



ON THE COVER:

Differentiating drug-related and state-related changes on electroencephalography during anesthetic-induced unconsciousness has remained difficult. In this issue of *ANESTHESIOLOGY*, Scheinin *et al.* demonstrate that the electroencephalogram effects of dexmedetomidine and propofol are strongly drug- and state-dependent in 47 healthy participants. Changes in slow-wave and alpha activity best detected different states of consciousness. Illustration by Sara Jarret, C.M.I.

- Scheinin *et al.*: Differentiating Drug-related and State-related Effects of Dexmedetomidine and Propofol on the Electroencephalogram, p. 22

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History of the Development of Anesthesia for the Dolphin: A Quest to Study a Brain as Large as Man's <i>J. G. McCormick and S. H. Ridgway</i>	11
Motivation to anesthetize dolphins came from the fact that scientists wanted to study the brain of the dolphin, a brain as large as man's, as well as the electrophysiology of the dolphin's sophisticated auditory system and sonar.	

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■ PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

-   **Differentiating Drug-related and State-related Effects of Dexmedetomidine and Propofol on the Electroencephalogram** 22
A. Scheinin, R. E. Kallionpää, D. Li, M. Kallioinen, K. Kaisti, J. Långsjö, A. Maksimow, T. Vahlberg, K. Valli, G. A. Mashour, A. Revonsuo, and H. Scheinin
- In humans rendered unresponsive with either propofol or dexmedetomidine, increased frontal alpha, increased slow-wave, and decreased beta activities were observed. Arousal in response to verbal or physical stimulation resulted in a reversion of the alpha and slow-wave activity, but not beta activity. The results suggest anesthetic effects on the electroencephalogram are a composite of the direct effect of the drugs on neuronal networks and the impact of the change in the state of consciousness itself. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-  **Supplemental Carbon Dioxide Stabilizes the Upper Airway in Volunteers Anesthetized with Propofol** 37
K. J. Ruscic, J. Bøgh Stokholm, J. Patlak, H. Deng, J. C. P. Simons, T. Houle, J. Peters, and M. Eikermann
- Elevation of end-tidal carbon dioxide by inhalation of carbon dioxide dose-dependently stabilized the airway as evidenced by decrease of upper airway closing pressure under propofol anesthesia in 12 nonobese adult volunteers. Phasic genioglossus activity dose-dependently increased with supplemental carbon dioxide and was a significant effect modifier for stabilizing the upper airway. Cortical arousal from anesthesia appeared to partly contribute to upper airway stabilization in the light propofol anesthesia group. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-   **Comparison of Anterior Suprascapular, Supraclavicular, and Interscalene Nerve Block Approaches for Major Outpatient Arthroscopic Shoulder Surgery: A Randomized, Double-blind, Noninferiority Trial** 47
D. B. Auyong, N. A. Hanson, R. S. Joseph, B. E. Schmidt, A. E. Slee, and S. C. Yuan
- This study suggests that anterior suprascapular block provides noninferior analgesia compared to interscalene block, and better preserves vital capacity. While supraclavicular block was associated with some vital capacity preservation compared to interscalene block, the analgesia provided by supraclavicular block did not meet noninferiority criteria.
-  **Auditory Icon Alarms Are More Accurately and Quickly Identified than Current Standard Melodic Alarms in a Simulated Clinical Setting** 58
 *R. R. McNeer, D. B. Horn, C. L. Bennett, J. R. Edworthy, and R. Dudaryk*
- In a simulated intensive care unit using primarily anesthesiology residents as test subjects, the ability to learn and identify standard and icon alarms was tested. In this setting, icon alarms were easier to learn and identify than standard alarms, while standard alarms were more likely to be perceived as having higher fatigue and task load. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-  **Current Ventilator and Oxygen Management during General Anesthesia: A Multicenter, Cross-sectional Observational Study** 67
S. Suzuki, Y. Mihara, Y. Hikasa, S. Okahara, T. Ishihara, A. Shintani, H. Morimatsu, on behalf of the Okayama Research Investigation Organizing Network (ORION) investigators
- In this multicenter, cross-sectional study of 1,498 patients at 43 hospitals, potentially preventable hyperoxemia and substantial oxygen exposure were common during general anesthesia, especially in patients receiving one-lung ventilation. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-   **Impact of Intravenous Acetaminophen on Perioperative Opioid Utilization and Outcomes in Open Colectomies: A Claims Database Analysis** 77
 *I. Wasserman, J. Poeran, N. Zubizarreta, J. Babby, S. Serban, A. T. Goldberg, A. J. Greenstein, S. G. Memtsoudis, M. Mazumdar, and A. B. Leibowitz*
- A minority of open colectomy patients receive intravenous acetaminophen, which is mostly used as a single-dose administration on the day of surgery. A variety of intravenous acetaminophen dosing regimens were not observed to decrease opioid utilization to a clinically significant threshold. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆  **Neuropsychological and Behavioral Outcomes after Exposure of Young Children to Procedures Requiring General Anesthesia: The Mayo Anesthesia Safety in Kids (MASK) Study** 89
D. O. Warner, M. J. Zaccariello, S. K. Katusic, D. R. Schroeder, A. C. Hanson, P. J. Schulte, S. L. Buenvenida, S. J. Gleich, R. T. Wilder, J. Sprung, D. Hu, R. G. Voigt, M. G. Paule, J. J. Chelonis, and R. P. Flick

This matched cohort study found that anesthesia exposure before age 3 yr was not associated with deficits in the primary outcome of general intelligence. Single exposures were not associated with deficits in other neuropsychological domains (assessed as secondary outcomes). However, multiple exposures were found to be associated with modest decreases in processing speed and fine motor coordination. Parents also reported that multiply exposed children have more difficulties with behavior and reading. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

BASIC SCIENCE

- γ -Aminobutyric Acid Type A Receptor Potentiation Inhibits Learning in a Computational Network Model** 106
K. P. Storer and G. N. Reeke


In a computational model of the hippocampus, propofol reduced polychronous group size in a dose-dependent manner. By contrast, modulation of theta oscillations did not affect group size. The results suggest formation of polychronous groups of neurons is more sensitive to the effect of propofol on the balance between excitation and inhibition than on theta oscillations.

- Noninvasive Tracking of Anesthesia Neurotoxicity in the Developing Rodent Brain** 118
R. Makaryus, H. Lee, J. Robinson, G. Enikolopov, and H. Benveniste

With either a single or multiple exposure to sevoflurane, a reduction in N-acetyl-aspartate was observed; this reduction led to a deviation in the normal trajectory in the developing brain. Effects of multiple anesthesia exposures with sevoflurane were more pronounced than a single exposure on both N-acetyl-aspartate trajectory and animal behavior. The results suggest that N-acetyl-aspartate may serve as a biomarker of the impact of anesthetic agents on the developing brain; however, further validation of its utility is necessary.

■ CRITICAL CARE MEDICINE

BASIC SCIENCE

- ◆  **Early-phase Innate Immune Suppression in Murine Severe Sepsis Is Restored with Systemic Interferon- β** 131
Y. Kusakabe, K. Uchida, Y. Yamamura, T. Hiruma, T. Totsu, Y. Tamai, H. Tsuyuzaki, K. Hasegawa, K. Chang, and Y. Yamada

In an established mouse model of sepsis (cecal ligation and perforation), severe *versus* mild sepsis was associated with increased mortality, less capacity of peritoneal inflammatory cells for phagocytosis, and decreased expression of focal and systemic cytokines and chemokine receptor expression on circulating neutrophils. These effects were reversed by the administration of the immune stimulant interferon- β after—but not before—severe sepsis was established. Interferon- β after the onset of peritonitis may restore impaired innate immunity and improve outcome. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- ◆  **Mechanical Ventilation Induces Desensitization of Lung Axl Tyrosine Kinase Receptors** 143
G. Otulakowski, D. Engelberts, M. Post, C. Masterson, and B. P. Kavanagh

Overdistention of lung endothelial cells caused an influx of calcium, which rendered Axl insensitive to the activating effects of its ligand. The immune regulatory and antiapoptotic effects of Axl in endothelial cells may thus be compromised by injurious mechanical ventilation. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

- Free Fatty Acid Receptor G-protein-coupled Receptor 40 Mediates Lipid Emulsion-induced Cardioprotection** 154
S. Umar, J. Li, K. Hannabass, M. Vaillancourt, C. M. Cunningham, S. Moazeni, A. Mahajan, and M. Eghbali

This study demonstrates that G-protein-coupled receptor 40 is expressed in the rodent heart and is involved in cardioprotection mediated by lipid emulsion against ischemia/reperfusion injury and bupivacaine-induced cardiotoxicity.

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◆ **Continuous Negative Abdominal Pressure Reduces Ventilator-induced Lung Injury in a Porcine Model** 163

T. Yoshida, D. Engelberts, G. Otulakowski, B. Katira, M. Post, N. D. Ferguson, L. Brochard, M. B. P. Amato, and B. P. Kavanagh

In a pig adult respiratory distress syndrome model, addition of continuous negative abdominal pressure (−5 cm H₂O) to positive end-expiratory pressure (PEEP), compared with PEEP alone (where transpulmonary pressure was matched in each group), resulted in better oxygenation, compliance, and homogeneity of ventilation, as well as less lung injury. PEEP with continuous negative abdominal pressure might be a treatment option for adult respiratory distress syndrome by recruiting atelectasis and minimizing ventilator-induced lung injury, but its efficacy and long-term effects in patients are not yet known. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

■ PAIN MEDICINE

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Spinal Protein Kinase M ζ Regulates α -Amino-3-hydroxy-5-methyl-4-isoxazolepropionic Acid Receptor Trafficking and Dendritic Spine Plasticity *via* Kalirin-7 in the Pathogenesis of Remifentanyl-induced Postincisional Hyperalgesia in Rats 173

L. Zhang, S. Guo, Q. Zhao, Y. Li, C. Song, C. Wang, Y. Yu, and G. Wang

The inhibition of protein kinase M ζ prevents remifentanyl-enhanced postoperative hyperalgesia in a rat incisional model. The intraoperative effects of remifentanyl in this rat model involve changes in dendritic spine morphology and function in the dorsal horn of the spinal cord. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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◆ **A Review of the Impact of Obstetric Anesthesia on Maternal and Neonatal Outcomes** 192

G. Lim, F. L. Facco, N. Nathan, J. H. Waters, C. A. Wong, and H. K. Eltzschig

Modern obstetric anesthesia care emphasizes multidisciplinary, evidence-based practice. Basic, translational, and clinical scientific research propels further evolution. This review article highlights recent advances in obstetric anesthesia and their impact on maternal-fetal-neonatal outcomes.

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