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Review

Part 1: Narrative overview of developmental care interventions for the preterm newborn

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ABSTRACT

The development of synaptic connections in the foetus' brain peaks during the third trimester of gestation. In case of preterm birth, the infant is vulnerable in the neonatal intensive care unit because of its immature and rapidly developing neurologic system. Therefore, developmental care interventions (DCI) are particularly important during the NICU hospitalization to optimize short and long-term outcomes, as well as neurodevelopment, in infants born prematurely. The aim of this article is to provide a narrative overview by summarizing findings of a thorough literature review on the latest findings regarding the effectiveness of six DCI on preterm infant's outcomes such as sleep, stress and neurodevelopment. Various DCI have been evaluated in empirical studies. Research related to these interventions is rapidly evolving but is still a priority in the neonatal research field.

1. Introduction

Neuroplasticity is the brain's capacity to modify its strength and number of synaptic connections and is particularly important during early life (Altimier and Philips, 2013). During gestation, the second phase of glial proliferation begins at 20 weeks as well as the organization phase which includes synaptogenesis, establishment and differentiation of neurons, lamination and neurite outgrowth and glial proliferation and differentiation (Tau and Peterson, 2010; Volpe, 2008). Most importantly, synaptic development peaks at 34–38 weeks of gestation (Volpe, 2008) and during early life (Altimier and Philips, 2013). Myelination process starts around the 28th week and peaks during the first postnatal year (Tau and Peterson, 2010). It is recognized that preterm birth is one of the primary disturbances to the central nervous pathways' myelination process (Volpe, 2008), which predisposes preterm infants to poor neurodevelopmental outcomes (Tau and Peterson, 2010). In fact, critical steps in the foetus's central nervous system (CNS) development occur from the 24th to the 40th week of gestation (Volpe, 2009). In case of a preterm birth, the infant hospitalized in the neonatal intensive care unit (NICU) is particularly vulnerable because of his/her immature CNS still rapidly developing, which may engender significant repercussions on neurodevelopment and other health outcomes. Prematurity-related CNS complications include attention deficits, sensory integration problems, cerebral palsy, learning disabilities (Verklan and Walden, 2015), significantly lower intellectual quotient scores (Breeman et al., 2015) and increased risk for autistic symptoms (Eryigit-Madzwamuse et al., 2015) reported in both children and adults born preterm.

Developmental care interventions (DCI) have been encouraged in the NICU care in order to optimize short and long-term neurodevelopmental outcomes in infants born preterm. According to Kenner and McGrath (2010), these DCI are classified in five core-measures including: protected sleep, assessment and management of pain, developmentally supportive activities of daily living, family-centered care and the healing environment. The latest systematic review regarding the effectiveness of DCI included in the five core-measures was updated in 2009 (Symington and Pinelli). It concluded that limited good quality evidence was available to support the benefits of DCI on infants' cognition, movements and behavior but no harmful effects have been reported (Symington and Pinelli, 2009). Noteworthy, researchers have evaluated the impact of DCI on neurodevelopment but they have also been interested in other variables, which could be influenced by these interventions such as stress reduction and sleep promotion because of their impact on the cortex development (Calciolari and Montirosso,

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2011). The aim of this article is to present a comprehensive narrative synthesis on the latest findings regarding the effectiveness of DCI on preterm infant's short and long-term outcomes as well as neurodevelopment.

2. Methods

A thorough literature review in the databases of CINAHL, Embase, PsycInfo, PubMed and Google Scholar was conducted according to interventions related to the five above-mentioned DC core-measures. Key words included: prematurity, neonatal intensive care unit, developmental care, positioning, pain management, pain, family centered care, feeding, breast milk, sleep promotion, sleep protection, light and noise, neurodevelopment and stress. Studies were selected for the review if they evaluated the effectiveness of these interventions on: a) preterm infant's short or long-term neurodevelopment or b) if they measured other outcomes which can influence neurodevelopment such as sleep, physiological stability, stress and/or pain responses and other health related outcomes. Following the method proposed by Green et al. (2006) for narrative overviews, recent studies evaluating DCI have been included in order to establish a comprehensive narrative synthesis of findings regarding these DC core-measures over the past 20 years.

3. Results

The following presents a narrative synthesis of findings regarding six DCI, included in the five core-measures, such as protected sleep, pain management, positioning, optimized infant-driven feeding to which human milk literature has been added, family-centered care and control of the environment.

3.1. Protected sleep

The infant's state system, which is also known as the states of consciousness, includes sleep-waking cycles and is directly related to the preterm infant's neurodevelopment (Arditi-Babchuk et al., 2009; Vandenberg, 2007). The development of the sensory system, plasticity of the brain, long-term memory and learning capacities are also dependent on the completion of sleep cycles (Graven and Browne, 2008). The only category of interventions which has been linked to the state system and protected sleep is the clustering of care. Clustering of care requires that caregivers modify the treatment processes provided to preterm infants in the NICU for longer sleep periods without interruptions (Pereira et al., 2013), which decreases the energy expenditure and physiological stress that result from frequent manipulations (Peng et al., 2014; Pereira et al., 2013). Theoretically, clustering of care optimizes preterm infant's neurodevelopment by providing longer periods of sleep without interruption and physiological stress, which allows the completion of sleep cycles that are beneficial for the neurodevelopment (Pereira et al., 2013). Indeed, manipulations related to treatment processes and care administered to preterm infants in the NICU interrupt sleep cycles, and are particularly stressful (Peng et al., 2009) and overstimulating (Blackburn, 1998). They can cause physiological instability which causes hypoxemia (Long et al., 1980), apnea, bradycardia, hyperventilation and increased intracranial pressure (Blackburn, 1998). A study describing the type, frequency and duration of manipulations received by premature infants over a 24 hour period concluded that the frequency of manipulations in the NICU is between 14 and 71 per day (Pereira et al., 2013). In general, clustering of care and procedures in the NICU would be a strategy to adopt to ensure complete sleep cycles in preterm infant and reduce stress-induced physiological instability (Liaw et al., 2012).

3.2. Assessment and management of pain

Untreated pain has long-term consequences on preterm infants' immature CNS and neurodevelopment, so managing pain during the NICU hospitalisation is considered as a DCI. A considerable number of painful procedures can lead to hyperactivity of the CNS, which changes the brain plasticity (Brummelte et al., 2012). Hypersensitivity to pain has also been reported in preterm born children at school age, 4 years (Crozier et al., 2016) and 7 years old (Valeri et al., 2016), whom had undergone numerous painful procedures during their NICU stay. Lower motor and intellectual development indices at 18 months have also been linked to the number of painful procedures preterm infants experienced while in the NICU (Grunau et al., 2009). Pain management in the NICU is still a current concern (Pillai Riddell et al., 2015) because painful procedures are accompanied by a pharmacological or non-pharmacological intervention only 50% of the time (Johnston et al., 2011).

3.2.1. Pharmacological interventions

According to a study including 150 ventilated preterm infants, continuous intra-venous administration of Morphine would not induce neurological consequences such as lower Intellectual Quotient (IQs) and would even enhance executive function skills at eight and nine years of age (de Graaf et al., 2013). On the other hand, some studies have linked administration of Morphine to lower indices of motor and intellectual development at eight months (Grunau et al., 2009), smaller head circumferences and poor social relationships at five and seven years of age (Ferguson et al., 2012). Moreover, administration of Morphine in infants born between 24 and 32 weeks of gestation has an impact on cerebral growth and motor and cognitive development at 18 months of corrected age (Zwicker et al., 2016). Thus, healthcare professionals should opt for pharmacological interventions to treat moderate to severe pain and non-pharmacological interventions for procedural pain (American Academy of Pediatrics et al., 2016).

3.2.2. Non-pharmacological interventions

In terms of non-pharmacological interventions, current evidence supports skin-to-skin contact (SSC), sucrose administration which can be associated with non-nutritive sucking (NNS), swaddling or tucking, as effective interventions to manage procedural pain in preterm infants. According to a Cochrane systematic review, SSC is an effective and safe intervention to reduce preterm infant's procedural pain (Johnston et al., 2017). As to sucrose administration, several systematic reviews recommend this intervention to manage pain during painful procedures, which has been reported as reducing facial expressions of pain and crying time (Gao et al., 2016; Harrison et al., 2017; Stevens et al., 2016). To increase sucrose effects, it could be combined with NNS and should be administered 3 min before the painful procedure (Pillai Riddell et al., 2015). Recently, Gao et al. (2016) didn't find any adverse effects in relation to repeated sucrose administration, although misconceptions still persist today about its potential adverse effects on preterm infant's brain development (Tremblay et al., 2017). Finally, according to a Cochrane review, swaddling or facilitated tucking could also reduce pain reactivity and promote immediate pain regulation during procedural pain (Pillai Riddell et al., 2015).

3.3. Developmentally supportive activities of daily living

3.3.1. Infant positioning

Positioning has been recognized as a DC intervention having short and long-term implications for the preterm infant's development (Sweeney et al., 2010) and more specifically on their cognitive function (King and Norton, 2017). Positioning is the use of blanket rolls or positioning tools to help the preterm infant maintain a position that mimics the fetal position: slight flexion of the neck, head and neck well aligned with the rest of the body, shoulders brought forward, upper and lower limbs contained near the body, symmetrical posture and spine slightly in flexion (Coughlin, 2017; Waitzman, 2007). As suggested by Blauw-Hospers et al. (2007), infant positioning that mimics the intra-

uterine position may be the intervention that enhances motor development the most and also has an effect on neurodevelopment of preterm infants. Infant positioning could enhance neurodevelopment by promoting physiological stability and sleep and facilitate stimuli integration, hence reducing stress, which could all influence brain development (King and Norton, 2017; Lavallée et al., 2018). Also, lack of therapeutic positioning of the preterm infant in the NICU can also induce serious complications for the motor system such as: long-term positional deformities caused by the stretching or shortening of ligaments, tendons or muscles, postural asymmetries (Waitzman, 2007) as well as neurobehavioral complication in the first year (Sizun et al., 2014).

As for short-term effects, a Cochrane review including five randomized controlled trials (RCTs; 114 preterm infants) concludes that there is a lack of evidence to support beneficial effects of positioning on preterm infants' central apneas, oxygen saturation and bradycardias when they are at room air (Ballout et al., 2017). On the other hand, another Cochrane review concludes that prone positioning is beneficial for ventilated preterm infants to improve oxygen saturation and decrease oxygen desaturation events (Rivas-Fernandez et al., 2016). Other studies have recommended prone positioning for preterm infants in the NICU to reduce oxygen needs, facilitate carbon dioxide elimination (Ammari et al., 2009), increase partial pressure of oxygen (Bembich et al., 2012), tidal lung volume and arterial oxygen saturation (Gouna et al., 2013). Therapeutic positioning has also been linked to the state system because it can increase sleep periods in the NICU (Kenner and McGrath, 2010) and reduce stress (Jarus et al., 2011), which are necessary for neurodevelopment (Graven and Browne, 2008). Observational and descriptive studies have shown better sleep periods in preterm infants positioned in lateral (Liaw et al., 2012) or in prone (Jarus et al., 2011).

3.3.2. Optimized infant-driven feeding and human milk

Breastfeeding remains the most physiological method of alimentation, that is less stressful compared to bottle feeding (Chen et al., 2000). More recent research has focused on strategies to facilitate the transition from gavage to breastfeeding to ensure long-term feeding with breast milk. In fact, learning of breastfeeding for preterm infants, that being the coordination of breathing, sucking and swallowing, is a challenge because of mother-infant separation in addition to motor and physiological immaturity (Oras et al., 2015). A recent literature review highlights that stable preterm infants are able to maintain physiological stability when they are breast-fed from 27 to 28 weeks of gestational age and can achieve exclusive breastfeeding more quickly (from 32.8 weeks of gestational age) when exposed to breast before 30 weeks (Lucas and Smith, 2015). To facilitate this process, the transition has to be progressive and should be cue-based, that being based on preterm infant's readiness to be breastfed (White and Parnell, 2013). SSC has also been identified as an intervention promoting breastfeeding as it provides to the preterm infant positive sensory stimulation and proximity with the mother (Oras et al., 2015).

Research results have been unanimous for the past decade in relation to supporting beneficial effects of breast milk for preterm infant feeding. Breast milk facilitates digestion, is adapted to preterm infant's nutritional needs (Schanler et al., 1999), strengthens their immune system, and protects them against gastrointestinal diseases to which they are exposed because of their immaturity (Koo et al., 2014; Lechner and Vohr, 2017). Moreover, evidence is accumulating that human milk consumption during NICU hospitalization has a positive impact on preterm infants' neurodevelopmental outcomes during infancy (Bier et al., 2002; O'Connor et al., 2003; Vohr et al., 2006), childhood (Belfort et al., 2016b; Gibertoni et al., 2015; Johnson et al., 2011; Roze et al., 2012; Tanaka et al., 2009), adolescence (Isaacs et al., 2010), and even adulthood (Sammallahti et al., 2017). For example, feeding preterm infants with breast milk has been linked to greater deep nuclear gray matter volume at term equivalent age and increased IQs at 7 years of age (Belfort et al., 2016a). The unique composition of breast milk, especially with regard to long-chain polyunsaturated fatty acids, plays an essential role in neurogenesis; however, the mechanisms by which breast milk enhances preterm infant's neurodevelopment remain to be fully investigated (Lechner and Vohr, 2017).

Mothers of preterm infants are at risk for insufficient breast milk production (< 500 ml/day; Hill et al. (2005)). Over the last few years, pasteurized donor human milk has become the preferred alternative method of feeding for preterm infants when maternal milk is insufficient or unavailable (American Academy of Pediatrics, 2012; Kim and Unger, 2010/2016; World Health Organization, 2017). This renewed interest in pasteurized donor human milk can be explained by a recent increase in the number of human milk banks worldwide and the cumulative supporting evidence. It is estimated that there are more than 500 human milk banks in 37 countries (Program for Appropriate Technology in Health, 2013). Compared to commercial formulas, pasteurized donor human milk decreases the incidence of necrotizing enterocolitis (Bertino et al., 2013; Espghan Committee on Nutrition et al., 2013; Quigley and McGuire, 2014), feeding intolerance (Bertino et al., 2013; Dritsakou et al., 2016a; Espghan Committee on Nutrition et al., 2013; Quigley and McGuire, 2014) and viral infections (Dritsakou et al., 2016a, 2016b). It could also have a protective effect against bronchopulmonary dysplasia (Espghan Committee on Nutrition et al., 2013) and accelerate the initiation of enteral feeding after birth (Utrera Torres et al., 2010). However, to date, there is no evidence of any beneficial effects on neurodevelopmental outcomes (Madore et al., 2017; O'Connor et al., 2016; Quigley and McGuire, 2014). The results of a systematic review show that breastfeeding rates at discharge are higher after the introduction of pasteurized donor human milk in NICUs (Williams et al., 2016). Yet, it has no impact on the volume of maternal milk administered during the neonatal period nor on rates of exclusive maternal breastfeeding at discharge (Williams et al., 2016). One of the included studies in the systematic review even reports a significant decline in maternal milk consumption during the neonatal period (Esquerra-Zwiers et al., 2014), which could jeopardize the pursuit of breastfeeding. These heterogeneous results can be explained in part by the diversity of utilizations of pasteurized donor human milk by healthcare professionals: a means to initiate enteral feeding early after birth (Williams et al., 2016), a bridge to breastfeeding until the establishment of a sufficient maternal milk production or a substitute to commercial formulas (Delfosse et al., 2013; Williams et al., 2016). Nevertheless, healthcare professionals should clearly mention the superiority of maternal milk when they introduce pasteurized donor human milk to parents of preterm infants (Meier et al., 2017).

3.4. Family-centered care

Family-centered care (FCC) is based on recognizing nine distinct elements (Shields et al., 2012) such as: a) family as a constant in the infant's life, b) collaboration with parents regarding infant's health care, c) racial, ethnic, cultural, and socio-economic statuses, d) families' strengths and coping methods, e) families' need for complete information, f) families' need of support and networking, g) child and family developmental needs as part of healthcare practices, h) need for emotional and financial support; and i) flexible, culturally competent and responsive to family needs healthcare. Thus, collaboration between healthcare professionals and families as well as acknowledging family's respect and dignity are at heart of NICU care (Ramezani et al., 2014). Family-centered care has beneficial effects on preterm infant's neurodevelopment by enhancing early parent-infant interactions during NICU hospitalization (Vanderveen et al., 2009). In fact, a meta-analysis looking at early interventions including parents (such as NIDCAP intervention, kangaroo care and other DCI) showed an overall positive effect on neurodevelopment in preterm infants (Vanderveen et al., 2009). An ongoing systematic review (Lavallée et al., 2017) also showing that interventions promoting parental participation in their

hospitalized preterm infants care to improve parental sensitivity also have beneficial effects on infant's cortical maturation (Welch et al., 2014), functional maturation (Myers et al., 2015), electroencephalogram (EEG) power (Welch et al., 2017) and Bayley scores (Teti et al., 2009; Welch et al., 2015). Higher parent visitation and holding during NICU hospitalization also improve neurobehavior of preterm infants at term age such as less arousal and excitability (Reynolds et al., 2013). Parental presence and holding have also been significantly associated with less infant stress at term age (Reynolds et al., 2013) which is related to improved cortex development (Calciolari and Montirosso, 2011). Finally, a recent RCT showed significantly better neurobehavioral performances in FCC infants compared to usual care infants (Yu et al., 2017). Moreover, FCC has been associated with improved long-term health outcomes in preterm infants, better parent-infant attachment, shorter hospital stays (Cooper et al., 2007), better weight gain, and increase in breastfeeding rates at the time of discharge (O'Brien et al., 2013; Yu et al., 2017). FCC has also shown benefits for parents such as reducing stress and increasing parental confidence (Cocroft, 2012).

In FFC, families are actively included in their preterm infant's care planning (Shields et al., 2012). This entails a modification of policies and programs in order to support healthcare professionals in this philosophy of care (Shields et al., 2012). Also, it has been reported that role negotiation between parents and healthcare professionals can be challenging (Trajkovski et al., 2015).

3.5. The healing environment

3.5.1. Control of the environment

Controlling the NICU environment, namely light and noise levels, is an integral DCI aimed at reducing preterm infants' stress (Lebel and Aita, 2013; Symington and Pinelli, 2009) by improving their autonomic stability (Altimier et al., 2015; Santos et al., 2015) and favoring their sleep (Calciolari and Montirosso, 2011), which are considered to enhance neurodevelopmental outcomes in preterm infants (Santos et al., 2015).

3.5.2. NICU light

Research conducted with regards to NICU lighting has mainly focused on studying the effects of cycled lighting (CL) on preterm infants' outcomes. A recent systematic review concludes that CL, which consists of respecting a 12-hr cycle day/night in the NICU, is a safe intervention and shortens preterm infants' days of hospitalization compared to continuous lighting or near darkness (ND) lighting (less than 20 lux over 24-hr; Morag and Ohlsson (2016)). Analysis of findings also show trends that CL, compared to ND, seems to be more favourable for weight gain and for reducing preterm infants' incidence of retinopathy and time spent crying (Morag and Ohlsson, 2016). Also, infants of 31 weeks gestational age exposed to CL by wearing an helmet during NICU hospitalization showed improved oxygen saturation, weight gain and consequently shorter length of hospitalization (Vasquez-Ruiz et al., 2014). On the other hand, another recent RCT concludes that preterm infants of 28 weeks gestational age or more can either be exposed to CL or ND lighting as, over a 24-hr period, as none of these lighting conditions was more promising for increasing their physiological stability or decreasing their motor activity level (Lebel et al., 2017). A new RCT examining the timing of the introduction on CL on preterm infants' outcomes concludes that there was no significant difference for length of hospitalization and neurodevelopment following discharge but a clinical significance was observed for weight gain favoring infants exposed to CL from 28 weeks post-menstrual age compared to those exposed from 36 weeks (Brandon et al., 2017).

3.5.3. NICU noise

Recent tendencies in interventions controlling NICU noise consist of evaluating the effects of reducing preterm infants' exposure to noise by covering their ears with earmuffs or earplugs on their short and long-term outcomes. An experimental study concludes that silicone earplugs wore by eight very low birth weight preterm infants' during their NICU hospitalization appears to favor mental developmental index at 18–22 months of corrected age (Abou Turk et al., 2009). Then, preterm infants who were randomized in crossover trials were physiologically more stable (lower heart and respiratory rates and improved oxygen saturation (Khalesi et al., 2017); and in more quiet sleep state during the 2-hr period they were wearing the earmuffs compared to the period when they were not wearing it (Duran et al., 2012; Khalesi et al., 2017). Findings of other studies with a RCT design also confirm that preterm infants wearing earmuffs 2-hr in the morning and 2-hr in the afternoon were more physiologically stable and had improved motor state (Abdeyazdan et al., 2014a) as well as greater weight gain (Abdeyazdan et al., 2014b) compared to those not wearing earmuffs. Although the findings of these studies confirm physiological, motor and sleep benefits for preterm infants wearing earmuffs, a recent study reports that earmuffs had no effect on intermittent hypoxia of preterm infants (Bott et al., 2015).

4. Limitations of this review

The aim of the narrative overview is to establish and summarize what has been written on a subject (Paré et al., 2015). Although a thorough method for the literature search was used, a systematic method has not been presented (Paré et al., 2015). Therefore, the possibility for a publication bias should be considered. Also, according to the narrative review method, the quality of the included articles has not systematically been appraised with explicit critical appraisal criteria or recognized tools (Green et al., 2006).

5. Conclusion

DCI and core-measures are a major interest and concern in research and clinical practice in order to optimize preterm infants' short and long-term outcomes and neurodevelopment. The efficacy of various interventions has been evaluated and recommendations for NICU clinical practice have emerged in the past decades to suit preterm infant's developmental needs. Nevertheless, more research is needed in this field to better understand how DCI work, their short and long-term effects, and how to implement them in NICUs worldwide. Recommendation for research and clinical practice will be addressed in a subsequent publication (part II). Evaluation of a combination of various DCI would be innovative as research mostly focused on assessing effects of individual DCI. Evaluation of DCI on preterm infants' neurodevelopment during the NICU hospitalisation would be beneficial in order to better understand their neurodevelopmental process before and after discharge to optimize their health outcomes and those of their family.

Conflicts of interest

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Ethical statement

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