◇ This Month in

ANESTHESIOLOGY

■ Pain-related Cerebral Activation Characterized by Magnetic Resonance Imaging in Healthy Volunteers. Kurata *et al.* (page 35)

Kurata *et al.* recruited five healthy, right-handed volunteers (four men, one woman) for four sets of experiments, which included delivery of pain stimuli and cognitive tasks, while characterizing subjects' brain activity using functional magnetic resonance imaging. The purpose of the study was not only to localize cerebral activation by various stimuli, but also to characterize the time course of signal intensity.

Study subjects took no psychoactive or analgesic medications for 24 h preceding the experiments. Each was fitted with a thermal stimulator on the right and left forearms and was trained in rating pain sensation on a scale of 0–10. After baseline pain thresholds were established, each subject was examined with four cycles of 15-s hot (47.2–49.0°C) pain stimulus (alternated with a 30-s control stimulus), first on one forearm and then on the other. The hot pain stimulus ("on phase") was limited to 15 s to reduce head motion–related artifacts on magnetic resonance imaging. Images of brain activation were obtained during pain stimulus experiments and also during visual (visually guided saccade) and motor (finger tapping) tasks. Visually guided saccade and finger tapping were also conducted in cycles, *i.e.*, 30 s of active task performance alternated with 30 s of rest conditions.

Voxel-wise *t* statistical maps were standardized and averaged across subjects. Blood oxygenation level–dependent signal time courses were analyzed at local maxima of representative activation clusters. The researchers found that pain stimulus on the right forearm activated the brain's secondary somatosensory (S2), superior temporal, anterior cingulate, insular, prefrontal cortices, premotor, and lenticular nucleus areas. Pain stimulus on the left forearm activated similar but fewer areas at lower signal intensity. Pain-related activation was statistically weaker and showed less consistent signal time courses than visually guided saccade or finger tapping–related activation. However, the pain-related signals decayed earlier before the stimulus ended, whereas the signal plateaus induced by visually guided saccade and finger tapping were well-sustained. Although the study used a block design of repeated identical stimuli and a short-duration pain stimulus, it showed that the bilateral S2 was robustly activated by somatic thermal pain in blood oxygenation level–dependent contrast functional magnetic resonance imaging.

■ Performance of Closed-loop Anesthesia System Assessed during Orthopedic Surgery. Absalom *et al.* (page 67)

In this study of 10 patients undergoing elective hip or knee replacement, Absalom *et al.* evaluated the performance of custom-made software to monitor and to automatically control propofol infusion in a closed-loop anesthesia system. Using the Bispectral Index (BIS) as the control variable, the system provides data management in the "monitor" mode, requesting electroencephalographic data at 5-s intervals and providing a graphical display of current and trend values. In "automatic" mode, the system automatically controls the propofol infusion after the operator has entered a target BIS value, a minimum propofol concentration, and the American Society of Anesthesiologists physical status of the patient. The system will not operate in automatic mode if the American Society of Anesthesiologists status is IV or V.

Patients received 0.5% epidural bupivacaine at T8 to provide preinduction anesthesia. General anesthesia was induced using the propofol target-controlled infusion system under manual control in monitor mode. When anesthesia was deemed to be clinically adequate and surgery had begun, the system was switched to automatic mode using BIS as the control variable. The adequacy of anesthesia was then assessed throughout the remainder of the procedure, both clinically and by calculating the median performance error, the median absolute performance error, and the mean offset of the control variable.

One anesthesiologist was in charge of clinical management of the patient, and another monitored the research equipment while also manually recording BIS, physiologic data, and blood and effect-site propofol concentrations at 5-min intervals. The target-controlled infusion system was switched back to manual mode when the surgeon began final closing, and the target propofol concentration was set to zero. Patients remained in the operating room until they had regained consciousness, laryngeal mask airways had been removed, and they could correctly state their date of birth. After surgery, none of the patients reported explicit recall of intraoperative events.

Operating conditions were adequate in 9 of the 10 patients. One began moving after hip manipulation by the surgeon, after about 45 min of stable anesthesia. In

three patients, the research team found oscillation of the measured BIS around the set point. The median performance error and median absolute performance error were 2.2 and 8.0%, respectively, and the mean offset of the BIS from the set point was 0.9. The researchers urge further study to determine whether control performance could be improved by alterations to the gain factors or by using an effect site–targeted, target-controlled infusion propofol system.

■ Effects of Carbon Dioxide Absorbents on Volatile Anesthetic Degradation Compared in Porcine Model. Kharasch *et al.* (page 173)

Because some carbon dioxide absorbents used in anesthetic machines contain sodium and potassium hydroxides identified as responsible for anesthetic breakdown and degradant formation, new absorbents with modified amounts or omission of strong bases have been developed. In this study of five to six experiments in 14 pigs, Kharasch *et al.* compared the effects of Amsorb® (a new absorbent without a strong base; Armstrong Ltd., Coleraine, Northern Ireland), Baralyme® (Chemetron Medical Division, Allied Healthcare Products, St. Louis, MO), and sodalime, in both fresh and partially dehydrated forms, on carbon monoxide (CO) and compound A formation, carboxyhemoglobin (COHb) concentrations, and anesthetic degradation.

After premedication with ketamine plus xylazine, anesthesia was induced with halothane, and instrumentation for blood sampling was completed. Pigs were randomly assigned to five or six experiments, each lasting 45 min, using anesthesia with sevoflurane, isoflurane, or desflurane, and one of the three absorbents. Baseline samples of breathing circuit gas and arterial blood were obtained before each experiment and at 5, 10, 15, 30, and 45 min after inspiration of sevoflurane, isoflurane, and desflurane to determine hemoglobin, COHb, and oxyhemoglobin amounts in blood and compound A and CO concentrations in gas samples.

For desflurane and isoflurane, the order of inspired CO and COHb formation was dehydrated Baralyme® >> sodalime > Amsorb®. For desflurane and Baralyme®, peak CO was 9,700 ± 5,100 parts per million (ppm), and the increase in COHb was 37 ± 14%. CO and COHb increases were undetectable with Amsorb®. Neither fresh nor dehydrated Amsorb® caused compound A formation from sevoflurane, whereas Baralyme® and sodalime caused 20–40 ppm compound A. Its failure to cause formation of toxic products suggests that Amsorb® may benefit patient safety. In addition, the decreases in anesthetic degradation seen in this study may address the issue of anesthetic consumption, thus lowering costs of anesthetics.

■ Does Isoflurane Protect against Delayed Cell Death after Simulated Cerebral Ischemia? Sullivan *et al.* (page 189)

To address the shortcomings of *in vitro* models of ischemia, Sullivan *et al.* developed an organotypic slice culture model of cerebral ischemia. Because the model retains cellular integrity and sensitivity to anoxia and allows serial measurement of cell survival over many days, the team was able to test whether isoflurane prevents delayed cell death of ischemia-sensitive hippocampal neurons after simulated ischemia.

Hippocampi of 6- to 28-day-old rats were harvested and kept in culture for 7–14 days before the study began. Presence of field potentials after 7 days in culture indicated the health of the cells and persistence of synaptic connections in the slices. Propidium iodide exclusion was used to establish that a high percentage of neurons in the CA1, CA3, and dentate cell fields were living. *In vitro* ischemia was simulated by anoxia combined with glucose-free media (oxygen–glucose deprivation). In the experiments involving isoflurane, the anesthetic was delivered to the chamber using a calibrated isoflurane vaporizer and remained throughout the ischemic injury period. In another experiment of 46 slices, the effect of 1% isoflurane on glutamate-induced delayed cell death was evaluated at 2, 3, and 7 days after injury. Delayed cell death was serially measured in each slide by quantifying the binding of propidium iodide to DNA with fluorescence microscopy.

Maximum cell death occurred 3–5 days after oxygen–glucose deprivation. CA1 neuronal cell death was 80 ± 18% after 3 days and 80–100% after 1 week. By the third day after oxygen–glucose deprivation, death of 70 ± 16% of CA3 neurons and 48 ± 28% of dentate gyrus neurons had occurred. Both 1% isoflurane and the *N*-methyl-D-aspartate antagonist MK-801 reduced cell death to levels similar to controls for 14 days after the ischemic injury. Isoflurane also reduced cell death caused by application of 100 but not 500 mM glutamate in CA1 and CA3 neurons. The researchers speculate that modulation of glutamate excitotoxicity may contribute to the protective mechanism.

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