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Detection of cerebral arterial gas embolism using regional cerebral oxygen saturation, quantitative electroencephalography, and brain oxygen tension in the swine

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HIGHLIGHTS

- Small amounts of cerebrovascular air can be detected by EEG and NIRS in the swine.
- These methods, however, are not as sensitive as intraparenchymal oxygen tension.
- Multimodal monitoring including EEG and NIRS may improve detection of air emboli.

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ABSTRACT

Background: Cerebral air emboli occur as a complication of invasive medical procedures. The sensitivity of cerebral monitoring methods for the detection of air emboli is not known. This study investigates the utility of electroencephalography and non-invasively measured cerebral oxygen saturation in the detection of intracerebrovascular air.
New method: In 12 pigs oxygen saturation was continuously measured using transcranial near-infrared spectroscopy and oxygen tension was continuously measured using intraparenchymal probes. Additionally, quantitative electroencephalography and microdialysis were performed. Doses of 0.2, 0.4, 0.8, and 1.6 ml of air were injected into the cerebral arterial vasculature through a catheter.
Results: Oxygen saturation and electroencephalography both reacted almost instantaneously on the air emboli, but were less sensitive than the intraparenchymal oxygen tension. There was reasonable correlation (ρ ranging from 0.417 to 0.898) between oxygen saturation, oxygen tension, electroencephalography and microdialysis values.
Comparison with existing methods: Our study is the first to demonstrate the effects of cerebral air emboli using multimodal monitoring, specifically on oxygen saturation as measured using near-infrared spectroscopy.
Conclusions: Our results show that non-invasively measured oxygen saturation and quantitative electroencephalography can detect the local effects of air emboli on cerebral oxygenation, but with reduced sensitivity as compared to intraparenchymal oxygen tension. Prospective human studies using multimodal monitoring incorporating electroencephalography and oxygen saturation should be performed.

Abbreviations: EEG, electroencephalography; rSO_2, regional cerebral oxygen saturation; NIRS, near-infrared spectroscopy; $PbtO_2$, brain oxygen tension; tBSI, temporal brain symmetry index; AUC, area under the curve.

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1. Introduction

Cerebral injury can occur as a complication of many invasive procedures, such as surgery and interventional radiology. Cardiac surgery carries the largest risk, with approximately 3% of patients suffering from stroke and 20-40% developing long-lasting post-operative cognitive deficits (Newman et al., 2006; Lombard and Mathew, 2010). Cerebral damage due to cardiac surgery is a multifactorial process, in which air emboli are a contributing factor (Carrascal and Guerrero, 2010).

In an effort to decrease the number of surgical cerebral complications, there is an increasing tendency to monitor brain function during high-risk procedures (Vohra et al., 2009). Two commonly used non-invasive methods for brain monitoring are electroencephalography (EEG) and regional cerebral oximetry (rSO_2) using near-infrared spectroscopy (NIRS). However, the ability of these methods to detect air embolism has never been investigated, and therefore, these techniques can currently not be used to detect emboli (Denault et al., 2007).

In the present study, we use an established porcine model of cerebral arterial gas embolism (van Hulst et al., 2005; Weenink et al., 2012) to test the hypothesis that rSO_2 and EEG can detect air embolization. We compared these two measurements with intraparenchymal brain oxygen tension ($PbtO_2$). We hypothesized that the localized nature of the PbO_2 measurements would make them less sensitive to the effects of the embolizations than the more regional rSO_2 and EEG measurements.

2. Materials and methods

2.1. General handling and preparation

After approval of the animal ethics committee of the Academic Medical Center, Amsterdam, The Netherlands (protocol number LEICA102643) and in accordance with European Community guidelines, 12 female Landrace pigs weighing on average 49 kg (SD 2.1 kg) were used for this study. Animals were premedicated with intramuscular ketamine 15 mg kg^{-1}, midazolam 2 mg kg^{-1}, and atropine sulfate 0.01 mg kg^{-1}, followed by tracheal intubation and volume controlled ventilation with an inspiratory oxygen fraction of 0.4, adjusted to maintain end-tidal carbon dioxide of 38–42 mm Hg. Anesthesia was continued with ketamine 10–15 mg kg^{-1} h^{-1}, sufentanil 5–10 μg kg^{-1} h^{-1}, midazolam 1.5 mg kg^{-1} h^{-1}, and pancuronium bromide 0.15 mg kg^{-1} h^{-1}. Antibiotic prophylaxis was given with 2 g ceftriaxone. Normoglycaemia (4–8 mmol l^{-1}) was maintained using continuous glucose administration. Further preparation was as described earlier (Weenink et al., 2012) and included invasive blood pressure measurement, a urinary catheter, temperature management to maintain normothermia, and placement of an Ascent Occlusion Balloon catheter (Johnson & Johnson, New Brunswick, NJ) in the right ascending pharyngeal artery. The ascending pharyngeal arteries are the primary feeding arteries of the porcine brain, supplying the bilateral internal carotid arteries through the rete mirabile (Weenink et al., 2011).

2.2. Experimental setup

In the prone position, two burr holes were created in the skull and two Licox $PbtO_2$ probes (Integra, Plainsboro, NJ), two microdialysis catheters (Carnegie Medicine AB, Solna, Sweden), one intracranial pressure (ICP) sensor (Codman, Raynham, MA), and one brain temperature probe (Integra) were placed in the brain parenchyma as depicted in Fig. 1. The temperature probe was used to correct $PbtO_2$ for actual brain temperature. The microdialysis probes were continuously flushed with artificial cerebrospinal fluid

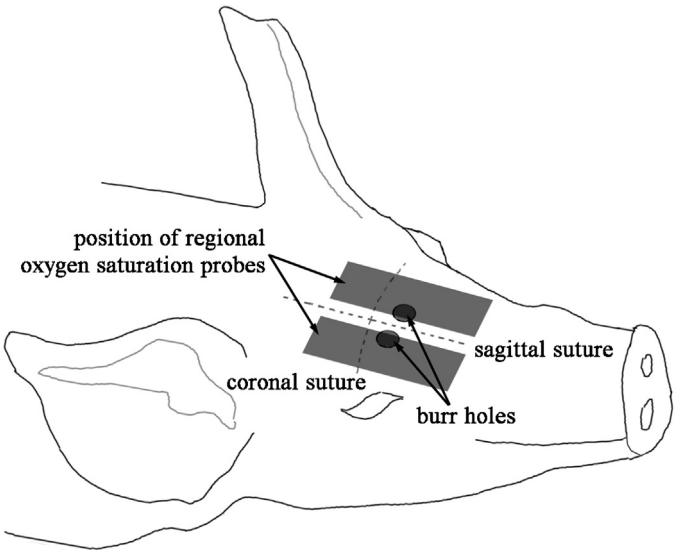

Fig. 1. Schematic drawing showing the setup of the cerebral probes. The burr holes are positioned 1 cm anterior to the coronal suture and 1 cm lateral to the sagittal suture. In each burr hole one brain oxygen tension probe and one microdialysis probe were inserted to a depth of 1 cm. In addition, the left burr hole contains an intracranial pressure probe and the right burr hole contains a brain temperature probe, both at a depth of 2 cm. The regional oxygen saturation probes were subcutaneously tunneled to the positions indicated by the gray rectangles.

(Carnegie Medicine AB) at a rate of 1 μl/min. Investigations by Bein et al. (2006) as well as our own preliminary experiments showed that in pigs of the size used in our experiments, transcutaneously obtained rSO_2 values are largely influenced by skin oxygenation. This phenomenon is larger in pigs than in humans (Davie and Grocott, 2012), probably due to the thicker skin and skull of pigs. We avoided this problem by placing the two Adult SomaSensor rSO_2 probes (Covidien plc, Dublin, Ireland) subcutaneously (Fig. 1), taking care to place the center of the probes over the burr holes. After careful hemostasis, the skin was closed over the probes and burr holes to prevent ambient light contamination. Nine needle electrodes (Ives EEG Solutions, Newburyport, MA) were placed in the skin as described earlier (Weenink et al., 2012), to measure EEG.

General parameters (heart rate, blood pressure, end-tidal carbon dioxide, body temperature, ICP, blood glucose) were recorded at 30 min intervals. Blood gas analysis was performed hourly. The EEG signal was continuously processed by calculation of the temporal brain symmetry index (tBSI) as described earlier (Weenink et al., 2012). In brief, tBSI calculates spectral changes in EEG by comparing the current EEG with a defined normal baseline. It is a normalized parameter within the range [0–1]. A higher tBSI value represents a larger deviation from the baseline EEG (van Putten, 2007). rSO_2 (measured using an INVOS 5100 C monitor (Covidien)) and $PbtO_2$ were continuously stored for offline analysis. The vials containing the effluent of the microdialysis probes were changed every 15 min.

2.3. Experimental protocol

In preliminary experiments (not published) injection of 0.5 ml air generally resulted in detectable changes in tBSI and $PbtO_2$ and 1.5 ml resulted in severe injury. We were interested in the smallest amount of air that would generate detectable injury, and therefore chose 0.2 ml as the lowest dose. In order to investigate the effect of larger doses as well as the effect of cumulative doses of air, we designed the following experimental setup using three groups. Group A received only the two largest doses (0.8 and 1.6 ml), group B started with a lower dose (0.4 ml, then 0.8 ml, then 1.6 ml), and group C started with the lowest dose (0.2 ml, then 0.4 ml, then