

The role of weighing-bathing sequence and postmenstrual age in eliciting adaptive/maladaptive responses in very low birth weight preterm infants

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Abstract

Purpose: In the neonatal intensive care unit, preterm infants are exposed to several stressful stimuli. Inappropriate stimulation led to high risk for short- and long-term neurocognitive disabilities. This study aimed to evaluate whether the sequence of execution of weighing/bathing nursing procedures and postmenstrual age (PMA) have any effect on preterm infants' stress responses.

Design and Methods: Prospective cross-sectional study on a sample of 21 preterm infants. Responses to the procedures were assessed using an observational sheet based on Als's Synactive Theory of Development. Autonomic and motor responses were scored according to five-point Likert scales. The order of execution of weighing/bathing nursing procedures and PMA were documented. Effects of weighing/bathing execution sequence and PMA on autonomic and motor response scores were analyzed by linear multiple regression analysis.

Results: The sequence of execution had a significant effect on the autonomic score during weighing (p = .035), evidencing more stress when weighing was executed first. A higher level of stress response on the autonomic score during both weighing (p = .015) and bathing (p = .018) procedure was independently associated with a lower infant PMA.

Conclusions and Practice Implications: The real-time recognition of adaptive/maladaptive responses allows nurses to personalize their approach to preterm infants, taking into account PMA and adjusting the appropriate sequence of execution of weighing/bathing nursing procedures.

KEYWORDS

NIDCAP, nursing, postmenstrual age, preterm infant, stability, stress

WHAT IS CURRENTLY KNOWN?

 In preterm infants admitted to neonatal intensive care unit, little is known about nursing practices or behaviors that can induce stress and, consequently, compromise an adequate brain development.

 Knowing what care practices or behaviors induce stress is paramount for nurses to minimize the impact of stressful procedures and create the best possible conditions for adequate brain development.

WHAT DOES THIS ARTICLE ADD?

- The sequence of execution of weighing/bathing procedures is relevant, since the autonomic functional subsystems show more stress when weighing is executed first.
- A higher level of stress response on the autonomic score during both procedures is independently associated with a lower infant postmenstrual age (PMA).
- The recognition of adaptive/maladaptive responses allows nurses to adjust the sequence of execution of weighing/bathing nursing procedures according to infant's PMA.

1 | INTRODUCTION

In developed countries, recent advances in neonatology have led to an increased survival rate for preterm infants with a very low gestational age (Glass et al., 2015). However, premature newborns need to spend even long periods in the neonatal intensive care unit (NICU), a setting very different from the uterine environment, where they are exposed to stressful stimuli such as painful diagnostic/ therapeutic procedures, frequent handling, and excessive light and noise levels, which are inherent to high-technology, lifesaving care (Cong et al., 2017).

The newborn is called to continuously interact with this inhospitable environment and the provided interventions, while her/his neurocognitive development is in a very critical phase (Lupien, McEwen, Gunnar, & Heim, 2009). Stress experienced during the NICU stay can thus have a dramatic negative impact on the newborn neurodevelopment (Liaw, Yang, Chou, Yang, & Chao, 2010; Weber & Harrison, 2018). Indeed, the stimulation of the sensory organs induced by the many stressors related to the environment and the care provided in the NICU may affect brain structure and functions (Ranger & Grunau, 2014; Smith et al., 2011), with a high risk for severe short- and long-term disabilities (Peters et al., 2009). Not surprisingly, neurodevelopmental outcome has been strongly identified as a benchmark to measure the effectiveness of newborn care (Aylward, 2014).

Any environmental stimulus should be considered as a potentially dangerous stress factor for the immature brain of preterm infants, particularly for those with a lower postmenstrual age (PMA; e.g., newborn's gestational age at birth plus postnatal age), who may exhibit exaggerated stress responses with a negative impact on brain maturation at term-corrected age (Sanders & Hall, 2018). When the many aspects of the stimulation provided are not appropriate, newborn's neurocognitive development can be affected (Graven & Browne, 2008). Consequently, knowing what care practices or behaviors induce stress is paramount for nurses to minimize the impact of stressful procedures and create the best possible conditions for adequate brain development, as stated by the approach known as developmental care (Peters et al., 2009).

According to Als's Synactive Theory of Development (Als, 1982, 1986), the stimuli induced by the many stressors related to the environment and the care provided in the NICU determine either adaptive or maladaptive newborn's responses, which can be assessed by observing five functional subsystems (i.e., autonomic, motor, state, attention/interaction, and self-regulatory) through which she or he interacts with the NICU physical and relational (family and caregivers) environments (Als, Butler, Kosta, & McAnulty, 2005). Nurses can establish how to perform care modalities in relation to infant's adaptive or maladaptive stress reactions observed during the procedures. Accordingly, tailored care behaviors and interventions can be chosen to reduce exposure to stressors (Als & Gilkerson, 1997), also paying attention that the outside stimulations of the sensory systems occur in appropriate sequence, intensity, and form. Although knowing if the sequence in which daily routine nursing procedures, such as bathing and weighing, are performed affect preterm infant's stress responses may be an important issue in preterm newborn care, this issue has never been studied before.

The aim of this study was to evaluate if (a) the sequence of execution of bathing and weighing nursing procedures and (b) the PMA have any effect on stress responses observed during a routine daily nursing of preterm infants born before the 33rd week of gestation.

2 | METHODS

2.1 | Study design, setting, and population

This was a prospective cross-sectional study carried out in a Level 3 NICU. All consecutive clinically stable preterm infants admitted to the unit over a 6-month period (from June to December 2017) with a gestational age <33 weeks and birth weight <1,500 g were considered eligible for inclusion in the study. Exclusion criteria were as follows: infants affected by either congenital or chromosomal abnormalities, or conditions that could interfere with behavior and growth, such as chronic lung disease, asphyxia, neurologic disorders, metabolic or cardiac disease, abdominal surgery, renal failure, retinopathy of prematurity higher than Stage 2, sepsis. Participants entered the study after their third day of life. The Independent Committee for Bioethics of the hospital approved the research (decree M/11-78/2014) and informed consent was obtained from parents after a full explanation of the study.

2.2 | Infant response assessment

To assess preterm infants' responses during bathing and weighing procedures, an observational sheet was used. For the construction of this tool, the Als's Synactive Theory of Development (Als & Gilkerson, 1997; Als et al., 2005) was referenced. As previously

described (Bembich et al., 2017), its items were derived from the Newborn Individualized Developmental Care and Assessment Program (NIDCAP) observation tool (Als et al., 1986). All items evaluated preterm neonates' autonomic and motor responses, referring to specific physiological or behavioral signs (Table 1). During each observation (e.g., bathing or weighing), all responses exhibited by the infant were detected and multiple signs, indicative of difficulty/stress, stability/adaption, or both, could co-occur.

The scoring of preterm infants' autonomic and motor responses was done according to five-point Likert scales, ranging from 1 (*indicating the highest difficulty/stress*) to 5 (*indicating the highest stability/adaption*, e.g., the lowest stress). Specific score attribution referred to the following criteria: score 1, when all the items of autonomic and/or motor function expressed Difficulty/Stress; score 2, when most of the items of autonomic and/or motor function expressed Difficulty/Stress; score 3, when there was an equal number of observed items expressing Difficulty/Stress and Stability/Competence in autonomic and/or motor function; score 4, when most of the observed items of autonomic and/or motor function expressed Stability/Competence; and score 5, when all the observed items of autonomic and/or motor function expressed Stability/Competence.

2.3 | Procedure

According to the international recommendation, as a holistic NICU care strategy focused on developmental care, environmental factors such as light, noise, and temperature were kept as far as possible in a range adequate to the inherent frailty of the preterm newborns (VandenBerg, 2007). For the study purposes, during the 15 min before

beginning daily nursing, any nonurgent medical or nursing care practice was suspended in order not to affect the baseline observation.

Participants were thus observed during two nursing procedures: weighing and bathing. The order of execution of such procedures with each individual infant was freely chosen by the nurse performing the assistance, based on her own professional criteria and experience. In any case, nurses were unaware of the purpose of the research. The execution of each procedure was standardized (see below) and was always performed by expert nurses in neonatal care who had been working in our NICU for at least 3 years. They all had basic training in the NIDCAP approach (Als et al., 1986), although none were NIDCAP certified. Although a standardized approach to preterm infant's care may appear in contradiction with a developmentally appropriate intervention, the execution of nursing procedures was standardized to control for variations due to each nurse's individualized and unique approach to caregiving.

Up to 34 weeks PMA, both procedures were performed inside the incubator and standardized as follows:

- Weighing: the infant was raised a few centimeters to reset the scale, gently replaced on the mattress on his or her back, and then weighed.
- Bathing: a sponge bath was provided, keeping the infant wrapped as much as possible. Bathing lasted for a few minutes, by moving the baby as little as possible.

At 35 and 36 weeks PMA, the procedures were standardized as follows:

1. Weighing: the scale was positioned next to the crib and the infant was wrapped in a towel (weighed separately) during the procedure, in

TABLE 1 Observational sheet^a

Diffuculty/distress	Stability/adaption		
Autonomic system score: 1 2 3 4 5			
Breathing (irregular, pause/apnea, slow/fast, gasping)	Breathing (regular)		
Color (unstable, pale, webb, red, dusky, blue)	Color (stable, pink)		
Visceral signs (regurgitation, hiccough, vomit/retch)	n) Visceral signs (quiet burp, no stress sign)		
Heart rate (tachycardia, bradycardia)	Heart rate (regular)		
Respiratory rate (dyspnoea, tachypnea)	Respiratory rate (regular)		
Peripheral oxygen saturation <85%	Peripheral oxygen saturation >85%		
Motor system score: 1 2 3 4 5			
Tremors/startles/clones	Smooth movements (limbs/trunk)		
Flaccidity/rigidity (limbs/trunk)	No flaccidity/rigidity (limbs/trunk)		
Arching/contortion of trunk	Flexed limbs		
Stretching/extending trunk	Trunk folded		
Limbs' extension movements	Hands on face/mouth		
"Airplane" (arms)	Clasped hands/feet		
"Salute" (arms)	Stabilize with hands		
"Sitting on air" (legs)	Stabilize with feet		
Finger splay	Sucking/Looking for sucking		

^aSource: Als et al. (1986).

which the neonate was moved rapidly from the crib to the scale and vice versa.

 Bathing: bathing by immersion outside the crib, initially wrapping the infant in a blanket, which was gradually removed. The duration depended on the reaction of the infant and was decided by the nurse.

All of the observed nursing procedures were preceded by removal of clothes and diapers. Once nursing ended, the infant was dressed, swaddled in a blanket, and positioned in a nest (handmade roll of soft material), to facilitate containment inside the incubator or crib, in the supine position. After that, the infant was left undisturbed.

Each observation was video-recorded by a nurse blinded to the purpose of the study and divided into two periods, with reference to the research aims: *execution of weighing* and *execution of bathing*, both lasting the time needed. Heart rate, respiratory rate, and peripheral oxygen saturation, as part of the autonomic response, were assessed via continued multiparametric monitoring (IntelliVue MP70; Royal Philips Electronics, The Netherlands). During bathing by immersion, data monitoring was possible by keeping the pulse oximeter probe on the infant's wrist.

Basing on video-recording, the infants' responses during nursing procedures were assessed on the same day of data collection, separately for weighing and bathing, using the observational sheet and the scoring system described above, by trained personnel blinded to research aims. Similarly to our previous study (Bembich et al., 2017), video-recording was focused on neonate's body (including extremities) and face. Since some responses could be difficult (e.g., skin color, visceral signs) or impossible (e.g., heart rate, respiratory rate and peripheral oxygen saturation) to detect from videotapes only, attention was paid to assess these specific few signs during real-time observation. Twenty percent of all video-recordings were independently evaluated by two coworkers. Assessment concordance across participants and caregiving procedures was checked by Cohen's *k* index, and a k = 0.90 was found for both routines.

2.4 | Data analysis

Scores of infants' autonomic and motor responses, collected during nursing execution, were analyzed by linear multiple regression analysis with two independent variables (regressors): (a) the sequence of execution of weighing and bathing nursing procedures, coded as 0 (sequence weighing/bathing) or 1 (sequence bathing/weighing) and, therefore, considered a dummy variable, and (b) the infant's PMA in weeks on the day of the observed nursing session.

This analysis was repeated on the autonomic or motor score, considered the dependent (predicted) variable, collected in each one of the nursing procedures assessed: (a) execution of weighing and (b) execution of bathing. Therefore, a total of four regression analyses were performed. The normal distribution of PMA in the sample was checked by Shapiro–Wilk test (W = 0.974; p = .83). The coefficient of

determination of the regression models was calculated based on the Nagelkerke R^2 and their overall significance was assessed through F test. All statistical analyses were conducted using SPSS version 22.0 for Windows (IBM Corp., Armonk, NY) and a p value of <.05 was considered significant.

3 | RESULTS

A total of 23 preterm infants with a gestational age <33 weeks and a birth weight of <1,500 g were admitted in the NICU during the study period. Two infants were excluded by their third day of life because they did not meet inclusion criteria (one infant had an intraventricular hemorrhage Grade 1, and one infant had an intraventricular hemorrhage Grade 2). Thus, a sample of 21 preterm infants (12 females, 9 males), with a mean gestational age of 28.6 ± 1.9 weeks (range: 26-32 weeks) and a mean birth weight of 1082.5 ± 345.1 g (range: 538-1,492g), constituted the final study population. At the time of data collection, their PMA ranged between 27 and 36 weeks. Concerning the sequence of nursing procedures, 11 infants had weighing preceding bathing and 10 infants had bathing preceding weighing.

The following results were observed through the linear regression analyses:

- 1. The sequence of execution of bathing and weighing procedures had a significant effect on the autonomic score during weighing (β = .410; $t_{(18)}$ = 2.280; p = .035; Figure 1), that evidenced higher difficulty/stress when weighing was executed first.
- The infant's PMA on the day of the observed nursing session had a significant positive effect (e.g., resulting in more stability/adaptation) on the autonomic score during the execution of both bathing



FIGURE 1 Mean autonomic (±standard error) score during weighing, when a different sequence of nursing procedure execution was performed (p = .035)

(β = .499; t₍₁₈₎ = 2.600; p = .018) and weighing (β = .481; t₍₁₈₎ = 2.676; p = .015).

All the other effects were not significant. A complete overview on linear regression analysis results is given in Table 2.

4 | DISCUSSION

The main result of this study is that preterm infants show higher difficulty/stress on the autonomic score during weighing, when such procedure is executed before than after bathing. Moreover, the infants' PMA has an independent positive significant impact on the stress response during both bathing and weighing procedures, irrespective of the order in which they are performed: the higher the infants' PMA, the lower the level of her or his stress responses in the autonomic system.

Each human responds to any stressful stimulus able to threaten the homeostasis by providing an adaptive response through a complex autonomic and neuroendocrine reaction, involving both parasympathetic and sympathetic autonomic nervous system, neuroendocrine system, and catecholamine and glucocorticoid release. At the same time, the organism activates concurrent mechanisms, which prevent the risk for an over-response by the stress system. Preterm newborns are not able to act an effective stress-related adaptive control, so that risk exists that stress response is excessive or maladaptive (Nicolaides, Kyratzi, Lamprokostopoulou, Chrousos, & Charmandari, 2015). The impact of the stresses encountered by immature brain in the early lifetime environment can alter the developmental template of preterm infants (Sanders & Hall, 2018).

To date, few studies have explored the relationship between stressing nursing procedures and the subsystem responses in terms of stress or stability behaviors, according to the Synactive Theory of Development (Als, 1982, 1986). Liaw et al. (2010) explored the relationship between nurses' behaviors and preterm infant behavioral responses during bathing, showing that stress was reduced and self-regulation was improved when nurses provided more support during the bath, in particular through the use of "containment" and "positional support." Conversely, nurses' behaviors such as "rapid and rough handling" of the baby or "chatting with other people" increased the newborns' stress. A further study (Bembich et al., 2017) analyzed the effects of weighing and bathing procedures on autonomic and motor stability of preterm infants. It was observed that weighing and bathing procedures stressed the infants up to 35 weeks' PMA. However, since nurses facilitated and supported infants after caregiving procedures through interventions such as swaddling and nesting, preterm newborns recovered autonomic and motor stability within 5 min.

The present study confirms and strengthens previous findings, underscoring that even very simple procedures such as turning or weighing the infant, changing the diaper and providing hygienic care may be overwhelming for the infants up to 35 weeks' PMA. Moreover, to the best of our knowledge, this is the first study demonstrating that planning the weighing as the first procedure to perform has an independent negative effect on stress responses in the autonomic system of preterm infants.

Newnham, Inder, and Milgrom (2009) asked a large group of experienced NICU physicians and nurses to rate, based on their clinical experiences and observations of behavioral and physiological responses, how stressful a range of common clinical situations were for preterm infants. Interestingly, they determined that the level of stress induced by procedures such as diaper changes, posture modification, being removed from incubator/crib, and being weighed decreases as an infant's PMA increases. The results of the present study confirm the subjective evaluations given by experienced NICU healthcare providers and, at the same time, underscore the effectiveness of evaluating the level of stress through more objective assessment methods as well.

However, assessing possible stress reactions and their intensity may be challenging in preterm infants. Indeed, due to a still disorganized central nervous system, the responses observed in these patients tend to express their stress more through alterations in vital signs or physiological reactions than with behavioral reactions (VandenBerg, 2007). Accordingly, bedside nurses should be trained to observe and capture every apparently negligible modification in the infant's physiologic normal patterns, either in the autonomic (e.g. skin color changes, abnormal breathing patterns, fluctuations in heart rate, oxygen desaturation) or in the motor system (e.g. abnormal flaccidity/rigidity or extension movements, occurrence of tremors), often occurring simultaneously, as pointed out by the Synactive Theory of Development (Als, 1982, 1986).

TABLE 2	Effect of nursing procedure sequence	(weighing/bathing vs. b	pathing/weighing) and	PMA (in weeks) or	n infant's autonomic a	and motor
response sc	ore, in each period considered by the	study design, as evider	nced by linear regress	sion analysis		

Period Subsystem score (dependent variable)	Performance of the regression model	Nursing procedure sequence	Postmenstrual age
Execution of weighing Autonomic score Motor score	$R^2 = .421; F_{(2,18)} = 6.552; p = .007$ $R^2 = .063; F_{(2,18)} = 0.603; p = .56$	β = .410* β = .057	β = .481* β = .241
Execution of bathing Autonomic score Motor score	$R^2 = .338; F_{(2,18)} = 4.596; p = .024$ $R^2 = .158; F_{(2,18)} = 1.692; p = .21$	β = .271 β = .199	β = .499* β = .333

*p < .05.

Another factor to be considered is that premature neonates are, in general, in an energy shortage state, as a result of a negative balance between-on one side-the low energy reserves related to the preterm condition and-on the other side-factors related to the acute illness, the stressful and painful stimuli, and the neurodevelopmental energy requirements. This energy dysregulation may lead to short- and longterm adverse impacts on both neurodevelopmental, metabolic and cardiovascular fields (Tan. Boskovic, & Angeles, 2018). Nurses should thus take into account that preterm infants' responses to stressful procedures may increase energy expenditure. Modifying care patterns can help to safeguard energy expenditure and prevent the undesired outcomes (Weintraub, Mimouni, & Dollberg, 2007). Interestingly, the finding of previous studies indicated that some preterm behaviors, such as grimace, sucking, diffusion squirm, fist, gape face, salute, and sneezing, are related to increased energy expenditure (Lin et al., 2014). Consequently, the presence of maladaptive responses should be taken into account by nurses as related to a higher amount of energy expenditure, while the intervention is provided.

On the other hand, some preterm infants may be exhausted as a result of the overwhelming impact of energy-expending stressful procedures, so that they may show a level of stress-related behavioral responses lower than expected due to their limited residual energy reserve. To prevent an uncorrected evaluation of infant's stress level in such cases, the assessment of these babies should be based mostly on the autonomic (e.g., heart rate increasing, oxygen desaturation) than on the motor subsystem (Walden, Sudia-Robinson, & Carrier, 2001).

The ability to recognize, in real-time, the adaptive or maladaptive responses of the newborn, also identifying the infant-specific stress evocation threshold in relation to the different care activities, is for nurses a pivotal aim. Based on the above consideration and on the results of the present study, we suggest that nurses should individualize the decision-making for each newborn in a given situation, to adopt the most appropriate nursing strategy, taking into account the PMA, the residual energy reserve, and the appropriate order of nursing procedure execution (weighing after bathing in the present study). This strategy might minimize stressors exposure and should also imply, in some cases, the cessation or delay of nursing, medical or physical therapy procedures that day with that specific preterm infant.

The adoption of the developmental care philosophy implies comprehensive behavioral observations of the premature newborn, on which basis providing individually-adapted care (Als, 2009). Results of the present investigation emphasize as the deployment of such a complex strategy implies that nurses had a high level of expertise and judgement for clinical decision-making, skills that are acquired over many years of professional practice. Unfortunately, NICUs are often forced to recruit new graduated nurses, whose level of expertise is very far from being adequate to address this complexity since nursing school programs do not routinely prepare their students for positions in such areas. Hospitals should develop focused learning programs for novice nurses to improve the effective achievement of these complex skills and develop clinical reasoning abilities (Square, 2010).

The impact of the stresses encountered by immature brain in the early lifetime environment can alter the developmental template of preterm infants. Innovative strategies are needed to guide and support optimal medical and nursing care of the preterm during the NICU experience (Sanders & Hall, 2018). It is imperative that a responsible application of neurobiological and behavioral research results is used to modify the NICU environments and to adapt the practice of care to foster good preterm infant development and ensure the best possible outcome (Graven & Browne, 2008). However acceptable, the achievement of such an objective is not simple or obvious and should, therefore, provide for a substantial rethinking of the NICU organization. The term "developmental clinician" (e.g., nurse or physician) has been coined to identify the transition from individual practice to a multidisciplinary approach based on shared knowledge and an individualized, family-inclusive team-approach to care, that still values the contribution of each single discipline. However, this approach does not ensure the adaptation of the entire NICU system to integrated developmental care (Browne, Vanden-Berg, Ross, & Elmore, 1999). Therefore, in addition, the practice position of the "development specialist" should be implemented in NICUs, with the aim to provide interdisciplinary leadership, education, mentoring, and systems change skills necessary for successful developmental programs (Kaye, 2016).

4.1 | Limitations

The findings of this study should be considered in light of some limitations. The sample size was rather small and this was probably due to the sampling strategy adopted in a small Level 3 NICU, like ours. Therefore, the results found to be not statistically significant may be due to the small sample size, rather than no effect; our findings need to be confirmed in larger populations. The independent impact on the stress response of the explored procedures was analyzed based on a limited number of predictors. It is possible that the stress response could be due to overlapping variables, such as auditory (e.g., noise level), visual (e.g., intensity of the light), and other potential environmental stressors (e.g., room temperature) inevitably present during the observations and not controlled by the study. This last aspect suggests caution with respect to our findings, as it could partially affect the generalizability of our results.

5 | CONCLUSIONS

The sequence of execution of weighing and bathing, two everyday routine nursing procedures, affects preterm infants' stress responses. Moreover, the procedure-induced levels of infants' stress responses decreased with their increasing PMA. Nurses should take these findings into account to personalize the approach to each infant, by adjusting the methods of execution of the procedures based on realtime recognition of the infant's adaptive or maladaptive responses. The observation of the infant should continue after completion of nursing procedures, to adopt appropriate personalized caregiving and environment interventions early on to facilitate the restoration of stability, according to the Synactive Theory of Development (Als, 1982, 1986).

6 | HOW MIGHT THIS INFORMATION AFFECT NURSING PRACTICE?

A personalized approach to the preterm infant, tuning interventions to his or her needs and difficulties, should be pursued by all health professionals involved in neonatal care (e.g., nurses, neonatologists, other medical specialties, physiotherapists, etc.). If systematically adopted for all stressful procedures under the Synactive Theory of Development (Als, 1982, 1986) and the NIDCAP approach (Als, 1986), this "routinely personalized" strategy may create better conditions for adequate preterm infant brain development. Further studies are needed to explore the effect of different nursing procedures on preterm infants' stress responses, as well as the impact of procedure-induced stress responses on infants' long-term neuro-cognitive outcomes.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ETHICS STATEMENT

The Independent Committee for Bioethics of the hospital approved the research (decree M/11-78/2014) and informed consent was obtained from parents after a full explanation of the study.

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REFERENCES

- Als, H. (1982). Toward a synactive theory of development. Infant Mental Health Journal, 3(4), 229-243.
- Als, H. (1986). A synactive model of neonatal behavioral organization: Framework for the assessment of neurobehavioral development in the premature infant and for support of infants and parents in the neonatal intensive care environment. *Physical & Occupational Therapy in Pediatrics*, 6(3-4), 3–53.
- Als, H. (2009). Newborn individualized developmental care and assessment program (NIDCAP): New frontier for neonatal and perinatal medicine. *Journal of Neonatal-Perinatal Medicine*, 2(3), 135–147.
- Als, H., Butler, S., Kosta, S., & McAnulty, G. (2005). The assessment of preterm infants' behavior (APIB): Furthering the understanding and measurement of neurodevelopmental competence in preterm and full-term infants. *Mental Retardation and Developmental Disabilities Research Reviews*, 11(1), 94–102. https://doi.org/10.1002/mrdd.20053
- Als, H., & Gilkerson, L. (1997). The role of relationship-based developmentally supportive newborn intensive care in strengthening outcome of preterm infants. *Seminars in Perinatology*, 21(3), 178–189.

- Als, H., Lawhon, G., Brown, E., Gibes, R., Duffy, F. H., McAnulty, G., & Blickman, J. G. (1986). Individualized behavioral and environmental care for the very low birth weight preterm infant at high risk for bronchopulmonary dysplasia: Neonatal intensive care unit and developmental outcome. *Pediatrics*, 78(6), 1123-1132.
- Aylward, G. P. (2014). Neurodevelopmental outcomes of infants born prematurely. Journal of Developmental and Behavioral Pediatrics, 35(6), 394–407. https://doi.org/10.1097/01.DBP.0000452240.39511.d4
- Bembich, S., Fiani, G., Strajn, T., Sanesi, C., Demarini, S., & Sanson, G. (2017). Longitudinal responses to weighing and bathing procedures in preterm infants. *The Journal of Perinatal & Neonatal Nursing*, 31(1), 67–74. https://doi.org/10.1097/jpn.0000000000228
- Browne, J. V., VandenBerg, K., Ross, E. S., & Elmore, A. M. (1999). The newborn developmental specialist: Definition, qualifications and preparation for an emerging role in the neonatal intensive care unit. *Infants & Young Children*, 11(4), 53–64.
- Cong, X., Wu, J., Vittner, D., Xu, W., Hussain, N., Galvin, S., ... Henderson, W. A. (2017). The impact of cumulative pain/stress on neurobehavioral development of preterm infants in the NICU. *Early Human Development*, 108, 9–16. https://doi.org/10.1016/j.earlhumdev.2017.03.003
- Glass, H. C., Costarino, A. T., Stayer, S. A., Brett, C., Cladis, F., & Davis, P. J. (2015). Outcomes for extremely premature infants. *Anesthesia and Analgesia*, 120(6), 1337–1351. https://doi.org/10.1213/ane.00000000 000705
- Graven, S. N., & Browne, J. V. (2008). Sensory development in the fetus, neonate, and infant: Introduction and overview. Newborn and Infant Nursing Reviews, 8(4), 169–172.
- Kaye, S. (2016). Historical trends in neonatal nursing: Developmental care and NIDCAP. The Journal of Perinatal & Neonatal Nursing, 30(3), 273–276. https://doi.org/10.1097/jpn.00000000000000000
- Liaw, J. J., Yang, L., Chou, H. L., Yang, M. H., & Chao, S. C. (2010). Relationships between nurse care-giving behaviours and preterm infant responses during bathing: A preliminary study. *Journal of Clinical Nursing*, 19(1-2), 89–99. https://doi.org/10.1111/j.1365-2702. 2009.03038.x
- Lin, H. C., Huang, L. C., Li, T. C., Chen, C. H., Bachman, J., & Peng, N. H. (2014). Relationship between energy expenditure and stress behaviors of preterm infants in the neonatal intensive care unit. *Journal for Specialists in pEdiatric Nursing: JSPN*, 19(4), 331–338. https://doi.org/10.1111/jspn.12087
- Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nature Reviews Neuroscience, 10(6), 434–445. https://doi.org/10.1038/nrn2639
- Newnham, C. A., Inder, T. E., & Milgrom, J. (2009). Measuring preterm cumulative stressors within the NICU: The Neonatal Infant Stressor Scale. Early Human Development, 85(9), 549–555. https://doi.org/10. 1016/j.earlhumdev.2009.05.002
- Nicolaides, N. C., Kyratzi, E., Lamprokostopoulou, A., Chrousos, G. P., & Charmandari, E. (2015). Stress, the stress system and the role of glucocorticoids. *Neuroimmunomodulation*, 22(1-2), 6–19.
- Peters, K. L., Rosychuk, R. J., Hendson, L., Cote, J. J., McPherson, C., & Tyebkhan, J. M. (2009). Improvement of short- and long-term outcomes for very low birth weight infants: Edmonton NIDCAP trial. *Pediatrics*, 124(4), 1009–1020. https://doi.org/10.1542/peds.2008-3808
- Ranger, M., & Grunau, R. E. (2014). Early repetitive pain in preterm infants in relation to the developing brain. *Pain Management*, 4(1), 57–67. https://doi.org/10.2217/pmt.13.61
- Sanders, M. R., & Hall, S. L. (2018). Trauma-informed care in the newborn intensive care unit: Promoting safety, security and connectedness. *Journal of Perinatology*, 38(1), 3–10. https://doi.org/10.1038/jp.2017.124
- Smith, G. C., Gutovich, J., Smyser, C., Pineda, R., Newnham, C., Tjoeng, T. H., ... Inder, T. (2011). NICU stress is associated with brain development in preterm infants. *Annals of Neurology*, 70(4), 541–549. https://doi.org/10. 1002/ana.22545

- Square, N. D. (2010). Modeling clinical applications in intensive care settings for nursing orientation. Advances in Neonatal Care: Official Journal of the National Association of Neonatal Nurses, 10(6), 325–329. https://doi.org/10.1097/ANC.0b013e3181fc881b
- Tan, J. B. C., Boskovic, D. S., & Angeles, D. M. (2018). The energy costs of prematurity and the neonatal intensive care unit (NICU) experience. *Antioxidants (Basel)*, 7(3), 37. https://doi.org/10.3390/antiox7030037
- VandenBerg, K. A. (2007). Individualized developmental care for high risk newborns in the NICU: A practice guideline. *Early Human Development*, 83(7), 433–442.
- Walden, M., Sudia-Robinson, T., & Carrier, C. T. (2001). Comfort care for infants in the neonatal intensive care unit at end of life. *Newborn and Infant Nursing Reviews*, 1(2), 97–105.
- Weber, A., & Harrison, T. M. (2018). Reducing toxic stress in the neonatal intensive care unit to improve infant outcomes. Nursing Outlook, 67, 169–189. https://doi.org/10.1016/j.outlook.2018.11.002

Weintraub, V., Mimouni, F. B., & Dollberg, S. (2007). Changes in energy expenditure in preterm infants during weaning: A randomized comparison of two weaning methods from an incubator. *Pediatric Research*, 61(3), 341–344. https://doi.org/10.1203/pdr.0b013e318030d1aa