Comparison of the qNOX and ANI Indices of Nociception during Propofol and Remifentanil Anaesthesia

J. Fontanet, E. Gabarrón, M. Jospin, M. Vallverdú, P.L. Gambus and E.W. Jensen

Abstract— **Movement responses to noxious stimuli during general anesthesia are regarded as a sign of nociception. We compared the qNOX Index and Analgesia Nociception Index (ANI) as predictors of movement during propofol and remifentanil anaesthesia. Both indices are compared using the calculated propofol/remifentanil effect site concentrations (Ce) and the response to noxious stimuli recorded in 20 patients. The ANI was transformed to 100-ANI in order to follow the same scale as qNOX, and make the statistical interpretation consistent. The prediction probabilities (remapped Pk-value) and their standard errors (SE) were obtained for the evolution of the indices versus Ce remifentanil: qNOX =0.78, SE=0.003; 100-ANI= 0.526, SE=0.004 (qNOX significantly larger). For the responses of noxious stimuli the Pk-value and their SE were: qNOX=0.71, SE=0.049; 100-ANI=0.68, SE=0.050. We conclude that the qNOX better predicts the Ce remifentanil while both qNOX and ANI detect equally well movement as a response to noxious stimulation.**

I. Introduction

Monitoring nociception under general anesthesia is currently an area which has not been completely solved although a number of different methods have been studied over the last decade. The proposed monitors can be divided into two groups, those based on analysis of brain signals such as electroencephalography (EEG) and Auditory Evoked Potential (AEP) [1,2] and those based on autonomic nervous system measures such as Heart Rate Variability (HRV) [3], baroreflex [4], Skin Conductance (SC) [5], or combinations of these [6]. There are main differences between the two approaches. Heart rate variability and skin conductance are correlated with sympathetic activity and therefore, monitors based on these parameters can measure the increase in sympathetic activity. However this is not necessarily related to pain or nociception because increase in the sympathetic activity can be caused by other factors not related to pain. The brain signal methods based on EEG are typically empirical in their origin as there is not clear consensus of which characteristics of the EEG change during analgesia.

The EEG is a direct measurement of brain activity and from the same recording a measure of hypnotic effect and a measure of pain/nociception can be developed. The qCON and qNOX indices are based on the combination of different frequency bands, which are fed into an Adaptive Neuro Fuzzy Inference System (ANFIS) which generates the output on a 0-99 scale. A vast number of publications have already been made on the validation of hypnotic effect monitors [7]-[9] whereas pain/nociception monitors for general anaesthesia are less explored [10].

The Analgesia Nociception Index (ANI) is an online HRV analysis based on electrocardiography (ECG) data derived from two single-use electrodes applied in V1 and V5 position on the chest. The ANI is obtained from the analysis of the high frequency (0.15-0.5Hz) of the HRV spectrum. It is displayed as a score from 0–100 with 0 reflecting a strong sympathetic tone and 100 (hence no pain) a strong parasympathetic tone [11].

The qNOX is decreasing when the effect increases, whereas the ANI uses the opposite scaling. Hence the ANI was transformed to 100-ANI, in order to follow the same scale as qNOX, and make the statistical interpretation consistent.

II. Methods

After institutional review board (IRB) approval and written informed consent data was recorded from 20 patients, scheduled for general anaesthesia in the Hospital Clinic of Barcelona.

Propofol and remifentanil were infused using a TCI system (Base Primea, FreseniusVial, France). The TCI system administered propofol and remifentanil according to the predictions of pharmacokinetic pharmacodynamic models. In both cases the TCI was targeting the effect site applying the Schnider model for propofol [12] and the Minto model for remifentanil [13].

The qNOX index was continuously measured and recorded to assess the nociception/antinociception balance. The data from qNOX index was stored in a PC with proprietary software, qCON display (Quantium Medical, Spain).The ANI was displayed and continuously recorded using the PhysioDoloris monitor (Metrodoloris, France). The remapped Pk-value [14] was used to assess the ability of the qNOX and ANI to predict movement as a response to noxious stimulation and to predict the Ce remifentanil. The remapped Pk-value avoids distinguishing if the index increases or decreases.

Movement as a response to laryngeal mask (LMA) insertion, skin incision, skin suture and LMA removal was recorded. Movement in the period of 1 minute after applying the stimuli was interpreted as a positive response to one of the nociceptive stimuli. The stimuli were classified as movers or non-movers. The mean value for the ANI and qNOX were calculated over 1 min period starting 30 seconds before the noxious stimulation event, entered in the Rugloop software. Because not all the data from the mean values

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followed a normal distribution a non-parametric Kruskal-Wallis test was used to find significant differences in the data, at $p<0.05$.To assess if there was significant difference between indices in terms of Pk-values the Student t-test was used.

III. Results

The Pk-value, SE and p-value were calculated for the qNOX and 100-ANI versus Ce remifentanil. The data with SQI (qCON signal quality index)<50 and ANI quality=0 was rejected for the study. It was calculated for the entire scale and for qCON <65. The reason for this was that the ANI is designed to work during general anaesthesia; hence a better measure could be expected when excluding the awake range. The results are shown in Table 1. The pooled approach for the 20 patients for Ce remifentanil and Ce propofol for entire scale is presented in Fig.1.

For the response to nociceptive stimuli the pre stimulus values found for qNOX were 57±30 (mean±std) for movers and 35±26 for non-movers, with Pk=0.71, SE=0.049 and $p<0.005$. Moreover the 100-ANI was 46±17 and 35±18 for movers/non-movers respectively, with Pk=0.69, SE=0.05 and $p<0.005$. The distribution is shown in Fig.2.

IV. Conclusion

A nociception monitor should correlate with the amount of analgesic administered to the patient, haemodynamic parameters and clinical signs of pain such as movement as response to noxious stimulation. The study shows that the qNOX and the ANI could predict whether a patient moves as a response to noxious stimulation during surgery. The prediction probability of Ce remifentanil was higher for qNOX than for ANI.

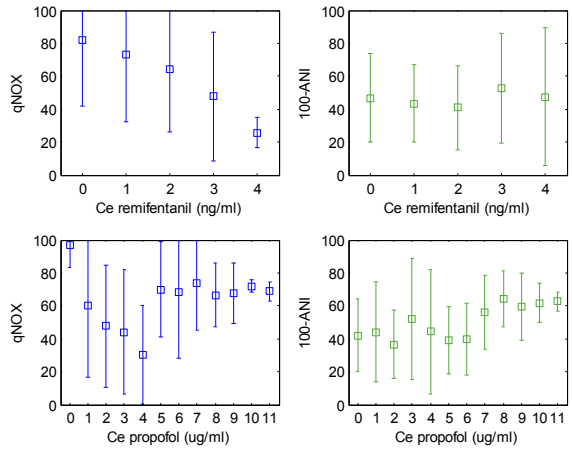

Figure 1. Indices qNOX and ANI versus the effect site concentration (Ce) of remifentanil and propofol. The mean with confidence interval of 90% are plotted for each value of Ce. . The qNOX y-axis was intentionally chosen to fit the scale of the monitor, 0-100, although cutting of the tail of some of the confidence intervals.

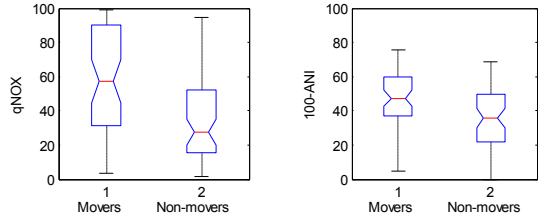

Figure 2. Indices qNOX and ANI for the response to nociceptive stimuli.

TABLE I. Results depending on the efect site concentration of remifentanil

Index	*Entire Scale*		*qCON<65*	
	qNOX	*100-ANI*	*qNOX*	*100-ANI*
Pk (SE)	0.78 (0.03)	0.53 (0.004)	0.75 (0.003)	0.54 (0.004)
p-value	<0.0005	<0.0005	<0.0005	<0.0005

Indices qNOX and ANI and qCON; Pk, prediction probability; SE, standard error

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