First Brazilian recommendation on physiotherapy with sensory motor stimulation in newborns and infants in the intensive care unit

Objective: To present guidelines on sensory motor stimulation for newborns and infants in the intensive care unit.

Methods: We employed a mixed methods design with a systematic review of the literature and recommendations based on scientific evidence and the opinions of physiotherapists with neonatal expertise. The research included studies published between 2010 and 2018 in the MEDLINE® and Cochrane databases that included newborns (preterm and term) and infants (between 28 days and 6 months of age) hospitalized in the intensive care unit and submitted to sensory motor stimulation methods. The studies found were classified according to the GRADE score by five physiotherapists in different regions of Brazil and presented at eight Scientific Congresses held to discuss the clinical practice guidelines.

Results: We included 89 articles to construct the clinical practice guidelines. Auditory, gustatory and skin-to-skin stimulation stand out for enhancing vital signs, and tactile-kinesthetic massage and multisensory stimulation stand out for improving weight or sucking.

Conclusion: Although all modalities have good ratings for pain or stress control, it is recommended that sensory motor stimulation procedures be tailored to the infant’s specific needs and that interventions and be carried out by expert professionals.

Keywords: Infant; Infant, newborn; Sensory motor stimulation; Neuropsychomotor development; Child development; Psychomotor performance; Intensive care units, neonatal

INTRODUCTION

Sensory motor stimulation (SMS) for newborns (preterm or term) and infants in the intensive care unit (ICU) is an early intervention that includes a series of strategies aimed at optimizing neuropsychomotor development (NPMD) by promoting sensory stimuli based on the level of functional development, gestational age (GA) at birth, and weight of this population. The primary aim of SMS is to organize human body systems. i.e., tactile, kinesthetic, vestibular, olfactory, taste, auditory, visual and/or a combination of these. In the ICU, newborns and infants are often in moderately to highly complex clinical situations that may lead to unstable neurological, hemodynamic and cardiorespiratory systems, requiring technical and scientific knowledge when conducting overall assessments of SMS candidates.
Despite technological advances and multiprofessional efforts, extremely premature (GA < 28 weeks) and extremely low weight (< 1,000g) newborns remain at high risk of death and functional disability (short, mid and long term). Approximately 20% to 50% of survivors are at risk of morbidity, including changes in weight-height growth and NPMD.(2)

Sensory motor stimulation facilitates typical NPMD and prevents or minimizes the harmful effects of the ICU environment and interventions on weight-height growth. As such, it can be applied to treat NPMD changes resulting from prematurity, diseases and/or alterations/complications in the prenatal, perinatal or intranatal period and postdelivery.(4-6)

The aim of the present study is to present clinical practice guidelines on SMS for newborns and infants in the ICU.

**METHODS**

**Study design**

We employed a mixed method design and the following four stages to create this document.

**Stage 1** - subject approval for the creation of this document and classification of SMS into the following:

**Recommendation**: the main findings are based on at least one clinical trial, considering scientific evidence on the benefits versus risks to newborns and infants hospitalized in the ICU, viability of comparisons with other intervention options, and confirmation of the reliability of the evidence presented to support the use or rejection of SMS in the clinical practice of physiotherapists.

**Guiding question**: the PICO domains are considered: **P**, Patient (newborn or infant); **I**, Intervention (any SMS intervention); **C**, Comparison (cross-sectional or prospective longitudinal comparison with itself; with the control, with no intervention or placebo; or with another SMS intervention) and **O**- Outcome (studies including weight-height outcomes and their indices; improved sleep quality; reduced pain; increase in any NPMD domain; other NPMD-related outcomes – example: arm circumference, bone growth – and weight-height growth).

**Stage 2** - a systematic search was conducted of the Medline and Cochrane databases for studies on SMS published between 2010 and 2018. The keywords used included controlled indexers contained in Health Sciences Descriptors (DeCS, available at http://decs.bvs.br/P/decsweb2014.htm) and/or in Medical Subject Headings (MeSH, available at http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=mesh); a number of free terms related to each SMS modality were also used (see below each subitem of the Recommendations in “descriptors”). The search terms were combined using the Boolean operators “OR” and “AND” and their corresponding Portuguese words. Five specialists conducted the systematic search and assessed the studies independently according to each SMS modality. Disagreements were resolved by common consent of all those present during the discussions and/or via Skype. The specialists were subdivided into pairs to write a report on the SMS interventions. All specialists were physiotherapists with neonatal expertise (experience ≥ 12 years) in SMS for newborns and infants (up to six months of age) in the ICU.

**Stage 3** - the partial data were presented to the public at different pediatric and neonatology congresses, where participants could give their opinions and offer suggestions and comments. The five specialists analyzed the suggestions and comments provided by the public at the aforementioned events and made pertinent changes to the document.

**Stage 4** - creation and writing of the document, in line with the three SMS modalities (unimodal and multimodal stimulation and exercises/mobilizations) and the types of interventions found in the literature (Figure 1).

![Figure 1 - Sensory motor stimulation modality recommendations for newborns and infants hospitalized in neonatal intensive care.](image)

**Inclusion and exclusion criteria**

Clinical trials that met the following criteria were included: (1) clinical study, controlled or not, comparative or not, randomized or not, or crossover; (2) the study included some type of SMS intervention; (3) study population consisting of newborns and/or infants and...
(4) neonatal ICU as the study site. Duplicate articles and review studies, case reports, editorials and letters to the editor were excluded. When deemed relevant, these were included in the introduction and/or comments of the document.

Quality assessment

The studies found were classified according to the modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) score. GRADE is the evidence rating system endorsed by the World Health Organization. It rates the quality of evidence on a 4-point scale (high, moderate, low and very low). Randomized trials start at a score of 4/4 (high) and can be downgraded based on methodological flaws. If no published literature was available, expert physiotherapists’ opinions were used. The GRADE ratings are shown in table 1, with clinical indicators presented by + signs, indicating the degree of scientific certainty: +, the recommendation was very weak; ++, weak; ++++, moderate and ++++, strong.

RESULTS

A total of 89 articles were included. The partial data were presented at different pediatric and neonatology congresses: The Brazilian Congress of Intensive Therapy (Congresso Brasileiro de Medicina Intensiva – CBMI-AMIB), Florianópolis (SC), 2014; the International Symposium of Cardiorespiratory Physiotherapy (Simpósio Internacional de Fisioterapia Cardiorrespiratória), Salvador (BA), 2014; CBMI-AMIB, Goiânia (GO), 2014; CBMI-AMIB Costa do Sauípe (BA), 2015; CBMI-AMIB Porto Alegre (RS), 2016; CBMI-AMIB Natal (RN), 2017; Pan-American Congress of Intensive Therapy Rio de Janeiro (RJ), 2017; CBMI-AMIB São Paulo (SP), 2018 and CBMI-AMIB Fortaleza (CE), 2018, with the participation of approximately 600 physiotherapists in the area of neonatal and pediatric intensive therapy from different regions of Brazil.

The clinical indicators classified by GRADE are shown in table 1. The tables 1S to 9S in the appendix 1 shows a summary of the data for the studies included.

DISCUSSION

Unimodal stimulation

Unimodal stimulation includes SMS interventions that provide only one type of sensory stimulation to newborns or infants, in line with the physiological development hierarchy of sensory subsystems, such as tactile→vestibular→taste→olfactory→auditory→visual.

Tactile stimulation

Recommendation: tactile stimulation is recommended to reduce stress, assessed by urine cortisol level, and applied using the gentle human touch (GHT) intervention; reduce pain intensity, as assessed by the Neonatal Infant Pain Scale (NIPS) and changes in heart rate (HR) and

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Table 1 - Classification of clinical indicators, scientific certainty and recommendations for sensory motor stimulation

| Clinical indicators | Tactile | Auditory | Olfactory | Gustatory | Tactile-kinesthetic* | Massage* | Skin-to-skin* | Multisensory* | Mobilizations* |
|---------------------|---------|----------|-----------|-----------|---------------------|---------|-------------|--------------|---------------|
| Reduce pain/stress or improve behavioral organization | +++ | +++ | +++ | ++++ | +++ | ++++ | ++++ | ++++ |
| Improve vital physiological events (regulate RR; HR; SpO2; temperature and reduce apnea episodes) | ++ | ++++ | +++ | | | | | ++++ |
| Improve sleep-wake cycles | + | + | + | + | | | | |
| Accelerate brain maturation | + | + | + | + | | | | |
| Improve weight or sucking or promote faster progression to total oral feeding | + | +++ | +++ | ++++ | ++++ | | | |
| Improve bone mass or muscle strength or muscle tone maturation | + | +++ | +++ | ++++ | ++++ | | | |
| Decrease length of hospitalization or reduce the number of morbidities | + | +++ | +++ | ++++ | ++++ | | | |

RR – respiratory rate; HR – heart rate; SpO2 – blood oxygen saturation. Degree of scientific certainty: ++++, strong; ++, moderate; +, weak; –, very weak. * Multimodal stimulation = sensory motor stimulation interventions that combine two or more types of sensory stimuli.
respiratory rate (RR) associated with pain stimuli, using the therapeutic touch (TT) intervention; and improve sleep state, as assessed by the Anderson Behavioral State Scale (ABSS) after the GHT intervention and the Yakson protocol. The clinical indicators classified by GRADE are shown in table 1.

Vestibular stimulation

**Recommendation:** some functional positioning methods, which can also be used for vestibular stimulation (for example, hammocks, frequently used in the ICU in Brazil), did not exhibit the degree of scientific evidence required for inclusion in unimodal stimulation and were therefore included in multimodal SMS.

Auditory stimulation

**Recommendation:** auditory stimulation is recommended to increase peripheral capillary oxygen saturation (SpO₂) and to reduce HR through exposure to male-sung lullabies; increase SpO₂ through exposure to a Brahms’ lullaby or one sung/recorded by the mother; decrease physiological (HR) and behavioral responses (sleep-wake state and facial expressions of pain) during and after pain stimuli; decrease resting energy expenditure through exposure to Mozart’s music (Mozart effect); lower HR and RR through exposure to lullabies and reduce HR during exposure to Mozart’s music; lower HR and RR using three types of interventions (lullabies, heartbeat-like sounds and sounds resembling breathing), better sucking behavior with heartbeat-like sounds and a rise in caloric intake and improved feeding behavior (sucking rate per minute) using lullabies; reduce the frequencies of adverse cardiopulmonary events (defined as the occurrence of apnea > 20 seconds and/or decline in HR to below 100bpm for babies with GA < 34 weeks or below 80bpm for infants > 34 weeks GA), poor sleep-wake cycle, and crying; lower peak HR while feeding, improve sucking, promote faster transition to oral feeding and shorten hospitalization time. One study did not reinforce the beneficial physiological and behavioral effects of lullabies for premature infants. The authors found no significant differences among the intervention (lullaby), placebo and control groups in terms of physiological and behavioral responses. The clinical indicators classified by GRADE are shown in table 1.

Olfactory stimulation

**Recommendation:** olfactory stimulation is recommended to prevent apnea using stimulation with vanilla fragrance and to reduce pain using odor stimulation with maternal milk. Olfactory stimulation is not recommended to decrease resting energy using vanilla fragrance and an unfamiliar odor (vanilla) had no noticeable calming effect on healthy full-term newborns subjected to a painful procedure. The clinical indicators classified by GRADE are shown in table 1.

Gustatory stimulation

**Recommendation:** gustatory stimulation using sensorial saturation, maternal milk, assisted suction, and sweetened solutions (glucose, sacralose and dextrose) is recommended to reduce pain. When sweetened solutions (glucose, sacralose and dextrose) and placebo stimulations were compared, the former decreased pain; only one study compared oral sucrose and EMLA® cream and the combination of sucrose with EMLA® cream had the greatest analgesic effect. The clinical indicators classified by GRADE are shown in table 1.

Visual stimulation

**Recommendation:** visual stimulation was included in multimodal SMS rather than unimodal stimulation due to the absence of scientific evidence that met the inclusion criteria of these recommendations.

Multimodal stimulation

Multimodal stimulation includes SMS interventions that combine two or more types of sensory stimuli, as follows: tactile-kinesthetic stimulation, therapeutic massage, skin-to-skin control and multisensory stimulation (Figure 1).

Kinesthetic tactile stimulation

**Recommendation:** kinesthetic tactile multimodal stimulation is recommended to improve weight gain and reduce hospitalization time, increase parasympathetic activity during sleep, improve muscle strength and bone mineralization, improve motor behavior performance, lower bilirubin levels, favor brain electrical activity maturation, favor more mature motor patterns and more regulated and organized behaviors, improve the motor component and shorten hospitalization time, improve fat deposition in preterm newborns and contribute to strengthening the immunological system and weight gain. The clinical indicators classified by GRADE are shown in table 1.
Massage therapy

Recommendation: multimodal SMS using massage therapy is recommended to increase weight gain,\(^{(58-60)}\) increase the frequency of defecation episodes,\(^{(61,62)}\) decrease transcutaneous bilirubin levels,\(^{(61-63)}\) reduce pain scores,\(^{(64)}\) and raise the state of alertness after massage.\(^{(65)}\) The clinical indicators classified by GRADE are shown in table 1.

Skin-to-skin contact

Recommendation: SMS using multimodal stimulation with skin-to-skin contact is recommended for newborns on mechanical ventilation,\(^{(66-70)}\) reduces pain during painful procedures,\(^{(71-77)}\) alleviates stress,\(^{(78,79)}\) controls body temperature,\(^{(80)}\) is associated with lower newborn salivary cortisol levels,\(^{(79)}\) improves the effectiveness of breastfeeding or weight gain,\(^{(81-85)}\) and decreases cost of hospitalization.\(^{(86)}\)

One study\(^{(84)}\) did not demonstrate a decline in the salivary cortisol levels of preterm newborns; other investigations\(^{(85,86)}\) produced no significant evidence in terms of average daily weight gain. The clinical indicators classified by GRADE are shown in table 1.

Multisensory multimodal stimulation

The multisensory stimulation combines different types of stimuli without being necessarily offered simultaneously. Its benefits depend on the maturity of the central nervous system and the sensory subsystems of newborns.\(^{(4,87,88)}\)

Recommendation: multisensory stimulation is recommended to improve the neuromotor score and muscle tone maturation of preterm newborns by applying the “auditory, tactile, visual and vestibular stimulus - ATVV” protocol, improve behavioral organization, raise the frequency of oral behaviors, extend the time spent in the alertness state,\(^{(89,90)}\) improve mother-baby interaction with ATVV\(^{(91)}\) and increase weight-height growth.\(^{(92)}\) The clinical indicators classified by GRADE are shown in table 1.

Exercises/mobilization

Exercises/mobilization (passive or active-assistive) can be initiated for clinically stable preterm newborns with high risk for bone metabolic disease and GA < 32 weeks and/or birthweight < 1000g.\(^{(93,94)}\) The Moyer-Mileur protocol\(^{(93)}\) was used in all the studies that met the inclusion criteria of these recommendations.

Recommendation: SMS using mobilizations performed by physiotherapists is recommended to increase weight, height and tibial length,\(^{(95)}\) raise the speed of tibial ultrasound propagation,\(^{(95,96)}\) increase arm circumference,\(^{(97)}\) increase bone formation markers and decrease bone resorption markers.\(^{(98,99)}\) The clinical indicators classified by GRADE are shown in table 1.

CONCLUSION

The only sensory motor stimulation modality that has a high degree of scientific certainty was multimodal skin-to-skin stimulation, followed by multisensory stimulation. All modalities have good ratings for pain or stress control. Auditory stimulation stands out for enhancing vital signs, and tactile-kinesthetic massage and multisensory multimodal stimulation stand out for improving weight or sucking. It is recommended that sensory motor stimulation procedures be tailored to the infant’s specific needs and that interventions and be performed by expert professionals.

AUTHORS’ CONTRIBUTIONS

C. Johnston, M.S. Stopiglia, S.N.S. Ribeiro, C.S.N. Baez and S.A. Pereira were responsible for the study ideation and design of the work; S.A. Pereira participated in the writing of the article and read and approved the final version of the manuscript.

AVAILABILITY OF DATA AND MATERIAL

The dataset used and analyzed during the current study is available from the corresponding author on reasonable request.

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RESUMO

Objetivo: Apresentar as diretrizes para estimulação sensório-motora para recém-nascidos e lactentes em unidade de terapia intensiva.

Métodos: Trata-se de um método de delineamento misto com revisão sistemática da literatura e recomendações com base na evidência científica e opiniões de fisioterapeutas especialistas em fisioterapia neonatal de estudos publicados entre 2010 e 2018 nas bases de dados MEDLINE® e Cochrane, que incluíu recém-nascidos (pré-termo e a termo) e lactentes (entre 28 dias e 6 meses de idade) admitidos à unidade de terapia intensiva e submetidos a métodos de estimulação sensório-motora. Os estudos encontrados foram classificados segundo o escore GRADE por cinco fisioterapeutas em diferentes regiões do país e apresentados em oito congressos científicos para discussão das diretrizes de práticas clínicas.

Resultados: Foram incluídos 89 artigos para construir as diretrizes de práticas clínicas. Estimulação auditiva, gustatória e contato pele a pele se destacaram por melhorar os sinais vitais, e a massagem terapêutica, assim como a estimulação multimodal tátil-cinestésica por melhorar o peso ou a sução.

Conclusão: Embora todas a modalidades tenham boas avaliações para controle da dor ou do estresse, é recomendado que os procedimentos de estimulação sensório-motora sejam adaptados às necessidades específicas da criança, e as intervenções sejam realizadas por profissionais experientes.

Descritores: Lactente; Recém-nascido; Estimulação sensório-motora; Desenvolvimento neuropsicomotor; Desenvolvimento infantil; Desempenho psicomotor; Unidades de terapia intensiva, neonatal

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APPENDIX 1

Table 1S - Studies included for unimodal tactile stimulation recommendations

| Author                      | Type of study       | Sample | Interventions                                                                 | Main outcomes                                                                 | Main results                                                                 |
|-----------------------------|---------------------|--------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Asadollahi et al. (11)      | Randomized controlled trial | n = 78 NB GA: 30 - 36 weeks Weight: 1,000g - 1,800g Without ventilatory support | Tactile stimulation performed 7 to 10 days after birth; interventions conducted 3 times a day for 5 consecutive days Randomized into 3 groups: Control Group, n = 24; the physiotherapist placed the palm of one hand on the NB’s forehead for 15 minutes (fingers on the eyebrows) and the other on the lower abdomen to support the spine and hip Gentle Human Touch Group, n = 27 Massage Group, n = 27 | The decrease in stress assessed by urine cortisol level | A decline in cortisol level in the Gentle Human Touch and Massage Group, but significantly higher in the latter |
| Ramada et al. (9)           | Prospective controlled trial | n = 40 NB (21 preterm NB and 19 term NB) GA: not informed Weight: not informed | Vital signs and pain level compared before and after therapeutic touch (physiotherapists kept their hands on each region for 3 minutes: head, anterior and posterior chest and regions of the body affected). Total time of 20 – 30 minutes | Assessment of vital sign variability (HR, RR, temperature) Pain assessment according to NIPS | Pain and vital signs declined after intervention (HR, RR) |
| Bahman Bijari et al. (10)   | Randomized controlled trial | n = 90 NB GA: 26 - 34 weeks Weight: 1,200g – 2,000g Without ventilatory support | Tactile stimulation performed 7 to 10 days after birth; interventions conducted twice a day for 5 consecutive days Randomized into 3 groups: Control Group, Gentle Human Touch Group and Yakson Group | Assessment of newborns’ behavioral status according to the ABSS scale | The newborns improved behaviorally, especially in the sleep phase, which increased in both the Gentle Human Touch and Yakson Groups |

NB - newborns; GA - gestational age; HR - heart rate; RR - respiratory rate; NIPS - Neonatal Infant Pain Scale; ABSS - Anderson Behavioral State Scale.

Table 2S - Studies included for unimodal auditory stimulation recommendations

| Author                      | Type of study       | Sample | Interventions                                                                 | Main outcomes                                                                 | Main results                                                                 |
|-----------------------------|---------------------|--------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| Taheri et al. (12)          | Double-blind randomized controlled trial | n = 52 NB GA: 33 ± 4 weeks (Intervention Group) GA: 34 ± 4 weeks (Control Group) Weight: not informed | Randomized into 2 groups (n = 26 each): (1) Intervention Group: submitted to auditory stimulation with lullabies, through earphones, at 50 - 60dB, for 20 minutes (2) Control Group: earphones with no music (silence). The two groups were observed for 40 minutes | HR and SpO2 assessment | Lullaby (male voice and without music) could significantly reduce heart rate and increase blood oxygen saturation of neonates |
| Jabraeili et al. (13)       | Double-blind randomized controlled trial | n = 66 NB GA: 29 - 34 weeks Postnatal age ≥ 3 days, Weight: ≤ 2,800g Without invasive or noninvasive ventilatory support | Randomized into three groups: (1) Lullabies Sung by the Mother Group (n = 21) (2) Brahms Lullaby group (n = 25) (3) Control Group (n = 20): ambient noises. The stimulus was presented at 65 - 70dB, for 15 minutes, between 10am and 7pm, in three consecutive sessions | SpO2 assessment | Lullabies sung by the mother and Brahms lullaby music can help to improve SpO2 in preterm |
| Shabani et al. (14)         | Randomized crossover clinical trial | n = 20 NB, but each infant was studied in two groups of experimental and control. So, totally 40 infants were studied GA: 29 - 36 weeks Birth weight: < 2,500g | Auditory stimulation was performed with Schwartz’ Transcultural music (combination of intrauterine sounds of a pregnant woman and a song sung by a female singer), through speakers placed 20cm from the NB’s ear, at 45 - 60dB, for 15 minutes | Physiological responses to pain (HR and SpO2) Sleep-wake state Pain level assessed by the NFCS scale | Playing music is an effective intervention which decreases the heart rate, sleep-wake state scores, and facial expressions of pain |
| Silva et al. (14)           | Non-controlled clinical trial | n = 12 NB GA ≤ 36 weeks Weight: not informed Spontaneous breathing | Auditory stimulation performed with classical music twice a day, for 15 minutes, 1 hour after breastfeeding, for 3 consecutive days, totaling 6 interventions The music was played inside the incubator at 45 to 55dB, (total noise = intervention + ambient noises) The speakers were placed outside the incubator, in front of the porthole (which remained open during the intervention), but near the NB’s head | Assessment of HR, RR, SpO2 BP (systolic and diastolic) and BT | Classical music can change the short-term physiological responses of NBs HR in one of the sessions, but increased it in the next session; besides, it led to the reduction of HR in two sessions and promoted different variations in SatO2 at when compared to the fifth and sixth session of music therapy |

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Keidar et al. \(^{[15]}\) Randomized crossover prospective clinical trial  
- n = 12 NB  
- GA: 30 - 37 weeks  
- Tube feeding  
- Weight: not informed  

Randomized for auditory stimulation with two types of music (Mozart and Bach) and control (no auditory stimulation), in random sequences, for three consecutive days. The music was always played midday through speakers placed 30 cm from the NB’s ear, at 65 - 70dB, for 30 minutes to one hour after feeding, with the infant in the prone position.

Primary outcome was resting energy expenditure. However, vital signs (HR, RR and SpO\(_2\)) were constantly recorded.  

Auditory stimulation with Mozart music (Mozart Effect) significantly decreased resting energy expenditure.

Amini et al. \(^{[16]}\) Randomized crossover clinical trial  
- n = 25 NB  
- GA: 29 - 36 weeks  
- Weight: 1,000g – 2,500g  

The NBs were randomly submitted to 2 days of classical music (Mozart), two of lullabies and 2 control days (no music). The stimulus was presented through speakers placed 30 cm from the NB’s ear, for 20 minutes, with the baby in the supine or prone position.

Assessment of vital signs (HR, RR and SpO\(_2\)). Lullabies lowered HR and RR. These effects continued after exposure. Classical music lowered HR, but the effect disappeared after exposure. Discontinued SpO\(_2\) did not change with the intervention.

Loewy et al. \(^{[17]}\) Randomized multcenter controlled trial with blind assessor  
- n = 272 NB  
- GA ≥ 32 weeks  
- Weight: not informed  

All the infants received 3 types of intervention:  
1. Lullabies  
2. Breathing-like sounds (Ocean disc)  
3. Heart beat-like sounds (Gato box)  

Each child received the three stimulation modalities three times a week (in the morning or afternoon), for two weeks, totaling 6 interventions. Auditory stimulation was conducted near the crib or incubator, at 55 - 65dB for 10 minutes. The incubator babies received the intervention through an open porthole.  

- Control group: did not receive auditory stimulation.

Primary: vital signs (HR, RR and SpO\(_2\)) and activity level. Secondary: feeding behavior (suckings per minute). Sucking behavior (frequency). Sleep pattern, calorie intake.

The three interventions positively influenced vital signs, sound and lullaby may improve feeding behaviors and sucking patterns and may increase prolonged periods of quiet-alert states and parent-preferred lullabies, sung live, can enhance bonding, thus decreasing the stress parents associate with premature infant care.

Doheny et al. \(^{[18]}\) Within-subject experimental study  
- n = 14 NB  
- GA: 26 to 32 weeks, and at least 27 weeks of age at the time of the study  
- Weight: not informed  

Submitted to routine hospital and maternal sounds (voice and heart beats), inside the incubator/crib, at 55 - 60 dBA, 4 times a day, for 30 minutes. Auditory stimulation with maternal sounds within 7 days of birth and continued until NICU discharge.

- Control group: did not receive auditory stimulation.

Frequency of adverse cardiorespiratory events (apnea > 20 seconds and/or HR decrease to below 100 bpm for babies < 34 gestational weeks or below 80 bpm for infants > 34 gestational weeks).

Cardiorespiratory events declined with age. Frequency was lower with exposure to maternal sounds. This effect was significant in infants with GA ≥ 33 weeks, suggesting a therapeutic window.

Olschar et al. \(^{[19]}\) Randomized controlled trial  
- n = 20 NB  
- GA: ≥ 32 weeks  
- Weight: not informed  

Neurologically healthy during the first 6 weeks of life, without ventilatory support.

Randomized into 2 groups (n = 10 each):  
1. Experimental Group: submitted to Brahms’ lullabies, through speakers placed 30 cm from the NB’s head inside the incubator, at 50 - 55 dBA for 20 minutes  
2. Control Group: no auditory stimulation with music.

Assessment of aEEG activity: Background pattern, sleep-wake cycle quality and periods of restful sleep in terms of frequency, duration and minimum and maximum amplitudes.

There were no statistically significant intergroup differences; however, the small sample was small.

Tramo et al. \(^{[20]}\) Randomized prospective controlled trial  
- n = 13 NB  
- GA: 30 weeks and 6 days to 34 weeks and 3 days  
- Weight: 1,200g – 2,600g  

at 1 to 25 days of life, without ventilatory support or oxygenation.

Randomized into 2 groups:  
1. Intervention Group (n = 7): submitted to auditory stimulation with lullabies, through speakers placed 50 cm from the infant’s head, inside the incubator, at 50 dBA for 10 minutes  
2. Control Group (n = 6): no auditory stimulation with music.

Assessment of physiological responses (HR, RR and SpO\(_2\)) and behavioral assessment (opening the eyes, head movements and crying) before and during and after heel puncture.

In both groups, HR and RR increased during the heel puncture procedure and nearly all the infants cried. During the 10-minute recovery period following heel puncture, HR and crying decreased significantly in the intervention group.

Yildiz et al. \(^{[21]}\) Quasi-experimental prospective study  
- n = 90 NB  
- GA: 30 - 34 weeks and exhibiting no sucking reflex  
- Weight: ≥ 1,000g  

Tolerating enteral diet.

Allocated to 3 groups (N = 30 each):  
1. Control Group: no intervention  
2. Sucking Group: the babies were given pacifiers  
3. Lullaby Group: Lullabies were played to the babies through speakers, placed at the infants’ feet in the incubator, at 65dB, during force feeding.

Assessment of peak HR, RR, and SpO\(_2\), before, during and after feeding, body weight, sucking success, transition period to oral feeding, and hospitalization time.

The pacifier group proceeded to total oral feeding faster, followed by the Lullaby Group. Sucking success was achieved by the pacifier group, followed by the Lullaby Group. The pacifier group had the shortest hospitalization time, followed by the Lullaby Group. There was no difference in RR, SpO\(_2\) and weight between the 3 groups.

Ailpour et al. \(^{[22]}\) Double-blind randomized placebo-controlled clinical trial  
- N = 90 NB  
- GA: 28 - 36 weeks  
- Tube feeding  
- Weight: not informed  

Randomized into 3 groups (n = 30 each):  
1. Intervention: auditory stimulation with lullabies, at 50 - 60 dB, through earphones, for 20 minutes, with the NB in the supine position  
2. Silence Group (placebo): NB in the supine position with earphones for 20 minutes, without music  
3. Control Group: no intervention; routine care.

Physiological responses (HR, RR and SpO\(_2\)) Behavioral responses assessed by the BSI scale.

No significant intergroup differences in terms of physiological and behavioral responses.
First Brazilian recommendation on physiotherapy with sensory motor stimulation in newborns and infants in the intensive care unit

Studies included for unimodal gustatory stimulation recommendations

| Author               | Type of study                      | Sample          | Interventions                                                                 | Main outcomes                                      | Main results                                                                 |
|----------------------|------------------------------------|-----------------|-------------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------------|
| Bernardi et al. [27] | Randomized prospective controlled clinical trial | n = 28 NB GA: 30 - 35 weeks Weight: not disclosed | Glucose solution associated to no nutritive suction versus sensorial saturation (14 each) comprising a 6-step protocol: Keep the NB in lateral position Maintain eye contact Massage face and back Talk to the baby gently but firmly Allow child to smell the fragrance of a baby oil (Babysella, Guieu Labs) on the therapist’s hands place 10% glucose on the baby’s tongue | Assess pain level during venipuncture using the PIPP scale | Sensorial saturation ameliorates the quality of life in NICU and reduces the pain threshold perceived by newborn |
| Bueno et al. [24]   | Randomized prospective controlled clinical trial | n = 113 NB GA: 34 - 36 weeks Weight: ≥ 2,000g | Stimulation with maternal milk versus glucose | Evaluate pain level by comparing stimulation with maternal milk versus glucose, before NB heel puncture, using the PIPP | No statistically significant differences were found between the interventions |
| Cignacco et al. [28] | Randomized prospective multicenter controlled clinical trial | n = 71 NB GA: 24 - 32 weeks Weight: not disclosed | Stimulation with sucrose, facilitated tucking, and a combination of both interventions during heel puncture and collected during the first 14 days of their NICU stay | Assess pain level by comparing sucrose versus assisted suction, during heel puncture of NBs, using the BPNS score (combination of items that evaluate physiological and behavioral status) | Sucrose, regardless of association, showed better efficacy in reducing pain |
| Mekkaoui et al. [26] | Randomized prospective controlled clinical trial | n = 125 NB GA: 28 - 37 weeks Weight: not disclosed | Randomized into five non-pharmacological interventions: Oral glucose stimulation Non-nutritive sucking Oral administration of glucose 30%; associated with pacifier suction Oral administration of glucose 30%; associated with formula milk Oral administration of age-appropriate formula milk | Assess pain level during heel puncture using the DAN scale | Among the five groups, NB who received 30% glucose, artificial milk, or sucking a pacifier showed better results |
| Ou-Yang et al. [27] | Randomized prospective controlled clinical trial | n = 123 NB AG: < 37 weeks Weight: not disclosed | Stimulation with distilled water (n = 48) versus 25% glucose water (n = 62) versus maternal milk (n = 62) | Assess pain level during heel puncture using the PIPP scale | Stimulation with maternal milk decrease pain level |

NB - newborn; GA - gestational age; HR - heart rate; PIPP - premature infant pain profile; SpO2 - blood oxygen saturation; VO2 - maximum oxygen volume; VCO2 - maximum carbon dioxide volume; NFCS - Neonatal Facial Coding System; BIIP - Behavioural Indicators of Infant Pain.

Table 3S - Studies included for unimodal olfactory stimulation recommendations

| Author               | Type of study                      | Sample          | Interventions                                                                 | Main outcomes                                      | Main results                                                                 |
|----------------------|------------------------------------|-----------------|-------------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------------|
| Ou-Yang et al. [30]  | Randomized prospective controlled clinical trial | n = 33 NB GA: 30 - 36 weeks Weight: > 1,500g | Randomized into two groups: Control Group: 17 NB submitted to routine care Intervention Group: 16 NB olfactory stimulation with vanillin solution | Pain assessment using PIPP and changes in vital signs (HR & SpO2) of NBs submitted to venipuncture | Significant pain reduction without changes in vital signs |
| Mekkaoui et al. [29] | Double-blind randomized placebo-controlled clinical trial | n = 71 NB GA: 24 - 32 weeks Weight: not informed Without ventilatory support | Olfactory stimulation with vanillin and associations without vanillin odour exposure for 2 consecutive days | Metabolic rate evaluated through indirect calorimetry; oxygen (VO2) and carbon dioxide (VCO2) consumption | There was no difference between the two groups in terms of resting energy expenditure |
| Cignacco et al. [28] | Randomized prospective controlled clinical trial | n = 125 NB GA: 30 - 37 weeks Weight: not disclosed | Randomized into five non-pharmacological interventions: Stimulation with sucrose, facilitated tucking, and a combination of both interventions during heel puncture and collected during the first 14 days of their NICU stay | Frequency of apnea episodes, arterial blood oxygen saturation and HR during heel puncture using the PIPP | There was a reduction in apnea episodes in the group submitted to vanillin solution There was no change in vital signs between groups |
| Baudesson de Chanville et al. [27] | Randomized prospective controlled clinical trial | n = 69 NB GA: ≤ 37 weeks Weight: 3,000g – 4,000g | Randomized into two groups: Control Group: 30 NB submitted to routine care Intervention Group: 39 NB olfactory stimulation with vanilla scent (7cm from the nose) for 3 minutes | Frequency of apnea episodes, arterial blood oxygen saturation and HR during heel puncture using the PIPP | There was a reduction in apnea episodes in the group submitted to vanillin solution |

Table 4S - Studies included for unimodal gustatory stimulation recommendations

| Author               | Type of study                      | Sample          | Interventions                                                                 | Main outcomes                                      | Main results                                                                 |
|----------------------|------------------------------------|-----------------|-------------------------------------------------------------------------------|---------------------------------------------------|-----------------------------------------------------------------------------|
| Bernardi et al. [27] | Randomized prospective controlled clinical trial | n = 28 NB GA: 30 - 35 weeks Weight: not disclosed | Glucose solution associated to no nutritive suction versus sensorial saturation (14 each) comprising a 6-step protocol: Keep the NB in lateral position Maintain eye contact Massage face and back Talk to the baby gently but firmly Allow child to smell the fragrance of a baby oil (Babysella, Guieu Labs) on the therapist’s hands place 10% glucose on the baby’s tongue | Assess pain level during venipuncture using the PIPP scale | Sensorial saturation ameliorates the quality of life in NICU and reduces the pain threshold perceived by newborn |
| Bueno et al. [24]   | Randomized prospective controlled clinical trial | n = 113 NB GA: 34 - 36 weeks Weight: ≥ 2,000g | Stimulation with maternal milk versus glucose | Evaluate pain level by comparing stimulation with maternal milk versus glucose, before NB heel puncture, using the PIPP | No statistically significant differences were found between the interventions |
| Cignacco et al. [28] | Randomized prospective multicenter controlled clinical trial | n = 71 NB GA: 24 - 32 weeks Weight: not disclosed | Stimulation with sucrose, facilitated tucking, and a combination of both interventions during heel puncture and collected during the first 14 days of their NICU stay | Assess pain level by comparing sucrose versus assisted suction, during heel puncture of NBs, using the BPNS score (combination of items that evaluate physiological and behavioral status) | Sucrose, regardless of association, showed better efficacy in reducing pain |
| Mekkaoui et al. [26] | Randomized prospective controlled clinical trial | n = 125 NB GA: 28 - 37 weeks Weight: not disclosed | Randomized into five non-pharmacological interventions: Oral glucose stimulation Non-nutritive sucking Oral administration of glucose 30%; associated with pacifier suction Oral administration of glucose 30%; associated with formula milk Oral administration of age-appropriate formula milk | Assess pain level during heel puncture using the DAN scale | Among the five groups, NB who received 30% glucose, artificial milk, or sucking a pacifier showed better results |
| Ou-Yang et al. [27] | Randomized prospective controlled clinical trial | n = 123 NB AG: < 37 weeks Weight: not disclosed | Stimulation with distilled water (n = 48) versus 25% glucose water (n = 50) versus maternal milk (n = 62) | Assess pain level during heel puncture using the PIPP scale | Stimulation with maternal milk decrease pain level |

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Continue...
| Authors                  | Design                          | n | GA/Weight | Interventions                                                                 | Before/After                                                                 | Measured Outcomes                                                                 |
|-------------------------|---------------------------------|---|-----------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Johnston et al.         | Randomized prospective controlled clinical trial | n = 124 NB  
GA: ≤ 32 weeks  
Weight: ≤ 1,500g | Administration of a 1mL dose of 25% glucose solution  
2 minutes before and immediately after the first retinopathy of prematurity (ROP) eye examination | Evaluate pain intensity during the first eye examination for retinopathy of prematurity in NB using the NIPS scale | Glucose decreases the pain level of the first eye examination for retinopathy of prematurity |
| Nimbalkar et al.        | Randomized prospective controlled clinical trial | n = 104 NB  
GA: > 28 weeks  
Weight: not disclosed | One group received lingual dextrose before orogastric tube placement and the other received a placebo | Evaluate pain reduction after orogastric tube placement, with lingual administration of 25% dextrose, using the PIPP scale | Lingual dextrose administration decreases pain level compared to the placebo group |
| Pandey et al.           | Randomized prospective controlled clinical trial | n = 105 NB  
IG: < 37 weeks  
(< 168 hours of life)  
Weight: not disclosed | Stimulation with 24% sterile sucrose solution (n = 53) versus distilled water (n = 52), both administered orally 2 minutes before orogastric tube placement | Evaluate pain level following orogastric tube placement using the PIPP scale | Sucrose reduced pain level compared to the placebo group |
| Sahoo et al.            | Randomized prospective controlled clinical trial | n = 160 NB  
GA: > 34 weeks  
Weight: not disclosed | Three groups randomized into: Stimulation with maternal milk (n = 50)  
25% dextrose (n = 62)  
Sterile water (n = 48) | Assess pain level after venipuncture using the PIPP scale and changes in HR, SpO2, and duration of crying | Dextrose and maternal milk reduced pain level compared to the placebo group |
| Scaramuzzo et al.       | Randomized prospective controlled clinical trial | n = 158 NB  
GA: > 37 weeks  
Weight: not disclosed | Randomized into two groups: stimulation with oral sucrose (n = 82) versus wrapping (n = 76) | Evaluate spontaneous fluctuations in skin conductance to measure pain and to compare oral sucrose with non-pharmacological analgesic packaging | Oral sucrose is more effective in reducing pain level |
| Al Qahtani et al.       | Randomized prospective controlled clinical trial | n = 90 NB  
GA: > 38 weeks  
Weight: not disclosed | Stimulation with EMLA cream (n = 30) versus oral sucrose (n = 30) versus combination of EMLA cream and oral sucrose (n = 30) | Assess pain level comparing EMLA use and oral sucrose in NBs during circumcision | The combination of sucrose with EMLA cream has the greatest analgesic effect |
| Dilli et al.            | Randomized prospective controlled clinical trial | n = 64 NB  
GA: 28 - 37 weeks  
Weight: not disclosed | Stimulation with sucrose on pacifier (n = 32) versus sucrose-free pacifier versus sterile water (n = 32) 30 seconds before eye examination | Evaluate effectiveness of oral sucrose combined with non-nutritive sucking to reduce pain level | Sucrose combined with non-nutritive sucking reduces pain level during eye examinations |
| Ravishanker et al.      | Randomized prospective controlled clinical trial | n = 150 NB  
GA: > 34 weeks  
Weight: not disclosed | Randomization into 3 groups: stimulation with 25% dextrose (n = 50) versus 10% dextrose (n = 50) versus distilled water (n = 50), 2 minutes before nasogastric tube placement | Assess pain level using the PIPP scale, crying duration, and changes in heart rate | 25% oral dextrose reduces pain level before nasogastric tube placement |
| Suhrab et al.           | Randomized prospective controlled clinical trial | n = 90 NB  
GA: > 37 weeks  
Weight: not disclosed | Randomization into three groups: stimulation with glucose (n = 30) versus oral sucrose (n = 30) versus placebo (n = 30), 2 minutes before vaccination | Assess pain intensity before the Hepatitis B vaccination using the NIPS scale | Both glucose and sucrose are equally effective in decreasing pain when administered before the Hepatitis B vaccination |
| Uzelli et al.           | Randomized prospective controlled clinical trial | n = 80 NB  
GA: > 33 weeks  
Weight: not disclosed | Oral glucose administration (n = 40) versus control group (n = 40) 2 minutes before intramuscular injection | Assess pain intensity using the NIPS scale | Oral glucose, even when used in low amounts, is effective in reducing pain before intramuscular injection |
| Katania et al.          | Randomized prospective controlled clinical trial | n = 24 NB  
GA: > 31 weeks  
Weight: not disclosed | Administration of 2mL dextrose (n = 12) versus control group (n = 12 PTNBs) 2 minutes before retinopathy of prematurity corrective laser surgery | Assess pain intensity using the PIPP scale before and 30 seconds after starting the laser treatment | A single dose of oral dextrose did not significantly reduce pain during laser treatment in premature neonates |
| Tutag Lehr et al.       | Randomized prospective controlled clinical trial | n = 56 NB  
IG: > 37 weeks  
(≤ 7 days of life)  
Weight: not disclosed | Randomized into 2 groups: stimulation with 24% sucrose (n = 29) versus sterile water (n = 27) 10 minutes before heel puncture | Evaluate pain and blood flow, in NB under the effect of oral sucrose, using laser doppler and NIPS scale | Blood flow and pain after heel puncture were less in NB who received 24% sucrose |
| Vezyroglou et al.       | Randomized prospective controlled clinical trial | n = 32 NB  
GA: < 37 weeks  
Weight: > 1,500g | Randomized into 2 groups: stimulation with glucose (n = 16) versus placebo group (n = 16), 3 minutes before oropharyngeal aspiration | Evaluate pain level using the PIPP scale | Pain level did not differ between the two groups |
| Medeiros et al.         | Randomized prospective controlled clinical trial | n = 90 NB  
GA: 28 - 36 weeks  
Weight: not disclosed | Randomization into 2 groups: stimulation with water (n = 46) versus sucrose (n = 44) to analyze specific hand-to-mouth and hand sucking behaviors | Assess motor behavior and behavioral status of NB by observing hand-to-mouth and hand sucking behavior | Oral stimulation had a positive influence on hand-mouth coordination, regardless of the stimulus (water or sucrose) |

NB - newborn; GA - gestational age; PIPP - Premature Infant Pain Profile; NICU - neonatal intensive care unit; RPNS - Bernese Pain Scale Neonatal Scale; DAN - Douleur Aigue Nouveau Ne scale; ROP - retinopathy of prematurity; NIPS - Neonatal Pain, Agitation and Sedation; HR - heart rate; SpO2 - blood oxygen saturation; NIPS - Neonatal Infant Pain Score; PTNB - preterm newborn.
### Table 5S - Studies included for multimodal tactile-kinesthetic stimulation recommendations

| Author          | Type of study                       | Sample | Interventions | Main outcomes | Main results                                                                 |
|-----------------|-------------------------------------|--------|---------------|---------------|-------------------------------------------------------------------------------|
| Ahmed et al.    | Prospective quasi-experimental      | n = 151 NB GA: 30 - 37 weeks Weight: 1,000g – 1,200g Without ventilatory support | Randomized into two groups: - Control Group: 76 NB submitted to routine care - Intervention Group: 75 NB submitted to tactile-kinesthetic stimulation for 15 minutes (3 times a day for 7 consecutive days) | Weight gain and length of hospital stay | Tactile kinesthetic group had greater weight gain and shorter length of hospital stay compared to the control group |
| Smith et al.    | Randomized prospective double-blind placebo-controlled clinical trial | n = 21 NB GA: 30 - 31 weeks Weight: 1,500g | Randomized into two groups: Control Group: 11 NB, therapists stood beside the incubator for 20 minutes twice a day Intervention Group: 10 NBs submitted to 20 minutes of massage + kinesthetic movement (Moyer-Mileur) twice a day | Autonomic nervous system function during sleep stages and assistive care, measured by HRV after 2 weeks of massage therapy performed twice a day | There was no difference in HRV between intervention group and control group |
| Smith et al.    | Randomized prospective single-blind controlled clinical trial | n = 21 NB GA: 29 - 32 weeks Weight: 1,500g | Randomized into two groups: Control Group: 20 NB, therapists stood beside the incubator for 20 minutes twice a day Intervention Group: 17 NB, 20 minutes of massage + kinesthetic movement (Moyer-Mileur) twice a day for 4 weeks | Heart rate variability through ECG | Massage improved the sample’s autonomic nervous system function |
| Haley et al.    | Randomized prospective single-blind controlled clinical trial | n = 40 NB GA: < 37 weeks Weight: 1,500g – 1,600g | Randomized into two groups: Control Group: 20 NB are placed in a supine position without tactile stimulation and without kinesthetic TKS Group: movement tactile/kinesthetic stimulation: 20 NB, 20 minutes of massage twice daily, 6 days per week for 2 weeks TKS = (1) legs from top of thighs to ankles and feet, (2) chest over ribs, (3) shoulders to hands, (4) head from crown to neck and including face, (5) back from neck to waist (performed with infant remaining in supine position) | Increase in anthropometry; in the quantitative measurement of the ultrasound-assessed tibial speed of sound; urine and blood markers | TKS improved bone strength; bone metabolism biomarkers suggest improved bone mineralization in the massage group. |
| Aliabadi et al. | Randomized controlled clinical trial | n = 40 NB GA: 29 - 32 weeks Weight: > 1,500g and < 2,499g | Randomized into two groups: Control Group: 20 NB; Intervention Group: 20 NB submitted to 15-minutes interventions divided into three phases: 5 minutes massage + 5 minutes. TKS + 5 minutes massage (field protocol), 3 times daily for 10 consecutive days | Behavioral state assessment | The group that received TKS showed better motor and regulation state |
| Chen et al.     | Randomized controlled clinical trial | n = 42 NB GA: 37 - 41 weeks Weight: 2,800g to 3,600g | Randomized into two groups: Control Group: 22 NB Intervention Group: 20 NB submitted to 15 to 20-minute interventions (touch therapy by field protocol), performed twice daily for 5 consecutive days | Assessment of bowel movement frequency, measurement of trancutaneous jaundice and serum bilirubin levels | The group that received massage (touch therapy by field protocol), showed lower bilirubin levels |
| Guzzetta et al. | Randomized controlled clinical trial | n = 20 NB GA: 30 - 33 weeks Stable hospitalized NB Weight: between the 25th and 75th percentile | Randomized into two groups: Control Group: 10 NB Intervention Group: 10 NB submitted to 15-minutes interventions divided into two phases: 10 minutes massage + 5 minutes. Kinesthetic movement, performed 3 times daily for 5 consecutive days over a period of 2 weeks (two-day interval between weeks) | ECG assessment of brain electrical activity | Massage favored a maturation process of brain electrical activity similar to that observed in utero |
| Ferreira et al. | Randomized controlled clinical trial | n = 32 NB GA: 31 - 33 weeks Weight: < 2,500g | Randomized into two groups: Control Group: 16 NB Intervention Group 16 NBs submitted to TKS | Assessment of behavioral state | TKS contribute towards adjustment and self-regulation of behaviour |
| Ho et al.       | Randomized controlled clinical trial | n = 20 NB GA: < 34 weeks Weight: < 1,500g | Randomized into two groups: Control Group: 12 NB received similar duration of light touch Intervention Group: 12 NB received massage therapy starting at 34 weeks post-conceptual age (15 minutes daily, 5 days/week for 4 weeks) | Assessment of motor performance using the TIMP scale | Improvement in motor performance (NB with low TIMP score before intervention); shorter length of hospital stay for intervention group |
Table 6S - Studies included for multimodal massage stimulation recommendations

| Author              | Type of study | Sample | Interventions                                                                 | Main outcomes                                                                 | Main results                                                                 |
|---------------------|---------------|--------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|
| Kumar et al. [54]   | Randomized    | n = 44 | Two groups: 23 in the control group                                           | Weight gain; serum triglyceride level; length and head circumference          | The massage group presented weight gain after 28 days and decreased weight loss within the first 7 days. There was no statistical difference regarding the other outcomes |
|                     | controlled    | GA: 29 - 32 weeks | 25 submitted to massage therapy using oil on both shoulders starting from the neck with baby in prone position, then the upper back to hip area followed by the upper and lower limbs, one at a time in supine position for 10 minutes, 4 times daily over a period of 28 consecutive days |                                                                                 |                                                                                |
|                     | clinical trial| Weight: < 1,800g                      |                                                                                 |                                                                                |                                                                                |
|                     |               |        |                                                                                 |                                                                                |                                                                                |
| Ang et al. [58]     | Randomized    | n = 120| Three groups: Massage therapy with oil (n = 40)                                | Weight gain                                                                    | There was greater weight gain in the oil massage therapy group compared to the other 2 groups |
|                     | controlled    | GA: 30 weeks | 5 minutes of massage 4 times a day for 7 days                                  |                                                                                |                                                                                |
|                     | clinical trial| Weight: not disclosed                 |                                                                                 |                                                                                |                                                                                |
|                     |               |        |                                                                                 |                                                                                |                                                                                |
| Diego et al. [65]   | Randomized    | n = 30 | Two groups: Massage Group (n = 40): upper limb massage before and after venipuncture | Number of bowel movements; transcutaneous bilirubin levels                    | The massage therapy group had a higher number of bowel movements and lower transcutaneous bilirubin levels |
|                     | controlled    | GA: 28 - 32 weeks | 20 underwent massage therapy. Type of massage therapy not disclosed. Intervention time: 20 minutes twice a day for 4 consecutive days |                                                                                |                                                                                |
|                     | clinical trial| Weight: not disclosed                 |                                                                                 |                                                                                |                                                                                |
|                     |               |        |                                                                                 |                                                                                |                                                                                |
| Lin et al. [70]     | Randomized    | n = 56 | Two groups: Control Group (n = 29)                                             | Length of hospital stay; weight gain; increased bowel movement frequency; microbilirubin level | There was an increase in bowel movement frequency and a decrease in bilirubin levels in the massage group; there was no difference between the groups for the other outcomes |
|                     | controlled    | GA: 30 - 40 weeks | 20 submitted to massage therapy with moderate pressure and oil (n = 17)         |                                                                                |                                                                                |
|                     | trial         | Weight: not disclosed                 |                                                                                 |                                                                                |                                                                                |
|                     |               |        |                                                                                 |                                                                                |                                                                                |
| Daili et al. [82]   | Randomized    | n = 50 | Two groups: Control Group (n = 25)                                             | Increased bowel movement frequency; transcutaneous bilirubin level             | There was a decrease in bilirubin levels in the massage group. There was an increase in bowel movement frequency in the control group on day 1. On the subsequent days, there was no difference between the two groups |
|                     | controlled    | GA: 36 - 40 weeks | 20 submitted to massage therapy with moderate pressure and oil (n = 17)         |                                                                                |                                                                                |
|                     |               | Weight: not disclosed                 |                                                                                 |                                                                                |                                                                                |
|                     |               |        |                                                                                 |                                                                                |                                                                                |
| Chik et al. [84]    | Randomized    | n = 80 | Two groups: Control Group (n = 40)                                             | Pain level reduction assessed by PIPP                                         | There was a reduction in pain score in the group submitted to massage therapy |
|                     | controlled    | GA: 30 to 40 weeks | 20 submitted to massage therapy with moderate pressure and oil (n = 17)         |                                                                                |                                                                                |
|                     | trial         | Weight: not disclosed                 |                                                                                 |                                                                                |                                                                                |
|                     |               |        |                                                                                 |                                                                                |                                                                                |
| Yates et al. [88]   | Randomized    | n = 23 | Two groups: Massage therapy the first day (n = 13)                             | Massage therapy can be used as an adjunct intervention to induce sleep        | Massage therapy did not induce sleep immediately after massage and infants are more wakeful following massage therapy |
|                     | cross-over    | GA: 32 - 48 weeks | 20 submitted to massage therapy with moderate pressure and oil (n = 17)         |                                                                                |                                                                                |
|                     | study         | Weight: not disclosed                 |                                                                                 |                                                                                |                                                                                |

NB - newborn; GA - gestational age; HRV – heart rate variation; ECG – electrocardiogram; TKS - tactile/kinesthetic stimulation group; TIMP - Test of Infant Motor Performance.
Table 7S - Studies included for multisensory skin-to-skin stimulation recommendations

| Author          | Type of study               | Sample                                                                 | Interventions                                                                                                                                  | Main outcomes                                                                                                                               | Main results                                                                                           |
|-----------------|----------------------------|------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Azevedo et al.  | Quasi-experimental study   | n = 43 GA: > 29 weeks Weight: not disclosed Hemodynamically stable, intubated receiving MV | A group evaluated longitudinally on 3 occasions: before, during and after the procedure for a duration of 90 minutes | Procedure safety Variables measured: HR, SpO₂, FiO₂, mean arterial blood pressure, and temperature                                           | Changes in the variables studied were not clinically significant (< 5% from baseline) although statistically significant. Skin-to-skin contact is a safe procedure for NBs receiving MV |
|                 | design                     |                                                                        |                                                                                                                                             |                                                                                                                                              |                                                                                                                                                                |
| Karlsson et al. | Quasi-experimental study   | n = 96 GA: 24 - 33 weeks Weight: > 500g Vulnerable preterm infants   | Vital signs, body temperature, and oxygen requirement data were prospectively recorded by each infant’s nurse before (baseline), during (3 time points), and after their first skin-to-skin contact. 17 clinically stable NBs receiving MV, 49 with nasal CPAP and 30 spontaneously breathing room air | Safety and physiological effectiveness of the procedure Evaluate the impact of the respiratory support. Variables measured: HR, SpO₂, FiO₂, transcutaneous partial pressure of carbon dioxide (TcPCO₂), and temperature | Changes in the variables studied were statistically significant. Skin-to-skin contact is an effective and safe procedure for vulnerable preterm infants |
|                 | design study               |                                                                        |                                                                                                                                             |                                                                                                                                              |                                                                                                                                                                |
| Lorenz et al.   | Prospective observational  | n = 40 GA: < 33 weeks Weight: > 500g Receiving ventilatory support (ETT, CPAP or HFNC) | rcO₂ was measured using near-infrared spectroscopy. Ninety minutes of skin-to-skin contact, with infants in incubators acting as their own control | Assessment of the NICU’s thermal balance and physical care environment during skin-to-skin Variables studied: Relative humidity and air temperature in the incubator and skin-to-skin environment; cerebral oxygenation and other physiological measurements in ventilated preterm infants did not differ between skin-to-skin contact, and incubator care | Early skin-to-skin initiation allows thermoregulation to occur in even the smallest NBs receiving intensive care, including mechanical ventilation Skin-to-skin is an important and safe care mode for extreme PTNBs, even with mechanical ventilation |
|                 | non-inferiority study      |                                                                        |                                                                                                                                             |                                                                                                                                              |                                                                                                                                                                |
| Park et al.     | Prospective clinical      | n = 31 GA: 25 - 32 weeks Weight: 760g – 1,740g                       | Two groups submitted to skin-to-skin contact: 25 - 28 weeks (n = 11) and 29 - 32 weeks (n = 20) | Determine the clinical characteristics and safety of skin-to-skin contact according to GA Physiological parameters were evaluated longitudinally for 60 minutes (15 minutes before, 30 minutes during and 15 minutes after the procedure). Variables studied: HR, RR, SpO₂, blood pressure, temperature | Changes in the variables studied were not clinically significant (< 5% from baseline) although some were statistically significant. At the same post-menstrual age, the lower GA group showed greater thermoregulation maturation compared to the higher GA group Skin-to-skin contact is a safe procedure for PTNBs even while receiving ventilatory support |
|                 | trial                      |                                                                        |                                                                                                                                             |                                                                                                                                              |                                                                                                                                                                |
| Okan et al.     | Randomized controlled     | n = 107 GA: > 37 weeks Age between 24 and 48 hours of life Weight: not disclosed Healthy NB | Three groups: Skin-to-skin contact group (N = 35) with maternal breast feeding; n = 38 skin-to-skin contact n = 36 placed in the crib, evaluated before, during and after the painful stimulus | Evaluate the effectiveness of skin-to-skin contact for pain reduction during heel puncture in FTNBs Assess whether the combination of skin-to-skin contact with breastfeeding provides greater analgesia than skin-to-skin contact alone Variables studied: Crying time after painful stimulus. Secondary outcomes: HR, SpO₂ | HR, SpO₂, and crying duration was significantly lower in the groups skin-to-skin and skin-to-skin contact with breastfeeding, compared to NBs in the crib who underwent the painful procedure Skin-to-skin contact before, during, and after a painful stimulus promotes a reduction in physiological and behavioral responses to pain in healthy FTNBs The combination of skin-to-skin contact with breastfeeding promotes an analgesic effect similar to skin-to-skin contact only |
|                 | clinical trial             |                                                                        |                                                                                                                                             |                                                                                                                                              |                                                                                                                                                                |
| Study               | Study Design                      | Sample Characteristics                                                                 | Main Interventions                                                                 | Main Findings                                                                                                                                                                                                 |
|---------------------|-----------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Saeidi et al. (72)  | Randomized controlled clinical trial | n = 80 GA: healthy full-term NBs Weight: not disclosed < 14 days of life in heated incubator | Two groups: skin-to-skin contact for 30 minutes (n = 30) and control (wrapped in blanket and placed next to mother, n = 30) | Evaluate the effect of skin-to-skin contact on pain intensity using the NIPS scale in healthy NBs undergoing a painful procedure (vaccination) Secondary outcomes: HR, SpO₂ and crying duration Mean pain intensity during the procedure, and 3 minutes after was significantly lower in the skin-to-skin contact group Kangaroo care may be used to decrease pain intensity in newborns undergoing painful procedures |
| Cong et al. (73)    | Randomized crossover clinical trial | n = 28 GA: 28 - 32 weeks Weight: not disclosed < 14 days of life | Three groups randomized into different procedure sequences, evaluated on 6 occasions: skin-to-skin for 30 minutes, skin-to-skin for 15 minutes, and standard care | Skin-to-skin effect (duration of 30 and 15 minutes) on the autonomic pain response of PTNBs subjected to heel puncture compared to standard care. Variables studied: HR variability, behavioral state Both skin-to-skin contact durations, before and during heel puncture, promote prolonged restful sleep after puncture. Kangaroo care has a significant effect on reducing autonomic pain responses in preterm infants. The findings support that KC is a safe and effective pain intervention in the neonatal intensive care unit |
| Nimbalkar et al.(74) | Randomized controlled clinical trial | n = 100 term and late preterm Weight: > 1,800g | Two groups: Intervention Group: SSC at 30 minutes to 1 hour after delivery and continue for as long as possible in the first 24 hours with each session lasting for minimum 60 minutes Control Group, after providing routine care under radiant warmer, NBs were kept clothed (including head cap) and covered with blanket with their mother (bedding in) for first 48 hours | Temperature and heart rate | The incidence of hypothermia in conventional care was significantly higher as compared with the SSC |
| Chidambaram et al.(75) | Randomized crossover clinical trial | n = 100 GA: 32 - 36 weeks Weight: < 2,500g Hemodynamically stable without dependence on oxygen. | Two groups: Control Group (n = 50) Skin-to-Skin Contact Group (n = 50) | PIPP score scale assessment 15 minutes before, 15 and 30 minutes after heel puncture PIPP scores at 15 and 30 minutes after puncture were significantly lower in the skin-to-skin contact group compared to the control group Skin-to-skin contact is effective in reducing pain in PTNBs subjected to heel puncture |
| Gao et al. (76)     | Randomized controlled clinical trial | n = 75 GA: < 37 weeks Weight: 2,030g | Two groups: Control group (n = 37) Skin-to-Skin Group (n = 38) | Evaluate the effectiveness of 30 minutes of skin-to-skin contact on behavioral and physiological responses of PTNBs undergoing heel punctures. During the first puncture procedure, all NBs were kept in the incubator. In the other three procedures, the NBs were randomized into skin-to-skin contact or standard incubator care; evaluators were blinded to the purpose of the study. Variables studied: facial expression, crying, and HR in 4 heel puncture procedures HR was significantly lower, crying and grimacing duration was significantly shorter (from time of heel puncture to recovery) across repeated heel puncture procedures in the skin-to-skin group compared to the control group The effect of repeated Kangaroo Mother Care analgesia remains stable in preterm infants over repeated painful procedures |
| Choudhary et al.(77) | Quasi-experimental crossover single-blind clinical trial | n = 140 Weight: > 1,000g | One group (n = 140): each NB was its own control GA < 37 weeks All NBs were divided into gestational age: 28 - 30 weeks (n = 80); 30 - 34 weeks (n = 60) and birth weight: 1,000g - 1,500 g (n = 88); 1,500 - 2,500g (n = 52) | Assessment of PIPP during heel puncture, HR, SpO₂, crying duration and recovery time | The effect of skin-to-skin contact was statistically significant in the PTNBs (30 - 34 weeks) and very low weight (1,000 – 1,500g) groups SpO₂ drop was lower (36% reduction) in the skin-to-skin contact group than in conventional care Crying duration was shorter in the skin-to-skin contact group than in conventional care, with a statistically significant difference PIPP scores were significantly lower with skin-to-skin contact Implementing skin-to-skin contact is a safe method of helping physiological and behavioral stability in PTNBs |

Continue...
| Reference                  | Design                        | Sample Size | Outcomes                                                                                           |
|----------------------------|-------------------------------|-------------|---------------------------------------------------------------------------------------------------|
| Kaffash et al. [78]        | Randomized quasi-experimental crossover trial | n = 134 NBs (8 PTNBs) | Received 8 weeks of skin-to-skin contact. Three groups: PTNBs received skin-to-skin contact for 8 weeks (16 EEG recordings during sleep, n = 8) compared to two groups (nN = 126): one group of PTNBs with corrected gestational age and another of FTNBs. Neurophysiology maturation of the neonatal brain by quantifying temporal characteristics (regularity and predictability) of sleep EEG signals. The group of PTNBs that received skin-to-skin contact exhibited more complex EEG signals compared to PTNBs of the same gestational age. Discriminant analyses show that PTNBs who received skin-to-skin contact at 40 weeks corrected age exhibit patterns closer to FTNBs than PTNBs not submitted to this intervention, at the same gestational age. |
| Neu et al. [79]            | Randomized controlled clinical trial | n = 79 GA: 32 - 35 weeks Weight: not disclosed | Three groups: Control Group (n = 24) Skin-to-Skin Contact Group (n = 29) Group Wrapped in Blanket (n = 26) Evaluate coregulation in salivary cortisol between mother and NB; coregulation defined as progressive reduction in the absolute difference between mother and NB cortisol levels during each 60-minute session of skin-to-skin contact. Variable studied: coregulation of salivary cortisol between mother and NB Decreased cortisol levels in mothers and NBs suggesting that skin-to-skin contact caused a decline in stress hormone levels. There was no significant difference in coregulation between the groups in nonstressful situations, co-regulation in salivary cortisol may not differ based on holding method. |
| Srivastava et al. [80]     | Randomized controlled clinical trial | n = 240 GA: any age Weight: > 2,500g Skin-to-skin in the first 30 minutes of life | Two groups: Control Group (n = 118) Skin-to-Skin Contact Group (n = 122) Variables studied: breastfeeding effectiveness, 6-week breastfeeding status, maternal satisfaction, thermoregulation, weight loss at hospital discharge and at first follow-up, and morbidity. Evaluate the impact of early skin-to-skin initiation on breastfeeding effectiveness and maternal satisfaction in relation to received NB breastfeeding status at hospital discharge Secondary outcomes: related to neonatal well-being (thermoregulation in the immediate postpartum period, NB weight parameters and morbidities during the first six weeks of life). Skin-to-skin contact contributed to greater breastfeeding effectiveness, more infants being exclusively breastfed at the first follow-up and at 6 weeks, greater maternal satisfaction, better immediate postpartum temperature gain, lower weight loss at hospital discharge and first follow-up, and lower morbidity when compared to the control group. |
| Jayaraman et al. [81]      | Randomized controlled clinical trial | n = 160 Weight: 1,000g – 1,800g | Two groups: early skin-to-skin contact initiated within the first 4 days of life (n = 80); late skin-to-skin contact, initiated after complete stabilization, defined as absence of respiratory support and intravenous fluids (n = 80) Evaluate the effects of early skin-to-skin contact initiation on exclusive breastfeeding, growth, mortality and morbidity compared to late initiation (during hospitalization and after hospital discharge) in low-weight NBs The early skin-to-skin contact group had higher proportion of exclusive breastfeeding, higher breastfeeding rate during hospitalization, and a higher proportion of exclusive breastfeeding up to one month after hospital discharge. The incidence of apnea and recurrent apnea requiring ventilation was significantly reduced in the early skin-to-skin contact group. There was no significant difference in mortality, morbidity, and growth during hospitalization and after hospital discharge. |
| Nagai et al. [82]          | Randomized controlled clinical trial | n = 73 Weight: < 2,500g Age: < 24 hours Relatively stable clinical conditions | Two groups: early skin-to-skin contact within the first 24 hours of life (n = 37). Control: conventional care performed initially with skin contact after 48 - 72 hours of life (n = 36). Evaluate the effectiveness of early skin skin contact initiation for relatively stable low-weight NBs in a resource-constrained country There were no differences in the incidence of morbidity. Weight loss from birth up to 24 hours (and up to 48 hours) of life was significantly lower in the early skin-to-skin contact group compared with the control group. The occurrence of adverse effects and length of hospitalization did not differ between the groups. |
| Sharma et al. [83]         | Randomized controlled clinical trial | n = 141 Weight: < 1,100g Clinically stable | Two groups: skin-to-skin contact (n = 71) and conventional care (n = 70) when NBs reached 1,150g. Assess weight gain (g/day) from start of randomization to full-term (40 weeks) Variables studied: weight gain (g/day) Secondary outcomes: weight, length and head circumference at 40 weeks; intra-hospital weight gain (g/day), length (cm/week) and head circumference (cm/week) following randomization; breastfeeding rates at hospital discharge and at full-term age; neonatal ICU readmissions (level III or intermediate care unit) Average weight gain, as well as weight, length and head circumference at term corrected age were comparable in both groups. There was a significant reduction in hospitalization time in the conventional care group and a significant increase in weight gain before discharge in the skin-to-skin contact group. |
...continuation

| Author                  | Type of study          | Sample                                                                 | Interventions                                                                 | Main outcomes                                    | Main results                                                                 |
|-------------------------|------------------------|-------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------------------------------|-------------------------------------------------------------------------------|
| Kanagabasai et al.      | Randomized controlled  | n = 50; GA: 28 - 36 weeks; Weight: 1,000g to 2,000g                     | Two groups: Control Group (n = 25); Multisensory Stimulation Group (n = 25) submitted to interventions in five 12-minute sessions per week until hospital discharge | Neuromotor development evaluation                  | The multisensory intervention group had better muscle tone                      |
| Medoff-Cooper et al.    | Randomized controlled  | n = 183; GA: 29 - 34 weeks; Weight: not disclosure                      | Two groups: Control Group (n = 93); Multisensory Stimulation (ATVV) Group (n = 90) to evaluate sucking organization PTNBs following a multisensory stimulation ATVV = 10' of auditory (female voice), tactile (moderate touch stroking or massage) and visual (eye to eye) stimulation, followed by 5' of vestibular stimulation (horizontal rocking) | Infant sucking was digitally recorded              | ATVV infants exhibited improved sucking organization during hospitalization    |
| White-Traut et al.      | Randomized controlled  | n = 195; GA: 29 to 34 weeks; Weight: not disclosure                     | Two groups: Control Group (n = 95) H-Hope Group (n = 90); ATVV protocol performed twice more maternal participatory guidance sessions by a nurse-community advocate team daily for 6 consecutive weeks | Behavioral state (frequency of oral behaviors and time of alertness) | The intervention group showed greater frequency of oral behaviors and increased alertness |
| White-Traut et al.      | Randomized controlled  | n = 198; GA: 29 to 34 weeks; Weight: not disclosure                     | Two groups: Control Group (n = 102) H-Hope Group (n = 96)                        | Improved mother-baby interaction during feeding and play at 6-weeks corrected age | The intervention group had better mother-baby interaction                        |
| White-Traut et al.      | Randomized controlled  | n = 182; GA: 29 - 34 weeks; Average weight = 1,985g                   | Two groups: Control Group (N = 94). H-Hope Group (n = 88); ATVV protocol performed twice daily for 6 consecutive weeks | Weight-length growth measured by weight and height | The intervention group had faster weight-length gain than the control group       |

GA - gestational age; BW - birth weight; HR - heart rate; SpO2 - oxygen saturation; FiO2 - fraction of inspired oxygen; NB - newborn; CPAP - continuous positive airway pressure; TcPCO2 - transcutaneous carbon dioxide pressure; NICU - neonatal intensive care unit; PTNB - preterm newborn; ETT - endotracheal tube; HFNC - high flow nasal cannula; reO2 - Regional cerebral oxygenation; HR - heart rate; cFTOE - cerebral fractional tissue oxygen extraction; AT - axillary temperature; RR - respiratory rate; FTNB - full-term newborn; KC - kangaroo care; PIPP - Premature Infant Pain Profile; KWC - kangaroo ward care.

Table 8S - Studies included for multisensory stimulation recommendations

GA - gestational age; ATVV - protocol Auditory, Tactile, Visual and Vestibular stimulus; PTNBs - preterm newborns; H-HOPE - Hospital to Home: Optimizing the Infant's Environment.
First Brazilian recommendation on physiotherapy with sensory motor stimulation in newborns and infants in the intensive care unit

### Table 9S - Studies included for multisensory skin-to-skin stimulation recommendations

| Author           | Type of study       | Sample                                      | Interventions                                                                 | Main outcomes                                  | Main results                                                                 |
|------------------|---------------------|---------------------------------------------|-------------------------------------------------------------------------------|------------------------------------------------|--------------------------------------------------------------------------------|
| Erdem et al.     | Randomized controlled | n = 28                                     | Two groups: Control Group (n = 14); Daily Mobilization Group (n = 14); Moyer-Mileur* protocol for 4 weeks (5 weekly sessions once a day) | Bone mineralization and anthropometric indices | The intervention group showed weight (p = 0.002) and height (p = 0.015) increase, as well as improved bone mineralization (p ≤ 0.001) compared to the control group |
| Tosun et al.     | Randomized controlled | n = 40                                     | Two groups: Control Group (n = 20); Intervention Group (n = 20); Moyer-Mileur protocol for 4 weeks (5 weekly sessions once a day) | Bone mineralization and anthropometric indices | The intervention group improved its bone mineralization (p ≤ 0.001) and anthropometric indices (p ≤ 0.001) compared to the control group |
| Vignochi et al.  | Randomized controlled | n = 30                                     | Two groups: Control Group (n = 15); Physiotherapy Group (n = 15); passive flexion-extension movements associated with mild joint compression/decompression for 15 minutes 5 times a week (until NB reaches 2,000g) | Bone metabolism                                | Imbalance between bone formation and resorption was lower in the intervention group |
| Litmanovitz et al. | Randomized controlled | n = 34 PTNBs                             | 3 Groups: Group 1 Control (n = 10); no interventions Group 2 (n = 13); mobilizations twice a day Group 3 (n = 11); mobilizations once a day. Mobilization started at the NB's 08 ± 2.4 days of life and continued for 4 consecutive weeks Mobilization protocols: passive mobilization consisting of flexion-extension of the extremities (upper and lower limbs) | Bone mineralization assessed by ultrasound | There was decreased bone loss in Group 2 compared to the other groups (p = 0.03), suggesting that passive mobilization performed twice a day may prevent demineralization |
| Chen et al.      | Randomized controlled clinical trial | n = 16                                   | 2 Groups Control Group (n = 8): routine care Intervention Group (n = 8): submitted to the Moyer-Mileur* protocol. | Bone mineralization assessed by ultrasound | There was an increase in bone mineralization in the intervention group compared to the control group |

GA: gestational age; PTNBs: preterm newborns; NB: newborn. * Moyer-Mileur* protocol is: Extension and flexion in the range of motion exercise against extremity resistance, performed for wrists, elbows, shoulders, ankles, knees, and hip-joints (acetabulo-femoral joints), 5 days/week for 4 weeks with one session a day. Each activity repeated 5 - 8 times.