

Infant Massage as a Stress Management Technique for Parents of Extremely Preterm Infants

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Introduction

Preterm birth, or birth prior to 37 weeks gestation, is a substantial contributor to infant mortality and comprises about 11.5% of all births.¹ A significant number of preterm infants experience cognitive and motor delays during development, with preterm birth accounting for roughly half of childhood disabilities.¹ Parents, especially mothers, experience increased anxiety, depression, and stress after a preterm birth.^{2,3} Parents of infants born extremely preterm, or before 28 weeks gestation, require prolonged medical intervention in the NICU and are at highest risk for developing mental health concerns.^{1,4} During this time, high risk of infant death and comorbidities among extremely preterm infants contribute to maternal feelings of helplessness and vulnerability to stress – creating a barrier to maternal-infant attachment.⁵ Further complicating this relationship is the parent’s limited involvement in their child’s care due to the complex medical management and decreased knowledge of how to safely interact with their fragile infant. Maternal anxiety and depressive symptoms have also been shown to negatively impact maternal-infant interaction, leading to worse developmental outcomes of the infant.⁶⁻⁸

Longitudinal studies have demonstrated that these negative developmental outcomes for the infant associated with parental psychological well-being may persist into middle childhood.⁹⁻¹⁴ Elevated maternal anxiety in the first month of life was found to impact the infant’s fine motor scores on the Bayley Scales of Infant Development at 20 months corrected age, in addition to increased behavioral problems noted in early childhood.⁹⁻¹¹ Mothers with decreased

psychological well-being shortly after their child's birth were found to provide more verbal cueing during play in middle childhood for their preterm infants. These infants also had a decreased attention span and were less social in middle childhood. These negative outcomes demonstrate the need to address parental psychological well-being in parents of extremely preterm infants in the postpartum period.¹² As a result, many hospital programs have implemented programmatic and institutional changes to incorporate the family into the infant's care in order to improve maternal outcomes and, consequently, infant outcomes.^{3,9-10,12}

Emerging evidence suggests that increased interaction within a mother-infant dyad, which is comprised of a mother and her infant, may lead to increased cohesiveness and reduced salivary cortisol, a biomarker for stress.^{13,14} Skin-to-skin contact has long been shown to be an effective strategy to achieve improved attachment, in addition to having a host of benefits for infants such as improved autonomic regulation, behavioral responses, and brain development.¹⁵ Skin-to-skin contact with either parent for neonates in the NICU leads to increased oxytocin levels and decreased cortisol levels in mothers, fathers, and infants, but cortisol only reached significance with infants.¹⁵ These changing hormonal levels were associated with improved responsiveness and synchrony in the parent-infant relationship as measured by videos of parent-infant interaction scored with the Dyadic Mutuality Code, an observational tool that measures reciprocal responsiveness in parent-infant dyads.¹⁵

Studies suggest a number of improved infant outcomes associated with maternally-administered infant massage, including a decreased pain response and improvements in weight gain, social engagement, overall development, responsiveness/attentiveness/alertness, mother-infant synchrony, mutual attentiveness, and improved infant temperament.¹⁸⁻²² The auditory-tactile-visual-vestibular (ATVV) intervention is an infant massage protocol that has previously

been studied and established for safe use in preterm infants and has been shown to be highly acceptable to mothers.^{16,17} Additionally, while research indicates that healthy, term infants have reduced cortisol after ATVV implementation, these outcomes have not been measured in preterm infants or their parents.¹³

Various treatment protocols involving infant massage, including ATVV, found decreased levels of anxiety, parenting stress, and depressive symptoms for mothers upon completion of the massage compared to mothers in control groups, both over time and in a single session.²³⁻²⁸ With ATVV participation specifically, mother-infant dyads demonstrated increased positive interactions and improved clarity of infant cues during feeding as defined by the Nursing Child Assessment Satellite Training – Feeding Scale.²⁹ Additionally, improvements from ATVV persisted after discharge at long-term follow up, with improved levels of maternal responsiveness during play and an improved home environment noted as compared to mother-infant dyads who did not complete this intervention.^{24,29}

To our knowledge, the published literature has examined the potential stress impact of preterm infant massage on infants and parents through self-report stress measures only instead of using objective, biological marker outcome such as salivary cortisol. Therefore, the aim of this study is to measure salivary cortisol in extremely preterm infants and their parents immediately before and after infant massage in order to detect potential changes in stress at the biological level. We hypothesize that parents performing the ATVV protocol with their extremely preterm infants in the NICU will lead to decreased levels of salivary cortisol in parents and their extremely preterm infants in a single massage session.

Methods

Subjects

This data was collected as part of the TEMPO (Therapist Education and Massage for Parent-Infant Outcomes) Study. The study design was a prospective single group, non-randomized study completed in the Neonatal Critical Care Center at UNC Children's Hospital. Data was collected as part of a prospective single cohort study funded by the PI's NIH KL2 training award (3KL2TR002490-02S1). Only infants who were born extremely preterm (less than or equal to 28 weeks gestation), were within their first 4 weeks of life, and with a biologic English-speaking mother or father available to participate were eligible for inclusion in the TEMPO study. Infants with any medical condition, such as abnormal bone density or a genetic abnormality, that would have limited the ability to perform massage or with parents that were unwilling to engage in all parts of the TEMPO study were excluded. All infants meeting the appropriate criteria were screened for inclusion when a PT referral was received, and families were approached by the principal investigator in the study for consent. Of the 32 parent-infant dyads enrolled, 6 were transferred to outside hospitals, and 2 infants died prior to massage education intervention. One mother declined salivary cortisol testing, and one mother could not be present for the massage session. In total, 21 mothers and 1 father completed the study. Infant massage was one of the main interventions provided in TEMPO and is the focus of this investigation.

Measures

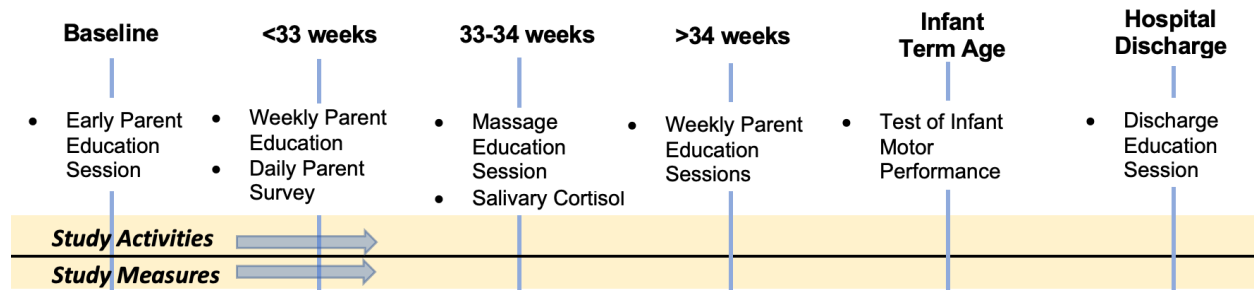
Salivary Cortisol: Salivary cortisol is a well-accepted biomarker for both physical and psychological stress, and this measurement technique is often preferred to more invasive forms of cortisol assessment (ex. blood draw) due to the possibility of increasing stress with a painful collection technique.³⁰ Additionally, salivary cortisol levels are commonly used to assess changes in a same day pre-post design.³¹⁻³⁴ These samples were taken utilizing procedures

outlined by Salimetrics (<https://salimetrics.com/saliva-collection-methods-devices/>).³⁵ Analyses were completed using Stata/MP 16.1.

Procedure

All TEMPO interventions were provided in addition to therapy standard care, which does not currently include infant massage. The included interventions and associated timeframes for TEMPO can be seen in Figure 1. Therapy standard care includes 1-2 sessions of physical therapy per week and spontaneous parent education if the parent is available during sessions. In the TEMPO intervention, weekly education sessions were planned in advance with parents, and multiple modes of instruction were used such as demonstration and handouts. Based on our experience in this study, infants were generally able to tolerate infant massage and regulate their temperature outside of an incubator at approximately 33-34 weeks gestational age and 1500 grams; other TEMPO interventions occurred before this point. Physical or occupational therapists leading the intervention monitored vitals throughout in order to ensure that the infant remained physiologically stable and appropriate for massage. While the therapist demonstrated how to perform massage on a doll and provided verbal cues, parents followed along and massaged their infants. The massage techniques consisted of moderately firm effleurage strokes to the extremities and gentle passive muscle elongation lasting 10-20 minutes in accordance with the White-Traut ATVV protocol.²¹ After 2 educational sessions conducted during concurrent physical therapy sessions, parents were encouraged to complete infant massage on their own when they visited their babies and were asked to record any massage they performed on a card at the bedside, which was used for other analyses in the TEMPO study.

Figure 1: Interventions and Timeframes for TEMPO Study



Salivary cortisol levels were collected by trained research personnel via buccal swab immediately before and after the second of two massage education sessions. For parents of twins, the first salivary cortisol sample was collected before massage with either child, and the second salivary cortisol sample was collected after massage with both infants was completed.

Results

Twenty-two parents completed the infant massage portion of this study. The majority of participants were mothers, married, not Hispanic or Latino, white, had a college or graduate degree, and had private insurance (Table 1). Infants had an average gestational age of 25.93 weeks. For 31.8% of mothers, this was their first pregnancy, and for 59.1% of mothers, this was their first time giving birth after 20 weeks gestation. Only one mother in this study had twins, and she performed infant massage on both twins. Insufficient levels of cortisol in infant samples prevented assessment of changes in infants; therefore, results for parents only are included in this study.

Table 1: Maternal Characteristics

Relationship to Infant	Mother 95.5% (21)	Father 4.5% (1)		
Marital Status	Married 72.7% (16)	Single 22.7% (5)	Unknown 4.6% (1)	
	High School Diploma	Partial College or Associate's Degree	College Degree	Graduate Degree

Highest Level of Education	9.1% (2)	27.3% (6)	27.3% (6)	36.3% (8)	
Medical Insurance	Private 59.1% (13)	Public Insurance 22.7% (5)	Self-Pay/Uninsured 9.1% (2)	Other 4.5% (1)	Unknown 4.5% (1)
Ethnicity	Not Hispanic or Latino 86.3% (19)	Hispanic or Latino 9.1% (2)	Unknown or Prefer Not to Say 4.5% (1)		
Race	White 59.1% (13)	Black 22.7% (5)	Unknown or Prefer Not to Say 13.6% (3)	More than One Race 4.5% (1)	
Number of Pregnancies (including current one)	Mean (SD) 2.76 (2.05)				
Number of Times Parent has given Birth to Baby of Gestation Age of 20 Weeks or More	Mean (SD) 1.52 (0.75)				
Gestational Age of Infant (Weeks)	Mean (SD) 25.93 (1.40)				

With the remaining 22 parents, results of a paired t-test revealed a significant difference in pre- to post-infant massage cortisol levels (18.01 ng/dl, [CI=2.6, 33.5] p=0.024). The cortisol test does not detect values <50 ng/dL, and 6 mothers measured <50 ng/dl at pre- and post-infant massage. In the remaining 16 samples with cortisol levels >50 ng/dl, average percent change from pre- to post-infant massage was 20.1%, which exceeds the recommended 15.5% threshold

to identify “responders” vs. “non-responders,” indicating a true stress response.³⁶ Additionally, a paired t-test with only those 16 samples revealed a larger and significant reduction in cortisol levels (26.47 ng/dL, [CI=4.40, 48.53], p=.016).

Table 2: Salivary Cortisol Levels from Pre- to Post-Infant Massage (Total Sample)

N	Average Change	Range of Change	Confidence Interval (95%)	p-value
22	-18.01 ng/dL	-108 to +55*	(2.6,33.5)	.024**

**Negative score indicates a decrease in salivary cortisol from pre- to post-massage while a positive score indicates an increase in salivary cortisol*

***p-value <.05 indicates significant difference*

Table 3: Salivary Cortisol Levels from Pre- to Post-Infant Massage (N = 16)

N	Average Change	Standard Error	Standard Deviation	Range of Change	Confidence Interval (95%)	p-value
16	-26.47 ng/dL	10.29	39.84	-108 to +55*	(4.40, 48.53)	.016**

**Negative score indicates a decrease in salivary cortisol from pre- to post-massage while a positive score indicates an increase in salivary cortisol*

*** p-value <.05 indicates significant difference*

Discussion

The key finding of this study revealed that participating in a single 20-minute massage session led by a NICU therapist led to a significant decrease in cortisol levels for parents of extremely preterm infants, which supported our hypothesis but we were unable to evaluate the impact of massage in infants due to insufficient levels of salivary cortisol collected.

Previous studies have also reported decreased stress as a result of ATVV or other massage interventions; however, these were more commonly assessed with self-report measures or over longer periods of time.²³⁻²⁸ Holditch-Davis et al. found that, in the long term, ATVV interventions led to decreased parenting stress and a faster decline in depressive symptoms after two months of intervention.²⁴ Two studies investigated state anxiety after one or two 8-minute infant massage sessions, which more closely aligns with the design of this study, and both found decreased levels of state anxiety as measured by the Spielberger State Anxiety Inventory for

parents immediately after the conclusion of infant massage.^{25,28} These studies were all performed with preterm infants <37 weeks gestational age rather than focusing exclusively on extremely preterm infants as in our populations. Nevertheless, these studies provide further support for our findings that massaging preterm infants leads to decreased parental stress levels. Most studies investigating the impact of infant massage on infants focused on long-term developmental outcomes, such length of hospital stay, time to transition to nipple feeding, and neuromotor scores, rather than short-term changes in stress.^{16,20,21} Despite our inability to assess salivary cortisol levels in extremely preterm infants in our cohort, White-Traut et al. has found that one session of ATVV intervention decreases levels of salivary cortisol in term infants¹³ and another by Vittner et al. found similar decreases after skin-to-skin contact.¹⁵

There is no clearly defined threshold for a minimal detectable change (MDC) or minimal clinically important difference (MCID) for salivary cortisol in the literature that we could reference to determine clinical significance. One study found that a change of 43.28 ng/dL was a threshold for distinguishing cortisol responders from nonresponders.³⁶ However, there are a number of reasons why using an absolute value to measure meaningful change may not be the most appropriate method. There are noted gender differences in both basal levels of salivary cortisol and absolute change in salivary cortisol levels in response to a stressful or relaxing event.^{34,37-39} Gender differences are also exacerbated in the postpartum period, as the hypothalamic-pituitary-adrenal (HPA) axis, which regulates salivary cortisol, is hyporesponsive in the immediate postpartum period for women, and men display increases in cortisol during this timeframe.^{40,41} Further, chronic stress can lead to decreased basal levels of salivary cortisol and decreased responsiveness of the HPA axis, which is seen among mothers of children with cerebral palsy and in parents the day after their child's admission to a pediatric ward on a

hospital.^{42,43} Due to these numerous factors that can influence salivary cortisol levels, MDC/MCID is not necessarily the most appropriate method to determine clinical significance of cortisol changes in this population.

In addition to quantifying an absolute value, Miller et al. also introduced the concept of calculating percent change as a way to identify clinically meaningful changes in salivary cortisol levels.³⁶ This method accounts for the numerous variables that can influence absolute levels of salivary cortisol and may a better representation of the magnitude of change. The average percent change in this study (20.1%) exceeded Miller's recommended percent change (15.1%) to identify cortisol responders from nonresponders, indicating that most parents' response reached clinical significance.³⁶ While this technique is on the whole effective, there may be some individuals, such as those with a history of chronic stress, who may be considered a "nonresponder" to intervention and will not demonstrate a shift in salivary cortisol due to decreased responsivity of the HPA axis.⁴²

Future research should seek to determine additional ways to quantify meaningful change in biomarkers like salivary cortisol. One method to consider is testing correlations between measures of salivary cortisol and self-report measures of perceived stress pre- and post-massage intervention; however, it is unclear how well self-report measures correlate with changes in salivary cortisol, as one study reported no correlation⁴⁴ and others reported mixed^{45,46} or strong correlations.^{47,48} Another method to detect clinical significance is to consider how cortisol levels change in relation to other hormones. Some evidence suggests that changes in cortisol and oxytocin, a hormone linked to bonding, are moderately correlated and should therefore be measured concurrently pre and post interventions designed to reduce stress and increase bonding.¹⁵ Elnazer et al. have found that changes over time, as measured by hair cortisol levels,

may be prevalent amongst individuals who do not show an immediate change in salivary cortisol levels, which could present as a more appropriate measure of change for chronic stress or for individuals who are deemed nonresponders.⁴⁹ Nevertheless, these areas continue to require future research to determine the best way to evaluate the relationship of salivary cortisol to clinical symptoms of stress in parents of extremely preterm infants.

Maternal satisfaction and improved health outcomes have been noted with massage-based interventions;¹⁷ however, more research on how to increase adherence to desired interventions is still needed.⁵¹ Parents report preferring multiple modes of instruction on how to interact with their infants, with direct observation of a physical therapist tending to be the most popular mode of instruction.⁵² It is also important to consider parent education level when designing intervention instructions.⁵³

Given these preliminary findings, results from studies examining salivary cortisol changes during skin-to-skin care, and studies demonstrating altered cortisol levels in parents of children with chronic health needs, we anticipate that regular maternally-administered massage will result in reduced salivary cortisol, which will, in turn, contribute to reduced maternal anxiety and depressive symptoms, leading to improved gross motor and behavioral outcomes for these infants in the long term.^{15,50} However, additional research in larger, randomized cohorts is needed to support this preliminary evidence.

This study had multiple limitations. The decreased sample size decreased the statistical power of our results, which makes it difficult to determine the true effect size of the intervention. Additionally, the laboratory test for salivary cortisol used in this study did not detect values below 50 ng/dL, so some changes may not have been detected, potentially leading to an

underestimation of the true change in salivary cortisol for some individuals. Future research should aim to assess these changes in a larger sample with a more sensitive laboratory measure.

Additionally, this study did not use any additional measures of short-term stress, such as the State-Trait Anxiety Inventory, to coincide with the biological measure, which should be considered in future research.⁵⁴ Lastly, we were not able to assess salivary cortisol changes in infants as sufficient levels of saliva were not collected using the sampling technique utilized in this study, which has been an issue in previous studies with infants as well.¹³ Prior studies investigating salivary cortisol changes in infants collected saliva over much longer periods of time by the nature of their intervention (ie. during skin-to-skin holding), which was not possible in this study because it would have required the infants being awoken at least 30 minutes prior to their care time.¹⁵ Other methods and timing for cortisol collection should be considered in future studies.

Conclusion

In this study, infant massage was determined to be a safe, low-risk intervention for use with extremely preterm infants once they have the ability to maintain their temperature outside of an incubator. The primary findings include the clinically significant decrease in maternal cortisol levels, indicating a decrease in stress as measured biologically, after one session of ATVV, which supported our hypotheses. Additionally, while further studies on the benefits for extremely preterm infants and long-term benefits for parents is warranted, this preliminary study supports integration of infant massage into clinical practice in neonatal intensive care units.

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