Predictive Performance of the Noxious Stimulation Response Index as a Measure of Anesthetic Potency during Sevoflurane, Propofol and Remifentanil Anesthesia

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Background and Goal of Study: The Noxious Stimulation Response Index (NSRI) is an anesthetic depth indicator related to the probability to tolerate laryngoscopy recently presented for propofol and remifentanil.[1] Previous data of the interaction of sevoflurane, propofol and remifentanil from three studies [2-4] were pooled and re-analysed.[5] With the modified parameter estimates the NSRI was calculated and the predictive performance of the new NSRI was compared with other parameters of drug effect to estimate tolerance to different stimulations.

Materials and Methods: We used data of three previously published studies.[2-4] 120 adult patients were randomized to different combinations of sevoflurane, propofol and/or remifentanil. All patients were assessed for tolerance to 'shake and shout' (TOSS) and laryngoscopy (TOL). One study tested tetanic stimulation (TTET) and insertion of laryngeal mask airway (TLMA).[4] We extracted the probability of tolerance to laryngoscopy (P_{TOL}) in 120 patients using response surface modeling. The new NSRI is calculated from P_{TOL} as follows:

$$NSRI = \frac{100}{1 + \left(\frac{P_{TOL}}{1 - P_{TOL}}\right)^{S}}$$

where S = slope factor = 0.63093. Bispectral index (BIS), end-tidal concentration of sevoflurane (ET_{SEVO}) and effect-site concentration of propofol (Ce_{PROP}) and remifentanil (Ce_{REMI}) was available for all patients (analysis 1). State and response entropy (SE, RE), composite variability index (CVI) and surgical pleth index (SPI) were available from the Sevo-Remi interaction study (analysis 2).[4] We used prediction probability (P_K) as performance measure.[6] Bootstrapping (n=1000) was used to determine 95% confidence intervals of the differences between P_Ks with significance being achieved if the confidence interval did not include zero ($p < 0.05$).

Results and Discussion: The parameter P_K per stimulus are summarized in Table 1. NSRI has the highest P_K for detecting TOL. Effect-site and end-tidal concentrations predict significantly worse. For TOSS, BIS has a significantly higher P_K than NSRI in analysis 1, but not in analysis 2. BIS, SE, RE and CVI were significantly worse at predicting TTET, TLMA and TOL. SPI performed poorly overall.

Conclusions: NSRI predicts tolerance to noxious stimuli better than EEG-derived parameters and single drug effect-site concentrations. Tolerance to shake and shout is equally well detected by NSRI, SE and RE, but significantly better by BIS. This NSRI seems a promising concept to measure anesthetic potency for both intravenous and inhaled anesthesia.

Table 1: Prediction probability (P_K) of parameters for estimating tolerance to each stimulus

Analysis 1 (n=120)	ET_{SEVO}	Ce_{PROP}	Ce_{REMI}	BIS	SE	RE	CVI	SPI	NSRI
TOSS	0.826*	0.694*	0.499*	**0.979***	N/A	N/A	N/A	N/A	0.939
TOL	0.728*	0.458*	0.668*	0.710*	N/A	N/A	N/A	N/A	0.926
Analysis 2 (n=40)	**ET_{SEVO}**	**Ce_{PROP}**	**Ce_{REMI}**	**BIS**	**SE**	**RE**	**CVI**	**SPI**	**NSRI**
TOSS	0.890	N/A	0.595*	**0.948**	**0.931**	**0.933**	0.917	0.565*	0.927
TTET	0.786*	N/A	0.687*	0.834*	0.838*	0.838*	0.829	0.526*	0.927
TLMA	0.815*	N/A	0.632*	0.825*	0.809*	0.809*	0.785*	0.567*	0.919
TOL	0.757*	N/A	0.719*	0.779*	0.779*	0.773*	0.738*	0.574*	0.948

N/A: No observations available for analysis, * $p<0.05$ in comparison to NSRI, bold values are higher than NSRI.

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