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The truth about anaesthesia

Staying asleep during surgery…

Anaesthesia has been routinely applied in surgery for more than a century. Yet there is still no 100% reliable way to measure the depth of anaesthesia. Even today, unintentional awareness during surgery occurs occasionally. The BRACCIA project aims to provide the basic understanding needed to supplement the anaesthesiologist's skill and judgement by improving quantitative monitoring.

Unrecognised awareness during surgery can be traumatic, and upsetting for the surgical team, as well as for the patient. Where a muscle relaxant is in use, it is possible for the patient to be fully conscious but unable to move or speak to communicate their distress. Of course, giving too much anaesthetic is bad for the patient and, taken to extremes, would cause death.

So the anaesthesiologist aims for a dosage only just sufficient to keep the patient reliably asleep. Existing anaesthetic monitors fail to provide perfectly reliable measures of depth of anaesthesia.

BRACCIA (Brain, Respiration And Cardiac Causalities In Anaesthesia) is an FP6 research programme funded by the European Commission. Its aim is to develop and apply mathematical techniques from non-linear science and complexity theory to explore the changes that take place in heart, respiration and brain rhythms and their mutual interactions during anaesthesia.

The project is unique in that experts in non-linear dynamics and biomedical physics met, communicated, and collaborated successfully in seeking an understanding of the non-linear dynamics of cardio-respiratory and brain function in the waking state and in anaesthesia. It brought together world leading experts from: the Royal Lancaster Infirmary, UK, and Ulleval Hospital, Oslo, Norway (to record clinical data and contribute professional knowledge of anaesthesia); the Institute of Physics in Potsdam, Germany (to pioneer new theories of phase synchronisation); the Institute of Computer Science, Academy of Sciences, Prague, Czech Republic (to pioneer an information theory approach to data analysis); the Physics Department, Lancaster University, UK, and the Faculty of Medicine, University of Ljubljana, Slovenia (to pioneer a coupled oscillatory approach to the complex dynamics of the cardio-respiratory and brain systems); EPFL, Lausanne, Switzerland (who, with the Potsdam and Lancaster groups, pioneered a new understanding of the physics of the interacting ensembles of oscillators that exist in the brain).

Chloroform was widely used for inducing anaesthesia

Scientific progress was expedited by twice-yearly meetings of the consortium, constant email and telephone exchanges, frequent inter-site visits, and the fact that the Coordinator Dr Aneta Stefanovska (Lancaster University) 'spoke' the languages of both the natural sciences and medicine.

A total of 60 surgical patients kindly agreed to have their anaesthesia monitored. Measurements were made of respiration, cardiac and brain activity, skin temperature, and the electrical resistance of the skin. They were carried out for two different types of anaesthetic agent, both without and with the use of a muscle relaxant (curare) plus assisted respiration. Measurements were also made in the waking state to clarify the differences. Complementary measurements were made on rats in Ljubljana.

The huge mass of data gathered from humans in the two hospitals, and from rats in Ljubljana, was then assembled centrally on the BRACCIA server from which it was collected by the analysis groups in Lancaster, Lausanne, Ljubljana, Potsdam and Prague.

Measurements were completed in February 2009, but data analysis will continue for years into the future, given the diverse methods available for its analysis and the new methods currently being developed, exploiting the huge quantity of high quality data carefully recorded under well characterised conditions.

Analysis methods applied so far include:

- Wavelet analysis to examine contributions from oscillatory processes at different frequencies, and how these change with time. Anaesthesia is found to bring a huge decrease in oscillation energy at

frequencies below that of respiration;

- Synchronisation analysis to determine the extent to which heart and respiration are synchronised (at, say, four beats per breath). The degree of synchronisation was found to depend on the particular anaesthetic used;
- Directionality analysis to quantify the direction of the cardio-respiratory interaction, and its changes during anaesthesia. Normally, respiration drives the heart but, under anaesthesia, there also appears to be some influence of the heart on respiration;
- EEG brain wave analysis, showing depth dependent changes in the power in particular frequency intervals (increases in the delta, theta and alpha intervals in anaesthesia, and decreases in gamma intervals), and clear evidence of depth dependent delta/theta interactions both in humans and rats;
- Pulse transit times of the blood pressure wave in travelling from the heart to an index finger, showing statistically significant changes, probably reflecting anaesthesia related changes in the stiffness of the blood vessels;
- Complexity analysis of the natural (healthy) variability in the heart rate, showing a decrease in complexity during anaesthesia.

Taken in conjunction with earlier studies, it is evident from the BRACCIA results that there is no single, simple, way to determine depth of anaesthesia. Rather, there are changes in both brain and cardiovascular processes. To get the full picture, all the different oscillations and their interactions need to be considered. BRACCIA has created a sophisticated system for non-invasive measurement of cardiovascular and brain oscillation signals, and has proposed several novel methods to study their interactions. BRACCIA results are leading to new data analysis software based on methods drawn from non-linear dynamics.

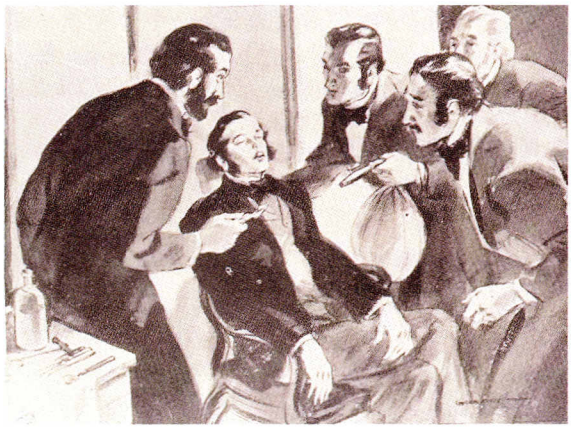

Fig. 1: Horace Wells, a Connecticut dentist, pioneered the use of nitrous oxide (laughing gas) in dentistry in 1844 while having one of his own wisdom teeth extracted. His next demonstration was such a catastrophic failure, however, that he gave up dentistry, became a chloroform addict, and subsequently committed suicide

Unlike existing anaesthesia monitors, based on single measures like heart rate variability or changes in brain rhythms, BRACCIA is proposing a single monitor combining many functions. It will provide an integrated measure of anaesthetic depth that can be expected to be more reliable than any measure determined from a single quantity.

About anaesthesia

Anaesthesia has been used, or attempted, with surgery since the earliest times. The 19th Century brought the discoveries of nitrous oxide and ether. These were used initially just for recreation, but Sir Humphrey Davy suggested applying nitrous oxide during surgery.

A Connecticut dentist, Horace Wells, pioneered the use of nitrous oxide (see Fig. 1) in 1844. From then on, anaesthesia was used more and more widely. Chloroform was added to the list of commonly used agents, and administered to Queen Victoria in giving birth to Prince Leopold and Princess Beatrice.

Modern practice relies on the notion of 'balanced anaesthesia', introduced by Gray and Rees in 1952. Different agents are used to produce the triad of unawareness, analgesia, and muscle relaxation, thus reducing the side effects of large doses of any one agent – but thereby introducing, through the use of muscle relaxants, the potential for unrecognised awareness.

Numerous techniques have been introduced to try to measure the degree of anaesthesia, none wholly successful. Many anaesthesiologists prefer to rely on close observation of the patient's movements, responses to stimuli, sweating, and other physiological indications of depth to supplement their calculations of the percentage of anaesthetic agent in the blood.

The results of BRACCIA are being embodied in a book 'Nonlinear Dynamics of Anaesthesia: from Theory to Clinical Application', written by the collaboration and edited by A Stefanovska, P V E McClintock, J Raeder and A F Smith, to be published by Springer in early 2010.

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