Résumé

Analyse de la structure des réponses à la douleur aiguë chez des nouveau-nés vulnérables

Bonnie Stevens, Linda Franck, Sharyn Gibbins, Patrick J. McGrath, Annie Dupuis et Janet Yamada
et par (en ordre alphabétique) Joseph Beyene, Carol Camfield, G. Allen Finley, Celeste Johnston, Karel O'Brien et Arne Ohlsson

Le but principal du projet était de déterminer la structure sous-jacente de la réponse du nouveau-né vulnérable à une intervention causant une douleur aiguë. Son but secondaire était d'analyser l'influence du contexte (p. ex. risque d'affection neurologique [AN] et âge gestationnel [AG]). L'étude d'une cohorte descriptive a permis d'établir le rôle des indicateurs sélectionnés relativement à la structure de la douleur chez le nourrisson. On a effectué une analyse de variance sur 19 indicateurs de la douleur à l'aide de trois analyses factorielles chez 149 nouveau-nés. La structure factorielle préliminaire comprenait des indicateurs comportementaux (p. ex. mouvements faciaux) et physiologiques (p. ex. saturation en oxygène, fréquence cardiaque). Les mouvements faciaux ont obtenu la variance la plus élevée pour toutes les solutions factorielles (29-39 %). Les indicateurs physiologiques expliquent 8 à 26 % de la variance additionnelle. On n'a observé aucune différence systématique entre les structures factorielles dans l'analyse des facteurs contextuels.

Mots clés : Nourrisson, douleur, évaluation, indicateurs, analyses factorielles

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Determining the Structure of Acute Pain Responses in Vulnerable Neonates

Bonnie Stevens, Linda Franck, Sharyn Gibbins, Patrick J. McGrath, Annie Dupuis, and Janet Yamada

and (in alphabetical order) Joseph Beyene, Carol Camfield, G. Allen Finley, Celeste Johnston, Karel O'Brien, and Arne Ohlsson

The primary purpose was to determine the underlying structure of the vulnerable infant's response to an acute painful procedure. The secondary purpose was to explore the influence of context (e.g., risk for neurological impairment [NI] and gestational age [GA]). A descriptive cohort design determined contributions of selected indicators to the structure of infant pain. The magnitude of variance for 19 pain indicators was assessed using 3 exploratory factor analyses in 149 neonates. The basic exploratory factor structure included behavioural (e.g., facial actions) and physiological (e.g., oxygen saturation, heart rate) indicators. Facial actions accounted for the greatest variance across all factor solutions (29–39%). Physiological indicators explained 8 to 26% additional variance. There were no consistent differences in the factor structures when contextual factors were explored.

Keywords: Infant, pain, assessment, indicators, factor analyses

Introduction

Pain assessment has become a standard of care for hospitalized patients. Although there has been a rapid proliferation of infant-pain measures over the past 2 decades, many of these instruments fall short of rigorous psychometric standards and are proliferated at the expense of refining existing measures that show promise. The most reliable and valid measures have been used to systematically evaluate pain-relieving interventions (Bellu, de Waal, & Zanini, 2005; Shah, Aliwalas, & Shah, 2006; Stevens, Yamada, & Ohlsson, 2004) and to provide evidence for the development of professional infant-pain guidelines and standards (Anand et al., 2006; Batton, Barrington, & Wallman, 2006). However, as clinicians become increasingly challenged with assessing acute pain in populations of infants who are extremely premature, of low birth weight, severely ill, or at risk for neurological or physical impairment, the question arises as to whether the way in which existing acute-pain

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measures are constructed is appropriate for assessing and managing pain in these vulnerable populations. To address this issue, contributions of indicators in real pain situations experienced by vulnerable infants can be examined and the underlying structure of existing measures explored.

Most frequently, measures of acute infant pain consist of multiple behavioural indicators or a composite of behavioural and physiological indicators. In the development of these measures, individual indicators of pain have been carefully generated, evaluated, and reduced based on observations of healthy preterm (Craig, Whitfield, Grunau, Linton, & Hadjistavropoulos, 1993; Holsti, Grunau, Oberlander, & Whitfield, 2004), term (Gibbins & Stevens, 2003), and older infants (Johnston, Stevens, Craig, & Grunau, 1993; Johnston, Stevens, Yang, & Horton, 1996), most often using heel lance as the pain stimulus. The majority of these measures consist of behavioural (e.g., facial actions, cry, body motions) and physiological (e.g., heart rate, respiratory rate, oxygen saturation, blood pressure) indicators. A few infant measures, such as the Premature Infant Pain Profile (PIPP; Stevens, Johnston, Petryshen, & Taddio, 1996), take contextual factors (e.g., gestational age [GA] and behavioural state) into account. Other examples include the Neonatal Infant Pain Scale (NIPS; Lawrence et al., 1993) where state of arousal is considered and the Neonatal Pain, Agitation and Sedation Scale (NPASS; Hummel, Puchalski, Creech, & Weiss, 2003) where pain scores are adjusted for GA, similar to the PIPP.

Consistent with the development of pain scales for individuals across all age groups, developers of most infant-pain scales have assumed that individual behavioural, physiological, and contextual indicators contribute equally to the infant's pain experience, as depicted in the particular instrument's scoring system. This assumption of equal contributions may preclude a comprehensive understanding of the underlying pain construct, which is known to be multidimensional (e.g., sensory, affective, and cognitive dimensions) in adults (Melzack & Casey, 1968; Price, 1999), or how indicators may be individually or collectively influenced by contextual factors (i.e., GA at birth and NI risk) that render the infant vulnerable. Thus, we are uncertain whether existing pain measures, which were most often developed with more mature and healthy neonates, are appropriate for use with vulnerable infant populations in the NICU.

The primary purpose of this study was to determine the underlying structure of the infant's response to an acute painful event. The secondary purpose was to explore the influence of two contextual factors: risk for NI and GA. Ultimately, the aim was to determine whether existing pain measures can be used with vulnerable infants.

Methods

Study Design and Sample

A descriptive cohort design was employed. Data were originally collected to compare the behavioural and physiological responses to painful procedures in infants at high, moderate, and low risk for NI (Stevens, McGrath, et al., 2007).

The sample comprised 149 neonates (GA > 25–40 weeks) at high (cohort A: $n = 54$), moderate (cohort B: $n = 45$), and low (cohort C: $n = 50$) risk for NI from three tertiary-level NICUs in Canada. Eligible neonates were: (a) hospitalized in the NICU, (b) > 25 weeks gestational age at birth, and (c) < 6 weeks of postnatal age. Maternal heroin or methadone addiction (defined by a history of active drug intake within 72 hours before delivery or a positive urine test from maternal urine) and pharmacologically induced paralysis in the infant precluded inclusion in the study.

Infants who met the inclusion criteria were stratified into three previously validated cohorts for NI (Stevens et al., 2003) defined as:

Cohort A: at high risk for NI — for example, perinatal asphyxia, IVH (Grade III or IV), or a syndrome or chromosomal anomaly

Cohort B: at moderate risk for NI — for example, acute disease processes such as persistent pulmonary hypertension of the newborn, severe meconium aspiration, meningitis, hydrocephalus, necrotizing enterocolitis

Cohort C: at low risk for NI — for example, respiratory distress requiring ventilation, sepsis.

Estimating inclusion of approximately 30 behavioural (facial actions, body movements, cry) and physiological (heart rate, oxygen saturation, heart rate variability [HRV]) indicators and using five subjects per variable, we concluded that 150 infants, or 50 per risk group, were required.

Pain Response Indicators

Of the originally estimated 30 indicators, 19 formed the basis for this analysis — 10 behavioural (7 facial action indicators, 3 cry indicators) and 9 physiological (3 oxygen saturation, 3 heart rate, 3 HRV). These indicators were selected based on their repeated validation across infant-pain measurement research. Each indicator was assessed in response to a routine heel-lance procedure in a standardized method described previously by Stevens, McGrath, et al. (2007). Of the original 30 indicators, 11 were excluded, for a variety of reasons. For example, although previous studies may have included all possible facial actions in the Neonatal Facial Coding System (NFCS) (Craig, Hadjistavropoulos, Grunau, & Whitfield,

1994; Grunau, Johnston, & Craig, 1990; Lilley, Craig, & Grunau, 1997), we included only 7 (brow bulge, eye squeeze, nasolabial furrow, open lips, vertical mouth stretch, horizontal mouth stretch, and taut tongue). Chin quiver and lip purse were removed from the analysis as 132/138 non-missing values recorded for this group of infants were 0 (indicating no facial action). Total facial action was excluded as this variable is obtained from a linear equation of other variables and therefore did not add any new information to the factor analysis. Body movements were excluded due to the poor feasibility of collecting data on body movements while bundling or containing the infant to conduct the heel lance and to accurately collect physiological data, in particular HRV data.

Data Collection

Data on behavioural and physiological indicators were collected using procedures previously developed and validated by Stevens and others (Stevens et al., 2003; Stevens, Pillai Riddell, Oberlander, & Gibbins, 2007). *Facial actions* were videotaped using an 8mm camcorder (Sharp, Panasonic, or Sony). Facial actions were coded according to the NFCS coding scheme (Grunau & Craig, 1987) by two trained research assistants on a second-to-second basis using videotapes replayed in real time. Each session was scored repeatedly for each facial action using laptop computer software written in BASIC that recorded the scores and allowed for information on artifacts to be included. A final score was calculated based on percentage of time the action was present for the block of time of interest. Intrarater and interrater reliability of 95% in videotape scoring has been consistently reported (Stevens et al., 2003).

Cries were audiotaped using a Sennheiser unidirectional microphone connected to a Sony 500 high-frequency audiotape recorder with an event-marking tone generator. A research assistant conducted cry analyses using CSPEECH (Milenkovic, 1998). The first cry from the stick phase of the heel lance was digitized at 20 kHz using a 16-bit analogue-to-digital converter and low-pass filtered with a high-frequency cut-off of 10 kHz to avoid aliasing. Cry analysis from Fast-Fourier transform spectroscopy was performed using a Pentium microcomputer with C-SPEECH SP that was modified to accommodate fundamental frequencies up to 4 kHz. Cries were analyzed by pitch, which is precisely measured as fundamental frequency (F_0). Intrarater reliability was 98%. Mean, minimum, and maximum F_0 were included in the analysis.

To collect *physiological indicators,* disposable ECG electrodes and pulse oximetry probes were placed on the infants and ECG, respiratory rate, and oxygen saturation were continuously recorded using a cardio-respiratory monitor and personal computer (1000 Hz sampling rate). Physiological indicators were recorded using a pulse oximeter (Nellcor

Pulse Oximeter, Model N-3000, Hayward, CA) and the SATMASTER data-collection system (EMG, Los Angeles). ECG segments of 128 seconds in the baseline/warming and immediate post-procedure/return to baseline phases were edited, linearly detrended, and analyzed for power spectral density using HRView software (Boston Medical Technologies, Boston). Data were recorded second-to-second and sampled at 100 Hz. Signals, digitalized in the pulse oximeter, were downloaded onto a personal computer. Standards defining specific frequency bandwidths commonly used to characterize and study power spectral analysis of HRV in infants were followed. Normalized power spectral values were calculated and reported for high-frequency power (0.15–1 Hz), low-frequency power (0.04–0.15 Hz), and the ratio of low-/high-frequency power.

Data on GA and NI risk status were retrieved from the infant's medical record.

Data Management and Statistical Analyses

A careful examination of all data indicators was undertaken and reasons for missing and unavailable data were ascertained. Data existed on 148/149 babies for all heart-rate indicators and on 146/149 babies for oxygen-saturation indicators. A difference score was created comparing baseline and stick phases of the heel-lance procedure and reported as such (e.g., mean HR difference). Of the 149 babies, HRV data were available for 106. Missing HRV data were attributable to movement artifact.

Complete facial action data were obtained on 135/149 babies with exclusion of the Taut Tongue indicator, where data existed for 129 babies. As Taut Tongue can be visualized only when infants have their mouth open, it is understandable why the coders could not view Taut Tongue in some infants. Cry data were available for 82/149 infants; the remainder did not cry. The incidence of crying in response to heel lance in preterm and sick babies has been noted previously as approximately 50% (Gibbins, Stevens, McGrath, & Yamada, 2007; Harrison, Johnston, & Loughnan, 2003).

A series of exploratory factor analyses with orthogonal transformation and varimax rotation were conducted. All factors with eigenvalues greater than 1.00 were included in the analyses; all indicators loading on factors > 0.4 were reported (Streiner & Norman, 2003). Factor analyses were first conducted on the total population of infants to address the primary research purpose. Sub-analyses were conducted by NI cohort groups and by GA age (i.e., two cohorts above and below the median number of weeks GA (31 weeks) to begin to explore the influence of contextual factors.

Table 1 *Summary of Factor Solutions Using Total Infant Samples*

Sample	Factor Solution	Eigenvalue	Rotated Factor Patterns, Indicators, and Proportion of Factor Variance
1. Total Sample with FA, HR, O2 (n = 124)	4 factors accounting for 93% of total variance	Factor 1 = 3.87 Factor 2 = 2.46 Factor 3 = 1.92 Factor 4 = 1.06	Factor 1 (FA) = 39% Factor 2 (O2 diff) = 25% Factor 3 (HR diff) = 19% Factor 4 (FA) = 11%
2. Total Sample with FA, HR, O2, HRV (n = 83)	5 factors accounting for 95% of total variance	Factor 1 = 4.29 Factor 2 = 2.66 Factor 3 = 1.64 Factor 4 = 1.55 Factor 5 = 1.02	Factor 1 (FA + min HR diff) = 36% Factor 2 (O2 diff) = 22% Factor 3 (FA) = 14% Factor 4 (HRV) = 13% Factor 5 (mean/max HR diff) = 8%
3. Total Sample with FA, Cry, HR, O2, HRV (n = 40)	5 factors accounting for 89% of total variance	Factor 1 = 4.51 Factor 2 = 3.95 Factor 3 = 1.94 Factor 4 = 1.74 Factor 5 = 1.32	Factor 1 (FA + min/mean HR diff) = 29% Factor 2 (Cry) = 26% Factor 3 (min/mean/max O2 diff + mean HR diff) = 13% Factor 4 (HRV) = 11% Factor 5 (FA) = 8%

FA = Facial Actions; HR = Heart Rate; O2 = Oxygen Saturation; HRV = Heart Rate Variability; diff = difference.

Results

Due to missing and unavailable data (i.e., from infants who did not cry and where HRV data were not available because infants were moving or crying), three separate factor analyses were performed on the total sample based on available data to address the primary research objective: sample 1, based on no missing data when the three cry and three HRV indicators were excluded (n = 124); sample 2, with no missing data when the three cry indicators were excluded (n = 83); and sample 3, with no missing data on any of the 19 variables (n = 40). Factor solutions, eigenvalues, the percentage of variance accounted for, rotated factor patterns, and the specific indicators (and proportion of additional variance) loading on individual factors are described in Table 1.

The factor solution from sample 1 was considered the most defensible due to the adequacy of the sample size. This solution represented the basic exploratory factor structure; key factors represented behavioural (i.e., facial activity) and physiological (i.e., oxygen saturation, heart rate) components of the infant's pain response. All three factor analyses involving the total sample resulted in either four or five factor solutions and accounted for 89 to 95% of the total variance. In each analysis, Facial Actions constituted the factor that accounted for the most variance (29–39%). In two of these analyses, this factor also included one of the heart-rate variables. Factors representing Oxygen Saturation, Cry, and HRV accounted for less variance in the factor solutions than Facial Actions but added anywhere from 8 to 26% additional variance to that resulting from Facial Actions.

To address the secondary research objective, we explored the influence of contextual variables (i.e., NI risk status and GA) on factor solutions. Individual factor analyses were conducted on sample 1 of the total sample only where 50 infants were in cohort A (high risk for NI), 39 were in cohort B (moderate risk for NI), and 35 were in cohort C (low risk for NI) (Table 2). Consistent with the basic exploratory factor structure, in each NI risk cohort Facial Action accounted for the most variance (38–42%) in infant pain response, with oxygen saturation and heart rate representing 20 to 27% and 11 to 20%, respectively, of the additional variance. Cry indicators and HRV indicators were not included in these factor solutions due to the limited amount of data on these variables.

A similar analysis was conducted to determine whether factor solutions varied by GA for infants who were less than and more than 31 weeks GA. No differences in factor solution or structure existed between the groups.

Table 2 *Summary of Factor Solutions Using Cohorts by Neurological Impairment (NI) Risk Status*

Sample	Factor Solution	Eigenvalue	Rotated Factor Patterns, Indicators, and Proportion of Factor Variance
Total Sample with FA, HR, O2 (n = 124)			
Cohort 1: high risk for NI (*n* = 50)	4 factors accounting for 93% of total variance	Factor 1 = 4.28 Factor 2 = 2.02 Factor 3 = 1.98 Factor 4 = 1.14	Factor 1 (FA) = 42% Factor 2 (FA) = 20% Factor 3 (min/mean/max O2 diff) = 20% Factor 4 (min/mean/max HR diff) = 11%
Cohort 2: moderate risk for NI (*n* = 39)	4 factors accounting for 90% of total variance	Factor 1 = 4.03 Factor 2 = 2.26 Factor 3 = 2.06 Factor 4 = 1.20	Factor 1 (FA) = 38% Factor 2 (min/mean/max O2 diff) = 21% Factor 3 (min/mean/max HR diff) = 20% Factor 4 (FA) = 11%
Cohort 3: low risk for NI (*n* = 35)	3 factors accounting for 85% of total variance	Factor 1 = 4.46 Factor 2 = 2.82 Factor 3 = 1.64	Factor 1 (FA) = 42% Factor 2 (min/mean/max O2 diff) = 27% Factor 3 (min/mean/max HR diff) = 16%

FA = Facial Actions; HR diff = Heart Rate difference; O2 diff = Oxygen Saturation difference; HRV = Heart Rate Variability.

Discussion

The development of infant pain assessment measures has expanded greatly in the past 2 decades, in response to demands for increasingly comprehensive standards of care and the need to increase our understanding of pain in neonates. However, many of these measures are devastatingly shy of being satisfactorily validated. The general developmental approach has been to utilize either multidimensional behaviour measures or a composite of behavioural and physiological indicators that, if validated, was undertaken in the healthiest infants in NICUs or from older populations where the most appropriate indicators are customized into measures for neonates. For example, the multidimensional behavioural NFCS (Grunau & Craig, 1990), consisting of 10 facial actions, was developed from the 44-facial-action Facial Coding System (Ekman & Friesen, 1978). Other researchers further adapted the original measures, added or deleted indicators, and established the construct validity with a different population of infants or a new pain paradigm. Stevens et al. (1996), in the PIPP, combined the three most frequently displayed facial actions from the NFCS with physiological (i.e., heart rate, oxygen saturation) and contextual (i.e., GA, behavioural state) indicators where sufficient evidence existed to support the construct of pain or factors known to influence it. In the original PIPP, factor analyses were performed on 124 preterm infants aged 32 to 34 weeks GA to determine the underlying structure of selected pain indicators. The three facial actions (Brow Bulge, Eye Squeeze, Nasolabial Furrow) accounted for 42.4% of the variance. An additional 35.8% of the variance was explained by physiological activity (19.1%) and behavioural state (16.7%), explaining 78% of the total variance (Stevens et al., 1996). These findings are consistent with those of the current study on the underlying structure of pain indicators, where up to 40% of the variance was explained by Facial Actions.

Pain assessment is now a standard component of care for all infants, including more vulnerable populations of infants (e.g., infants with low, very low, and extremely low birth weight; infants who are neurologically, physically, and pharmacologically compromised; and infants who may be critically ill or receiving end-of-life care). However, questions remain as to whether the underlying structure of the acute-pain response is similar in the population with whom the measures were developed. Ultimately, this knowledge could assist in determining whether existing measures are applicable for assessing pain in these infants or whether new indicators are warranted.

In the present analyses, Facial Actions consistently accounted for the maximum amount of variance amongst all indicators examined, across all factor solutions. These Facial Action factors were not identical in terms

of the indicators that loaded onto them or their individual indicator weightings. Most often, Brow Bulge, Eye Squeeze, and Nasolabial Furrow had amongst the highest loadings on the Facial Action Factor. However, given the limited sample sizes and the varying amounts of missing or unavailable data, it would not be prudent to delve into this depth of analysis or to make broad and sweeping conclusions about particular Facial Actions from these data. Similar and consistent results across these analyses and previous analyses (Stevens, McGrath, et al., 2007) suggest with some certainty that Facial Actions are the most important but not the only contributors to the assessment of acute pain in neonates.

In two of the factor solutions, one or more of the Heart Rate indicators loaded with the most heavily weighted facial actions. However, Heart Rate indicators also loaded on a separate factor that accounted for varying amounts of significant variance. This result may reflect the lack of specificity in pain responses in infants, especially in distinguishing it from the more global concept of stress.

Although predominant, the leading factor containing the Facial Action indicators (and sometimes one or more of the Heart Rate indicators) accounted for approximately 40% of the total variance, when up to 95% of total variance was explained by the three to five factors in the factor solutions. Indeed, the remaining two to four factors, in any given solution, contributed important additional information in terms of the total explained variance, up to approximately 25% and rarely less than 10%. This finding was consistent across factor solutions, supporting the claim that a composite of indicators contributed to the overarching construct of infant pain.

Until recently, our knowledge of the mechanisms of pain in neonates was limited primarily to our understanding of nociception and pain responses at the periphery and at the level of spinal activation. Recently, Bartocci, Bergqvist, Lagercrantz, and Anand (2006) and Slater et al. (2006) explored cortical responses to a painful stimulus using Near Infrared Spectroscopy (NIRS). The primary hypothesis in each of these studies was that acute pain would cause hemodynamic changes associated with activation of the somatosensory cortex. Slater et al. noted that noxious stimulation via heel lance produced a clear cortical response, measured as an increase in total hemoglobin concentration in the contra-lateral somatosensory cortex in infants as young as 25 weeks GA. Similarly, Bartocci et al. noted increases in hemoglobin concentrations in both hemispheres following tactile stimulation with further significant increases followed by noxious stimulation (i.e., venipuncture). These data suggest that noxious information is being transmitted to the neonatal cortex from 25 weeks GA, highlighting the potential for higher-level pain processing and potentially pain perception. Therefore, determination

of specific pain indicators at very early GA may be necessary to supplement or replace existing acute-pain indicators.

No categorical differences were noted in factor loadings or factor solutions by either GA or NI risk status in this study. This suggests that, in this early exploratory work to determine the influence of contextual variables, there is no difference in the underlying structure of the responses, although the magnitude of actual responses is not captured. We need to be very cautious in interpreting this result due to the limited sample sizes for the subanalyses involving these cohorts. In our previous research (Stevens, McGrath, et al., 2007), using regression analyses, the magnitude of facial actions in infants at the least risk for NI (cohort C) was greater following the pain stimulus. A significant cohort by phase (of the heel lance) interaction existed for total facial expression ($F[6,409] = 3.50$, $p = .002$), and four individual facial actions. Cohort B had higher minimum ($F[2,79] = 3.71$, $p = .029$) and mean ($F[2,79] = 4.04$, $p = .021$) cry pitch. A significant phase effect existed for low- and high-frequency HRV ratio ($F[2,216] = 4.97$, $p = .008$), with the greatest decrease in cohort A. Significant cohort by phase interactions were found for low- and high-frequency HRV. Overall, all infants responded to the most painful phase of the heel lance; however, infants at moderate and high risk for NI demonstrated decreased intensity of responses on some indicators. These results indicate that the underlying structure of the response was consistent. Factors such as severity of illness, time since previous painful procedures, and current medication status may be important to consider in terms of the situational context.

No differences in factor solutions were noted in the two groups of infants defined by GA greater than and less than 31 weeks. Gibbins et al. (2007) report that responses to painful procedures in infants with extremely low birth weight (i.e., < 28 weeks GA) were similar across behavioural and physiological responses, compared to older infants, but the responses were proportional to GA, with the youngest infants showing the least amount of change. Infants less than 28 weeks GA had significantly lower minimum oxygen saturation and higher minimum heart rate following a heel lance than infants greater than 28 weeks GA. When controlling for NI risk status, GA was still a significant factor in responsiveness. The categorization of age cohorts (i.e., greater than and less than 31 weeks GA) or the particular pain indicators used for the comparisons, although developmentally defensible, may have influenced these analyses in light of the small cohort sizes.

Overall, the results are generally consistent with the underlying structure of the PIPP and with the multivariate composition of existing composite infant-pain measures. Greater variance was explained when additional indicators such as cry characteristics and HRV were added in

the factor solutions, although the populations examined in relation to the influence of context were small. Therefore, the conclusions need to be considered with caution. The results are limited by the contextual variables included in these analyses. Further research, including additional and novel pain behavioural and physiological indicators and contextual variables beyond NI risk status and GA, should be considered, especially with infants who are the most immature, critically ill, fragile, or vulnerable.

The research is also constrained by the pain indicators that were selected for entry into this factor analysis in consideration of the sample size. Many other behavioural and physiological variables could have been included; behavioural indicators such as finger splay and fisting (Holsti et al., 2004) and physiological indicators such as cortisol, hemodynamic intracranial pressure changes, and palmer sweating may also be important to consider in the youngest age group of infants. In previous measurement research by Stevens and others (Stevens et al., 1996), the potential list of available indicators was minimized based on sensitivity and specificity, high correlations with other indicators, and feasibility (for an in-depth discussion on selection of pain indicators in infants, see Stevens, Pillai Riddell, et al., 2007).

Indicators (e.g., cry) that were included in this study are also problematic when assessing pain in infants. Except for mechanical ventilation, which precludes the infant's ability to voice a cry, we continue to be perplexed as to why particular infants fail to cry following a heel lance. The complexity of issues surrounding cry has frequently rendered cry a questionable indicator for inclusion in infant pain-assessment measures. This rationale is not sufficient for removing cry from our potential list of infant-pain indicators and for failing to study other cry characteristics in addition to fundamental frequency (pitch) and duration. Peak spectral energy, phonation, jitter, and other temporal characteristics (latency, expiration, pause, inspiration, rhythmicity) should also be explored in future cry analyses.

This research is relevant in light of the directions for research proposed by Anand et al. (2006), where the search for a gold standard in pain assessment is still paramount. At present, this research, in addition to work by Gibbins et al. (2007) and others, suggests that these infants' pain responses in terms of facial expression, heart rate, and oxygen saturation are consistent (although dampened) with their more mature counterparts and therefore may serve as a useful starting point for assessment of acute pain. Results from our explanatory factor analyses can also be helpful in guiding future confirmatory factor analyses that may be undertaken to test specific hypotheses regarding the number of factors, factor loadings, and factor intercorrelations.

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Comments or queries may be directed to Bonnie Stevens, Associate Chief of Nursing Research, Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8 Canada.

Bonnie Stevens, RN, PhD, is Professor, Lawrence Bloomberg Faculty of Nursing and Faculty of Medicine, University of Toronto; and Signy Hildur Eaton Chair in Paediatric Nursing Research and Associate Chief of Nursing Research, Hospital for Sick Children, Toronto, Ontario, Canada. Linda Franck, RN, PhD, is Professor and Chair, Children's Nursing Research, UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom. Sharyn Gibbins, RN, PhD, is Director, Interdisciplinary Research, Sunnybrook Health Sciences Centre, Toronto. Patrick J. McGrath, OC, PhD, FRSC, FCAHS, is Professor of Psychology, Pediatrics, and Psychiatry and Canada Research Chair, Dalhousie University; and Psychologist and Vice-President, Research, IWK Health Centre, Halifax, Nova Scotia, Canada. Annie Dupuis, PhD, is Biostatistician, Research Institute, Hospital for Sick Children, Toronto. Janet Yamada, RN, MSc, is Research Associate, Research Institute, Hospital for Sick Children.

Joseph Beyene, PhD, is Biostatistician, Research Institute, Hospital for Sick Children. Carol Camfield, MD, FRCPC, is with the Department of Pediatric Neurology, IWK Health Centre. G. Allen Finley, MD, FRCPC, FAAP, is Medical Director, Pediatric Pain Management, IWK Health Centre. Celeste Johnston, RN, DEd, is James McGill Professor, School of Nursing, McGill University, Montreal, Quebec, Canada. Karel O'Brien, MB, FRCPC, and Arne Ohlsson, MD, FRCPC, are with the Department of Pediatrics, Mount Sinai Hospital, Toronto.