

# Propofol and Remifentanil Differentially Modulate Frontal Electroencephalographic Activity

David TJ Liley<sup>1,2</sup>, Nicholas C Sinclair<sup>2</sup>, Tarmo Lipping<sup>3</sup>, Bjorn Heyse<sup>4</sup>, Hugo EM Vereecke<sup>4</sup>, Michel MRF Struys<sup>4,5</sup>

<sup>1</sup> Swinburne University of Technology, Melbourne, Australia <sup>2</sup> Cortical Dynamics Ltd, Perth, Australia  
<sup>3</sup> Tampere University of Technology, Pori, Finland <sup>4</sup> Ghent University, Ghent, Belgium <sup>5</sup> University of Groningen, Groningen, The Netherlands.

**Overview** – A recently developed, physiologically inspired, electroencephalographic method for monitoring anaesthetic drug action is expected to show superior performance compared to existing heuristic approaches<sup>1</sup>. It is hypothesised that this method is capable of dissociating the effects hypnotic and analgesic agents have on frontally recorded electroencephalographic activity. Such a feature is absent from all other existing processed electroencephalographic depth of anaesthesia monitoring approaches. In order to test this hypothesis electroencephalogram collected during propofol-remifentanil anaesthesia was evaluated using a physiologically constrained fixed order times series analysis method.

**Methods** – Forty five ASA I patients were randomly allocated to one of three groups based on target effect site remifentanil concentration (0, 2, 4 ng/ml). Subsequently all patients received stepwise increased targeted effect site concentrations of propofol until loss of response to all measures of alertness and sedation. At each step change the Observer's Assessment of Alertness/Sedation score was determined. Raw electroencephalogram was continuously acquired from a bipolar frontal montage and analysed offline using a fixed order autoregressive moving average model to give derived measures of Cortical State (CS) and Cortical Input (CI). CS is designed to quantify the response of cortex to arbitrary input whereas CI is designed to quantify the magnitude of actual input to cortex.

**Results** – CS was found to clearly decrease with increasing levels of unconsciousness ( $P_k = 0.814$ ) whereas CI was largely independent of the OAA/S assessed state ( $P_k = 0.527$ ). Regression analysis revealed that CS was significantly negatively correlated with predicted effect site propofol concentration but uncorrelated with predicted effect site remifentanil concentration. In contrast CI was strongly correlated with target effect site concentrations of both propofol and remifentanil. In particular it was observed that CI decreased with increasing remifentanil concentration.

**Conclusion** – Because CS responds principally to variations in target effect site propofol concentrations and is strongly correlated with OAA/S assessed levels it may represent an alternative measure of hypnosis to existing indices. In contrast as there is a clear dependency of CI on target remifentanil concentrations it may be useful as a measure of analgesic efficacy and the nociceptive – antinociceptive balance, though prospective studies with noxious stimuli will be needed to validate such speculations.

## References

1. Liley DT, Leslie K, Sinclair NC, Feckie M: Dissociating the effects of nitrous oxide on brain electrical activity using fixed order time series modeling. *Comput Biol Med* 2008; 38: 1121-30.