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Development of a pain monitoring device focused on newborn infant applications: The NeoDoloris project

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Abstract

Heart rate variability (HRV) reflects the autonomic nervous system activity on the organism. Sympathetic and parasympathetic influences in response to painful or stressful stimuli can be measured by the variations of RR intervals. After the elaboration of an automated index evaluating parasympathetic tone in adults (Analgesia Nociception Index, ANI), we choose to adapt this technology to neonates. A work system analysis of the maternity and the neonatal intensive care unit has established the needs for such an application and users’ requirements the application should meet. Based on these observations, neonatal applications have been developed for an automated analysis of neonatal HRV in high frequencies only (<0.15 Hz) which is representative of parasympathetic activity. Technical developments have resulted in two specific devices (one ambulatory and one monitor) displaying a unique index: the Newborn Infant Parasympathetic Evaluation (NIPE). Several clinical studies have been carried out and they have shown that the NIPE index is able to evaluate prolonged pain, acute pain, discomfort, and comfortable stimulations. The NIPE index assesses the parasympathetic tone and could be a good decision support for medical staff. Long term studies are needed in order to evaluate the neuro-developmental benefits of continuously parasympathetic evaluation on neonates.

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1. Introduction

In order to improve the quality of cares during hospitalization, pain assessment is essential for medical teams. In neonatology units, neonates are daily confronted to painful or stressful acts that could alter their later development [1]. Indeed, during the perinatal life, the stress could program the organism by a long-term programming of the hypothalamic-pituitary axis and lead to aberrant response to stressful stimuli later in life or in an increased risk to develop metabolic disorders [2–5]. Presently, pain and/or discomfort assessment is mainly based on behavioral pain scales. Medical teams have access to the Neonatal Facial Coding System (NFCS) [6], the Neonatal Acute Pain (Doulour Aiguë du Nouveau-né, DAN) [7], the Premature Infant Pain Profile (PIPP) [8] or the Neonatal Pain and Discomfort Scale (Echelle de Douleur et d’Inconfort du Nouveau-né, EDIN) [9]. However, with such scoring systems by items like facial movements, body movements or comfort ability, these scales are subjected to a huge inter and intra-observer variability.

Painful or stressful stimuli imply physiological events through the autonomic nervous system (ANS) influence. The ANS is a part of the central nervous system and is activated for the control and the regulation of involuntary bodily functions.

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It is divided in two arms; the sympathetic nervous system and the parasympathetic nervous system. Sympathetic fibers are stimulated during stressful situations and act directly on organs in favor of an adaptive response to an intern or extern stimuli. On the other hand, parasympathetic fibers are more activated during rest events like the digestion. These two arms are continually counter-balanced in order to maintain a homeostatic state; this is the notion of sympathetic–parasympathetic balance.

The real-time effect of the ANS on the body regulation is visible by the analysis of heart rate variability (HRV). Indeed, the variations in the time interval separating two heart beats reflect the ANS activity. The first interest on HRV was born 50 years ago, and from an important amount of research we are now able to say that in very low frequencies (≤0.04 Hz), HRV corresponds to thermoregulatory and endocrine systems like renin–angiotensin–aldosterone system. In the low frequencies (0.04–0.15 Hz), we can analyze both parasympathetic and sympathetic tones, and finally, in the high frequencies (0.15–0.4 Hz), only the parasympathetic activity is represented [10].

From these observations, the university hospital of Lille has developed algorithms allowing studying the ANS parasympathetic response to a painful stimulus; the Analgesia Nociception Index (ANI) [11]. Firstly tested in adult patients under general anesthesia [12–16], the ANI application has been extended to conscious patients, during delivery or in post-anesthesia care unit [17–19].

Regarding the good results obtained in adult studies with this HRV index and the need to assess pain objectively with young patients, we decided to adapt this new technology to the particular context of neonatology. In the frame of the ANR TECSAN 2011 NeoDoloris project, we therefore developed new monitoring devices adapted to the physiological and environmental particularity of newborns’ pain monitoring.

In a first step, this project aimed to define the needs of clinicians and nurses for the pain assessment in maternity and in neonatal intensive care units and to define users’ requirements for a pain monitor for the newborns clinical context. Based on the results of this work system analysis, the Human–Computer Interface and the technical design of an existing device and the ANI algorithm were adapted in order to obtain two dedicated medical devices. Finally, we used each device in different clinical settings in order to prove their efficiency.

2. Method

2.1. Analysis of the intended context of use

An analysis of the intended context of use has been perform to adapt the ANI technology for two particular clinical contexts where newborns’ pain monitoring is needed: the neonatal intensive care unit (NICU) and the maternity unit (MU). This is the first step of a usability engineering process that aims at “reducing, as far as possible, the risk of use error due to the ergonomic features of the device and the environment in which the device is intended to be used (design for patient safety, IEC 62366 norm in conformity with the European Union Medical Device Directive (Official Journal L 247) [20,21])”.

The study was carried out in the university hospital of Lille. Clinicians and nurses were interviewed and observed during their daily work in the NICU and in the MU. The first result of that study was that pain management differs from one clinical context to another. In MU, most of newborns are healthy at birth and do not need to be monitor in their first hours of life, except if they experienced complications during deliveries (cephalhemaetoma, fractures...). Painful acts are limited and not too much invasive. Contrary to MU, in NICU each patient is continuously monitored and pain evaluation is processed during all along the hospitalization [23]. The number of potentially painful or stressful procedures is around 10 acts/day/neonates [1] and it is essential to minimize the pain or discomfort feeling.

MU and NICU evaluate the neonatal pain in the same way, using clinical observations and behavioral pain scales (mainly EDIN [9]). However, MU medical staff acts when they see signs of pain and they administrate pain killer (acetaminophen) when needed (e.g. to newborns after assisted deliveries). On the other hand, NICU medical staff controls continuously the environment in order to avoid the discomfort and anticipates the treatment on the basis of the patient knowledge. This analysis of the intended context study allowed the adaptation by the technical teams to develop a monitor that corresponds to clinicians’ expectations. The design requirements issued from this study are presented in Table 1 [22].

2.2. Technical development

Following the clinical context of use study, we planned to develop two devices: an ambulatory monitor for puntual pain assessment for MU and a continuous monitor system for NICU.

The ambulatory monitoring device is based on the use of a photoplethysmographic sensor (easiest to positioned than ECG) in order to facilitate the sensor device installation. On the other hand, the NICU monitoring device collects the ECG signal through an analog link with the newborn’s multiparametric monitoring system in order to avoid the need of any additional sensor. Each device therefore integrates its own algorithm for heart beat detection.

Even if signal sources are different (ECG vs photoplethysmographic), the NIPE computation remains the same for the two devices.

Briefly, the NIPE index is based on continuous cardiac signal (ECG or plethysmographic waveform) processing. The detection of each heart beat is realized and the RR series is computed as the time evolution of the period between two heart beats. RR series are re-sampled at 8 Hz and mean centered and normalized in a 64 s moving window. A wavelet based high pass filter over 0.15 Hz is applied in order to keep parasympathetic related variations only, which are mainly influenced by the respiration cycle.

After RR filtering, local maxima and minima are detected in the 64 s window. Lower and upper envelopes are plotted in order to compute 4 areas under curves (one area/16 s: A1, A2,
Table 1
Main requirements concerning the neonatal application.

<table>
<thead>
<tr>
<th></th>
<th>MU</th>
<th>NICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device design</td>
<td>Implementing a medical device near babies who are supposed to be in good health may question the parents. Therefore, device’s design should be as “friendly” as possible.</td>
<td>The implementation of the device will not affect the parents’ feelings: therefore, its design may still be medical.</td>
</tr>
<tr>
<td>Data capture process</td>
<td>In MU, when a baby is monitored, the heart rate could be retrieved by the physiological monitor; however, most of the baby being not monitored, a data capture directly through ad hoc sensors would be required.</td>
<td>To avoid adding another sensor (already up to five), it would be preferable to retrieve data from an already implemented physiological monitor, e.g. electrocardiograph.</td>
</tr>
<tr>
<td>Transportability</td>
<td>It is plausible that one monitor will be used punctually for several patients. Moreover, babies are often moved inside and outside the unit. It is then mandatory that the device be easily transportable.</td>
<td>Due to continuous monitoring, each patient must have its “own” monitor. Since patients are rarely moved, the portability of the monitor is not an essential feature.</td>
</tr>
<tr>
<td>Interface and functions</td>
<td>To support the monitoring of the evolution of pain index while data are retrieved punctually, the device must allow (i) recording measures for each identified patient and (ii) displaying in an understandable way those punctual measures. It might be necessary to provide support for the index interpretation. The monitoring of the evolution of the index requires only a mid-long-term monitoring span to supervise the evolution of patients’ discomfort.</td>
<td>The monitoring of the evolution of the index must support very-short term (minutes range) and also mid- and long-term monitoring to allow clinicians managing pain according to therapeutic acts and also to supervise the evolution of patient’s discomfort.</td>
</tr>
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Note: From [22].

Fig. 1. Normalized and filtered RR series. A1, A2, A3 and A4 are computed between lower and upper envelopes. Lower area (AUCmin) is then selected and NIPE is computed.

A3 and A4, Fig. 1). AUCmin is detected as the minimum value of A1, A2, A3 and A4.

In order to obtain a value normalized between 0 and 100, we defined a Newborn Infant Parasympathetic Evaluation (NIPE) index as: NIPE = 100 * (5.1 * AUCmin + 1.2)/12.8.

Where 12.8 corresponds to the maximum area under the curve value (A1 + A2 + A3 + A4 = 64 * 0.2 = 12.8 cf. Fig. 1) and where the linear equation’s values (5.1 and 1.2) were defined empirically on a 200 patients population in order to keep a good correlation between the visual information and the numerical value.

In clinical practice, a NIPE close to 100 corresponds to a high level of comfort. On the opposite, a NIPE close to 0 can be interpreted to a very low comfort level which could be related to a high stress level. The algorithm is computed continuously by sliding the moving window with a 1 s moving period. NIPEmin is then computed as the record’s last 20 min mean value, but the software gives also a value of instantaneous NIPE (NIPEi) for short-term analysis of neonatal high frequencies HRV [23].

In an architectural point of view, the ambulatory monitoring system integrates a signal conditioning unit for the plethysmographic waveform acquisition, a Microchip DSPIC-33F (µP1), a mikromedia PIC24 graphic card (µP2) including a display unit and a lithium battery (Fig. 2).

µP1 integrates the plethysmographic waveform signal processing up to NIPE computation as described in the signal acquisition and processing section. Digitalized pulse wave samples, and NIPEi values are transmitted in real time to the second
microcontroller (µP₂) for data displaying; a specific user interface has been developed for NIPE ambulatory use (Fig. 3). This user interface allows continuous display of pulse wave. A bar graph displays NIPE instantaneous value, and elementary descriptive statistics of NIPE (min, max and mean) are displayed on the right side of the screen. Touch sensitive screen zones permit device and pulse wave gain re-initialization.

In an architectural point of view, the NICU monitoring system integrates a signal conditioning unit for the ECG signal acquisition, a Microchip DSPIC-33F (µP₁) and a touch screen panel PC (Fig. 4).

Digitalized ECG is transmitted in real time to the Panel PC for signal processing and data displaying: a specific user interface has been developed for NIPE use in NICU. This user interface allows continuous display of ECG, NIPE and a 20 min mean of the NIPE index (NIPEₘ). A bar graph displays NIPEₘ value. This interface also allows NIPE recording and trends visualization up to 72 h before (Fig. 5).

3. Clinical validation

The establishment of the feasibility and usability of the NIPE monitor is only possible if we test the two devices in clinical situations.

3.1. In NICU

Preliminary data revealed a good correlation between the NIPE index and the behavioral EDIN score. The authors studied the NIPE index on a population of preterm infants with a gestational age upper than 34 weeks (n = 28). Patients were included between 2 and 72 h after a major surgical procedure. HRV was recorded during 2 h and an EDIN score determination was made. Patients were subdivided in two groups: a “low EDIN” determined by an EDIN score <5 that corresponds to no significant pain or discomfort and a “high EDIN” group with an EDIN score ≥5 (maximal score 15) that reflects a significant discomfort or a painful patient. The NIPE index was significantly lower in the “high EDIN” group compared to the “low EDIN” group (P = 0.009). Moreover EDIN score and NIPE index were correlated (P < 0.01) [24].

In NICU, great cares are taken in order to avoid any environmental disturbances. The light intensity and the noise are controlled for better conditions of hospitalization. Treatments are administered daily to preterm infants in NICU. Some of them are pharmaceuticals (acetaminophen, opioids), but some non-pharmaceuticals techniques can be used like the administration of saccharose before a heel prick, the cocooning or the skin-to-skin contact [25,26]. The impact of cocooning associated to a reading by the mother or a third person was studied by Alexandre et al. on preterm infants in NICU with a gestational age of 37 weeks at the inclusion time. Ten infants were included and HRV was recorded 10 min before, during and 10 min after the cocooning + reading period. Results showed a great increase of the parasympathetic activity illustrated by the NIPE index when authors compared the values before and after cocooning (P < 0.05), without significant differences with a reading by the mother or by a third person [27].
3.2. In MU

The parasympathetic activity was evaluated during the first hours of life on full-term infants born by spontaneous vaginal deliveries or by assisted-vaginal deliveries (forceps, vacuum or both, n = 35 per group). The NIPE index and the EDIN score were studied. In the group of infants born by assisted-deliveries, the number of infants with an EDIN score ≥5 was significantly higher (P < 0.0001) and the NIPE index was significantly reduced (P = 0.005). Moreover, a significant inverse correlation between the NIPE index and the EDIN score was found (P = 0.016) (publication in progress).

In another study, the ambulatory device was used 2 months after birth on 14 infants. The aim of the study was to investigate the gate response to a noxious stimulus on infants born by assisted-deliveries. After a vaccination, infants showed an increased behavioral response to pain (determined by the DAN score) (P = 0.011) [7] and the NIPE index was significantly reduced (P = 0.008) (clinical study in progress).

4. Discussion

The development of new monitor devices with algorithms to evaluate the neonatal pain and/or discomfort was confirmed by clinical studies. Two applications have been developed in accordance with clinicians’ needs in MU and NICU. Studies aimed to show that NIPE index is adapted to reflect the parasympathetic activity have been performed within 4 situations: prolonged and acute pain assessment as well as discomfort, and comfort evaluation. The results presented above showed that the NIPE index is correlated to existing pain scales in different clinical settings for a preterm or a full term infants, and can be a new tool for medical staff with the goal of improving the development cares.

We detailed the efficiency of the NIPE index to detect prolonged pain in newborns with the study carried out with post- operative infants and with the pain assessment just after birth by forceps, vacuum or both [24]. The NIPE index is also able to show an increasing response of the parasympathetic part of ANS by non-pharmaceuticals acts like cocooning [27]. Further studies are needed in order to evaluate the response of the NIPE index to an acute pain in NICU.

The parasympathetic tone is severely reduced when infants were born prematurely [28]. The maturity of ANS is not completely achieved and contact stimulation like cocooning, skin-to-skin and massages have proved their efficiency on the improvement of ANS activity but also on feeding and growth [29–31]. Even if medical staff, particularly in NICU, takes care of neonates who spend a lot of time in hospital, it seems important to evaluate the parasympathetic activity of newborn.

The short term impact of neonatal parasympathetic tone assessment by the NIPE index has been proved. Now, we need to test the added value of the NIPE index in long-term neurodevelopment of preterm infants who benefit to nurses trained to interpret to NIPE index and act appropriately. A daily use of such devices could considerably improve the neonatal well-being in order to improve their long term neuro-developmental diagnosis. A prospective randomize study will start in the upcoming month in order to evaluate the clinical benefit of the NICU device use.

5. Conclusion

The HRV analysis method is non-invasive, and the NIPE index is an objective value that can be a good decision support for the medical staff. More clinical trials are needed if we want to know the long term clinical benefit of this technology. Following this project, two patents were deposited and the NICU monitoring system is EC marked and marketed since May 2014.

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References


