MedStorm

Real-time Pain Management

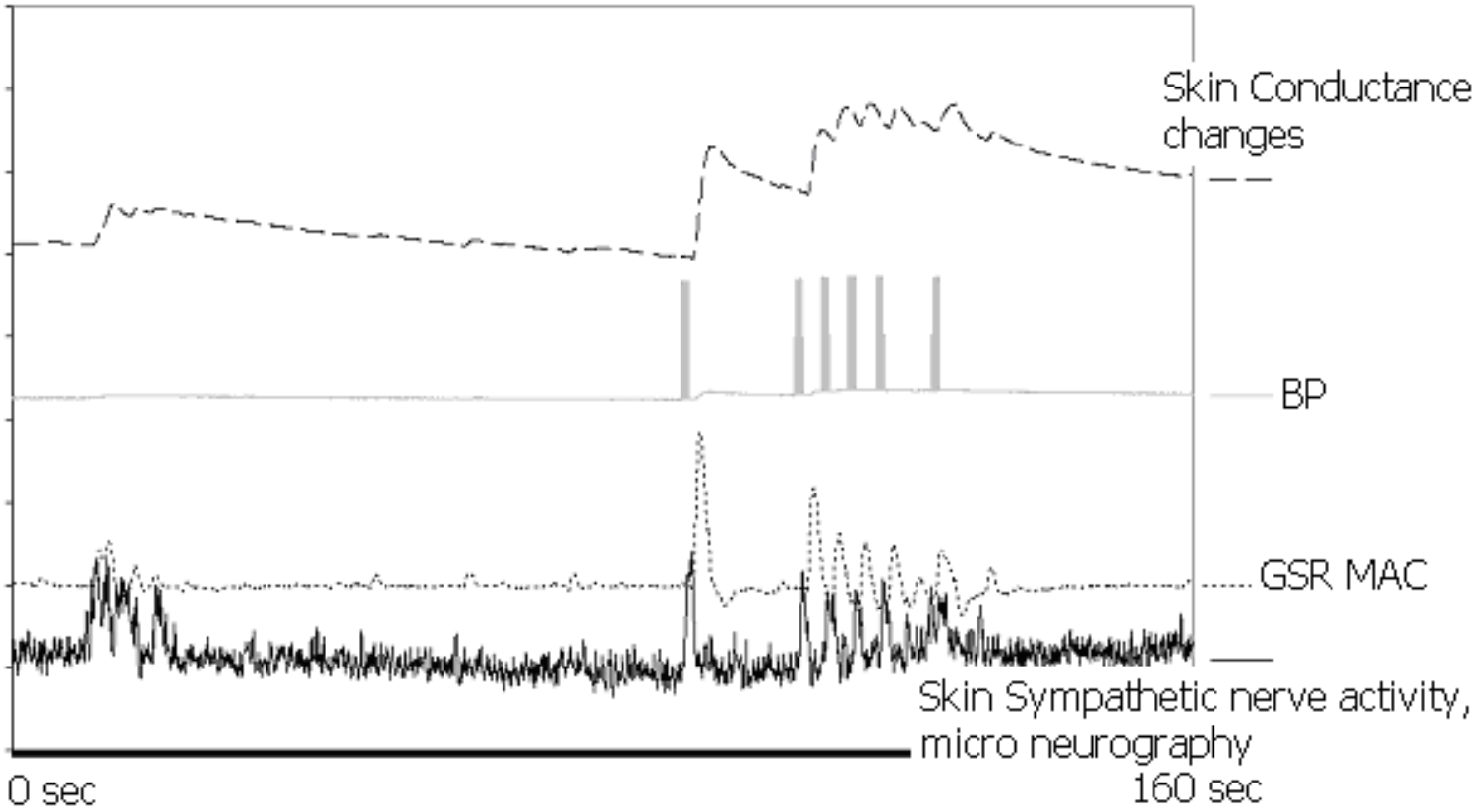
Improved personalized pain management by tailoring the need of analgesia

The Pain-Nociceptive Sensor

Fight / flight reaction – primitive nociceptive spinal reflex (emotional sweating)

Painful stimulus elicits a skin symphatetic response by the sweat glands, increasing secretion. Sweat contains water and electrolytes, which **increases electrical conductivity**, and **lowering the electrical resistance** of the skin.

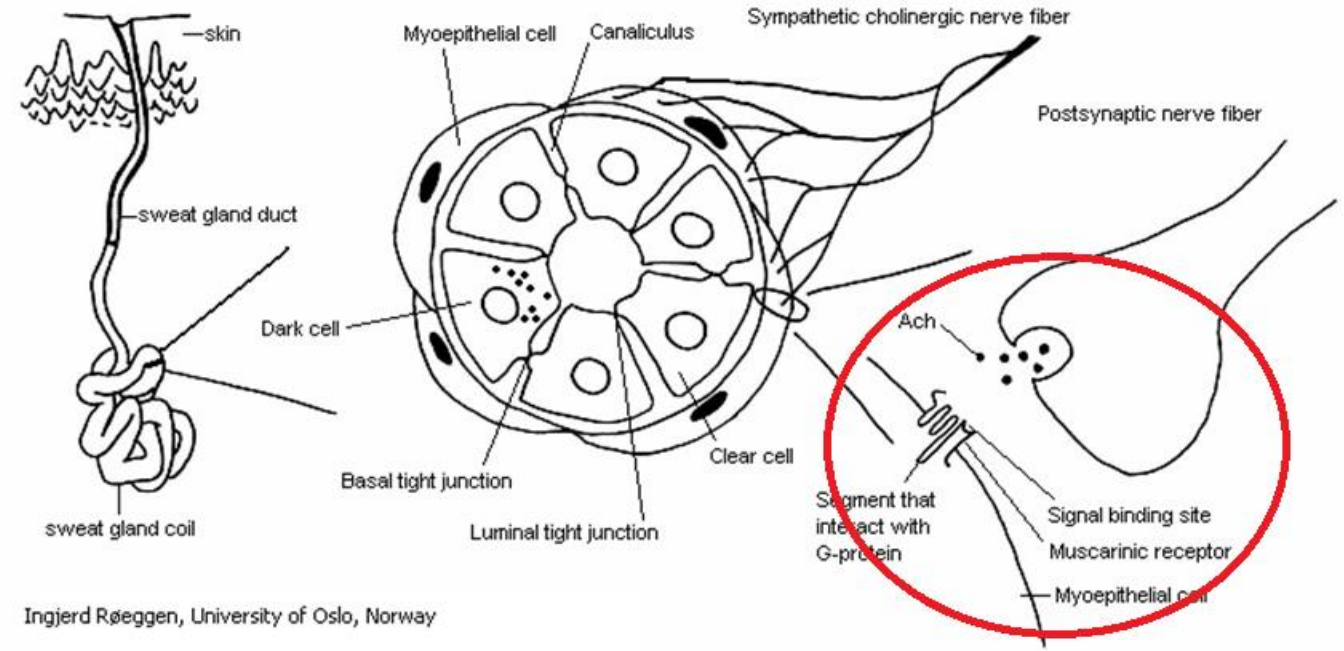
Firing rate in the skin sympathetic nerves
→ Number of skin conductance peaks



Correlation between the firing rate in the skin sympathetic nerves and the number of skin conductance peaks. Moreover, small bursts in the sympathetic nerves give small skin conductance peaks and huge bursts in the sympathetic nerves give huge skin conductance peaks.

Gjerstad AC, Storm H, Wallin G. Evaluation of the skin conductance method by using microneurographi, abstract, ISAP, Chicago 06. Presentation of skin sympathetic nervous system.

The PainSensor assess changes in skin conductance, palmary and plantar



When the skin sympathetic nervous system is firing, sweat is released within **1-2 sec** and the conductance increases. When the sweat is reabsorbed the conductance decreases. **This process creates one skin conductance peak**.

One skin conductance peak:

Skin sympathetic nervous system fires

↓

Sweat released within 1-2 sec

↓

Conductance increases

↓

Conductance decreases when sweat reabsorbs into skin

“The PainSensor - Skin conductance algesimeter (SCA)”

The PainSensor uses number of skin conductance peaks per sec as an index

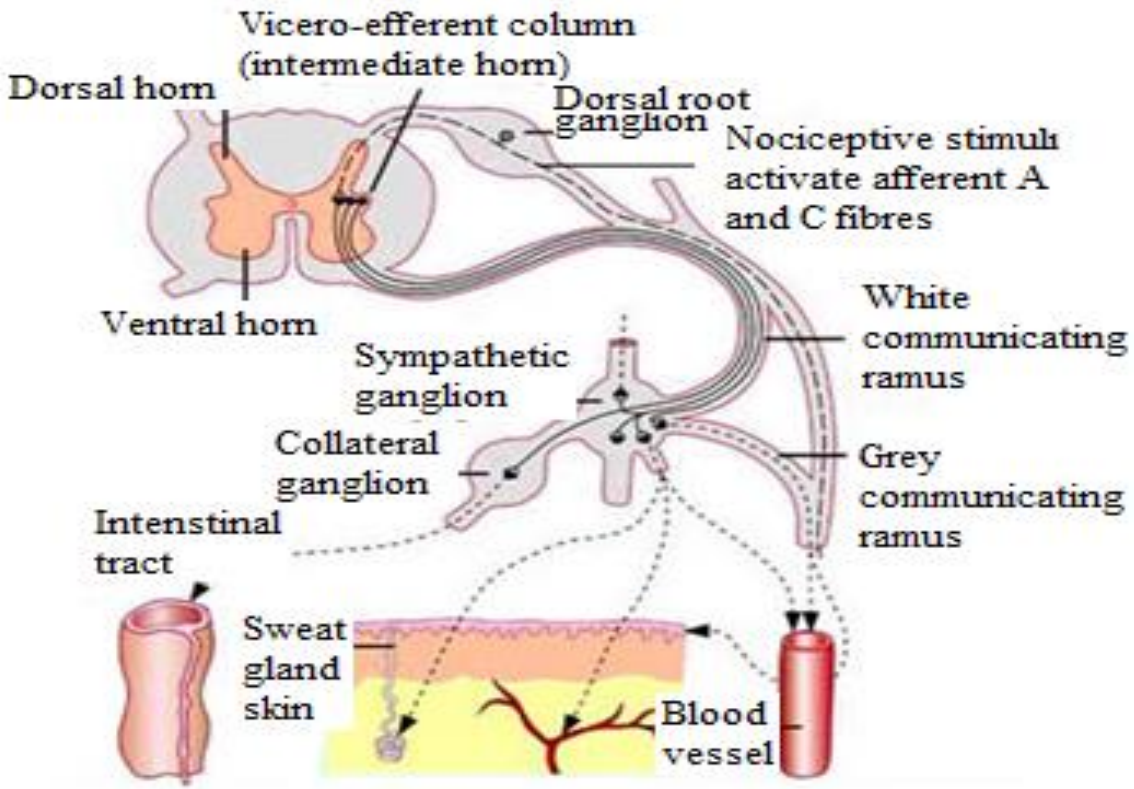
Since acetyl choline acts on the muscarine receptors, the skin conductance peaks are **not influenced** by blood circulatory changes, medication acting on the blood circulation, respiratory distress, general hypoxia, or neuro muscular blockers. Also not influenced by low oxygenation levels.

Not influenced by:

- Hemodynamic instability
- Respiratory distress
- adrenergic medication
- beta-blockers
- alfa-2 agonists
- neuromuscular blockers
- Atropine (in clinical doses).

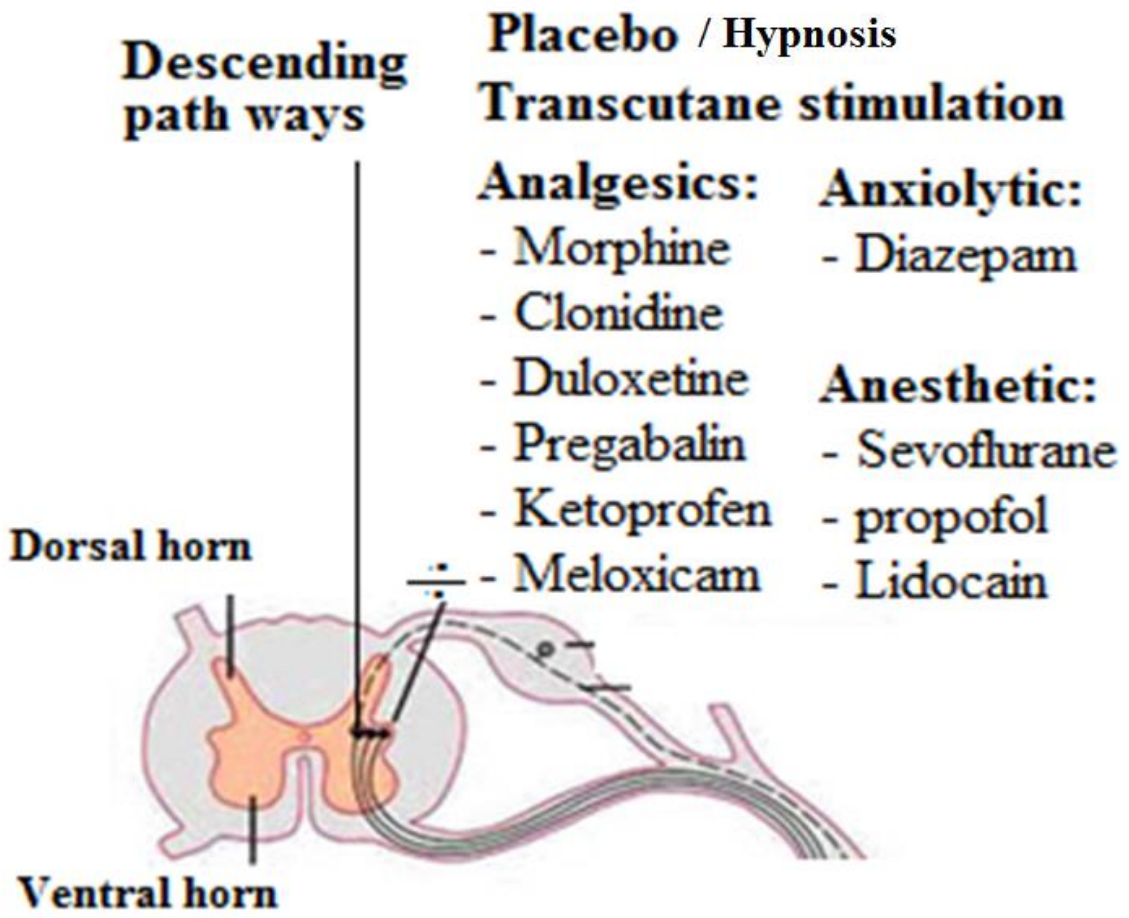
- **The skin conductance peaks reacts immediately to a pain stimulus (1-2 sec).**
- **Not influenced by environmental temperature**
- **Can be used for all age-groups - preterm infants (24 weeks gestational age) to adults**
  - There is low variation between and within individuals, which made it possible to develop an index for all patients

The nociceptive spinal reflex response



The nociceptive spinal reflex correlates with the strength of the elicited stimulus different from the clinical observational pain scores.

The PainSensor tailor the need of analgesia at the spinal pain port:



The PainSensor assesses the response to painful stimuli at the spinal level where analgesia acts. Analgesia decreases the response by inhibiting the nervetransmission.

Validation studies

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Validation studies

80+ supportive validation studies

5 theses

”**Pain skin conductance**” in Pubmed: more than **6000** papers.

Validation studies

Operation room / Anaesthesia

- **14** Anesthesia

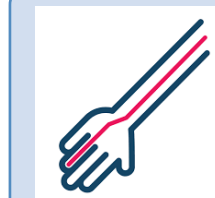
NICU / Paediatrics

- **36** pain and other stimuli in infants and children

ICU

- **12** ICU

Regional nerve block



- **1** regional nerve block

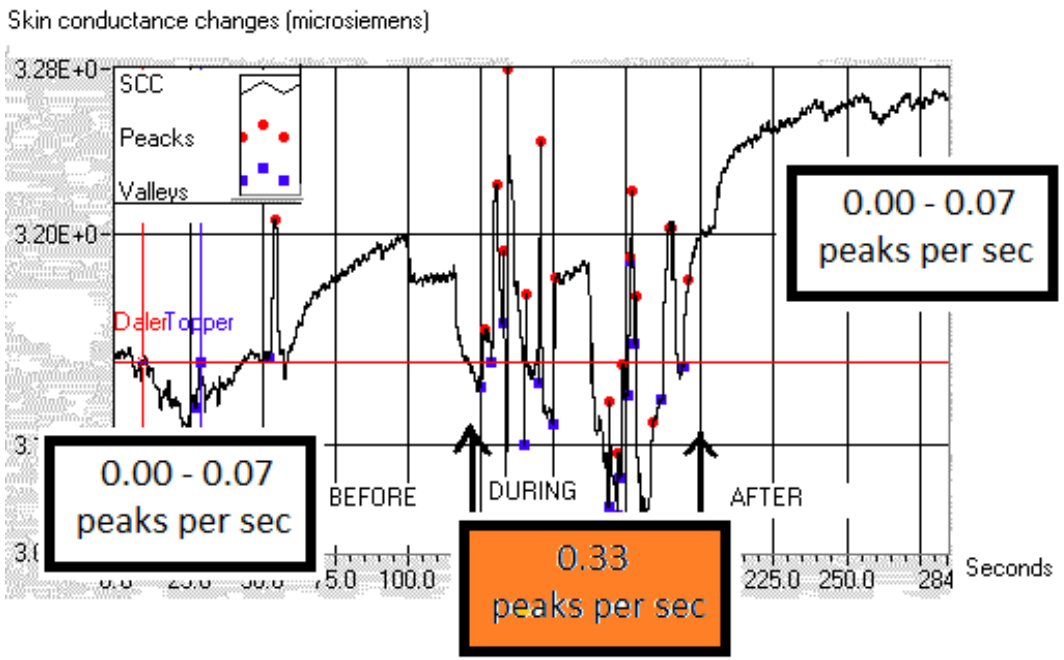
Post operative

- **6** postoperative pain, adults and children
- **2** withdrawal symptoms

The technology

- **13** validation of the technology on volunteers
- **2** development of software program
- **1** review paper of clinical utility
- **1** pain threshold

Neonatal intensive care units (NICU)



The registration curve is before, during and after heel stick for blood sampling.

WHITE: 0.00-0.07 peaks per sec 0-1	**The infant is calm (15 infants studied 6 times asleep, peaks per sec: median: 0.00 range 0.00-0.04).**
LIGHT YELLOW: 0.14 peaks per sec 2-3	**The infant is calm and moves a little**
YELLOW: 0.21-0.027 peaks per sec 4	**The infant is active, the infant pain/discomfort threshold is reached [observe the infant]**
ORANGE: 0.33 peaks per sec 5-6	**The infant is probably in pain/discomfort [evaluate the situation]**
RED: 0.40 peaks per sec or more 7-10	**The infant is in increasing pain/discomfort**

Based on observational pain scores and NIDCAP

The index (peaks per second) increases during painful procedures from gestation age 24 weeks, and is not influenced by gestational and postnatal age. In total, 500 preterm infants have been examined before during and after painful procedures. All the studies performed show that the index increases during these procedures.

Eye examination for retinopathy in the NICU

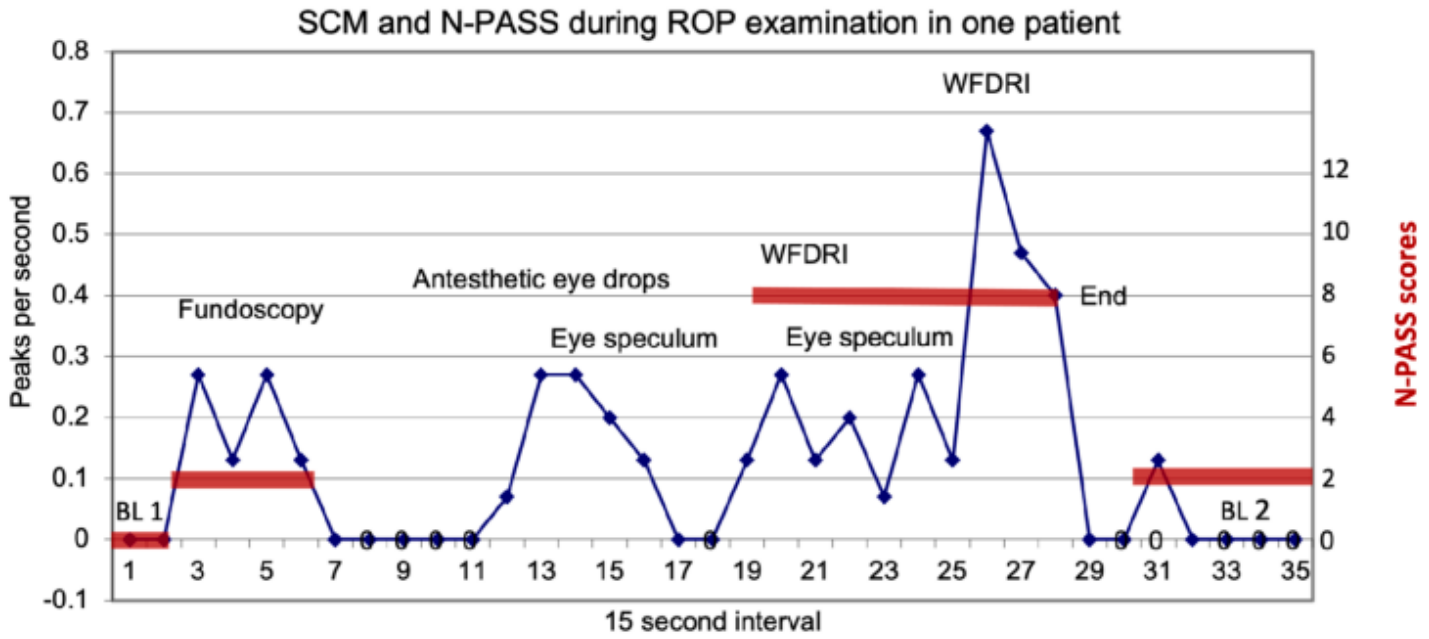


Fig. 4. Example of SCM and N-PASS scores during one ROP examination in one patient.

Skin conductance measurement as a selective and continuous pain assessment method during eye examinations for retinopathy of prematurity Munsters J, Sindelar R et al. Global Pediatrics 4 (2023) 100056

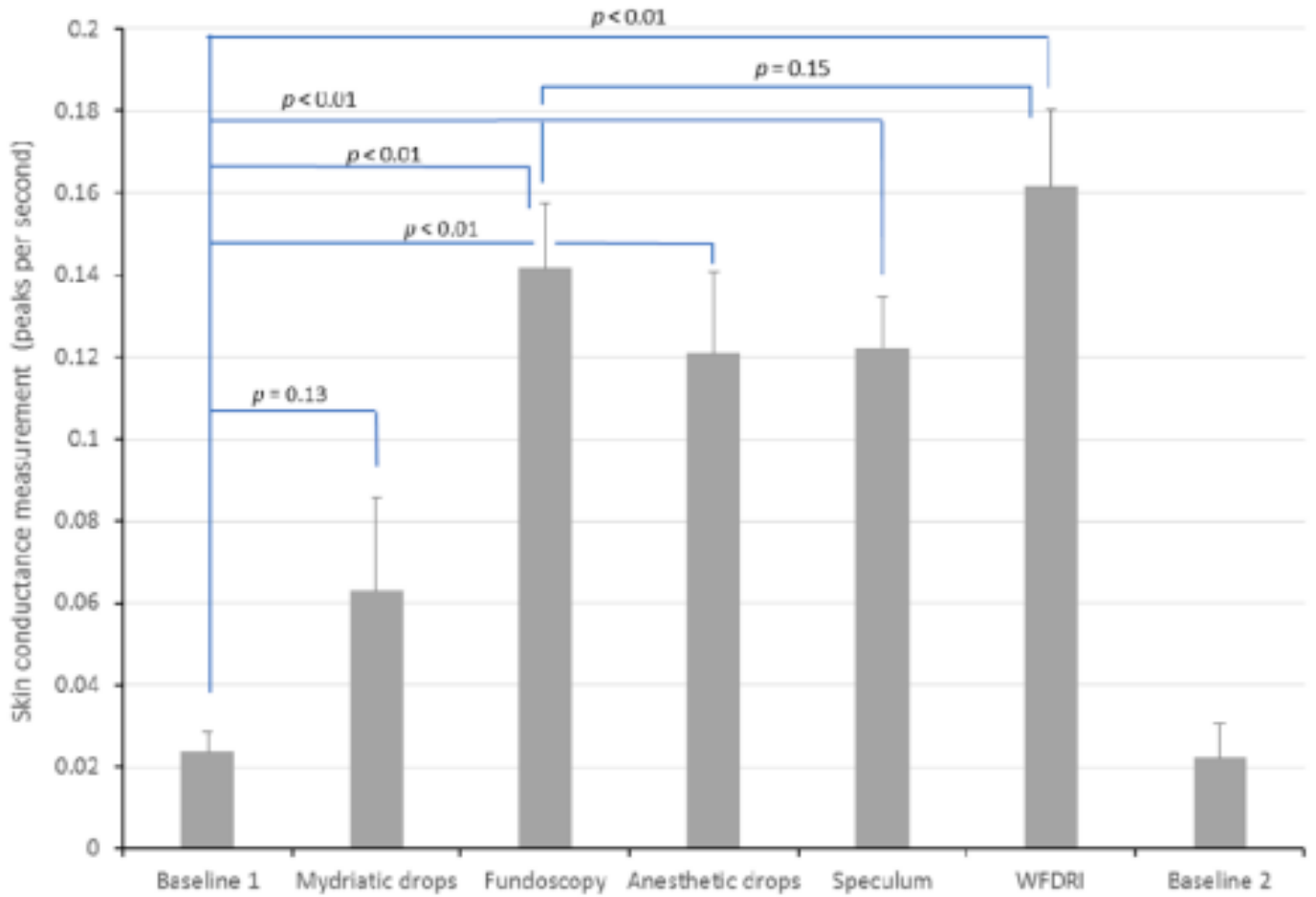


Fig. 1. Skin conductance measurements during different stages of ROP examination. Mean and standard error of mean.

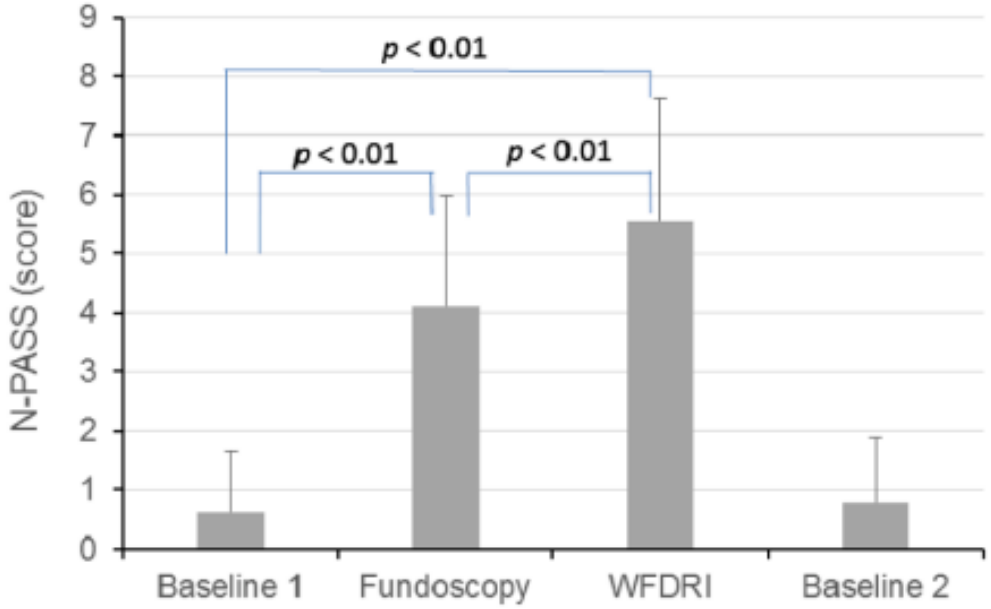
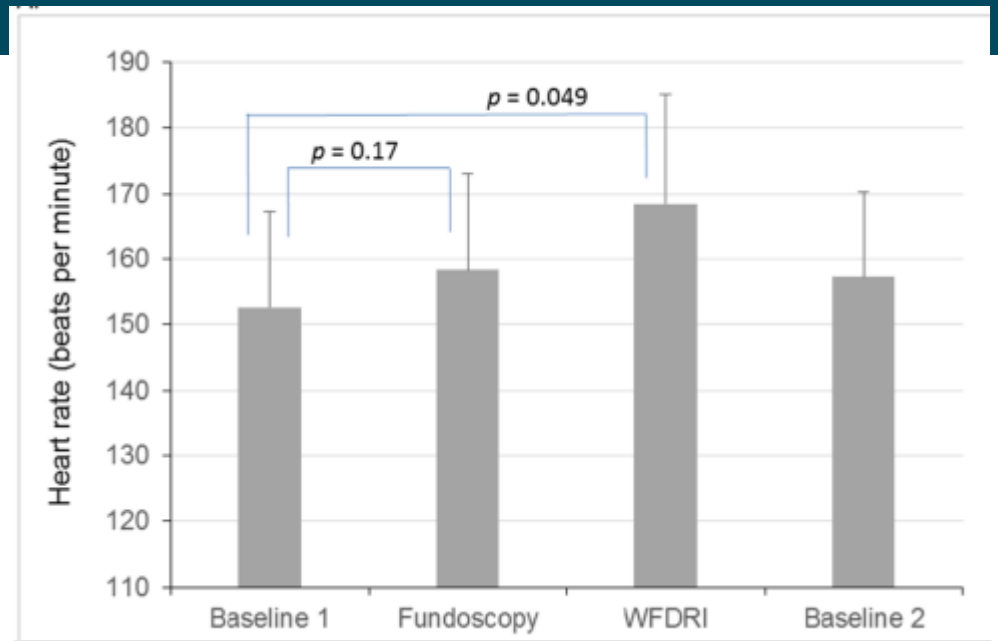
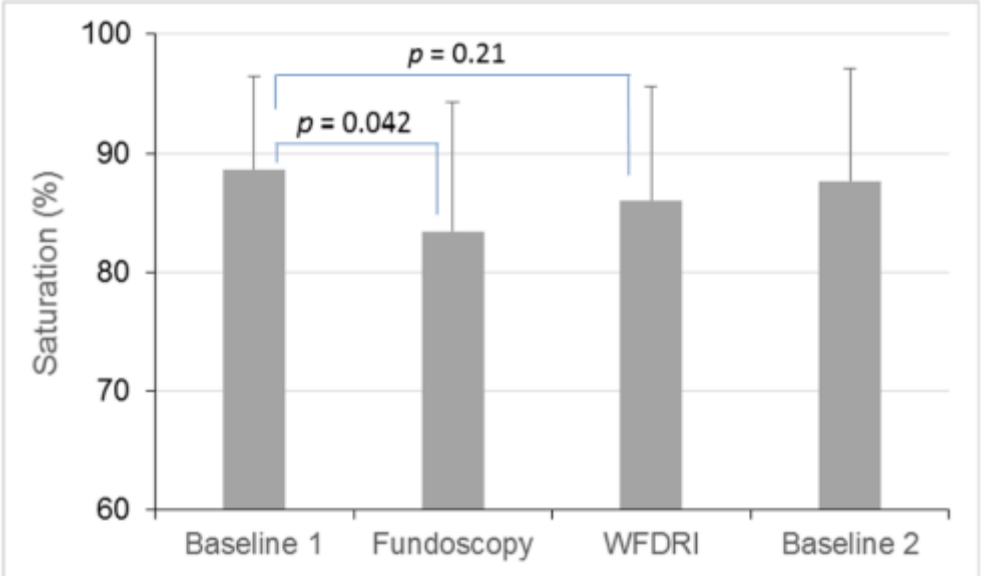


Fig. 2. N-PASS scores during ROP examination. Mean and standard deviations.

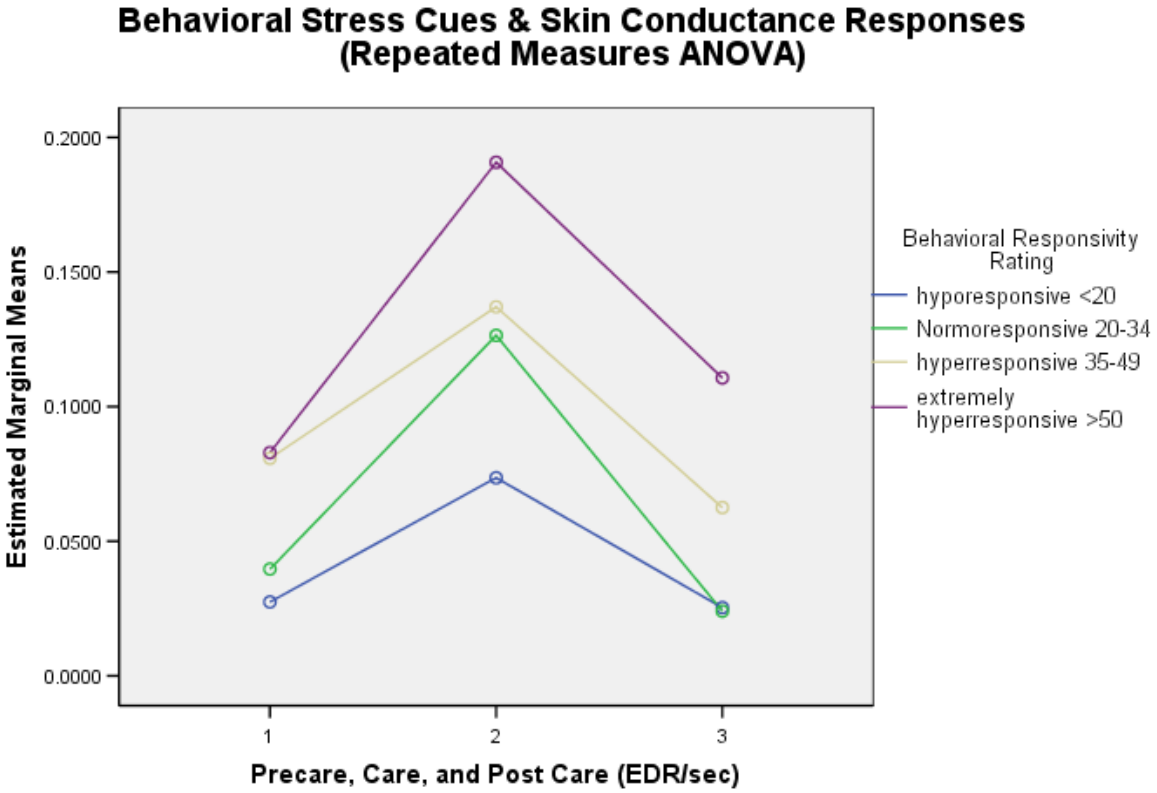




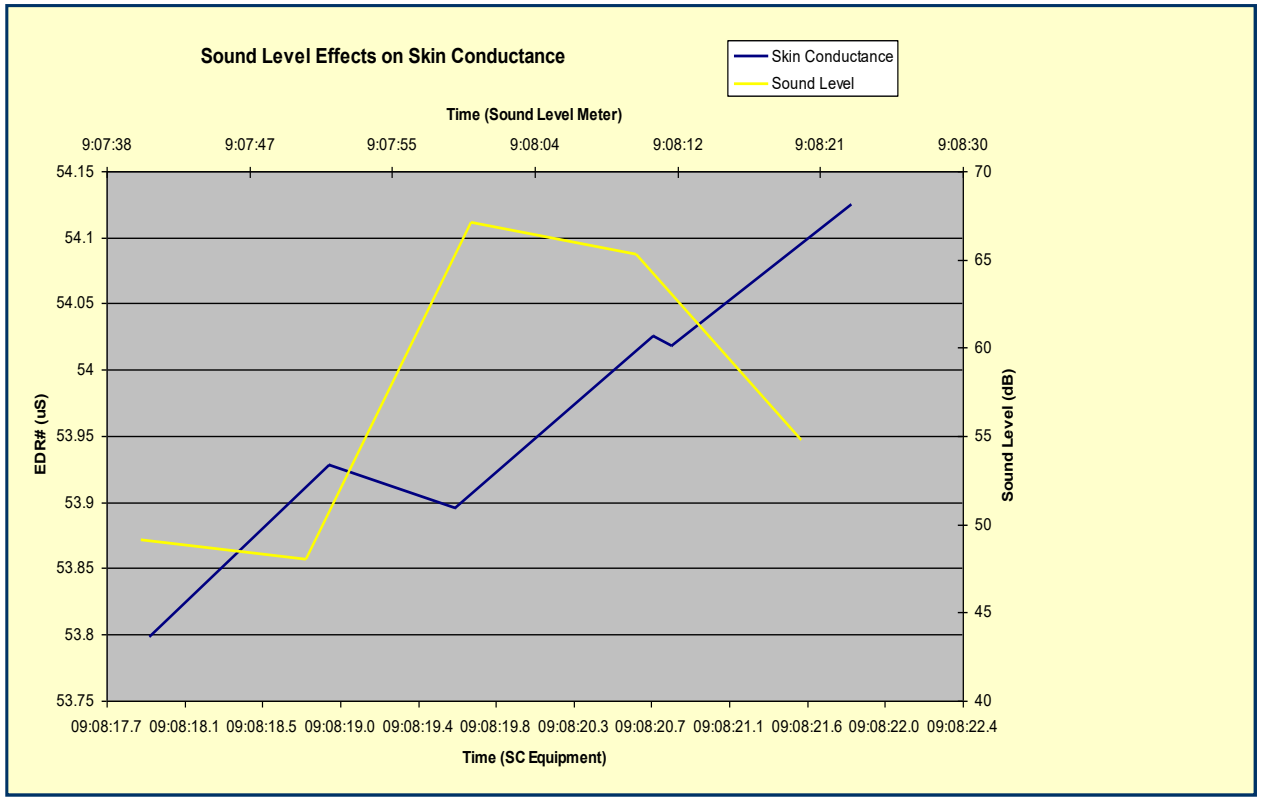
Observational scores compared to Skin conductance response

Measures of Stress Vulnerability in LBW Infants: An Integrative Biobehavioral Approach to Stress Reactivity Measurement

Kim Kopenhaver Haidet, PhD, CNNP, Penn State Univeristy, US:



A measure of pain and emotional stress



Salavitabar A, Haidet KK, Adkins CS, Palmer C, Storm H. Preterm infants sympathetic arousal and associated behavioral responses to sound stimuli in the neonatal Intensive care units. Advances in Neonatal Care 2010:10(3):158-166.

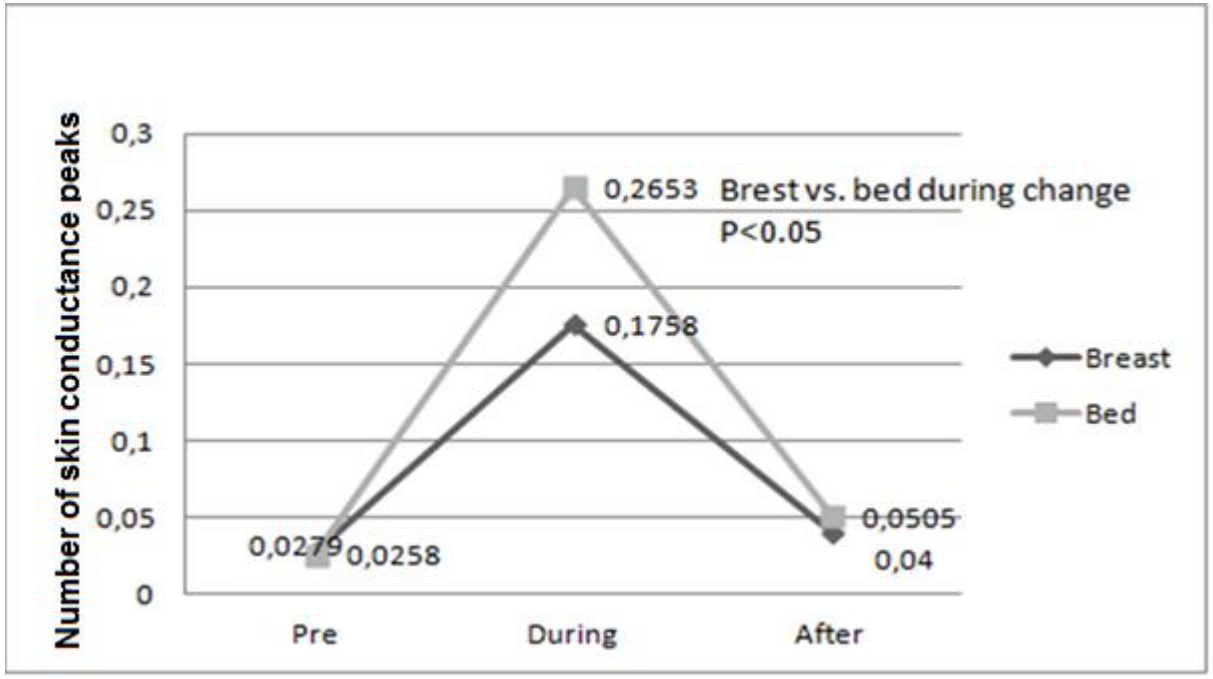
Thirty infants without severe illness, Score for Neonatal Acute Physiology (SNAP) < 10, were studied at postnatal day 4-5 during nursing procedure

NIDCAP® behaviors during nurse care showed a negative statistical significant association to the SNAP score (R=-0.45, P=0.05) and days to full enteral feeding (R=-0.53, P= 0.01) different from the physiological parameters.

Zeiner V, Storm H, Kopenhaver Doheny K. Preterm Infants' Biological and Behavioral Stress Responses to Nurse Handling in the NICU. The Journal of Maternal-Fetal & Neonatal Medicine accepted for publication 2015

Diaper change in bed versus Kangaroo Mother care (KMC)

	Before	During	After
SpO21	97 (2.4) (92-100)	92 (5.5) (80-100) **	98 (2.1) (94-100) **
SPO22	96.8 (2.5) (92-100)	91.6 (6.4) (80-100) **	97.2 (2.1) (94-100) **
HR1	155 (13) (138-180)	173 (17) (146-209) ***	156 (15) (128-185) ***
HR 2	156 (10) (142-178)	167 (19) (120-199) *	156 (12) (142-177) **
SC peaks/sec KMC	0.03 (0.05) (0.00-0.20)	0.18 (0.07) (0.05-0.35) ***	0.04 (0.07) (0.00-0.27) ***
SC peaks/sec bed	0.03 (0.03) (0.00-0.10)	0.27 (0.14) (0.08-0.44) ***	0.05 (0.07) (0.00-0.30) ***



Lene Tandle Lyngstad, Bente Silnes Tandberg*, Hanne Storm** MD, PhD, Birgitte Lenes Ekeberg*, Atle Moen, MD, PhD*. Does skin-to-skin contact reduce stress during diaper change in preterm infants? Stress during change of diapers in preterm infants and the effect of kangaroo mother care. Early Hum Dev. 2014 Apr;90(4):169-72.*

There were statistical differences for physiological measures during the no- painful- and hypoxic events:

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	POS	SCR/sec	HR	RR
No-event	95 (3)	0,07 (0,10)	163 (10)	68 (28)
Painful- event	88 (8)	0,27 (0,21)	166 (20)	57 (24)
Hypoxic-event	69 (4)	0,03 (0,03)	153 (25)	61 (21)
P-value	0.002	0.011	NS	NS

NAKSTAD B., NORDHEIM T., HOVDE H., STORM H. (2014). Skin Conductance changes differ between painful stimuli and general hypoxia different from peripheral oxygen saturation. European Academy of Paediatric Societies (EAPS 2014), Barcelona, October.

Application areas

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INDICES AND APPLICATION AREAS

Operating theatres

- Pain Index
- Awakening index
- Nerveblock index

Intensive care units

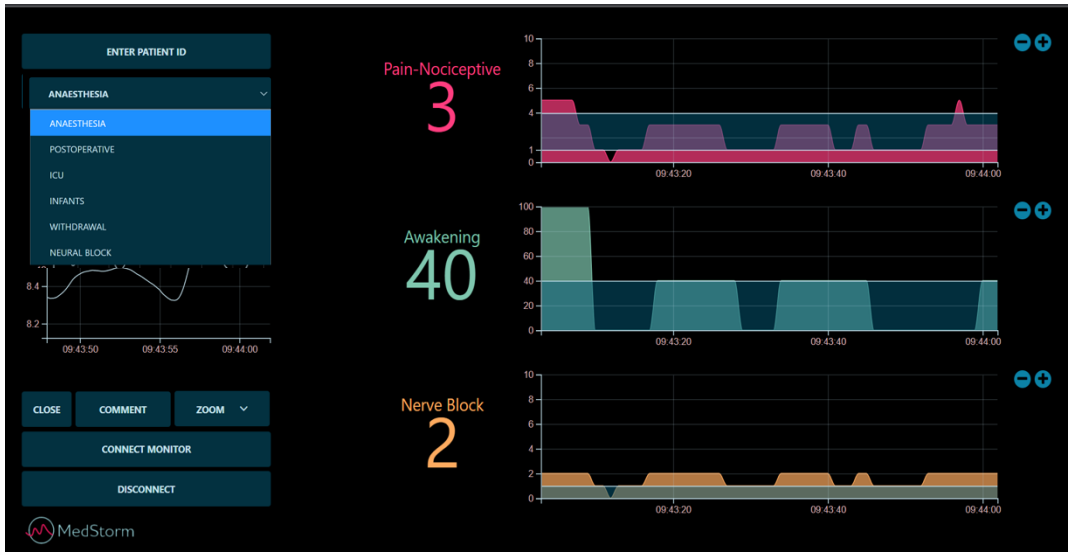
- Pain Index
- Awakening index

Post-operatively

- Pain Index

Neonatal intensive care units (NICUs) and paediatric intensive care units (PICUs)

- Pain Index



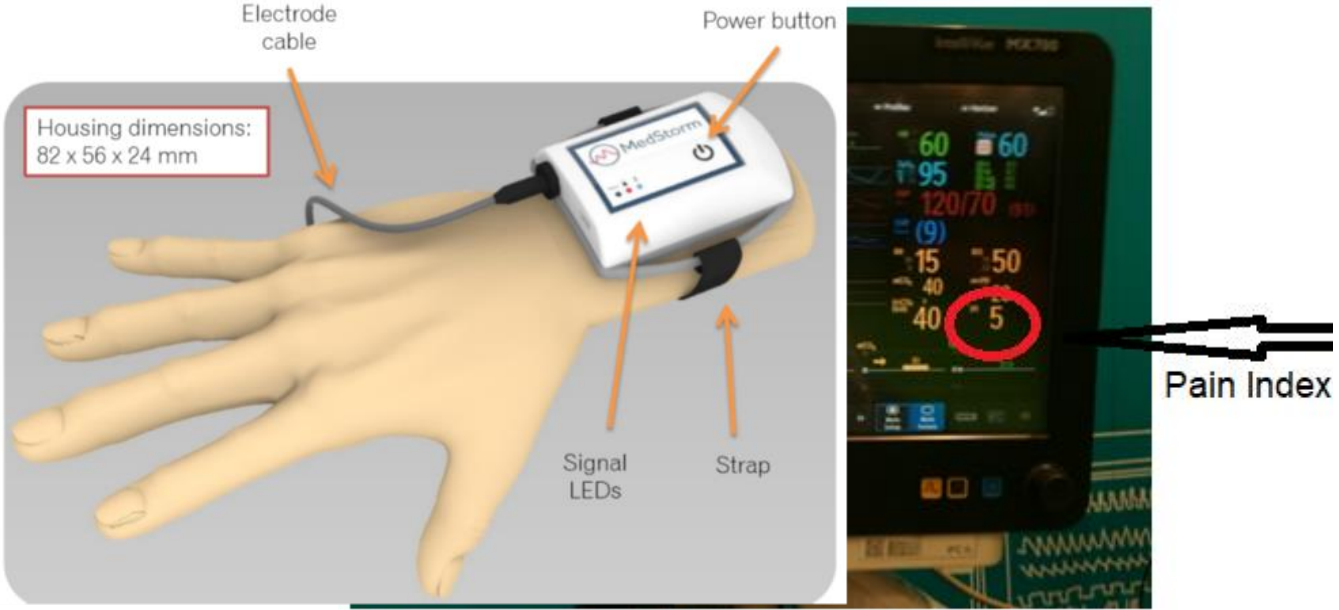
The Pain-Nociceptive Sensor

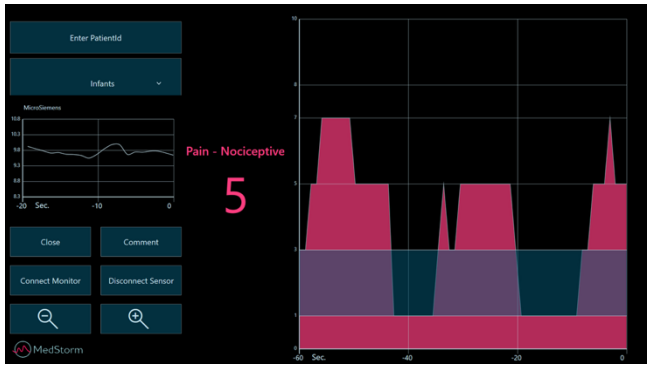
MedStorm's low cost, PainSensor with electrodes

- PainSensor will be CE-MDR approved 2023
- Accurate, real time and objective pain assessment
- Intergrates with of existing patient monitoring systems (Masimo, Mindray, Philips, Draeger-SDC, HL7 GE)
- Pain Index transferred to patient data monitoring systems
- Simple, real-time readout number to improve pain management

Electrodes:

PainSensor:





PainIndex for infants

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Quick guide PainSensor

Neonates from 23 weeks & infants

The index shall only be used to titrate the need of analgesia:

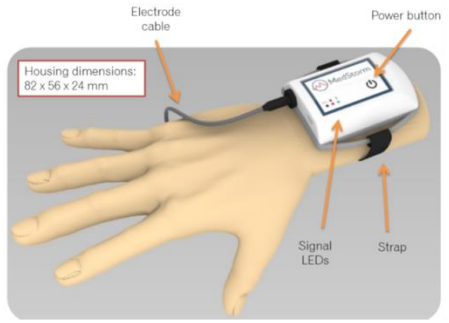
Pain Index	Peaks per second Reflect how often the sympathetic nerves of the skin fire	Indication during painful events
0	0.00 - 0.06	Analgetics can be reduced
1	0.07 - 0.12	Analgesics is probably not needed
3	0.13 - 0.19	More analgesics may possibly be needed
5	0.20 - 0.26	More analgesics may probably be needed
7	0.27 - 0.32	More analgesics may be needed
8	0.33 - 0.39	More analgetisk are necessary
10	0.40 or higher	More analgetisk are necessary

Suggested use-cases to titrate the need of analgesia:

- **Postoperatively**
- **Artificial ventilated**
- **Asphyxiated**

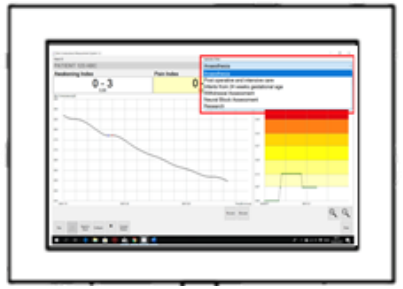
To assess emotional stress the device can be used on general basis, but the index is not valid.

The different interface options for showing the indices

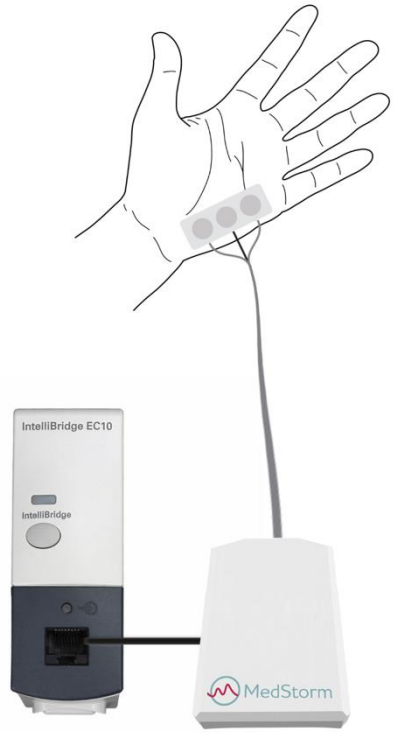


Bluetooth Connection

Monitors without bluetooth connection need to connect via the «cubist box» which is connected to the intellivue bridge

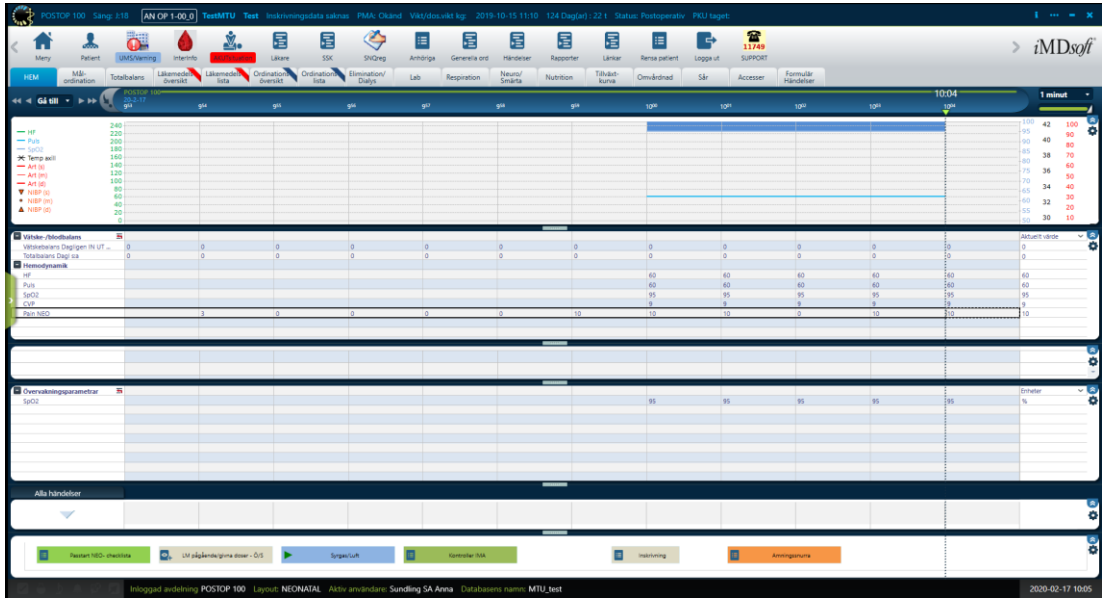


The index can also be shown on a stand alone monitor. More information is available here.



The PainSensor can be connected with the Philips monitor with a cable. Intended to be ready in 2021.

Connectivity Philips patient monitor



Why assessing pain in infants – return of investment

- Infants are shown to remember pain with e.g. stronger response to pain stimulus (immunization) 3 months after circumcision*.
- Less development of sepsis and even death, extra stay in the NICUs* will be reduced.
- Pain can cause intra-cerebral hemorrhage in preterm infants causing long term side effects like cerebral palsy (spasticity), hearing loss, vision problems and learning disabilities*.
- Reduce of abstinence**, extra stay in hospitals will be reduced.
- Pain-Nociceptive Sensor devices helps titrate and assess the effictiveness of opioid-sparing approaches during Surgery***.
- Emotional stress in infants like pain may decrease weight gain and development, and length of hospital stay may increase*.

*Storm H, Pain assessment in neonates. Published by IGI Global http://igi-global.com/AuthorsEditors/AuthorEditorResources/CallForBookChapters/CallForChapterDetails.aspx?CallForContentId=02f37e9d-dfc7-4596-9a47-cadff82a5a9c.
**1. Oji-Mmuo CN, Michael EJ, McLatchy J, Lewis MM, Becker JE, Doheny KK (kdoheny@hmc.psu.edu). Skin conductance at baseline and postheel lance reflects sympathetic activation in neonatal opiate withdrawal. Acta Pædiatrica. Published by John Wiley & Sons Ltd 2016 105, pp. e99–e106 e99.
2. Schubach NE, Mehler K, Roth B, Korsch E, Laux R, Singer D, von der Wense A, Treszl A, Hünseler C. Skin conductance in neonates suffering from abstinence syndrome and unexposed newborns. Eur J Pediatr. 2016 Jun;175(6):859-68.

***Kehlet H, Dahl JB. The value of 'multimodal' or 'balanced analgesia' in postoperative pain treatment. *Anesth Analg* 1993; 77: 1048-1056.
Coeckelenbergh S, Doria S, Patricio D, Perrin L, Engelman E, Rodriguez A, Di Marco L, Van Obbergh L, Estebe JP, Barvais L, Kapessidou P. Effect of dexmedetomidine on Nociception Level Index-guided remifentanil antinociception: A randomised controlled trial. *Eur J Anaesthesiol.* 2021 May 1;38(5):524-533. doi: 10.1097/EJA.0000000000001402. PMID: 33259449

Demonstration

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Thank you

(Time for a demonstration)

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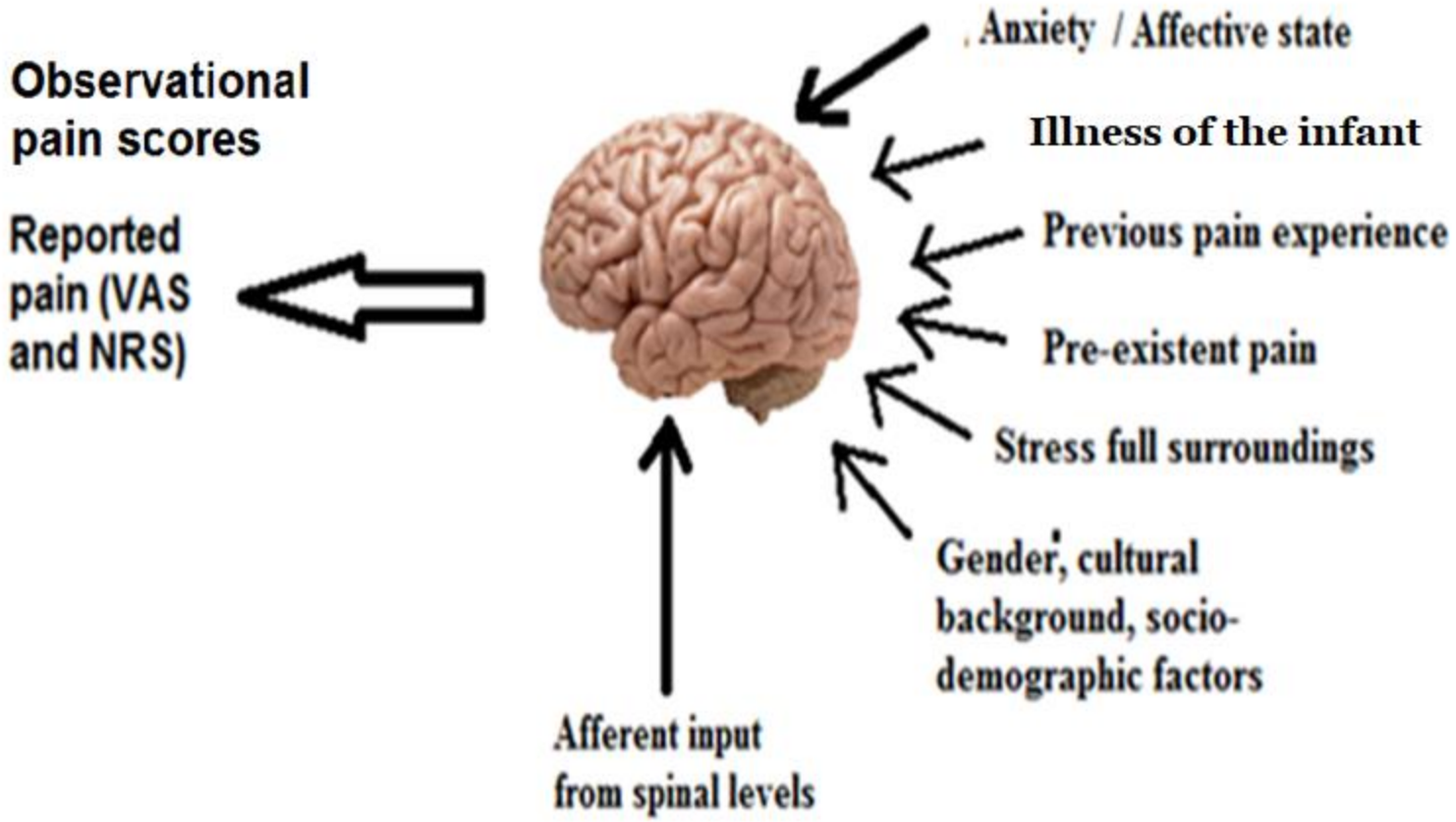
Why using the Pain-Nociceptive Sensor from Med-Storm Innovation - The physiology

Pain assessment in patients who may verbally communicate, strengths and weakness:



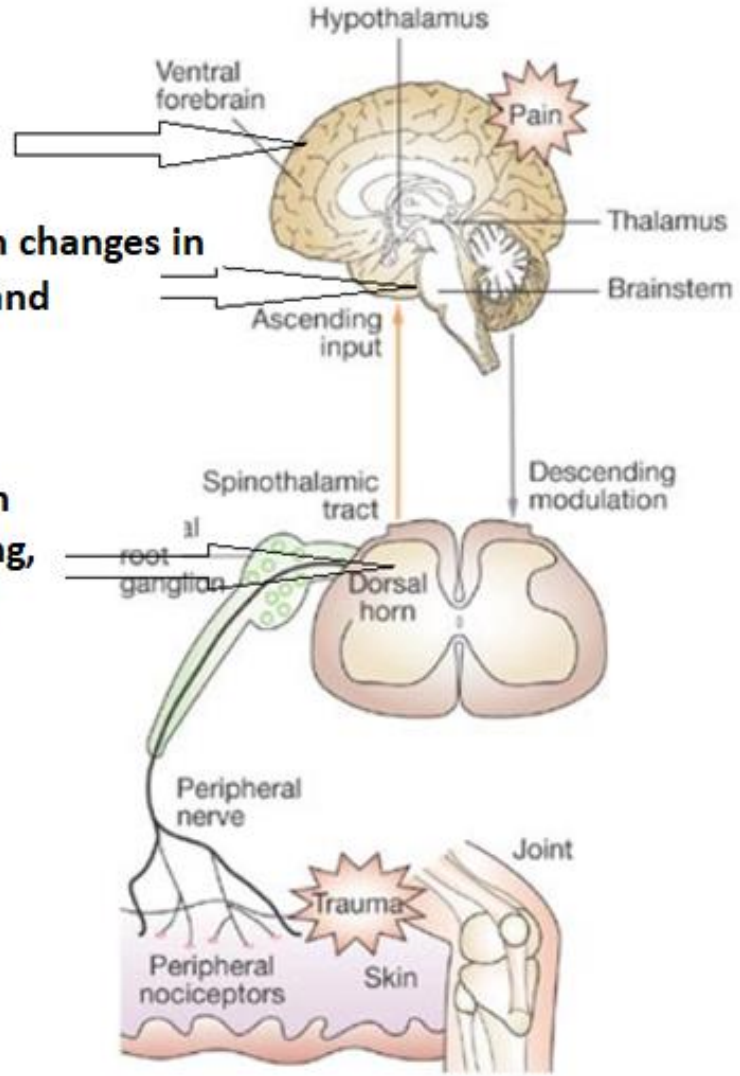
Lidén Y, Landgren O, Arnér S, Sjölund KF, Johansson E. Procedure related pain among adult patients with hematologic malignancies. *Acta Anaesthesiol Scand*. 2009;53(3):354-363.

Assessment of nociceptive responses in the sedated patients:

EEG-monitors

Monitors based on changes in blood circulation and respiration

Monitors based on emotional sweating, changes in blood circulation and respiration



The Sympathetic nerve activity assessed by Microneurographi

Vaughan GM.

Handbook of clinical neurology, vol 117.
Automomic nervous system. R.M. Buijs and D.F. Swaab, Editors © 2013 Elsevier B.V. All rights reserved

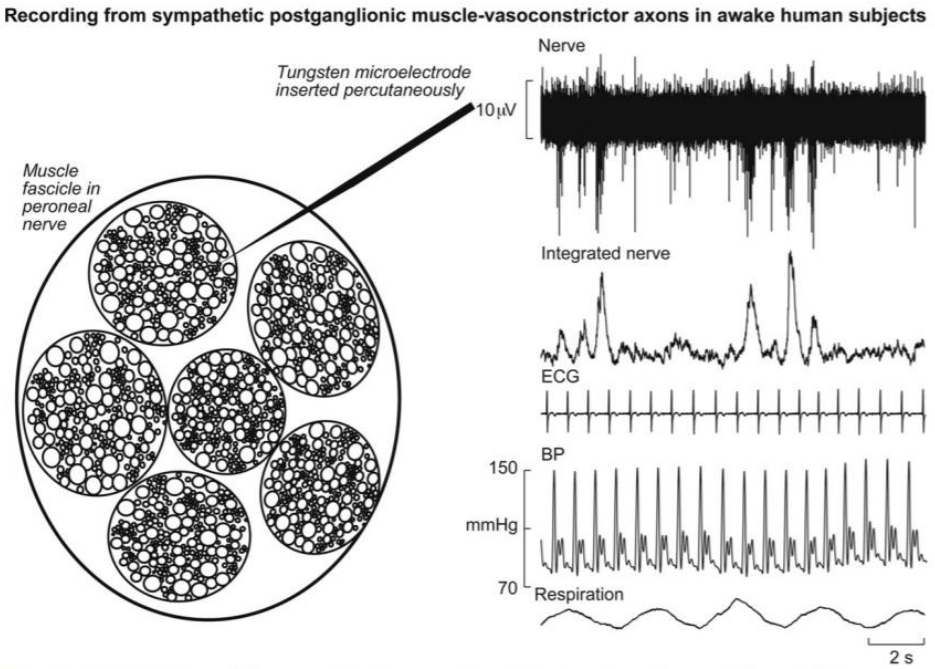


Fig. 28.1. Spontaneous bursts of muscle sympathetic nerve activity recorded via a tungsten microelectrode inserted into a muscle fascicle of the fibular nerve.

1. Muscle sympathetic nerve activity (MSNA) is muscle nerve fascicle influences NOL-index, Surgical stress index– may also influence the **parasympathetic nervous** system: heart rate variability, Mdoloris and partly Medasense – the epinephrines

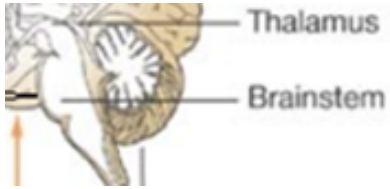
2. Skin sympathetic nerve activity (SSNA) is skin nerve fascicle

A. The skin sympathetic nerves responsible for temperature dependent sweating by vasoconstriction to the skin with hair.

B. The skin sympathetic nerves responsible for emotional sweating palmary and plantar - influences Skin Conductance Algesimeter (partly NOL-index) – acetylcholine acting on muscarinic receptors.

The sympathetic nervous system:

Surgical Stress Index, the NOL-index (Mdoloris indirectly) - MSNA (vaso-constriction) is activated (different from the SSNA) during:

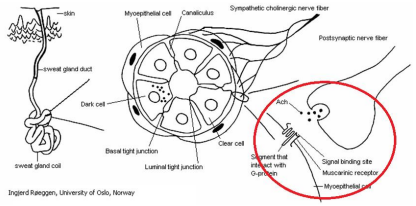


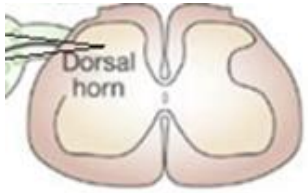
- Orthostatic hypotension and syncope (baroreflex control)
- Decreasing during inspiration and increasing during expiration
- Individual differences / decreases by age / increase by increase in BMI
- Cardiovascular, cardio-respiratory and renal diseases
- Parkinson's disease, panic disorders, depression and pure autonomic failure (also influencing SSNA)
- Medication acting on blood circulation and respiration (e.g. epinephrines, beta-blockers, the hypotensive effect of alfa2-agonists – **important for opioid free and opioid reduced anaesthesia.**

SSNA – hairy skin (vaso-constriction) is activated during hyperhidrosis (different from MSNA)

The Skin Conductance Algesimeter (partly the NOL-index) SSNA – palmar and plantar (acetyl choline acting on muscarinic receptors):

- Arousal in awake patients
- Atropine (not in clinical doses)





Skin Conductance Algesimeter - Sensitivity and Specificity in different patient populations

The PainNociceptive Sensor index, peaks per sec, to assess pain during intensive and postoperative care as well as during anaesthesia

	Sensitivity	Specificity
Postoperative (NRS > 4) all patients	90 %	70-75%
Intensive care (VAS > 30 mm) patients without moderate and severe anxiety	92 % and 91%	92 %
Anaesthesia, Surgical stress score Anaesthesia without stimuli	86%	86% 100%

*Preliminary results

Storm H, Günther A, Sackey JP, Bernhardsson J, Bjärtå A. Measuring pain – physiological and self-rated measurements in relation to pain stimulation and anxiety. Acta Anaesthesiol Scand. 2019;1–8.

Hansen JO, Storm H, Boglino-Hörlin A, Le Guen M, Gayat E, Fischler M. Skin conductance as a pain assessment tool during chest tube removal: An observational study. Eur J Pain. 2017 Eur J Pain. 2017 Jul;21(6):987-996.

Ledowski T, Storm H et al. Monitoring of skin conductance to assess postoperative pain intensity. British Journal of Anaesthesia 2006;97(6):862-5.

Ledowski T, Bromilow J, Wu J, Paech MJ, Storm H, Schug SA. The assessment of postoperative pain by monitoring skin conductance: results of a prospective study, Anaesthesia. 2007 Oct;62(10):989-93

Hullett B, Chambers N, Preuss J, Zamudio I, Lange J, Pascoe E, Ledowski T, Monitoring Electrical Skin Conductance A Tool for the Assessment of Postoperative Pain in Children? Anesthesiology 2009; 111:513–7