World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(REVIEW ARTICLE)

The effect of music on the structure and function of the preterm neonatal brain: A systematic review

Kleoniki Xatzi [1], Grigorios Karampas [2], Antigoni Sarantaki [3], Maria Tigka [3,*], Aikaterini Lykeridou [3] and Dimitra Metallinou [3]

[1] *Rea Maternity Hospital, Athens, Greece.*
[2] *Second Department of Obstetrics and Gynaecology, Aretaieio University Hospital, National and Kapodistrian University of Athens, Athens, Greece.*
[3] *Department of Midwifery, School of Health and Care Sciences, University of West Attica, Athens, Greece.*

World Journal of Advanced Research and Reviews, 2025, 26(01), 2327-2334

Publication history: Received on 10 March 2025; revised on 14 April 2025; accepted on 16 April 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.26.1.1334

Abstract

Introduction: Preterm birth poses significant risks to neonatal brain development due to disrupted in-utero maturation. Music, as a structured auditory stimulus, has emerged as a potential non-invasive intervention to support neurodevelopment in preterm neonates. This systematic review evaluates the effects of music exposure on the structure and function of the preterm neonatal brain.

Methods: Following PRISMA guidelines, a systematic search of PubMed, Google Scholar, and ScienceDirect was conducted for English-language studies from 2014–2024. Inclusion criteria focused on studies involving preterm neonates receiving music-based interventions with outcomes related to brain structure or function. Out of 608 screened records, 9 studies met eligibility criteria and underwent quality assessment using reliable tools.

Results: Nine studies involving 283 neonates (118 preterm with music exposure) were included. Interventions ranged from parental singing to recorded music. Neuroimaging and electrophysiological assessments revealed that music exposure enhanced auditory processing, functional connectivity, and cortical structure. Notably, music-stimulated brain regions extended beyond auditory cortices, engaging networks related to emotion, memory, and motor planning. Several studies indicated that music-exposed preterms exhibited brain patterns more closely resembling those of full-term neonates.

Conclusions: Music-based interventions show promising neuroprotective and neurodevelopmental effects in preterm neonates, enhancing both structural maturation and functional connectivity. Given its safety and potential long-term benefits, music therapy may be a valuable addition to neonatal care. Further large-scale, longitudinal studies are needed to establish standardized protocols and assess long-term outcomes.

Keywords: Preterm Neonates; Music Therapy; Neurodevelopment; Brain Plasticity; Auditory Stimulation; Neonatal Intensive Care Unit

1. Introduction

Preterm birth is a significant global health concern, with premature neonates facing a range of developmental challenges due to their underdeveloped physiological systems. One of the most vulnerable organs in preterm neonates is the brain, which, due to early birth, may be exposed to a host of developmental risks such as abnormal neural maturation, altered

* Corresponding author: Maria Tigka.

synaptic connectivity, and impaired cognitive function [1]. As neonatal care continues to advance, various therapeutic approaches have been explored to improve the long-term neurological outcomes of preterm neonates [2]. Among these interventions, music has emerged as a promising tool to stimulate neural development and promote optimal brain function in this fragile population [3].

The impact of auditory stimulation, particularly music, on brain development has been a subject of growing interest in recent years. Research has shown that early auditory experiences can significantly influence brain plasticity, which is crucial for the cognitive and sensory development of preterm neonates [4]. Music, in particular, is thought to provide a structured auditory environment that might help foster neural connections, enhance sensory processing, and promote positive emotional regulation [3]. This notion stems from evidence suggesting that music-based interventions may not only improve physiological markers such as heart rate, respiratory rate and oxygen saturation [5] but could also have long-lasting effects on neurodevelopment [3,6].

Despite the promising nature of these findings, there remains a lack of consensus regarding the specific mechanisms through which music affects the developing brain of preterm neonates. Studies have demonstrated varying results, with some showing improvements in neurological outcomes [3,5,7,8] while others report minimal effects [6,9]. This discrepancy may be due to differences in study design, music type, timing, and intensity of exposure. Therefore, a comprehensive and systematic evaluation of the existing literature is essential to provide a clearer understanding of the role of music in neonatal brain development, particularly in preterm neonates.

This systematic review aims to evaluate the current evidence on the effects of music on the structure and function of the preterm neonatal brain. By synthesizing findings from multiple studies, we seek to identify patterns and highlight the potential therapeutic benefits of music for enhancing neurodevelopmental outcomes in preterm neonates. Ultimately, this review will contribute to the growing body of knowledge on non-invasive interventions in neonatal care and may inform future clinical practices that integrate music-based therapies into Neonatal Intensive Care Units (NICUs) worldwide.

2. Materials and Methods

This systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

2.1. Inclusion Criteria

The PICO framework was employed to structure this review (Table 1). PICO is an acronym representing four essential elements of clinical research: Population, Intervention, Comparison, and Outcome. This approach facilitates the formulation of focused clinical questions and guides the targeted search for evidence supporting the research hypothesis.

Table 1 PICO Elements of the Review

Population	Studies involving preterm neonates, defined as those born before 37 weeks of gestation.
Intervention	Studies specifically investigating the effects of music-based interventions on preterm neonates. These interventions may include live music, recorded music, or other forms of music therapy.
Comparison	Studies that include a control group receiving either no musical intervention or an alternative intervention, to assess the comparative effectiveness of music therapy.
Outcomes	Studies reporting either primary or secondary outcomes related to structural and/or functional changes in the brain attributed to music exposure. These outcomes may include neuroimaging findings (e.g. MRI, CT), neurological assessments, EEG data, or developmental milestones related to brain function.

CT: computed tomography; EEG: electroencephalogram; MRI: magnetic resonance imaging

Eligible studies included randomized controlled trials (RCTs), case-control studies, experimental studies, and cohort studies. Only English-language studies published between 2014 and 2024 were included.

2.2. Exclusion Criteria

- Population: Studies focusing on full-term neonates, older infants, children, or adults; or studies without subgroup analysis by gestational age.
- Intervention/Exposure: Studies examining multimodal interventions where music is not a distinct variable, unless its specific effect can be clearly isolated.
- Outcomes: Studies that do not report outcomes related to brain structure or function, or outcomes unrelated to neurodevelopmental processes.
- Study Design: Case reports, editorial articles, and narrative reviews lacking primary data were excluded.

The systematic search was conducted across the following scientific databases: PubMed, Google Scholar, and ScienceDirect. Search terms and keywords were carefully selected to capture relevant studies involving preterm neonates, music therapy, brain structure, and brain function. Keywords used included: "premature neonates," "preterm neonates," "preterm brain development," "music therapy and brain plasticity," "music therapy and brain development in preterm neonates," "music intervention in NICU," and "neurodevelopment in preterm neonates."

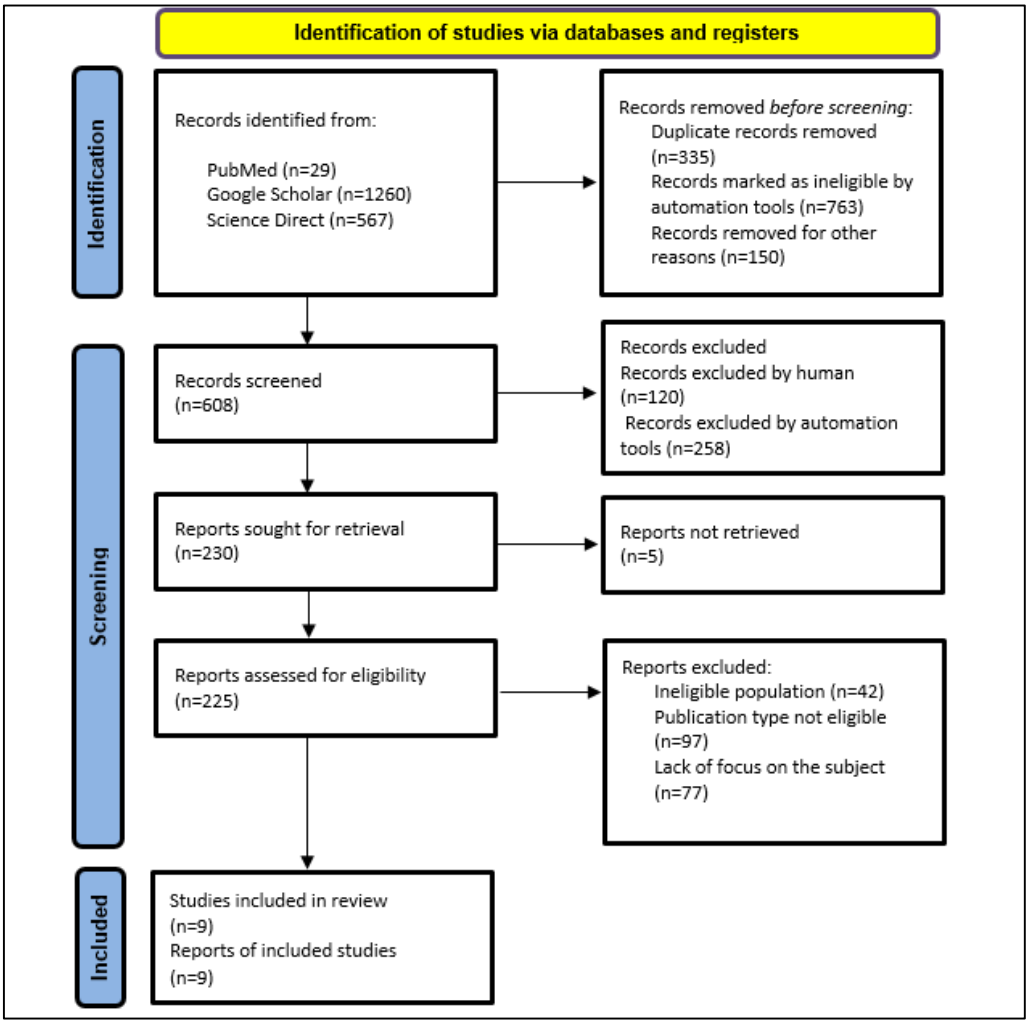

Figure 1 PRISMA flowchart illustrating the study selection process for the systematic review

During the initial screening phase, the titles and abstracts of identified records (n = 608) were rigorously assessed for relevance to the research objectives. Records deemed irrelevant were excluded (n = 383). The full-text articles of potentially eligible studies (n = 225) were then thoroughly reviewed for inclusion, based on the predefined criteria. Any exclusions were explicitly justified.

A comprehensive quality assessment was conducted to evaluate the methodological rigor and risk of bias of the included studies. This evaluation aimed to identify potential biases and methodological limitations. The following tools were used: a) RoB 2 tool for randomized studies, assessing factors such as randomization process, deviation from intended

interventions, and completeness of outcomes, b) ROBINS-I for non-randomized intervention studies and c) ROBINS-E, which provides a structured approach for assessing bias in observational epidemiological studies, focusing on the causal effect estimated by the outcome. This tool allows in-depth evaluation of the strength and nature of evidence regarding the potential effect of exposure [10]. The search strategy is illustrated in Figure 1 [11]. As this review is based solely on published literature, ethical approval was not required.

3. Results

Table 2 Summary of Included Studies

Study	Country	Design	Sample (total)	Intervention	Outcome Measures	Key Findings
Partanen et al. (2022) [12]	Sweden	RCT	21	Parental singing during kangaroo care	MEG responses to auditory stimuli	Enhanced auditory discrimination; stronger father engagement
Ren et al. (2022) [13]	China	Observational	10	Mozart Sonata K.448, 3 min	fNIRS, dynamic functional connectivity	Innate music-processing networks; broad functional synchronization
Ren et al. (2021) [14]	China	RCT	20	Mozart K.448, 12 min/day for 3 days	fNIRS (pre/post)	No significant short-term connectivity changes; left-lateralized activation
Loukas et al. (2022) [15]	Switzerland	Cohort study	46	NICU music, 8 min, 5x/week	RS-fMRI	Enhanced connectivity in emotion/memory regions; exposure-dependent effects
Sa de Almeida et al. (2020) [16]	Switzerland	RCT	45	Vollenweider music, 8 min, 5x/week	fMRI, DTI	Improved maturation of emotional neural circuits
Lordier et al. (2019a) [7]	Switzerland	RCT	27	Vollenweider music, 8 min, 5x/week	fMRI (PPI analysis)	Stronger connectivity in rhythm-processing areas; enhanced musical structure recognition
Lordier et al. (2019b) [8]	Switzerland	RCT	45	NICU music exposure	Resting-state fMRI	Improved salience and sensorimotor network connectivity
Ren et al. (2019) [17]	China	RCT	16	Mozart K.448, 3 sessions	fNIRS, EEG	Reduced hemodynamic complexity; neurovascular protection
Webb et al. (2015) [18]	USA	RCT	40	Maternal voice and heartbeat playback	Cranial ultrasound	Increased auditory cortex thickness; early auditory plasticity

dFC = dynamic functional connectivity; DTI = diffusion tensor imaging; fNIRS = functional near-Infrared spectroscopy; MEG = magnetoencephalography; PPI = psychophysiological interaction; RCT = randomized controlled trial; RS-fMRI = resting-state functional magnetic resonance imaging

This systematic review included nine (N=9) studies that analyzed data from a total of 283 neonates. Among these, 118 were preterm neonates who received music-based interventions, 107 were preterm controls who did not receive any music exposure, and 58 were full-term neonates included as comparison groups. The studies were conducted in

Switzerland, China, Sweden, and the United States. The majority of studies were randomized controlled trials, while others followed observational or cohort designs.

The music interventions employed across the studies varied in content and delivery. Some studies focused on parental singing during kangaroo care, while others utilized recorded classical music, such as Mozart's Sonata K.448, or maternal voice and heartbeat recordings. In several cases, the interventions involved original instrumental compositions specifically designed for the neonatal intensive care environment. The duration and frequency of music exposure ranged from short daily sessions lasting only a few minutes (3-12 minutes) to repeated exposures over several weeks. Most interventions began as early as 28 weeks of gestational age and continued up to term-equivalent age or until discharge from the NICU.

To evaluate the effects of music on brain structure and function, the studies employed a range of neuroimaging and electrophysiological methods, including functional near-infrared spectroscopy (fNIRS), functional magnetic resonance imaging (fMRI), resting-state fMRI, diffusion tensor imaging (DTI), electroencephalography (EEG), and cranial ultrasound. These methods allowed researchers to investigate both structural changes and functional connectivity within the developing neonatal brain.

The findings across studies consistently suggested that music exposure has a beneficial impact on the brain development of preterm neonates. Enhanced auditory processing and stronger neural responses to sound were observed in neonates who received music-based interventions, especially those involving parental singing or emotionally significant auditory stimuli. In several studies, increased functional connectivity was reported in brain regions related to emotion regulation, sensory processing, and memory integration. Some studies also identified structural changes, such as increased thickness of the auditory cortex, in neonates exposed to maternal voice recordings.

Moreover, preterm neonates who received music exposure often demonstrated neural connectivity patterns that more closely resembled those of full-term neonates. Although short-term interventions did not always produce statistically significant changes in brain connectivity, they often activated relevant auditory and emotional circuits, indicating early responsiveness to music stimuli (Table 2).

Overall, the results suggest that music-based interventions can promote experience-dependent brain plasticity and support the development of auditory and emotional networks in preterm neonates. These effects were most evident in studies employing longer or more frequent exposures, particularly when the musical stimuli were familiar, personalized, or emotionally meaningful. Music therapy, therefore, emerges as a promising complementary approach for enhancing neurodevelopmental outcomes in the preterm neonatal population.

4. Discussion

The synthesis of the nine studies included in this systematic review reveals a range of compelling findings regarding the effects of music therapy on the brain development of preterm neonates. Collectively, these studies highlight music as a powerful sensory stimulus capable of influencing both structural and functional neural maturation during a critical period of neurodevelopment.

One of the most striking insights emerging from this review is the multidimensional neural engagement triggered by music exposure. Rather than being confined to the auditory cortex, musical stimuli appear to recruit widespread brain networks. Studies by Ren et al. (2021, 2022) [13,14] and Lordier et al. (2019a, 2019b) [7,8] consistently demonstrate activation in brain areas such as the Broca's area, premotor and supplementary motor cortices, the anterior cingulate cortex, and the superior temporal gyrus. These findings suggest that music engages not only auditory pathways but also circuits involved in emotion regulation, motor planning, attention, and language-related processing. This widespread activation supports the hypothesis that preterm neonates possess a significant degree of neuroplasticity, responding to music in ways that extend beyond basic acoustic perception.

In parallel, several studies report structural brain adaptations in response to music exposure. Changes in the auditory cortex, particularly increased cortical thickness and improved white matter integrity, have been observed in preterm neonates exposed to maternal voice or recorded music [16,18]. These results imply that early sensory experiences can shape the architecture of the developing brain, potentially laying the foundation for enhanced perceptual and cognitive functions. Moreover, music-related activation of regions involved in emotional processing suggests a role for music in supporting the maturation of neural networks essential for socio-emotional functioning [8,16].

Another dimension of critical importance is the potential for long-term effects. While many studies focus on neural responses during or shortly after the intervention period, some findings indicate more durable benefits. For example, Sa de Almeida et al. (2020) [16] and Partanen et al. (2022) [12] provide evidence for sustained microstructural maturation, stronger language-related auditory discrimination, and increased neural efficiency in preterm neonates exposed to music. These observations raise the possibility that music interventions during NICU hospitalization may have lasting developmental implications that extend into early childhood.

The studies also reveal complex patterns of brain connectivity associated with music exposure. Both functional and structural connectivity appear to be enhanced, particularly in areas related to memory, multisensory integration, and affective processing [7,8,12]. This increased connectivity not only reflects more efficient inter-regional communication but also hints at the potential for music to scaffold early cognitive functions by linking sensory and higher-order networks during a formative developmental window.

An additional noteworthy finding relates to the potentially protective vascular effects of music. Research by Ren et al. (2019) [17] suggests that exposure to specific musical stimuli, such as Mozart's compositions, may reduce cerebral hemodynamic complexity. This finding implies that music might contribute to regulating cerebral blood flow and promoting vascular stability, thus expanding the therapeutic scope of music interventions beyond cognitive and emotional domains.

Beyond the studies included in this review, additional literature supports the therapeutic benefits of music in neonatal care. For instance, Haslbeck et al. (2020) [19] demonstrated that creative music therapy (CMT) can enhance functional brain activity and connectivity in networks underlying higher-order cognitive, socio-emotional, and motor functions in preterm neonates. Similarly, Standley (2010) [20] found that music reinforcement for non-nutritive sucking can improve feeding behaviors and support neurodevelopment in premature neonates.

Taken together, the evidence presents a multifaceted picture of how music therapy may positively influence the developing brain of preterm neonates. The observed effects span a spectrum of neural domains—including perceptual, cognitive, emotional, and even vascular systems—emphasizing the depth and breadth of music's impact. These findings support the view that music is a potent environmental factor capable of guiding neurodevelopmental trajectories during the most vulnerable phase of postnatal maturation.

Ultimately, this review positions music therapy as a promising, non-invasive intervention that not only enhances immediate neural responsiveness but may also foster long-term developmental gains. Its ability to elicit structural remodeling, strengthen functional connectivity, and support cognitive and emotional regulation underscores its value as an adjunctive approach in neonatal intensive care. Future longitudinal studies are needed to further examine whether these early neural enhancements translate into improved language acquisition, emotional resilience, and cognitive performance in later life.

4.1. Suggestions for further research

While the current evidence is encouraging, further investigation is necessary to better understand the full potential of music therapy in neonatal care. Longitudinal research is particularly needed to determine whether the observed neural enhancements lead to lasting cognitive, linguistic, and emotional benefits as the child develops. Future studies should also explore the optimal characteristics of music interventions, including their timing, duration, and type—whether live, recorded, or parent-delivered—in order to establish standardized, evidence-based protocols.

In addition, larger and more diverse randomized controlled trials would strengthen the reliability and generalizability of existing findings. It would also be beneficial to examine how music therapy interacts with other aspects of neonatal care and whether its effects vary across different populations and clinical settings. Including physiological and biochemical measures, such as stress markers or autonomic regulation, could provide deeper insights into the mechanisms by which music exerts its effects. Lastly, practical studies assessing the feasibility and cost-effectiveness of integrating music therapy into routine neonatal care could help pave the way for broader clinical adoption.

5. Conclusion

This review demonstrates that music-based interventions can positively influence the structural and functional brain development of preterm neonates. The findings suggest that music enhances auditory processing, strengthens neural connectivity, and may support long-term developmental outcomes. Given its non-invasive nature and potential

neuroprotective effects, music therapy appears to be a valuable addition to neonatal care. However, further research is needed to confirm these benefits and guide best practices for clinical implementation.

Compliance with ethical standards

Disclosure of conflict of interest

All authors declare that they have no conflicts of interest.

References

[1] Chau V, Synnes A, Grunau RE, Poskitt KJ, Brant R, Miller SP. Abnormal brain maturation in preterm neonates associated with adverse developmental outcomes. Neurology. 2013;81(24):2082-2089. doi:10.1212/01.wnl.0000437298.43688.b9

[2] Molloy EJ, El-Dib M, Soul J, Juul S, Gunn AJ, Bender M, Gonzalez F, Bearer C, Wu Y, Robertson NJ, Cotton M, Branagan A, Hurley T, Tan S, Laptook A, Austin T, Mohammad K, Rogers E, Luyt K, Wintermark P, … Newborn Brain Society Guidelines and Publications Committee. Neuroprotective therapies in the NICU in preterm infants: Present and future (Neonatal Neurocritical Care Series). Pediatric Research. 2024;95(5):1224-1236. doi:10.1038/s41390-023-02895-6

[3] Pino O, Di Pietro S, Poli D. Effect of musical stimulation on placental programming and neurodevelopment outcome of preterm infants: A systematic review. Int J Environ Res Public Health. 2023;20(3):2718. doi:10.3390/ijerph20032718

[4] Di Fiore JM, Liu G, Loparo KA, Bearer CF. The effect of early postnatal auditory stimulation on outcomes in preterm infants. Pediatric Research. 2024;96(6):1389–1396. https://doi.org/10.1038/s41390-024-03329-7

[5] Shahbazi F, Fattahi-Darghlou M, Moslehi S, Dabiri-Golchin M, Shahbazi M. Effect of music therapy on behavioral and physiological neonatal outcomes: A systematic review and dose-response meta-analysis. PLoS One. 2025;20(1):e0316674. doi:10.1371/journal.pone.0316674

[6] Haslbeck FB, Mueller K, Karen T, Loewy J, Meerpohl JJ, Bassler D. Musical and vocal interventions to improve neurodevelopmental outcomes for preterm infants. Cochrane Database Syst Rev. 2023;9(9):CD013472. doi:10.1002/14651858.CD013472.pub2

[7] Lordier L, Loukas S, Grouiller F, Meskaldji DE, Vollenweider A, Borradori-Tolsa C, Hüppi PS. Music processing in preterm and full-term newborns: A psychophysiological interaction (PPI) approach in neonatal fMRI. Neuroimage. 2019a;185:857-864. doi:10.1016/j.neuroimage.2018.03.078

[8] Lordier L, Meskaldji DE, Grouiller F, Pittet-Metrailler A, Vollenweider A, Borradori-Tolsa C, Lazeyras F, Grandjean D, Van De Ville D, Hüppi PS. Music in premature infants enhances high-level cognitive brain networks. Proceedings of the National Academy of Sciences. 2019b;116(24):12103-12108. doi:10.1073/pnas.1817536116

[9] Gaden TS, Ghetti C, Kvestad I, Bieleninik Ł, Stordal AS, Assmus J, Arnon S, Elefant C, Epstein S, Ettenberger M, Lichtensztejn M, Lindvall MW, Mangersnes J, Røed CJ, Vederhus BJ, Gold C. Short-term music therapy for families with preterm infants: A randomized trial. Pediatrics. 2022;149(2):e2021052797. doi:10.1542/peds.2021-052797

[10] Higgins JPT, Morgan RL, Rooney AA, Taylor KW, Thayer KA, Silva RA, Lemeris C, Akl EA, Bateson TF, Berkman ND, Glenn BS, Hróbjartsson A, LaKind JS, McAleenan A, Meerpohl JJ, Nachman RM, Obbagy JE, O'Connor A, Radke EG, ... Sterne JAC. A tool to assess risk of bias in non-randomized follow-up studies of exposure effects (ROBINS-E). Environment International. 2024;186:108602. doi:10.1016/j.envint.2024.108602

[11] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, … Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi:10.1136/bmj.n71

[12] Partanen E, Mårtensson G, Hugoson P, Huotilainen M, Fellman V, Ådén U. Auditory processing of the brain is enhanced by parental singing for preterm infants. Frontiers in Neuroscience. 2022;16:772008. doi:10.3389/fnins.2022.772008

[13] Ren H, Jiang X, Meng L, Lu C, Wang L, Dai C, Chen W. fNIRS-Based Dynamic Functional Connectivity Reveals the Innate Musical Sensing Brain Networks in Preterm Infants. IEEE transactions on neural systems and rehabilitation engineering: a publication of the IEEE Engineering in Medicine and Biology Society. 2022;30:1806-1816. doi:10.1109/TNSRE.2022.3178078

[14] Ren H, Zou L, Wang L, Lu C, Yuan Y, Dai C, Chen W. Evaluation of the short-term music therapy on brain functions of preterm infants using functional near-infrared spectroscopy. Frontiers in Neurology. 2021;12:649340. doi:10.3389/fneur.2021.649340

[15] Loukas S, Lordier L, Meskaldji D, Filippa M, Sa de Almeida J, Van De Ville D, Hüppi PS. Musical memories in newborns: A resting-state functional connectivity study. Human Brain Mapping. 2022;43(2):647-664. doi:10.1002/hbm.25677

[16] Sa de Almeida J, Lordier L, Zollinger B, Kunz N, Bastiani M, Gui L, Adam-Darque A, Borradori-Tolsa C, Lazeyras F, Hüppi PS. Music enhances structural maturation of emotional processing neural pathways in very preterm infants. NeuroImage. 2020;207:116391. doi:10.1016/j.neuroimage.2019.116391

[17] Ren H, Jiang X, Xu K, Zou L, Wang L, Lu C, Liu X, Chen W. Evaluation of the effects of Mozart music on cerebral hemodynamics in preterm infants. In 2019 IEEE Biomedical Circuits and Systems Conference (BioCAS), Nara, Japan, 2019 (pp. 1–4). doi: 10.1109/BIOCAS.2019.8919100

[18] Webb AR, Heller HT, Benson CB, Lahav A. Mother's voice and heartbeat sounds elicit auditory plasticity in the human brain before full gestation. Proceedings of the National Academy of Sciences. 2015;112(10):3152-3157. doi:10.1073/pnas.1414924112

[19] Haslbeck FB, Jakab A, Held U, Bassler D, Bucher HU, Hagmann C. Creative music therapy to promote brain function and brain structure in preterm infants: A randomized controlled pilot study. Neuroimage Clin. 2020;25:102171. doi:10.1016/j.nicl.2020.102171

[20] Standley JM, Cassidy J, Grant R, Cevasco A, Szuch C, Nguyen J, Walworth D, Procelli D, Jarred J, Adams K. The effect of music reinforcement for non-nutritive sucking on nipple feeding of premature infants. Pediatr Nurs. 2010;36(3):138-145.