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Brain monitor puts patients at ease

KEY POINTS

- **A Swinburne researcher and his commercial partner have developed a brain monitoring system to improve the safety and recovery of people undergoing surgery**
- **Anaesthetists are constrained by current technology, which cannot separately monitor consciousness and pain in patients**
- **Investors are being sought for the technology to be on the market by 2013**

Awakening during surgery is a nightmare that haunts patients and doctors alike, but Swinburne scientists have found a way to allow both patients and doctors to rest easy BY MANDY THOO

"I FELT MY CHEST being cut open and blood being mopped away. I heard and felt the saw cutting through my chest bone," Norman Dalton told the UK's *The Independent* newspaper in 2004 in a harrowing account of his heart bypass operation. "I could feel every cut and saw the doctors made. I couldn't scream out to tell."

Dalton's horrifying experience – known in medical jargon as 'intra-operative awareness' – is one of the most common complications of anaesthesia. Annually, about 2000 patients have some form of awareness during surgeries performed in Australian hospitals, according to the *Medical Journal of Australia*, and 45 per cent of the insurance claims lodged against anaesthetists relate to this phenomenon. The lack of technology to accurately monitor the state of the brain during anaesthesia is considered to be the main reason for over- and under-sedation. While surgical patients fear the trauma of 'feeling the knife', hospitals and medical staff are equally afraid of ensuing litigation.

Now, a team of researchers and entrepreneurs with the vision to end this angst has developed a technology called the Brain Anaesthesia Response (BAR) monitoring system. The BAR monitor, a world-first device to replace existing Electroencephalography (EEG) monitors, results from a joint venture between Swinburne University of Technology and Cortical Dynamics Ltd.

The BAR monitor improves on the currently used electroencephalogram EEG monitors by incorporating the latest advances in our understanding of the mechanisms responsible for brain activity, allowing doctors to better optimise anaesthetic delivery. It has the potential to improve the patient experience, reduce recovery times and lower the costs of anaesthesia, creating a significant global market opportunity.

Pain monitoring gap

The BAR monitoring system has taken 10 years

Louis Delacretaz (left) and Associate Professor David Liley (right) demonstrate use of the device that will save patients from waking surgical nightmares on compliant collaborator Dr Bruce Whan.

to develop and was originally the brainchild of Swinburne Associate Professor David Liley with Louis Delacretaz, founding managing director of Cortical Dynamics, also involved in its development.

"In any application of anaesthesia, we always try to achieve a balance between unconsciousness and pain relief," Associate Professor Liley says. "Current anaesthetic methods involve giving the patient a combination of opioid and hypnotic drugs and monitoring their status with EEG-based monitors.

"However, the downfall of these EEG monitors is that they use arbitrary, rule-of-thumb determinations to analyse brain signals and translate them into something that tells us about consciousness. In most cases the monitors can only tell if the patient is awake or asleep, but not if he or she is in pain."

Associate Professor Liley is the lead researcher and originator of the BAR monitor. His research on the topic has appeared in peer-reviewed journals such as *Anesthesiology, Physical Review E* and *Network: Computation in Neural Systems*.

Associate Professor Liley explains that the way anaesthetists determine the amount of anaesthetic used on patients is based on a 'black box' system in which the internal workings are largely obscure.

"Research has gathered thousands of EEG responses from surgical patients and produced an average of what a patient needs. This is a top-down approach where the estimation is based on rule-of-thumb data-mining and not on the requirements of the individual as determined by scientific principles."

Meanwhile, he says the question of how the brain reacts to analgesic agents – painkillers – has remained unanswered, and this is what has limited conventional EEG monitors: "Standard EEGs also lack the ability to monitor the effects of other anaesthetic drugs, such as nitrous oxide, better known as sleeping gas."

Return to fundamentals

Associate Professor Liley took the view that the logical way to solve the anaesthesia challenge was to return to fundamentals: find out what mechanisms underpin the generation of the brain's electrical activity to determine how it is affected by hypnotic and analgesic agents, and develop a scientific way to measure this.

His solution was to develop a technology that defines the patient's hypnotic and analgesic states separately.

A 10-year research program has subsequently pioneered a new method for detecting and monitoring the brain's physiological reaction to sedative drugs.

In the course of this research, Associate Professor Liley analysed brainwave data provided by clinical collaborators in Belgium. Forty-five patients were anaesthetised with propofol, a common hypnotic drug, and a synthetic opioid, remifentanil, a powerful, short-acting analgesic agent. The group used two measures derived from their understanding of the EEG to explore brain reactions: cortical state (CS), to measure the brain's responsiveness to stimuli, and cortical input (CI), to quantify the strength or magnitude of such stimuli reaching the brain.

"The results showed that our BAR algorithm was able to detect the effects of remifentanil – the analgesic opioid – separately from the effects of the hypnotic drug propofol," he says.

"We found that CS was affected only by the propofol action, whereas CI was systematically affected by the amount of remifentanil, the pain killer with which the patient was administered.

"Because CS reflects hypnosis, and CI reflects the level of analgesia, we have been able to develop a method that will allow doctors to monitor both of these states independently of one another. This will supply what is missing in current EEG monitors. Doctors will be able to tell if the patient needs more hypnotic drugs or sedative agents, whereas conventional EEG monitors can't separate these two states, making optimal drug delivery more difficult."

Associate Professor Liley says the innovation combines a better scientific understanding of how the brain responds to anaesthetic drugs with development of the best mathematical algorithms to measure its responses.

He says that the BAR monitor is also able to detect anaesthetic drugs that are currently unidentified by existing EEG monitors.

Elderly will be major beneficiaries

With the science sorted, the next step in developing a useable technology was its commercialisation, which is where Cortical Dynamics Ltd has been crucial.

Louis Delacretaz, who raised the initial capital for the company, says the first question is always whether a good research idea will also be a good business opportunity. He says that by addressing something lacking in the operating theatre and the medical marketplace, the BAR monitor was seen as a brilliant idea and potentially viable commercial product.

Mr Delacretaz says the market need is partly driven by the ageing population and a subsequent increase in the number of surgical interventions on frailer people. He says there are two million general anaesthetics performed each year in Australia and 1.3 billion worldwide, and the company plans to distribute the product as widely as possible.

Cortical Dynamics was established in Melbourne in 2004 by Mr Delacretaz and Associate Professor Liley to raise funds to commercialise the technology.

"It's quite difficult to raise the capital for a start-up company in Australia and it took us 12 months," Mr Delacretaz says.

It has long had the support of Perth-based BPH Energy Ltd (formerly BPH Corporate Ltd, formerly Biopharmica Ltd), which commercialises a portfolio of Australian biomedical technologies. Cortical Dynamics is now working towards making an initial public offer (IPO) of its shares to fund further development. If the IPO is successful, Cortical Dynamics hopes to apply for admission to the official list of the Australian Securities Exchange in 2011.

Dr Bruce Whan, Director of the Swinburne Knowledge commercialisation unit and a director of Cortical Dynamics, says the technology is expected to offer substantial financial benefits to hospitals and healthcare systems that choose to adopt it. "Being able to finetune the application of anaesthetic agents can avoid issues of under- or over-sedation, potentially reducing side-effects and their impact on the patient experience, including recovery times and after-care expenses," he says.

"Hospitals on the other hand can avoid litigation and run more efficiently due to the earlier mobility of post-anaesthetic patients. This leads to higher turnover rates in surgery. By reducing use and wastage, it also reduces the costs of anaesthesia."

Mr Delacretaz says market research carried out at the company's start-up revealed medical professionals were concerned about the credibility of conventional EEG monitors for monitoring the state of anaesthesia.

"Anaesthetists thought that the workings of the normal EEG monitors were not robust," Mr Delacretaz says. "They felt that there wasn't much scientific evidence to support their mechanisms and that the monitors are sometimes inaccurate.

"Apart from addressing the biggest drawback with conventional EEG monitors, the BAR technology has the potential to expand research into neuro-diagnostic fields like Alzheimer's dementia and other degenerative neurological illnesses.

"This is because our system is based on basic research into how the brain operates and how it responds to drugs."

He also says that the device will not cost more than current EEG monitors.

"Our next step is to perform clinical trials to test the technology and, if all goes well, the BAR monitor should be available to the market in two years," Dr Whan says.

"Ten years in the making, we have been through the journey of having an initial concept to actually holding the BAR monitor in our hands. We hope that it will bring a new day to the world of monitoring the function of the brain."