Journal of Perinatology (2020) 40:1770–1779
https://doi.org/10.1038/s41372-020-0756-4

ARTICLE

Evaluating physiologic outcomes of music interventions in the neonatal intensive care unit: a systematic review

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Received: 14 September 2019 / Revised: 2 June 2020 / Accepted: 22 July 2020 / Published online: 31 July 2020

Abstract

Music is widely used in the neonatal intensive care unit. The objectives of this systematic review are: (1) clarify the current literature in regards to the impact of music on neonatal physiologic parameters, (2) highlight the variability in definitions utilized for music interventions, and (3) provide a foundation for future music therapy research focused on influencing neonatal physiology. A systematic literature review was conducted in accordance with PRISMA guidelines, with search terms including "music," "music therapy," "neonates," "newborn," and "NICU." Four hundred and fifty-eight studies were reduced to 16 clinical trials divided based on methodological description of music intervention. Our review highlights variability in the existing literature specifically on neonatal physiological impact of music. Future studies should focus on consistent and well-defined data collection, utilization of standardized definitions for music interventions, and consideration of more sensitive markers of physiology, such as heart rate variability, to enhance study rigor and reproducibility.

Introduction

Music therapy, according to the American Music Therapy Association is "the clinical and evidence-based use of music interventions to accomplish individualized goals within a therapeutic relationship by a credentialed professional who has completed an approved music therapy program" and can be used to treat physical and psychological conditions using various modalities, including vocals and instruments [1]. Having been extensively studied in mothers and infants, music therapy literature currently has a stronger literature base for nonphysiological outcomes (i.e., maternal anxiety) and lacks robust data evaluating neonatal physiologic impact. Currently available data suggest that music therapy may have an impact on infant behavior and physiological parameters, in addition to increasing factors such as maternal–infant bonding [2].

Previous reviews have reported on the impact of music for neonates often focusing on behavioral interventions or the impact on maternal and/or maternal–child factors. For example, a systematic review evaluated 20 studies focused on live vs. recorded music in premature infants admitted to the NICU. In this review, authors divided outcomes into three categories: (1) physiological parameters, (2) growth and feeding, and (3) behavioral state, relaxation and pain. When considering the impact on physiologic parameters, live music improved heart rate in two of four studies and recorded music improved heart rate in two of six studies. They were unable to conduct meta-analysis due to multiple study variations, which included outcome measures and timing of interventions [3]. A 2016 meta-analysis found that most music interventions consisted of lullabies, frequently provided by a parent. Positive effects were found on respiratory rate (less than four breaths per minute) [4]. Similarly, another meta-analysis demonstrated improvement of heart rate and oxygen saturation after exposure to music therapy in preterm infants [5]. While other psychosocial considerations, such as attachment, are also impacted, the effect of music on these parameters is beyond the scope

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of this review. One additional review noted heterogenous and inconsistently defined methods in many studies under the heading of "music therapy" [6]. Taken together, despite evidence of an impact of music therapy on maternal and maternal–infant outcomes most existing reviews focus on nonphysiological parameters, and secondarily, there appear to be frequent misclassifications of music interventions with few studies adhering to standardized definitions of music therapy and music medicine.

Music medicine is defined as music interventions lacking the interaction between a trained music therapist and the patient, and is conducted in the absence of a treatment plan with nonmusical, therapeutic goals [7]. The misrepresentation of music medicine as "music therapy" is rampant in the published literature and is an important consideration in interpreting the significance of studies. Certification as a music therapist (designated as MT-BC) requires advanced education and, according to AMTA, the music therapist must be appropriately credentialed and maintain vigorous continuing education in order to practice. The goal of a music therapist is to work with an array of diverse populations to meet an individual's unique needs via a systematic therapeutic process [8]. In the NICU setting, a music therapist should undertake advanced training in NICU music therapy prior to working with this population and their caregivers given the importance of ensuring music implementation at a safe decibel level and appropriately monitoring the infant for signs of overstimulation. While any board-certified music therapist with or without advanced training may practice music therapy in the NICU setting, the ethical question of working with vulnerable populations without the highest level of training must be considered for best practice. The harmful effects of overstimulation are known and understood by a trained NICU music therapist, with their priority being patient safety and well-being [9]. While trained musicians may work in medical settings and music may be utilized in multiple settings not directed by a certified music therapist, studies seeking to better understand the range of benefits of music therapy need to adhere to established definitions of "music therapy" in order to enhance study reproducibility and minimize variations. Furthermore, the literature needs to carefully report study methodology in order to appropriately classify "music therapy" and "music medicine," as the misrepresentation of "music therapy" as any musical intervention (with or without a trained music therapist) is detrimental to music therapy professionals and limits the building of interdisciplinary research and clinical care teams.

The objectives of this systematic review are to (1): clarify the current literature in regards to the impact of music interventions on neonatal physiologic parameters (2), highlight the variability in definitions utilized for music interventions, and (3) provide a foundation for future music therapy research focused on influencing neonatal physiology. Demonstration of physiological effects in the neonate is expected to enhance and expand the utility of music therapy as a noninvasive, low-cost intervention for a variety of medical conditions in high-risk neonates.

Methods

A literature review was conducted between December 1, 2018 and April 5, 2019 in accordance with PRISMA guidelines, using the PubMed, CINAHL, and PsycInfo databases (Fig. 1). Search terms included "music and neonates," "music and newborn," "music therapy and neonates," "music therapy and newborn," "music and NICU," "music therapy and NICU," and included MeSH terms (music therapy, infants, newborns, newborn infant, newborn infants, neonate, neonatal ICU, newborn intensive care units, newborn ICU). Searching was supplemented with references from included papers. Inclusion criteria were: (1) a minimum sample size of ten, (2) music directed toward a neonate in the NICU, (3) inclusions at least one physiologic outcome including heart rate, respiratory rate, oxygen saturation, and/or energy expenditure, (4) publication in a peer review journal within the last 15 years, and (5) written in English. Exclusion criteria included: (1) insufficient documentation of data collection methods or outcomes, (2) sample size < 10, (3) absence of direct measurements of physiologic outcomes, (4) review articles, and (5) studies that included only behavioral outcomes, sleep, growth, and/or pain. After removal of duplicates, 458 published studies reduced to sixteen clinical trials, divided based on methodological description into music therapy and music medicine.

One reviewer evaluated abstracts for inclusion and exclusion criteria for this review. For studies deemed to meet all criteria, two reviewers performed full-text review and data extraction. Data extraction included study title, first author, publication year, journal, total sample size, and citation. The study under review was then classified by study type, such as randomized/non-randomized control trial, case–control, or cohort study. Next, study outcomes were assessed and data collection methods stratified by: (1) software, (2) manual collection from monitor, (3) manual collection from subject. Data collection and music intervention procedures were recorded with respect to dose, frequency, and duration. Results for each physiologic variable were abstracted to capture improvement or no change/negative effect. All included studies were classified as either music therapy or music medicine by a board-certified music therapist based on the following criteria: music therapy must be an intervention designed and performed by a trained, licensed music therapist based on the following criteria: (1) therapy must be an intervention

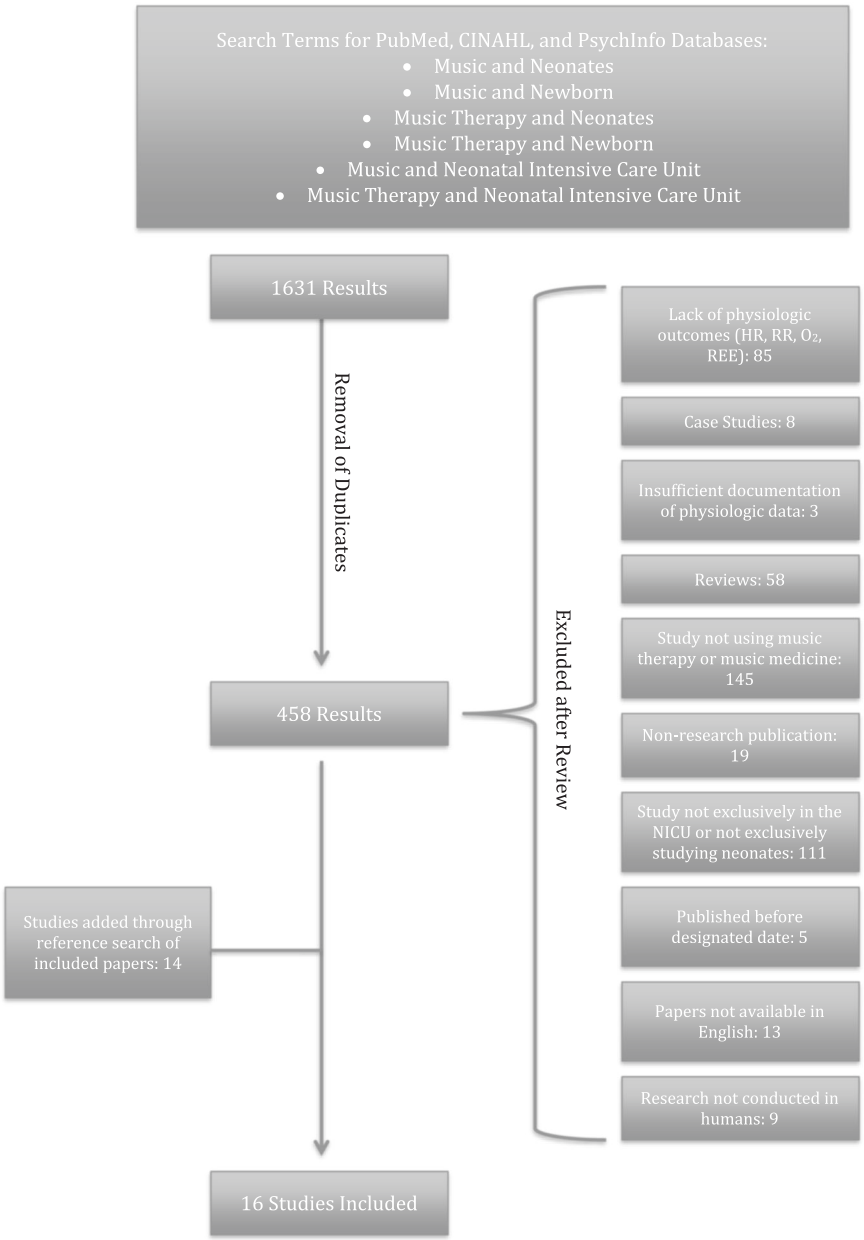

Fig. 1 Systematic search strategy and results.

designed and performed by a trained music therapist (2), music therapy was provided in accordance with AMTA definition, and (3) music therapy involves interaction between the music therapist and patient. Music medicine was defined as the use of music interventions, e.g., recorded music or live music performed by a general musician or parent. A board-certified music therapist abstracted included studies for music modality, dose, and duration, which are tabulated in Table 1.

Methodological rigor of included studies were assessed by National Institute of Health Guidance for Assessing the Quality of Controlled Intervention Studies Tool [10] by two independent reviewers. Discrepancies were resolved by discussion and group consensus, and findings are reported in Table 2. Due to heterogeneity in study design, music intervention, and primary outcomes, we could not assign each study as "good," "fair," or "poor" without risk of bias.

To better characterize the musical aspects of the included studies, Robb's reporting guidelines for music-based interventions was used (CITE). A board-certified music therapist reviewed the included studies utilizing this set of criteria. Results are reported in Table 3.

Results

Search revealed 1631 studies, and after removal of duplicates, 458 studies were identified based on search criteria.

Table 1 Studies evaluating music interventions in NICU.

Authors (ref. No.)	Total *N*	Multi-site vs. single-site	Music therapy vs. music medicine	Music modality evaluated, dose and duration	Certified music therapist involvement	Clinician (e.g., MD, DO) involvement	Physiologic outcomes			
							HR	O_2	RR	REE
Alipour et al. [18]	90	Single-site	Music medicine	Prerecorded music once for 20 min	Not co-authored	Co-authored	(−)	(−)	(+)	N/A
Amini et al. [11]	25	Undisclosed	Music medicine	Lullaby or classical music lasting 20 min for 4 days	Not co-authored	Co-authored	(+)	(−)	(+)	N/A
Arnon et al. [12]	31	Single-site	Music medicine	30 min of live music and recorded music: each randomly selected 3 days in a row for 6 months	Neither co-authored nor acknowledged	Co-authored	(+)	(−)	(−)	N/A
Badr et al. [17]	42	Single-site	Music medicine	Recorded songs listened to prenatally, or lullaby twice a day for 10 min every 8 h before, during, and after heel stick	Not co-authored	Co-authored	(−)	(−)	(+)	N/A
Caparros-Gonzalez et al. [19]	17	Multi-site	Music medicine	Prerecorded "relaxing" music 20 min, 3 times per day for 3 days	Not co-authored	Not co-authored	(−)	(−)	(+)	N/A
Keidar et al. [26]	12	Single-site	Music medicine	30 min of prerecorded classical music for 3 days	Not co-authored	Co-authored	N/A	N/A	N/A	(+)
Keith et al. [13]	24	Single-site	Music medicine	18 min of MT-recommended music twice per week	Co-authored	Not co-authored	(+)	(+)	(+)	N/A
Lai et al. [20]	30	Multi-site	Music medicine	Parent-selected prerecorded lullaby music 60 min per day for 3 days	Not co-authored	Not co-authored	(−)	(−)	(−)	N/A
Loewy et al. [14]	272	Multi-site	Music therapy	Live music 3 times per week for 2 weeks: Ocean Disc, Gato Box, or Lullaby	Co-authored	Co-authored	(+)	(+)	(−)	N/A
Lubetzky et al. [27]	20	Single-site	Music medicine	30 min of Mozart 1 time	Not co-authored	Co-authored	N/A	N/A	N/A	(+)
Ranger et al. [21]	21	Multi-site	Music medicine	15 min live harp music	Not co-authored	Co-authored	(−)	(−)	(−)	N/A
Rossi et al. [16]	80	Single-site	Music medicine	Heartbeat, Mozart, or Beethoven one time for 40 min, 1 h after feeding during procedure	Not co-authored	Co-authored	(+)	(+)	N/A	N/A
Schlez et al. [22]	52	Single-site	Music medicine	Harp for 30 min 1 time	Not co-authored	Co-authored	(−)	(−)	(−)	N/A
Schwilling et al. [15]	20	Multi-site	Music medicine	15 min live music, 3 days in a row (MT did consult, not the treatment)	Co-authored	Co-authored	(+)	(+)	N/A	N/A
Taheri et al. [23]	52	Single-site	Music medicine	Male-voiced recorded lullabies, 20 min per day for 3 days	Not co-authored	Not co-authored	(−)	(−)	N/A	N/A
Ullsten et al. [24]	38	Single-site	Music therapy	Live lullabies implemented one time only during blood sampling	Co-authored	Co-authored	(−)	(−)	(+)	N/A

HR heart rate, *RR* respiratory rate, O_2 oxygen saturation, *REE* resting energy expenditure.

(+) denotes an improvement in physiological parameter with music intervention.

(−) denotes either no change or a negative effect in physiological parameter with music intervention.

N/A denotes that the physiological parameter was not evaluated.

Table 2 Assessing methodological quality of included studies via NIH Guidance for Assessing the Quality of Controlled Intervention Studies Tool.

	Alipour	Amini	Arnon	Badr	Caparros-Gonzalez	Keidar	Keith	Lai	Loewy	Lubetzky	Ranger	Rossi	Schlez	Schwilling	Taheri	Ullsten
1. Was the study described as randomized, a randomized trial, a randomized clinical trial, or an RCT?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
2. Was the method of randomization adequate (i.e., use of randomly generated assignment)?	NR	Yes	NR	Yes	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	NR	NA	Yes	Yes
3. Was the treatment allocation concealed (so that assignments could not be predicted)?	NR	NR	NR	Yes	Yes	NR	NR	Yes	Yes	NR	Yes	NR	NR	NA	NR	NR
4. Were study participants and providers blinded to treatment group assignment?	NA	NA	NA	NA	Yes	NR	No	No	Yes	NR	NA	NR	NA	NA	NA	NA
5. Were the people assessing the outcomes blinded to the participants' group assignments?	Yes	NR	Yes	Yes	Yes	NR	NR	Yes	NR	NR	No	NR	Yes	NA	Yes	NR
6. Were the groups similar at baseline on important characteristics that could affect outcomes (e.g., demographics, risk factors, co-morbid conditions)?	Yes	NA	NA	NA	Yes	NA	NA	Yes	NA	NA	NA	Yes	NA	Yes	NR	NA
7. Was the overall drop-out rate from the study at endpoint 20% or lower of the number allocated to treatment?	NR	No	No	No	No	NA	NA	No	NA	NA	NA	NR	NA	NR	NR	NA
8. Was the differential drop-out rate (between treatment groups) at endpoint 15 percentage points or lower?	NR	No	No	No	Yes	NA	NA	No	NA	NA	NA	NR	NA	NR	NR	NA
9. Was there high adherence to the intervention protocols for each treatment group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Were other interventions avoided or similar in the groups (e.g., similar background treatments)?	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11. Were outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	Yes	Yes	No	Yes	Yes	Yes	NR	Yes	NR	Yes	Yes	Yes	NR	Yes	Yes	Yes
12. Did the authors report that the sample size was sufficiently large to be able to detect a difference in the main outcome between groups with at least 80% power?	Yes	NR	NR	Yes	Yes	Yes	NR	Yes	Yes	NR	NR	NR	Yes	NR	Yes	NR
13. Were outcomes reported or subgroups analyzed prespecified (i.e., identified before analyses were conducted)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
14. Were all randomized participants analyzed in the group to which they were originally assigned, i.e., did they use an intention-to-treat analysis?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

NR not reported, *NA* not applicable.

Table 3 Reporting guidelines for music-based interventions.

Authors	Theory	Musical content	Unit of delivery	Delivery schedule	Interventionist	Setting	Lullaby/SOK used?
Alipour et al. [18]	P/BA	Preselected, recorded lullaby music via headphones	60 individual sessions, 30 no music	One session, 20 min	Study researchers	NICU	Lullaby—"Good Night, Kid"
Amini et al. [11]	P/BA	Preselected, recorded music via speaker 30 cm from ears	25 infants split into 6 combination groups	20 min for 6 days; 4 days music, 2 days control	Study researchers	NICU	Classical music (Mozart) and lullaby—Iranian Folk Song
Arnon et al. [12]	P/BA	Live and recorded music, played 1 m from infants' bed	31 infants	30 min for each intervention, 3 consecutive days	Two musicians	NICU	Live lullaby accompanied by frame drum and harp
Badr et al. [17]	P/BA	Prerecorded music; maternally selected or standard lullaby	42 infants	10 min every 8 h twice a day	Study researchers	NICU	Song of kin and lullaby
Caparros-Gonzalez et al. [19]	P/BA	Prerecorded "relaxing" music; via speaker 20 cm from left ear	17 infants	20 min 3 times a day for three days (a.m., noon, p.m.)	Study researchers	NICU	Prerecorded synthesized "relaxing" music
Keidar et al. [26]	P/BA	Prerecorded, preselected Bach/ Mozart via speaker 30 cm from ears	12 infants	30 min a day for 3 days	Study researchers	NICU	No lullaby or SOK
Keith et al. [13]	P/BA	Prerecorded lullaby, speakers placed on both sides of infant	24 infants	18 min of music twice in 1 week	Nursing researcher	NICU	Lullaby sung by female vocalist
Lai et al. [20]	P/BA	Prerecorded, parent selected	15 mother–infant dyads	60 min per day for 3 days	Study researchers	NICU	Western vocals, instrumental lullaby, or Taiwanese lullaby
Loewy et al. [14]	P/BA	Live music: parent-selected lullaby, Ocean disc, or Gato Box	272 infants	3 times a week for 2 weeks	Music therapist	NICU	Song of kin
Lubetzky et al. [27]	P/BA	Prerecorded Mozart via speakers 30 cm from ear	20 infants	One 30 min session a day for 2 days	Study researchers	NICU	Baby Mozart CD, possibly some lullaby-like melodies
Ranger et al. [21]	P/BA	Live harp music	21 infants	One 15 min session	Author, a hand harpist	NICU	Harp, could resemble lullaby
Rossi et al. [16]	P/BA	Prerecorded Mozart, Beethoven, Heartbeat Sound Recordings	80 infants	One 40 min session	Study researchers	NICU	No lullaby or song of kin
Schlez et al. [22]	P/BA	Live, preselected harp music with multicultural approach	52 mother–infant dyads	One 30 min session	Musician	NICU	Harp playing culturally relevant melodies, resemble lullaby
Schwilling et al. [15]	P/BA	Live kantele music, utilizing pentatonic scale	20 infants	15 min of music for 3 consecutive days	Author, a musician	NICU	Harp playing pentatonic scale, resemble lullaby
Taheri et al. [23]	P/BA	Prerecorded male voice lullabies via Mp3 using headphones	26 received music, 26 received none	20 min of music for 3 consecutive days	Study researchers	NICU	Lullaby
Ullsten et al. [24]	P/BA	Live lullaby	38 infants	One session	Music therapist	NICU	Lullaby

P/BA physiological/behavioral approach, *NA* not applicable.

Abstract review resulted in inclusion of 22 studies in full-text review. Of those, six were determined to be excluded based on the above described exclusion criteria. In total, 16 clinical trials are included in this systematic review (Table 1) and annotated with a (+) to demonstrate statistically significant results.

Heart rate

Fourteen of the included studies used heart rate as an outcome [11–24]. Most studies collected heart rate data from a traditional monitor used in the NICU or a pulse oximeter; however, one reviewed study did not disclose their data collection method [13]. A total of six studies found that music resulted in significantly decreased heart rate [11–16], while eight studies found no significant effects [17–21, 23, 24]. Notably, music therapy was used in one study with a significant result [14] and in one dissenting study [24]. Live music was used in three studies (two music medicine and one music therapy) with a significant effect [12, 14, 15] and three studies (two music medicine and one music therapy) found no change in heart rate [21, 22, 24]. Sample sizes for the included studies were varied (range 20–272). It must be noted that infant heart rates are expected to have high variability, averaging between 90 and 180 beats per minute within the 1st year [25], thus, interpreting the significance of heart rate changes can be challenging.

Oxygen saturation

Fourteen of the included studies used O_2 saturation as an outcome, with 12 utilizing music medicine and 2 utilizing music therapy [11–24]. Four studies found a significant increase in oxygen saturation with music [13–16] with one study utilizing music therapy [14] and three utilizing music medicine [13, 15, 16]. Ten studies found no effect [11, 12, 17–24]. Two of the studies with an effect (one music therapy and one music medicine) utilized live music [14, 15], while two music medicine studies used recorded music [13, 16]. Of the ten dissenting studies, one used music therapy [24], and nine used music medicine [11, 12, 17–23]. Four dissenting studies (including the one music therapy study) provided live music [12, 21, 22, 24], while six used recorded music [11, 17–20, 23].

Respiratory rate

Eleven of the included studies used respiratory rate as an outcome with nine utilizing music medicine and two utilizing music therapy [11–14, 17–22, 24]. Of those, six (five music medicine and one music therapy) found a significant decrease in respiratory rate as an effect of music [11, 13, 17–19, 24], while five (four music medicine and one music therapy) found no statistically significant effect [12, 14, 20–22]. Of those that demonstrated a significant effect, one was music therapy and provided live music [24], while the rest were music medicine utilizing recorded music [11, 13, 17–19, 24]. Of the dissenting studies, one utilized music therapy [14] and four used music medicine [12, 20–22]. Three (including the one music therapy study) provided live music [14, 21, 22], two provided recorded music [18, 20], and one provided both live and recorded music, neither of which produced a significant effect [12].

Energy expenditure

Two music medicine studies used resting energy expenditure as an outcome [26, 27]. Both found that Mozart music resulted in significantly decreased resting energy expenditure, as collected by a Deltatrac II Metabolic Monitor. It should be noted that indirect calorimetry, while an effective test when done correctly, is subject to inaccuracies [28].

Findings in music therapy vs. music medicine

Rigorous methodology is crucial to determining the true physiologic benefit of music for NICU newborns—current practice guidelines require that music therapy be provided by a trained music therapist [29]. Unfortunately, the current literature exploring the physiologic impact of music treatment fails to consistently apply accepted music therapy definitions in their methodological descriptions leading to inaccuracies as to whether the modality utilized was music therapy or music medicine [7]. Of the 16 studies reviewed, 14 consist of music medicine [11–13, 15–23, 26, 27] and only 2 music medicine studies [13, 15] and 2 music therapy [14, 24] studies listed a certified music therapist as a co-author. Of these, 10 out of 14 found significant effects on at least one physiologic variable. Only two studies utilized music therapy that met AMTA defined criteria, and of these, both reported a statistically significant effect in at least one physiologic variable [14, 24]. Notably, while one music medicine study had certified music therapist supervision, music was delivered by an uncertified musician [21], while one music medicine study utilized a musician with NICU experience and did not indicate expertise [22].

Discussion

Music therapy for neonates has a broad literature base and recent meta-analyses provide evidence in support of an impact of music therapy on maternal outcomes and the maternal–infant relations. However, when specifically exploring the relation between music interventions and

neonatal physiology, the data are less clear. Despite a significant number of existing studies, careful review of over 400 studies reporting music interventions in the NICU, only 16 studies directly evaluated physiologic outcomes with sufficient reporting detail and rigor. Eight of these studies reported on sample sizes of 30 or less. Of these eight studies, none were music therapy and six reported positive effects in at least one physiologic variable. In the eight studies that were larger than 30 subjects, two were music therapy and six reported positive effects in at least one physiologic variable. Of the studies that reported positive effects, the majority reported effects on HR. While intriguing, given the expected wide variability in heart rate in the infant of between 90 and 180 beats per minute [25], the clinical significance and implications of a decrease of between <2 [14] and ~40 bpm [12] remain uncertain.

Physiologic measures

Twelve studies reported a positive effect on physiological outcomes, specifically six on HR, four on oxygen saturation, six on RR, and two on REE. However, of the studies that reported positive effects, five had a sample size of 30 or less subjects, raising concerns about statistical power and generalizability. Beyond issues of sample size, variable methods of music intervention delivery further challenge data interpretation. Recorded music, which is the majority of the musical modalities in the studies included in our systematic review, has not been shown to be efficacious in the NICU environment [30]. For the six studies using live music [12, 14, 15, 21, 22, 24], four total (two music therapy and two music medicine) found positive effects on physiologic parameters [12, 14, 15, 24] and two music medicine studies did not [21, 22]. As such, the current data are insufficient to confirm physiological benefit to the infant.

This systematic review does not demonstrate any negative effects of music medicine or music therapy when used in the NICU. Future studies should focus on clear, consistent methodologies (in both music therapy definitions and interventions as well as physiological measures) in order to build evidence for clinical trial design to generate reproducibility. Even published meta-analyses and systematic reviews focused on behavioral effects note similar limitations. Beyond this, there is an absence of data on long-term outcomes [4, 31].

Non-physiologic outcomes

The majority of published studies examining the effects of music in neonatal care focus on non-physiologic outcome parameters, including pain, weight gain, behavioral state, sleep pattern, length of stay, and subjective measures of progress as evaluated by the infant's parents. Although beyond the scope of this systematic review, if these outcomes are analyzed, data collection must be standardized and include the use of validated parental and infant measures.

Future directions

Caution must be used in extrapolating statistically significant findings as clinically significant, given the high variability of physiological measurements, specifically heart rate and respiratory rate, in neonates. We recommend that future studies utilize more sensitive markers of physiological function, such as heart rate variability and auditory evoked potentials, to better determine impact of music therapy on the dynamic biological systems in neonates. As music therapy represents a low-cost, low-risk intervention, targeted studies evaluating these specific parameters can guide clinicians to utilize music therapy. For example, music therapy could potentially enhance physiological and clinical stabilization of the autonomic nervous system associated with a variety of neonatal conditions, such as neonatal opioid withdrawal and prematurity, potentially reducing hospital costs associated with prolonged NICU admissions. Future studies should ensure that study design is evidence based, and all data collection methods and procedures are described in publication. For the most part, those studies with a demonstrated statistically significant effect have limited effect sizes, drawing into question the clinical significance of the intervention. In addition, longer-term follow-up should be performed in order to truly gauge outcomes.

Limitations

The studies evaluated in this systematic review were restricted to peer-reviewed journals. Data from conference presentations and other forms of gray literature were, therefore, excluded and is one of our limitations; however, given the variation in review processes for gray literature, peer-reviewed journal articles minimize concerns regarding study rigor. While meta-analyzing these studies would be beneficial in determining the physiologic efficacy of music interventions, the lack of methodologic consistency includes difference methods and time points of data collection, as well as different study durations and music intervention schedules. Taken together, meta-analysis stemming from our current systematic review would be flawed.

The variable methods of collecting physiologic data also likely affected results. In particular, leaving unknown the number of physiologic data points and specific data collection methods, including how final data for analysis were prepared, resulted in varied effects between studies. This is

further exacerbated by small sample sizes that can make statistically significant results difficult to achieve. In addition, our systematic review is focused solely on physiological outcomes (such as heart rate), and other psychosocial and environmental factors, such as caregiving environment, though important, are beyond the scope of this review. Despite these scientific gaps, the use of music modalities is widespread in NICUs, perhaps, in part, due to the absence of reported adverse effects. Investigators evaluating music therapy in neonates ought to use sensitive and validated measures, including heart rate variability, auditory evoked potentials, and validated behavioral coding systems.

Conclusion

Music medicine and music therapy, though widely used in the NICU environment, are limited with regard to data on their impact on physiological outcomes in neonates, despite more robust data on psychosocial outcomes, such as behavior, attachment, and caregiver anxiety. Discrepancies between studies may be largely due to small sample size and different intervention and data collection methods, yet no study has demonstrated music to be harmful to neonates. Future studies should focus on robust study design and data collection, as well as being adequately powered to detect intervention effects, in order to draw firm conclusions on the efficacy of music on neonatal physiology. Although the current data are promising, more multidisciplinary research is needed to evaluate the impact of music therapy as a low-cost, low-risk intervention within neonatal care.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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