◇ This Month in

# ANESTHESIOLOGY

## ■ Response to Acoustic Stimuli during Propofol Anesthesia. Plourde *et al.* (page 448)

Plourde *et al.* used blood oxygenation level dependent functional magnetic resonance imaging with noise mitigation strategies to assess brain response to complex auditory stimuli. Seven healthy volunteers were recruited for the study, and imaging data were recorded during a single 4-h session. Data were obtained during four different conditions: awake; during sedation, with a blood propofol concentration of 0.6 μg/ml; during anesthesia, when subjects were unconscious (propofol concentration of 4.6 μg/ml); and during recovery, about 45 min after the end of propofol infusion.

Other monitoring during the study period included pulse oximetry, intraarterial blood pressure, and on-line concentration of oxygen and carbon dioxide in inspired and expired gas. Volunteers breathed spontaneously and received supplemental oxygen (5 l/min) by facemask during baseline, sedation, and recovery phases of the study. The digitized auditory stimuli were arranged in 10-s blocks and delivered binaurally at mean intensity of 88–90 dB sound pressure. Word stimuli consisted of common English words (4 lists of 10 words—one for each condition) and scrambled words presented in a similar manner. Other sounds included human nonspeech vocalizations (laughter, moaning, etc.) and nonvocal sounds such as environmental noises (wind, waves) and musical sounds. Participants' memory for words was tested after 22–26 h.

During all four conditions, including anesthesia, all sounds elicited greater activations than silence bilaterally in primary auditory cortices and adjacent regions within the planum temporale. The magnitude of activations during sedation and anesthesia was reduced by 40–50%. Anesthesia abolished voice-specific activations in the superior temporal sulcus. Scrambled words elicited more activation than normal words bilaterally in planum temporale during anesthesia. The next day, subjects only recognized words presented during baseline plus recovery, correlating with activity that had been shown in the right and left planum temporale. It appears that primary and association auditory cortices remain responsive to complex auditory stimuli under anesthesia. However, the ability for higher-level analysis of auditory stimuli is lost during anesthesia.

## ■ Adding Simulator-based Assessment to Anesthesia Board Examinations. Savoldelli *et al.* (page 475)

Anesthesia board examinations in most countries rely on traditional written and oral tests to determine residents' fitness for independent clinical practice. In this study reported by Savoldelli *et al.*, two independent examiners scored performances of 20 senior anesthesia residents who were assessed by both oral examination and a simulator-based examination. The goal was to assess residents' competence in similar content domains using two different evaluation modes. Using a previously validated global rating scale developed by the Anesthesia Oral Examination Board of the Royal College of Physicians and Surgeons of Canada, different examiners rated the residents' performance during oral examinations and during resuscitation and trauma scenarios performed on simulation mannequins. The researchers found that interrater reliability was good to excellent across scenarios and modalities. The within-scenario between-modality score correlations were moderate. Forty percent of the average score variance was accounted for by the participants and 30% by the interaction between participant and modality. The residents' scores on the oral examination were not a good predictor of how they performed in a simulator-based assessment. Therefore, simulation might be considered a useful adjunct to the oral board examination process to more thoroughly gauge clinical competence of senior anesthesia residents.

## ■ Will Isoflurane Pretreatment Reduce Lung Injury from Endotoxin? Reutershan *et al.* (page 511)

Lipopolysaccharide, a major component of the outer membrane in gram-negative bacteria, plays a major role in the development of acute respiratory distress syndrome, characterized by an excessive infiltration of neutrophils (polymorphonuclear leukocytes, or PMN), among other responses. Both *in vitro* and *in vivo* studies have suggested that volatile anesthetics might inhibit PMN recruitment by modulating the release of chemotactic cytokines. Accordingly, Reutershan *et al.* investigated the effect of isoflurane pretreatment on endotoxin-induced lung injury in male C57Bl/6 mice.

Groups of at least four mice were exposed to aerosol-

ized lipopolysaccharide from *Salmonella enteritidis* for 30 min in a custom-built cylindrical chamber. Such exposure usually results in a time-dependent PMN recruitment into all compartments of the lung, peaking between 12 and 24 h. Groups of mice were randomly assigned to receive isoflurane, delivered in a separate chamber using an agent-specific vaporizer, at 1, 4, 6, 12, or 24 h before endotoxin exposure, or 1 h after endotoxin exposure. Mice in the control group did not receive isoflurane.

The authors used flow cytometry to determine neutrophil recruitment into the pulmonary vasculature and migration into lung compartments. Capillary protein leakage, formation of lung edema, and concentration of chemokines in bronchoalveolar lavage were assessed from samples obtained from each group of mice. Inhalation of the endotoxin induced significant neutrophil migration into all lung compartments. When given 1 or 12 h before endotoxin exposure, isoflurane pretreatment inhibited PMN recruitment into lung interstitium and alveolar spaces. This effect was also observed when isoflurane was given within the first hour after endotoxin exposure. However, pretreating with isoflurane 4, 6, or 24 h before exposure did not inhibit PMN recruitment. When mice received isoflurane pretreatment 1 or 12 h before endotoxin exposure, they also experienced reduced protein leakage and pulmonary edema. Production of keratinocyte-derived chemokines (CXCL 1) and macrophage inflammatory protein 2 (CXCL 2/3) in the bronchoalveolar lavage was reduced with isoflurane pretreatment when given 1 h, but not 12 h, before endotoxin exposure. From these results, the authors surmise that different mechanisms may be responsible for early and late protective effects of isoflurane pretreatment. Further investigation to elucidate the molecular targets of volatile anesthetics in the lung will help to find more specific modulators of inflammatory response in acute lung injury and acute respiratory distress syndrome.

## ■ Are Cyclooxygenase-2 Inhibitors Safe for Postsurgical Pain in Noncardiac Patients? Nussmeier *et al.* (page 518)

In 113 centers in 14 countries, Nussmeier *et al.* conducted a randomized, double-blind trial comparing parenteral parecoxib in combination with oral valdecoxib to placebo given after noncardiac surgery. A total of 1,062 patients, scheduled to undergo major orthopedic, abdominal, gynecologic, or noncardiac thoracic surgery, participated in the study. Primary endpoints were the occurrence of predefined adverse events, including cardiovascular events such as myocardial infarction; cerebrovascular events including a new ischemic or hemorrhagic event; peripheral vascular events such as deep-vein thrombosis; renal events; gastroduodenal complications; and wound-healing complications. Secondary endpoints included patients' pain ratings, use of supplemental opioid analgesics, and reports of adverse events due to opioids.

Patients assigned to the study drug group received parenteral parecoxib the day of surgery and for 2 days afterward, followed by oral valdecoxib for the remainder of the 10-day treatment period. Electrocardiograms, clinical laboratory assessments, and vital signs were analyzed at baseline, at the time of transition from intravenous to oral medication, and at the final visit (between day 11 and 14). Patients were contacted by telephone 30 days after their last dose of study medication and questioned about the occurrence of serious or clinically relevant adverse events.

The occurrence of predefined adjudicated adverse events was similar between the two groups. Patients receiving placebo consumed more morphine than did patients receiving the cyclooxygenase-2 inhibitors. Placebo patients also reported higher pain ratings on study days 2–10 and reported more opioid-related side effects on days 2–6. It appears that parecoxib and valdecoxib are useful adjuncts to opioids for treatment of postoperative pain in noncardiac surgery patients. However, further study will be needed to determine the drugs' safety in patients with known atherosclerotic disease scheduled for noncardiac surgery.

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