Comparisons of EEG Measures of Hypnosis and Anti-Nociception in Response to Stimuli During Propofol Remifentanil Anesthesia

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Introduction & Aims

Hypnosis and analgesia constitute two important components of anesthesia. Nociception induced responses during anesthesia result from inadequately inhibited ascending sensory signals. Current electroencephalogram (EEG) derived measures do not provide accurate information on this sub-cortical activity. The neurophysiology-based EEG measures Cortical Input (CI) and Composite Cortical State (CCS) have been shown to be differentially influenced by analgesic and hypnotic medications respectively,[1] and thus could function as independent analgesia and hypnosis drug effect monitors.

Using these EEG derived measures to optimize anesthetic drug dosing before and during noxious stimulation could maximize patient safety and improve operating conditions while minimizing adverse effects.

In the current study we aimed to evaluate how well:

- The individual EEG derived measures (BIS, CVI, CI, CCS) and
- Combinations thereof (BIS/CVI versus CCS/CI)

measured <u>before</u> stimulation and <u>after</u> the administration of a test stimulus (OAA/S) could separate patients responsive and non-responsive to a subsequent tetanic stimulation.

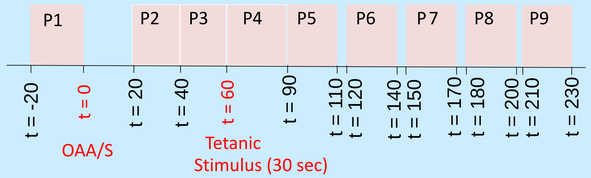

Fig.1 Timeline of study period (seconds). Median value of CCS, CS, BIS and CVI during each of 9 time periods (P1 to P9) was calculated. t = 0 represents the start of the OAA/S observation

Methods

In a previously published study[2] patients were randomly assigned to receive different combinations of hypnosis (propofol administered by closed loop to reach BIS target 50 or 70) and anti-nociception (target effect-site remifentanil concentrations of 0, 2, 4 or 6 ng/ml). Raw EEG was recorded. After a 17.5 min stabilisation period, at t = 0 in Fig. 1, an OAA/S (Observer's Assessment of Alertness/Sedation; fig 2) was performed. Thereafter, from t = 60 to 90 sec, a tetanic stimulus (100 Hz, 60 mA) was applied. The CCS, CI, BIS and CVI were calculated from the EEG for the period -20 sec until +230 sec.

For the current study we calculated the median values of these parameters during 9 time periods (P1 to P9 in Fig 1) before and after the application of the OAA/S and tetanic stimulus.

Score	Responsiveness
5	Responds readily to name spoken in normal tone
4	Lethargic response to name spoken in normal tone
3	Responds only after name is called loudly and/or repeatedly
2	Responds only after mild prodding or shaking
1	Responds only after painful trapezius squeeze
0	No response after painful trapezius squeeze

Fig.2 The Observer's Assessment of Alertness/Sedation scale (OAA/S)

Patients were classified as responsive if the OAA/S was >=1 and/or there was a purposeful response to the tetanic stimulus, otherwise they were classified as non-responsive. Prediction probability's were calculated for individual measures (data not shown). Scatterplots were constructed to visually judge the ability of individual and combined measures to distinguish responders from non-responders.(Fig.4) K-means classification was used to quantify this.

References

1. Liley et al. Anesthesiology 113 (2):292-304
2. Sahinovic et al. Anesth Analg 119 (2):288-301

Results

Median CI, CCS, CVI and BIS values during the 9 time periods are shown in fig. 3. Before stimulation, at P1, neither individual nor combinations of measures could differentiate responders from non-responders as both groups seem visually intertwined (fig 4a and 4b). After the application of the OAA/S (P2) distinction between responders and non-responders improved but only in the combined measures plane (CCS/CI and BIS/CVI) as shown in fig 4b and 4c. K-means classification showed that CI and CCS combined have higher sensitivity (75.8% vs 42%, P=0.006) and specificity (52% vs 24%, P = 0.0159) than CVI and BIS combined in differentiating responders from non-responders (Fig. 4).

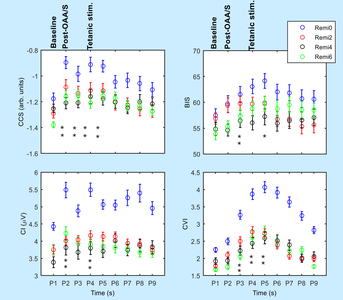

Fig.3 Mean (SD) EEG measures (a) CCS, (b) CI, (c) BIS and (d) CVI of the different remifentanil groups across the time periods. Significant differences shown are between P1 (baseline) and other time points (*P<0.05, ** P<0.01).

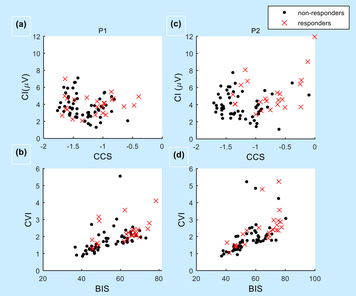

Fig.4 CCS/ CI and BIS/CVI used in combination. (a) and (b) show measures at P1 (baseline) and (c) and (d) at P2 (after OAA/S stimulus).

Conclusion

1. Individual parameters and combinations of parameters, measured <u>before</u> a stimulus, are all poor predictors of subsequent response to stimulus.
2. The combination of CCS and CI, measured <u>after</u> the OAA/S stimulation, better separates responders from non-responders than BIS and CVI, & individual parameters.