Non-linear Multi-parameter Approach for evaluation of Nociception Level during General Anesthesia

Ben-Israel Nir, M.Sc., Zuckerman Galit, M.Sc., Kliger Mark, Ph.D., Katz Yeshayahu, Ph.D. M.D., Edry Ruth, M.D.,

Background

Direct indicators for the assessment of nociception level during general anesthesia have been investigated in recent years. Among these indicators: the linear combination of the normalized heart rate (HR) and pulse wave amplitude (PA) [1]; the high frequencies of heart rate variability (HRV-HF) [2]; and the skin conductance level (SCL) and number of skin conductance fluctuations (NSCF) [3].

The objective of this study is to enhance the concept of using physiological parameters for the assessment of nociception level. By using an advanced regression technique, that enables a non-linear combination of several physiological parameters, we seek to provide a reliable and robust indicator for the nociception level that outperforms any individual parameter or their linear combination.

Methods

24 ASA I-II patients (10M,14F, mean age 47± 13.5) scheduled for elective surgery under general anesthesia were enrolled. Following premedication with Midazolam (1–2 mg), general anesthesia was induced by propofol (1.5–3 mg/kg), fentanyl (1.5–3 µg/kg), and rocuronium (0.7 mg/kg); and maintained with isoflurane (0.6–1.2%), remifentanil (0.2 µg/kg*min) or fentanyl (2 µg/kg), and atracurium as required.

The patients' ECG, Plethysmograph, and Skin Conductance were recorded and sampled by the MP 100 system (Biopac System Inc., Goleta, CA, USA). The physiological parameters HR, PA, HRV-HF, SCL, NSCF, and their derivatives were extracted and were used as predictor variables. Random-Forest regression technique [4] was used to derive a novel indicator NoL, which estimates Nociception Level from the predictor variables. The NoL values were further non-linearly normalized into a graduated scale between 0 and 100 using a sigmoid function.

A Combined Index of Stimulus and Analgesia (CISA) was defined as a combination of stimulus level (a number representing the intensity of the surgical event ranked by anesthesiologist) and scaled remifentanil effect-site concentration to represent a nociception level and as an observed variable in the regression model:

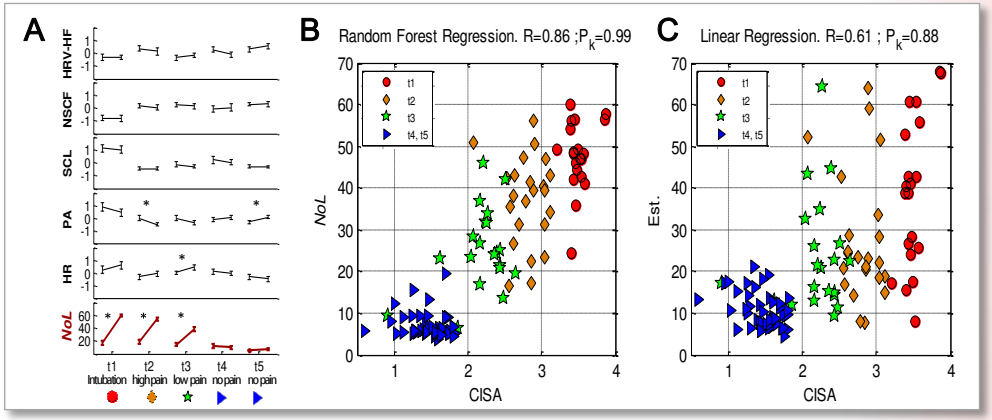
$$\mathbf{CISA = Stimuli\ Level - Ce_{Remi}}/\alpha + \beta$$

5 time-points were chosen for comparisons: t1 = intubation; t2 = first incision/trocar; t3 =other painful stimuli (gastric tube placement, small incision, etc.); t4 =no pain, before skin incision; t5 = no pain, about 20 minutes before awakening. Correlation coefficient (R) and prediction probability (Pk) were evaluated to examine the regression performance. Statistical comparison was conducted using Wilcoxon test for paired groups with 5% significance level.

Results

NoL indicator, which estimates Nociception Level from the predictor variables, significantly increased during all noxious stimuli (t1–3) as opposed to the other individual parameters. Fig. 1A shows the behavior of each of the parameters and the NoL indicator before and during time-points t1–5.

When the *NoL* was examined versus the observed variable CISA (Fig 1B), R=0.86 and Pk=0.99 were obtained. For comparison, an ordinary linear LS regression (Fig 1C) resulted in lower correlation (R=0.61).



Conclusions

The proposed *NoL* indicator derived from the non-linear combination of multiple parameters outperformed (in the sense of R, Pk, and t-test significance) individual parameters and their linear combinations in detecting response to intraoperative noxious stimulus under GA. Further validations in various surgical scenarios are necessary to strengthen the results of this pilot study.

Summary

A non-linear multi-parameter approach for the evaluation of a novel indicator for nociception level (*NoL*) during general anesthesia is proposed. Validation shows that the NoL outperformed individual physiological parameters (commonly used as indirect measurement for nociception level) and their linear combinations in detecting response to a noxious stimulus.

Literature

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[4] Breiman L. Machine Learning J, 2001; 45:5-32.