***Review Article***

# The skin conductance-based non-invasive pain assessment instrument for infants

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## Introduction

Implementation of pain management in hospitalised infants encounters problems due to inadequate pain assessment in painful procedures, lack of knowledge of pharmacological / non-pharmacological pain management and inconsistency in implementing correct pain management techniques. Thus, the infant's pain is often either over-treated or under-treated. Recent evidence indicates that the fetus and newborn can feel and respond to painful stimuli[1]. The infant's pain response is higher than in adults due to an immature inhibitory function resulting in low pain tolerance[2].

Assessment of pain in an infant is challenging because he or she cannot express pain clearly. Measurement of pain in infants has been conducted using subjective tools and has relied on idiosyncratic factors and cognitive biases in health workers. To minimize this, currently used machine-based tools can improve consistency, utilise objectivity and promote effectiveness[3]. Skin conductance (SC) is a non-invasive method for measuring pain in infants. Studies show increasing use of SC to measure infant pain in the past several years[4]. Many recent studies find SC to be an objective[5], simple, non-invasive, rapid and accurate tool to detect autonomic reflex function in the neonate[6].

This review of infant pain measurement and SC-based pain measurement is derived from database publications Springer, Sage, Oxford, and Wiley. All articles were searched by keywords and Booleans. Data extraction was carried out based on the theme determined by researcher, specifically an overview of basic pain in an infant, pain response, SC, electro-dermal activity (EDA), measurement procedures, parameter analysis and comparison with other pain-related physiological and behavioural scales.

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## Basic review of pain in infants

International Association for Study of Pain (IASP) has updated the definition of pain to clarify that "the inability to communicate verbally does not negate the possibility that an individual is experiencing pain". Another perspective states that "pain in infants is the inherent quality of life that appears early in ontogeny to serve as a signalling system for tissue damage; measurement of neonatal pain is highly dependent on the observer's judgment and indicators in the signalling system must be subjectively observed and determined by others"[7]. Injury early in life provides learning about pain in individuals. Infants already have a complete organ structure, both anatomically and functionally, to feel pain and be able to respond to pain by showing changes in behaviour. This behavioural change is interpreted as infant pain. Pain in infants is the result of a complex interaction between the signalling system and modulation system of the central nervous system (CNS) caused by the stimulus (tissue damage/injury), causing discomfort in the infant's perceptions and sensation, so demonstrating physical, behavioural, and biochemical responses.

## Infants' pain mechanism

Nociception is a physiological mechanism involved in the pain phenomenon. It depends on the ability of the nerves to detect the presence of stimuli (harmful / noxious) and send information containing these stimuli to the brain for interpretation. Nociception does not require conscious reports from the body to feel pain. It provides a precise description of a baby's response caused by tissue-impaired stimuli from the body[8]. The level and character of an infant's pain response is age-dependent. After birth, nociceptors (peripheral pain receptors) that respond to mechanical, thermal and chemical stimuli, and peripheral sensitization (primary hyperalgesia) will

develop in areas of tissue injury. Nociceptors will be activated specifically by pain / noxious stimuli. The receptors transduce the hazard information into electricity and transmit it from the periphery to the CNS along the nerve axons. The presence of these inflammatory mediators saturates and activates nociceptors, making them more sensitive. There are two main types of fibres, A-delta and C. The routes of all pain fibres vary to the endpoint but their final location is the posterior horn. The pain pathway connects peripheral receptors to the spinal cord and are transmitted from the spinal cord to the thalamus and the external cerebral layer. Individuals experiencing pain require a complete pain transmission system[9].

**Pain response in infants**

Pain response in neonates and infants is related to contextual, behavioural, physiological / autonomic and biochemical aspects[2,3] (Table 1).

**Table 1:** ***Infant's pain response and indicators***

| Contextual | Behavioural | Physiological / autonomic | Biochemical |
|---|---|---|---|
| *Age*<br>Gestational age<br>Postnatal age | *Vocalization*<br>Crying sound / time | *Vital signs*<br>Heart rate<br>Respiratory rate<br>Periphery skin temperature | *Increased norepinephrine* |
| *Weight* | *Facial expression* | *Brain dynamic*<br>Intracranial pressure<br>Cortical activity | *Increased epinephrine* |
| *Health state*<br>Illness severity | *Body movement*<br>Gross motor movement<br>Flexion reflex to body core | *Palmar sweating* | *Increased glucagon* |
| *Therapeutic*<br>Intervention: Analgesic use | *Awakening-sleep cycle* | *Oxygen saturation* | *Increasing corticosteroid* |
| *Pain experience*<br>Number of previous procedure | | *Vagal tone* | *Decreasing prolactin* |
| *Gender* | | *Periphery blood flow* | *Decreased insulin level* |
| *Behavioural state* | | *Skin conductance activity* | *Decreased immunity* |
| *Caregiver*<br>Parent<br>Healthcare professional | | *Muscle activity* | *Increasing corticosteroid* |

**Infant pain assessment**

Pain measurement when carried out in a suitable population will increase accuracy (Figure 1). Strategies for using pain assessment tools in pre / non-verbal individuals are shown in Figure 2

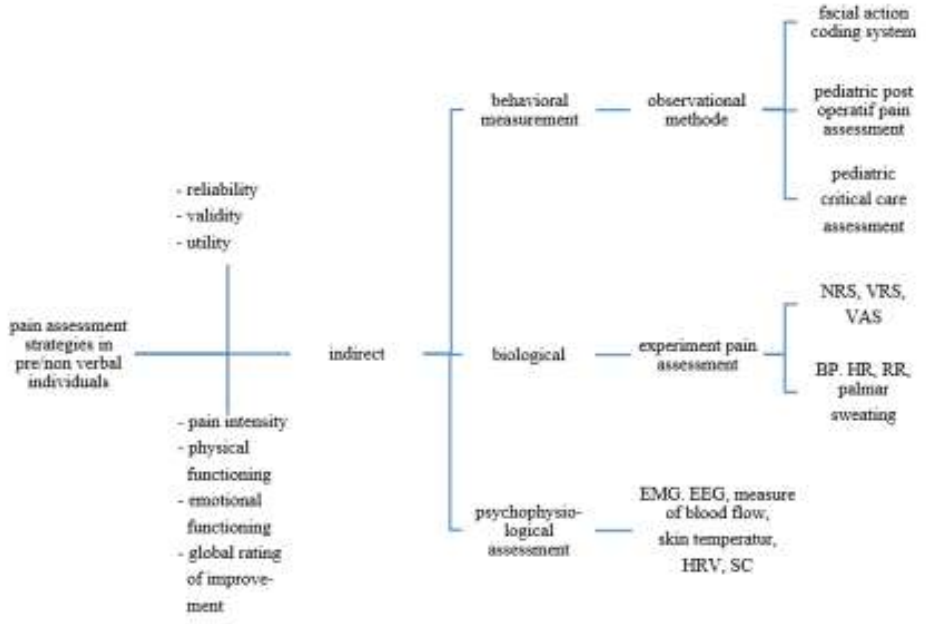


**Figure 1:** ***Strategies for using pain assessment tools in pre/non-verbal individual***

*NRS: Numeric rating scale, VRS: Visual rating scale, VAS: Visual analog scale, BP: Blood pressure, HR: Heart rate, RR: Respiratory rate, EMG: Electromyography, EEG: Electroencephalography, SC: Skin conductance*

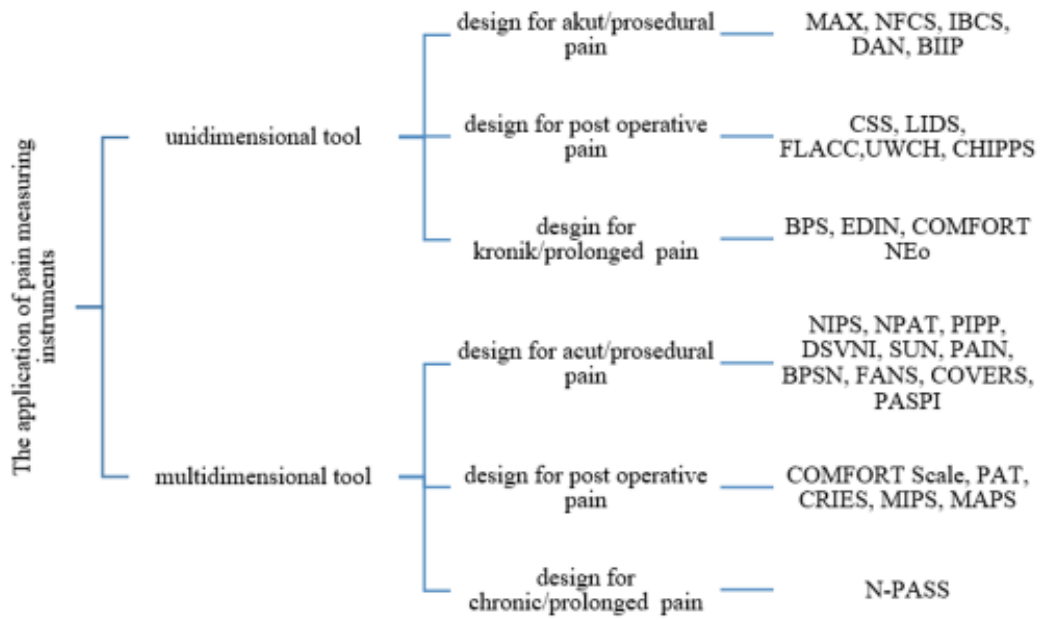


**Figure 2:** ***The application of pain measuring instruments based on the infant's pain cases***

*MAX: Maximally discriminative facial coding system, NFCS: Neonatal facial coding system, IBCS: Infant body coding system, DAN: Acute pain in newborn, BIIP: Behavioural indicator of infant pain, CSS: Clinical scoring system, LIDS: Liverpool infant distress scale, FLACC: Face, legs, activity, cry, consolability, UWCH: University of Wisconsin Children's Hospital pain scale, CHIPPS: Children's and infant's postoperative pain scale, BPS: Behavioural pain score, EDIN: Neonatal pain and discomfort scale, NIPS: Neonatal infant pain scale, NPAT: Neonatal pain assessment tool, PIPP: Premature infant pain profile, DSVNI: Distress scales for ventilated newborn infants, SUN: Scale for use in newborns, PAIN: Pain assessment in neonates, BPSN: Bernese pain scale for neonates, FANS: Faceless acute neonatal pain scale, COVERS: COVERS neonatal pain scale, PASPI: Pain assessment scale for preterm infants, PAT: Pain assessment tool, CRIES: Crying, requires O2 for saturation, increased vital signs (heart rate and blood pressure), expression, sleepless, MIPS: Modified infant pain scale, MAPS: Multidimensional assessment pain scale,* N-PASS: *Neonatal pain, agitation and sedation scale*

Pain assessment should be based on self-report and observational, behavioural and physiological indicators[10]. Neonates and infants react to pain by behavioural, biological, and psycho-physiological responses. Unidimensional (Single) indicators seem to be less effective than multi-dimensional pointers in that they are not comprehensive. Multidimensional pain measurement instruments are recommended for use in a clinical setting as many adopt several pain indicators and are therefore expected to be more accurate. However, these instruments usually take a long time and are sometimes difficult to apply in clinical practice. The addition of a non-invasive machine-based assessment tool to detect various indicators of infant pain and evaluate them in a more consistent, sustainable, and minimally biased manner is recommended. A new trend in current research is the use of neurophysiological imaging methods which are non-invasive.

**Skin conductance (SC)**

SC is a term used when there is a change in the electrical attribute of the skin which occurs autonomously due to the active sympathetic nerves. SC measurement (SCM) assesses the electrical current generated on the two skin sites which have provided the electrical potentials. Changes in EDA result from sympathetic neuronal activity; therefore, EDA can indicate emotional and cognitive states. SC indicates the electrical properties of the skin in response to sweat secretion by the sweat glands[11,12]. SC is divided into two phenomena, tonic and phasic. The major distinction is related to the time scale and related to the stimulation of the electrical response generation. SC is measured in micro Siemens (µS). The EDA recording technique is called exosomatic because it uses an external current on the skin. Exosomatic techniques include direct current (DC) or alternating current (AC). SC uses DC which maintains a constant voltage. Also, there is a DC measurement that maintains a constant current which is called skin resistance. As for AC, a measurement that maintains an effective voltage constant results in a skin admittance measurement, and AC that maintains an effective current constant produces skin impedance[13]. SCM is also known as SC activity (SCA), skin conductance response (SCR), EDA, electrodermal response (EDR), or galvanic skin response (GSR).

**Electrodermal mechanism**

Increasing sympathetic cutaneous nerves, which activate muscarinic receptors, will influence SC. Sweat is released from the sweat glands on to the surface of the skin. Before the sweat is reabsorbed, the SCM assesses the sweat conductance of the epidermis along with noxious stimuli[14]. Changes in

SC are related to sweat gland activity. One of them is the eccrine gland, innervated by sympathetic nerves. The sympathetic nerves via acetylcholine acting on muscarinic receptors, innervate the sweat glands. All muscarinic receptors, together with G-protein, mediate their effect within seconds. The change in SC reflects sweat secretion from these glands. Sweat is an electrolyte solution and the more ducts and pores of the skin are filled by sweat, the more conductive it is. The sympathetic branch of the autonomic nervous system (ANS) controls eccrine sweating. This suggests that SC reflects the fluctuations in sympathetic ANS, which accompany various psychological processes. The mechanisms and pathways involved in central nervous control of eccrine perspiration are relatively complex and recent functional magnetic resonance imaging (fMRI) studies have shown that SC level (SCL) and SCR are associated with activity in different brain areas[4].

EDA follows an efferent peripheral sudomotor pathway. The hypothalamus, the centre of the sudomotor control that regulates sweat secretion directly and which is the main centre of thermoregulation, plays an important role in EDA signals. It is known that the elicitation of the CNS in humans has three pathways: (1) ipsilateral influence of the limbic system through the hypothalamic thermoregulation area (EDA-1 route); (2) contralateral influence of the cortical and basal ganglia premises (EDA-2 route); and (3) reticular effects. The sudomotor reflex is controlled by the limbic system. The amygdala and hippocampus are limbic structures mostly involved specifically in the control of hypothalamic functions related to the activity of the sudomotor nerve. The amygdala plays a role in excitatory function, while the hippocampus plays an inhibitory role. In particular, the amygdala plays a key role in controlling sweating in response to emotional stimulation[11,14]. Stimulation of the hippocampus causes EDR in humans. This stimulation produces the highest EDR, followed by the anterior and posterior hippocampi, and left and right anterior gyri, which play an important role in the cortical control of EDA. The amygdala and hippocampus have different effects on EDA in terms of information processing. Basal ganglia also play a role in the overseeing of EDA. The EDA inhibition centre is in the caudate nucleus (part of the striatum). EDA regulatory centres are located in several parts of the pallidum[11].

**Measurement procedure**

The following procedures were performed before applying electrodes to infants in previous studies: providing a comfortable / neutral thermal environment[5,15], keeping clean[5,15], giving feeds[5,15] 1 hour prior[16], restricting stimulation[5,17] for at least 1 hour[15], minimal handling, giving a pacifier, and giving 25% oral glucose[15], or sucrose[18], then placed on the open-bed[19], wearing nappies and a top[5], opening the cover of both legs, one hand and part of the abdomen, and cleaned the skin area by rubbing alcohol[20] or normal physiological saline[21] for 30 seconds[20]. After the electrodes have been applied, then the area where the electrodes are placed is wrapped[22,23] and the cable secured with a band around the ankle area[24].

Conventional EDA measurements are carried out on the palm area and fingers. Suggested locations for electrode placement are 1) fingers, 2) distal wrist, 3) central wrist, 4) vertical wrist, 5) chest, 6) foot (instep), 7) calf, 8) forehead, 9) neck, 10) shoulders, 11) back, 12) buttocks, 13) stomach, 14) armpits, 15) upper arms, and 16) femur. The electrodes used are made of silver / silver chloride using a paste/gel. The radius of the phalanx is the gold standard of EDA measurement, and the location on the sole is the closest to the fingers[12].

The SC measurement tool uses three electrodes in its recording, which are the measurement, the counter-current, and the reference (the M, C, and R) electrodes. The SCM (by Med-Storm) suggests applying the electrode to the heel of the neonate[12]. The C electrode is put on the medial side of the foot over the abductor hallucis muscle adjacent to the plantar surface. The M electrode is put midway between the phalanges and a point just below the ankle. The R is located on the dorsal side of the foot[25]. The studies used an SC apparatus from Varioport-B © by Becker Meditec two electrodes)[17], a Q Sensor SC (two electrodes) [23], and Sensormedic (two electrodes). The studies recorded result time calculation of the infant's SC measurement for 5 sec[26], 15 sec[24,27,28], 30 sec[27], 4 min[5], and 1 hour[27]. The time calculation for the SC measurement is adjusted according to the duration of the pain stimulus being performed at that time.

**SC parameters / analysis**

SC analysis readings start when the SC apparatus software is connected to the electrodes, then automatically defines peaks above the 0.02 μsiemens (Med-Storm) amplitude threshold. The detector will record the quality of the SC signal, then the SC is read with various analysis parameters related to electric waves. The SC parameters in previous studies varied and peak/sec (PpS) was the most frequently used parameter, following by the number of wave peaks/sec (NWP/s) [4] (Table 2).

**Table 2:** ***Skin conductance parameters/analysis used in the previous study***

| Analysis | Abbreviations | References |
|---|---|---|
| *NWP/s* | Number of wave peaks/sec | 15,16,19,20,22,24–27 |
| *PpS* | Peak/sec | 5,16,18,19,21,25 |
| *AUC* | Area under curve | 15,17,21,22 |
| *SCRs* | Skin conductance response/sec | 24,29 |
| *EDRs* | Electrodermal response/sec | 20,26 |
| *Basal level* | - | 26 |
| *NSCF/s* | Number of skin conductance fluctuations /sec | 27 |
| *ASCF/s* | Amplitude skin conductance fluctuation/sec | 17 |
| *MLSC* | Mean level of skin conductance | 17 |
| *SCA* | Skin conductance activity | 30 |
| *Peak value* | - | 26 |
| *Number of peaks* | - | 27 |
| *Mean basal level* | - | 20 |
| *Mean peak amplitude* | - | 20 |
| *EDA* | Electrodermal activity | 23 |

Parameters such as NWP/s and area under curve (AUC), are derived from real-time SC changes[15,22,27]. NWP/s are calculated over a 1-hour measurement period and will be better at 15 or 30-s time frames[27]. A study shows the AUC scale is better used in chronic pain conditions at an analysis time of more than three minutes. There are different findings of AUC where AUC is at the very sensitive and specific parameter in scaling the level of pain, while other findings suggest that AUC has a lower sensitivity[15].

Pain assessment in infants using SCM needs more attention and focus in its analysis because of the individual uniqueness of the infants. Variation in study findings is found, such as evidence that the peak/sec (PpS) has high validity across all gestational age categories[21]. This is different from the findings which stated that, with increasing postnatal age (PNA), there will be higher scores in SC parameters (three parameters); these are the number of skin conductance fluctuations/sec (NSCF/s), amplitude skin conductance fluctuation/sec (ASCF/s), and mean level of SC. The main parameters used in infants are skin conductance response (SCR) frequency, amplitude, and basal level[10].

**SC and other pain physiological and behavioural scales**

SC and heart rate were reported to be significantly similar[20]. Likewise, respiratory rate[20,29], oxygen saturation[16,20,24,30] and skin temperature[27]. Vital signs as previously described are easy physiological indicators to monitor chronic conditions, but they are not recommended for measuring pain since vital signs are affected by the clinical condition of the infant and other contextual factors. The importance of showing the validity and reliability of a tool is the comparison of its value with the gold standard value. Researchers have carried out experiments, and even a scoping review that describes the validity of SC based on past research[4] and so, in this article, we find an overview of SC and its comparison with another pain scale. Recent studies have reported a significant relationship between SCM and Neonatal Infant Pain Scale (NIPS)[19,22,30], Neonatal Facial Coding System (NFCS)[22,26], Premature Infant Pain Profile–Revised (PIPP-R)[28], Bernese Pain Scale for Neonates (BPSN)[17], Comfort–b[15], Prechtl Scale[17], Newborn Individualized Developmental Care and Assessment Program (NIDCAP)[20,29], Acute Pain in Newborn (APN) score[5] and crying time. However, there are variations of previous studies report related similarity of SCM with other physiological and behavioural pain tools.

**Conclusion**

The purpose of this literature review is to describe SC as a determiner and a measurer of infants' pain, which includes a review of the term 'pain' in infants. Descriptions of the literature and scientific evidence regarding pain assessment in infants with the SC apparatus suggest that SC has good potential to be used as a pain assessment tool in infants. It is possible to overcome the shortcomings of manual pain assessment, although we still have to consider other sources of information in the judgment of the infants' pain scale. Based on the literature and the findings described, it is necessary to study more broadly SC-based infant pain measurement and compare it with other more objective pain indicators, such as Near-infrared spectroscopy NIRS, functional magnetic resonance imaging (fMRI), and electroencephalography (EEG). Research, testing, and scientific evidence are expected to provide adequate sources of information before they are applied in a clinical setting. Subsequent studies such as diagnostic tests to determine sensitivity and specificity may further support the benefits of using SC for application in daily clinical practice.

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**References**

1. Anand KJS. Effects of perinatal pain and stress. *Progress in Brain Research* 2000; **122**: 117-29. https://doi.org/10.1016/S00796123(08)62134-2

2. Cong X, McGrath JM, Cusson RM, Zhang D. Pain assessment and measurement in neonates: An updated review. *Advamces in Neonatal Care* 2013; **13**: 379–95. https://doi.org/10.1097/ANC.0b013e3182a41452 PMid:24300956

3. Zamzmi G, Kasturi R, Goldgof D, Zhi R, Ashmeade T, Sun Y. Machine-based multimodal pain assessment tool for infants : A review. 07/01/2016. University of South Florida.

4. Hu J, Modanloo S, Squires J, Harrold J, Harrison D. The validity of skin conductance for assessing acute pain in infants: A scoping review. *Clinical Journal of Pain* 2019; **35**(8): 713-24. https://doi.org/10.1097/AJP.0000000000000721 PMid:31094936

5. Maillard A, Garnier E, Saliba E, Favrais G. Prematurity alters skin conductance and behavioural scoring after acute stress in term-equivalent age infants. *Acta Paediatrica* 2019; **108**(9): 1609-15. https://doi.org/10.1111/apa.14777 PMid:30851198

6. Storm H. Changes in skin conductance as a tool to monitor nociceptive stimulation and pain. *Current Opinion in Anaesthesiology* 2008; **21**: 796–804. https://doi.org/10.1097/ACO.0b013e3283183fe4 PMid:18997532

7. Anand KJS, Craig DK. New perspective definition of pain. *Pain* 1996; **67**: 3–6. https://doi.org/10.1016/03043959(96)03198-3

8. Hatfield LA. Neonatal pain : What's age got to do with it ? *Surgical Neurology International* 2014; **5**(Suppl 13): S479-S489. https://doi.org/10.4103/2152-7806.144630 PMid:25506507 PMCid:PMC4253046

9. Bellieni CV, Johnston C, Campbell-yeo M, Benoit B, Disher T. Neonatal pain: Neurophysiology, recognition, prevention and management with nonpharmacological interventions. in *Neonatology* (eds. Buonocore, G., Bracci, R. & Weindling, M.) 365–381 (Springer, Cham, 2018). doi:G. Buonocore et al. (eds.), Neonatology https://doi.org/10.1007/978-3-319-29489-6_175

10. Storm H. Skin conductance and the stress response from heel stick in preterm infants. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 2000; **83**: F143-7. https://doi.org/10.1136/fn.83.2.F143 PMid:10952711 PMCid:PMC1721148

11. Boucsein W. *Electrodermal Activity*. (Springer Science+Business Media, 2012). doi:10.1007/978-1-4614-1126-0. https://doi.org/10.1007/978-1-4614-1126-0

12. van Dooren M, de Vries JJGGJ, Janssen JH. Emotional sweating across the body: Comparing 16 different skin conductance measurement locations. *Physiology and Behavior* 2012; **106**: 298–304. https://doi.org/10.1016/j.physbeh.2012.01.020 PMid:22330325

13. Braithwaite JJ, Watson DG, Jones R, Rowe M. A guide for analysing electrodermal activity (EDA) & skin conductance responses ( SCRs ) for psychological experiments. (University of Birmingham, 2015).

14. Greco A, Valenza G, Scilingo EP. Advances in electrodermal activity processing with applications for mental health. (Springer International Publishing, 2016). https://doi.org/10.1007/978-3-319-46705-4

15. Tristão RM, Garcia NVM, De Jesus JAL, Tomaz C. COMFORT behaviour scale and skin conductance activity: What are they really measuring? *Acta Paediatrica* 2013; **102**: 402–6.

https://doi.org/10.1111/apa.12325
PMid:23782068

16. Lyngstad LT, Tandberg BS, Storm H, Ekeberg BL, Moen A. Does skin-to-skin contact reduce stress during diaper change in preterm infants? *Early Human Development* 2014; **90**: 169–72. https://doi.org/10.1016/j.earlhumdev.2014.01.011 PMid:24548816

17. Schubach NE, Mehler K, Roth B, Korsch E, Laux R, Singer D, *et al.* Skin conductance in neonates suffering from abstinence syndrome and unexposed newborns. *European Journal of Pediatrics* 2016; **175**(6): 859–68. https://doi.org/10.1007/s00431-016-2716-8 PMid:27026377

18. Meesters NJ, Simons SHP, Rosmalen JV, Holsti L, Reiss IKM, Dijk MV. Acute pain assessment in prematurely born infants below 29 weeks: A long way to go. *Clinical Journal of Pain* 2019; **35**: 975–82. https://doi.org/10.1097/AJP.0000000000000762 PMid:31513054

19. Beken S, Hirfanoglu IM, Gucuyner K, Ergenekon E, Turan O, Unal S, *et al.* Cerebral haemodynamic changes and pain perception during venipuncture: Is glucose really effective? *Journal of Child Neurology* 2014; **29**: 617–22. https://doi.org/10.1177/0883073813511149 PMid:24334348

20. Salavitabar A, Haidet KK, Adkins CS, Susman EJ, Palmer C, Storm H. Preterm infants' sympathetic arousal and associated behavioral responses to sound stimuli in the neonatal intensive care unit. *Advances in Neonatal Care* 2010; **10**(3): 158-66. https://doi.org/10.1097/ANC.0b013e3181dd6dea PMid:20505427

21. Macko J, Moravcikova D, Kantor L, Kotikova M, Humpolicek P. Skin conductance as a marker of pain in infants of different gestational age *Biomedical Papers of the Medical Faculty of the University Palacky, Olomouc, Czechoslovakia* 2014; **158**: 591–5. https://doi.org/10.5507/bp.2013.066 PMid:24089027

22. de Jesus JAL, Campos Júnior D, Storm H, Da Rocha AF, Tristão RM. Skin conductance and behavioral pain scales in newborn infants. *Psychology and Neuroscience* 2015; **8**: 203–10. https://doi.org/10.1037/h0101058

23. Zimmerman E, Thompson K. A pilot study: The role of the autonomic nervous system in cardiorespiratory regulation in infant feeding. *Acta Paediatrica* 2016; **105**: 286–91. https://doi.org/10.1111/apa.13289 PMid:26613548

24. Røeggen I, Storm H, Harrison D. Skin conductance variability between and within hospitalised infants at rest. *Early Human Development* 2011; **87**: 37–42. https://doi.org/10.1016/j.earlhumdev.2010.09.373 PMid:21041044

25. Baleine J, Milesi C, Mesnage R, Novais ARB, Combes C, Durand S, *et al.* Intubation in the delivery room: Experience with nasal midazolam. *Early Human Development* 2014; **90**: 39–43. https://doi.org/10.1016/j.earlhumdev.2013.10.007 PMid:24331827

26. Dalal PG, Doheny KK, Klick L, Britcher S, Rebstock S, Bezinover D, *et al.* Analysis of acute pain scores and skin conductance measurements in infants. *Early Human Development* 2013; **89**: 153–8. https://doi.org/10.1016/j.earlhumdev.2012.09.008 PMid:23046994

27. Valkenburg AJ, Niehof SP, Van Dijk M, Verhaar EJM, Tibboel D. Skin conductance peaks could result from changes in vital parameters unrelated to pain. *Pediatric Research* 2012; **71**: 375–9. https://doi.org/10.1038/pr.2011.72 PMid:22391638

28. Avila-Alvarez A, Pertega-Diaz S, Gomez LV, Alonso AS, Rey HR, Barbeito DE, *et al.* Pain assessment during eye examination for retinopathy of prematurity screening: Skin conductance versus PIPP-R. *Acta Paediatrica* 2020; **109**(5): 935-42.

https://doi.org/10.1111/apa.15066
PMid:31630433

29. Zeiner V, Storm H, Doheny KK. Preterm infants' behaviour and skin conductance responses to nurse handling in the NICU. *Physiology and Behaviour* 2018; **176**: 139–48.

30. Gokulu G, Bilgen H, Ozdemir H, Sarioz A, Memisoglu A, Gucuyener K, *et al.* Comparative heel stick study showed that newborn infants who had undergone repeated painful procedures showed increased short-term pain responses. *Acta Paediatrica* 2016; **105**(11): e520–e525. https://doi.org/10.1111/apa.13557
PMid:27557529