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Enhancing sensory experiences for very preterm infants in the NICU: an integrative review

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Abstract

OBJECTIVE—Very preterm infants hospitalized in the neonatal intensive care unit (NICU) experience alterations in sensory experiences. Defining types, timing and frequency of sensory-based interventions that optimize outcomes can inform environmental modifications. The objective of this study was to conduct an integrative review on sensory-based interventions used with very preterm infants in the NICU to improve infant and parent outcomes.

STUDY DESIGN—The data sources include MEDLINE, CINAHL, Cochrane Library and Google Scholar. Studies were identified that used sensory-based interventions in the NICU with preterm infants born < 32 weeks gestation, were published in a peer-reviewed journal between 1995 and 2015, and measured outcomes related to infant and parent outcomes. Studies were extracted from electronic databases and hand-searched from identified reference lists.

RESULTS—Eighty-eight articles were identified (31 tactile, 12 auditory, 3 visual, 2 kinesthetic, 2 gustatory/olfactory and 37 multimodal). There was evidence to support the use of kangaroo care, music and language exposure, and multimodal interventions starting at 25 to 28 weeks postmenstrual age. These interventions were related to better infant development and lower

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AUTHOR CONTRIBUTIONS

RGP conceived of the original idea to do an integrative review to inform a clinical practice guideline on sensory-based interventions in the NICU. She was involved with data synthesis, and wrote the first draft of the manuscript. She oversaw all parts of the project and approved the final version of the manuscript submitted. RG and AH conducted the literature review and identified articles appropriate for the integrative review. They were involved in identifying the articles, assessing each for quality and wrote the first draft of the evidence table. They critically reviewed the manuscript's content and approved the final version of the manuscript submitted. LCR assisted with the analysis processes, reviewed and revised the manuscript, and approved the final manuscript as submitted, and was also responsible for reporting the studies in the evidence table and ensured the accuracy of the evidence table. SO assisted with the analysis processes, reviewed and revised the manuscript, and approved the final manuscript as submitted, and made the PMA tables that demonstrate the PMA at which interventions have been investigated. JS was involved in idea conception, study design, data synthesis and ensured accuracy of the studies reported. She oversaw all parts of the project. She provided intellectual content to the manuscript and approved the final version that was submitted.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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maternal stress, but not all findings were consistent. Limitations included lack of consistent outcome measures, study quality and gaps in the literature.

CONCLUSIONS—Most research identified interventions that were done for short periods of time. It is unclear what the potential is for improving outcomes if positive sensory exposures occur consistently throughout NICU hospitalization. Until more research defines appropriate sensory-based interventions to use with infants born very preterm in the NICU, information from this review can be combined with expert opinion and parent/family values to determine best practice.

INTRODUCTION

Very preterm infants, those born < 32 weeks estimated gestational age (EGA), have a high incidence of long-term morbidity, which is not fully explained by clinical course or the presence of brain injury.^{1–8} A less-studied influence on long-term outcome is the neonatal intensive care unit (NICU) environment, which may influence neural development of very preterm infants during a sensitive period of brain growth.⁹ The NICU environment can be fraught with excess light and sound,^{10–12} as well as other chaotic types of stimulation, when infants lack mature coping mechanisms. As such, minimal stimulation, interaction and/or reduction of environmental exposures have become common NICU practices.^{10,13,14}

Based on current practice models that aim to minimize sensory exposure and facilitate parent–child interaction, hospitals throughout the United States and abroad are renovating NICU spaces to include private rooms. However, it may be important to focus attention on the sensory environment in private NICU rooms where near-complete sensory abatement is possible. We previously investigated differences in neurodevelopmental outcomes in very preterm infants hospitalized in an open ward NICU compared with private rooms,¹⁵ and found alterations in brain structure by term equivalent age and significantly poorer language outcomes in preterm infants in low stimulation private rooms.¹⁵ These results complement other studies that have demonstrated the importance of development during the NICU period¹⁶ and the need for positive sensory exposures to optimize outcomes.^{17,18} A recent editorial also questioned whether NICU infants are at risk for sensory deprivation in low-stimulation private rooms.¹⁹

While noxious sensory stimulation during periods of medical fragility may be detrimental to health,^{12,20,21} the appropriate amount of optimal sensory stimulation for very preterm infants is poorly defined, understood and implemented. Positive sensory exposures can have lifelong implications on learning, memory, emotions and developmental progression.²² Further, it is well understood that infants receive multidimensional sensory exposures in utero in the final months of pregnancy,²³ but the very preterm infant in the NICU misses potentially important, timed exposures that may facilitate neural pathways. An intentional, enhanced sensory environment has the potential to improve infant experiences and promote optimal outcomes for both infants and parents. Careful consideration of an appropriate sensory-based intervention plan should include interventions that have evidence to support their use in this vulnerable population. Important considerations include (1) ensuring that sensory interventions are appropriately timed according to the infant's readiness to accept and benefit from stimuli, based on the sequential order of development and maturation of the

sensory system;¹⁶ (2) making adaptations available for infants with limiting medical conditions; and (3) ensuring that the amounts and types of interventions across different levels of maturation are defined. However, before an intentional enhanced sensory environment can be defined, a comprehensive review of current evidence is critical. While there are existing reviews of developmental care, neurodevelopmentally supportive care, kangaroo care and single intervention exposures,^{24–31} to date, reviews on the current state of the science on multisensory exposure for very preterm infants across postmenstrual age (PMA) in the NICU are lacking.

MATERIALS AND METHODS

Purpose

The purpose of this integrative review was to identify evidence for sensory exposures for very preterm infants in the NICU in relation to their impact on neurodevelopmental outcomes of the infant as well as outcomes of the parents. It was of interest to also define the type, amount and timing of sensory-based interventions in the NICU.

Procedures

An integrative review was used to highlight the most relevant evidence related to sensory exposure in the NICU from a range of clinical research methodologies. Various study designs (systematic reviews, randomized controlled trials, quasi-experimental, crossover or single-group repeated measure studies) published in the last 20 years were included. Studies prior to 1995 were excluded to eliminate studies that were done well before current advances in NICU culture, practice and care. The population of interest was very preterm infants born 32 weeks gestation who were hospitalized in the NICU and had a sensory-based intervention that commenced prior to 36 weeks PMA. Very preterm infants (born > 32 weeks gestation) were the population of interest, as we sought to define optimal sensory exposures among the most fragile and vulnerable infants who were hospitalized in the NICU for significant periods of time. Infants born 432 weeks gestation were excluded, as sensory exposures in the NICU are shorter in duration, many times lasting only a few days or 1 week, consistent with shorter length of stay, in comparison with very preterm infants, who can be hospitalized in the NICU for several weeks or months. Studies that imposed a quantifiable environmental sensory exposure during the NICU stay were included. Studies that identified unimodal interventions were described in their respective categories (tactile, auditory, vestibular, kinesthetic, visual or olfactory/gustatory), while interventions that included more than one type of sensory exposure or those that compared one sensory exposure with a different type of sensory exposure were included in the multimodal category. The comparison group received no identified sensory intervention or standard of care, varying levels of the same or similar intervention, or a different sensory exposure. interventions could be performed by health-care workers, study investigators or parents. Relevant outcomes included infant behavioral outcomes, infant physiology, maternal mental health and parental outcomes. Physiology and behavior were included as outcomes, as it was felt that they could be tied into development in the very preterm infant. Samples of healthy infants were excluded, as this review was intended to define sensory exposures for infants who represent medically complex very preterm infants in the NICU.

Studies with sample size < 30 and no a priori calculation of power that was met were excluded. This was done to focus energies on studies with adequate sample size in order to make inferences from statistical analyses investigating associations. Finally, studies that included outcomes of pain or breastfeeding were excluded, as it was felt that they warranted their own review. See Table 1 for the exclusion criteria for this review. See Table 2 for search criteria and keywords.

Search strategy

A systematic search for studies published from January 1995 to October 2015 was performed using databases including MEDLINE (via PubMed), CINAHL (Cumulative Index to Nursing and Allied Health Literature), the Cochrane Library and Google Scholar. Reference lists of included studies were also searched for relevant literature. Searches were performed separately for each type of sensory exposure.

Study screening

One reviewer (authors, AH or RG) screened studies for inclusion. Studies were screened first by title. In situations where the title was unclear, the abstract was retrieved for review. The full text articles of potentially relevant studies were reviewed for final inclusion. If relevance of an intervention or inclusion of a study was unclear, it was resolved through discussion with the review team (authors: RP, AH, RG and JS).

Data extraction

One reviewer performed data extraction (authors, AH or RG) that was checked for accuracy by a second reviewer (authors, AH or RG). Extracted information included study design, sample size, country of origin, intervention (including frequency, duration, timing), EGA at birth, PMA at intervention, study inclusion/exclusion criteria and study outcomes and results. When results from the same sample were reported in multiple publications, they were reported together in this review as a single study. When it was unclear if samples came from the same cohort, authors were contacted for confirmation.

Study quality

Assessment of study quality was independently performed by two reviewers (AH and RG), and disagreements regarding study quality were resolved by discussion among the two reviewers until consensus was achieved. Systematic reviews were assessed for methodological quality using the Documentation and Appraisal Review Tool (DART).³² The remaining studies were assessed for quality using a modified version of a tool developed by the United Kingdom's National Institute for Health and Care Excellence (NICE).³³ The tool evaluates studies for *selection bias* (randomization, allocation concealment, group comparability at baseline), *performance bias* (groups received the same care, blinding of participants and health-care workers), *attrition bias* (equal follow-up time, completion of treatment, complete outcome data), *detection bias* (appropriate length of follow-up, precise definition of outcomes, valid and reliable outcomes, blinding of investigators or outcome assessor) and *other bias* (statistical methods, issues related to specific study designs). Each

factor was rated as yes/adequate, no/inadequate or unclear. Several of these factors were not relevant for single-group repeated measures studies.

Synthesis of findings

Given the significant heterogeneity of studies and their outcomes, study findings could not be combined quantitatively but were summarized qualitatively. Evidence related to each type of sensory intervention was defined across each PMA to determine at what age of maturity evidence existed to support specific interventions.

RESULTS

See Figure 1 for a breakdown of the articles reviewed during the integrative review process. See Figure 2 for evidence of the different types of interventions that have been studied across different PMA. See Supplementary Appendix SA for the 88 studies included in this review. See Supplementary Appendix SB for the quality assessment tables.

All articles that were included in the review and their details are available in Supplementary Appendix SA. Many of the outcomes were related to physiology or sleep, which did not have a direct and clear tie to development or parent outcomes. In addition, some of the significant differences that were reported had questionable clinical significance. Therefore, only outcomes that included clinically relevant developmental outcomes or parent mental health are synthesized below in the text.

Tactile

Thirty-one articles, representing 26 different cohorts, were identified on tactile sensory interventions.^{34–64} Three studies were on gentle human touch,^{34–37} two on massage^{38–40} and 21 on kangaroo care.^{41–64} Gentle human touch treatment length and duration ranged from 10 to 15 min over a course of 5 to 15 days. Tactile massage, which included tactile only portions with no kinesthetic component, consisted of 15-min treatments three times per day for 9 to 10 days.^{38–40} The duration of kangaroo care interventions ranged from 30 min⁵¹ to continuous kangaroo care after the infant stabilized.⁶⁰ In three studies the treatment length and duration were unspecified.^{45,58,60}

One study investigated the impact of gentle human touch on developmental outcomes, and no difference in behavioral organization was found.³⁵ One study investigated the effects of massage on the mother and found better mother–infant interaction.³⁸ There were 11 studies that investigated the impact of kangaroo care on infant development or parent mental health. Infants receiving kangaroo care looked more intently at a stimulus with less gaze aversion^{46,48} and demonstrated better mental development at 6, 12 and 24 months as well as better cognitive development at 5 and 10 years.⁴⁷ Parents who participated in kangaroo care demonstrated fewer depressive symptoms and a better mood,^{45,47,48} some decreases in measures of stress,⁶³ better mother–infant interaction^{46,50} and better maternal self-esteem.⁵⁰ Mothers who provided kangaroo care also were more adept at providing a developmentally appropriate environment for the infant.⁴⁶ However, not all studies found significant differences in outcomes among those receiving kangaroo care. No differences in infant social interaction⁴⁸ as well memory, social emotional health and developmental outcome at

age 1 year⁵⁴ have been reported. No differences in IQ at 5 and 10 years⁴⁷ have also been reported. Other studies reported no differences in maternal depression,^{47,54} stress,^{54,56,63} anxiety,⁵⁴ parent attitude toward baby or parent emotion,⁵³ and parent interaction with infant.^{54,63} Negative responses to kangaroo care included some alterations in temperature stability when kangaroo was done between 25 and 27 weeks PMA, some bradycardic and hypoxic events starting at 32 weeks PMA⁴⁴ and poorer sleep states.^{42,44,49,59,61,64} However, there are inconsistent findings with others reporting better temperature stability, improved physiology and sleep following kangaroo care.^{42,44,49,50,61}

Auditory

Twelve articles, representing 11 different cohorts, pertained to auditory interventions,^{65–76} including 2 on live music/singing,^{72,73} 5 on recorded music/singing/maternal voice^{66,68,70,71,74} and 2 on recorded maternal biological sounds.^{75,76} Treatment lengths ranged from 45 s to 45 min and were done one to four times per day over a course of 1 to 21 days.^{65–76} There were differences across studies regarding whether the auditory exposure was live or recorded. Music was related to improved feeding behaviors and less parent stress.⁷² Maternal voice was related to fewer stress responses, better neurobehavior at term and better developmental outcome at 3 and 6 months.⁷⁴

Visual

Three articles pertained to visual interventions,^{77–79} one of which was a systematic review consisting of eight articles.⁷⁸ No studies investigated the effects of visual stimulation using objects or people to focus visual attention and pursuit. All studies reported on the effects of cycled light. Cycled light was started at birth for several studies, and the intervention continued throughout hospitalization. No differences in neurobehavior at 32 and 38 weeks PMA were observed in relation to cycled light compared with other light environments.⁷⁸

Kinesthetic

Two articles pertained to kinesthetic interventions, both of which specifically investigated physical therapy.^{80,81} One of the articles was a systematic review consisting of 11 studies.⁸⁰ Treatment duration varied, but most included specific exercises performed five times, repeated five times per week over 4 weeks. There were no studies that assessed the impact of physical activity/kinesthetic interventions on neurodevelopmental outcomes.⁸⁰

Gustatory and olfactory

Three articles pertained to olfactory/gustatory interventions, all of which specifically investigated the effects of oropharyngeal colostrum, breast milk odor or mother's scent.^{82–84} Treatment duration ranged from every 3 h for 3 days to continuously until discharge. There were no studies that specifically investigated the effect of gustatory/olfactory stimulation on infant development or maternal mental health outcomes.

Multimodal

Thirty-seven articles on multimodal interventions, representing 32 different cohorts, were identified as part of this review.^{18,85–120} Eight articles were on the Auditory, Tactile,

Vestibular, Visual (ATVV) intervention originally described by Rosemary White-Traut, two on the Family Nurture intervention,^{99,113} three on the Hospital to Home: Optimizing the Premature Infant's Environment (H-HOPE) intervention,^{114,115,120} one on massage with aromatic oil,¹¹² three on use of kangaroo care coupled with auditory stimuli^{87,108,111} and 20 described a massage intervention that was coupled with a kinesthetic component.^{85,86,89–98,100,102–107,109}

ATVV interventions were related to better developmental outcomes,¹⁸ improved tolerance of handling³¹ and better feeding.^{117,119} ATVV has also been related to mothers having a more rapid decline in depressive symptoms and less parenting stress.¹⁰¹ However, several studies also reported no significant differences in outcomes of infants receiving ATVV, including no differences in neurobehavior and neurodevelopment¹¹⁸ and no differences in infant responsiveness.¹⁰¹

The Family Nurture Intervention reported no difference in relationship to maternal caregiving behaviors among those receiving the intervention.^{99,113}

Only one study reports parent and infant outcomes in relation to the H-HOPE; trends are reported, but no statistically significant differences in parent child interaction were found.^{114,115,120}

Massage interventions, which include a kinesthetic component, were related to significant decreases in maternal stress behaviors,^{100,104} better neurobehavior¹⁰³ and better mental development at age 2 years.^{105,107} However, some studies also reported no differences in psychomotor development^{105,107} or father's stress¹⁰⁴ among those receiving multimodal massage.

Kangaroo care plus singing as well as kangaroo care plus live harp were also shown to be related to decreased maternal anxiety.^{87,108}

Vestibular

No studies pertaining to isolated vestibular stimulation met inclusion criteria. However, see section on multimodal stimulation for articles that used vestibular stimulation in conjunction with other sensory exposures.^{18,88,101,110,116–119}

DISCUSSION

Key findings of this review include that there is a growing body of evidence supporting the use of early tactile, auditory, kinesthetic, visual, olfactory/gustatory and multimodal sensory-based interventions in the NICU with very preterm infants. However, there are significant differences in sensory exposures, outcomes, dosages and timing of sensory interventions across the literature that make it challenging to combine studies for a cohesive understanding of appropriate sensory exposures across PMA. Consistent relationships of sensory exposures to outcomes were not observed across studies. In addition, there are gaps in our understanding of appropriate timing of interventions, and several studies fail to elucidate the PMA that sensory interventions commenced. In addition, there is little evidence to suggest there are improved long-term outcomes related to sensory interventions. Finally, studies

identifying sensory-based interventions contain many methodological issues that make it difficult to appropriately interpret results across studies. However, current evidence identified in this review can be combined with expert clinical opinion and patient/family values to identify the ideal landscape for sensory-based interventions for very preterm infants in the NICU. Such work can lay the foundation for establishing sensory exposure guidelines that outline the type, dose, timing and frequency of appropriate sensory-based interventions for future investigation.

There is little evidence to suggest there are improved long-term outcomes from sensory interventions, which was the main focus of this review. An absence of evidence does not mean these interventions do not improve long-term outcomes. There is some evidence in this review to support the use of kangaroo care, music and language exposure, and multimodal interventions starting at 25 to 28 weeks PMA. Such interventions have been demonstrated to have positive relationships with infant development, sleep and physiology, as well as lower maternal stress. However, most of the research identified interventions that were done for short periods of time over only a few days. For example, some interventions were limited to 1 day for 1 to 1.5 h, others to 45 s twice per day over a course of 2 to 6 weeks, and still others ranged from 15 to 45 min over a course of 1 to 6 days.^{30,41,49,51,65–67,69,70,87,90–96,100,103,104,108} It remains unclear what the potential is for improving outcomes if such sensory exposures occurred consistently throughout NICU hospitalization. Moreover, evidence related to vestibular, kinesthetic and olfactory/gustatory interventions is not as well defined. There are also significant gaps in the literature related to most interventions. Despite the gaps in the literature, outlining where evidence exists, as done in our PMA tables can enable a better understanding of where more research is needed.

While some evidence to support the benefits of sensory-based interventions, as well as existing gaps, were identified in this review, very few risks of conducting sensory interventions were uncovered. As most NICUs in the United States are converting their spaces to ones with private rooms, sensory abatement is possible if families are not present and not at the center of care. Therefore, it is important that we build appropriate models of care within the new environments to optimize outcomes for very preterm infants and their families. This review identified some inconsistent benefits of sensory-based interventions. While more research is needed, it should not keep us from providing age-appropriate positive sensory exposures to very preterm infants. The development and implementation of a clinical practice guideline on sensory-based interventions can aid in guiding parent participation and health-care professionals in fostering important early interactions in order to optimize both infant and parental outcomes. Our next step will be to take the evidence identified in this review and couple it with expert clinical opinion and patient/family values in order to develop a clinical practice guideline. Appropriately timed sensory interventions that are supported by current evidence and places the parents at the center of the infant's care, which can be done within the context of developmental care across PMA.

This is the first review, to our knowledge, identifying the literature on multiple modes of sensory-based interventions in the NICU for very preterm infants. Other reviews related to neonates focus on developmental care, neurodevelopmentally supportive care or individual interventions.^{24,25,28,29} Individualized developmental care is a system of care in which there

is continuous assessment of infant behavior mixed with modifications to caregiving of the preterm infant; a clinical practice guideline for individualized developmental care was established in 2007.¹²¹ This work is important, as it aids in the understanding of modifying the environment early in development to support the unique needs of the preterm infant, provides guidance on how to assess and when/how to intervene, gives specific criteria for light levels (cycling, avoiding direct light) and defines maximum intensity (not to exceed 50 decibels) of sound. A review of developmental care was conducted by Symington in 2006 and includes components of positioning, clustering care, modifications of sensory stimuli and individualized developmental care interventions.²⁵ In a systematic review of neurodevelopmentally supportive care, 42 elements of care were identified, which included interventions such as family centered care, flexion positioning, modifying caregiving and reducing environmental stimuli.²⁴ There were also elements of sensory interventions identified with this review, which include components of olfactory stimulation, reducing sensory monotony, kangaroo care, positive tactile stimulation, teaching parents to interact with the preterm infant, uterine environment, and day and night cycle. However, previous reviews do not address the appropriate dosage and timing of sensory exposures, which this review attempts to better define.

Limitations of included studies

There is a possibility of publication bias, where only studies reporting positive outcomes were published and included in this review. In addition, most studies included multiple outcome measures, many of which did not reach statistical significance. Many outcomes that did have statistical significance were challenging to interpret and many may not have been clinically significant. We included multiple research designs in an effort to capture all appropriate literature related to improving the sensory environment, so lower quality non-randomized designs could have biased the review findings. Of the studies that were randomized, many did not specify their methods clearly or report allocation concealment. This, in addition to incomplete or weak assessments of participants at baseline, placed many of these studies at high risk for selection bias. While participants could not be blinded, and it may be difficult to blind parents and health-care workers to the intervention, few studies attempted to blind the outcomes assessor. Completeness of treatment and follow-up was also difficult to ascertain, as studies infrequently reported the number of infants by group with complete outcomes data and reasons for loss to follow-up. Most interventions were very short and were not conducted across the majority of hospitalization. In addition, many studies did not give clear descriptions of inclusion criteria including EGA at birth, and the PMA at the start and end of intervention. Finally, generalizability of many of the studies is limited.

Limitations of this review

Owing to resource limitations, this review did not include non-English language studies or non-published literature, and only one reviewer screened studies and performed data extraction. Exclusion of studies with a sample size less than 30 may have excluded relevant literature, though this was an attempt to exclude lower quality studies with convenience sampling and limited external validity. Articles published more than 20 years ago were excluded, so it is possible that important research from a time when there were rapid

transformations in providing or minimizing sensory stimuli in the NICU has been excluded. The size and scope of this review also did not allow us to follow-up with individual study authors in situations where methods or data were missing or unclear. When possible, we attempted to rate the methodological quality as unclear and explained our reason for judgment in these cases. In addition, this review is limited by lack of common interventions and outcomes, making it difficult to combine results into a cohesive whole. Finally, this review did not include literature on sensory exposures among infants born between 33 and 36 weeks gestation, which eliminated many research articles that define sensory exposures on healthier preterm infants. A review on this other population of preterm infants is warranted to define appropriate exposures, but the intent of the current review was to identify literature that defines the impact of sensory exposures in very preterm infants, who have different vulnerabilities and spend significant amounts of time in the NICU at the start of their lives.

In conclusion, early positive sensory exposures have been identified as being safe and potentially important for optimizing infant and parent outcomes in the NICU. However, a cohesive plan of sensory exposure is difficult to establish solely from the literature. This review is an important start of identifying the evidence that can support early sensory exposures in the NICU. Coupling these findings with expert clinical opinion, as well as parent input, could lead to the development of a clinical practice guideline that can inform appropriate sensory exposures across PMA in the NICU that aims to optimize outcomes. Defining a clinical practice guideline for sensory-based interventions is the next step.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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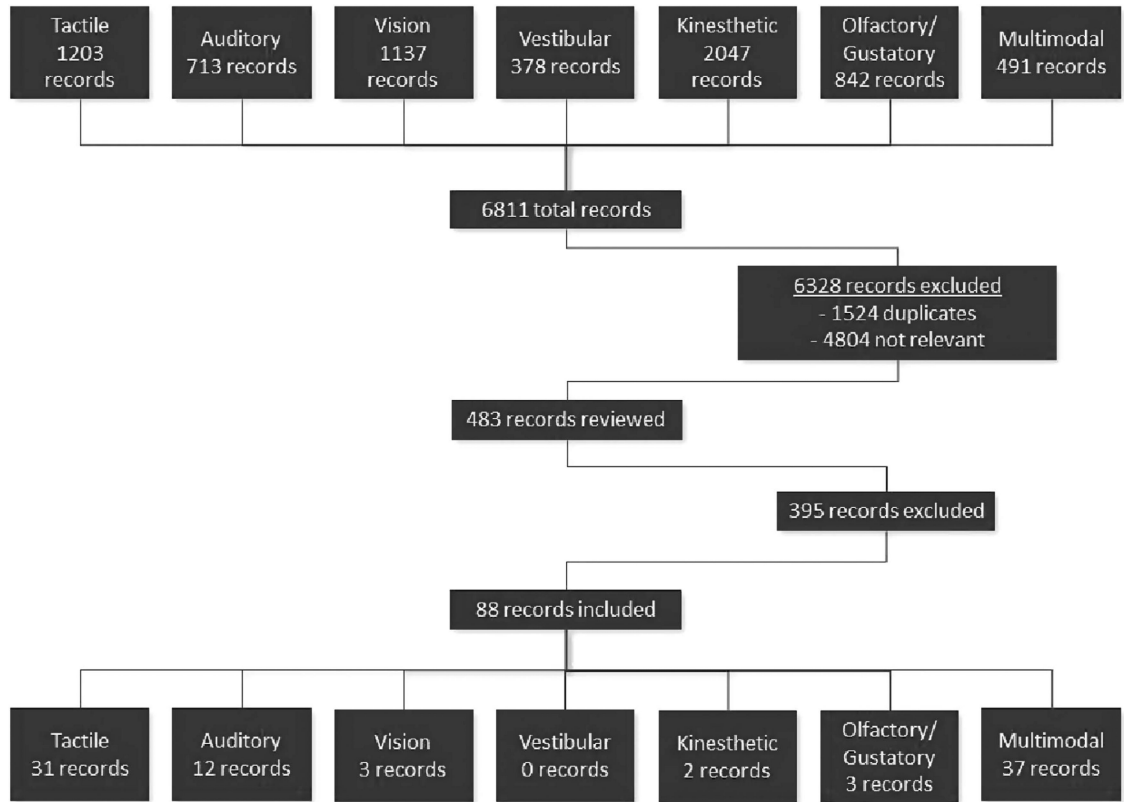


Figure 1.
Flow diagram of articles identified in the integrative review.

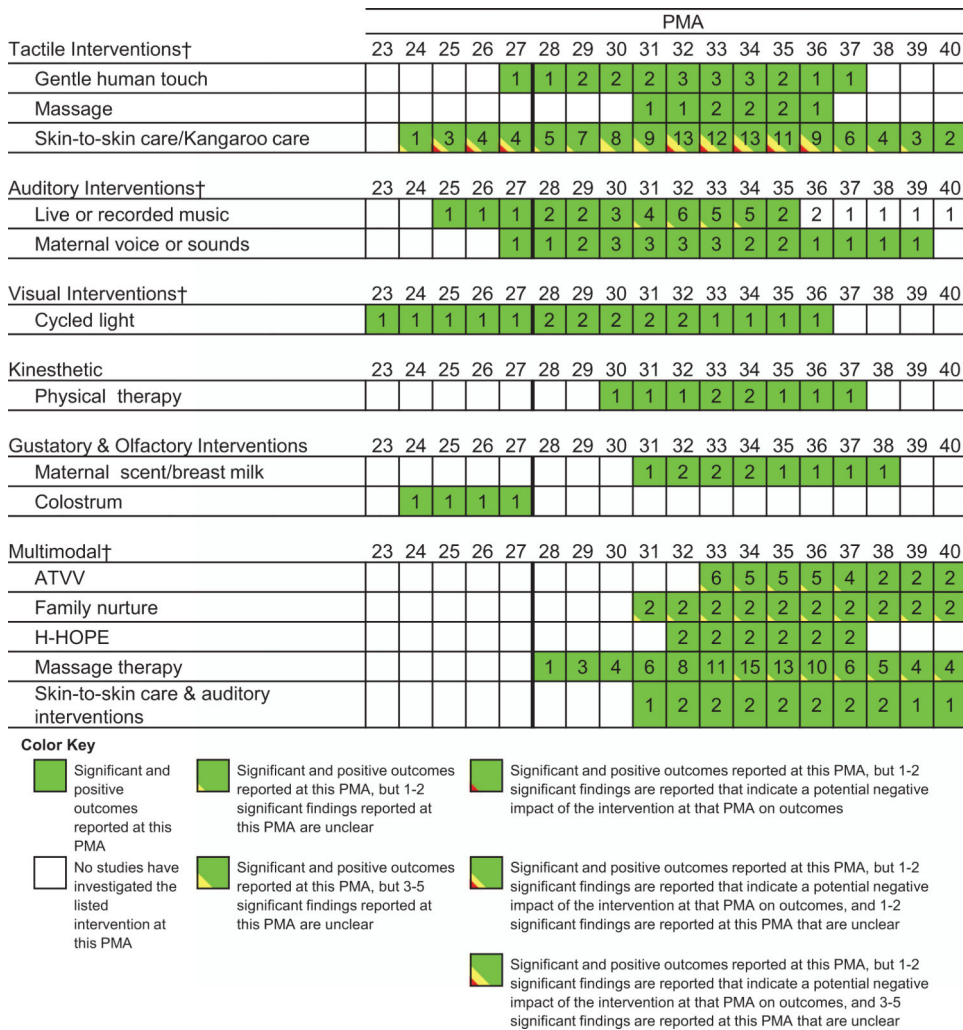


Figure 2. Different interventions studied across PMA. This figure demonstrates where evidence currently exists related to sensory exposures at different PMA and defines when interventions were deemed beneficial (green), unclear (yellow) or potentially negative (red). There were many outcomes studied that did not reach statistical significance, and these are not represented here in this figure. Studies across this review exhibited a large variety of outcomes, making them challenging to compare quantitatively. Also, many studies found statistically significant results that did not appear to be clinically significant (e.g., SpO₂ higher in one condition (97.13%) than another (96.38%, $P = 0.01$));⁷² therefore, it is unclear what these outcomes mean in a global, developmental context. Numbers in squares represent the number of studies that have investigated the listed intervention for each PMA. Some studies did not list sufficient information to estimate PMA at intervention and, thus, were not included in this table (see Supplementary Appendix SA).

Table 1

Study exclusion criteria

<p><i>Population</i></p> <p>Populations with mean or median gestational age greater than 32 weeks</p> <p>Populations with mean or median postmenstrual age greater than 36 weeks at time of intervention</p> <p>Populations with a purposeful sample of healthy infants (defined as 3 or more of the following factors: never on oxygen, never on medications, no intraventricular hemorrhage or other perinatal brain injury, or if Apgar scores were >7 at 1 or 5 min)</p> <p><i>Interventions</i></p> <p>Interventions aimed at reduction of external stimuli (e.g. headphones to reduce noise)</p> <p>Interventions aimed at reducing pain (e.g. during heel stick or endotracheal suctioning)</p> <p>Breastfeeding interventions</p> <p>Therapeutic touch (non-touch, energy-balancing technique)</p> <p>Pacifier-activated sound (includes use of a learning element)</p> <p>Vibrating pacifiers (includes use of a learning element)</p> <p>Breathing bear (no direct intervention to the infant)</p> <p>NIDCAP (interventions individualized for each infant rather than a uniform, quantifiable intervention)</p> <p><i>Non-relevant outcomes</i></p> <p>Apnea</p> <p>Incidence of retinopathy of prematurity</p> <p>Breastfeeding measures or feeding outcomes</p> <p><i>Study design and other factors</i></p> <p>Studies published before 1995</p> <p>Studies with a sample size < 30 without an <i>a priori</i> power calculation or sample size not attained</p> <p>Observational studies</p> <p>Pilot or feasibility studies</p> <p>Studies without a comparison group (case reports or case series)</p> <p>Systematic reviews that included studies with different EGA and PMA criteria</p> <p>Primary studies included as part of a relevant systematic review</p> <p>Non-English language studies</p> <p>Studies not published in a peer-reviewed journal (conference abstracts or dissertations)</p> <p>Studies with unclear or incomplete methods, statistical analysis or results</p>
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Abbreviations: EGA, estimated gestational age; NIDCAP, Newborn Individualized Developmental Care and Assessment Program; PMA, postmenstrual age.

Table 2

Search criteria, keywords and sample search strategy

Subject	Keywords	MeSH Terms
Auditory	music therapy, music, Bach, Mozart, lullaby, singing, maternal AND (heartbeat OR voice OR speech OR sound), auditory stimulation, adult talk, parent talk	Music Therapy; Singing; Acoustic Stimulation; Voice; Speech
Gustatory/Olfactory	colostrum, oral immune therapy, sucrose, flavor, gustatory, taste, oral hygiene, oral care, buccal care, smell, scent, olfactory, odor	Colostrum; Sucrose; Taste Perception; Taste; Flavoring Agents; Oral Hygiene; Smell; Olfactory Perception; Odors
Kinesthetic	kinesthetic, range of motion, physical therapy, exercise, physical activity, physiotherapy, passive limb movement, extension AND flexion	Kinesthesia; Range of Motion; Articular; Musculoskeletal Manipulations; Motor Activity; Physical Therapy Modalities; Movement; Exercise
Tactile	tactile stimulation, touch, tactile, massage, skin contact, skin-to-skin, kangaroo care, kangaroo mother care, acupressure	Touch; Tactile stimulation; M technique; TAC TIC; Massage
Vestibular	rock, bounce, swing, hammock, vestibular	Vestibule; Labyrinth; Motion; Proprioception
Vision	Eye contact, eye engagement, visual contact, visual engagement, eye-to-eye, mobile, light AND (cycled OR exposure OR dim OR reduction), visual AND (stimulus OR toy OR intervention OR novelty OR pattern)	Photostimulation; Pattern Recognition; Visual; Color Perception; Lighting; Light
Multimodal ^a <i>combined with</i>	multimodal, multiple sensory, ATVV	
Infant	infant, newborn, neonate, preterm, premature, low birth weight, LBW, VLBW, ELBW	Infant; Infant, Premature; Infant, Low Birth Weight
<i>Sample search strategy</i>		
Population		1 Infant[mh] OR infant ^a [tiab] OR newborn ^a [tiab] OR neonat ^a [tiab] 2 preterm ^a [tiab] OR pre-term ^a [tiab] OR prematur ^a [tiab] OR 'low birthweight' [tiab] OR 'low birth weight' [tiab] OR lbw[tiab] OR vlbw[tiab] 3 1 AND 2 4 Infant, Premature[mh] 5 Infant, Low Birth Weight[mh] 6 #3 OR #4 OR #5 7 Music therapy[mh] OR music ^a [tiab] OR Bach[tiab] OR Mozart[tiab] OR lullab ^a [tiab] OR Singing[mh] OR singing[tiab] 8 Mothers[mh] OR mother ^a [tiab] OR maternal[tiab] 9 Voice[mh] OR voice[tiab]
Interventions		

Subject	Keywords	MeSH Terms
Combined		10 Speech[mh] OR speech[tiab] 11 'sound simulation'[tiab] 12 #9 OR #10 OR #11 13 #8 AND #12 14 Acoustic Stimulation[mh] 15 'auditory stimulation'[tiab] 16 heartbeat ^a [tiab] OR 'heart beat'[tiab] 17 'adult talk'[tiab] OR 'parent talk'[tiab] 18 #7 OR #13 OR #14 OR #15 OR #16 OR #17 19 #6 AND #18

^a Searches of individual sensory categories also generated multimodal studies for inclusion.