

# **Adaptive Neuro Fuzzy Inference System (ANFIS) for Modelling the Effect of Propofol and Remifentanil Combination Using qCON and qNOX Indices During Induction**

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**Introduction:** The objectives of this study were to describe the relationship between the effect site concentrations of propofol (CeProp) and remifentanil (CeRemi) versus the qCON and qNOX indices of hypnotic effect and pain/nociception by using an adaptive neuro fuzzy inference system (ANFIS) and to estimate their values that correspond to loss of consciousness and no response to nociceptive stimulation during anesthesia induction.

**Methods:** Data were recorded from 284 patients scheduled for general anaesthesia with a combination of propofol and remifentanil. The qCON 2000 monitor (Quantium Medical, Barcelona, Spain) was used to calculate the qCON and qNOX. Both indices are derived from the frontal electroencephalogram<sup>1</sup>. The TCI system (Base Primea, FreseniusKabi AG, Bad Homburg, Germany) administered propofol and remifentanil according to the predictions of pharmacokinetic and pharmacodynamic models. The data from the TCI system (CeProp and CeRemi) were recorded with Rugloop (Demed, Belgium). Loss of eye-lash reflex (LER) was assessed during the transition from awake to anesthetized, and used as the indicator that consciousness was lost. Movement as a response to laryngeal mask (LMA) insertion in the period of one minute after applying the stimuli was interpreted as the response to the nociceptive stimuli. The patients were classified as movers or non-movers and the values for the qCON and qNOX over the 1 min period before and after LER and LMA insertion were considered for the analysis.

Firstly, an ordinal logistic regression was performed in order to obtain the qCON and qNOX values and the confidence interval (CI) associated with a 25% and 50% probability of being awake and response to LMA insertion. Then, the qCON and qNOX data were fitted with CeRemi and CeProp by using ANFIS, a fuzzy logic-based modeling approach. ANFIS has the advantage to be a data-driven approach that does not assume an underlying mathematical model governing the relationship between the anesthetic drugs and the response effect. The models were developed on half of the patients and validated on the other half, by calculating the mean absolute error (MAE) and the prediction probability (Pk).

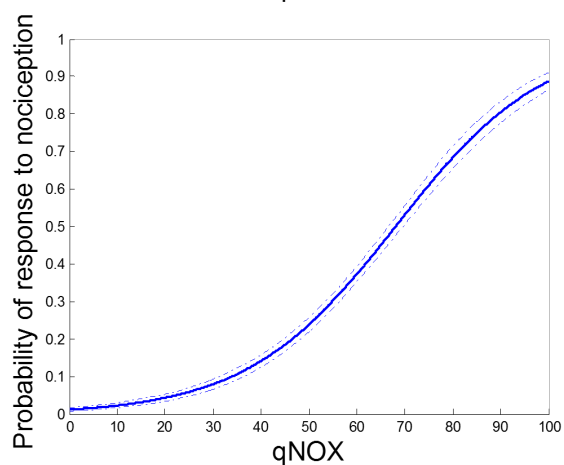
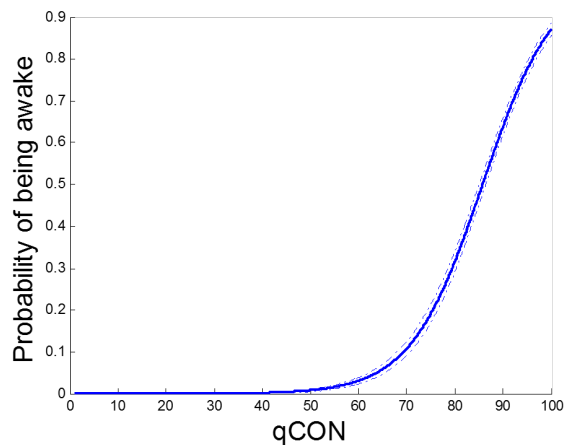
**Results:** The results of the ordinal logistic regression established that the values of qCON of 85.8 (CI: 85.0; 86.5) and 77.6 (CI: 76.5; 78.5) are associated with a 50 % and 25 % of probability of being awake, while the values of qNOX of 68.1 (CI: 66.5; 69.6) and 51.1 (CI: 52.6; 49.4) are associated with a 50 % and 25 % probability of loss of response to LMA insertion. Figure 1 shows the results of the ordinal logistic regression and the ANFIS models of qCON and qNOX. The results of the validation of the qCON ANFIS model gave MAE=16.01 and Pk=0.791 (standard error: 0.001), while for the qNOX ANFIS were MAE=17.27 and Pk=0.815 (standard error: 0.002).

**Discussion and Conclusion:** In conclusion, by using an ANFIS modeling approach it was possible to study the relationship between propofol and remifentanil predicted concentrations and hypnotic and analgesic effects during induction, in patients under general anesthesia. A qCON value of 75 corresponds to probability of being awake lower than 25 % while a qNOX of about 50 provided a probability of response to LMA insertion lower than 25 %. The qCON ANFIS surface shows higher slope with respect to CeProp, while the qNOX ANFIS surface shows a decrease with respect to CeRemi at high CeProp values. This suggests that at certain CeProp concentrations, the administration of CeRemi induces a decrease of qNOX.

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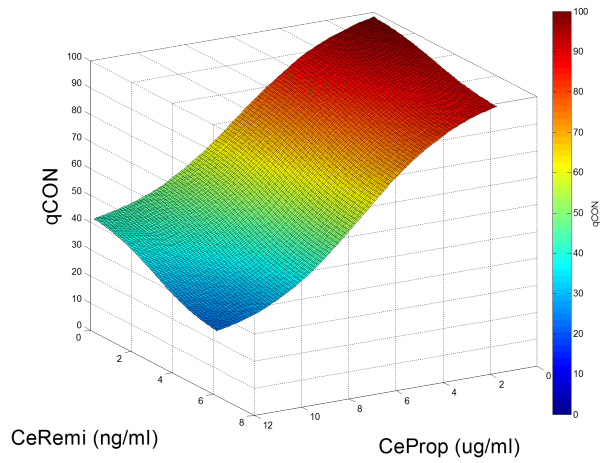
**References:**

1 Jensen, E. W., Valencia, J. F., Lopez, A., Anglada, T., Agustí, M., Ramos, Y., Serra R., Jospin, M., Pineda, P., Gambus, P. (2014). Monitoring hypnotic effect and nociception with two EEG-derived indices, qCON and qNOX, during general anaesthesia. *Acta Anaesthesiologica Scandinavica*, 58(8), 933-941.



(a)

(b)



(c)

(d)

Figure 1 – Ordinal logistic regression of (a) qCON vs. loss of consciousness and (b) qNOX vs. response to LMA insertion with the respective confidence intervals (dashed curves); results of the ANFIS models of (c) qCON and (d) qNOX versus CeRemi and CeProp.