



ON THE COVER:

Machine learning, the tool currently driving the development of artificial intelligence, has recently seen exponential growth in its sophistication and influence. In this issue of ANESTHESIOLOGY, we explore three examples of machine learning applied to our field. Lee *et al.* use machine-learning techniques to predict postoperative mortality from electronic health record data. Kendale *et al.* predict hypotension by leveraging data available during induction, and Hatib *et al.* predict hypotension using data from high-fidelity arterial line waveforms. In an accompanying Editorial View, Mathis *et al.* describe what the practicing anesthesiologist needs to know about artificial intelligence for anesthesia. Illustration by Annemarie Johnson, Vivo Visuals.

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PERIOPERATIVE MEDICINE

CLINICAL SCIENCE

-   **Development and Validation of a Deep Neural Network Model for Prediction of Postoperative In-hospital Mortality** 649
  *C. K. Lee, I. Hofer, E. Gabel, P. Baldi, and M. Cannesson*
- The authors' neural network model was comparable in accuracy to, but potentially more efficient at feature selection than logistic regression models. Deep neural network-based machine learning provides an alternative to conventional multivariate regression. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-   **Machine-learning Algorithm to Predict Hypotension Based on High-fidelity Arterial Pressure Waveform Analysis** 663
 *F. Hatib, Z. Jian, S. Buddi, C. Lee, J. Settels, K. Sibert, J. Rinehart, and M. Cannesson*
- A machine-learning algorithm based on thousands of arterial waveform features can identify an intraoperative hypotensive event 15 min before its occurrence with a sensitivity of 88% and specificity of 87%. Further studies must evaluate the real-time value of such algorithms in a broader set of clinical conditions and patients. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-   **Supervised Machine-learning Predictive Analytics for Prediction of Postinduction Hypotension** 675
S. Kendale, P. Kulkarni, A. D. Rosenberg, and J. Wang
- Among 13,323 patients undergoing a variety of surgical procedures, 8.9% experienced a mean arterial pressure less than 55 mmHg within 10 min of induction start. While some machine-learning algorithms perform worse than logistic regression, several techniques may be superior. Gradient boosting machine, with tuning, demonstrates a receiver operating characteristic area under the curve of 0.76, a negative predictive value of 19%, and positive predictive value of 96%. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-   **Liposomal Bupivacaine Does Not Reduce Inpatient Opioid Prescription or Related Complications after Knee Arthroplasty: A Database Analysis** 689
  *L. Pichler, J. Poeran, N. Zubizarreta, C. Cozowicz, E. C. Sun, M. Mazumdar, and S. G. Memtsoudis*
- Retrospective analysis of a national observational data set showed that liposomal bupivacaine use for total knee arthroplasty is increasing. Liposomal bupivacaine use was not associated with clinically meaningful reductions in inpatient opioid use, opioid-related complications, or resource utilization in patients who received modern pain management including a peripheral nerve block. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*
-   **Anesthesia Care Team Composition and Surgical Outcomes** 700
 *E. C. Sun, T. R. Miller, J. Moshfegh, and L. C. Baker*
- Using national claims data for 443,000 Medicare beneficiaries, the influence of care team composition on inpatient mortality, inpatient length of stay, and inpatient spending was evaluated. There were no significant differences in mortality, length of stay, or inpatient spending between the care team models. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Preoperative Epoetin- α with Intravenous or Oral Iron for Major Orthopedic Surgery: A Randomized Controlled Trial 710

P. Biboulet, S. Bringuier, P. Smilevitch, T. Loupec, C. Thuile, M. Pencole, G. Maissiat, G. Dangelser, and X. Capdevila

Hemoglobin concentration the day before surgery was 1 g/dl greater in 50 patients randomized to intravenous iron than in those assigned to oral iron. About half the patients given oral iron reported gastrointestinal symptoms. Intravenous iron is preferable to oral iron as a supplement to epoetin- α .

Complications in Pediatric Regional Anesthesia: An Analysis of More than 100,000 Blocks from the Pediatric Regional Anesthesia Network 721

B. J. Walker, J. B. Long, M. Sathyamoorthy, J. Birstler, C. Wolf, A. T. Bosenberg, S. H. Flack, E. J. Krane, N. F. Sethna, S. Suresh, A. H. Taenzer, D. M. Polaner, on behalf of the Pediatric Regional Anesthesia Network Investigators

In a prospective multicenter cohort of more than 100,000 blocks in children, there were no cases of permanent neurologic deficit associated with regional anesthesia. The rate of transient neurologic deficit was low at 2.4 per 10,000, and the incidence of local anesthesia toxicity was also low at 0.76 per 10,000.

BASIC SCIENCE

 **Breakdown of Neural Function under Isoflurane Anesthesia: *In Vivo*, Multineuronal Imaging in *Caenorhabditis elegans*** 733



M. R. Awal, D. Austin, J. Florman, M. Alkema, C. V. Gabel, and C. W. Connor

Even though exposure to 4% isoflurane prevented movement, neurons in the movement circuitry remained highly active. However, the coordination among the neurons of the command circuitry was lost in comparison to the awake state. The data suggest that the primary cause of the lack of motion in worms is not the suppression of neuronal activity *per se* but rather the loss of coordination between neurons in the command circuit.

 **Anesthetics Have Different Effects on the Electrocorticographic Spectra of Wild-type and Mitochondrial Mutant Mice** 744

C. W. Carspecken, S. Chanprasert, F. Kalume, M. M. Sedensky, and P. G. Morgan

While isoflurane and halothane suppressed electrocorticography in all frequency bands in control mice, in *Ndufs4* knockout mice, both agents decreased power in the higher frequency bands (beta, gamma), whereas activity in the lower bands (delta, theta, and alpha) was maintained. Ketamine also decreased power in the *Ndufs4* knockout mice in the beta and gamma frequency bands only. The data indicate that in *Ndufs4* knockout mice, an energetic state in glutamatergic neurons impacts anesthetic sensitivity, and this sensitivity is reflected in cortical electrical activity. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Stereoselective Ketamine Metabolism by Genetic Variants of Cytochrome P450 CYP2B6 and Cytochrome P450 Oxidoreductase 756

P.-F. Wang, A. Neiner, and E. D. Kharasch

Several genetic variants of CYP2B6 and P450 oxidoreductase have diminished ketamine *N*-demethylation activity. Variants do not have altered stereoselectivity of ketamine metabolism. Results suggest candidate polymorphisms of CYP2B6 and P450 oxidoreductase for clinical evaluation.

CRITICAL CARE MEDICINE

CLINICAL SCIENCE

  **Standardized Unloading of Respiratory Muscles during Neurally Adjusted Ventilatory Assist: A Randomized Crossover Pilot Study** 769



F. Campoccia Jalde, F. Jalde, M. K. E. B. Wallin, F. Suarez-Sipmann, P. J. Radell, D. Nelson, S. Eksborg, and P. V. Sackey

This pilot study of 10 patients titrated neurally adjusted ventilatory assist to different levels of diaphragm unloading; less unloading was associated with greater diaphragm activity and improved ventilation of dependent lung. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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D. G. Ririe, M. D. Boada, M. K. MacGregor, S. J. Martin, T. J. Strassburg, S. A. Kim, J. C. Eisenach, and T. J. Martin

In a rat model of incisional pain, attention was impaired after injury and improved with an opioid analgesic. Diminished activity of the medial prefrontal cortex was found and may contribute to pain-induced impaired attention.

Effect of Thoracic Epidural Anesthesia in a Rat Model of Phrenic Motor Inhibition after Upper Abdominal Surgery 791

W.-S. Chae, S. Choi, D. Sugiyama, G. B. Richerson, T. J. Brennan, and S. Kang

Upper abdominal incision in rats reduced phrenic motor output for several days after surgery. Thoracic epidural anesthesia using bupivacaine reduced incision-induced alterations in phrenic motor output. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

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Association between Performance in a Maintenance of Certification Program and Disciplinary Actions against the Medical Licenses of Anesthesiologists 812

Y. Zhou, H. Sun, A. Macario, M. T. Keegan, A. J. Patterson, M. M. Minhaj, T. Wang, A. E. Harman, and D. O. Warner

The introduction in 2000 of certificates that require participation in a program to maintain certification was not associated with a significant change in the incidence of disciplinary license actions. Completing maintenance of certification program requirements in a timely fashion was associated with a lower incidence of license actions. *SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT*

Reducing the Incidence of Substance Use Disorders in Anesthesiology Residents: 13 Years of Comprehensive Urine Drug Screening 821

M. G. Fitzsimons, K. Baker, R. Malhotra, A. Gottlieb, E. Lowenstein, and W. M. Zapol

The Massachusetts General Hospital randomly tested residents over a period of 13 yr. There was no detected substance abuse among residents during the testing period in 1,002 resident years, *versus* four incidents in the previous 719 resident years. This intriguing, but statistically fragile, result needs to be confirmed in other settings and other anesthesia clinicians.

REVIEW ARTICLE

Neurocognitive Function after Cardiac Surgery: From Phenotypes to Mechanisms 829

M. Berger, N. Terrando, S. K. Smith, J. N. Browndyke, M. F. Newman, and J. P. Mathew

Postoperative delirium and cognitive dysfunction occur frequently after cardiac surgery and are associated with decreased quality of life and increased mortality risk. This review discusses the potential mechanisms that may underlie these complications and questions for future study.

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