

Alternatively, out of concern for the physiologic fragility of very preterm infants (e.g., born ≤ 30 weeks' GA) in the NICU, researchers have examined a wide

range of comforting or relaxing touch techniques. These supplemental touch techniques include *therapeutic touch*—a non-contact, energy balancing therapy;¹⁸ *Gentle Human Touch* (GHT)—a still touch without stroking or massaging;¹⁹⁻²² *touch and caressing-tender in caring* (TAC-TIC therapy)—a *gentle/light systematic stroking touch*;²³⁻²⁴ and IM with kinesthetic stimulation.²⁵ These studies have incorporated varying protocols resulting in limited or inconsistent results.

Recently, a novel alternative to providing these conventional techniques to hospitalized high-risk infants was introduced, called the M Technique.²⁶ The M Technique is a gentle, structured stroking technique aimed at reducing stress and anxiety in fragile intensive care patients who are unable to tolerate conventional massage.²⁷⁻²⁸ The M Technique does not require frequent infant repositioning and can be delivered based on infant cues. Each movement and sequence is done in a set number of repetitions using a set pattern, pressure, and speed making it easy to learn and easily reproducible for research and clinical practice.²⁷ To our knowledge, no studies have examined the effects of the M Technique on infants born very preterm. Therefore, our goal was to explore the application of the M Technique in hospitalized preterm infants within a level IIIC NICU who were born less than 30 weeks' EGA and were no greater than 30 completed weeks' PMA at the time the M Technique[®] commenced. In order to achieve our goal, a feasibility study was conducted to determine whether the M Technique intervention is appropriate for this population of infants and whether further efficacy testing should be employed.

Methods

Sample and Setting

Ten very preterm infants admitted to the level IIIC NICU in a large Midwestern academic pediatric hospital were recruited from February 2011 to May 2011 for this pilot study to explore the application of the M Technique. Inclusion criteria were (1) infants born less than 30 weeks' gestation (determined by Ballard), (2) 30 weeks' PMA at time of the M Technique intervention (appropriate for gestational age), and (3) no evidence of major brain injury (e.g. Grade IV intraventricular hemorrhage). Infants with septic shock, non-intact skin, respiratory failure (e.g., supplemental FiO₂ requirement >75%), severe brain injury, persistent tachycardia, bradycardia or those deemed unstable as determined clinically by the attending physician, were excluded.

Procedures

The NICU research committee and the hospital's Institutional Review Board approved the study. Parents of infants who met the sample selection criteria were contacted by one of the study team members. After parent consent was obtained, each participant was scheduled to receive the M Technique intervention.

M Technique Training: The principal investigator (PI) participated in a three-day adult, pediatric, and neonatal M Technique[®] certification class given by the developer, Jane Buckle. All infants received the intervention once, which was administered by the PI and lasted approximately 5 minutes. Specific criteria were identified for the M Technique to be discontinued if the infant demonstrated signs of persistent physiological distress (e.g., heart rate <100 or >200 beats per minute for 15 seconds or more, or arterial oxygen saturations levels <85% for longer than 30

seconds) or if the infant required an increase in supplemental FiO₂ concentration during the M Technique administration. None of the infants exhibited these signs of physiological distress during the M Technique period; therefore, it was not necessary to discontinue the technique before the end of the 5-minute period.

The M Technique was provided according to a detailed protocol (see Sidebar-M Technique Protocol). The protocol was similar to the M Technique intervention designed by Buckle²⁷ and used in infants following craniofacial surgery.²⁶ The M Technique is a method of structured touch that follows a systematic set structure and pattern. Each movement and sequence follows a distinctive pattern that is not modified. Planned modification or termination of the stroke was only to be done if the infant demonstrated signs of physical or behavioral distress. It was not necessary to terminate the intervention but a brief 5-to 10-second pause was warranted in two of the participants to promote self-regulation during administration of the intervention. Each stroke within each movement is repeated three times. The rationale for this set repetition is to decrease anxiety in the individual receiving the technique. For example, when the first stroke is provided, the receiver will take notice; the second stroke, the receiver recognizes the stroke; the third stroke, the receiver anticipates what is going to happen and begins to relax. The M Technique uses a set pressure of 3 (more than a tickle) where 0 is no pressure and 10 is crushing pressure. The speed of the M Technique is slow, constant and rhythmical. The M Technique can be provided on any part of the body but for this study the technique was delivered to the infant's back while in a prone position.

Outcomes Measures

The aim of this feasibility study was to explore the impact of the M Technique on physiologic, behavioral, and state responses in very preterm infants. The M Technique was provided once over a 5 minute period. Physiologic parameters (heart rate, respiratory rate, and oxygen saturation), behavioral variables (signs of distress and relaxation cues) and behavioral state (Anderson Behavioral State Scale—ABSS) were continuously measured beginning 5 minutes before, during, and up to 10 minutes after the intervention.

Infant Physiological Measures: Heart rate (HR), respiratory rate (RR), and oxygen saturations (SaO₂) were measured continuously beginning 5 minutes before, during, and up to 10 minutes after the intervention. The HR, RR, and SaO₂ measures were obtained via a Philip's monitoring system and Nellcor pulse oximeter and confirmed by a member of the research team who separately tracked each autonomic response. This research team member, a neonatal occupational therapist, documented autonomic responses at baseline and every minute throughout the data collection period. The same individual collected these data throughout the study.

Infant Behavioral Measures: Observations of each infant's positive (e.g., eyes widened, face brightened, hands to mouth, hands opened and relaxed, pink, relaxed breathing, relaxed posture) and distressed (e.g., brow bulge, eyes clinched, fingers splayed, crying, fussing, grimace, hiccup, self-repositioning) behavioral cue responses were measured and documented at baseline and continuously throughout the entire data collection period. A member of the research team continuously monitored both positive and distressed infant behavioral cues. This research team member is a neonatal nurse

practitioner with over 30 years of neurodevelopmental supportive care experience and is trained in infant observations. This same member of the research team measured the behavioral cues throughout the entire study.

Infant Behavioral State (IBS): Twelve categories of infant behavioral state (e.g., quiet sleep, irregular sleep, active sleep, very active sleep, drowsy, alert inactivity, quiet awake, active, very active, fussing, crying, and hard crying) were measured using the Anderson Behavioral State Scale.²² The ABSS allows for classification of behavior into states from sleep to awake to crying. Infant behavioral state was assessed and documented at baseline and every minute throughout the entire data collection period by a member of the research team, trained to reliability. This trained research team member is a neonatal physical therapist with more than 20 years experience in neurodevelopmental supportive care. For one-third of the observations, a second member of the research team independently judged behavioral states to ensure reliability. Inter-rater reliability was assured at a level >90% throughout the study. However, to ensure consistency, the same member of the research team recorded each infant's behavioral state throughout the study.

Statistical Analysis:

All data were analyzed in SPSS 18 software. Descriptive statistics were used to analyze infant characteristics, physiological, behavioral state and cue responses. *P*-values were calculated based on a one-sample *t* test and a Wilcoxon signed-rank test to determine differences from baseline in the physiologic parameters during and after the M Technique session.

Results

Table 1 summarizes the characteristics of the participating infants' birth weight, gestational age (GA) and average PMA when the M Technique commenced. Additional infant characteristics are summarized revealing that the majority of the infants were black (70%), females (80%), receiving caffeine (80%) and supplemental oxygen (70%) when the M Technique commenced.

Physiological Responses

Although heart rate (HR), respiratory rate (RR), and arterial oxygen saturation (SaO₂) data were collected continuously, for the analyses reported here, data were averaged at baseline and during the M Technique at 1-minute intervals and then at 5 minutes and 10 minutes after the M Technique. Descriptive analysis revealed that baseline HR (*mean* 173 bpm) and RR (*mean* 65 bpm) progressively decreased throughout and at the end of the intervention (Table 2). Oxygen saturations increased over the course of the intervention (Table 2). A difference from baseline in the physiologic parameters during and after the M Technique was observed (Table 3). A decrease in HR occurred from baseline to the lowest level during the intervention ($p=0.006$). In addition, a decrease in HR occurred from baseline to the end of the intervention ($p=0.02$). A decrease in RR occurred from baseline to the lowest RR level during the intervention ($p>0.001$). Finally, an increase in SaO₂ levels occurred from baseline to the highest SaO₂ level during the intervention and from baseline to the highest SaO₂ level 5 minutes after the M Technique ($p=0.04$, $p=0.02$, respectively).

Behavioral State Responses

The majority of infants were in an active or very active state at baseline with a few being fussy or crying (Table 4). No infant was awakened from a quiet sleep state to initiate the M Technique therapy. For the ABSS scoring the higher the behavioral state score, the more active or fussy the infant. The average behavioral state scores decreased from baseline (*mean* 5.1) to after the M Technique session (*mean* 2.0), indicating a more quiet sleep state.

Behavioral Cue Responses

Table 5 provides a summary of the percent of times infants displayed distressed or positive behavioral cues. More positive behavioral cues were observed than distressed sign throughout, at the end, and after the M Technique session. Figure 1 provides a graph depicting the cues by time point. Distressed behaviors decreased over time and were non-existent within 4 minutes after the M Technique therapy commenced and continued 5 and 10 minutes after the M Technique session. Similarly, positive behavioral responses increased over time and all participants displayed positive behavioral cues within 4 minutes after the M Technique commenced and continued 5 and 10 minutes after the M Technique session.

Discussion

Results from this study suggest that a 5-minute infant-driven M Technique intervention has no adverse effect on very preterm infants' physiologic parameters, behavioral cues and state. These physiologic results are consistent with other supplemental comforting touch studies including therapeutic touch¹⁸ and TAC-TIC²³⁻²⁴ therapies in which heart rate or oxygen saturations were not adversely affected in very

preterm infants. However, unlike the present study, these studies did not examine infant behavioral state or behavioral cues, which may further support the relaxing effects of these supplemental touch techniques. Similar to the present study, GHT studies¹⁹⁻²² have examined physiologic and behavioral state and/or cues to evaluate its effect on hospitalized very preterm infants. The majority of the GHT studies have resulted in no adverse physiologic effects and a reduction in negative behavioral effects. In a pilot study, Harrison and colleagues²⁰ demonstrated that infants who received GHT had less time in active sleep ($p=0.008$), less motor activity ($p=0.003$) and less behavioral distress ($p=0.033$) during the GHT intervention compared to baseline but these same benefits were not observed post-GHT periods. However, in a larger randomized controlled trial, Harrison and colleagues²¹ did report a decrease in oxygen saturations across the three phases of GHT at baseline, during and post-intervention. Although a statistically significant ($p<0.001$) decrease in oxygen was observed, it did not appear to be clinically significant. Additionally, 19% of the infants in the GHT group had to have one or more GHT sessions terminated early due to a decrease in heart rate or decrease in oxygen saturations. The investigators of the GHT study²¹ noted that the infants with decreased oxygen saturations were those infants who were lower in GA and birth weight and had higher morbidity levels compared to infants who did not require early termination of the GHT sessions. This decrease in oxygen saturation did not occur in the current study. Although the present study does not report morbidity levels, infants within the present study are of similar GAs and birth weights and are slightly younger in PMA compared to the GHT study.²¹ No infant in the current study required early termination of the M Technique. It's important to note that this adverse

effect on oxygen saturations may not have been observed in the present study because the M Technique intervention was only delivered once and to only ten patients.

Overall, results from this study suggests that this type of structured and systematic stroking may have a relaxing effect as evidenced by a lower HR, increased SaO₂, an increase in quiet sleep, and less behavioral distress signs. Although more research is needed to determine both the short and long-term benefits of the M Technique, results of this study suggest that NICU nurses can provide and/or encourage parents to provide a structured comforting touch method that is infant-driven, easy to learn, and relatively short in duration.

The major limitations of this study are the size and sampling technique. Since the purpose of this feasibility study was to explore the application of a novel the M Technique in hospitalized very preterm infants in a level IIIC NICU, a typical power calculation was not applied. However, data from this study will aid in determining estimated sample size for future studies. As with any study using a convenience sample, sampling bias is a limitation because the small numbers of participants are challenging to represent the entire very preterm infant population. Given the small sample size, lack of randomization, and convenience sample, caution should be used in generalizing these findings to all very preterm infants in a level IIIC NICU. Finally, the examiner was not blinded and knew that the intervention was administered which may have resulted in bias in their recording of behavior and state. This would not have influenced the physiological measures.

A further limitation was the short-term nature of this study and the immediate outcome measures. No intermediate or long-term outcomes were collected and

analyzed. Because the M Technique was only administered once, the number of times per day and the number of days the M Technique can be delivered in order to achieve maximum benefit were not studied and are unknown.

Although feasibility studies may have a number of limitations, well-designed and constructed feasibility studies can inform investigators about the research process.³⁰ Strengths of this feasibility study allowed the development of a workable and realistic research protocol in order to design our next phase of study. In addition, logistical problems (e.g., timing of the intervention and coordination of the research team) were identified, successful recruitment approaches and data collection methods were refined, and data were obtained in order to aid in determining estimated sample size for future studies. Finally, this feasibility study provides evidence for future funding bodies that (a) the research team is competent and knowledgeable and that (b) the next main phase of study is worth funding.

Conclusion

The M Technique can be easily delivered to very preterm infants in a level IIIC NICU who are 30 weeks' PMA without notable adverse effects and with evidence of positive behavioral and physiological impact. Based on the findings of this feasibility study, our next proposed study is to systematically test the cumulative effect of the M Technique on infant neurodevelopment in hospitalized very preterm infants. Additional research is needed with a larger, randomized, systematic methodological design to determine the short- and long-term effects, specifically as related to brain growth, long-term neurobehavioral development, as well as decreased stress. Although not a component of this study, future research is also needed to evaluate the

effectiveness of a parent-delivered M Technique and the potential impact on parent mental and emotional health and parent-infant synchrony.

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SIDEBAR: M Technique Protocol

- Timing of the M Technique therapy was based on a schedule that best supported each infant, generally at least, 1.5-2 hours post feeding (*if on a q 3-hour feeding schedule*).
- Prior to, during, and after the M Technique administration, each infant's behavioral and physiological cues and state were closely examined to avoid overstimulation. Administration of the technique was *not* commenced if the infant was in a quiet sleep state.
- Prior to commencing the M Technique, the PI confirmed with the attending physician and bedside nurse whether or not the infant was still considered a candidate to receive the M Technique. At this point, the nurse was instructed to place the infant in a midline prone position with extremities in flexion (supported by developmental positioning aids) after routine care.
- Baseline data obtained
- Hands warmed prior to commencing M Technique
- Confirmed infant was in prone position and the upper half of the positioning aid was opened, keeping the lower extremities and buttocks in a well supported flexed position.
- *Let your presence be known*—hands cupped with one hand resting gently on infant's head and the other on the infant's lower back/buttocks (offer gentle still touch/containment)
- Stroking began using a pressure of 3 (0-10) or moderate pressure with a set rhythmic sequence, each stroke repeated 3 times.
- Stroking was applied to the infant's back using the pads of the 2nd & 3rd fingers of both hands
- Total duration— 5 minutes (approximately 20 seconds per stroke)
- Ended with still gentle touch/containment

Table 4.1: Infant Characteristics

Infant Characteristics (<i>n</i> = 10)	Mean ± SD
Birthweight, gms	1160± 198 Range 860-1420
Gestational Age, wks	27.9± 0.9
Postmenstrual Age on day of study, wks	30± 0
Male	2 (20%)
Female	8 (80%)
Black	7 (70%)
Caffeine	8 (80%)
Room Air	3 (30%)
Nasal Cannula	3 (30%)
High Humidity Nasal Cannula	3 (30%)
SiPAP with Back-up Rate	1 (10%)

Table 4.2: Descriptive Mean \pm standard deviation (SD) and Range for Heart Rate and Respiratory Rate and Oxygen Saturations prior to and at 1 minute intervals during and 5- and 10-minute intervals following the administration of the M Technique

Physiologic Parameters (n = 10)	Baseline Mean \pm SD Range	1 min Mean \pm SD Range	2 min Mean \pm SD Range	3 min Mean \pm SD Range	4 min Mean \pm SD Range	5 min Mean \pm SD Range	5 min Post-M Mean \pm SD Range	10 min Post-M Mean \pm SD Range
Heart Rate	173 \pm 23 133-215	171 \pm 16 147-198	168 \pm 16 142-192	165 \pm 17 130-192	165 \pm 14 140-189	163 \pm 15 131-185	166 \pm 16 131-186	164 \pm 13 134-178
Resp Rate	64 \pm 17 30-83	52 \pm 20 33-85	54 \pm 17 35-83	53 \pm 14 36-84	51 \pm 17 35-78	54 \pm 14 38-80	55 \pm 17 25-78	59 \pm 16 30-85
Oxygen saturation	95 \pm 5 85-100	94 \pm 6 84-100	95 \pm 6 83-100	94 \pm 8 77-100	96 \pm 5 86-100	97 \pm 3 90-100	97 \pm 3 87-100	97 \pm 3 89-100

Table 4.3: Change in Heart Rate, Respiratory Rate, and Oxygen Saturation from Baseline

Difference from Baseline*	Mean	Mean Difference ± SD	P†
<i>Heart Rate</i>			
<i>Baseline</i>	173		
Lowest during intervention	163	-15.2 ± 13.6	0.006
Highest during intervention	171	-0.5 ± 8.1	0.85
At end of intervention	163	-12.8 ± 14.9	0.02
5 min post-intervention	166	-7.6 ± 11.1	0.06
10 min post-intervention	164	-9.8 ± 14.1	0.06
<i>Respiratory Rate</i>			
<i>Baseline</i>	64		
Lowest during intervention	51	-25.7 ± 15.2	0.0005
Highest during intervention	54	3.9 ± 15.3	0.44
At end of intervention	54	-8.7 ± 16.8	0.14
5 min post-intervention	55	-9.5 ± 17.1	0.11
10 min post-intervention‡	59	2 (-9, 6)	0.68
<i>O2 saturation</i>			
<i>Baseline</i>	95		
Lowest during intervention	94	-3.1 ± 5.3	0.10
Highest during intervention	97	2.9 ± 3.9	0.04
At end of intervention	97	2.0 ± 4.1	0.16
5 min post-intervention	97	2.3 ± 2.7	0.02
10 min post-intervention	97	2.2 ± 3.5	0.08

*Calculated as value at time-point (during intervention, end of intervention, etc.) minus baseline value

†P value based on one-sample *t*-test

‡Median (25th, 75th percentile) presented.

P value based on Wilcoxon signed rank test

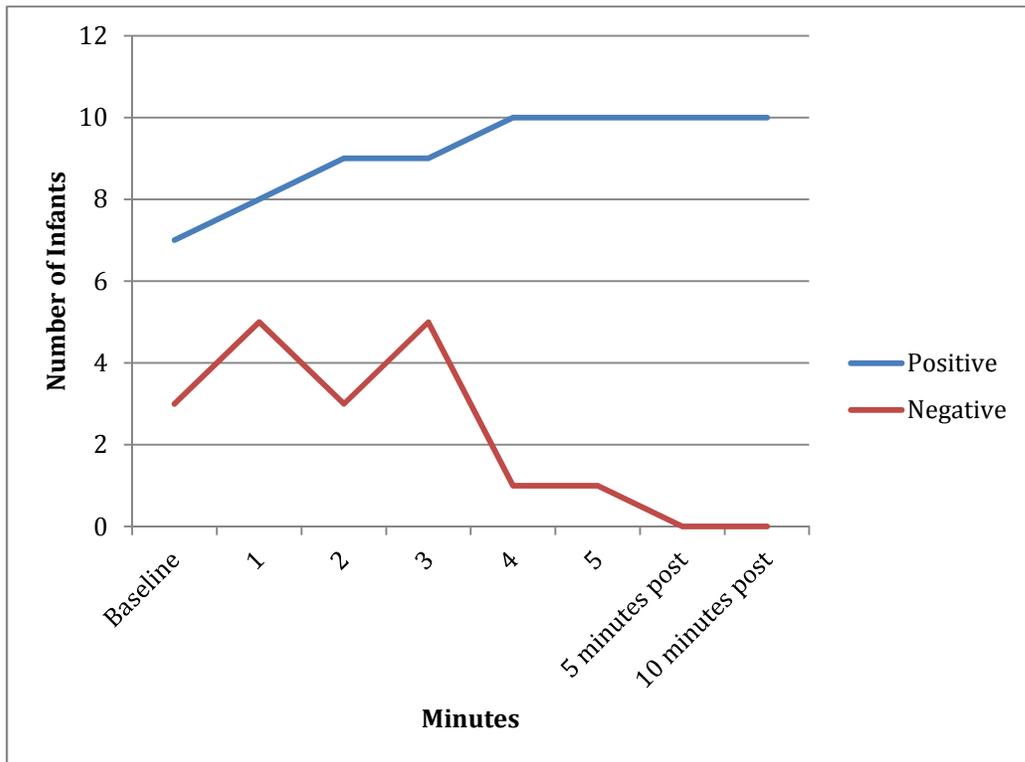
Table 4.4: Descriptive Data of Infant Behavioral State (IBS) Using the Anderson Behavioral State Scale (ABSS) Score

ABSS (<i>n</i> = 10)	Mean ± SD Range
ABSS at Baseline	5.1±2.08 3-9
ABSS at 1 Minute	3.8±2.70 2-10
ABSS at 2 Minutes	2.8±1.32 1-5
ABSS at 3 Minutes	2.2±.79 1-4
ABSS at 4 Minutes	2.4±.70 2-4
ABSS at 5 Minutes	2.0±.47 1-3
ABSS at 5 Minutes Post M	2.0±.82 1-4
ABSS 10 Minutes Post M	2.6±1.17 1-5

Table 4.5: Descriptive Data of Infant Behaviors

Distressed/Negative and Positive Behaviors (n = 10)	
Distressed/Negative and Positive Behaviors (n = 10)	Percent
Brow bulge	20.0
Crying	20.0
Eyes clinched	30.0
Fingers splayed	20.0
Fussing	10.0
Grimace	50.0
Hiccup	20.0
Self-repositioned	40.0
Eyes widened	20.0
Face brightened	20.0
Hands open and relaxed	60.0
Hands to mouth	70.0
Relaxed breathing	90.0
Relaxed posture	100.0
Pink	100.0

Figure 4.1: Negative and Positive Infant Cues by Time Point



CHAPTER 5

RESULTS

Infant Characteristics

SPSS 18 (Chicago, Illinois) was used for data analysis. Of the 10 infants who were randomly assigned to the treatment group, one infant developed necrotizing enterocolitis (NEC) with perforation of the gastrointestinal tract requiring emergency surgery and was withdrawn from the study. Therefore, data from a total of 18 infants (9 infants in each of the treatment and control groups) were analyzed for this study. Descriptive statistics and Mann-Whitney U statistical techniques were conducted to determine the equivalency of the two groups at birth and before the intervention at 30 weeks' PMA (Tables 1-3, respectively). There were no differences among the experimental and control groups in terms of birth weight, gestational age (GA), CRIB (acuity) score, and 1-minute and 5-minute Apgar scores. The majority of infants in both groups were white (55.6%), females (55.6%), on caffeine (100%), and receiving assisted ventilation (100%).

Table 5.1

Descriptive-Continuous Variables of Infant Characteristics at Birth^a

Infant Characteristics	M Technique Group			No M Technique Group			P-value ^b
	Mean	SE	Range	Mean	SE	Range	
Birth weight, (g)	970	71.01	630-1190	966.11	79.21	740-1460	0.730
**Gestational age, (weeks)	26.67	.441	26-29	26.67	.441	26-29	1.000
Apgar score 1 min	3.89	.964	1-8	4.22	.846	0-7	1.000
Apgar score 5 min	5.11	.696	2-8	6.44	.555	4-8	0.161
CRIB score	5.11	1.39	1-13	3.78	1.26	1-12	0.436

Note: SE=Standard Error of Mean. Min=Minute. CRIB=Critical Risks Index for Babies.

^aInfant characteristics between the M Technique and No M Technique groups were not statistically different ($P>0.05$).

^bMann-Whitney U

**Matched with controls

Table 5.2

Descriptive-Categorical Variables of Infant Characteristics at Birth^a

Infant Characteristics	M Technique Group	No M Technique Group
	Frequency (%)	Frequency (%)
Gender ^a		
Male	4 (44.4)	4 (44.4)
Female	5 (55.6)	5 (55.6)
Race ^a		
Black	4 (44.4)	4 (44.4)
White	5 (55.6)	5 (55.6)

^aInfant characteristics matched for study design

Table 5.3

Descriptive-Categorical Variables of Infants at 30 weeks PMA (day 1 of study)

Infant Characteristics	<u>M Technique Group</u> Frequency (%)	<u>No M Technique Group</u> Frequency (%)
Assisted Ventilation		
HHNC	4 (44.4)	7 (77.8)
CPAP	2 (22.2)	1 (11.1)
SiPAP	3 (33.3)	1 (11.1)
Supplemental Oxygen		
Yes	8 (88.9)	6 (66.7)
No	1 (11.1)	3 (33.3)
Patient Room Design		
Single	5 (55.6)	5 (55.6)
Open Bay	4 (44.4)	4 (44.4)
Caffeine		
Yes	9 (100.0)	9 (100.0)
No	0 (0.0)	0 (0.0)

Note: HHNC=High Humidity Nasal Cannula. CPAP=Continuous Positive Airway Pressure. SiPAP=Bi-level Continuous Positive Airway Pressure.

Specific Aim One

Examine the neurobehavioral and growth velocity impact of the M Technique for hospitalized very preterm infants. Our working hypothesis: Very preterm infants (≤ 30 weeks gestation) who receive the M Technique intervention will have improved **(1)** neurobehavioral development [NICU Network Neurobehavioral Scale (NNNS)]; **(2)** higher growth velocity (infant weight data were collected at the beginning and end of protocol), compared to the control group.

Very Preterm Neurobehavioral Outcome at 35 Weeks' PMA

Descriptive analysis was used to determine the mean NNNS summary score for each group. A Mann-Whitney's U test was used to determine differences in the NNNS summary scores between the treatment and control groups. The results of the analysis summarized in Table 4 did not reveal a significant difference in the 12 NNNS summary scores between the M Technique group and the non M Technique group.

Table 5.4

Comparison of the Study Cohort NNNS Summary Scores at Near Term Equivalent

Summary score	<u>M Technique</u> Group Mean ^a (SE) ^b	<u>No M Technique Group</u> Mean ^a (SE) ^b	P-value ^c
Attention	3.32 (0.26)	3.67 (0.49)	0.596
Handling	0.61 (0.03)	0.61 (0.03)	0.961
Quality of Movement	3.14 (0.22)	3.04 (0.24)	0.790
Regulation	4.33 (0.24)	4.03 (0.17)	0.298
Nonoptimal reflexes	7.44 (0.84)	7.78 (0.36)	0.560
Asymmetric reflexes	2.89 (0.84)	2.56 (0.63)	0.610
Stress abstinence	0.37 (0.02)	0.38 (0.02)	0.477
Arousal	3.78 (0.32)	3.64 (0.28)	0.561
Hypertonicity	1.00 (0.33)	1.89 (0.48)	0.185
Hypotonicity	1.00 (0.29)	0.78 (0.32)	0.480
Excitability	4.89 (0.82)	5.67 (0.69)	0.349
Lethargy	5.78 (1.19)	7.33 (1.29)	0.399

^aDescriptive Statistics

^bStandard Error

^cMann-Whitney U

Growth Velocity Results

Descriptive analysis was used to determine the mean, standard error (SE) and range of weights at both 30 weeks' and 35 week's PMA. A Mann-Whitney's U test was used to determine differences between the weights at the two different time points. The results of the analysis summarized in Table 5 did not reveal a significant difference between the two groups at baseline (30 weeks' PMA) ($p= 0.860$), after the 5-week intervention at 35 weeks' PMA ($p= 0.627$), or a difference in growth velocity between the two groups ($p= 0.161$).

Table 5.5

Infant Weights Between the 2 groups at 30 weeks' PMA (day 1 of study) and 35 weeks' PMA (completion of study).

Timepoints	<u>M Technique Group</u> Mean ^a (SE/Range)	<u>No M Technique</u> <u>Group</u> Mean ^a (SE/Range)	<i>P</i> -value ^b
Weight at 30 weeks PMA, g.	1171.67 (68.35/790-1470)	1186.11 (53.51/950-1500)	0.860
Weight at 35 weeks PMA, g.	2335.00 (125.11/3010)	2256.67 (134.23/1660-3000)	0.627
Difference in weight from 30 weeks to 35 weeks' PMA	1163.33 (64.67/990-1540)	1070.56 (85.36/710-1500)	0.161

Note: PMA=Postmenstrual Age. SE=Standard Error of Mean.

^aDescriptive Statistics

^bMann-Whitney U

The results of these analyses do not support our working hypothesis for specific aim one.

Specific Aim Two

Examine the physiological and behavioral state impact of the M Technique for hospitalized very preterm infants. Our working hypothesis: Very preterm who receive the M Technique intervention (experimental group only) will have improved physiologic stability (HR, RR, oxygen saturation) and behavioral state (e.g., ABSS) changes from baseline at 3 different time points over the course of the 5-week intervention.

Physiological Responses

Although heart rate (HR), respiratory rate (RR), and arterial oxygen saturation (SaO₂) data were collected continuously, for the analyses reported here, data were collected and analyzed at baseline and during the M Technique at 1-minute intervals and then at 5 minutes and 10 minutes after the M Technique at three different time points over the course of the 5-week intervention. Due to the small sample size characteristic of pilot studies and insufficient degrees of freedom at the 3 different time points (30, 32, and 34 weeks' PMA), a repeated measures analysis of variance (RMANOVA) could not be conducted. However, the 3 time points all had the same trend toward physiologic stability and there were no differences between HR, RR and SaO₂ for each individual infant between the 3 time points. Therefore, HR, RR, and SaO₂ at the 3 different time points were treated as independent measurements and the RMANOVA with a Greenhouse-Geisser correction determined that mean HR, RR, and SaO₂ differed significantly between from baseline to 10 minutes post the M Technique

intervention ($F = 41.116, p < 0.0005$). These results were also confirmed after accounting for the repeated measurements from the 3 time periods (30, 32, and 34 weeks' PMA) with the SAS mixed model statistical analysis conducted at UMKC by Dr. An-Lin Cheng (Verbeke & Molenberghs, 2009). We can conclude that the M Technique elicits a statistically significant reduction in HR and RR and an increase in SaO₂ over time, from baseline to 10 minutes post-delivery, suggesting an improved physiologic stability in these high-risk very preterm infants.

These physiologic changes over time are well illustrated in figures 1- 4. Figure 1 provides a visual snapshot of each infant's heart rate at 30 weeks' PMA at each experimental time point controlled during these studies. The red line represents the group HR mean +/- standard errors (SE). Figures 2 – 4 illustrate the group HR, RR, and arterial SaO₂ means (+/- SE) over the 3 different time points for the treatment group at baseline and during the M Technique at 1-minute intervals and then at 5 minutes and 10 minutes after the M Technique. HR and RR progressively decreased throughout and up to 10 minutes following the M Technique intervention (Figures 2 – 3). Oxygen saturations increased over the course of the intervention and up to 10 minutes following the M Technique intervention (Figure 4)

**Effects of the M Technique
on the Heart Rate of each Preterm Infant at 30 Weeks**

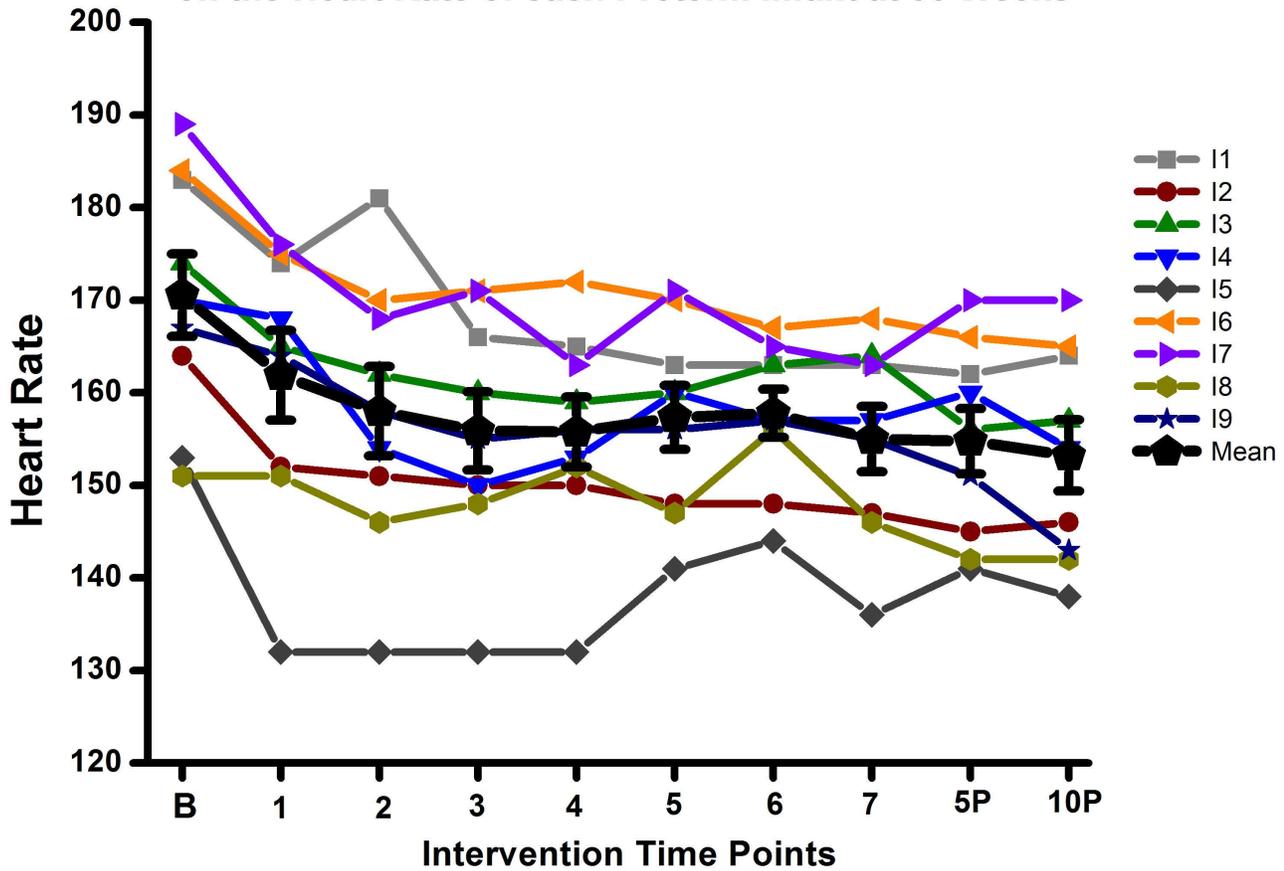


Figure 5.1. Line graph showing experimental subjects' heart rate (HR) from baseline to 10 minutes post intervention at 30 weeks' PMA. The black line indicates the group mean heart rate and standard error (SE) over time and clearly depicts the reduction of HR over time.

**Effects of the M Technique
on the Mean Heart Rate of Very Preterm Infants**

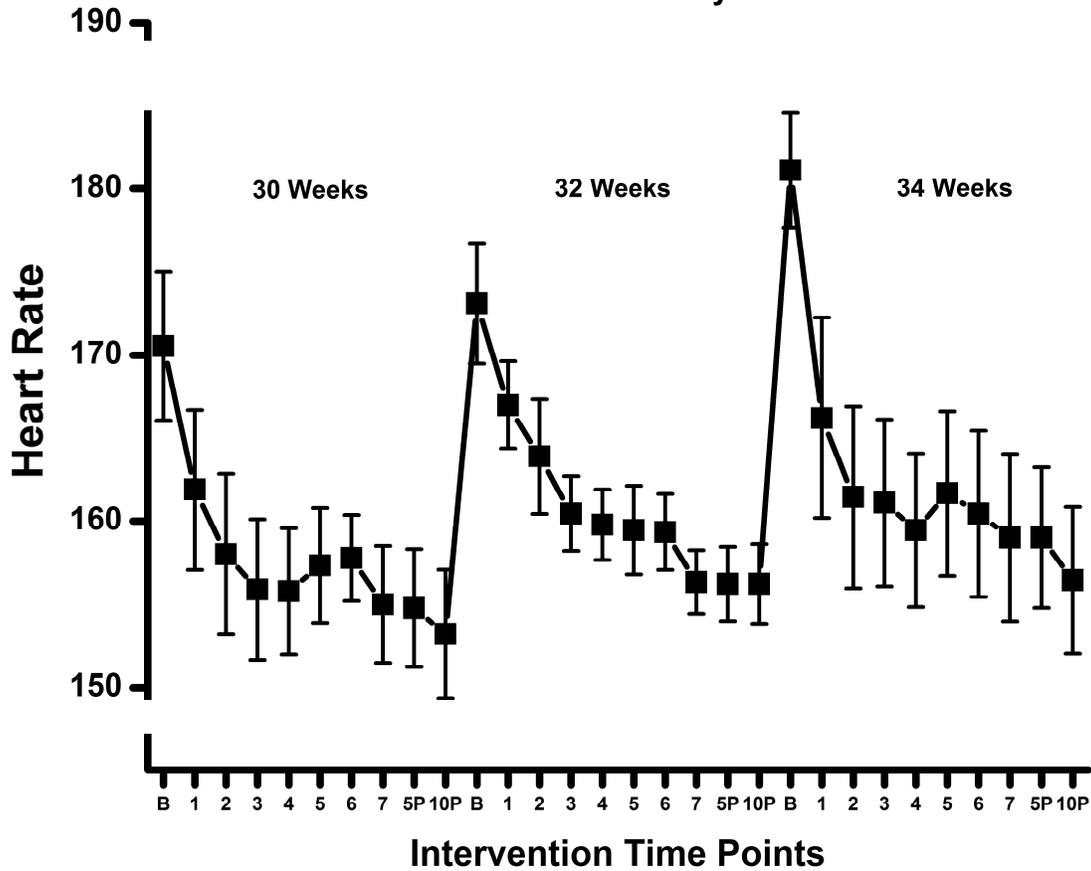


Figure 5.2. Line graph shows the mean heart rate (HR +/- SE) for experimental subjects from baseline to 10 minutes post intervention at 30, 32, and 34 weeks' PMA making evident the decrease in mean HR over time at each PMA studied. Only the experimental group received the M Technique intervention.

**Effects of the M Technique
on the Respiratory Rate of Very Preterm Infants**

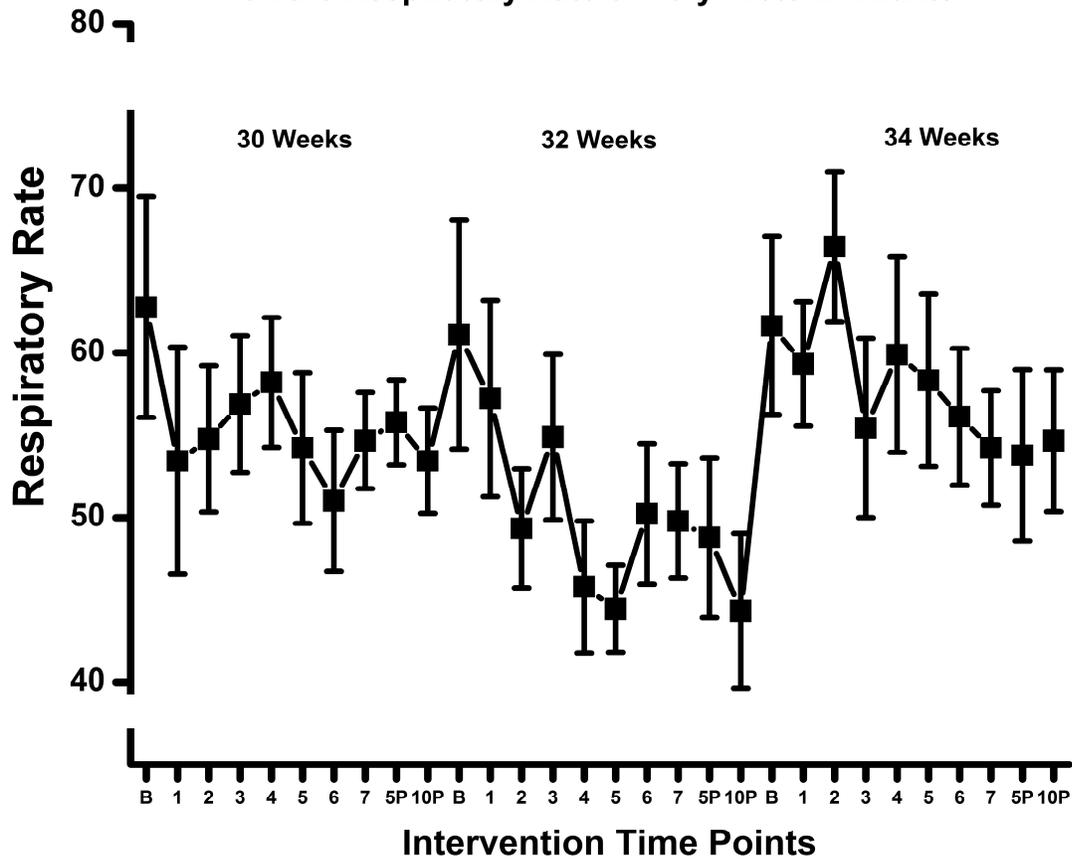


Figure 5.3. Line graph showing shows the mean respiratory rate (RR +/- SE) for experimental subjects from baseline to 10 minutes post intervention at 30, 32, and 34 weeks' PMA making evident the decrease in mean RR over time at each PMA studied.

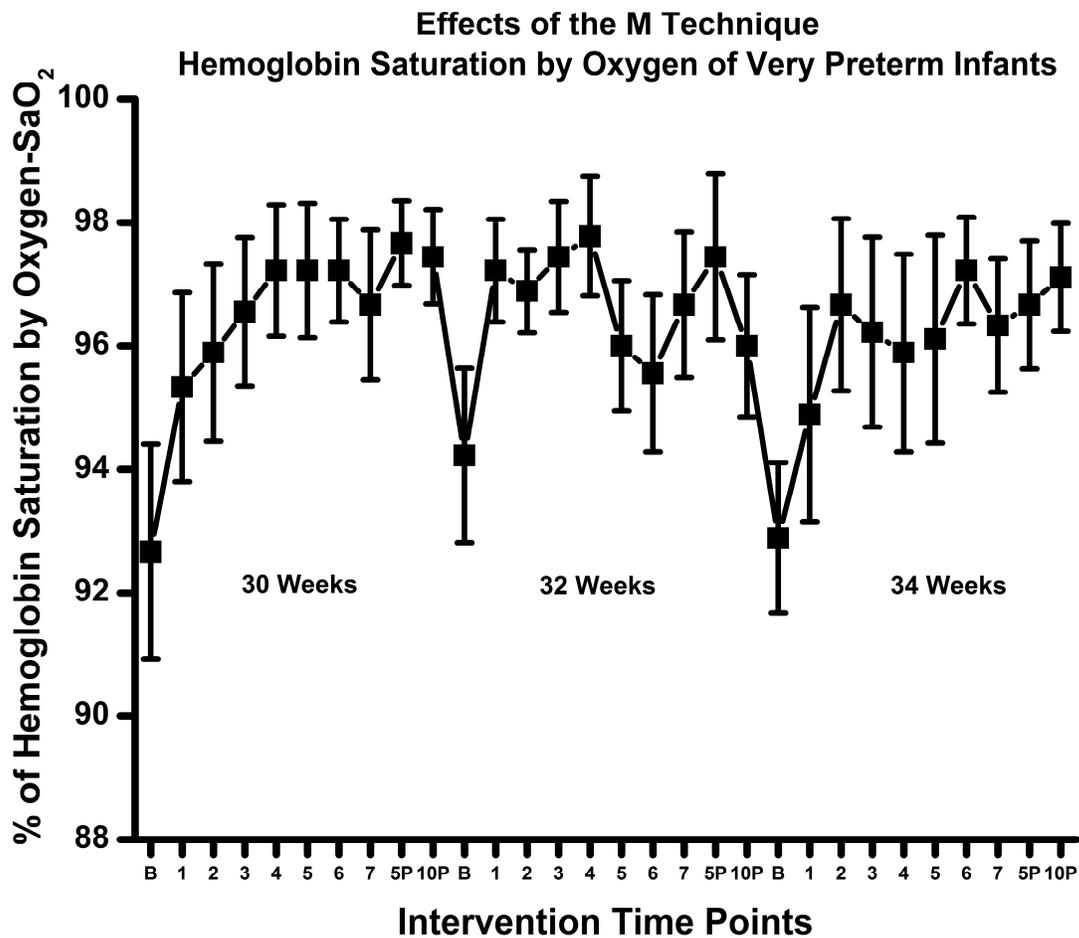


Figure 5.4. Line graph showing shows the mean hemoglobin oxygen saturation percentage (SaO₂ +/- SE) for experimental subjects from baseline to 10 minutes post intervention at 30, 32, and 34 weeks' PMA making evident the increase in mean SaO₂ over time at each PMA studied.

Behavioral State Responses

The majority of infants were in a drowsy to an active awake state at baseline with few being fastidious or crying at all 3 time points (*Range=3-11*). None of the infants were awakened from a quiet sleep state to initiate the M Technique therapy. For the ABSS scoring the higher the behavioral state score, the more active or fastidious the infant. The average behavioral state score decreased from baseline (*Mean=6.11*) at all three time points resulting in infants being in a predominately quiet sleep state (*Mean=1.40*) at completion through 10 minutes following the M Technique session.

Similar to the physiologic analysis, ABSS scores at the 3 different time points (30, 32, and 34 weeks' PMA) were treated as independent measurements and the RMANOVA with a Greenhouse-Geisser correction determined that the mean ABSS differed significantly between time points from baseline to 10 minutes post the M Technique intervention ($F = 38.564, p < 0.0005$). These results were also confirmed after accounting for the repeated measurements from the three PMA periods (30, 32, and 34 weeks' PMA) with the SAS mixed model statistical analysis conducted at UMKC by Dr. An-Lin Cheng (Verbeke & Molenberghs, 2009). We can conclude that the M Technique elicits a statistically significant reduction in ABSS scores over time, from baseline to 10 minutes following the M Technique intervention, suggesting an improved behavioral state changes over time.

These behavioral state changes are illustrated in Figure 5 which represents the group ABSS means and SE over the 3 different time points for the treatment group at baseline and during the M Technique at 1-minute intervals and then at 5 minutes and 10 minutes after the M Technique. ABSS scores progressively decreased during, throughout and up to 10 minutes following the course of the M Technique, resulting in a more quiet sleep state.

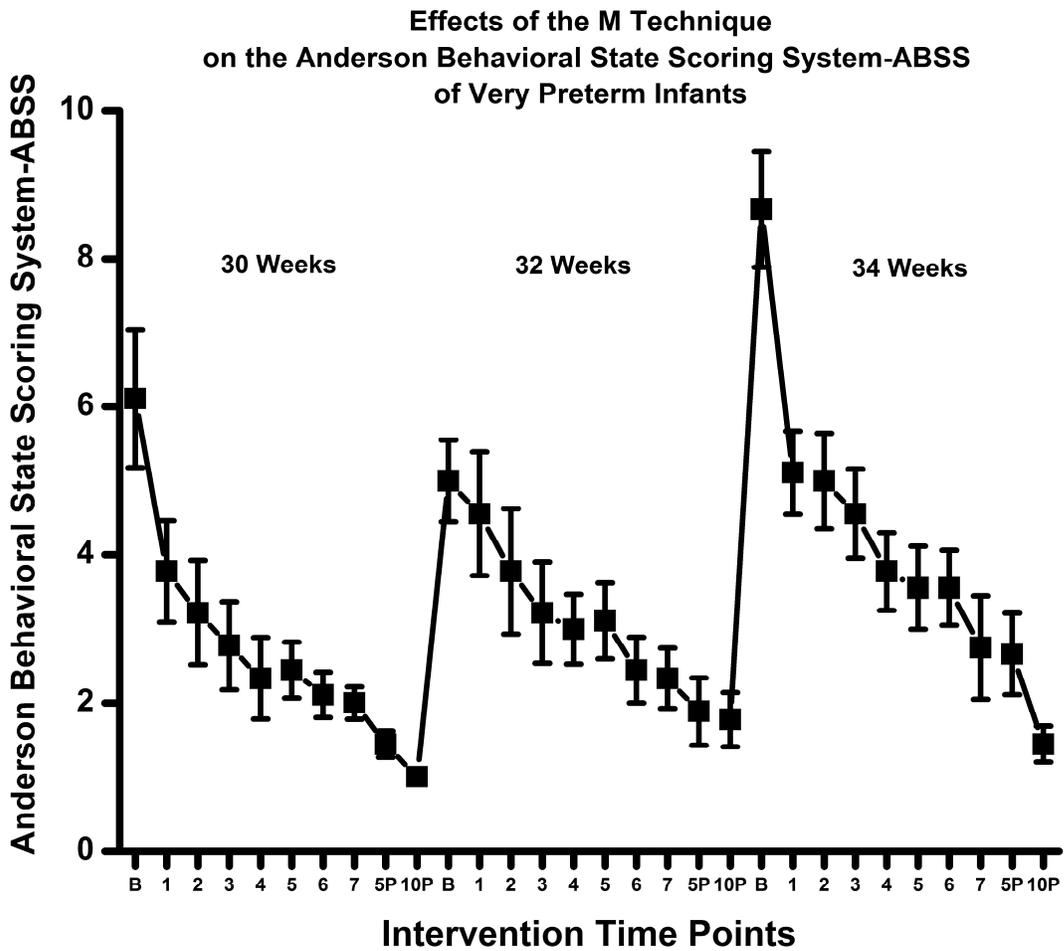


Figure 5.5. Line graph showing shows the mean Anderson Behavioral State Scoring System (ABSS +/- SE) for experimental subjects from baseline to 10 minutes post intervention at 30, 32, and 34 weeks' PMA clearly illustrates the reduction in mean ABSS over time at each PMA studied.

CHAPTER 6

DISCUSSION

Findings from this study have both clinical and research implications for neonatal health care providers and families. This study is one of the first to evaluate the effects of the M Technique on neurobehavioral development in infants born very preterm. It also demonstrates the feasibility and the potential utility of the M Technique and the use of the NNNS in the NICU.

Specific Aim One

Very Preterm Infant Neurobehavior

Findings from this study suggest that the M Technique does not influence neurobehavior in infants born very preterm. Few massage or comforting touch studies have examined the effects of neurobehavioral development of high-risk, very preterm infants. The majority of touch studies examining neurobehavior have been conducted in healthy infants greater than 30 weeks' GA with birth weights greater than 1,200 grams (Arora, Kumar, & Ramji, 2005; Field, et al., 1986; Harrison, Olivet, Cunningham, Bodin, & Hicks, 1996; Scafidi, Field Schanberg, 1993) and one study specifically examined cocaine exposed preterm infants (Wheeden et al., 1993). Similar to the present study, a recent meta-analysis concluded that neurobehavioral outcomes of these combined studies (excluding gentle human touch studies) yielded no significant differences between the massage and control groups (Wang, He, & Zhang, 2013). Because of the small number of studies, small sample sizes, and the heterogeneity that exists between the studies, the analysis was underpowered and the strength of the conclusion is weak. Gentle human touch studies were not included in the meta-analysis

because of the lack of evidence to support its effect on weight gain in preterm infants (Wang et al., 2013). However, consistent with the present study and the meta-analysis results, Harrison and colleagues (1996) did not observe a difference in the neurobehavioral subscales between the GHT and control groups.

Neurobehavior refers to the physiological and behavioral systems dynamically influencing each other, and their quality is dependent upon neural feedback (Lester & Tronick, 2004; Sullivan, Miller, Fontaine, & Lester, 2012). Multiple methods of neurobehavioral assessment have been developed (Brazelton, 1973; Lester & Tronick, 2004; Daily & Ellison, 2005). In the aforementioned studies, neurobehavioral evaluations were administered at the end of a 10-day massage or GHT intervention, approximately at 36 weeks' PMA. The neurobehavioral tool used to evaluate these healthy preterm infants was the Brazelton (1973) Neonatal Behavioral Assessment Scale (NBAS), which includes items focused on the infant's capacity to self-regulate and to interact with environmental stimuli. Although used with various populations, the NBAS was developed to describe the behavior of normal, term, and healthy infants. Therefore, due to the high-risk nature of the very preterm infants in this present study, the NNNS was used as a comprehensive assessment of neurological integrity and behavioral function (Lester & Tronick, 2004).

NNNS Summary Score

While there were no differences observed between the treatment and control groups of this presents study, this cohort of infants demonstrated less optimal neurobehavioral scores across all domains by near term equivalent which is consistent with other published NNNS mean summary scores of very preterm infants at term

equivalent (Brown et al., 2006; El-Dib, Massaro, Glass, & Aly, 2012; Pineda et al. 2012). For instance, when compared to previously reported NNNS summary scores of very preterm infant at term equivalent (Brown et al., 2006; El-Dib et al., 2012), infants in this present study cohort had lower scores for *attention*, *quality of movement*, *regulation*, and *arousal*. These same infants had higher scores for *handling*, *nonoptimal reflexes*, *asymmetric reflexes*, *stress abstinence*, *hypertonicity*, *hypotonicity*, *excitability* and *lethargy*. However, it's important to acknowledge that very preterm infants in these published reports (Brown et al., 2006; El-Dib et al., 2012) were evaluated closer to 40 weeks' PMA (e.g., 40-44 weeks' PMA) compared to this present study's cohort at 35 weeks' PMA, likely resulting in a difference in mean summary scores. According to Pineda and colleagues (2012), significant changes in neurobehavior occur in the last six weeks of development, before term equivalent. Because of these rapid changes, a difference is likely to exist between very preterm infants evaluated at near term (e.g., 35-36 weeks' PMA) compared to term (e.g., 40-44 weeks' PMA). This period of rapid brain growth provides a window of opportunity for health care professional to support infant development by maximizing early therapy interventions, such as occupational, physical, and speech therapies, to optimize neurodevelopment in these at-risk infants. Therefore, it is hypothesized that if the M Technique intervention would have continued to discharge and the timing of the administration of the NNNS performed at term equivalent (40-44 weeks' PMA), differences between the experimental and control groups may have reached significance and differences between this cohort and the published very preterm mean summary scores would not have differed.

To date, only one RCT trial has examined the long-term neurodevelopmental impact of massage on infants born very preterm (Procianoy, Mendes, & Silveira, 2010). Procianoy et al. (2010) examined the effects of a mother-delivered massage therapy program on neurodevelopmental outcomes at two years corrected age and found that infants who received routine massage had significantly higher Mental Development Index scores on the Bayley Scales of Infant Development (BSID—II), suggesting routine massage combined with skin-to-skin care improves neurodevelopmental outcomes at two years of age. More research is needed to determine if this improved neurodevelopment is continued past 2 years of age and if the same effect can be seen with very preterm infants who receive the M Technique soon after birth through discharge.

Infant Weight

The effect of massage on daily weight gain in healthy preterm infants (greater than 30 weeks' GA) is well reported (Diego, Field, & Hernandez-Reif, 2005; Dieter, Field, Hernandez-Reif, Emory, & Redzepi, 2003; Ferreira & Bergamasco, 2010; Gonzalez, et al., 2009; Adamson-Macedo, 1985; Field et al., 1986; Scafidi, Field & Schanberg, 1993; Wheeden, 1993). However, similar to other studies examining the effects of massage on body weight in very-low-birth-weight infants (VLBW; <1500 g), our study found no difference in body weight between the infants who received the M Technique and the control group (Guzzetta et al., 2009; Mendes & Procianoy, 2008). Similarly, no differences in weight gain were seen between the infants who received gentle human touch and the control group (Harrison, Williams, Berbaum, Stem, & Leeper, 2000; Modrin-Talbot, Harrison, Groer, & Younger, 2003). The topic of infant

nutrition is a complex phenomenon for infants born very preterm who are either VLBW or extremely-low-birth-weight (<1,000 g) (ELBW) and reside in the NICU. These infants are born at a time of rapid brain and body growth. Initiating and maintaining growth in these high-risk infants is often challenging and complicated due to their disease state. Often, growth rates lag behind resulting in extrauterine growth restriction because of their disease state, including pulmonary disease or sepsis. Although infants in the experimental group in this present study started with lower birth weights compared to the control group infants, the infants who received the M Technique had higher weights at the end of the 5-week intervention, even though it was not significant.

Specific Aim Two

Immediate Physiological Infant Response

This is the first comforting touch study to examine infant physiologic and behavioral state responses over a period of five weeks. The majority of massage or gentle human touch studies are conducted over a 5 to 10 day period. Similar to our feasibility study (Smith et al., 2012), findings from this present study suggest that infants born very preterm can tolerate an infant-driven systematic stroking touch method, the M Technique, that promotes physiologic stability and indications of relaxation. No studies have examined immediate physiologic responses in very preterm infants as a result of providing systematic touch with moderate pressure stroking over a 5-week period. The majority of studies have examined slightly older gestational age infants and their response to gentle human touch (e.g., still touch, containment, no stroking) with the main outcomes resulting in no significant difference in oxygen

saturation or heart rate before, during or after the intervention indicating no adverse effect (Harrison et al., 1996, Modrcin-Talbott et al., 2003). These studies support the notion that gentle human touch for preterm infants does not cause changes in heart rate and oxygen saturation. However, in a larger randomized controlled trial, Harrison and colleagues (2000) reported a decrease in oxygen saturations across the 3 phases of GHT at baseline, during, and after the intervention and 19% of the infants in the GHT group had to have 1 or more GHT sessions terminated early because of a decrease in HR or a decrease in oxygen saturations. Preterm infants who received GHT and had decreased oxygen saturations were those infants who were lower in gestational age (GA range between 27 – 33 weeks) and birth weight (BW range between 796-1998 grams) and had higher morbidity levels (morbidity range not reported) than the infants who did not require early termination of the GHT sessions, suggesting the need for caution and close monitoring in these very small infants (Harrison et al., 2000). This decrease in oxygen saturation did not occur in the present study.

Two studies have examined the immediate physiologic effects of the *Touch and caressing-tender in caring* (TAC-TIC) therapy, a systematic, sequence of stroking in ventilated very preterm infants (Adamson-Macedo, de Roiste, Wilson, de Carvalho, & Dattani, 1994; de Roiste & Bushnell, 2000). Intubated very preterm infants received a 3 to 4 minutes of systematic, sequenced stroking all over the body for an average of seven to nine sessions. Similar to our findings, de Roiste & Bushnell (2000) demonstrated a significant decrease in heart rate from the “during-to-after” stroking intervention but unlike our findings, these investigators did not observe a significant decrease in heart rate from “before-to-during” or “before-to-after” stroking intervention

(de Roiste & Bushnell, 2000). In addition, these infants' respiratory rates increased significantly from the "during to after" phases but no differences were found across the "before to during" and the "before to after" phases. These respiratory rate findings are different from the present study findings, which demonstrated a decrease in respiratory rates from baseline, during, and post M Technique intervention delivery. Both TACTIC therapy studies (Adamson-Macedo et al., 1994; de Roiste & Bushnell, 2000) measured infants' transcutaneous arterial oxygen tension (TcPO₂) and found no difference in TcPO₂ in any of the before, during, or after phases. These investigators also conclude that no change in TcPO₂ indicates that this method of touch can be delivered without adverse effects and the unlikelihood of exacerbating infant distress.

The results of the present study clearly suggest that the M Technique has positive immediate physiologic effects from baseline through 10 minutes post intervention, suggesting a relaxing and soothing effect, which is different from the aforementioned studies. Whether or not these positive physiologic responses have long-term implications needs further investigation.

Immediate Infant Behavioral State Response

To our knowledge, no infant massage or M Technique studies have examined behavioral state outcomes in this population of infants born very preterm who received the intervention starting at 30 weeks' PMA. Studies that have examined the immediate behavioral response to touch are restricted to gentle human touch, which include infants born at slightly older gestational ages and do not receive moderate pressure stroking (Harrison et al., 1996, 2000; Modrcin-Talbott et al., 2003). Similar to the GHT studies, infants in the present study had decreased levels of active sleep and motor

activity during the touch intervention, however, these differences were significant in the present study from baseline up to 10 minutes following the M Technique intervention. In addition, infants in the present study also demonstrated consistent trends of increased periods of quiet sleep from baseline, during, and post-M Technique intervention which is different from the GHT studies that did not observe a significant increase in quiet sleep during this same time period (Harrison et al., 1996, 2000; Modrcin-Talbott et al., 2003).

Consistent with our feasibility study (Smith et al., 2012), very preterm infants receiving the M Technique demonstrated positive ABSS scores over time suggesting a more quiet sleep state during and following the M Technique sessions. However, unlike our feasibility study, very preterm infants in the present study received 30 applications of M Technique intervention over the course of 5 weeks, versus once in the feasibility study, and the behavioral state scores remained consistently low during and following the interventions. These study results suggest that a 7-minute infant-driven M Technique intervention can be delivered multiple times to hospitalized very preterm infants starting at 30 weeks' PMA.

Conclusion

This case-control pilot study is one of the first to examine and support the cumulative effect of an infant-driven M Technique intervention that incorporates a series of stroking movements performed using a set pressure, sequence, and repetition in hospitalized very preterm infants over a five-week period starting at 30 weeks' PMA. This study demonstrates the utility and feasibility of multiple M Technique applications in high-risk infants in a level IV NICU starting at 30 weeks' PMA with

notable evidence of positive physiological and behavioral state impact. These results indicate that hospitalized very preterm infants can tolerate an infant-driven systematic stroking method of touch resulting in soothing or relaxing effects. Although no differences were found between the M Technique and control groups on neurobehavior and growth velocity, this study supports that the M Technique intervention does not adversely affect these at-risk infants and was deemed appropriate and beneficial for this population. Due to the small sample size and study design limitations, caution should be taken in generalizing the results of this study to all very preterm infants. This study provides the framework for further investigation. Additional research is needed with a larger, randomized, systematic methodological design to determine the short- and long-term effects, specifically as related to brain growth, long-term neurobehavioral development, as well as decreased stress. Although not a component of this study, future research is also needed to evaluate the effectiveness of a parent-delivered M Technique and the potential impact on parent mental and emotional health and parent-infant synchrony.

Limitations

There are several limitations to this study. First, the design of the study was limited to using retrospective case controls in order to match subjects to the experimental group. Although strict criteria were used to match subjects according to GA, race, and gender, a threat to internal validity exists due to selection bias. Second, the small sample size and lack of randomization limits the ability to generalize findings and control for additional confounding variables. Our study was based on a practical, but relative small sample size of 9 infants per group, which might mask some of the

additional differences that might exist between different groups of infants subjected or not to the M Technique intervention. Third, the primary investigator provided the majority of the M Technique interventions and had vested interest in the results; however, the PI was not responsible for collecting the data. Fourth, we did not take into account the number of skin-to-skin (SKS) care sessions or parent-infant interactions between the two groups of infants nor did we account for the physical and occupational therapy sessions these infants received as part of their standard care. All infants received standard therapy protocols administered by neurodevelopmentally trained neonatal physical and occupational therapists. These therapists incorporate infant massage into part of their routine protocol. This NICU environment incorporates a strong emphasis on optimizing developmental care consistent with supporting sleep cycles and neurodevelopment. Infants within this NICU are routinely provided positioning support to facilitate optimal physiological development. In addition, the unit adheres to reducing the stresses of the NICU by minimizing noise and light and promoting longer rest periods. Parent involvement, a commitment to developmental care, routine therapy that incorporates infant massage and the number of parent-infant interactions were not accounted for and could explain the possibility of no differences seen in the experimental and control groups. Fifth, this study did not take into account alterations in brain structure or white matter injury that is more accurately detected by MRI than cranial ultrasound, that may further explain poor neurobehavior in the very preterm infant at term (Inder, Warfield, Wang, Huppi, & Volpe, 2005; Inder, Anderson, Spencer, Wells, & Volpe, 2003). The MRI of one of our intervention subjects (Subject 109) at term equivalent revealed periventricular leukomalacia (a form of white matter

injury) and poor brain development. However, upon further analysis, the NNNS summary scores were virtually the same controlling for the inclusion of this subject. Six, this study only examined immediate (e.g., physiologic and behavioral state) and short-term (e.g., pre and post-weights and NNNS) outcomes and did not examine long-term developmental effects. For instance, longer-term neurodevelopmental outcomes at two years of age (and beyond) could have been incorporated, including the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) (Bayley, 2006). In addition, because the study only consisted of a 5-week intervention, the M Technique was discontinued once the subjects in the experimental group received 30 sessions. This decision to terminate the M Technique intervention after 30 sessions and prior to discharge was difficult because parents, staff, members of the research team, and the medical care team requested continuation of the M Technique sessions until discharge. Seventh, one infant was withdrawn from the study prior to completion after receiving 25 of the 30 M Technique sessions. The subject was withdrawn because he acquired necrotizing enterocolitis with bowel perforation, requiring emergent surgery. Attrition is a threat to internal validity. Eighth, this study did not take into account any perinatal factors that may have influenced neurobehavior. While the relationship between perinatal variables and preterm infant neurobehavior at term is complex, studies have demonstrated that maternal antenatal steroids positively affect neurobehavior in infants born very preterm (Brown et al., 2006). Ninth, the variability of the infant's state prior to administration of the NNNS is another limitation of this study. Proper administration of the NNNS times is dependent on the presence of proper state. Six states are recognized by the NNNS including quiet sleep, active sleep, drowsy, quiet

awake, active awake and crying. The optimum time to administer the NNNS is 2 hours after feeding, since it allows the examination to start while the infant is in a sleep state and gradually changes to a state of wakefulness, which can be challenging in an intensive care environment. However, it is not clear how this variation may have affected the results as all items were still administered accordingly. In addition, it's important to note that the NNNS evaluation is only one snapshot or window of time and does not take into account variables that may have occurred immediately before or after the evaluation. Finally, the examiner was not blinded to observing and recording behavioral state data and knew that the intervention was administered, which may have resulted in bias in the recording, but is very unlikely that such observation would have influenced the physiologic or NNNS measures.

Recommendations for Future Research

Strengths of this dissertation study despite its aforementioned limitations include the fact that it allowed modification of an existing workable and realistic protocol that could be administered multiple times over several weeks, which will enhance the design of the next phase of research. This modified protocol has also allowed us to extend *comforting touch* to a length of period rarely explored in this population and field of research. Logistical barriers were also identified, requiring detailed coordination of the research team, and include timing of the intervention as it relates to the infant's:

- hands-on care schedule,
- feeding schedule,
- procedure schedule (such as eye exams), and

- parent/family interaction schedule.

The identification and broader understanding of these logistical issues also led to refinement of successful recruitment approaches and data collection methods, as well as gathering of data that will aid in determining estimated sample size for future studies. Thus, this pilot study provides evidence for future funding bodies that the research team is knowledgeable and competent to carry out the next phase of study and that the next phase is worth funding. It is our goal that the next phase of study will be fruitful and foster new transformational knowledge that will be applied to the lives of very preterm infants and their families.

The M Technique can be easily delivered to very preterm infants in a level IV NICU who are 30 weeks' PMA without notable adverse effects and with evidence of positive physiologic and behavioral state impact. Additional research is needed with a larger, randomized, systematically methodological design to determine both short- and long-term effects as it relates to brain growth, long-term neurobehavioral development, as well as decreased stress. Future research is also needed to evaluate the effectiveness of parent-delivered M Technique session and the potential impact on parent mental and emotional health and parent-infant synchrony. These future research studies should incorporate a modifiable infant-driven M Technique protocol starting prior to 30 weeks' PMA to determine timing, duration, and frequency of this novel approach.

Implications for Practice

Findings from this study build upon the science of touch for very preterm infants and are important because much of the care delivered to this high-risk population includes minimal stimulation, resulting in limited comforting touch

stimulation (Smith, 2012). This study is one of the first to support an infant-driven systematic method of stroking touch with over a five-week period starting at 30 weeks' PMA. Importantly, while the majority of infant massage studies incorporate a 15-minute massage intervention, including 10 minutes of moderate pressure stroking and 5 minutes of kinesthetic stimulation, this study demonstrates that positive physiological and behavioral state changes occurred after only 7 minutes of the M Technique intervention, resulting in a lesser need of time commitment and effort by caregivers. Neonatal health care professionals can apply a potentially cost-effective, infant-driven comforting touch strategy, the M Technique, aimed at reducing stress and optimizing the sensory experience of very preterm infants. More importantly, neonatal health care professionals can teach parents to deliver the M Technique, which could ultimately have infant, parent, and infant-parent dyad implications with beneficial outcomes for the infants, their families, the healthcare system, and society in general.

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APPENDIX A

IRB AUTHORIZATION AGREEMENT BETWEEN WUSTL AND UMKC

Washington University
IRB Authorization Agreement

This Agreement is made and entered into this 27th day of December, 2011, by and between Washington University, a Missouri charitable and educational institution ("WU"), and the Curators of the University of Missouri on behalf of University of Missouri – Kansas City ("UMKC").

Whereas, WU faculty members desire to conduct the research project(s) described in Attachment A to this Agreement ("Research Projects") in collaboration with UMKC; and

Whereas, WU and UMKC mutually desire that the WU IRB serve as the Institutional Review Board (IRB) of record to review and approve Research Project protocols involving human research participants that will be conducted by full-time WU faculty members and employees in collaboration with UMKC.

Now, therefore, in consideration of the premises set forth above and the mutual covenants set forth below, WU and UMKC agree as follows:

1. WU IRB shall provide IRB review for the Research Projects identified in Attachment A to this Agreement.

WU OHRP Federalwide Assurance (FWA) Number: FWA00002284
WU IRB Registration Numbers: IRB00000163, IRB00001723, IRB00000164,
IRB00000165, IRB00002167, IRB00000166, IRB00000167, IRB00001730,
IRB00000988, IRB00002168 and IRB00005594.

2. UMKC shall rely upon WU IRB review for the Research Projects identified in Attachment A to this Agreement.

UMKC OHRP Federalwide Assurance (FWA) Number: 1026 0000 388

3. The authorized Officials signing below agree that UMKC may rely on the WU IRB review, approval, and continuing oversight provided under WU's FWA for the Research Projects identified in Attachment A to this Agreement.

4. UMKC remains responsible for ensuring compliance with the WU IRB's determinations and with the terms of its OHRP-approved Assurance for research conducted at UMKC facilities. Relevant minutes of IRB meetings shall be made available to UMKC upon request.

5. The review, approval, and continuing oversight performed by the WU IRB shall satisfy the requirements of the HHS regulations for the protection of human subjects at 45

CFR 46, the requirements of WU's OHRP-approved FWA, and the HIPAA Privacy regulations at 45 CFR Parts 160 and 164.

6. Either party shall have the right to terminate this Agreement with or without cause upon 30 days written advance notice to the other party. WU shall also have the right to terminate this Agreement immediately upon written notice to UMKC in the event that (1) the Research Project is terminated; (2) UMKC is debarred from participation in federally funded research; (3) UMKC is determined to have violated any of the provisions of this Agreement or federal, state or local laws or regulations; or (4) if applicable, a subcontract entered into between the Parties to this Agreement with respect to a Research Project identified on Attachment A to this Agreement is terminated.

7. The Parties will each maintain their own separate general and professional liability coverage in the amounts of \$1,000,000 per occurrence and \$3,000,000 in the aggregate for each policy. Such insurance will be for claims, costs, or liability for a loss, damage, injury or loss of life resulting from their respective participation in this Agreement, and any relevant protocols developed under the Research Project.

8. WU agrees to defend, indemnify and hold harmless UMKC, its employees, officers and trustees from and against all claims, costs, and liabilities, including attorney fees and expenses, arising directly from performance of WU of its duties and obligations under this Agreement.

9. UMKC agrees to defend, indemnify and hold harmless WU, its employees, officers and trustees, as well as the WU IRB and its individual members, from and against all claims, costs, and liabilities, including attorney fees and expenses, arising out of performance of UMKC or any of its employees, students or agents, of the duties and obligations under this Agreement.

10. This Agreement will be governed and construed in accordance with the laws of the State of Missouri.

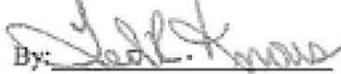
11. This Agreement, and the duties and obligations associated with this Agreement, may not be assigned by either party without the prior written consent of the other party.

12. No Amendments or changes to this Agreement shall be effective unless made in writing and signed by the other party.

WASHINGTON UNIVERSITY

By: 
Larry J. Shapiro, MD
Executive Vice Chancellor for
Medical Affairs and Dean

UNIVERSITY OF MISSOURI -
KANSAS CITY

By: 
Ted R. Norris, Ph.D.
Associate Vice Chancellor for Research
University of Missouri - Kansas City

APPENDIX B
INFORMED CONSENT

INFORMED CONSENT DOCUMENT

Project Title: Impact of a Novel Relaxation Method of Touch (M Technique®) on Neonatal Neurobehavioral Development Among Very Preterm Infants.

Principal Investigator: Joan Smith

Research Team Contact: Joan Smith 314-454-6037

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights as a research participant. By signing this form you are agreeing to participate in this study.

If you have any questions about anything in this form, you should ask the research team for more information.

You may also wish to talk to your family or friends about your participation in this study.

Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because your child was born before 30 weeks' gestation, is a patient in the neonatal intensive care unit (NICU), and is now at least 30 weeks' post-menstrual age.

The purpose of this research study is to systematically test the cumulative effect of the M Technique® on infant brain development in hospitalized infants born very preterm. Survival rates for preterm infants (less than 30 weeks gestation) have improved a lot with advances in medical care. However, babies born prematurely have a higher risk for developmental problems. Often the NICU is stressful for the developing premature baby and strategies to modify the baby's environment are needed to decrease stress. Touch is one of the first human senses to develop and is the foundation of your baby's communication. Positive gentle human touch can be beneficial for babies.

The M Technique® is a relaxation technique that has been specifically developed as a structured and systematic relaxation method of touch for hospitalized intensive care patients. This technique incorporates a series of stroking movements performed in a set sequence for patients who are too fragile to tolerate a traditional massage. The M Technique® will be administered to your baby's back. Our research team studied the effects of a onetime application of the M Technique® on other NICU babies similar to yours. We found evidence of positive physiological and behavioral changes. There were no adverse effects. No studies to date have examined multiple applications of the M Technique® in hospitalized very preterm infants. The M Technique® will be delivered by an experienced neonatal nurse practitioner or therapist trained in the M Technique® method. The technique will be delivered to your son/daughter once he/she reaches 30 weeks post-menstrual age. After you provide consent, your child will be randomly assigned to either a control group (routine NICU care) or a treatment group (routine NICU plus the M Technique®). This means that the study treatment you receive will be determined purely by chance, like flipping a coin. Your child's participation in this study will help us to better understand whether the Technique® is suitable and beneficial for preterm babies in the NICU.

WHAT WILL HAPPEN DURING THIS STUDY?

- During your baby's stay in the NICU, he/she is being asked to allow an experienced neonatal nurse practitioner or therapist to deliver the M Technique[®] once he/she reaches 30 weeks' post-menstrual age (PMA). If your baby is in the treatment group, the relaxation technique will be delivered to your son/daughter's back and will last no longer than 15 minutes. A member of the research team will monitor your child's behavior prior to, during and up to 10 minutes after delivering the M Technique[®]. If your child is in the treatment group, the M Technique[®] will be provided 6 times per week, no closer than 6 hours apart, for 5 weeks, for a total of 30 applications. During this time, you may choose to stay and watch your child receive the Technique[®] or you may choose to leave.
- The delivery of the technique will take place at your child's bed space within the NICU.
- We will use specific medical information that is collected as part of your child's routine clinical care (heart rate, respiratory rate, oxygen saturations, weight) and record your child's behavioral state (specifically looking at your child's cues and sleep-wake states).
- At the end of the 5 weeks, a neurobehavioral evaluation will be administered in your child's room by a trained occupational therapist that is certified in the use of neurobehavioral measures.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 20 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your child's involvement will last for 5 weeks. If your child is part of the treatment group, he/she will receive the M Technique[®] 6 times per week for a total of 5 weeks. Each M Technique[®] session will last no longer than 15 minutes.

WHAT ARE THE RISKS OF THIS STUDY?

Your child may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks, or risks that we did not anticipate, associated with being in this study. There are no foreseeable risks to participating in this study. However, even though unlikely, your baby may exhibit signs of stress during the administration of the M Technique[®]. Typically, preterm infants show their stress cues by demonstrating physiologic changes such as heart rate, respiratory rate, or oxygen saturations or they demonstrate behavioral cues such as crying, facial grimacing, finger splaying, hiccoughs, and eyes clinched. However, to minimize this risk, the M Technique[®] will be delivered based on your baby's cues and will be delivered by an experienced neonatal nurse practitioner or therapist trained in recognizing infant stress signs. The M Technique[®] will be delivered once your baby shows signs that he/she is ready to be touched.

WHAT ARE THE BENEFITS OF THIS STUDY?

We don't know if your child will benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because a better understanding of whether or not babies born very preterm are able to tolerate a technique that could provide relaxation, comfort and decrease stress could aid in their development.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study.

WILL I BE PAID FOR PARTICIPATING?

You will not be paid for being in this research study.

WHO IS FUNDING THIS STUDY?

The research team has received funding from the St. Louis Children's Hospital Research Grant program to conduct this research study.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

It is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities
- Hospital or University representatives, to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and be available to your health care providers who are not part of the research team.
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants.) The Institutional Review Board has reviewed and approved this study.

To help protect your confidentiality, we will retain electronic information in a secure format using password-protected computer records. Hard copy and the records will be identified only by study number and stored in a locked file cabinet. The site PI, in a separated locked file cabinet, will keep a log of study numbers and de-identifying data. All file cabinets containing data are inside a locked office in a corridor accessible only with badge access. If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect your treatment or the care given by your health provider.

your insurance payment or enrollment in any health plans.
any benefits to which you are entitled.
However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
Your signature and this form will not expire as long as you wish to participate.
You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
- To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at <http://hrpo.wustl.edu> (or use the direct link: <http://hrpohome.wustl.edu/participants/WithdrawalTemplate.rtf>) or you may request that the Investigator send you a copy of the letter.
 - **If you revoke your authorization:**
 - ! The research team may only use and share information already collected for the study.
 - ! Your information may still be used and shared if necessary for safety reasons.
 - ! You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send in a withdrawal letter. A sample withdrawal letter can be found at <http://hrpo.wustl.edu> under Information for Research Participants.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the researchers might decide to end your participation in this research study earlier than planned. This might happen because your baby was showing stress cues and in our judgment it would not be safe for him/her to continue.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Joan Smith (314) 454-6037 or Terrie Inder (314) 454-6148. If you experience a research-related injury, please contact: Joan Smith (314)454-6037 or Terrie Inder (314) 454-6148.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office, 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO

63110, (314) 633-7400, or 1-(800)-438-0445 or email hrpo@wusm.wustl.edu. General information about being a research participant can be found by clicking "Participants" on the Human Research Protection Office web site, <http://hrpohome.wustl.edu>. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Parent/Guardian Name and Relationship to Participant:

Do not sign this form if today's date is after EXPIRATION DATE: 07/17/13.

(Child's name – printed)

(Signature of Parent/Guardian)

(Date)

(Name of Parent/Guardian – printed)

OPTIONAL Parent/Guardian Name and Relationship to Participant:

Do not sign this form if today's date is after EXPIRATION DATE: 07/17/13.

(Child's name – printed)

(Signature of Parent/Guardian)

(Date)

(Name of Parent/Guardian- printed)

(Relationship to participant – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that he or she understands the risks, benefits, and procedures involved with participation in this research study.

(Signature of Person who Obtained Consent)

(Date)

(Name of Person who Obtained Consent - printed)

APPENDIX C
INFANT DEMOGRAPHIC DATA COLLECTION FORM

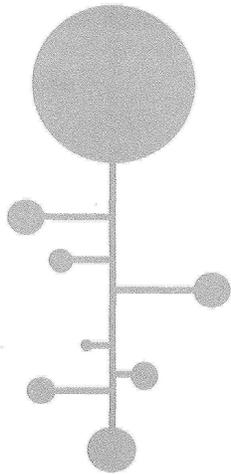
Infant Demographic Data Collection Form

Infant Study ID #	_____
Male/Female	_____
Gestational Age	_____
Birth Weight	_____
Race	_____
Admitting Diagnoses	_____
*Postmenstrual Age	_____
*Current Diagnoses	_____
Critical Risks Index for Babies (CRIB Score)	_____
*Current Weight	_____

Note: Collection starts at admission to the study and throughout.
*Characteristics obtained more than once.

APPENDIX D

NICU NETWORK NEUROBEHAVIORAL SCALE (NNNS)



nicu
Network
Neurobehavioral
Scale
Scoring Sheet



Child's Name/I.D. Number: _____
Examiner's Name: _____
Administration Start Time: _____
Administration End Time: _____

Date Tested

Year	Month	Day
<input type="text"/>	<input type="text"/>	<input type="text"/>

Child's Date of Birth

<input type="text"/>	<input type="text"/>	<input type="text"/>
----------------------	----------------------	----------------------

Child's Chronological Age

<input type="text"/>	<input type="text"/>	<input type="text"/>
----------------------	----------------------	----------------------

Prematurity Adjustment

<input type="text"/>	<input type="text"/>	<input type="text"/>
----------------------	----------------------	----------------------

Child's Corrected Age

<input type="text"/>	<input type="text"/>	<input type="text"/>
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Notes:

· P A U L · H ·
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PART I. EXAMINATION

A. Pre-Examination Observation
 1. Initial state observation

B. Habituation (States 1 and 2)
 2. Response decrement to light
 3. Response decrement to rattle
 4. Response decrement to bell

C. Unwrap and Supine
 5. Posture (States 1, 2, 3, 4, and 5)
 6. Skin color (States 1, 2, 3, 4, and 5)

7. Skin texture
 Is the infant in State 1, 2, 3, 4, or 5?

Yes	No
1	2

If yes,

Yes	No
1	2

 a. Desquamation

1	2
---	---

 b. Excoriations (abrasions)

1	2
---	---

 c. Loose skin

1	2
---	---

 d. Deep creases around the eyes and nose

1	2
---	---

8. Movement (States 1, 2, 3, and 4)
 9. Response decrement to tactile stimulation of the foot (States 1, 2, and 3)

D. Lower Extremity Reflexes (States 3, 4, and 5)
 10. Plantar grasp

If asymmetry, describe the less optimal side.

▼ L	▲ L	▼ R	▲ R
<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4

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D. Lower Extremity Reflexes (States 3, 4, and 5)—Continued

If asymmetry, describe the less optimal side.

11. Babinski reflex	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
12. Ankle clonus	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
13. Leg resistance	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
14. Leg recoil	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
15. Power of active leg movements	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
16. Popliteal angle	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4

E. Upper Extremities and Face (States 3, 4, and 5)

If asymmetry, describe the less optimal side.

17. Scarf sign	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
18. Forearm resistance	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
19. Forearm recoil	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
20. Power of active arm movements	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
21. Rooting	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
22. Sucking	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4
23. Grasp of hands	<input type="checkbox"/>	<input type="checkbox"/>	▼ L	▲ L	▼ R	▲ R
			1	2	3	4

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I. Infant Supine on Examiner's Lap (States 4 and 5)—Continued

39. Orientation animate auditory

--	--
40. Orientation animate visual & auditory

--	--

J. Infant Spin (States 3, 4, and 5)

If asymmetry, describe the less optimal side.

41. Tonic deviation of head and eyes

--	--
42. Nystagmus

--	--



K. Infant Supine in Crib (States 3, 4, and 5)

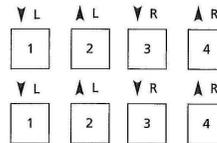
If asymmetry, describe the less optimal side.

43. Defensive movements

--	--
44. Asymmetrical tonic neck reflex (ATNR)

--	--
45. Moro reflex

--	--



PART II. EXAMINER RATINGS

L. Summary Items

46. Orientation handling procedures

- Was infant in State 4 or 5?

Yes	No
1	2

If yes,

- | | Yes | No | | Yes | No |
|---|-----|----|---------------------|-----|----|
| a. Repeated time out | 1 | 2 | f. Swaddling | 1 | 2 |
| b. Hand holding/Ventral pressure | 1 | 2 | g. Rocking/Walking | 1 | 2 |
| c. Auditory stimulation (voice or rattle) | 1 | 2 | h. Sucking/Pacifier | 1 | 2 |
| d. Jiggling/Vertical rocking | 1 | 2 | i. Other | 1 | 2 |
| e. Covering/Wrapping | 1 | 2 | | | |

L. Summary Items—Continued

47. Alertness (States 4 and 5)	<input type="text"/>	<input type="text"/>	57. Amount of startle during exam (States 3, 4, 5, and 6)	<input type="text"/>	<input type="text"/>
48. General tone—Predominant tone (States 4 and 5)	<input type="text"/>	<input type="text"/>	58. Lability of skin color (As infant moves from States 1 to 6)	<input type="text"/>	<input type="text"/>
49. Motor maturity (States 4 and 5)	<input type="text"/>	<input type="text"/>	59. Lability of states (All states)	<input type="text"/>	<input type="text"/>
50. Consolability with intervention (States 6 to 4 and below)	<input type="text"/>	<input type="text"/>	60. Self-quieting activity (States 6 and 5 to 4, 3, 2, 1)	<input type="text"/>	<input type="text"/>
51. Peak of excitement (All states)	<input type="text"/>	<input type="text"/>	61. Hand-to-mouth facility (All states)	<input type="text"/>	<input type="text"/>
52. Rapidity of build-up (All states with State 6 at least 15 seconds)	<input type="text"/>	<input type="text"/>	62. First predominant state	<input type="text"/>	<input type="text"/>
53. Irritability (All states)	<input type="text"/>	<input type="text"/>	63. Second predominant state	<input type="text"/>	<input type="text"/>
54. Spontaneous activity (States 3, 4, and 5)	<input type="text"/>	<input type="text"/>	64. Post-Examination state observation	<input type="text"/>	<input type="text"/>
55. Elicited activity (States 3, 4, and 5)	<input type="text"/>	<input type="text"/>	65. Order of administration	<input type="text"/>	<input type="text"/>
56. Tremulousness (All states)	<input type="text"/>	<input type="text"/>			

PART III. STRESS/ABSTINENCE SCALE

M. Physiological

	Yes	No		Yes	No
66. Labored breathing	<input type="text"/>	<input type="text"/>	67. Nasal flaring	<input type="text"/>	<input type="text"/>
Physiological Subtotal				<input type="text"/>	<input type="text"/>

N. Autonomic

	Yes	No		Yes	No
68. Sweating	<input type="text"/>	<input type="text"/>	71. Sneezing	<input type="text"/>	<input type="text"/>
69. Spit-up	<input type="text"/>	<input type="text"/>	72. Nasal stuffiness	<input type="text"/>	<input type="text"/>
70. Hiccoughing	<input type="text"/>	<input type="text"/>	73. Yawning	<input type="text"/>	<input type="text"/>
Autonomic Subtotal				<input type="text"/>	<input type="text"/>

O. CNS

	Yes	No		Yes	No
74. Abnormal sucking	<input type="checkbox"/> 1	<input type="checkbox"/> 2	80. Hypertonia	<input type="checkbox"/> 1	<input type="checkbox"/> 2
75. Choreiform movements	<input type="checkbox"/> 1	<input type="checkbox"/> 2	81. Back arching	<input type="checkbox"/> 1	<input type="checkbox"/> 2
76. Athetoid postures and movements	<input type="checkbox"/> 1	<input type="checkbox"/> 2	82. Fisting	<input type="checkbox"/> 1	<input type="checkbox"/> 2
77. Tremors			83. Cortical thumb	<input type="checkbox"/> 1	<input type="checkbox"/> 2
a. Low frequency / High amplitude	<input type="checkbox"/> 1	<input type="checkbox"/> 2	84. Myoclonic jerks	<input type="checkbox"/> 1	<input type="checkbox"/> 2
b. High frequency / Low amplitude	<input type="checkbox"/> 1	<input type="checkbox"/> 2	85. Generalized seizures	<input type="checkbox"/> 1	<input type="checkbox"/> 2
78. Cogwheel movements	<input type="checkbox"/> 1	<input type="checkbox"/> 2	86. Abnormal posture	<input type="checkbox"/> 1	<input type="checkbox"/> 2
79. Startles	<input type="checkbox"/> 1	<input type="checkbox"/> 2			
CNS Subtotal				<input type="checkbox"/>	<input type="checkbox"/>

P. Skin

	Yes	No		Yes	No
87. Pallor	<input type="checkbox"/> 1	<input type="checkbox"/> 2	90. Overall cyanosis	<input type="checkbox"/> 1	<input type="checkbox"/> 2
88. Mottling	<input type="checkbox"/> 1	<input type="checkbox"/> 2	91. Circumoral cyanosis	<input type="checkbox"/> 1	<input type="checkbox"/> 2
89. Paroxysmal cyanosis	<input type="checkbox"/> 1	<input type="checkbox"/> 2	92. Periocular cyanosis	<input type="checkbox"/> 1	<input type="checkbox"/> 2
Skin Subtotal				<input type="checkbox"/>	<input type="checkbox"/>

Q. Visual

	Yes	No		Yes	No
93. Gaze aversion during orientation	<input type="checkbox"/> 1	<input type="checkbox"/> 2	98. Sustained spontaneous nystagmus	<input type="checkbox"/> 1	<input type="checkbox"/> 2
94. Pull down during orientation	<input type="checkbox"/> 1	<input type="checkbox"/> 2	99. Visual locking	<input type="checkbox"/> 1	<input type="checkbox"/> 2
95. Fuss/cry during orientation	<input type="checkbox"/> 1	<input type="checkbox"/> 2	100. Hyperalertness	<input type="checkbox"/> 1	<input type="checkbox"/> 2
96. Obligatory following during orientation	<input type="checkbox"/> 1	<input type="checkbox"/> 2	101. Setting sun sign	<input type="checkbox"/> 1	<input type="checkbox"/> 2
97. End point nystagmus during orientation	<input type="checkbox"/> 1	<input type="checkbox"/> 2	102. Roving eye movements	<input type="checkbox"/> 1	<input type="checkbox"/> 2

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Q. Visual—Continued

	Yes	No		Yes	No
103. Strabismus	<input type="checkbox"/> 1	<input type="checkbox"/> 2	105. Other abnormal eye signs	<input type="checkbox"/> 1	<input type="checkbox"/> 2
104. Tight blinking	<input type="checkbox"/> 1	<input type="checkbox"/> 2			
Visual Subtotal				<input type="checkbox"/>	<input type="checkbox"/>

R. Gastrointestinal

	Yes	No		Yes	No
106. Gagging/choking	<input type="checkbox"/> 1	<input type="checkbox"/> 2			
107. Loose and/or watery stools	<input type="checkbox"/> 1	<input type="checkbox"/> 2			
108. Excessive gas, bowel sounds	<input type="checkbox"/> 1	<input type="checkbox"/> 2			
Gastrointestinal Subtotal				<input type="checkbox"/>	<input type="checkbox"/>

S. State

	Yes	No		Yes	No
109. High-pitched cry	<input type="checkbox"/> 1	<input type="checkbox"/> 2	113. Extreme irritability	<input type="checkbox"/> 1	<input type="checkbox"/> 2
110. Monotone-pitched cry	<input type="checkbox"/> 1	<input type="checkbox"/> 2	114. Abrupt state changes	<input type="checkbox"/> 1	<input type="checkbox"/> 2
111. Weak cry	<input type="checkbox"/> 1	<input type="checkbox"/> 2	115. Inability to achieve quiet awake state (4)	<input type="checkbox"/> 1	<input type="checkbox"/> 2
112. No cry	<input type="checkbox"/> 1	<input type="checkbox"/> 2			
State Subtotal				<input type="checkbox"/>	<input type="checkbox"/>

Stress/Abstinence Total

NICU Network Neurobehavioral Scale (NNNS™) by Barry M. Lester & Edward Z. Tronick.
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APPENDIX E

ANDERSON BEHAVIORAL STATE SCALE (ABBS)

ANDERSON BEHAVIORAL STATE SCALE (ABSS)

EYES OPEN OR CLOSED

- 12 HARD CRYING: VERY RED FACE; CLINCHED FISTS; VERY PROLONGED EXHALATION; AUDIBLE OR SILENT CRY; ENTIRE BODY VERY TENSE
- 11 CRYING: RED FACE; PROLONGED EXHALATION; AUDIBLE OR SILENT CRY; GENERAL BODY TENSION (RED FACE)
- 10 FUSSING: NORMAL COLOR; SLIGHTLY PROLONGED EXHALATION; WHIMPERS; (PRE-CRY GRIMACE; SNORTS)

EYES OPEN

- 9 VERY ACTIVE: TOTAL BODY MOVEMENT; TWISTING OR LIFTING TRUNK; TURNING HEAD SIDE TO SIDE
- 8 ACTIVE: WHOLE LIMB MOVEMENT
- 7 AWAKE, QUIET: EYES DON'T FIX AND FOLLOW; SAME MOVEMENT AS 6
- 6 ALERT INACTIVITY: EYES FIX AND FOLLOW; NO MOVEMENT OR SLIGHT SLOW MOVEMENT OF FACE, HAND, FOOT, HEAD, FOREARM, OR LOWER LEG; (EYE CONTACT)

EYES OPENING AND CLOSING

- 5 DROWSY: QUIET OR SOME MOVEMENT; DULL GLAZED APPEARANCE TO EYES

EYES CLOSED

- 4 VERY ACTIVE SLEEP: TOTAL BODY MOVEMENT; TWISTING TRUNK

- 3 ACTIVE SLEEP: IRREGULAR RESPIRATION; WHOLE LIMB MOVEMENT; (RAPID EYE MOVEMENT; FACIAL GRIMACES)
- 2 IRREGULAR QUIET SLEEP: IRREGULAR RESPIRATION; NO MOVEMENT OR SLIGHT, SLOW MOVEMENT OF FACE, HAND, FOOT, HEAD, FOREARM, OR LOWER LEG; (BRIEF APNEA)
- 1 REGULAR QUIET SLEEP: REGULAR RESPIRATIONS: FAINT OR NO MOVEMENT; (SLIGHT MOVEMENT OF FINGERS AND TOES)

SUCKING: HAND = H; FINGER - F; THUMB - T; PACIFIER = P;

OTHER: HICCOUGHS = C; YAWN = Y; TWITCH = W; MOUTHING = M.

USE ONLY ONE LETTER

RULES FOR SCORING ABSS

1. SCORE THE HIGHEST NUMBER THAT OCCURS DURING A 30-SECOND INTERVAL.
2. IF THE BABY HAS EYE PATCHES ON, ASSUME THE EYES ARE CLOSED, UNLESS THEY ARE SEEN TO BE OPEN.
3. IF SOMEONE IS WORKING WITH THE INFANT, WAIT UNTIL 1 MIN. AFTER THE INTERVENTION; THEN SCORE AROUSAL FOR 30 SEC.
4. IF STATE 6 OCCURS AT ANY TIME DURING THE OBSERVATION, SCORE THE AROUSAL LEVEL AS 6, EVEN IF A HIGHER NUMBER OCCURS.
5. IF ONE EYE IS OPEN AND ONE EYE IS CLOSED, SCORE THIS A STATE 5.
6. ITEMS IN PARENTHESES NEED NOT BE PRESENT.

APPENDIX F

SLCH RESEARCH GRANT AWARD LETTER



One Children's Place

St. Louis, Missouri 63110

May 9, 2012

Joan R. Smith, MSN, RN, NNP-BC

Neonatal Nurse Practitioner

St. Louis Children's Hospital

Dear Ms. Smith:

I am pleased to inform you that your project entitled, "Impact of a Novel Relaxation Method of Touch on Neonatal Neurobehavioral Development Among Very Preterm Infants" has been selected for funding in the amount of \$5000 through the St. Louis Children's Hospital Research Grant program. This grant is made possible by generous contributions to the St. Louis Children's Hospital Foundation. To access the funds as needed, please contact either Dr. Karen Balakas or Lisa Carroll at 454-4216 or lbc5945@bjc.org.

Please complete the following steps to begin the implementation process:

- Sign and return the enclosed Letter of Agreement to Dr. Karen Balakas at SLCH
- Develop an IRB proposal for the Washington University's HRPO. Please contact me if you need assistance accessing or completing the required forms.
- Provide a copy of the Washington University IRB approval to Dr. Karen Balakas before beginning work on your project.
- Submit quarterly progress updates and expenditures as indicated on the attached form yearly by the following dates:
 - April 1st
 - July 1st
 - October 1st
 - January 1st

Sincerely,

[Karen Balakas, PhD, RN, CNE](#)

Director, Clinical Research Partnerships

APPENDIX G
NANN SMALL GRANT AWARD LETTER



National
Association of
Neonatal
Nurses

**National Association of Neonatal Nurses
Research Institute Small Grants Award Program**

July 20, 2012

Dear Joan Renaud Smith:

On behalf of the National Association of Neonatal Nurses (NANN) thank you for submitting your application, ***Impact of a Novel Relaxation Method of Touch on Neonatal Neurobehavioral Development Among Very Pre term Infants***, for the 2012 Small Grants Award Program. Congratulations, your application was chosen to receive one of these awards, a \$5,000 grant.

Each application was assigned to three reviewers, all of whom are active neonatal researchers. The reviewers noted the high quality of applications submitted and the many strong candidates for research funding. You should be very proud of this accomplishment! Your passion for neonatal nursing is evident as well as your commitment to advancing nursing research.

Attached are your comments regarding your grant submission. Please use these constructively as you move forward in conducting your research. At the NANN Conference in October in Palm Springs, you will be acknowledged for your achievement. One of the requirements in receiving this Small Grants Award is that you attend the 2012 NANN Educational Conference in Palm Springs, CA, October 17-20th. Registration and housing are now open and you can save \$100 by registering before September 17th. Please go to the conference page at www.NANN.org to register and acquire your housing information.

To confirm that you will be accepting this award and attending the NANN conference, please email Kristi AR Conley, NANN Education Manager, kconley@NANN.org. At that point, you will have someone 'assigned' to you as a NANN point of contact for you and your mentor.

Funds will be distributed once we have proof of IRB approval. Please submit to the NANN offices as soon as possible. To submit your IRB approval or should you have any questions, please contact Kristi AR Conley, NANN Education Manager, 847-375-04835 or the email address above.

Sincerely,

Jacqueline M. McGrath
Chair, Research Institute Steering Council

4700 W. Lake Avenue • Glenview IL 60025 • 800-451-3795
www.nann.org

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VITA

Joan Smith (nee Renaud) was born and raised in St. Louis, Missouri. She is the youngest of nine children. Her primary education was received through the private, Catholic school system. After graduating with her Associate's Degree in Nursing in 1986, she secured a job in the neonatal intensive care unit (NICU) at St. Louis Children's Hospital. That same year she married her husband Steve. After completing her Master's Degree in Nursing and a Post-Master's Neonatal Nurse Practitioner (NNP) Certification, she became pregnant and delivered premature twin boys; Robert and Alan, at 29 weeks' estimated gestational age. It was at this time that Joan experienced firsthand what it was like to be a neonatal parent and became very interested in family-centered and neurodevelopmental care. Three and half years later, Joan and Steve gave birth to a healthy full-term baby girl, Carolyn.

Joan continues to work as a NNP in the NICU at St. Louis Children's Hospital and has been the recipient of several nursing research grant awards and the 2011 St. Louis Magazine Excellence in Pediatric Nursing Award. She is a member of several national nursing organizations, an Executive Committee Member for the Academy of Neonatal Nurses, and serves as a member of the Board of Directors and Program Service Committee for the Missouri March of Dimes. Joan has numerous publications, is on the Editorial Board for the Journal of Perinatal and Neonatal Nurses, and is a manuscript reviewer for three neonatal nursing journals.