BPH Corporate Ltd

BPH Corporate [ASX: BPH] ASX Announcement

3 May 2010

Companies Announcements Office
Australian Securities Exchange Limited
10th Floor, 20 Bond Street
SYDNEY NSW 2000

Dear Sir/Madam,

Cortical Dynamics Poster Presentation at the Australian and New Zealand College of Anaesthetists (ANZCA) and Faculty of Pain Medicine

BPH Corporate [ASX: BPH] investee company Cortical Dynamics (Cortical), has presented an important poster at the ANZCA Annual Scientific Meeting in New Zealand on the 1 May 2010. The poster entitled *"Propofol and Remifentanil Differentially Modulate Frontal Electroencephalographic Activity" was* presented as part of the moderated Poster Session *(please see attached).*

Professor David Liley of Cortical commented that "the results detailed in this poster show unequivocally that physiologically motivated approaches to analyzing the brain's electrical activity can deliver more sensitive approaches to monitoring brain activity during surgery. In particular these results suggest that the states of unconsciousness and analgesia might be able to be independently monitored, potentially enabling anaesthesia during surgery to be more optimally delivered."

BPH is working with Cortical to develop and commercialise the BAR Monitor. Cortical is working towards listing on the Australian Securities Exchange (ASX) later this year.

Yours sincerely,

David Breeze
Chairman

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Propofol and Remifentanil Differentially Modulate Frontal Electroencephalographic Activity

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Overview

A recently developed, physiologically inspired, electroencephalographic method for monitoring anaesthetic drug action is expected to show superior performance compared to existing heuristic approaches[1,2,3] (Figure 1).

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 time 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 (OAA/S) 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 (Figure 2).

Results

CS was found to clearly decrease with decreasing levels of consciousness ($P_k = 0.814$) whereas CI was largely independent of the OAA/S assessed state ($P_k = 0.527$) (Figure 3).

Regression analysis (hierarchical linear modelling) revealed that CS was significantly negatively correlated with predicted effect site propofol concentration but uncorrelated with predicted effect site remifentanil concentration (Figure 4).

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, because of the clear dependency on target remifentanil concentrations CI may be useful as a measure of analgesic efficacy and the nociceptive – antinociceptive balance. Prospective studies with noxious stimuli will be needed to validate such speculations.

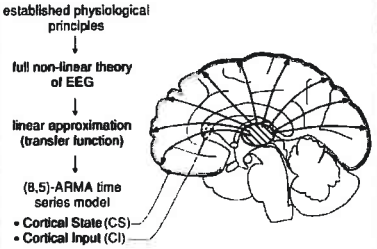

Figure 1: Schematic outline of the physiologically inspired electroencephalographic analysis method. Theory[3] suggests that the electroencephalogram (EEG) can be modelled as the result of the cortex acting as a linear filter on its (pseudorandom) input. This allows the derivation of measures of the responsive state of the cortex (Cortical State) and the magnitude of the input to cortex (Cortical Input). ARMA = autoregressive moving average.

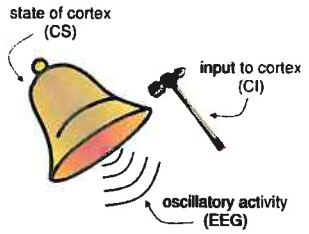

Figure 2: The general concept of the measures of Cortical State (CS) and Cortical Input (CI) can be illustrated using the highly simplified analogy of a bell being struck by a hammer. The sound of the bell ringing is dependent on both the resonant frequency of the bell and how hard it is struck. Analogously, the electroencephalogram (EEG), when modelled as the output of a linear filter, is dependent on both the resonant state of the cortex (CS) and the magnitude of the input to cortex (CI).

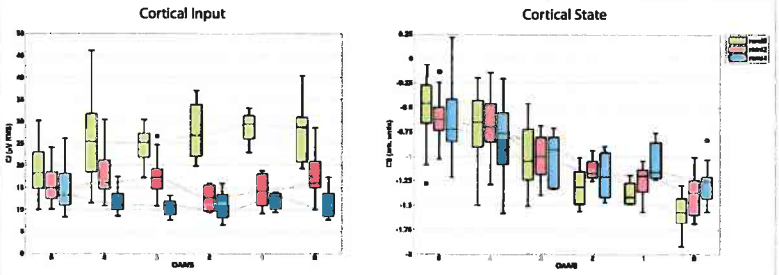

Figure 3: Box and whisker plots for derived electroencephalographic measures as a function of the Observer's Assessment of Alertness/Sedation (OAA/S) level for no remifentanil (remi0), 2 ng/ml remifentanil (remi2) and 4 ng/ml remifentanil (remi4) treatment groups. Boxes represent inter-quartile ranges, lines enclosed within boxes (and connected lines) median values, whiskers the largest (smallest) non-outlier and circles outliers (defined as values extending a further 1.5 times the inter-quartile range – equivalent to approximately 3 standard deviations for normally distributed data).

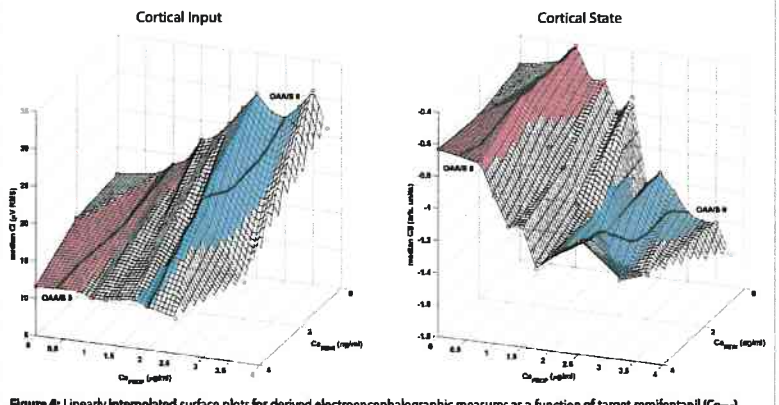

Figure 4: Linearly interpolated surface plots for derived electroencephalographic measures as a function of target remifentanil (C_{eREMI}) and propofol (C_{ePROP}) concentrations. Mesh represents the linearly interpolated surface through data (red circles). Inter-quartile (25th – 75th percentile) ranges of target propofol concentration for a given Observer's Assessment of Alertness/Sedation (OAA/S) level and remifentanil level are shown as shaded (OAA/S 5 = red, OAA/S 0 = blue) patches on the interpolated surface. Median values correspond to the respective solid black line.

[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
[2] Liley DT, Sinclair NC, Lipping T, Heyse B, Vereecke HE, Struys MM: Propofol and remifentanil differentially modulate frontal electroencephalographic activity. Anesthesiology, accepted April 2010. Article in press
[3] Liley DT, Cadusch PJ, Gray M, Nathan PJ: Drug-induced modification of the system properties associated with spontaneous human electroencephalographic activity. Phys Rev E Stat Nonlin Soft Matter Phys 2003; 68: 051906