



“A philosophy....can help us choose the best approach from an ethical point of view, such as the philosophy of person/family-centered care

—Jacques Sizun

## Translating Data on Brain Development Into Practice

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One of the goals of the neonatal teams is to support and protect the developing brain in the Newborn Intensive Care Unit (NICU), as the baby only has ‘one brain for life.’<sup>1</sup> Medical treatments, such as antenatal steroids and magnesium sulfate, have been shown to be effective in preventing brain damage in preterm infants. In parallel, environmental and behavioral strategies have been proposed under the generic term of ‘developmental care’ or ‘brain care.’ Developmental care is an emerging science and needs to be as evidence-based as possible so that healthcare providers are in a position to choose the best strategies for care, and in order for healthcare teams to be trained effectively, and parents and

families to be provided with the best and most comprehensive information available.

Brain plasticity is ‘the ability of the nervous system to change its activity in response to intrinsic or extrinsic stimuli by reorganizing its structure, functions, or connections.’<sup>2</sup> Brain plasticity is an opportunity for the newborn, as it offers a chance for rehabilitation after brain damage. Brain plasticity is also a challenge: an early hostile environment could alter the steps of brain development, such as synaptogenesis. In case of prematurity, synaptogenesis occurs while infants are hospitalized in the newborn intensive care unit.

This article focusses on the effects, as described in recent systematic reviews,

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of some approaches aimed at preventing the negative impact of frequent stressors on brain development in the NICU. The stressors are sleep deprivation, pain, mother-child separation, and sensory dysstimulation.

## Stressors in the NICU

### Sleep deprivation

Animal studies, mostly conducted on rodents, have provided useful insights with regard to sleep deprivation.<sup>3</sup> These studies have shown that sleep deprivation may result in: oxidative stress, neuroinflammation via chronic microglial activation, and the accumulation of the abnormal proteins p-Tau and amyloid- $\beta$  in the cerebral cortex. These studies have also shown a neurogenesis decline via complement activation, which alters the balance of Fragile X-Mental Retardation Protein expression.<sup>3</sup> In addition, the impact of chronic sleep deprivation on behavioral development has been demonstrated. Sare et al<sup>4</sup> found short- and long-term changes in behaviors of sleep-deprived mice, measured by activity in an open field arena. Males demonstrated decreased sociability and increased repetitive behaviors. This data from preclinical studies show that sleep deprivation in the neonatal period has long-lasting behavioral changes, possibly modulated by gender.

### Pain

A meta-analysis by Steinbauer et al<sup>5</sup> concluded that neonatal pain has a large effect on neuronal cell death in rodents. The higher number of neonatal pain events was significantly asso-

ciated with increased neuronal cell death, increased anxiety, and depressant-like behavior. Boggini et al<sup>6</sup> summarized the impact of pain on preterm infants' brain development demonstrated by MRI studies. A volume reduction of white and gray matter structures at neonatal and school ages is associated with early postnatal pain exposure. However, there is a possible bias, as the most severe clinical conditions are associated with higher exposure to painful procedures.

### Mother-child separation

Maternal separation, an early stressful experience, can negatively impact the newborn's nociceptive system development and pain responses at different levels<sup>7</sup> (Table 1). Epigenetic mechanisms are implicated in the long-term effects of this early life stress that could also impact the next generation.

### Sensory Stimuli

During prenatal development in mammals, the sensory systems do not become functional at the same time, but rather in a specific and invariant sequence: first tactile, then vestibular > chemical > auditory > visual.<sup>8</sup> This differential timing of sensory system onset could benefit the earlier developing sensory systems as it allows them to develop without competition or interference from later developing sensory systems. In the case of preterm birth, the sensory stimuli are numerous, intense, simultaneous, chaotic, and physically different from those observed in utero.<sup>9</sup> This could negatively impact synaptogen-

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## Editorial

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The influence of NIDCAP is steadily increasing, as evident from the comprehensive body of work it encompasses. In this edition, Jacques Sizun presents compelling proof of NIDCAP's efficacy by examining current research and practical applications.

Notably, there has been a surge in publications citing NIDCAP's principles across multiple languages, underpinning its growing global recognition.

The path of our global outreach remains unwavering. The NIDCAP Federation International, driven by dedicated members, continues to propel the frontiers of this approach. Through leadership, we are privileged to embark on journeys of discovery with our valued members. An insightful introduction to Monique Oude Reimer-van Kilsdonk hailing from the Netherlands, offers a glimpse of our diverse membership.

Joy Browne enriches our understanding of APIB through a survey of our members, providing valuable insights that deepen our appreciation of its implementation.

A pivotal facet of the NFI is our community of family members. Nina Nikolova's poignant account from Bulgaria exemplifies how adversity can be the catalyst for assisting fellow families.

I invite the members and readers of the Developmental Observer to share their journeys with developmental care. We warmly welcome your reflections on training, practice, interesting case studies, and the invaluable lessons drawn from personal experiences. Your contributions stand to strengthen the Developmental Observer and the information to move developmental care forward.

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Cover image by Emmanuel Angelicas

**Table 1: Overview of maternal separation on the nociceptive system**  
[adapted from Melchior et al.<sup>7</sup>]

Gastro-intestinal tract	Dorsal root ganglion	Spinal cord	Higher brain centers
<ul style="list-style-type: none"> <li>- Increased permeability of the mucosal layer</li> <li>- Inflammation</li> <li>- Change in microbiota composition</li> </ul>	<ul style="list-style-type: none"> <li>- Increased excitability of afferent neurons</li> <li>- Increased expression of Nav 1.8</li> <li>- Decreased expression of Kv1.2</li> </ul>	<ul style="list-style-type: none"> <li>- Increased activity of superficial and deeper layers</li> <li>- Changes in neurotrophic factors expression</li> </ul>	<ul style="list-style-type: none"> <li>- Differential activation of the pain matrix</li> <li>- Alteration of descending controls of pain</li> <li>- Central inflammation</li> </ul>

esis. According to Bourgeois, ‘experimental models provide an additional example showing that a perturbation at an early neurodevelopmental stage may have a late and long-lasting effect of disorganization despite an apparently normal intermediate period.’<sup>10</sup>

The research data shows evidence for the importance of prevention of pain, stress, mother-child separation and inappropriate stimulation in the NICU. What is the evidence for the strategies that reduce these stressors?

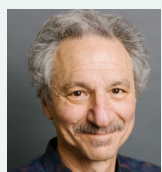
## Strategies for Reducing Stress

### Sleep support strategies

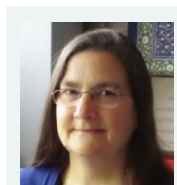
A systematic review found that swaddled preterm newborns arouse less and sleep longer.<sup>11</sup> Swaddling stimulates sleep continuity, as shown under laboratory conditions and in descriptive studies. The effect is most consistent in periods of Quiet Sleep (QS), but not always consistent during Rapid Eye Movement (REM) sleep.

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## Editorial Board



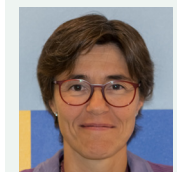
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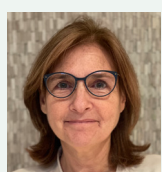
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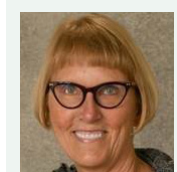
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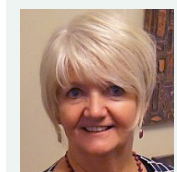
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A Cochrane Review of non-nutritive sucking (NNS) found four studies reported on behavioral states with different methods of reporting states.<sup>12</sup> Two studies reported no effect, one study reported the most frequent transition was from QS to drowsy for the NNS group, and one study reported that sleep states were more frequent in the NNS group.

The impact of skin-to-skin on sleep in neonates has been clearly demonstrated.<sup>13</sup> According to a review from the American Academy of Pediatrics,<sup>13</sup> skin-to-skin increases frontal brain activity during both quiet and active sleep, supports a more mature sleep organization, with increased total and quiet sleep, decreased REM sleep and arousals from sleep, and improves sleep cycling. Therefore, the best strategy to protect sleep is to encourage parents to be present in the NICU and to provide extensive skin-to-skin for their infant.

In a study of infants receiving regular care versus developmental care practices (covering the incubator, decreasing environmental noise, using supportive bedding, and promoting state transition by hand swaddling, non-nutritive sucking, or grasping), sleep time was increased both in AS and QS states.<sup>14</sup>

In a systematic review of randomized control studies on the effects of music therapy on premature infants,<sup>15</sup> recorded music interventions were not associated with a significant effect on behavioral states. Live music interventions were shown to improve sleep in three out of four studies, however, behavioral states were defined with different non-validated tools. Due to the heterogeneity of type and duration of interventions, gestational age of the subjects, and outcome measures, there was not enough evidence to recommend music therapy.

### **Pain control strategies**

Numerous clinical trials and meta-analyses have demonstrated the efficacy of non-pharmacological interventions on the behavioral expression of pain in newborns: swaddling, flexed position, non-nutritive sucking, oral sucrose, breastfeeding or mother's milk, and skin-to-skin. Association and/or superiority of interventions are less studied.<sup>16</sup> More trials studying the impact of these interventions on the cortical response and the effect of structured parent involvement are needed.

### **Maternal Separation Strategies**

New World Health Organization (WHO) guidelines advise that kangaroo mother care should start immediately after preterm birth without an initial period in an incubator.<sup>17</sup> These recommendations are based on recent trials demonstrating the positive impact of very early skin-to-skin on survival or cardiorespiratory stabilization.<sup>18,19</sup>

Mother-newborn couplet care is considered the best strategy to support the zero-separation concept. However, the current evidence is scarce.<sup>20</sup> The Stockholm Neonatal Family Centered Care Study demonstrated a 5.3-day reduction in total length of stay and a reduced risk of moderate-to-severe bronchopulmonary dysplasia in the Couplet-care group.<sup>21</sup>

Believing that all these interventions could be integrated with an evidence-based global approach, Roué et al collaborators identified eight principles that do not need more research before routine use.<sup>22</sup> These include free 24-hour parental access, pain management, environmental influences, support of skin-to-skin, and sleep protection.

### **Science, Philosophy, and Human Rights**

While the scientific evidence is strong, science alone cannot guide all aspects of care for hospitalized newborns. A philosophy - 'a theory that acts as a guiding principle for behavior' - can also help us choose the best approaches from an ethical point of view, such as the philosophy of person/family-centered care. In this case, scientific evidence is not then necessary. Instead, the ethical reflection, both individually and as a group, can inspire and enrich the approach. Moreover, in a study concerning the participation of NICU parents in medical rounds, some parents argued that it was not a philosophical question, but just the expression of human rights, their 'right' to be present, and their 'right' to participate in the decisions concerning their baby.<sup>23</sup> Although science is an important factor in determining best practice, the respect of human rights is also very important.

### **Guidelines**

In order to put the science and philosophy to practice it is necessary to have access to the data and for clear guidelines/recommendations/standards to be formulated and followed. Many guidelines are easily accessible and can guide high quality care in the NICU.

### **Gap Between Research and Practice**

Despite the existence of scientific evidence and easily accessible recommendations from national or international agencies and organizations, a significant gap exists between knowledge and practice. An example is a multisite survey across 13 NICUs in Paris about procedural pain in newborns.<sup>24,25</sup> One NICU used non-pharmacological interventions for painful procedures only 2.4% of the time, whereas another NICU used these strategies 81% of the time. They also measured the difference in pain control during the day and the night and found that the babies were more protected from pain during the day than at night. The only difference was parental presence. There is high evidence for the importance of parental presence, yet implementation is lacking. Why is there such a difference between these units given they all have access to the same research? Another study, the French EPIPAGE study<sup>26</sup> showed that there was little range in difference across units on medical interventions, but there was a large difference across units in the use of behavioral strategies. It was also shown that there was no significant difference between the cluster of infants who received intensive medical intervention and those who received more behavioral interventions. Although there is a high level of research on the benefits of

behavioral strategies there is great difference in the implementation of these strategies which has an effect on the comfort and care of the baby and ultimately on the baby's outcome.

## NIDCAP Training and implementation of brain-care practices

The French EPIPAGE study gives us information on the implementation of medical and nursing practices such as skin-to-skin, breastfeeding support, and pain control, and the association with professional education and training.<sup>26,27</sup> The authors observed large unit-level variations not explained by differences in infants' characteristics across units, but possibly explained by neurodevelopmental care policies and training. The NIDCAP training compared with no training was significantly associated with early kangaroo-mother-care (KMC) initiation: [OR, 3.5; 95% CI, 1.8–7.0] and sufficient perceived maternal information on infants' pain [aOR (95% CI) 2.6 (1.7–4.1)].<sup>26,27</sup> There has been much evidence on the effectiveness of NIDCAP on the infants' outcome, but this was one of the first studies to show the influence of NIDCAP training on evidence based care practices.

How can we explain this? Dominique Haumont identified ten points where NIDCAP impacts early developmental care, including assessment of pain, kangaroo care, and sleep organization.<sup>28</sup> The tenth point identified NIDCAP training as a tool for change. NIDCAP is not a prescribed protocol, instead NIDCAP implementation is said to be 'process-guided': a continuous process requiring flexible procedures and not procedurally-based attitudes. NIDCAP is also 'relationship-based' as it provides a new way of thinking about our relationships with the babies, the parents, and our colleagues. The third aspect is 'system-oriented' thinking as a change in any part of the system has an effect on the whole system.<sup>29</sup>

## Conclusion

- Research highlights the vulnerability of the developing brain in hospitalized newborns.
- Developmental care practices are evidence-based.
- A research-practice gap exists.
- NIDCAP could bridge this gap.

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