26 November 2015

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

Dear Sir/Madam,

Cortical Dynamics Poster Presentation at American Society of Anesthetists Conference 2015

Please find attached an update from BPH Energy Ltd (ASX: BPH) investee company Cortical Dynamics Ltd. BPH Energy currently holds 3.89% of Cortical Dynamics but has the option to increase its holding to in excess of 10% through the conversion of its secured loan.

Yours Sincerely

Deborah Ambrosini
Company Secretary

BPH Energy Limited ACN 095 912 002
PO Box 317, North Perth, Western Australia 6906
14 View Street, North Perth, Western Australia 6006
admin@biopharmica.com.au www.biopharmica.com.au
T: +61 8 9328 8366 F: +61 8 9328 8733

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10th Floor, 20 Bond Street
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Dear Sir/Madam,

Cortical Dynamics Poster Presentation at American Society of Anesthetists Annual Meeting

Cortical Dynamics Ltd ("**Cortica**l"), is pleased to provide a copy of the poster entitled *"Comparisons of EEG measures of Hypnosis and Anti-Nociception in Response to Stimuli During Propofol Remifentanil Anesthesia"* that was recently presented at the 2015 Annual Meeting of the American Society of Anesthesiologists in San Diego *(please see attached).*

The paper was presented by Mr Marko Sahinovic who was one of the co-authors on this paper with Cortical's principal research scientist Dr Mehrnaz Shoushtarian.

Yours Sincerely

David Breeze
Executive Director

About Cortical

Cortical is an Australian based medical device technology company that has developed a next generation Brain Function Monitor. The company is focused on commercialising the intellectual property developed at Swinburne University. The core-product the Brain Anaesthesia Response (BAR) monitor has been developed with the objective of better detecting the effect of anaesthetic agents on brain activity, aiding anaesthetists in keeping patients optimally anaesthetised.

The BAR monitor improves on currently used electroencephalogram (EEG) technologies by incorporating the latest advances in our understanding of how the brain's rhythmic electrical activity, the

electroencephalogram (EEG), is produced. The approach used is fundamentally different from all other devices currently available in the market in that its underlying algorithm produces EEG indexes which are directly related to the physiological state of the patient's brain.

The global brain monitoring market in 2012 was valued at $1.08 billion and is poised to grow at a CAGR of 8.6% to reach $1.63 billion by 2017. The global brain monitoring devices market is broadly segmented into three categories based on its product, application, and end-user. Fueling market growth is the various technological advancements which are leading to high functionality, lower costs, ease of operation, and miniaturization of devices.

Initial marketing in will focus on TIVA (Total Intravenous Anaesthesia), a method of inducing and maintaining general anaesthesia without the use of any inhalation agent. This is becoming more widely accepted, particularly in Western Europe.

Cortical's technology has a versatility that goes beyond depth of anaesthesia and may be applied to other EEG based markets, such as Neuro-diagnostic, drug discovery, drug evaluation and the emerging Brain Computer Interface (BCI) market.

There are considerable opportunities offered by subsequent expansion of the company's core technology through developing the product to carry out additional functions including neuro-diagnostics of changes in brain and memory functions to provide early warning of degenerative diseases, pain response and tranquiliser monitoring for trauma patients in intensive care units.

The BAR monitor is protected by five patent families in multiple jurisdictions worldwide consisting 16 granted patents.

Cortical Dynamics Ltd
ACN 107 557 620
PO box 317, North Perth, WA, 6906
14 View Street, North Perth, Western Australia
T: + 61 8 6467 9525 F: +61 8 9328 8733
contact@corticaldynamics.com www.corticaldynamics.com

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

M.M. Sahinovic, M.D.[1], M. Shoushtarian, Ph.D.[2], A.R. Absalom, M.D.[1], A. Kalmar, M.D.[1], H. Vereecke, M.D.[1], D. Liley, M.B.[3], M.M.R.F. Struys, M.D.[1]

1. University Medical Center Groningen, Groningen, Netherlands, 2. Cortical Dynamics Ltd., Melbourne, Australia, 3. Swinburne University of Technology, Hawthorn, Australia

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.

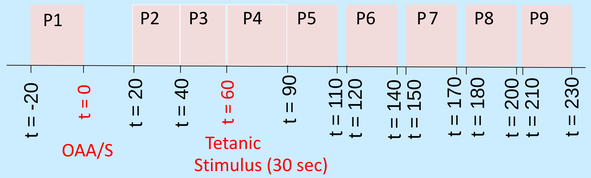

Fig.1 Timeline of study period (seconds). Median value of CCS, CS, BIS and CVI during each of 9 time periods (P1 to P9) was calculated. t = 0 represents the start of the OAA/S observation

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).

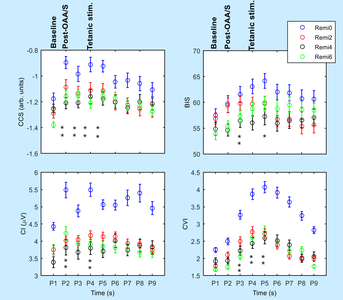

Fig.3 Mean (SD) EEG measures (a) CCS, (b) CI, (c) BIS and (d) CVI of the different remifentanil groups across the time periods. Significant differences shown are between P1 (baseline) and other time points (*P<0.05, ** P<0.01).

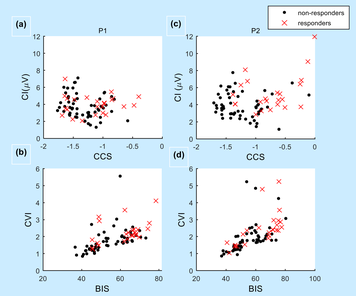

Fig.4 CCS/ CI and BIS/CVI used in combination. (a) and (b) show measures at P1 (baseline) and (c) and (d) at P2 (after OAA/S stimulus).

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.