3 May 2013

ASX Market Announcements
Australian Securities Exchange Limited
10th Floor, 20 Bond Street
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Cortical Dynamics Ltd – Cortical Dynamics Presents Results of Clinical Trial at the Annual Scientific Meeting of the Australian and New Zealand College of Anaesthetists (ANZCA) in Melbourne

Please find attached an operational update from BPH Energy Ltd (**ASX: BPH**) investee company Cortical Dynamics Ltd.

Yours sincerely,

Deborah Ambrosini
Director and Company Secretary

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BPH Energy Limited
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Cortical Dynamics Presents Results of Clinical Trial at the Annual Scientific Meeting of the Australian and New Zealand College of Anaesthetists (ANZCA) in Melbourne

Cortical Dynamics Ltd ("**Cortical**"), an investee company of BPH Energy Limited (ASX: BPH), is pleased to announce that the results of a major clinical trial involving the BAR monitor are to be presented on 4th May at the 2013 Annual Scientific Meeting of the Australian and New Zealand College of Anaesthetists held in Melbourne.

The clinical trial, involving 25 patients undergoing elective coronary artery bypass surgery, was designed to evaluate the ability of the BAR monitor to distinguish between two different doses of the widely used intravenous analgesic fentanyl, in addition to assessing the immunity of the BAR monitor to a range of intra-operative mechanical and electrical artifacts known to complicate the EEG measurement of anaesthetic action.

The principle investigator in the trial was Dr Desmond McGlade, Senior Staff Anaesthetist, from the Department of Anaesthesia at St Vincent's Hospital in Melbourne. Cortical worked closely with Dr McGlade and his team during the study to ensure the integrity of all data collecting protocols and procedures.

A detailed analysis of the trial results indicated that the BAR Monitor's Cortical Input (CI) index differed significantly between the two different fentanyl doses. In contrast the BAR Monitor's Cortical State (CS) index, and the simultaneously recorded BIS™ index were unchanged.

The ability of the CI index to distinguish between the two different fentanyl doses indicates that the BAR Monitor may be useful for the intra-operative monitoring of analgesia. Further, given that during this study the CS index was highly correlated with the BIS™ index, it suggests that the BAR monitor may find significant utility in the delivery of optimal and balanced surgical anaesthesia.

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Cortical's Chairman, David Breeze said, "This is an exciting result as it shows, on the basis of an independent clinical trial, that the BAR Monitor has features and sensitivities that existing market leading products do not possess. The fact that we are able to present this important result at the ANZCA meeting means we can immediately discuss ways in which the BAR Monitor can best be integrated into existing clinical practice."

About the BAR Monitor

The BAR monitoring system measures a patient's brain electrical activity, the electroencephalogram (EEG), in order to indicate how deeply anaesthetised a patient is during an operation via an adhesive sensor applied to the forehead. The BAR monitor is designed to assist anaesthetists and intensive care staff in ensuring patients do not wake up unexpectedly, as well as reducing the incidence of side effects associated with the anaesthetic.

The BAR monitor improves on currently used EEG monitors by utilising advances in understanding of how the brain's electrical activity is produced, and how it is affected by anaesthetic and sedative drugs. The BAR's unique physiological approach is aimed at independently monitoring the hypnotic and analgesic states associated with anaesthesia, a feature no known existing EEG based depth-of-anaesthesia monitor is able to achieve. Objective monitoring of hypnotic and analgesic state will lead to improved anaesthetic and surgical outcomes, by reducing recovery times and minimising drug costs.

About Cortical Dynamics

Cortical Dynamics is a medical technology company that was established in 2004 to commercialise intellectual property relating to brain function monitoring developed by Professor David Liley and his scientific team at Melbourne's Swinburne University of Technology.

Yours Sincerely

David Breeze
Chairman

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Validation of the Brain Anaesthesia Response Monitor During Anaesthesia for Cardiac Surgery: a Double-Blinded Randomised Controlled Trial Using Two Different Doses of Fentanyl

Mehrnaz Shoushtarian[1], Desmond P McGlade[2], Louis Delacretaz[1], David TJ Liley[1,3]

1. Cortical Dynamics Ltd, Perth, Australia 2. St. Vincent's Hospital, Melbourne, Australia 3. Swinburne University of Technology, Melbourne, Australia

Introduction

The Brain Anaesthesia Response Monitor (BAR Monitor, Fig.1) non-invasively monitors the cerebral function in response to anaesthetic and sedative agents. Unlike other monitors, which use a heuristic approach, the BAR Monitor uses a physiologically inspired method of EEG analysis[1]. Two indices, Cortical State (CS) and Cortical Input (CI) are calculated by the monitor. These indices have been shown to respond differentially to varying levels of hypnotic and analgesic agents[2].

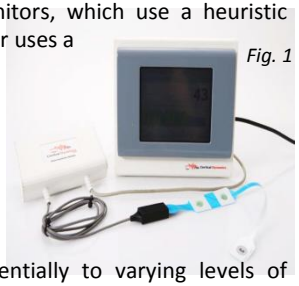


Fig. 1

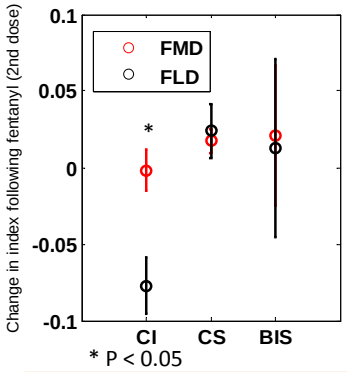
Hypothesis

We hypothesised that the CI index, a putative measure of the nociceptive-antinociceptive balance, would be able to distinguish between two patient groups receiving different doses of the synthetic opioid fentanyl administered between induction of anaesthesia and surgical skin incision.

Methods

- Twenty-five patients scheduled to undergo elective first-time CABG were recruited, of whom 20 were suitable for analysis.
- Patients were randomised to receive either fentanyl 12μg/kg total (fentanyl low dose, FLD) or 24 μg/kg total (fentanyl moderate dose, FMD); fentanyl was given in two divided doses (2/3 following induction, 1/3 prior to skin incision).
- Anaesthesia induction and maintenance was performed using a propofol infusion titrated to maintain a Bispectral Index (BIS™) value between 40 and 60.
- BIS™ and CS/CI were simultaneously recorded using two sets of electrodes applied to the forehead.
- Depth of anaesthesia Indices (CI, CS and BIS) were averaged over 20 seconds at two events: at the time of skin incision, which was on average, 1 minute 48 seconds after the second fentanyl bolus, and 3 minutes before.
- The relative difference in indices at the two time-points was compared between groups.

Results



* P < 0.05

The relative change in CI was greater in the FLD group compared with the FMD group ($F(1, 18) = 10.7$, $p = .004$). BIS and CS showed no significant difference between the groups. CS has previously been shown to represent a measure of hypnosis[2].

Conclusion

The ability of the CI index to differentiate the two groups by fentanyl dose indicates that the BAR Monitor may be useful in the titration of fentanyl as an anti-nociceptive agent during cardiac surgery.

References

1. *Liley 2003, Phys Rev E 68: 051906*
2. *Liley et al. 2010, Anesthesiology 113(2):292-304*

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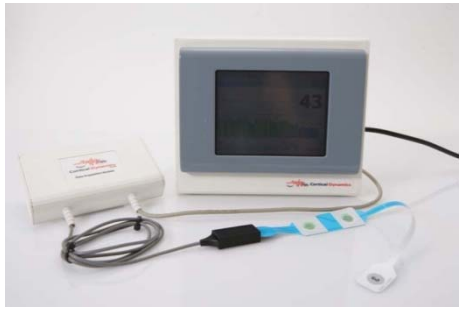
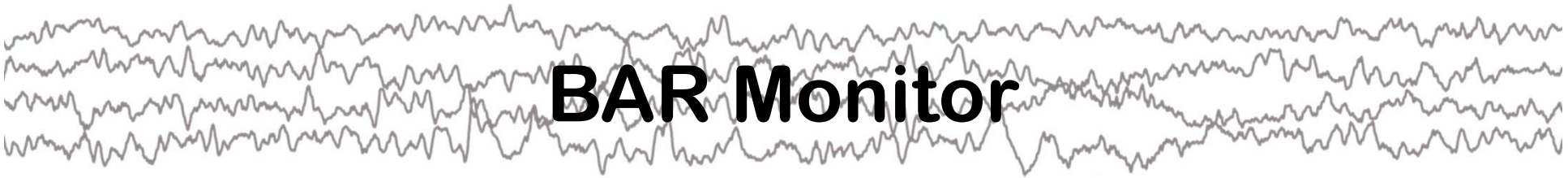


Introduction

- EEG-based depth of anaesthesia monitors are commonly used due to sensitivity of the EEG to anaesthetic agents
- All current monitors (e.g. BIS, Entropy, etc.) use QEEG, MLAEP, or combination to select features which best correlate with clinical endpoints
- These features are combined to produce a dimensionless index between 0 and 100
- All current measures are heuristically derived



BAR Monitor

$$\tau\,\partial h(r,t+\xi)/\partial t \;=\; -h(r,t+\xi)+\Psi(h)I(r,t)$$

Passive electrical properties and reversal potentials

$$(\mathrm{I}\partial/\partial t+\gamma)^2 I(r,t) \;=\; \gamma\Gamma\{N^{\beta}S(h)+\phi(r,t)+p(r,t)\}$$

Transmitter kinetics, intra-cortical connectivity and cable delays

$$\{(\mathrm{I}\partial/\partial t+v\Lambda)^2-\frac{3}{2}v^2\nabla^2\}\phi(r,t) \;=\; N^{\alpha}v^2\Lambda^2 S_e(h_e)$$

Conduction delays and cortico-cortical connectivity

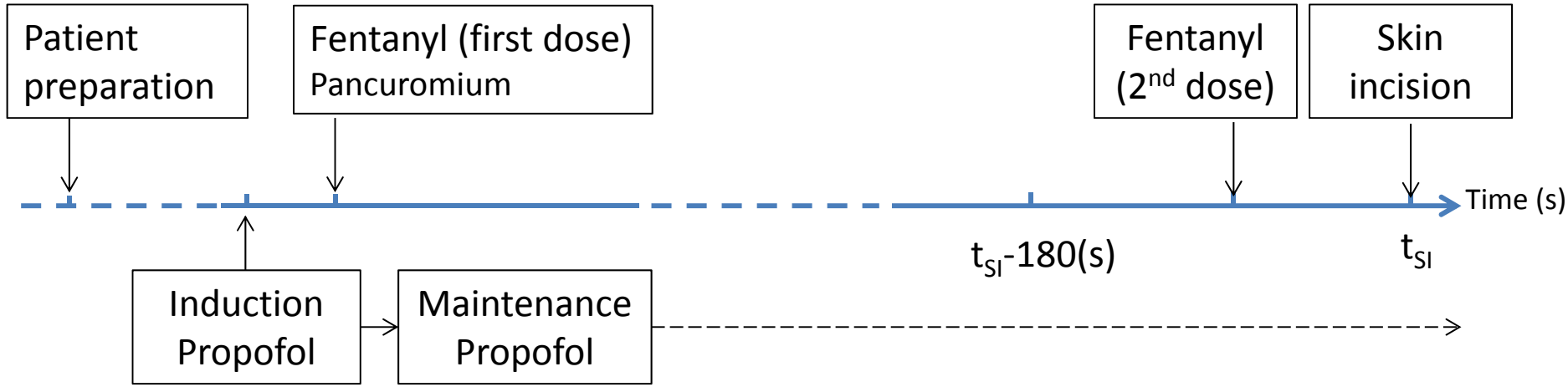
linearised

- Cortical State (CS): Resonant state of cortex
- Cortical Input (CI): Input to cortex

Methods

Recruitment and Randomisation	25 patients primary CABG low risk factors Fentanyl Low Dose 12 μg/kg total (8 μg/kg + 4 μg/kg) Fentanyl Moderate Dose 24 μg/kg total (16 μg/kg + 8 μg/kg)
↓	
Premedication **Preoperative Preparation**	Lorazepam 2 mg, Oxycontin 10 mg BAR and BIS Sensors applied IV, Arterial and Pulmonary Artery Catheters inserted Midazolam 0.5 mg to maintain OAA/S 4 (mild sedation only)
↓	
Induction and Maintenance	Propofol 1 mg/kg over 60 seconds then 6 mg/kg/h, titrated to BIS 40-60
↓	
Following Induction **Prior to Skin Incision**	Fentanyl Dose 1, Pancuronium 0.12 mg/kg; intubate after 3 minutes Fentanyl Dose 2
Haemodynamic Management	Vasoactive agents used to maintain SBP 100-140 mmHg and HR 45-90

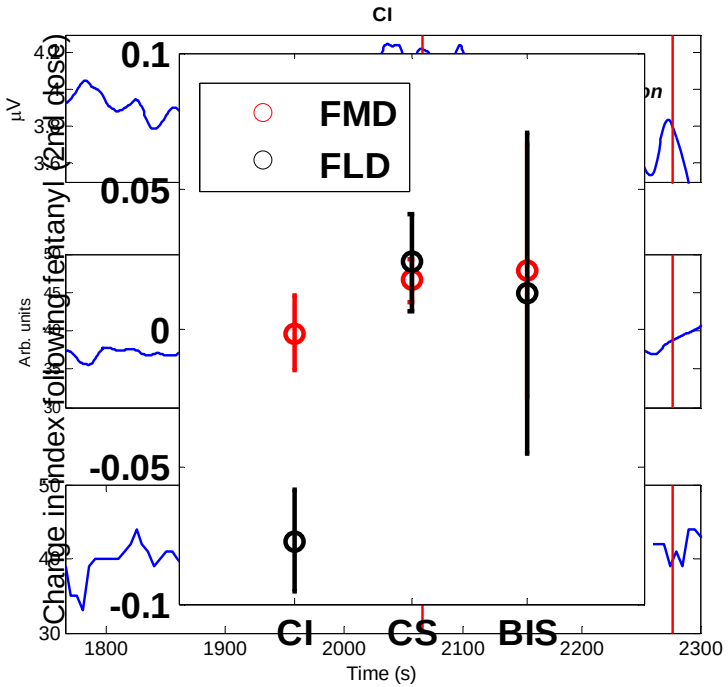
Methods



Relative difference in BIS, CI and CS at time of skin incision and 3 minutes before calculated

Results

- 20 patients suitable for analysis
- The relative change in CI was greater in the FLD group compared with the FMD group ($F(1, 18) = 10.7$, $P = .004$).
- BIS and CS showed no significant difference between the groups.



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StV

Conclusion

The ability of the CI index to differentiate the two groups by fentanyl dose indicates that the BAR Monitor may be useful in the titration of fentanyl as an intraoperative anti-nociceptive agent