Title page

Informative title

Development, evaluation and adaptation of a critical realism informed theory of procedural pain management in preterm infants: the PAIN-Neo theory

Short running title

PAIN-Neo theory

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Title. Development, Evaluation and Adaptation of a Critical Realist-informed Theory of Procedural Pain Management in Preterm Infants: The PAIN-Neo theory

Abstract

Aim. To present the development, the evaluation, and the adaptation of the PAIN-Neo theory.

Design. Theory development.

Data Sources. A review of literature was conduct from 1980 to 2021.

Results. Using a critical realism paradigm, this paper presents the PAIN-Neo theory, which was developed from an analysis of existing theoretical perspectives on pediatric procedural pain, empirical studies conducted with preterm infants, and the research team's pain management expertise. The theory was then empirically tested and fine-tuned.

Implications for nursing. The PAIN-Neo theory highlights that the neonatal nurse is part of a larger picture as she is influenced by factors related to her unit, hospital and country of practice. This theory emphasizes the importance of parental involvement in pain management, which is consistent with family-centered nursing practices.

Conclusion. The PAIN-Neo theory reflects the complexity of pain management nursing. This theory is innovative and specific enough to guide practice, structure research projects, and contribute to the body of knowledge in the discipline of nursing.

No Patient or Public Contribution.

Impact:

- **What problem did the study address?**
  Procedural pain in preterm infants is complex, and managing it is becoming increasingly recognized as the cornerstone of high-quality patient care. Yet, there is a lack of conceptual clarity of this phenomenon.
- **What were the main findings?**
  The PAIN-Neo theory improves the understanding of procedural pain management in preterm infants with the three stakeholders (preterm infant, healthcare professional and parents).
- **Where and on whom will the research have an impact?**

This theory will help neonatal clinicians and researchers improving preterm infants' pain management.

What does this paper contribute to the wider global clinical community?

- Pain assessment and management is a worldwide concern.
- The theory was developed from empirical studies conducted in different countries.
- The theory can be adapted to different neonatal units' contexts.

Keywords: nursing theory development; neonates; NICU; procedural pain; PAIN-Neo Theory; critical realism

AIMS

This article aims to present the development, the evaluation, and the adaptation of a theory, from the critical realism perspective, on the procedural pain management of preterm infants in the neonatal unit.

BACKGROUND

Each preterm infant undergoes an average of 43 painful procedures per entire hospital stay, such as blood sampling, nasal suctioning, or venous line insertion, during the first two weeks of their hospitalization in the neonatal unit (Orovec et al., 2019). Untreated pain has significant consequences for preterm infants' neurological development, resulting in impaired intellectual, motor, visual, and sensory development, as well as language, comprehension, and memory disorders, predicting a lower IQ in these children (Boggini et al., 2021). Despite growing evidence documenting the consequences of repeated, untreated pain on preterm infants' neurodevelopment, there is a critical lack of effective interventions in this field (Hatfield et al., 2019), resulting in the need for further research to prevent the repercussions of pain.

Pain in preterm infants is a complex phenomenon and influenced by many factors related to the specific characteristics of the preterm infant (i.e. gestational age, previous painful interventions), healthcare professionals, and parents. Adding to this complexity, there is a lack of conceptual clarity of this phenomenon in neonatal practice and research. Pain management in neonatology is suboptimal with only half of the painful procedures being relieved (Orovec et al., 2019). Also, Walco et al. (2018) noted a lack of theories on procedural pain in preterm and newborn infants to adequately guide research, casting light on the need to develop specific theories to incorporate the particularities of this population.

According to our recent critical review of theories in procedural pain in infants (De Clifford-Faugère & Aita, 2021), six theories were identified and analyzed in pediatrics, two were specific

to younger infants (two to twelve months for Pillai-Riddell's theory and six months to twelve years for Huth and Moore's theory). None of which addressed procedural pain in preterm infants. In addition, parents were rarely mentioned in these theories even though collaboration with them is crucial in a family-centered care perspective. The six theories in pediatric pain appear to have been developed through a post-positivist philosophical view (De Clifford-Faugère & Aita, 2021). While in a post-positivist perspective, the research goal is to evaluate, explain, and predict the effect of a variable A on B, for critical realism, science aims to explain what the mechanisms are, how they are activated, and under what conditions they arise. Realist research is characterized by a focus on causal chains that are operationalized by the CMO configuration: Context-Mechanism-Outcome, meaning that the interaction between the context and mechanism(s) will lead to an outcome (Emmel et al., 2018). The decision to take a critical realist point of view is highly relevant to introduce a new way of understanding the pain phenomenon by pinpointing different CMO configurations, thus encouraging reflection on the complexity of pain management in neonatology. The development of a specific theory for preterm infant pain would further the understanding of the phenomenon of procedural pain in this particularly vulnerable population in addition to directing research in neonatology to optimize the assessment and management of preterm infant pain.

DESIGN

The development, evaluation, and adaptation of the PAIN-Neo theory was conducted from a critical realist perspective involving the search for CMO configurations in the theoretical literature and empirical studies.

METHOD

Critical realism: Key features

The epistemology of critical realism is relativist, since knowledge is relative to experience, and

then to representations made by individuals in particular contexts (Bhaskar, 1997). Ontology is central to critical realism and postulates that reality exists apart from our knowledge of it. Bhaskar (1997) proposes a stratified ontology, i.e. a vision of reality in three layers: real (deep), actual, and empirical. These CMO configurations have mainly been studied in sociology (Emmel et al., 2018), therefore, we propose a definition of these concepts applicable to nursing (see Table 1).

*** Insert Table 1

Development, evaluation, and adaptation of the PAIN-Neo theory

According to critical realism, the process of theory development includes existing theories about the phenomenon under study, current empirical knowledge, and the experience of the researchers, including any personal observations they may have made (Bhaskar, 1997). A recent analysis of theory development strategies, conducted on 23 theories developed in nursing, identified that researchers use several sources of data to conceptualize their theory: existing theories in the field (65% of researchers), a review of the empirical literature (61%), studies conducted by the researchers proposing the theory (35%), and by the researchers' clinical expertise (22%) (Im, 2018). It is interesting to note similarities in the sources of data identified in nursing theories and those recommended by critical realism (theoretical sources, empirical sources, and team expertise).

The development process of the PAIN-Neo theory is illustrated below (Figure 1) and includes all of the proposed sources. Based on critical realism methodology (Emmel et al., 2018), the development, evaluation, and adaptation of the PAIN-Neo theory consisted of five steps: 1) conducting a literature review of the theoretical perspectives in pediatric pain and an analysis of CMO configurations brought forward by these theories; 2) conducting a literature review of the empirical studies for each stakeholder (preterm infant, healthcare professionals, and parents) and an analysis of CMO configurations; 3) compiling the knowledge and expertise of our research team, which resulted in embedding the proposed theory with developmental care; 4) developing

the PAIN-Neo theory; 5) performing the empirical evaluation of the theory and then adapting it based on the study's findings. The evaluation of the links proposed in the theory was carried out through two studies with the following objectives: 1) During an olfactory stimulation intervention performed in the context of a painful procedure (context), to evaluate the inhibitory mechanisms of pain regulation that are potentially involved (mechanisms) as well as the effects of the intervention on the pain response of the preterm infant (outcomes); and 2) To evaluate which contextual factors (individual and institutional) specific to the nurse working in neonatology (context) influence her clinical judgment (mechanism – not evaluated) for pain assessment and management in preterm infants (outcomes). The five planned steps have been completed.

The PAIN-Neo theory is concerned by pain assessment and management during the preterm infant's hospitalization in the NICU. It was essential to develop a theory involving all three actors, as well as the contextual factors and underlying mechanisms for each of them.

*** Insert Figure 1

RESULTS

Objective 1. Development of the theory

Step 1. Literature review of pediatric pain theory

Our analysis of the review of pediatric pain theories (De Clifford-Faugère & Aita, 2021) identified the different CMO configurations transferable to procedural pain in preterm infants (see Table 2). The configurations were classified in four levels: the individual level, i.e. the CMO specific to each actor (preterm infant, health professional, parents); the painful procedure level, such as the type or duration of the stimulus; the social level, referring to the relationship between one or more actors; and the institutional level (policies of the neonatal unit). Nevertheless, in procedural pain, some theories highlight a social interaction between parents and healthcare professionals to improve pain

management interventions. Also, inter-professional collaboration between nurses, physicians, and pharmacists was an important concept that emerged from the analysis of the theories.

*** Insert Table 2

Step 2. Literature review of empirical studies

Empirical studies were reviewed and analyzed to identify the various CMO configurations for each stakeholder. Different keywords were used: pain, preterm infants, signs of pain, consequences, healthcare professionals, pain assessment, pain management interventions, factors, parents, and NICU (see Table 3).

Preterm infant

The inhibitory systems modulate pain through three mechanisms: in the spine (gate theory), at the brainstem level, and on the cortical level (Purves et al., 2019). To give a few examples of inhibitory modulatory mechanisms involved in pain management interventions: massage seems to generate a mechanism at the spine, and sucrose does not appear to have an effect at the cortical or spinal level, but acts at the brainstem (Fitzgerald, 2015). Odors, light, and noise, non-nutritive sucking and wrapping/positioning seem to activate mechanisms at the cortical level. Skin-to-skin contact combining auditory, vestibular, visual, olfactory, and tactile stimulation appear to activate mechanisms at all three regulation levels. Given that pain has affective and sensory-discriminative components, different mechanisms could be at play at the cortical level (Purves et al., 2019).

Contextual factors that may influence the pain response have been identified in previous studies with preterm infants. The individual factors are: gestational age, Apgar score (adaptation to extrauterine life) at one and five minutes of life, disease severity, sex, state of arousal during the painful event, ventilatory support, and number of previous painful procedures. Contextual factors related to the procedure characteristics, such as duration, type of sampling, as well as the physical

environment (light, noise, positioning), also influence pain. Very few studies have looked at the social factors that may influence pain in preterm infants during a painful procedure, such as the number of people around the newborn or parental presence on the stress of preterm infants.

Observed signs of pain (outcomes) are related to the activation of the sympathetic system and generate an automatic response (Buonocore & Bellieni, 2017). These signs of pain can be grouped into four categories: 1) physiological parameters (i.e. heart and respiratory rates); 2) behavioural parameters (facial expressions [i.e. eyes squeezed closed] and motor expressions [i.e. axial tone]); 3) biological parameters, such as salivary cortisol; and 4) neurological parameters that can be measured by EEG or near-infrared spectroscopy (NIRS). It is important to note that a cortical response may be present even in the absence of facial expressions in preterm infants. Repeated, untreated pain reportedly affects stress in preterm infants and on neurodevelopmental outcomes from the age of corrected term (Boggini et al., 2021). Also, repeated pain during hospitalization in neonatology can lead, in former preterm infants, to an amplified reaction to pain at seven years of life (memory).

Healthcare professionals

Professionals play a central role in assessing and implementing pain management interventions with preterm infants, as these latter cannot express themselves verbally. In order to properly assess pain in preterm infants, the American Academy of Pediatrics (2016) recommends using standardized scales, such as the Premature Infant Pain Profile (PIPP), the Neonatal Facial Coding System (NFCS), or the Neonatal Pain, Agitation, and Sedation Scale (N-PASS). Systematic and appropriate pain assessment promotes the use of pain management interventions.

Since emotional availability influences the sensitivity of healthcare professionals, this may be a mechanism in the process of assessing and managing pain in preterm infants (Buonocore & Bellieni, 2017). Professional education appears to be a key individual factor to consider in

procedural pain management, including professionals' capacity for observation, clinical judgment, and decision-making. Indeed, a lack of knowledge and negative attitudes towards pain are barriers to pain management in preterm infants (Muteteli et al., 2019). However, it has been shown that the experience of nurses and access to continuing education promote optimal pain management in neonatology (Mohamadamini et al., 2017). And yet, knowledge of the interventions to be performed is not sufficient for the practical application of this information by healthcare professionals (De Clifford-Faugere, Aita & Le May., 2018).

According to Gibbins et al. (2015), the factors influencing healthcare professionals in pain management are: 1) their individual characteristics, namely their discipline (e.g. nurses seem be more sensitive to preterm infant pain than other professionals), education, personality, personal experience, and observation skills; 2) the context of the neonatal unit (workload, unit priorities, and approaches); 3) the preterm infant's characteristics (age, days of life, comorbidities, pain expression skills), their immediate environment (infant's face hidden by medical equipment interfering with assessment of facial expressions to pain), and contextual factors of the procedure (frequency and invasiveness).

Clinical practice guidelines for pain management are an essential resource for neonatal healthcare professionals on the unit and will contribute to optimal pain management in preterm infants. However, lack of equipment and resources (i.e. no sucrose, not enough staff to place babies skin to skin) may be limiting factors in providing pain management interventions for preterm infants.

Parents

In light of the empirical studies, there seems to be a mechanism of pain memory as well as social mechanisms, with the parents. The parents are experiencing great stress due to the uncertainty of their infant's survival and the technicality of the environment, among others, which can alter their

parental role and family dynamics (Caporali et al., 2020; Govindaswamy et al., 2019). Procedural pain generates stress in parents because they feel unable to protect their infant (Govindaswamy et al., 2019) and may influence the stress of the preterm infant, which may in turn increase their pain response. With preterm infant birth, the infant's hospitalization and atypical communication, such as their absence of crying during pain, complicates the establishment of the parent-infant relationship and disturbs the integration of the parental role (Govindaswamy et al., 2019). Parents need to be informed about painful procedures and the importance of support, i.e. professionals who are sensitive to their infant's pain, offer them emotional support, and encourage them to be involved in care (coping mechanism) (Govindaswamy et al., 2019).

Parents should be considered partners in care, through quality communication, involvement in pain management, professional counseling, and knowledge of their role, as parents in the neonatal unit (Palomaa et al., 2016). Parental presence on the unit is valuable for the preterm infant during pain management interventions when mothers and fathers can be directly involved, such as through skin-to-skin contact. This pain management intervention not only allows the parents to be involved in the care, it also provides them the opportunity to observe and be sensitive to their infant's signs so they can respond. To date, little is known about the father's desire to be involved in the pain care of his preterm infant and factors influencing his participation (McNair et al., 2020).

*** Insert Table 3

Step 3. Experience and expertise of the team in pain management

Our research team was composed of clinical and research experts in pain and developmental care. Considering that the development of the theory was guided by the knowledge and clinical expertise of our team, we viewed the three stakeholders (preterm infant, healthcare professional, and parents) as having an equal level of importance. Although the preterm infant is the one undergoing the

painful procedure, the parents and healthcare professionals are involved in managing the infant's pain. The shared responsibility between the healthcare professional and the parents points to family-centred care. Thus, the proposed theory is intended to reflect this evolution in care, through the philosophy of developmental care.

Pain assessment and management is part of developmental care for preterm infants. Kenner and McGrath (2011) organized developmental care into five categories: 1) sleep protection; 2) pain assessment and management; 3) support with daily activities including positioning and feeding; 4) family-centered care; and 5) environment (light, noise, and odor). All five of these categories, which are central to nursing, have been considered in this theory in order to guide nurses in carrying out effective interventions. Based on the literature (Lavallée et al., 2019), we propose links between pain and the other four categories of developmental care (see Figure 2). This reflection has led to a deeper understanding of the specificity of preterm infant pain by identifying contextual factors from the empirical data, such as the presence of parents, the intensity of sound and light, the presence of a pleasant or unpleasant odor, and the adequacy of positioning. When assessing pain in a preterm infant, it is difficult to distinguish between the pain response and the stress response, so the pain experience should include pain and stress as a whole experience without trying to distinguish between the two.

*** Insert Figure 2

Step 4. The pain-neo theory

First, a triangle is used to represent family-centered care, where each stakeholder is at one end. The presence of a relational mechanism is postulated between each person (preterm infant, health professional and parents); i.e. the interactions between the parents and their infant to decode pain, between the parents and the nurse for collaboration, and between the nurse and the infant to

evaluate, intervene, and readjust pain management interventions. In the center of the triangle, pain expression, pain assessment, and pain management interventions are represented. Feedback arrows illustrate the dynamic nature of the process of pain assessment / implementation of pain management interventions / pain expression by the preterm infant. Though the preterm infant is involved only in the expression of pain, the healthcare professional and the infant's parents are shown in the assessment of pain and interventions.

This theory identifies three stages of pain assessment: initial, reactive, and regulation. The initial assessment includes the preterm infant's pain, but also the individual factors of the preterm infant, the physical environment, and parental factors. Then, the assessment of pain reactivity corresponds to the immediate response to the stimulus, while pain regulation concerns the return to homeostasis. The purpose of this monitoring is to evaluate the effect of the intervention and be able to individualize care. Indeed, pain management is part of developmental care, one of the main principles of which is the individualization of care. Pain management interventions are used for to prevent or reduce pain then adjusted according to the continuous evaluation. Evidence-based pain management interventions for preterm infants are skin-to-skin contact, sweet solutions (i.e. sucrose) with non-nutritive sucking and positioning.

CMO configurations are presented for each of the stakeholders. For the preterm infant, procedural pain begins with a stimulus, with or without skin abrasion, where the type, duration, and intensity of the stimulus will influence the signs of pain (see Figure 3). This stimulus will lead to a painful experience for the preterm infant. It is important to note that the painful experience consists of stress and pain, which current knowledge of the signs does not distinguish. These signs (outcomes) constitute the expression of the painful experience. This theory specifies that pain in the preterm infant is manifested by physiological, behavioural, biological, and neurological signs. Pain assessment that considers these different signs gives rise to a thorough and systemic

understanding of the pain experience. With a view to deepening understanding of mechanisms of action of the interventions performed with this population, the following four mechanisms of pain regulation are proposed: 1) spinal; 2) brainstem; 3) cortical (affective); and 4) cortical (sensory-discriminative). In addition, preterm infants' pain is also influenced by the physical environment and by individual contextual factors (context), such as gestational age, corrected age, sex, Apgar score at one and five minutes of life, presence of ventilatory support, severity of illness, number of previous painful procedures, and state of arousal-sleep. Moreover, a memory mechanism of the infant's painful experience may contribute to building the memory and thus influence the next painful procedures. Also, pain can have consequences on long term outcomes such as sleep, neurodevelopment, chronic pain, and stress.

For healthcare professionals, the neurophysiological mechanisms of sensitivity and empathy to pain, and the cognitive mechanisms of observation and analysis are involved in assessing pain. Furthermore, the implementation of pain management interventions is influenced by cognitive mechanisms of clinical judgment and decision-making. The healthcare professional's assessment and interventions will also differ according to individual contextual factors, such as discipline, education, personal experience of pain, and skills, but also according to factors stemming from their work team (team support and interprofessional collaboration) and their unit (workload, practice guidelines, unit acuity). Relational mechanisms are postulated between members of the care team and on the unit related to team dynamics. The healthcare professional who assesses and intervenes appropriately within their context will have greater job satisfaction and less stress (outcomes).

Several individual parental factors (context) are considered such as: age, gender, socioeconomic status, anxiety level, personal experience with pain, information retained (knowledge), culture, and beliefs. Parental involvement in pain care can create a stress or a coping

mechanism that can be reflected in family dynamics, parenting, and presence on the unit. Presence on the unit (outcome) is valuable for the preterm infant when pain management interventions involving the parent, such as skin-to-skin contact, are performed. In addition, the influence of parental stress on the preterm infant's stress is illustrated by an arrow that shows the influence of parental stress (mechanism) on the preterm infant's individual factors. Mechanisms of observation and sensitivity to the signs their infant expresses are also postulated as part of the parent's assessment of pain.

*** Insert Figure 3

Objective 2. Evaluation of the links proposed in the theory

The evaluation of the links proposed in the theory was carried out in two studies, each conducted with one of the stakeholders described in the theory, i.e. a systematic review with meta-analysis for preterm infants and quantitative study for nurses. i.e. premature infants and health professionals.

The systematic review with meta-analysis was guided by the following PICO question "What is the effectiveness of olfactive stimulation interventions on full-term and preterm neonates' pain response during a painful procedure compared to standard of care?". The evaluated intervention was an olfactory stimulation, to isolate the preterm infant's pain regulation mechanisms, understand whether these latter were activated by the intervention, and evaluate the effects of this intervention (De Clifford-Faugere et al., 2020). The results of the meta-analysis for preterm infants showed that olfactive stimulation interventions using a familiar odour (i.e. breast milk, vanilla following a period of habituation to the odour) were significantly effective compared to an unfamiliar odour on pain reactivity ($p=0.002$) and regulation ($p=0.02$), which are the two measurement time proposed in the PAIN-Neo theory. The studies included in the systematic review assessed pain according to signs identified in the PAIN-Neo theory: physiological signs,

behavioural signs, and biological signs, the latter was rarely used with preterm infants (only two studies). Although, no study has considered neurological signs, those are innovative in pain measurement in the NICU.

A secondary analysis of data collected from the international comparative study of nurses in France and Canada validated nurses' perceptions, assessment of and interventions for pain management, and examined the individual and contextual factors influencing their assessment and implementation of pain management interventions (De Clifford-Faugère, Aita et al, 2022). Mixed model analyses identified significant ($p<0.05$) contextual factors at the institutional level (country, hospital, work shift, and unit acuity, and pain assessment tools used on the unit) and at the staff level (implementation of developmental care practices). The study findings showed that factors related to the implementation of developmental care practices (family-centered care, skin-to-skin contact, and light environment) significantly influenced nurses' pain assessment and relief interventions ($p<0.05$); however, these factors had not been identified in previous empirical studies. The individual factors we found to influence nurse assessment and interventions ($p<0.05$) were age, years of nursing experience, level of training, pain perceptions, and having had their own preterm infant. Specifically, our results showed that higher neonatal pain perception scores predicted better pain assessment by nurses, which influenced the implementation of pain management interventions by these latter.

Objective 3. Adaptation of the pain-neo theory

The systematic review with meta-analyses confirmed the adequacy of the links proposed in the PAIN-Neo theory regarding the different pain measurement times, as the meta-analysis was done according to the two measurement times of pain reactivity and pain regulation. The baseline measurement time is necessary to calculate the reactivity and regulation times. Also, different signs

of pain have been used by the included studies (physiological, behavioral, biological). and neurological signs were kept in the PAIN-Neo theory as they are an innovative way to measure pain in preterm infants.

Hypotheses about the mechanisms activated during an olfactive stimulation intervention could also be formulated. Current knowledge of the central nervous system supports the potential impact of olfactive stimulation interventions on the emotional and affective components of pain. Indeed, the olfactory system is anatomically linked to the limbic system (emotionality), which is involved in pain perception (Purves et al., 2019). Thus, the mechanism of action would be at the cortical level, as corroborated by animal studies (Shipley et al., 2003) and found in the PAIN-Neo theory. In conclusion, no new elements were added or removed from the PAIN-Neo theory following the evaluation of the links proposed.

In the second study with nurses, the individual and contextual factors postulated in the PAIN-Neo theory that were empirically supported were: age, years of nursing experience, level of training, perceptions of pain, unit acuity and assessment tools. New factors could be added considering the significant results: having giving birth to a preterm infant, work shift, hospital, and country. As for the factor of having given birth prematurely, our study is the first to address this variable, which was added to the theory. One hypothesis is that having had a preterm infant increases the nurse's sensitivity to neonatal pain (Buonocore & Bellieni, 2017). In addition, this is the first study to show a link between pain management and developmental care practice, which provides empirical support for the Step 3 (Figure 2). Several factors present in the theory could not be empirically validated in this study and should be the subject of subsequent research. These include beliefs, level of anxiety, emotional availability, and skills (relational, observational and technical). Also, our study did not find the physical environment (light and noise) influenced the

nurse's assessment and interventions, contrary to what had been represented in the theory. Further research should be conducted to clarify the influence of the environment. In conclusion, among the factors postulated in the PAIN-Neo theory, unit acuity, pain assessment tools used in the unit, age, years of nursing experience, level of education, and nurses' perceptions of pain were found to be significant; environment, education (last degree obtained), having children, and having had a child hospitalized were not significant variables. In addition, several new factors tested in this study—country, hospital, work shift, and having had a premature child—could be added to the PAIN-Neo theory.

DISCUSSION

Rigour of the PAIN-Neo theory

The PAIN-Neo theory seems to offer the best possible explanation for the data analyzed. Indeed, this theory leads to reflection on the different CMO configurations found at both theoretical and empirical levels and proposes an innovative vision of procedural pain management. The adaptation made following the evaluation improved this aspect, simplifying the theory by streamlining it for a more pleasing visual and retaining the complete and thorough explanation in the text. Emmel et al. (2018) emphasize the importance of being confident in the data used to apply the theory and the need to integrate multiple sources (theoretical and empirical), as well as the fact that there is enough relevant and useful data on any one aspect to ensure plausibility of the theory with consistent arguments. As explained in the PAIN-Neo theory development process, the evidence identified comes from theoretical, empirical, experiential sources, and thus reinforcing theory plausibility. It is important to point out that the PAIN-Neo theory is not intended to be universal; rather, it proposes convincing explanatory elements specific to neonatal pain management (Emmel et al.,

2018).

Limitations

The lack of empirical studies conducted with parents diminishes the study's explanatory value in terms of parent-related items. For example, the theory posits that parents may be involved in assessing their infant's pain, but no empirical study has assessed this assumption. Also, the theory states "parents" to maintain inclusivity. However, the PAIN-Neo predominantly presents mothers' viewpoint, as the reviewed empirical studies for the development of the theory mainly included mothers.

Implications for practice

The PAIN-Neo theory highlights that the neonatal nurse is part of a larger picture as she is influenced by factors related to her unit, hospital and country of practice. In addition, the PAIN-Neo theory emphasizes the importance of parental involvement in pain management, involving a progressive transfer of responsibilities between the nurse and the parent, which is consistent with family-centered nursing practices. Also, the PAIN-Neo theory reflects the complexity of pain management nursing and thus could guide the development of clinical guidelines considering contextual factors of all actors.

Implication for research

The PAIN-Neo theory improves our understanding of procedural pain management in preterm infants and helps guide research projects conducted with preterm infants, healthcare professionals and parents (Table 4). Furthermore, since the theory was developed from a critical realist philosophical perspective, it can be applied regardless of research method as long as the study seeks to answer the question, "What works, for whom, how and in what context?" The PAIN-Neo theory can guide quantitative, qualitative, and mixed-methods research. For example, a lack of knowledge persists on the mechanisms of action of non-pharmacological interventions with preterm infants.

A better knowledge of the mechanisms involved in each intervention would make it possible to optimally combine these latter. Nurses' individual factors, such as beliefs, level of anxiety, and emotional availability, as well as their relational, observational, and technical skills, could be investigated.

Implication for nursing knowledge

As a professional discipline, research issues must emerge from the practice to meet nurses' needs (Risjord, 2010), as in the case of procedural pain in preterm infants. Science and practice are in continuous interaction to renew nursing practice and improve populations' health (Risjord, 2010). Resulting theoretical knowledge interacts with practice, since the more knowledge increases, the more new forms of practice are possible (Bhaskar, 1997). Furthermore, knowledge from nursing can be used by other disciplines, thus contributing to a network of knowledge (Risjord, 2010); the PAIN-Neo theory could be relevant to other disciplines, such as public health, medicine or psychology.

CONCLUSION

The aim of this article was to propose a theory consistent with the management of procedural pain in preterm infants that would integrate the specificities of pain in this population. We developed the PAIN-Neo theory based on a review of the literature on pediatric pain theory, on an exhaustive literature review of empirical studies on pain in preterm infants, and on our professional experience. This theory is innovative and specific enough to guide practice, structure research projects, and contribute to the body of knowledge in the discipline of nursing.

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Conflict of interest statement

The authors declare no conflicts of interest.

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Legends for tables and figures

Table 1. Definition of the Mechanism, Context and Outcome (CMO)

Table 2. Context-Mechanisms-Outcomes transferable to preterm infants, drawn from the analysis of pediatric pain theories, according to various actors

Table 3. Context-Mechanisms-Outcomes identified as being empirically involved in infants' procedural pain, according to various actors

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Figure 1. Process of development for the theory

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Figure 3. The PAIN-Neo theory

Table 1. Definition of Mechanism, Context and Outcome (CMO)

CONTEXT	The context is defined at different levels: individual, collective, institutional, and societal. It consists of the physical environment and cultural, economic, socio-political, and psychological factors. It involves all the elements present that can influence the outcomes. The context is central since it is necessary for the activation or non-activation of mechanisms and allows us to understand why or how specific interventions work.
MECHANISM	The mechanisms would exist at four levels: material (physical and chemical), individual (psychological, cognitive, and emotional), group and social (families, professionals), and institutional. The mechanisms are the ways of acting of the elements of reality, existing at each of the four levels previously mentioned, reflecting the existence of causal laws. Some mechanisms can produce immediate effects (i.e. chemical reaction) while others will produce short, medium or long term effects.
OUTCOME	The outcome or outcomes are observed at different levels: individual, group and social, community, institution, society, depending on the nature of the research. They may be observed in the short, medium or long term, and may be expected or not.

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Table 2. Context-Mechanisms-Outcomes transferable to preterm infants, drawn from the analysis of pediatric pain theories, according to various actors

CMO	Preterm infants	Parents	Healthcare Professional
C	**Individual level** • Age • Sex • Developmental stage (including brain maturity) • Motor skills • Genetics (i.e. endogenous opioid receptor density) • Level of anxiety, stress • Previous pain experience and memory • Threshold of sensitivity to pain • Calm or agitated physical environment • Nutrition **Procedure characteristics** • Invasive procedure • Duration of procedure **Social level** • Presence of a parent • Presence of strangers	**Individual level** • Sex • Socio-economic status • Level of anxiety, stress • Personal experience • Sense of control • Information received **Group level** • Family culture and beliefs about pain	**Individual level** • Relational, technical and observational skills • Knowledge (i.e. signs of pain, child's developmental level, pathology) • Biological dispositions (allowing for empathy) • Personal experience and beliefs about pain • Level of anxiety, stress **Group level** • Family requests • Team dynamics • Practice standards, protocols (evidence-based) • Unit organization **Institutional level** • Policies • Healthcare system organisation
M	**Individual level** • Nociceptive mechanism • Mechanisms of pain regulation • Emotional mechanism (stress) **Social level** • Relational mechanism with the parent • Relational mechanism with the health professional	**Individual level** • Stress mechanism • Mechanism of adaptation to the unit **Social level** • Relational mechanism with the infant • Relational mechanism with the health professional	**Individual level** • Neurophysiological mechanisms that enable sensitivity and empathy to pain • Cognitive mechanisms: clinical judgment, decision making **Social level** • Relational mechanism with the infant or child • Relational mechanism with the parent • Relational mechanism with the team
O	<u>Short-term:</u> Pain reactivity and regulation, stress, adverse effects of interventions <u>Long-term:</u> Pain memory	Parental Anxiety Family dynamics	Anxiety Job satisfaction

Table 3. Context-Mechanisms-Outcomes identified as being empirically involved in infants' procedural pain, according to various actors

CMO	Preterm infants	Parents	Healthcare Professional
C	**Individual level** • Gestational age and postnatal age • Apgar score • Severity of illness • Sex • State of arousal • Ventilatory support • Number of previous retrievals **Level of physical environment and nature of the procedure** • Type of procedure (invasiveness) • Duration • Frequency of procedures • Light intensity • Sound intensity • Positioning **Social level** • Parental presence	**Individual level** • Stress • Parental sensitivity **Social level** • Informations given by prefessionals • Support from professionals	**Individual level** • Discipline • Education (initial or continuing) • Professional experience • Personal experience (i.e. having children) • Beliefs • Knowledge • Sensitivity • Emotional disposition • Critical thinking skills • Observation skills **Physical environment level** • Acuity of the unit • Visibility of preterm infant's face **Group level** • Interprofessional collaboration • Support from team members **Institutional and unit level** • Workload • Unit orientations • Assessment tools used • Implementation of evidence-based practices and practice guidelines • Continuing education opportunities
M	**Individual level** • Memory mechanism • Pain regulation mechanisms (spinal, brainstem, cortical) **Social level** • Relational mechanism with the parent • Relational mechanism with the healthcare professional	**Individual level** • Observation mechanism • Stress mechanism **Social level** • Relational mechanism with the infant • Relational mechanism with the healthcare professional	**Individual level** • Emotional mechanism (sensitivity) • Cognitive mechanism (observation, clinical judgment, and decision making) **Social level** • Relational mechanism with the infant • Relational mechanism with peers
O	Signs of pain Neurodevelopment Sleep	Parenting Family dynamics Presence at the bedside	Pain assessment Performance of interventions

Table 4. Recommendations

Recommendations for future research to test the theory	Recommendations for the application of the PAIN-Neo theory
Investigate the different mechanisms involved in the healthcare professional's pain management (clinical judgment, decision making...) Evaluate the relational mechanisms of the collaboration process between parents and healthcare professionals Investigate in what context and by what mechanisms a parent can be involved in pain assessment Examine the unique contribution of fathers to pain assessment and management Investigate the mechanisms of pain regulation involved in preterm infants during different interventions to combine them according to their mode of action and optimize the effectiveness of the interventions. Understand the mid- and long-term consequences of procedural pain on sleep and chronic pain. Evaluate the different responses to pain as well as the different effective interventions according to the types of stimuli. Continue to evaluate the links between pain and other developmental care categories.	Could guide the development of clinical guidelines including the assessment and reassessment, the different pain management interventions in prevention and adjustment, consequences of untreated pain and the deafferents factors to considered during pain management. Highlights that healthcare professionals are part of a larger picture as they are influenced by factors related to her unit, hospital and country of practice. This pointing out the importance of, clinical guideline and interprofessional collaboration. Enphase this importance of the sharing responsibilities between parents and healthcare professionals in clinical practice.

Figure 1. Process of development for the theory

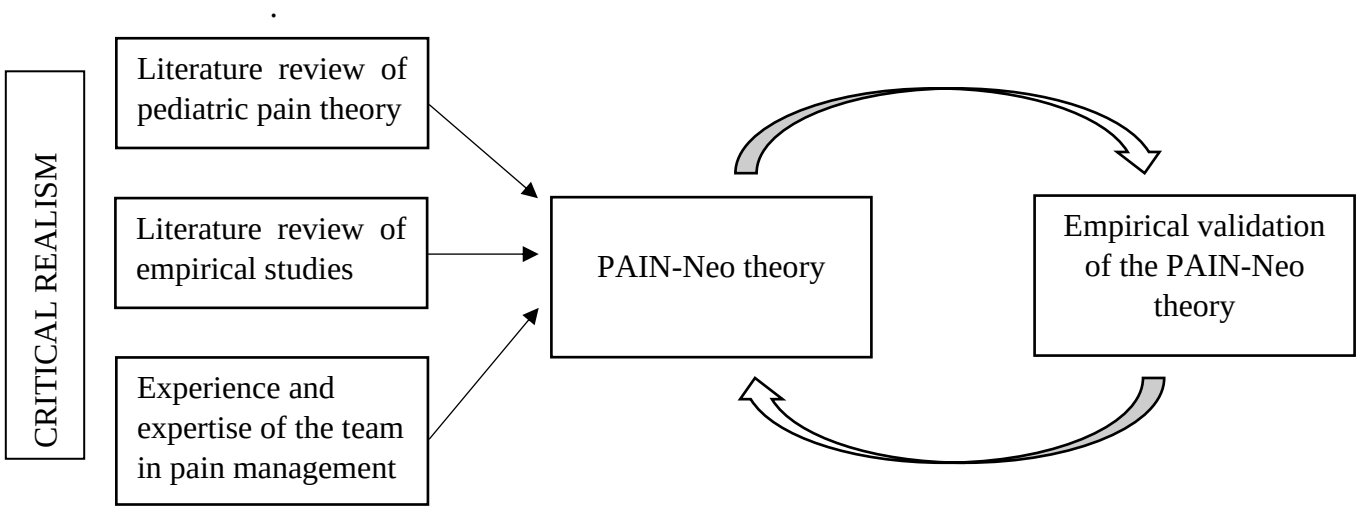
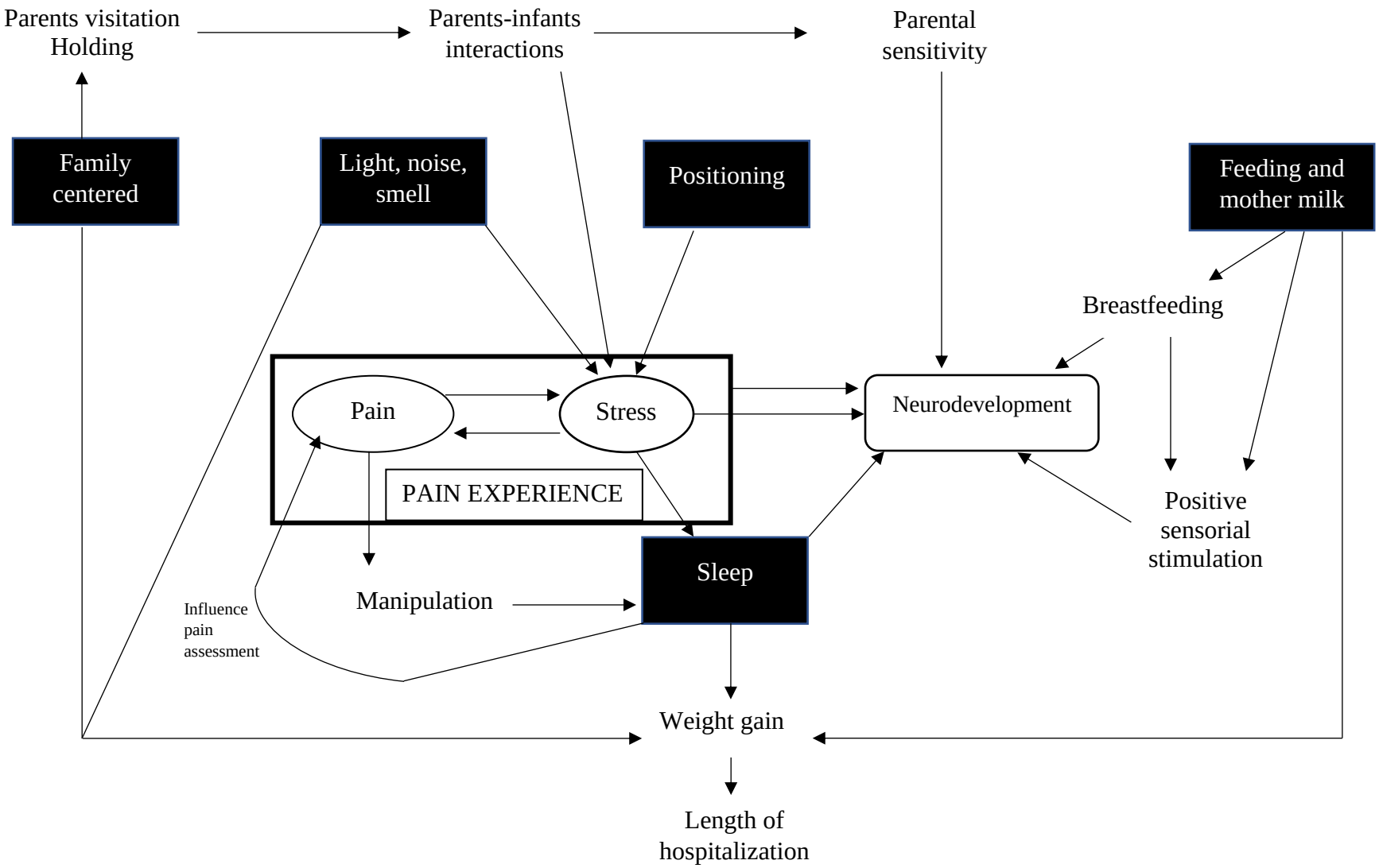
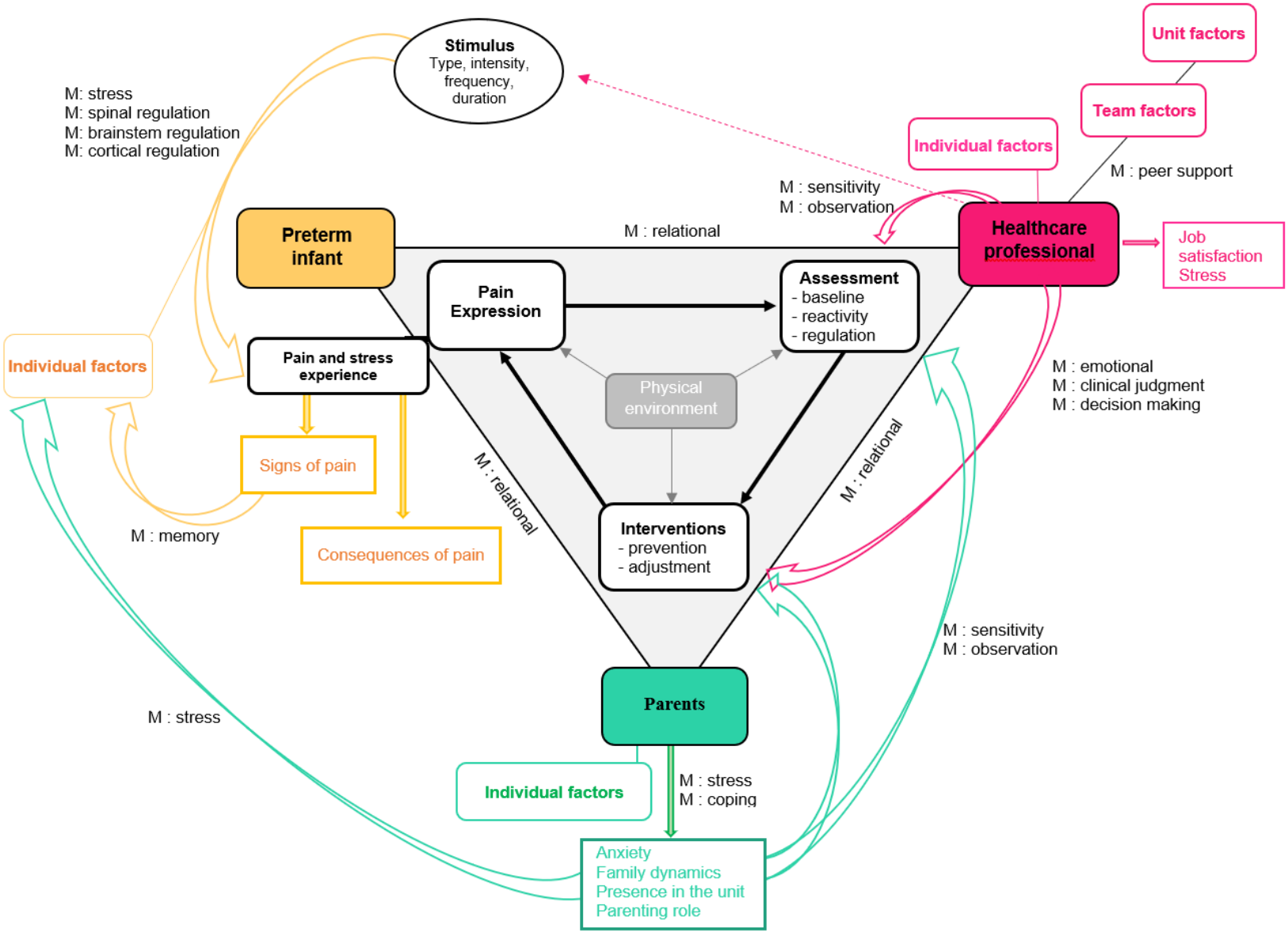


Figure 2. Empirical links between developmental care components



Legend: Boxes in black are developmental care categories; Pain experience is composed of pain and stress

Figure 3. The PAIN-Neo theory



Legend

M = mechanism; the arrows represent mechanisms; the arrows ⇨ lead to the outcomes that are named in the square boxes; the factors are elements of the context that can influence the outcomes.

Explanation of colors:

- Context-Mechanism-Outcomes (CMO) configurations: Yellow for preterm infant; Pink for healthcare professional; Green for parents.
- Grey triangle symbolizes family-centered care with a relational mechanism between each stakeholder.
- In the middle, physical environment (light, noise, smell) is represented in grey and could influenced pain expression, pain assessment and pain management interventions
- In the middle, black feedback arrows illustrate the dynamic nature of the process of pain assessment / implementation of pain management interventions (i.e. skin to skin, sucrose) / pain expression by the preterm infant.

Preterm infant

- **Signs of pain** are physiological, behavioral, biological, and neurological.
- **Consequences** of pain on short, mid, and long term: neurodevelopment, sensitivity to pain, sleep, and chronic pain
- **Individual factors** that could influenced the tree inhibitory **mechanisms** of pain regulation and stress **mechanism** are: gestational age, corrected age, sex, Apgar score at one and five minutes of life, presence of ventilatory support, severity of illness, pain sensitivity threshold, number of previous painful procedures, and state of arousal-sleep
- The pain experienced during a painful procedure will increase according to the number of previous procedures through a memory **mechanism** of the infant's painful experience and may influence the next painful procedures (increase the number of previous painful procedures in individual factors).

Healthcare professionals

- **Individual factors** are discipline, age, years of experience, training (initial and continuous), personal and professional experience of pain, beliefs, and knowledge on pain, having giving birth to a preterm infant, level of anxiety, emotional availability, and skills (relational, observational, and technical).
- **Team factors** are team dynamics, team support, and interprofessional collaboration (with a mechanism peer support).
- **Unit factors** are workload, work shift, unit acuity, practice guidelines, in the unit, assessment tools implanted in the unit, hospital and country where the unit is located.
- Professionals' **outcomes** of job satisfaction and stress are postulated. Pain assessment and interventions done by professionals are also **outcomes.**
- The professional will perform the stimulus (dotted arrow), then will evaluate pain through sensitivity and observation **mechanisms** and then intervene to manage pain through emotional, decision making and clinical judgment **mechanisms.**

Parents

- **Individual factors** are age, sex, gender, socioeconomic status, level of anxiety, personal experience (with pain, during pregnancy and delivery), information retained (knowledge), parental sensitivity, feeling of control, culture, and beliefs
- **Parental outcomes** are anxiety, family dynamics, parenting, and presence on the unit.
- **A mechanism** of stress could impact the parental outcomes but also the preterm infant. Also, a coping mechanism could be present. A mechanism of sensitivity and observation would allow the parent to be involved in pain assessment and perform interventions.