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The effect of music therapy on weight gain among preterm infants: *Confounding variables*

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Abstract

Preterm infants, especially those born before 32 weeks of gestation, experience extrauterine growth restriction (EUGR). Poor weight gain is associated with adverse neurocognitive outcomes. Many factors influence EUGR, including clinical and behavioral factors and developmental care philosophies. This perspective view describes factors that affect weight gain among preterm infants during their stay in the Neonatal Intensive Care Unit (NICU) and evaluates whether studies that used music therapy interventions to augment weight gain reported these factors. We recommend that trials addressing weight gain during MT interventions should be conducted throughout hospitalization in the NICU or after medical stability is achieved until discharge. The studies should evaluate in detail the sustained effects of music therapy interventions on weight gain, be powered to detect significant differences in weight gain, include factors that directly influence weight gain (such as level of prematurity, appropriate or small for gestational age, chronic morbidities associated with prematurity, and information on nutritional care, developmental care and family-centered care philosophies in the NICU). The use of accurate methods to assess weight gain, such as individual Z-scores should be considered. Furthermore, other anthropometric measurements needed for growth assessment, such as head circumference and length should be evaluated, as well. We also recommend that the elements of music therapy interventions influencing weight gain should be described in detail.

Keywords*: Developmental care, Growth restriction, Music therapy, Preterm infants, Weight gain*

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Introduction

Preterm infants, especially those born before 32 weeks of gestation and/or weighing less than 1500 g at birth, experience extrauterine growth restriction (EUGR) [1–3]. This is defined as slower than expected growth during Neonatal Intensive Care Unit (NICU) hospitalization. The prevalence of EUGR ranges from 13% to 60% in various reports, making it a major health concern in this vulnerable population [4–7]. Optimal postnatal growth is important and should include anthropometrics such as weight, head circumference and length [8]. Monitoring the growth of preterm infants is complex, as the optimal parameter indicating EUGR is not yet defined [8–13]. Weight is the most easily obtained anthropometric measurement and it is used in both clinical care and research.

Poor weight gain is associated with adverse neurocognitive outcomes in cases of EUGR [14,15]. Slower weight gain patterns may persist into infancy and adulthood, especially for extremely premature infants or those born small for gestational age (SGA) [4,6]. Conversely, rapid postnatal growth is supposedly harmful, as it may increase the risk of later metabolic diseases such as hypertension and insulin resistance [4,16–18].

Many factors influence EUGR, including clinical, nutritional, and developmental supportive care philosophies. Hence, studies have been conducted to evaluate these relationships. Music therapy intervention studies for preterm infants have shown beneficial effects across some domains [19–21], although few studies have investigated music interventions to enhance weight gain in this population [22–29]. The possible mechanisms reported were increased sucking ability and feeding rate and hence, caloric intake [22]; increased oral volume intake and oral feeds per day, and faster time to full oral feedings with the Pacifier Activated Lullaby device (PAL) [29]. Other possible explanations for better weight gain during music therapy interventions were

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decreasing resting energy expenditure [23,30] and parents being more attuned to their infant's needs during feedings [23].

The objectives of this perspective view are to identify some of the important factors that influence weight gain in preterm infants and how music therapy intervention studies that evaluated weight gain as an outcome addressed them. These factors are detailed in Table 1.

Table 1. *Factors affecting weight gain in preterm infants*

Parameter	Categories of parameter			
Prematurity	Extreme prematurity (born < 28 weeks of gestation)	Very premature (born < 32 weeks of gestation)	Moderate prematurity (born < 34 weeks of gestation)	Late prematurity (born < 37 weeks of gestation)
Small for gestational age (SGA)	Symmetric SGA[1]	Asymmetric SGA[2]		
Chronic morbidities associated with prematurity	Bronchopulmonary dysplasia[3]	Intraventricular hemorrhage[4]	Periventricular leukomalacia[5]	Necrotizing Enterocolitis[6]
Nutritional Care	Type and route of feeding	Intake	Feeding protocols	
Growth monitoring	Weight gain	Length and head circumference	Z-score[7] and percentiles	Growth charts
Developmental care modalities	Developmental care	Family centered care	Family integrated care	
Research-related factors	Powered to detect weight gain differences	Long-term intervention	Infant's stability	

[1]Symmetric SGA: infant with weight, head circumference and length below the 10th percentile of growth chart.
[2]Asymmetric SGA: weight below the 10th percentile, with head circumference and length relatively preserved.
[3] Bronchopulmonary dysplasia: oxygen requirements at 36 weeks of gestation.
[4]Intraventricular hemorrhage: bleeding into the ventricles in the brain.
[5] Periventricular leukomalacia: a form of white-matter brain injury, characterized by necrosis of the white matter near the lateral ventricles.
[6]Necrotizing enterocolitis: a devastating intestinal disease which may lead to short bowel syndrome and growth retardation.
[7]Z-score: the number of standard deviations an individual weight is above or below the mean cohort value.

Clinical factors and weight gain

Weight gain is associated with gestational age at birth. Preterm infants who are born before 32 weeks of gestation (very preterm infants) and especially those who are born before 28 weeks of gestation (extremely preterm infants) are at risk for EUGR, as their immature bodily systems such as the gastrointestinal tract are still not developed enough to maintained and utilize the high demands of nutritional intake needed for optimal growth [1,2,31]. Infants born (SGA (below the tenth percentile of expected weight for gestational age at birth) are at higher risk of growth problems [32–34].

Chronic morbidities associated with prematurity can increase energy needs and may lead to decreased nutritional intake and utilization. Bronchopulmonary dysplasia (BPD) affects the respiratory system and results in higher caloric expenditure due to high respiratory effort. Furthermore, infants with BPD may be fluid restricted, and may receive medications that affect normal metabolism [35]. Intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL) may lead to severe brain damage, resulting in impaired oral feeding skills [17,36]. Necrotizing enterocolitis (NEC), especially when it leads to short bowel syndrome, affects gastrointestinal tract absorption [37,38].

The type and amount of nutritional support and the prespecified nutritional treatment protocols during NICU hospitalization are important components of weight gain among preterm infants [39–41]. Even without major morbidities, inadequate nutritional intake (such as low energy and protein intake [42], enteral versus parenteral feeding [43], breast milk versus other types of milk [44,45], and lack of growth monitoring [46]), may have a negative influence on weight gain while the infant is in the NICU. Feeding protocols attributing to decision-making for consistent nutritional care have been shown to enhance growth [46].

The accuracy of calculating weight gain velocity for preterm infants is affected by the method used and by the infant's age when it is measured [47,48]. A meta-analysis of studies using weight gain calculations, demonstrated a trend towards using Z-scores to measure weight gain rather than grams per day [49]. A Z-score is the number of standard deviations an individual weight is above or below the mean cohort value. The calculation of Z-scores requires a growth reference chart from which standard deviations can be calculated. There are several growth charts in regular use for preterm infants to which individual weights are compared [7,13,50]. The optimal method for monitoring weight gain is yet to be determined [7,51].

Developmentally Supportive Care and weight gain

Developmentally supportive care is a multidisciplinary-based care philosophy. It has developed along with the ever-increasing success in treating preterm infants [52]. The different types of developmental care (DC) continue to evolve [53]. Developmentally supportive care involves controlling and arranging environmental factors, focusing on the needs of preterm infants and their families as the main aspect of care and meeting these needs to enable optimal adaptation of the

preterm infant to extrauterine life [54]. DC interventions in relation to weight gain, aim to reduce stress and discomfort in order to reduce energy expenditure and allow caloric intake to be used for growth [55].

In general, developmentally supportive care can be classified into several different categories [56]. The main categories include, individualized care [54], handling techniques and transition support, management of the external environment, positioning of the baby, feeding methods, pain management, knowledge of infant development, family centered care (FCC) and family integrated care (FIC), and adjusting the design and structure of the NICU [53]. Almost all of these types of caregiving can affect the stability and future development of the infant [52]. Only a few studies have evaluated the association between developmentally supportive care and weight gain. The sleep duration and weight gain of preterm infants were positively influenced by environmental conditions, such as controlling levels of noise and light [57]. In another study [58], preterm infants in a NICU with rooms designed for individual families weighed more at discharge, had a greater rate of weight gain, required fewer medical procedures, had a lower gestational age at full enteral feed, and fewer cases of sepsis, as well as better attention, less physiologic stress, less hypertonicity, less lethargy, and less pain. NICU differences in weight at discharge and rate of weight gain were mediated by increased developmental support.

A Cochrane review analyzing massage interventions for preterm infants demonstrated that they improved daily weight gain by 5.1 grams. However, the reviewer's conclusion was that the evidence is weak and does not warrant wider use of preterm infant massage [59]. A study using a retrospective comparative design, evaluated the effects of training 10% of a nursing staff in the Neonatal Individualized Developmental Care and Assessment Program (NIDCAP) on 25 preterm infant outcomes [55]. Preterm infants treated according to the NIDCAP, had a greater rate of weight gain, among other benefits. Findings suggest that benefits of developmental care are achievable even when only a portion of the staff is trained in the NIDCAP. In an integrative review, kangaroo care was also shown to a positive impact on weight gain [60].

Family Centered Care (FCC) is a philosophy of care that is guided by a set of core principles recognizing the importance of the family in the care and well-being of a hospitalized, preterm infant. Principles of family- and patient-centered care specific to the neonatal intensive care context include, free and unrestricted access to the NICU 24 hours a day for parents; psychological support to parents, including but not limited to educational and developmental support; supportive NICU environment that minimizes noxious sensory stimuli while assuring the presence of a parent's voice; consistent assessment and treatment of pain; developmentally appropriate postural support; skin-to-skin contact with parents; support for breastfeeding, and promoting good sleep quality [61]. The intent of FCC is to stabilize the infants during their stay in the NICU and reduce the caregivers' stress. Family Centered Care has been related to significant benefits in increased rates of breastfeeding, fewer nosocomial infections and shorter length of stay, as well as enhanced weight gain [62].

The FIC model of neonatal care builds upon principles of FCC, but takes the concept of parental involvement further by establishing parents as primary caregivers, and positioning families as the center of care [63]. Parents receive educational, structural and psychological support that help them successfully assume their parenting and primary caregiving roles in the NICU [63]. A recent multicenter, cluster-randomized study from Canada, Australia and New Zealand showed significant benefits in weight gain and breastfeeding, as well as decreased parental anxiety and stress, using developmental supportive care and FIC [64]. This advantage was also shown in a similar study from China [65]. Therefore, it seems that the developmental supportive care modalities, FCC and FIC, are important components to consider when studies evaluating the influence of music therapy interventions on weight gain are designed and reported.

Music therapy and weight gain

In this section concerning the effect of music therapy on weight gain in preterm infants during NICU hospitalization, only studies that used a certified music therapist who underwent advanced training in NICU music therapy prior to working with this population and their caregivers, were included. These criteria were based on the importance of ensuring music is implemented at a safe decibel level and the infant is appropriately monitored for signs of overstimulation. We did not survey all the studies involving MT interventions and weight gain in the literature [19, 66] but describe a few pivotal articles emphasizing the importance of other confounding factors associated with weight gain, which need to be addressed (see Table 2).

Table 2: *Factors associated with weight gain in some of the music therapy studies that included certified therapists for preterm infants during NICU hospitalization*

Author (ref. no.)	Loewy et al. (22)	Ettenberger et al. (23)	Standley et al. (29)	Chorna et al. (25)	Cevasco et al. (26)
Music therapy intervention	Lullaby, Ocean disc and Gato box	Song of Kin lullaby style during KC	PAL	PAL, mothers voice	PAL

Theoretical foundation for the effectiveness of music to impact feeding behavior	Gato box-increased sucking rate, Song of Kin Lullaby increased feeding and caloric intake	MT promotes relaxation (might lead to lower Resting Energy Expenditure and better feeding). Data to support these theories were not shown	Augment sucking behavior	Augment sucking behavior	Augment sucking behavior
Length of study (days)	2 weeks	NM	5 days	5 days	4 days
Level of prematurity	VP	VP, MP	MP, LP	LP	LP
SGA included	Yes	NM	NM	NM	NM
Chronic morbidities	NM	NM	NM	IVH, PVL	NM
Nutritional intervention	NM	NM	NM	NM	NM
Growth monitoring	NM	Weight gain per day during the intervention period	Weight gain during study period	Discharge weight	Weight gain per day of trial
Study powered for weight gain differences	NM	NM	NM	Done, but did not detect differences	NM
Developmental Care modalities	NM	Kangaroo care	NM	Kangaroo Care	NM
Family Centered Care	NM	Yes	NM	NM	NM
Family Integrated Care	NM	NM	NM	NM	NM
Study outcomes	Song of Kin resulted in higher levels of caloric intake and feeding behavior	Increased infant weight gain per day during the intervention period	Shorter duration of gavage feeding	Improved oral feeding skills	Trend toward greater weight gain with PAL

MT, Music Therapy; SGA, small for gestational age; EP, extreme prematurity; VP, very premature, MP, moderate prematurity; LP, late prematurity; NM, not mentioned; PAL, Pacifier Activated Lullaby; IVH, intraventricular hemorrhage; PVL, periventricular leukomalacia.

Loewy et al. [22] conducted an in-depth study that measured the effects of three live music therapy interventions as part of the First Sound: Rhythm, Breath and Lullaby model. This model includes the use of lullaby, Ocean disc and Gato box. The Gato box is an instrument that can provide a rhythm with a soft timbre that simulates the heartbeat sound a fetus hears in the womb. The rhythm provided by the Gato box was entrained to the infants' observed sucking pace. Data collected from 272 preterm infants in 11 NICUs, included physiological functions, such as sucking measured by sucking pattern grading, feeding measured by sucks per minute and caloric intake throughout a 2-week period.

The Gato box intervention significantly improved sucking patterns compared to the control phases (P = 0.01). Other beneficial results related to weight gain were evaluated by comparing two types of lullabies: 'Song of Kin' (parents' preferred song adapted to a lullaby rhythm) versus "Twinkle, Twinkle Little Star", a well-known lullaby that was sung when a song of kin was not chosen by parents. The Song of Kin method was associated with higher levels of caloric intake (P = 0.01) and increased feeding (P = 0.02), as compared with "Twinkle, Twinkle Little Star". The suggested beneficial effect of the Song of Kin, is that an entrained, culturally menaingful melody and rhythmic pattern that supports infants' sucking behavior enhances intermittent sucking-and orders a rhythmic behavior that is critical to maintaining the suck-swallow-breath function.

Therefore, it led to higher caloric intake and better feeding behavior. Furthermore, Song of Kin is preferred by parents; thus, motivating and enabling a DC experience for both parents and infants. However, although feeding and sucking behavior was enhanced, caloric intake by the music intervention, indicated by weight gain in the study groups was not reported. Confounding variables affecting weight gain were also not reported in some of the other NICUs indicated in Table 1.

A Colombian study [23] investigated the effects of combined family-centered MT intervention during Skin-to-Skin Care (SSC, kangaroo care) in 36 preterm infants and their parents, compared to a historical control group. Most sessions used the Song of Kin intervention (22). The data collected related to weight gain included birth weight, weight at start of SSC, weight gain during the intervention period (measured each day of the MT intervention), and weight at hospital discharge. The study results reported statistically significant increases in weight gain per day during the intervention period for the MT group, compared to a historical control group (24.20 g/day vs. 18.54 g/day; P = .036).

The researchers suggested two possible mechanisms for weight gain in the MT group: a more relaxed state of the babies during MT sessions, which may have led to lower resting energy expenditure and therefore better weight gain, or parents were better attuned to their infants during feeding, which enabled increased weight gain. The study reported some of the confounding variables affecting weight gain in this population, such as gestational age 28-34 weeks of

gestation, medically stable, birth weight less than 2000 grams, with kangaroo care implemented in this NICU. However, other factors affecting weight gain, such as inclusion of SGA infants, their specific chronic morbidity and severity, the amount of caloric intake during that period and calculating weight gain in relation to the cohort reference (Z-score) were not reported.

Several studies evaluated enhancement of oral feeding using the Pacifier Activated Lullaby (PAL) device [24–27,29]. All MT interventions were carried out by a certified music therapist. The PAL plays recorded lullabies in response to an infant's sucking activity. It has beneficial effects in increasing the endurance and rate of non-nutritive sucking in preterm infants. PAL studies investigated whether its effect on non-nutritive sucking would also be reflected in improved feeding skills. One of the first studies evaluating the PAL mechanism, included 32 preterm infants who failed to make the transition from gavage to bottle feeding [27], infants were randomly assigned to an experimental group of 15-20 minutes of the PAL intervention conducted 30-60 minutes before the last nipple-feeding opportunity of the day, compared to a control group that received standard care with no PAL intervention.

The music played by the PAL included a repertoire of familiar lullabies sung by female vocalists. Significant positive effects on feeding rate were found for the PAL group post-intervention, however the benefit of PAL on weight gain was not reported [27]. Another study evaluated sucking behavior using PAL with music selected by the music therapists, including traditional lullabies sung by a young female vocalist with minimal instrumental accompaniment [29]. The lullabies highlighted soft, soothing melodies, intended to avoid the music evoking stimuli, such as changes in volume or tempo. As the infant began sucking, the music turned on for 10 seconds and turned off until the infant sucked again, making the music stimuli contingent on the sucking activity. Over a course of 5 days, infants received either 1 or 3, 15-minute PAL trials. The study groups were further stratified into 32-, 34-, or 36-weeks postmenstrual age. Results showed that only the 34-week-old infants using PAL had significantly shorter duration of gavage feeding. Three PAL sessions compared to 1 resulted in shorter gavage feedings ($P < 0.05$). Weight gain during the 5-day protocol was similar between the study and control groups.

In another study evaluating the effect of PAL on weight gain, definite trends toward greater weight gain with PAL were demonstrated. However, individual variability within groups was greater than group differences, leading to no significant differences in statistical analysis [26].

Chorna et al. [25] evaluated the use of Pacifier Activated Music (PAM), applied in a FCC approach using the mothers' recorded voices. Ninety-four dyads of mothers and preterm infants 34-35 weeks postmenstrual age, who were taking at least half their feedings enterally and less than half orally, were randomly assigned to receive 5 daily 15-minute sessions of either PAM with mother's recorded voice or no PAM, along with routine nonnutritive sucking and maternal care in both groups. Before the study, the mothers met the music therapist who modeled and simplified the songs to record. Results demonstrated a beneficial effect of the PAM intervention in terms of achieving full oral feedings quicker. The oral feeding rate, volume of oral intake (measured the first day after the last PAM intervention) and number of oral feedings per day increased, as compared to the control group ($P < 0.01$ for each outcome). The sucking pressure in the PAM group increased an average of 15 mmHg between the first and last day of the intervention. No significant difference in weight gain was found between the study and control groups. None of the studies that evaluated PAL or PAM reported on other confounding variables affecting weight gain.

Conclusions and implications for future research

This article provides a perspective on the use of MT interventions to enhance weight gain in preterm infants in the NICU. It details the important clinical and behavioral factors related to weight gain in this vulnerable population. Considering these factors, we analyzed MT interventions that address possible effects on weight gain and feedings skills. Although the various MT interventions were shown to be beneficial and seemed to conclude that MT is associated with better weight gain, this effect could not be firmly established. Some of the MT interventions were short-term, implemented for a period of a few days to a few weeks and not over a prolonged period of NICU hospitalization [24–27,29,67]. Others did not report clinical factors, such as gestational age at birth and postmenstrual age at study entry [26,29], whether the study population was appropriate or SGA [23,25], chronic morbidities associated with prematurity [22,29], or nutritional intake [27,29]. Most studies measured weight gain in grams per day as the growth parameter. None used Z-scores which relate weight to a reference population [49]. A few studies did not detail the developmental care and FCC or FIC philosophies used in the NICU and whether the study and control groups were similar or differed in that sense [26,67]. Several variations of MT have been trialed (Table 2); therefore, it is difficult to conclude which mechanism might have contributed more to weight gain of preterm infants in the NICU [20].

The variety of studies that use MT interventions confirm that the interactions of MT, nurturing, caring, calming, and connecting, are achievable, but their effect on weight gain, which has short- and long-term consequences for the well-being of preterm infants, needs further research to address this issue. Future trials that address weight gain during MT interventions should be long-term, during most of the NICU hospitalization period, powered to detect weight gain differences, should describe clinically relevant morbidities of

preterm infants in the study cohort, and specify developmental care and FCC philosophies carried out in the NICU.

Methods of measuring weight gain, such as individual Z-scores can aid in interpreting weight gain in terms of comparison to a growth chart [49]. We also recommend using length and head circumference for comprehensive growth monitoring. To the best of our knowledge, studies including these parameters are in progress [68,69]. The LongStep study [68], a multi-national study which examines the effect of MT interventions on parent-infant bonding as the primary outcome, also addresses issues concerning weight gain in the NICU. MT interventions may become a low-cost, low-risk, family-integrated, standard intervention from birth, for preterm infants and their parents and may be found to support growth, neurobehavioral development, well-being and secure attachment in this vulnerable group.

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