

Monitoring Electrical Skin Conductance

A Tool for the Assessment of Postoperative Pain in Children?

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Background: **Monitoring changes in electrical skin conductance has been described as a potentially useful tool for the detection of acute pain in adults. The aim of this study was to test the method in pediatric patients.**

Methods: **A total of 180 postoperative pediatric patients aged 1–16 yr were included in this prospective, blinded observational study. After arrival in the recovery unit, pain was assessed by standard clinical pain assessment tools (1–3 yr: Face Legs Activity Cry Consolability Scale, 4–7 yr: Revised Faces Scale, 8–16 yr: Visual Analogue Scale) at various time points during their stay in the recovery room. The number of fluctuations in skin conductance per second (NFSC) was recorded simultaneously.**

Results: **Data from 165 children were used for statistical analysis, and 15 patients were excluded. The area under the Receiver Operating Characteristic curve for predicting moderate to severe pain from NFSC was 0.82 (95% confidence interval 0.79–0.85). Over all age groups, an NFSC cutoff value of 0.13 was found to distinguish between no or mild *versus* moderate or severe pain with a sensitivity of 90% and a specificity of 64% (positive predictive value 35%, negative predictive value 97%).**

Conclusions: **NFSC accurately predicted the absence of moderate to severe pain in postoperative pediatric patients. The measurement of NFSC may therefore provide an additional tool for pain assessment in this group of patients. However, more research is needed to prospectively investigate the observations made in this study and to determine the clinical applicability of the method.**

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CHILDREN'S pain is a global public health issue.[1] Early assessment and treatment of acute pain in children is crucial, not only for humanitarian and ethical reasons, but because prolonged states of pain in childhood may have significant long-term effects, leading to disability and suffering later in life.[2]

Most pain scoring systems used in clinical practice rely on patient cooperation and communication. However, especially younger children may be less able to understand, tolerate, or describe their pain in a way that health professionals can understand. As a result, pediatric pain is often poorly assessed and inadequately managed.[1] Recent investigations[3,4] in adults have shown that changes in the number of fluctuations of skin conductance per second (NFSC) reflect acute postoperative pain when compared with a patient self-rating of pain on a numeric scale. In one of these studies, a cutoff value of NFSC (0.1) distinguished between no or mild *versus* moderate or severe pain with 89% sensitivity and 74% specificity,[4] suggesting the method as a suitable tool for the assessment of acute pain.

The aim of this prospective, blinded observational study was to assess NFSC as a marker of pain status (none-mild *vs.* moderate-severe) determined by different traditional pain scoring systems in children in the postoperative setting.

Materials and Methods

Institutional Review Boards' (Ethics Committee of the Princess Margaret Hospital for Children, Perth, WA, Australia) approval was obtained for this prospective, blinded, observational study, and the trial was registered with the Australian Clinical Trials Register (ACTRN12607000474459). A total of 180 children, aged 1–16 yr undergoing elective surgery, were recruited after written informed consent was obtained from the parents and children–as appropriate–on the day of surgery. Exclusion criteria were the presence of major systems disease (diabetes mellitus, cardiovascular, renal, hepatic, neuronal), developmental delay, congenital syndromes, pacemakers, autonomic neuropathy, American Society of Anesthesiologists Anesthetic Risk score 3–5, medication with drugs suspected or known to interact with the method of skin conductance (SC) monitoring (*e.g.*, atropine, glycopyrrolate, ketamine, clonidine, β-adrenoreceptor-blockers), lack of access to patient's hand, and history of contact reaction to adhesive tapes.

Intraoperatively, the attending anesthetists used a general anesthetic technique of their choice, with attention

to maintaining normothermia and avoidance of above-specified drugs.

Pain scores were obtained in 3-min intervals from arrival in the recovery room until discharge. Different pain scores are usually used in different age groups to account for the age-related different levels of neurocognitive development, children were divided into three age groups. Pain in the 1–3 yr group was assessed by using the Face, Legs, Activity, Cry, and Consolability score,[5] in the 4–7 yr group by using the Revised Faces Pain Scale,[6] and in the 8-16 yr group by using the Visual Analogue Scale; all scoring systems ranged between 0 and 10 points (0 representing no, 1–3 mild, 4–5 moderate, and 6–10 severe pain). Simultaneously, NFSC was recorded by a second observer. In addition, an anxiety score (Modified Yale Preoperative Anxiety Scale, m-YPAS)[7] was obtained preoperatively in children aged 3–12 yr (age range for which m-YPAS has been validated) to control for the influence of anxiety on NFSC readings. The treatment of postoperative pain was per standard clinical practice at the study institution (fentanyl/morphine for moderate-severe pain and non-opioid analgesics for mild pain).

Discharge from the recovery unit occurred per standard clinical practice, *i.e.*, when the patient was deemed comfortable, awake, and behaviorally appropriate with stable basic observations.

Skin Conductance Monitoring

NFSC was obtained *via* aMEDSTORM AS 2005 monitor (Medstorm Innovations, Oslo, Norway) by using a three-electrode system (measurement, counter, reference) and single-use Ag/AgCl pediatric electrocardiogram electrodes (Neotrode, ConMed Corp., Utica, NY). Electrodes were placed on the patients' hands (measurement, thenar eminence; counter, hypothenar eminence; reference, back of hand) on arrival in recovery. The equipment used an alternating current of 88 Hz and an applied voltage of 50 Mv (highest density 2.5 μA). The monitor was connected to a laptop computer *via* a standard serial port connection to display and process the obtained data. The software was able to automatically define peaks and troughs within the mean skin conductance (amplitude threshold for detection 0.02 μS) and to calculate NFSC from this data. A data sampling rate of 15 s and a monitor refresh rate of 15 s were chosen for this investigation.

Statistical Analysis

On the basis of these results of two former publications by the authors related to NFSC as a tool for assessment of postoperative pain in adults,[3,4] 60 subjects per age group was deemed to be sufficient to obtain a substantial amount of pain readings in the moderate-severe range. However, a formal sample size calculation was not performed because NFSC has not been used in this age group before. A pain score of no more than 3 was considered no to mild pain, and a score greater than 3 was considered moderate to severe pain. NFSC values were then analyzed in relation to simultaneous dichotomous pain scores by using receiver operating characteristic (ROC) curves. Separate ROC analyses were performed on data for three age groups, 1–3 yr, 4–7 yr, and 8–16 yr. Univariate and multivariate logistic regression analyses using generalized estimating equations to handle the repeated measurements on each patient were used to assess unadjusted and adjusted relationships between dichotomized pain and NFSC variables. Age, body temperature, and anxiety were assessed as potential confounding variables. We assumed an exchangeable correlation structure for the generalized estimating equations models, and we used robust variance estimates for all hypothesis tests. All *P* values were two-sided, and a *P* value less than 0.05 was considered significant. ROC analyses were performed by using Stata 10.0 (StataCorp, College Station, TX). All other analyses were performed by using SAS for Windows 9.1 (SAS Institute, Cary, NC).

Results

Data from 1,255 pairs (standard pain score + NFSC) of pain assessments in 165 patients were evaluated. The mean age of patients was 6.9 yr (SD = 4.49). The median (interquartile range, IQR) operation time was 40 (30–50) min and the median (IQR) recovery time was 30 (25–30) min. Sixty patients were recruited from each of three age groups: 1–3 yr, 4–7 yr, and 8–16 yr. Data from 15 patients were excluded because of technical difficulties with the skin conductance monitoring or a violation of the study protocol: nine from the 1–3 yr group and six from the 4–7 yr age groups. Characteristics of patients by age group are given in table 1.

The median (IQR) number of pain assessments was 7 (6–9), with a minimum of 3 and a maximum of 18. The median (IQR) NFSC was 0.07 (0–0.27), with 45.8% (n = 574) of measurements equal to or greater than 0.13. The median (IQR) pain rating was 0 (0–2), with 18% (n = 226) of ratings classified as moderate to severe pain, defined as a rating of at least 4. Characteristics of the NFSC measurements and pain ratings by age group are given in table 1.

The area under the ROC curve for predicting moderate to severe pain from NFSC was 0.82 (95% confidence interval [CI] 0.79–0.85). A data-determined NFSC cutoff value of at least 0.13 resulted in a test sensitivity of 90.3% and specificity of 64.0% to identify time points with moderate/severe pain out of all pain assessments (table 2). On the basis of the resulting positive and negative predictive values (table 2), clinical application of NFSC of at least 0.13 as a cutoff value to detect moderate/severe pain in our subjects would have resulted in 64.5% (1-positive predictive value) of patients being overtreated (incorrectly defined as in moderate/severe pain)

Table 1. Characteristics of the Sample

	Age Group			
	1–3 yrs	4–7 yrs	8–16 yrs	Full Sample
Characteristics of data				
Number of patients	51	54	60	165
Total number of pain assessments	426	377	452	1255
Pain assessments per patient, median (IQR) [minimum–maximum]	8 (6–10) [3–15]	7 (5–8) [4–13]	7 (5–9) [3–18]	7 (6–9) [3–18]
Characteristics of patients				
Age, yrs, mean (SD)	2.3 (0.81)	5.5 (1.21)	12.1 (2.50)	6.9 (4.49)
Anxiety score, mean (SD)	6.9 (3.39)	7.0 (1.61)	6.1 (1.36)	6.7 (2.12)
Operation time, min, mean (SD)	42.1 (36.24)	46.7 (48.79)	60.7 (36.16)	50.4 (41.29)
Body temperature, °C, mean (SD)	36.4 (0.57)	36.2 (0.49)	36.3 (0.48)	36.3 (0.51)
Recovery time, min, mean (SD)	30.9 (7.66)	29.0 (7.79)	28.8 (9.70)	29.5 (8.50)
Characteristics of measurements				
Pain rating category, n (%)				
None (0)	315 (73.9)	310 (82.2)	281 (62.2)	906 (72.2)
Mild (1–3)	30 (7.0)	30 (8.0)	63 (13.9)	123 (9.8)
Moderate (4–5)	38 (8.9)	12 (3.2)	53 (11.7)	103 (8.2)
Severe (6–10)	43 (10.1)	25 (6.6)	55 (12.2)	123 (9.8)
NFSC, median (IQR) [minimum–maximum]	0.13 (0–0.60) [0–2.65]	0 (0–0.13) [0–1.57]	0.07 (0–0.20) [0–2.72]	0.07 (0–0.27) [0–2.72]

IQR = interquartile range; NFSC = number of fluctuations per second; SD = standard deviation.

but only 3.2% (1-negative predictive value) of patients undertreated (incorrectly defined as in no/mild pain).

Separate ROC analyses by age group showed some variation in the accuracy of predicting moderate to severe pain from NFSC (fig. 1). The area under the ROC curve was smallest for the 1–3 yr age group (area 0.76; 95% CI 0.71–0.80), largest for the 4–7 yr group (area 0.93; 95% CI 0.90–0.96), and virtually identical to the sample result for the 8–16 yr age group (area, 0.83; 95% CI 0.78–0.87). Differences in test characteristics for the three age groups can be mostly attributed to the relatively lower prevalence of moderate to severe pain in the 4–7 yr age group and slightly higher prevalence in the 8–16 yr group (table 2). The former produces a more accurate negative test result, and the latter produces a more accurate positive test result.

Odds ratios for the association between pain ratings and NFSC were calculated. Based on the complete sample of observations, the odds of moderate to severe pain were significantly higher for patients with NFSC of at least 0.13 relative to those with NFSC less than 0.13 ($P < 0.0001$), both unadjusted and when adjusted for age and body temperature (table 3). When using data from patients who also provided anxiety scores (a total of 814 pain assessments), the odds of moderate to severe pain were again significantly higher for patients with NFSC of at least 0.13 relative to those with NFSC less than 0.13 ($P < 0.0001$), both unadjusted and when adjusted for anxiety (m-YPAS), age, and body temperature. Overall, adjusting the odds ratios for potential confounders (anxiety score [m-YPAS], body temperature, age) did not substantially alter the unadjusted values, suggesting no influence of the factors in our cohort (table 3).

Table 2. Characteristics of Skin Conductance Test Using the Number of Fluctuations in Skin Conductance per Second (NFSC) of at least 0.13 as a Positive Test Result

Group	Prevalence of Moderate to Severe Pain	Sensitivity (%)	Specificity (%)	PPV	NPV
Whole sample	18.0	90.3	64.0	35.5	96.8
Age 1–3 years	19.1	93.8	52.0	31.5	97.3
Age 4–7 years	9.8	97.3	72.9	28.1	99.6
Age 8–16 years	23.9	85.2	67.1	44.9	93.5

NPV = negative predictive value; PPV = positive predictive value.

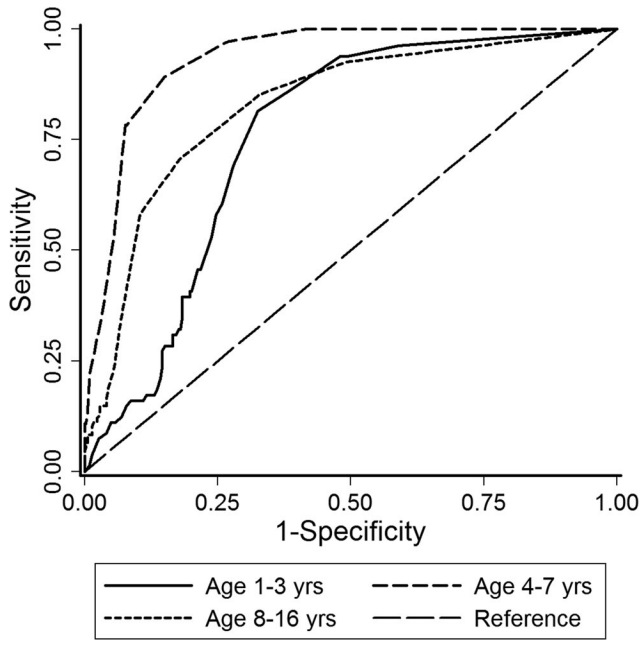

Fig. 1. Receiver operating curves (ROC) for the parameter number of fluctuations in skin conductance per second (NFSC) to identify all time points with moderate or severe pain as measured by standard pain scores.

Table 3. Odds Ratios and 95% Confidence Limits for Predicting Pain (Moderate–Severe *vs.* None–Mild) from the Number of Fluctuations in Skin Conductance Dichotomized at 0.13 (Less Than 0.13 *vs.* at Least 0.13)

Adjustment Variable(s)	Odds Ratio*	95% LCL	95% UCL
All valid observations (n = 1,254)			
Unadjusted	7.56	4.49	12.73
Age, body temperature	7.95	4.75	13.30
Observations with anxiety scores (n = 814)			
Unadjusted	11.46	5.73	22.93
Anxiety score	11.50	5.73	23.07
Anxiety score, age, body temperature	12.29	6.02	25.10

Results are from generalized estimating equations assuming an exchangeable correlation structure. Confidence limits are based on robust standard errors. All $P < 0.0001$.

* Odds ratio greater than 1 indicates higher odds of moderate–severe pain for the number of fluctuations in skin conductance per second (NFSC) of at least 0.13.

LCL = lower confidence limit; UCL= upper confidence limit.

Discussion

Though the method of monitoring changes in the electrogalvanic properties of the skin has been described by Fere as early as 1888, it has not been used as a tool for the assessment of postoperative pain until two recent publications found a strong relationship between postoperative pain and the SC parameter NFSC in adults.[3,4]

Previous research in neonates focused on absolute values of SC parameters but failed to provide values that would allow the clinician to discriminate between pain that is well controlled (no or mild) and pain that needs urgent attention (moderate or severe).[8,9] To our knowledge, the current study is the first to describe the use of skin conductance as a tool for pain assessment in children of all ages.

In our observational study, a cutoff value for NFSC (0.13) allowed us to identify time points with moderate or severe postoperative pain with 90% sensitivity and 64% specificity. These results match with the previously described characteristics in adult postoperative patients (Ledowski *et al.*[4]: sensitivity 89%, specificity 74%) as well as with results for the ability of NFSC to indicate intraoperative painful stimuli; Storm *et al.*[9]: sensitivity and specificity 86%). However, the NFSC cutoff values used in adult studies were generally lower (Ledowski *et al.*[4]: 0.1; Storm *et al.*[9]: 0.05).

If NFSC had been used in our cohort to guide pain treatment by using an NFSC value below the cutoff to exclude moderate and severe states of pain (NFSC as negative predictor), only 3.2% of children in moderate or severe pain would have remained undiagnosed and hence potentially undertreated. In contrast, use of NFSC values higher than the cutoff to identify states of moderate or severe pain (NFSC as positive predictor) would have resulted in an overtreatment (incorrectly diagnosed as moderate or severe pain) in 64.5% of patients. The difference in the potential clinical usefulness of NFSC as either negative or positive predictor for moderate/severe pain reflects the test's high sensitivity and lower specificity, with the consequence of relatively more false-positive than false-negative results. This can be partially explained by the fact that we chose to emphasize sensitivity when choosing a cutoff to minimize undertreatment of pain. Also contributing to the difference in the positive and negative predictive value of NFSC was the relatively low prevalence (18%) of moderate and severe pain in our subjects. Virtually independent of a test's intrinsic accuracy (sensitivity and specificity), a negative test will be more accurate than a positive one when the prevalence of an event is low; the opposite being true when the prevalence is high.[10] In modern anesthesia, the prevalence of moderate and especially severe postoperative pain is likely to be low, and any diagnostic tool for the assessment of pain would be expected to produce more false-positive than false-negative diagnoses.

Our investigation focused on the SC parameter NFSC because it has been shown to be less influenced (compared to mean SC) by electrode placement or type of electrodes. However, other parameters have been studied in the past; Harrison[11] showed no correlation between the mean SC or the amplitude of fluctuations and a painful stimulus and confirmed that NFSC did increase significantly with a painful stimulus in neonates.

A clear limitation of the SC method to assess pain is the fact that SC reflects palmar sweat gland filling, hence ultimately sympathetic tone. Therefore, all factors that influence sympathetic tone (*e.g.*, anxiety, nausea) might theoretically alter the reaction of SC or its parameters to painful stimuli. In children, anxiety associated with parental separation or an unfamiliar environment may well influence sympathetic tone and therefore skin conductance. We did not study state anxiety in the recovery room, but we found that preoperative anxiety measured by m-YPAS did not affect the strong association between pain ratings and NFSC. In addition, studies in adults comparing bispectral index data and SC measures during emergence from general anesthesia have demonstrated a strong effect of arousal on sympathetic tone and subsequently SC.[12,13] However, Storm[14] has claimed that painful stimuli with/without arousal did produce different waveforms of the fluctuations in skin conductance, hence a potential chance to electronically eliminate arousal as a confounder. Measuring the effect of arousal on sympathetic tone was not the subject of our investigation. Thus we are unable to comment on its extent in our cohort. Despite these limiting factors, our results suggest a strong relationship between NFSC and acute postoperative pain.

For correct interpretation of our current and formally published results, it needs to be emphasized that there is currently no reliable standard for the assessment of acute pain in adults and children. All scoring systems used in our trial and previous trials are highly observer-dependent (*e.g.*, nurse-rated pain scores) or rely on patient cooperation

(visual analogue or numeric rating scales). All systems lack clearly specified sensitivities/specificities in the description of pain states as the subjectivity of pain does not allow comparison with absolute values for pain.

Further work, especially related to the limitations of the method, is therefore required to define the precise role of NFSC assessments in the management of pediatric pain.

We conclude that NFSC, especially when used as a negative predictor, may play an important role for the assessment of acute pediatric pain. In particular, NFSC may facilitate pain assessment in children with developmental or communication difficulties. However, as NFSC may be influenced by factors other than pain, the method should not be used as a sole tool for pain assessment, and further research is required to determine the clinical applicability of the method.

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