Journal-related Activities and Other Special Activities at the 2016 American Society of Anesthesiologists Annual Meeting

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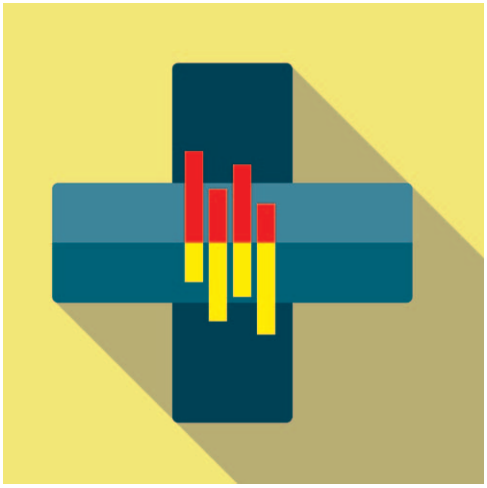

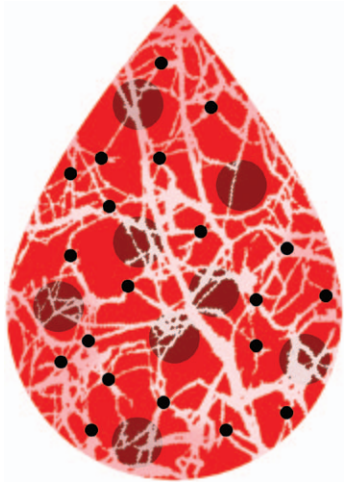

Initial Results of Clinical Trials

Sunday, October 23, 1:10 PM to 3:10 PM, McCormick Place, W375b

This year ANESTHESIOLOGY will sponsor four sessions at the Annual Meeting of the American Society of Anesthesiologists (ASA).

Moderators

Daniel I. Sessler, M.D., Cleveland Clinic, Cleveland, Ohio; and Paul S. Myles, M.B.B.S., M.P.H., M.D., F.F.A.R.C.S.I., F.A.N.Z.C.A., Monash University, Melbourne, Victoria, Australia.

ANESTHESIOLOGY is sponsoring its second Major Trials Session at the 2016 Annual Meeting of the ASA. The session will provide a high-profile, large audience forum for initial presentation of major randomized clinical trial results. It is designed for substantial trials, usually randomized and blinded, with a clinically important primary outcome. Articles selected for the Trials Session will be simultaneously published in the journal and have a press release.

25th Annual Journal Symposium: Coagulation 2016: New Drugs and New Data

Sunday, October 23, 2016, 9:00 AM to 12:00 PM, McCormick Place, W375c

The 2016 Journal Symposium titled "Coagulation 2016: New Drugs and New Data" addresses managing bleeding and coagulopathy in a perioperative setting. It will feature the following moderator and speakers.

Moderator

Michael J. Avram, Ph.D., Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Speakers

1. Critical Quality of Clot Structure

Alisa S. Wolberg, Ph.D., F.A.H.A., University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

The figures were recreated by Annemarie B. Johnson, C.M.I., Medical Illustrator, Vivo Visuals, Winston-Salem, North Carolina.

Submitted for publication July 6, 2016. Accepted for publication July 14, 2016. Department of Cardiovascular Anesthesiology, Baylor College of Medicine, Texas Heart Institute, Houston, Texas (C.D.C.); Department of Anesthesiology, Brigham and Women's Hospital/Harvard Medical School, Boston, Massachusetts (D.J.C.); Department of Anesthesiology, Chiba University Graduate School of Medicine, Chiba, Japan (S.I.); Department of Anesthesiology, Duke University School of Medicine, Durham, North Carolina (J.H.L.); and Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois (M.J.A.).

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2. **Anticoagulation Management for Surgery and Regional Anesthesia**

   Marc Samama, M.D., Ph.D., F.C.C.P., Cochin and Hotel-Dieu University Hospitals, Paris, France

3. **Managing New Anticoagulants: Purified and Recombinant Strategies for Prevention and Treatment of Bleeding**

   Jerrold H. Levy, M.D., Duke University, Durham, North Carolina

Description

In a perioperative setting, managing bleeding and coagulopathy are critical for clinicians. Perioperative bleeding is due to multiple causes, including fibrinolysis, activation of inflammatory pathways, consumption of coagulation factors, dilutional changes, and other factors. Additionally, an increasingly frequent cause of bleeding is the perioperative use of anticoagulation and antiplatelet agents that until recently have no well-established reversal methods. New direct-acting oral anticoagulants are frequently utilized for management of both venous thromboembolic prophylaxis and therapy, as well as stroke prevention in patients with atrial fibrillation. As a result, new data and therapeutic approaches have emerged for understanding critical aspects of clot formation for hemostasis, management of perioperative anticoagulation especially for regional anesthesia, and specific antidotes for the novel anticoagulants. Three experts will introduce these topics for the first 90 min of the symposium, with 25-min presentations and 5-min discussions. The speakers will discuss three different considerations from the basic science of clot structure, to new data and guidelines about managing perioperative anticoagulation, and novel considerations for the use of recombinant and purified therapeutic approaches to reverse anticoagulation and treating bleeding and coagulopathy.

These lectures will be followed by oral presentations of 12 abstracts, summarized below, that were selected for their relevance to the symposium topic. The full text for each abstract can be found at the ASA abstract Web site.

JS01

"Anticoagulation Based on Heparin Dose–Response Technique Fails to Predict Heparin Bolus Dose Requirement during Cardiac Surgery" by Junko Ichikawa, M.D., Takahito Marubuchi, M.D., Tetsu Mori, M.D., Mitsuharu Kodaka, M.D., Makiko Komori, M.D., Department of Anesthesiology, Tokyo Women's Medical University Medical Center East, Tokyo, Japan. The accuracy of Hepcon Heparin Management System Plus–based heparin administration in achieving target activated clotting time (ACT) and desired heparin concentration was evaluated prospectively in 86 patients undergoing cardiac surgery with cardiopulmonary bypass. Blood samples for baseline ACT, predicted heparin dose–response (HDR), and predicted heparin concentration were obtained after induction of anesthesia. A kaolin ACT of 450 s was a target value for the HDR on the Hepcon Heparin Management System, and unfractionated heparin was administered based on the estimated dose. Kaolin ACT was measured 3 min later. There was wide variation in the heparin concentrations required to reach target ACT, which was achieved in 31.4% of patients. Correlation between calculated and measured HDR was poor, although the predicted heparin concentration was strongly correlated with the measured concentration.

JS02

"Report on 5-Yr Experience with Obstetric Hemorrhage Protocol" by Cathleen Peterson-Layne, M.D., Ph.D., Nicole R. Guinn, M.D., Evelyn Lockhart, M.D., Holly Ann Muir, M.D., Duke University Hospital, Durham, North Carolina; University of New Mexico, Albuquerque, New Mexico. Quality improvement data collected from the time of implementation of an obstetric hemorrhage protocol (OHP) to present (2010 to 2015) were reviewed. The OHP was activated 121 times in a setting of approximately 16,000 deliveries in that time. The introduction of tranexamic acid (TXA) and fibrinogen concentrate to the OHP addressed the inhibition of fibrinolysis and rapid treatment of hypofibrinogenemia. Point-of-care coagulation testing allowed for detection of coagulopathy, facilitating goal-directed therapy. Interval analysis after process improvement changes suggests that they led to improved hemorrhage management as measured by reduced erythrocyte transfusion. Indicators of severe maternal morbidity associated with maternal hemorrhage, intensive care unit (ICU) admission, or transfusion of four or more blood products were also reduced.

JS03

"Aminocaproic Acid Is Associated with Decreased Cognition Early after Cardiac Surgery Compared to Tranexamic Acid" by Yinghui Low, M.D., Mary Cooter, Ph.D., Niccolo Terrando, Ph.D., Miles Berger, M.D., Mihai V. Podgoreanu, M.D., Mark Stafford-Smith, M.D., Mark F. Newman, M.D., Joseph P. Mathew, M.D., Rebecca Y. Klinger, M.D., Duke University Hospital, Durham, North Carolina; University of California - San Francisco, San Francisco, California; Duke University Medical Center, Durham, North Carolina. The antifibrinolytic drugs TXA and epsilon-aminocaproic acid (EACA) are used to reduce blood loss and transfusion requirements in cardiac surgery. The hypothesis that there would be a difference in postoperative cognitive dysfunction (POCD) after cardiac surgery between patients who received TXA and those who received EACA was tested in a cohort of 155 patients, 69 of whom received TXA and 86 of whom received EACA. POCD was defined as a decline from baseline of greater than or equal to 1 SD in one or more of the five cognitive domains. After propensity score adjustment, multivariate analysis demonstrated a higher 6-week POCD in patients who received EACA (59.3%) than in those who received TXA (46.4%; odds ratio [OR], 3.28; 95% CI, 1.48 to 7.62).

JS04

"The Effect of Remote Ischemic Preconditioning on Platelets and Coagulation in Healthy Volunteers" by Nathan J. Clendenen, M.D., M.S., Denis V. Snegovskikh, M.D., Trevor M. Banack, M.D., Yale University, New Haven, Connecticut; Yale University, Wallingford, Connecticut. Remote ischemic preconditioning (RIPC) aims to reduce injury to vital organs by inducing ischemia in a limb before a systemic ischemic insult. Because platelets may play a role in transferring a signal from the ischemic limb to distant tissues, a study was conducted in four healthy volunteers to identify platelet markers of RIPC after two and four cycles of blood pressure cuff inflation to 200 mmHg for 5 min and release for 5 min. RIPC induced mild platelet activation measured by P-selectin expression, changed surface expression of CXCR4 by 20% after two cycles, progressively reduced the percent of monocytes aggregated with platelets, decreased clot formation time, and increased maximum lysis measured by rotational thromboelastometry (ROTEM).

JS05

"Effectiveness of Dual Antiplatelet Therapy, Thrombelastograph® with Platelet Mapping and Effect of Therapy Suspension" by Davide Cattano, M.D., Ph.D., Tyrone Burnett, Jr., B.S., Tariq Syed, M.S., Chunyan Cai, Ph.D., The University of Texas Health Science Center at Houston (UTHealth), Houston, Texas. Thrombelastograph® Platelet Mapping (Haemoscope Corp., USA) is a whole blood assay that can potentially determine the efficacy of antiaggregation therapy. This prospective observational study assessed the ability of Thrombelastograph® Platelet Mapping to detect platelet inhibition secondary to dual antiplatelet therapy (APT) before surgery in 239 patients who were receiving or had recently suspended aspirin and clopidogrel therapy. The median time of clopidogrel suspension was 1 day and that of aspirin suspension was 0.5 day. The level of preoperative inhibition of arachidonic acid– and/or ADP-induced platelet aggregation after short-term interruption of APT was low, with decreasing inhibition after longer interruption of therapy. Platelet function commonly recovered at 5 days, and about 30% of patients were not effectively inhibited by clopidogrel.

JS06

"Coagulation Standards and New Oral Anticoagulants" by Huong-Tram Vu Hoang, M.D., Evan G. Pivalizza, M.D., Davide Cattano, M.D., Anesthesiology, McGovern Medical School UTH Houston, Memorial Hermann TMC Houston, Houston, Texas. New oral anticoagulants are used in the prophylaxis and treatment of venous thrombotic events, as well as stroke and systemic embolism in nonvalvular atrial fibrillation. Routine coagulation data (prothrombin time, partial thromboplastin time [PTT], and thromboelastography) collected for 120 patients taking the new oral anticoagulants rivaroxaban, dabigatran, or apixaban were reviewed to determine their effects on these standard laboratory tests. Rivaroxaban, dabigatran, and apixaban had variable effects on clinical coagulation assays. While the PTT may not be useful in screening in special circumstances and in patients for whom laboratory measurements may be necessary for perioperative anticoagulation management, the prothrombin time was prolonged. Thromboelastography indices of fibrin formation were within the normal range, suggesting that global clot formation was preserved.

JS07

"Mixing Study in Patients with Activated Prolonged Partial Thromboplastin Time" by Honorio T. Benzon, M.D., Meghan Park, B.A., Paul Lindholm, M.D., Ph.D., Northwestern University Feinberg School of Medicine, Chicago, Illinois. A retrospective study looked at the results of the PTT mixing studies done since January 2010 on 131 patients with prolonged activated PTT but not on any anticoagulant when seen in the preoperative clinic. In a mixing study, the patient's blood is mixed with normal plasma, and the test is repeated at 1 h. In the presence of prolonged activated PTT, mixing studies identify the presence of deficiencies of clotting factors involved in the intrinsic pathway (correction into the reference normal range) or the presence of an anticoagulant inhibitor (no or very mild correction), with the 1-h result differentiating between immediate and time-dependent inhibitors. Mixing study results were classified into eight categories, and most underwent further workup.

JS08

"The Utilization of Thromboelastometry to Identify HIT and Hypercoagulable States" by Michelle Shirak, M.D., Gebhard Wagener, M.D., Columbia University Department of Anesthesiology, New York, New York. The ROTEM parameter maximum clot firmness (MCF) can be used to assess the risk of thromboembolic events in noncardiac surgery patients. The ability of parameters of hypercoagulability derived from ROTEM to identify patients with heparin-induced thrombocytopenia and predict thromboembolic complications was tested in a prospective study of 23 postoperative cardiac surgical patients. There was no significant difference in MCF between the 13 patients who developed thromboembolic complications and those who did not. Six patients who were platelet factor 4 positive for heparin-induced thrombocytopenia had longer MCF.

JS09

"The Hemostatic System in Scoliosis Surgery: Alteration of D-dimer and Fibrinogen Kinetics by Tranexamic Acid" by Ryan P. Pong, M.D., Alicia Edwards, M.B.A., Grete H. Porteous, M.D., Jean-Christopher Leveque, M.D., Rajiv K. Sethi, M.D., Virginia Mason Medical Center, Seattle, Washington. A potential contributor to the coagulopathy seen in scoliosis surgery is the activation of the fibrinolytic system. The hypothesis that the addition of the antifibrinolytic

TXA to the perioperative protocol will decrease the fall of fibrinogen and decrease the rise of D-dimer (a product of fibrinolysis) was tested in a retrospective analysis of data from patients who underwent surgery for the treatment of adult *de novo* scoliosis, nine of whom were cared for before the addition of TXA to the perioperative protocol and 9 of whom were cared for after its addition. Fibrinogen consumption was reduced from 230 ± 130 to 67 ± 102 mg/dl (P = 0.01), and the rise of D-dimer was attenuated from 7.5 ± 6.2 to 2.8 ± 4.4 μg/ml (P = 0.09) with the addition of TXA to the protocol.

JS10

"High- *versus* Low-dose Tranexamic Acid to Reduce Transfusion Requirements in Pediatric Scoliosis Surgery" by Joshua A. Wetzler, Brian C. Cho, M.D., Stephen L. Freiberg, M.D., Daniel Johnson, B.S., Susan Goobie, M.D., F.R.C.P.C., Nina Nami, M.D., Steven M. Frank, M.D., Johns Hopkins University, Baltimore, Maryland; Boston Children's Hospital, Boston, Massachusetts. Blood loss and transfusion requirements were quantified for two commonly used TXA dosing regimens in a retrospective analysis of records of 116 pediatric patients who underwent posterior spinal fusion for correction of idiopathic scoliosis. Seventy-two patients received a 10 mg/kg loading dose with a 1 mg kg^{-1} h^{-1} maintenance dose (low dose), and 44 patients received a 50 mg/kg loading dose with a 5 mg kg^{-1} h^{-1} maintenance dose (high dose). Compared to the low-dose TXA group, the high-dose TXA group had decreased estimated blood loss (695 ± 372 *vs.* 968 ± 756 ml; P = 0.01) and a decrease in both intraoperative (0.3 ± 0.8 *vs.* 0.9 ± 1.7 units; P = 0.01) and whole hospitalization (0.4 ± 1.0 *vs.* 1 ± 1.9 units; P = 0.04) erythrocyte transfusion requirements.

JS11

"The Use of Low-dose Tranexamic Acid to Reduce Red Blood Cell Transfusion during Complex Multilevel Spine Fusion" by Natalie Moreland, M.D., Louanne M. Carabini, M.D., Ryan J. Vealey, M.D., John Patrick F. Bebawy, M.D., Antoun Koht, M.D., Michael J. Avram, Ph.D. University California at Los Angeles, Los Angeles, California; Northwestern University Feinberg School of Medicine, Chicago, Illinois. The hypothesis that low-dose TXA would reduce intraoperative total erythrocyte transfusion during complex spinal deformity correction was tested in a randomized, double-blind, placebo-controlled trial of low-dose TXA in 61 patients undergoing multilevel spinal fusion. The volume of total erythrocytes (millimeter) transfused was less in the TXA group (placebo group median, 1,460 ml *vs.* TXA group median, 1,140 mL; median difference, 460 ml; 95% CI, 15 to 914 ml), with a decrease in cell saver transfusion (P = 0.043) and a decrease in PRBC transfusion that did not reach statistical significance. Hemoglobin concentrations measured immediately postoperatively did not differ between groups.

JS12

"Pathogen-reduced Cryoprecipitate Demonstrates Retention of Fibrinogen, Factor VIII, Factor XIII, and von Willebrand Factor Activity 120 h Post Thaw" by Anne North, Ph.D., Travis Berry, B.A., Jeremy Puckett, B.A., Tovo David, Ph.D., Melissa VonGoetz, M.S., Marc Stern, M.B.A., Melody Holtan, M.B.A., Jessica Hanover, M.D., Nina Mufti, Ph.D., Cerus Corporation, Concord, California. Cryoprecipitate has a shelf life of 4 to 6 h after thawing because of factor VIII instability and concerns over bacterial contamination and growth at room temperature. Preparation of cryoprecipitate from pathogen-reduced prepooled plasma reduces the risk of transfusion-transmissible infections and may allow extended storage of thawed cryoprecipitate at 22°C. Pathogen-reduced cryoprecipitate and control cryoprecipitate were thawed at 37°C and stored at 22°C until sampled aseptically at 0, 6, 24, 48, 72, and 120 h post thaw. Fibrinogen, factor XIII, and von Willebrand factor concentrations in pathogen-reduced cryoprecipitate remained stable over storage, while factor VIII activity declined steadily over storage. Both fibrinogen and factor VIII concentrations met U.S. Code of Federal Regulations, guidelines for single containers of cryoprecipitate.

Best Abstracts: Clinical Sciences and Basic Sciences

ANESTHESIOLOGY will sponsor two Best Abstract Sessions this year, one in basic science and another in clinical science. These abstracts were chosen by a panel of editors, who examined the highest scoring abstracts from the ASA subcommittees, choosing those with important scientific and clinical application and novelty. Subsequently, a combination of these editors and appointees from the ASA will choose one abstract in each category to receive the Best Abstract award for basic and clinical sciences at the meeting in Chicago, Illinois. Following are summaries of the excellent abstracts that will be presented.

Best Abstracts: Clinical Science

Saturday, October 22, 1:15 PM to 3:15 PM, McCormick Place, W476

Moderators

Charles D. Collard, M.D., St. Luke's Episcopal Hospital and the Texas Heart Institute, Baylor College of Medicine, Houston, Texas; Deborah J. Culley, M.D., Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; and Shiroh Isono, Chiba University Graduate School of Medicine, Chiba, Japan

5038

"National Impact of Anesthesiology Providers on Outcomes after High-risk Surgery" by S. Kheterpal, M.D., M.B.A., M. Housey, M.S., A. Shanks, Ph.D., Anesthesiology, University of Michigan, Ann Arbor, Michigan. There are no robust analyses of national data spanning a range of

procedures evaluating the impact of the anesthesiology provider on surgical outcomes. We hypothesized that a measurable proportion of outcome variation can be attributed to variation in anesthesiology practice and provider across vascular, cardiac, and colorectal surgery. Data were acquired from the Medicare Provider Analysis and Review files, which contain all hospital discharges for Medicare recipient acute care. Using International Classification of Diseases, Ninth Revision, codes, we identified all patients who underwent abdominal aortic aneurysm repair, coronary artery bypass graft (CABG), or colectomy procedures from 2010 to 2013 and linked to part B professional claims to identify the primary surgeon and anesthesiologist using anonymized codes. After adjusting for patient, procedure, hospital, and surgeon covariates, the anesthesiology provider is responsible for approximately 3.1 to 4.5% of mortality/morbidity variation in three common high-risk procedures, similar to a surgeon effect of 4.2 to 5.2%.

786

"Interrelationship of Preoperative Anemia, Postoperative Anemia, Acute Kidney Injury, and Mortality after Coronary Artery Bypass Grafting Surgery" by Patrick J. Nailer, M.D., Manuel Fontes, M.D., Ishwori Dhakal, M.Sc., Jorn A. Karhausen, M.D., Mihai V. Podgoreanu, M.D., Mark Stafford-Smith, M.D., Miklos D. Kertai, M.D., Ph.D., Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina. The relationship between anemia and acute kidney injury (AKI) after CABG surgery has not been clearly defined. The authors used multivariable logistic regression and Cox proportional hazard models to examine the interrelationship between preoperative anemia, postoperative anemia and postoperative AKI, and long-term mortality in 4,217 adult patients who underwent CABG surgery. Preoperative anemia was defined as hemoglobin less than 13 g/dl in men and less than 12 g/dl in women, while postoperative anemia was defined as the median of the lowest in-hospital values measured for the first 10 postoperative days. In the risk-adjusted model for postoperative AKI, preoperative anemia (OR, 1.27; 95% CI, 1.04 to 1.56; $P = 0.02$), postoperative anemia (OR, 1.38; 95% CI, 1.17 to 1.63; $P = 0.0001$), and the combination of pre- and postoperative anemia (OR, 1.93; 95% CI, 1.58 to 2.35; $P < 0.0001$) were associated with an incremental risk of postoperative AKI. Similarly, preoperative anemia (hazard ratio [HR], 1.29; 95% CI, 1.09 to 1.52; $P = 0.003$) and the combination of pre- and postoperative anemia (HR, 1.23; 95% CI, 1.04 to 1.47; $P = 0.02$) were significantly associated with long-term mortality in the risk-adjusted Cox model. These data suggest that anemia before and/or after CABG surgery is associated with an incremental risk of postoperative AKI. Furthermore, only preoperative anemia and the combination of pre- and postoperative anemia had a significant relation with long-term mortality after CABG surgery.

4413

"Brain Activity Predictive of Arousal during Propofol or Dexmedetomidine Anesthesia: Who's Going to Wake Up and Why?" by Michael T. Alkire, M.D., Annalotta Scheinin, M.D., Oskari Kantonen, M.D., Jaakko Långsjö, M.D., Kaike Kaisti, M.D., Timo Laitio, M.D., Roosa Kallionpää, M.Sc., Katja Valli, Ph.D., Antti Revonsuo, Ph.D., Harry Scheinin, M.D., Department of Anesthesiology, University of California, Irvine, California. Clinicians are often faced with the challenge of preventing patient movement under "light" general anesthesia. The authors examined neuroimaging data in volunteers receiving dexmedetomidine or propofol anesthesia who subsequently later moved in response to stimulation. The average targeted concentrations for achieving a loss of responsiveness (LOR) were 1.5 ng/ml for dexmedetomidine and 1.87 μg/ml for propofol. Cerebral blood flow using O_{15}-H_2O as a tracer was imaged using positron emission tomography on a Siemens high-resolution research tomograph during the LOR. After achieving LOR, subjects were tested for arousal to awakening with loud voice or mild physical stimulation without changing the drug dose. Future arousal to consciousness was predicted in the LOR scans by greater activity ($P < 0.001$) in the posterior cingulate cortex (Brodmann area 23) for dexmedetomidine, whereas for propofol, it was predicted by increased activity in the medial dorsal thalamus and visual cortical Brodmann area 18. At a more liberal statistical threshold ($P < 0.05$, uncorrected), a network effect was evident between the two agents that centered on the posterior cingulate cortex and also involved visual areas, thalamus, and Broca area (Brodmann 44) in the left frontal lobe. These data suggest that brain regions responsible for imminent arousal differ depending on which anesthetic is being used, as well as a multiple pathway arousal model that may involve the posterior cingulate, visual cortex, thalamus, and Broca area.

3694

"Delayed Detection of Esophageal Intubation in Anesthesia Malpractice Claims" by Marzieh Roza Honardar, M.D., Karen L. Posner, Ph.D., Karen B. Domino, M.D., Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington. In 1991, identification of carbon dioxide in the expired gas to verify endotracheal intubation became an ASA standard of basic anesthetic monitoring. The authors of this study aimed to identify factors associated with delayed detection of esophageal intubation in anesthesia malpractice claims after this change in monitoring standards. The authors analyzed 45 claims for delayed detection of esophageal intubation from the Anesthesia Closed Claims Project Database, and factors associated with delayed detection were abstracted from claim narratives. The authors found that 49% of the cases with delayed detection of esophageal intubation occurred during anesthesia care in the OR or a NORA location with elective

cases accounting for 29% and resuscitation for 38%. In 76% of claims, esophageal intubation was recognized during resuscitation and in 13% not until autopsy. In 60% of cases, a quantitative or qualitative carbon dioxide detection device was available at the time of intubation. The most common reasons for delayed detection were associated with carbon dioxide monitoring (73%), such as not using or ignoring end-tidal carbon dioxide or equivocal change in calorimetric carbon dioxide. In 33% of cases, late detection was associated with confusion over differential diagnosis, most often bronchospasm. Cardiac arrest without cardiac output contributed to delayed detection in 13%. Communication problems occurred in 27% of esophageal intubation claims and were more common when the anesthesiologist was called to help in a nonanesthesia location (43%) than during anesthesia care in the OR/NORA (9%; $P = 0.017$). Nearly, all esophageal intubations with delayed detection resulted in patient death or severe brain damage (96%). Sixty-seven percent resulted in payment made on behalf of the anesthesiologist with a median payment of $665,000 (interquartile range, $236,000 to $1,213,500). The authors conclude that although end-tidal carbon dioxide monitoring has been a standard of care for confirmation of endotracheal tube placement since 1991, carbon dioxide detection issues and differential diagnosis errors contributed to persistence of delayed detection of esophageal intubation in malpractice claims.

3981

"Impact of Temperature on Cognition and Brain Connectivity following Hypothermic Surgical Circulatory Arrest" by Rebecca Y. Klinger, M.D., M.S., Jeffrey Browndyke, Ph.D., Tiffany Bisanar, B.S.N., Mary Cooter, M.S., Miles Berger, M.D., Ph.D., Mihai V. Podgoreanu, M.D., Jorn A. Karhausen, M.D., Mark F. Newman, M.D., G. Chad Hughes, M.D., Joseph P. Mathew, M.D., M.B.A., Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina. The optimal temperature for hypothermic circulatory arrest remains unclear. The authors hypothesized that deep hypothermia would reduce postoperative cognitive decline and preserve functional brain network connectivity when compared with high-moderate (HM) hypothermia. Thirty-four patients undergoing hypothermic circulatory arrest for elective proximal aortic reconstructive surgery (ascending aorta + aortic valve or root) with concomitant proximal (hemi-) arch replacement completed a battery of neurocognitive tests at baseline and 4 weeks postoperatively. Fifteen of these patients also underwent resting functional magnetic resonance imaging. Patients were categorized into three groups on the basis of nasopharyngeal temperature at the initiation of circulatory arrest as defined above: deep, low-moderate (LM), and HM. Cognitive function (mean Z score of predefined domains) was compared between the three groups using ANOVA or Kruskal–Wallis tests. Voxel-wise intrinsic connectivity contrast analyses were used to identify group (temperature) × time (pre-/postsurgery) differences in resting-state functional connectivity (RSFC) patterns associated with perioperative cognitive changes, adjusting for baseline cognitive abilities. Statistical significance was established using multiple comparison-corrected cluster-wise topological p-FDR less than 0.05 (peak $P < 0.001$). In 14 patients treated with deep hypothermia, 10 with LM, and 10 HM, the neurocognitive change score from baseline to 4 weeks was lower in patients subjected to HM hypothermia (global mean Z score: -0.04 ± 0.40 [HM] *vs.* 0.26 ± 0.21 [deep] and 0.17 ± 0.51 [LM]; $P = 0.17$], representing an effect size difference of 0.99 between the deep and HM groups. The largest differences were seen in short-term memory (HM: -0.15 ± 0.37 *vs.* deep: 0.32 ± 0.37 *vs.* LM: 0.17 ± 0.51; $P = 0.04$) and executive function (HM: 0.02 ± 0.53 *vs.* deep: 0.56 ± 0.67 *vs.* LM: 0.56 ± 1.48; $P = 0.03$). Group × time comparisons of RSFC change revealed significant gray-matter regional differences in the right parahippocampal, mesial frontal, and posterior cingulate cortices between deep and HM hypothermia groups associated with perioperative short-term memory changes. Short-term memory decline in the HM hypothermia group was associated with perioperative decreases in intrinsic RSFC in the posterior cingulate and mesial frontal cortices and increases in the parahippocampal RSFC. These data suggest that deep hypothermia may be superior to HM hypothermia in mitigating against postoperative cognitive decline and in preserving functional brain connectivity after circulatory arrest for arch surgery.

4494

"Early Surgery Confers 1-Yr Mortality Benefit in Hip-Fracture Patients" by Kamal Maheshwari, M.D., Jeffrey A. Planchard, M.D., Jing You, M.S., Wael M. Ali Sakr Esa, M.D., Leif Saager, M.D., Alparslan Turan, M.D., Andrea M. Kurz, M.D., General Anesthesia, Outcomes Research, Anesthesia Institute, Cleveland Clinic Foundation, Cleveland, Ohio; Anesthesia Institute, Cleveland Clinic Foundation, Cleveland, Ohio. Hip fracture is a major cause of morbidity and mortality among older surgical patients and is associated with a 1-yr mortality as high as 33% with or without surgery. Accordingly, there is a debate about the timing of surgery as early surgery may provide a survival benefit. The authors of this study evaluated the relationship between the timing of surgery and 1-yr mortality in 720 patients (more than 65 yr) who underwent hip fracture surgery between March 25, 2005, and February 28, 2015. One-year mortality was derived from the Ohio Death Index, U.S. Social Security Death Index, and PHDS. The authors used a multivariable logistic regression analysis adjusting for baseline clinical status and the surgical factors. Among the 720 patients, 159 patients (22%) died within 1 yr after their surgical procedure. The median time from hospital admission to the start of operation was 30 h. Delaying surgery was significantly associated with increased 1-yr mortality. The estimated OR was 1.05 (95% CI, 1.02 to 1.08) for each

increase of 10 h ($P = 0.001$). These results suggest that mortality is improved with early surgery and that for every 10-h delay from hospital admission to surgery, the 1-yr mortality increased by 5% after adjusting for confounders. On the basis of these results, the authors suggest that hip fracture surgery should not be delayed, as delaying surgery is associated with an increased 1-yr mortality.

4166

"A Randomized Controlled Trial Comparing Combined Spinal–Epidural Dosing Strategies for External Cephalic Version" by L.A. Chalifoux, M.D., R.J. McCarthy, Pharm.D., J.T. Sullivan, M.D., M.B.A., Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois. Breech presentation is the leading cause of cesarean delivery (CD). ACOG recommends that external cephalic version (ECV) is offered whenever possible to reposition the fetus for vertex vaginal delivery, thus avoiding the morbidity associated with CD. Anesthetic techniques for ECV have evolved from no analgesia to intravenous opioids to neuraxial techniques. We conducted a prospective, patient and OB blinded, randomized clinical trial to assess the impact of combined spinal–epidural bupivacaine dosing on the success rate of ECV for breech fetal position and the incidence of vaginal *versus* CD. There was no difference among groups in ECV success ($P = 0.990$) or mode of delivery ($P = 0.7$). OB perception of abdominal relaxation did not differ significantly ($P = 0.162$). CD indication ($P = 0.779$) and rates of crash CD (one in each group) were also similar among groups. There was a dose-dependent decrease in visual analog scale pain scores and increase in incidence of hypotension with increasing bupivacaine dose. Time to discharge was significantly longer as dose was increased. We conclude that anesthetic dose bupivacaine does not offer a significant increase in ECV success or NSVD compared to standard analgesic dosing but does incur additional risk of hypotension and prolonged length of stay.

3810

"Changes in the Propofol-induced Frontal Electroencephalogram in Children with Autism Spectrum Disorder" by E.C. Walsh, B.S., J.M. Lee, B.A., K. Terzakis K, D.W. Zhou, M.S., P.G. Firth, M.D., E.S. Shank, M.D., T. Buie, M.D., E.N. Brown, M.D., Ph.D., P.L. Purdon, Ph.D., Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts. Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by deficits in social interaction and restricted, repetitive patterns of behavior, interests, and activities. The underlying pathophysiology remains poorly understood, but aberrant development of γ-aminobutyric acid–mediated (GABAergic) circuits has been implicated. To investigate differences in how ASD patients respond to the GABAergic agent propofol, we compared the frontal electroencephalogram during propofol sedation in ASD patients *versus* age-matched neurotypical patients. ASD patients had significantly decreased total electroencephalogram power ages 7 to 10 yr relative to neurotypical patients ($P < 0.05$) during maintenance propofol. α power (8 to 13 Hz) was significantly reduced in patients between ages 17 and 23 yr ($P < 0.05$). We observed no significant difference in coherence in any frequency band. We found that ASD patients experienced burst suppression more than twice as often as neurotypical patients (28.57 *vs.* 12.30%; $P < 0.01$). We noted that ASD patients, despite having a significantly higher incidence of burst suppression, tended to receive lower doses of intraoperative agents. These results suggest that ASD patients respond differently to propofol compared to neurotypical patients, showing changes in age-dependent electroencephalogram power and greater sensitivity to burst suppression. This may reflect underlying dysfunction of GABAergic circuits.

4245

"Delirium in the Postanesthesia Care Unit: Risk Factors and Clinical Significance" by Paul S. Garcia, M.D., Ph.D., September D. Hesse, Ph.D., Darren Hight, Ph.D., Matthias Kreuzer, Ph.D., Amy Gaskell, M.B., B.S., Simon Lee, M.D., Nicholas Taylor, B.S., Paran Devari, B.S., Matthew K. Whalin, M.D., Ph.D., Jamie Sleigh, M.B., Ch.B., Anesthesiology, Emory University/Atlanta VA Medical Center, Decatur, Georgia; Anesthesiology, Emory University, Atlanta, Georgia; University of Auckland, Hamilton, New Zealand; Anesthesiology, Emory University, Decatur, Georgia; Anesthesiology, University of Auckland, Hamilton, New Zealand; Emory Anes. Smart Key 9648, Atlanta, Georgia; Anesthesiology, Waikato DHB/University of Auckland, Hamilton, New Zealand. Postoperative delirium is associated with an increased risk of morbidity and mortality in older surgical patients. A significant proportion of older patients develop signs of hypoactive delirium in the recovery room, but the clinical significance of delirium in the postanesthesia care unit (PACU-D) is unclear. The authors evaluated electroencephalogram patterns and other potential risk factors to determine whether they were associated with PACU-D and whether PACU-D was associated with adverse perioperative outcomes in a study involving 626 patients from multiple sites in patients receiving a general anesthetic. The authors collected data on comorbid medical conditions, perioperative variables, and frontal electroencephalogram during anesthetic maintenance and emergence. Patients were assessed using the CAM-ICU after 15 min of routine postoperative care and motoric subtype characterized *via* Richmond Agitation and Sedation Scores. Thirty-day outcomes, including length of stay, readmission rate, and ICU admissions, were noted on a chart review. Twenty percent of patients were tested positive for PACU-D. Age, renal failure, and preexisting neurologic disease were associated with PACU-D in univariable analysis, but in multivariate analysis, electroencephalogram emergence trajectories

(OR [95% CI], 1.98 [1.03 to 3.80]; $P = 0.04$), case duration (OR [95% CI], 1.34 [1.07 to 1.68]; $P = 0.01$), and preexisting neurologic disease (OR [95% CI], 2.35 [1.03 to 5.38]; $P = 0.04$) remained significant. Patients with PACU-D were at an increased risk for readmission and had longer hospital stays after their operation (effect sizes [95% CI], 2.17 [1.13 to 4.17]; $P = 0.03$ and 2.07 [1.38 to 3.16]; $P = 0.0006$). The authors conclude that this study demonstrates that PACU-D can be predicted intraoperatively and that PACU-D (like other forms of delirium) is a predictor of adverse outcomes in older surgical patients.

5111

"Carbon Dioxide Reverses Effects of Propofol on Upper Airway Collapsibility and Breathing in Healthy Volunteers" by Katarina J. Ruscic, M.D., Ph.D., Janne Bøgh Nielsen, B.Sc., Daniel Diaz-Gil, Jeroen Simons, M.D., Matthew Meyer, M.D., Carl E. Rosow, M.D., Ph.D., Eric T. Pierce, M.D., Ph.D., Robert Kacmarek, Ph.D., Matthias Eikermann, M.D., Ph.D., Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts; Department of Anesthesiology, Herlev Hospital, Copenhagen, Denmark; Department of Respiratory Care, Massachusetts General Hospital, Boston, Massachusetts. General anesthesia dose-dependently increases upper airway collapsibility and decreases minute ventilation. Preclinical data demonstrate that respiratory depression by propofol can be reversed with carbon dioxide administration. The authors tested the hypothesis that carbon dioxide insufflation during steady-state propofol anesthesia restores airway patency and restores minute ventilation in a secondary analysis of data from a randomized controlled crossover study involving 12 healthy volunteers, aged 18 to 45 yr, where propofol was titrated to identify the threshold for suppression of the motor response to electrical stimulation. The authors measured nasal and epiglottic pressures during normal, unassisted breathing and in response to external airway occlusion. Subjects wore a nasal mask connected to a high-airflow circuit. Respiratory airflow was determined using a pneumotachometer, and end-tidal carbon dioxide was monitored with an infrared analyzer. Mask pressures were monitored with an open catheter attached to a pressure transducer, and airway pressures were measured at the level of the epiglottis with an intranasal Millar pressure catheter. Upper airway collapse was induced by external airway occlusion. P_{close} was defined as the inspiratory nasal plateau pressure observed after airway occlusion, while epiglottic pressure continued to decrease until the end of the inspiration attempt. Carbon dioxide was added to the inspired air to produce elevations of end-tidal carbon dioxide to 4 and 8 mmHg above baseline. For evaluation of the effects of depth of anesthesia and level of carbon dioxide insufflation on upper airway collapsibility, the authors used mixed models, including the main effect of depth of anesthesia and of carbon dioxide level on P_{close} (primary) and minute ventilation (secondary) as fixed effects, while allowing intercepts to vary (random intercepts model). The authors report that propofol anesthesia dose-dependently increases upper airway collapsibility (significant increase in P_{close}, $P < 0.001$) and significantly decreases minute ventilation ($P < 0.001$). Carbon dioxide insufflation (4 and 8 mmHg above end-tidal carbon dioxide) decreases P_{close} (indicating a more patent airway, $P = 0.028$) and increases minute ventilation across levels of propofol ($P < 0.001$). The authors conclude that carbon dioxide insufflation reverses the depressant effects of propofol on upper airway patency and minute ventilation.

Best Abstracts: Basic Science

Sunday, October 23, 1:15 PM to 3:15 PM, McCormick Place, W476

Moderators

Charles D. Collard, M.D., St. Luke's Episcopal Hospital and the Texas Heart Institute, Baylor College of Medicine, Houston, Texas; Deborah J. Culley, M.D., Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; and Shiroh Isono, Chiba University Graduate School of Medicine, Chiba, Japan

5128

"Isoflurane Anesthesia during the First 2 Weeks of Life Alters Long-term Behavioral Development in Rhesus Macaques" by Ansgar Brambrink, M.D., Ph.D., Kristine Coleman, Ph.D., Nicola Robertson, M.Sc., Lauren D. Martin, D.V.M., Greg Dissen, Ph.D., Martha Neuringer, Ph.D., Oregon Health & Science University, Portland, Oregon; Oregon National Primate Center, Oregon Health and Science University, Beaverton, Oregon; Oregon National Primate Center, Oregon Health and Science University, Portland, Oregon; Oreon National Primate Center, Oregon Health and Science University, Portland, Oregon. General anesthetics, at clinically relevant doses, can trigger widespread neuroapoptosis and are associated with behavioral and cognitive impairments in the developing brain of animals, including nonhuman primates. Few studies have investigated the effects of infant anesthesia exposure on neurobehavioral development after infancy. To do so, the authors treated infant rhesus monkeys to isoflurane for 5 h once on postnatal days 6 to 8 (1× isoflurane; n = 8), three times between postnatal days 6 and 12 (3× isoflurane; n = 7), or not at all (control; n = 8). Infants were reared in large social groups with their dams for approximately 12 months, at which time they were housed in indoor pens with 5 to 6 other study subjects. The authors measured temperament and anxiety at 24 months using the Human Intruder test and used generalized linear modeling to examine the relationship between treatment and anxiety behavior. The authors found that at 2 yr of age, 3× isoflurane subjects froze more than controls, a finding that has been linked with a behaviorally inhibited temperament ($\beta = 0.42$; $P < 0.001$).

The 3× isoflurane monkeys were also more likely than controls to threaten the human stranger making direct eye contact ($\beta = 0.82$; $P < 0.001$). Interestingly, the 1× isoflurane animals were more likely than controls to display anxious behaviors in the stare condition ($\beta = 1.24$; $P < 0.001$). The authors conclude that isoflurane anesthesia can have long-lasting neurobehavioral effects in rhesus macaques, manifesting as anxiety and/or behavioral inhibition at 2 yr of age.

5076

"Administration of Subanesthetic Ketamine during Isoflurane Anesthesia Induces Burst Suppression but Accelerates Recovery" by Viviane Hambrecht-Wiedbusch, Ph.D., Duan Li, Ph.D., George A. Mashour, M.D., Ph.D., Department of Anesthesiology, University of Michigan, Ann Arbor, Michigan. Acetylcholine is known to be critical for cognitive function and wakefulness and is suppressed in the cortex by most general anesthetics. The authors investigated the hypothesis that a single intraperitoneal injection of ketamine (25 mg/kg) during isoflurane anesthesia causes an increase in cholinergic tone in the prefrontal cortex, high-frequency cortical activity, and accelerated recovery from isoflurane anesthesia in a rat model. Animals were randomly assigned to a control (saline injection) or ketamine group. A microdialysis probe was inserted and acetylcholine samples were collected every 12.5 min. During the entire experiment, electroencephalographic signals were recorded. Additionally, the time required for recovery from anesthesia was measured. A single dose of subanesthetic ketamine caused not only a significant increase in burst suppression ratio ($P < 0.0001$) but also a significant 44% reduction in wake-up time ($P = 0.005$). Ketamine also caused a significant increase in acetylcholine release from the prefrontal cortex during the first 62.5 min of the recovery phase. These findings suggest that the addition of the anesthetic ketamine during inhaled anesthesia not only increases anesthetic depth but also accelerates the recovery of consciousness, possibly through cholinergic mechanisms.

4426

"Battery of Behavioral Tests in Mice to Study Postoperative Delirium" by Mian Peng, M.D., Ph.D., Ce Zhang, M.D., Yuanlin Dong, M.D., Yiying Zhang, M.D., Harumasa Nakazawa, M.D., Ph.D., Masao Kaneki, M.D., Ph.D., Zhongcong Xie, M.D., Ph.D., Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. Postoperative delirium is associated with increased morbidity, mortality, and cost. The authors employed a battery of behavioral tests in mice, including natural and learned behavior, to determine the effects of laparotomy under isoflurane anesthesia on these behaviors. Mice (n = 14 in the control and anesthesia/surgery groups) were tested at 24 h before and at 6, 9, and 24 h after the anesthesia/surgery. Composite Z scores were calculated for each of the mice. Brain levels of ATP and reactive oxygen species were measured. The Seahorse XFp Analyzer was applied to test the bioenergetics of isolated brain mitochondria. Cyclosporin A, an inhibitor of mitochondria permeability transient pore, was used to determine the mitochondria-associated mechanisms of these behavior changes. Anesthesia/surgery selectively impaired behavior, including the buried food test, the open-field test, and the Y maze test. The composite Z score further quantitatively demonstrated the anesthesia/surgery-induced behavior impairment in the mice (1.539 *vs.* 0.000; $P = 0.0007$). The anesthesia/surgery decreased brain ATP levels and increased brain reactive oxygen species level. However, the anesthesia/surgery did not significantly change the oxygen consumption rate or respiratory control rate as compared to controls. Cyclosporin A selectively ameliorated the anesthesia/surgery-induced reduction in ATP levels and the increases in latency to eat food. These findings suggest that anesthesia/surgery selectively impairs natural and learned behavior in mice and induces brain energy deficits and oxidative stress. Moreover, these findings demonstrate a potential animal model to study postoperative delirium and suggest that energy deficits could contribute to postoperative delirium.

4443

"Severe Pulmonary Hypertension and Right Ventricular Dysfunction Is Associated with Changes in Ubiquitin–Proteasome System" by Soban Umar, M.D., Ph.D., Shannamar Dewey, Ph.D., Ali Navid Said, B.Sc., Aldrin Gomes, Ph.D., Mansoureh Eghbali, Ph.D., Department of Anesthesiology, University of California Los Angeles, Los Angeles, California. The ubiquitin–proteasome system (UPS) is responsible for degradation of intracellular proteins. The authors investigated the role of UPS in pulmonary hypertension (PH) and right ventricular (RV) dysfunction using a rat model. Rats received monocrotaline to develop PH and RV failure (RVF). Serial echocardiography was performed to monitor cardiopulmonary hemodynamics. Cardiac catheterization was terminally performed to record RV systolic pressure. Proteasome subunits and ubiquitinated proteins were determined by Western blot. Proteasome activity was measured in lungs with fluorescent substrates. Subcellular localization of proteasomal subunits was determined in isolated RV myocytes by high-resolution confocal microscopy. RVF was associated with significant downregulation of a7 (a subunit of 20S, 0.05 ± 0.001 in controls *vs.* 0.04 ± 0.002 in RVF; $P < 0.05$), RPT4 (the 19S regulatory proteasomal subunit, 0.25 ± 0.008 in controls *vs.* 0.18 ± 0.01 in RVF; $P < 0.05$), and PA28a (4.83 ± 0.17 in controls *vs.* 3.17 ± 0.17 in RVF; $P < 0.01$) protein levels in lungs. The activity of b1 26S and b2 26S subunits increased, whereas the activity of b1 20S and b2 20S decreased in RVF lungs. The activity of b5 26S and b5 20S subunits in lungs remained unchanged. In RV myocytes, confocal microscopy showed that RVF was associated with disappearance of core 20S in the nuclei and in the t-tubules. RPT4 was also reduced both in the nucleus and

in the t-tubules in isolated myocytes from the RVF group only. Western immunoblots from CTRL and RVF stained with the antibody detecting mono- and polyubiquitinated proteins showed significantly lower ubiquitination in lungs of the RVF group. These data suggest that severe PH and RV dysfunction are associated with changes in the UPS.

4348

"GTS-21, an α7-acetylcholine Receptor Agonist, Attenuates Body Mass, Muscle Mass, and Muscle Function Loss in Rats Having Systemic Inflammation with and without Disuse Atrophy" by Stefan J. Schaller, M.D., Manfred Blobner, M.D., J.A. Jeevendra Martyn, M.D., Klinik für Anaesthesiologie, Klinikum rechts der Isar der TUM, Munich, Germany; Massachusetts General Hospital, Boston, Massachusetts. Critical illness is associated with muscle mass loss and weakness that has been attributed to disuse atrophy and systemic inflammation. The authors investigated whether the antiinflammatory properties of GTS-21, an α7-acetylcholine receptor (α7AChR) agonist, would mitigate these changes in rodents. Systemic inflammation was induced with *Corynebacterium parvum* (Cp) without and with disuse atrophy and body mass, tibialis muscle mass and force, and α7AChR expression were compared to saline-treated control animals. Methemoglobin levels (a marker of systemic inflammation) were increased in the Cp group but significantly reduced by GTS-21 ($P = 0.049$). Body weight in control animals increased but decreased in Cp groups without and with superimposed disuse ($P = 0.005$). CTS-21 attenuated body weight loss in the Cp with disuse group from 30 ± 16 to 14 ± 10 g ($P = 0.011$). Similarly, tibialis mass was reduced in the Cp group and in those animals with superimposed disuse when compared to controls ($P < 0.001$). GTS-21 attenuated tibialis mass loss in both the Cp group ($P = 0.028$) and the CP with disuse group ($P = 0.004$). Maximal tetanic tensions were decreased in both Cp groups ($P < 0.001$), but this was attenuated by GTS-21 in the Cp group with disuse group ($P = 0.029$). Cp up-regulated muscle α7AChR protein expression, whereas GTS-21 decreased α7AChR expression. From this study, the authors conclude that GTS-21, a highly specific α7AChR agonist, modulates systemic inflammation resulting from Cp administration in rats.

4981

"Cortical Sensory Processing and Propofol-induced Loss of Consciousness in Nonhuman Primates" by Y. Ishizawa, M.D., Ph.D., S.R. Patel, Ph.D., O.J. Ahmed, Ph.D., E.N. Brown, M.D., Ph.D., E.N. Eskandar, M.D., Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts. The effect of general anesthetics on cortical sensory processing is poorly understood. We have studied cortical sensory processing during transition from wakefulness to propofol-induced loss of consciousness in the primary somatosensory and frontal premotor network in nonhuman primates. LEP-evoked responses to tactile and auditory stimulation indicate discontinuous transition at loss of consciousness to a significantly prolonged duration of the response, suggesting a decrease in temporal selectivity under propofol. Together with previously reported loss of multisensory response in single-neuron spikes, our results suggest that spatiotemporal is selectively impaired in sensory processing in this network during propofol-induced unconsciousness.

5131

"Effects of Region-specific Knockout of Ndufs4 on Volatile Anesthetic Response" by P.G. Morgan, M.D., R. Ramadasan-Nair, Ph.D., J. Hui, B.S., L. Itsara, Ph.D., M.M. Sedensky, M.D., Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington. The cellular circuitry and the brain regions involved in mediating anesthesia are not well elucidated. We knocked out the mitochondrial protein Ndufs4 in specific regions of the mouse brain and analyzed the contribution of regional mitochondrial defects to isoflurane or halothane sensitivity. Ndufs4 knockout in the central medial thalamus confers increased sensitivity for a tail clamp to isoflurane and halothane, while a similar loss in the vestibular nucleus confers resistance. Since the central medial thalamus is involved in maintaining consciousness by glutamatergic relaying to the cortex, visual analog scale and mitochondrial dysfunction may increase sensitivity through suppressing this signaling. In contrast, the vestibular nucleus sends inhibitory signaling to the spinal cord; suppression of these signals may lead to anesthetic resistance.

4728

"State Repertoire and Self-organized Criticality of Mesoscopic Cortical Dynamics Are Not Altered during Anesthetic-induced Unconsciousness" by Anthony G. Hudetz, Ph.D., Jeannette A. Vizuete, Ph.D., Siveshigan Pillay, Ph.D., George A. Mashour, M.D., Ph.D., University of Michigan, Ann Arbor, Michigan; Medical College of Wisconsin, Milwaukee, Wisconsin; University of Wisconsin-Madison, Madison, Wisconsin. Consciousness has been linked to the repertoire of brain states and to self-organized criticality at various spatiotemporal scales. At a mesoscopic scale, cortical neuronal populations may form synchronized ensembles whose characteristics are presumably state dependent. The authors used desflurane anesthesia, which is thought to modify consciousness by altering information integration in cortical and thalamocortical circuits, to test their hypothesis. Spontaneous neuronal activity was recorded in the primary visual cortex of chronically instrumented, unrestrained rats under stepwise decreasing steady-state levels of desflurane and local field potentials were recorded. The authors found that n local field potentials formed compact, spatially contiguous activity patterns (CAPs) that were not due to chance. The frequency distribution of CAP sizes followed a power law

with slope −1.5 in deep anesthesia, suggesting the presence of self-organized criticality, but the distribution deviated slightly from the power law as the animals regained consciousness. The average number of CAPs was increased in both wakefulness (0% desflurane) and deep anesthesia (8% desflurane). The entropy of CAP sizes was highest in wakefulness but changed insignificantly at desflurane concentrations associated with the return of the rats' righting reflex. The types of recurring CAPs categorized by K-means clustering were conserved at all anesthesia levels and wakefulness, although the proportion of various types did change in a concentration-dependent manner. From this study, the authors conclude that neither the repertoire nor self-organized criticality of local population activity can account for anesthetic suppression of consciousness, suggesting that the latter may depend more on large-scale or temporally longer scale dynamics or changes outside of primary sensory cortex.

4442

"Inhibition of Free Fatty Acid Receptor G-protein–coupled Receptor-40 Abolishes Cardioprotection Conferred by Intralipid in Two Rodent Models of Bupivacaine Cardiotoxicity and Ischemia–Reperfusion Injury" by S. Umar, M.D., Ph.D., J. Li, M.D., Ph.D., A. Mahajan, M.D., Ph.D., M. Eghbali, Ph.D., Anesthesiology, University of California Los Angeles, Los Angeles, California.

We have previously shown that intralipid protects the heart against ischemia–reperfusion (I/R) injury and bupivacaine cardiotoxicity. We explored whether cardioprotective effects of intralipid are mediated, at least in part, through G-protein–coupled receptor-40 (GPR40) in two animal models of I/R injury and bupivacaine cardiotoxicity.

Results: Bupivacaine cardiotoxicity: bupivacaine caused asystole. Intralipid gradually improved HR and left ventricular (LV) function fully recovered within 5 min of intralipid. However, GPR40 antagonist GW1100 (GW) pretreatment prevented intralipid rescue, with no recovery even after 10 min. I/R injury: intralipid significantly improved rate pressure product. GW prevented intralipid prevention with significantly lower rate pressure product. LV-developed pressure was also lower in intralipid + GW. Intralipid + GW also showed lower LV dP/dt_{max} and LV dP/dt_{min} compared with intralipid. Our data demonstrate for the first time that GPR40 is involved in cardioprotection mediated by intralipid against bupivacaine-induced cardiotoxicity and cardiac I/R injury, as pretreatment with a selective GPR40 antagonist prevented intralipid's rescue in both models.

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Competing Interests

The authors declare no competing interests.