

Communicating Complex Information in the Journal Anesthesiology

ASCPT 2017 Annual Meeting Workshop

Communicating Complex Information to Influence
Decisions: What Works and What Doesn't

Thursday, March 16, 2017

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Anesthesiology - Executive Editor

ANESTHESIOLOGY



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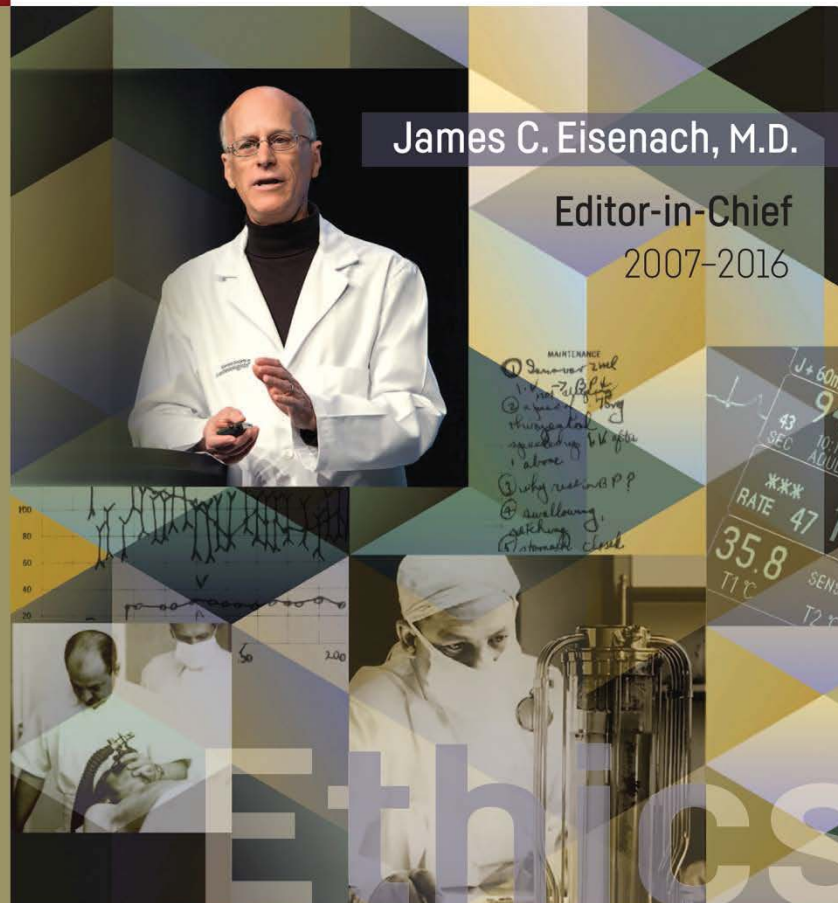
- 2016 Impact Factor: 5.555
- Number of subscribers: 52,000
- Number of original research articles and published each year: 168
- Number of editorials published each year: 72
- Number of Reviews and Clinical Concepts and Commentaries published each year: 12

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Emery Rovenstine, Robert Dripps, and the Evolution
of the Practice of Anesthesiology

Evan D. Kharasch, M.D., Ph.D.
Editor-in-Chief 2016 -



Monthly Issue Planner

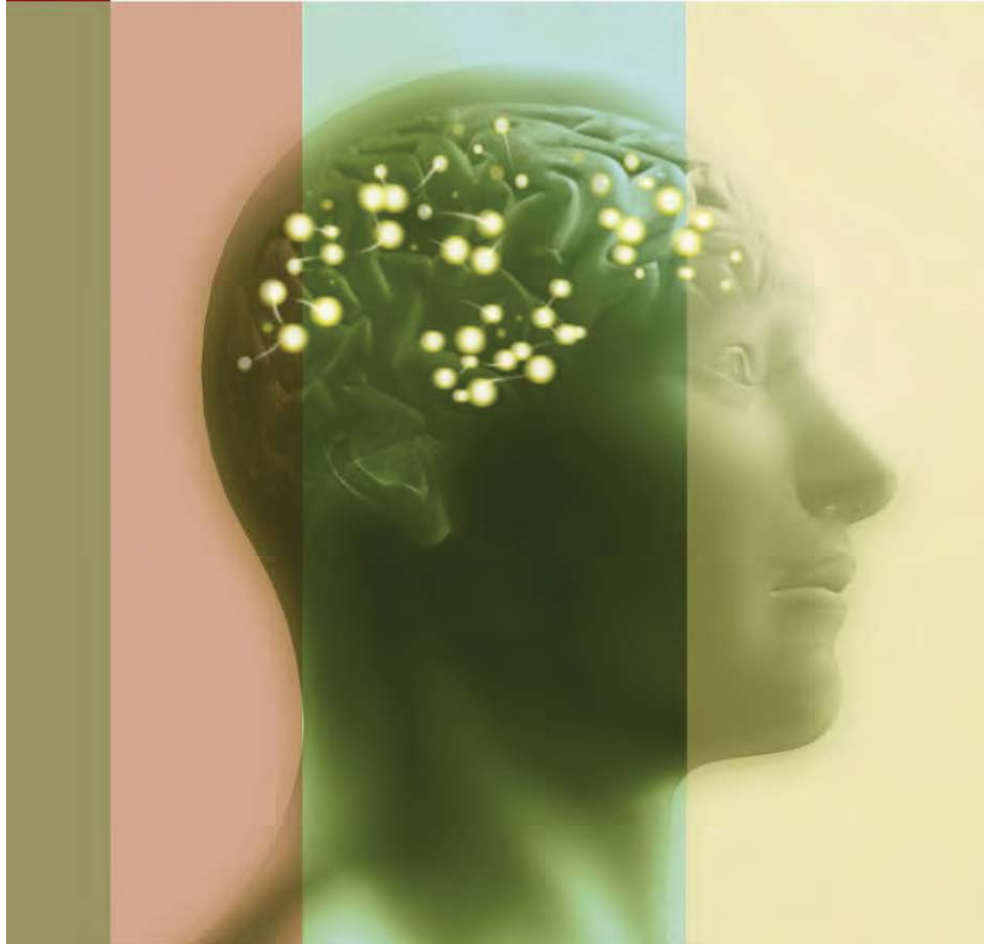
Date Added	Status	Ready (0) Future (1) Issue	Sent to MJA	Seen by MJA/ PR	Press Release	This Month	Free Article	Audio Podcast	Video Abstract	HotTopic	EDK Basic/ Clinical	EDK Issue Order	Manuscript No.	Corresponding Author	Article Type	Article Title	
8/4/2016	LWW	0	N/A	N/A							clinical	1	ALN-D-16-00731	Jamie W. Sleigh	01Editorial	Another brick in (some kind of) wall.	
8/3/2016	LWW	0	N/A	N/A							clinical	2	ALN-D-16-00776	George Alexander Mashour	01Editorial	Network-Level Mechanisms of Ketamine Anesthesia	
											basic	3		Kane Pryor			
8/4/2016	Acc/MP	0	N/A	N/A							clinical	4	ALN-D-16-00922	Robert L. Owens	01Editorial	Better sleep in the ICU: Blue pill or Red pill... or no pill?	
8/4/2016	Acc/MP	0	N/A	N/A							basic	5	ALN-D-16-00942	Maurizio Cereda	01Editorial	Early regional inflammation: the seeds of lung injury	
8/4/2016	LWW	0	N/A	N/A							basic	6	ALN-D-16-00730	Albert Dahan	01Editorial	Potent opioid analgesia without respiratory depression - Could it be possible?	
7/27/2016	LWW	0	N/A	N/A							clinical	7	ALN-D-16-00517	Robert A. Bjork	01Editorial	Commentary on the Potential of the MOCA-Minute program	
8/4/2016	Acc/MP	0	8/4/2016			8							8	ALN-D-16-00890	J. David Clark	03Special Article	Preclinical Pain Research: Can we do Better?
7/26/2016	LWW	0	7/26/2016										9	ALN-D-16-00369	Sukumar P. Desai	03Special Article	Sites related to Crawford Williamson Long in Georgia
7/26/2016	LWW	0	7/26/2016			2	X		X	Neural Correlates of Anesthetic-Induced Unconsciousness MA	clinical	10	ALN-D-15-01427	Daniel Golkowski	04Periop Med + Ed	Neural Correlates of Sevoflurane-Induced Unconsciousness Identified by Simultaneous Functional Magnetic Resonance Imaging and Electroencephalography	
8/3/2016	LWW	0	8/3/2016	Yes		3	X			Neural Correlates of Anesthetic-Induced Unconsciousness MA	clinical	11	ALN-D-15-01384	Vincent Bonhomme	04Periop Med + Ed	Resting state network-specific breakdown of functional connectivity during ketamine alteration of consciousness in volunteers	
7/26/2016	LWW	0	7/26/2016			5					clinical	12	ALN-D-16-00031	Gaspard Montandon	04Periop Med	Distinct cortical signatures associated with sedation and respiratory rate depression by morphine in a pediatric population	
7/26/2016	LWW	0	7/26/2016								clinical	13	ALN-D-16-00161	Jurgen C. de Graaff	04Periop Med	Reference values for non-invasive blood pressure in children under anesthesia. A multi-centered retrospective observational cohort study.	
8/4/2016	Acc/MP	0	8/4/2016								clinical	14	ALN-D-15-01495	Eric C. Cheon	04Periop Med	Unplanned, Postoperative Intubation in Pediatric Surgical Patients: Development and Validation of a Multivariable Prediction Model	
7/26/2016	Acc/MP	0	7/26/2016			1	X	X		Neural Correlates of Anesthetic-Induced Unconsciousness MA	basic	15	ALN-D-15-01378	George Alexander Mashour	04Periop Med + Ed	Neural Correlates of Wakefulness, Sleep, and General Anesthesia: An Experimental Study in Rat	
7/26/2016	LWW	0	7/26/2016								basic	16	ALN-D-16-00071	Douglas E. Raines	04Periop Med	Sedative-Hypnotic Binding to 11 β -Hydroxylase	
7/26/2016	LWW	0	7/26/2016		X	4	X				basic	17	ALN-D-15-01397	Warren M. Zapol	04Periop Med	Exposure Of Stored Erythrocytes To Nitric Oxide Prevents Transfusion-Associated Pulmonary Hypertension	
7/26/2016	LWW	0	7/26/2016								basic	18	ALN-D-16-00262	Richard L Horner	04Periop Med	Enhanced thalamic spillover inhibition during non rapid-eye-movement sleep triggers an electrocortical signature of anesthetic hypnosis	
7/26/2016	Acc/MP	0	7/26/2016								clinical	19	ALN-D-15-01452	Dong-Xin Wang	04Critical Care + Ed	Low-Dose Dexmedetomidine Improves Sleep Quality Pattern of Elderly Patients after Non-cardiac Surgery in the Intensive Care Unit: A Pilot Randomized Controlled Trial	
7/26/2016	Acc/MP	0	7/26/2016			6					basic	20	ALN-D-15-01475	Marcos F. Vidal Melo	05Crit Care + Ed	Lung Metabolic Activation as an Early Biomarker of the Acute Respiratory Distress Syndrome and Local Gene Expression Heterogeneity	
7/29/2016	LWW	0	8/4/2016								basic	21	ALN-D-15-01455	Fu-ming Shen	05Critical Care	The vagus nerve attenuates hepatocyte apoptosis upon ischemia reperfusion via $\alpha 7$ nicotinic acetylcholine receptor on Kupffer cells in mice	
8/4/2016	LWW	0	8/4/2016								basic	22	ALN-D-15-01207	Philippe Sitbon	06Pain Medicine + Ed	STR-324, a stable analogue of opiorphin, causes analgesia in post-operative pain by activating endogenous opioid receptor-dependent pathways	
8/4/2016	Acc/MP	0	8/4/2016								basic	23	ALN-D-15-01161	Jing Wang	06Pain Medicine	AMPAKines Target the Nucleus Accumbens to Relieve Postoperative Pain	
7/26/2016	LWW	0	7/26/2016			7	X	X			clinical	24	ALN-D-15-01560	Huaping Sun	11Education + Ed	Association between Participation in an Intensive Longitudinal Assessment Program and Performance on a Cognitive Examination in the Maintenance of Certification in Anesthesiology Program® (MOCA®)	
8/4/2016	Acc/MP	0	8/4/2016								clinical	25	ALN-D-15-01146	Kiki M.J.M.H. Lombarts	11Education	Re-design of the System for Evaluation of Teaching Qualities in Anesthesiology Residency Training (SETQ Smart)	

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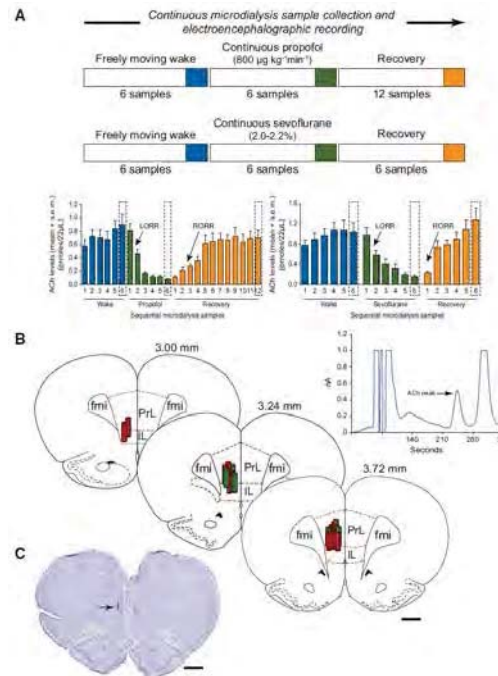
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Neural Correlates of Anesthetic-induced Unconsciousness

Pal D, Silverstein BH, Lee H, Mashour GA
**Neural Correlates of Wakefulness, Sleep, and
General Anesthesia**
An Experimental Study in Rat
Anesthesiology 2016; 125:929-42



Handling Editor's Summary of Wakefulness and Unconsciousness

What We Already Know about This Topic

- Accumulating evidence suggests that fragmentation of cortical networks occurs during physiologic, pharmacologic, and pathologic states of unconsciousness
- Cortical connectivity and acetylcholine levels were examined in relation to changes in behavioral arousal due to propofol or sevoflurane anesthesia and normal sleep in rat

What This Article Tells Us That Is New

- Disruption of cortical connectivity in high γ band correlated with anesthetic- and sleep-induced unconsciousness, while θ connectivity correlated with cholinergic tone and cortical activation
- Functional fragmentation of high-frequency activity in the cortex may be a common network-level mechanism of unconsciousness during general anesthesia and sleep

Executive Editor's Summary of Wakefulness and Unconsciousness

THIS MONTH IN

ANESTHESIOLOGY



929 Neural Correlates of Wakefulness, Sleep, and General Anesthesia: An Experimental Study in Rat

The relationship of cortical acetylcholine and electroencephalographic (EEG) indices of corticocortical connectivity—coherence and symbolic transfer entropy—was studied in rats before, during, and after propofol- and sevoflurane-induced unconsciousness. These EEG indices were also analyzed during wakefulness, slow wave sleep (SWS), and rapid eye movement (REM) sleep in other rats. EEG coherence and frontal-parietal directed connectivity in the high gamma (85 to 155 Hz) bandwidth were present during wakefulness and were disrupted during physiological (SWS and REM sleep) and pharmacological (propofol and sevoflurane) states of unconsciousness. Coherence and bidirectional frontal-parietal connectivity in the theta (4 to 10 Hz) bandwidth were present during states of cortical activation (low amplitude—fast wave electroencephalogram) with (wakefulness) or without (REM sleep) behavioral arousal, and correlated with cortical acetylcholine concentrations. Coherence and frontal-parietal directed connectivity in high gamma band were not mediated by cholinergic mechanisms. *See the accompanying Editorial View on page 832.* (Summary: M. J. Avram. Illustration: A. Johnson, Vivo Visuals.)



929 Neural Correlates of Wakefulness, Sleep, and General Anesthesia: An Experimental Study in Rat

The relationship of cortical acetylcholine and electroencephalographic (EEG) indices of corticocortical connectivity—coherence and symbolic transfer entropy—was studied in rats before, during, and after propofol- and sevoflurane-induced unconsciousness. These EEG indices were also analyzed during wakefulness, slow wave sleep (SWS), and rapid eye movement (REM) sleep in other rats. EEG coherence and frontal-parietal directed connectivity in the high gamma (85 to 155 Hz) bandwidth were present during wakefulness and were disrupted during physiological (SWS and REM sleep) and pharmacological (propofol and sevoflurane) states of unconsciousness. Coherence and bidirectional frontal-parietal connectivity in the theta (4 to 10 Hz) bandwidth were present during states of cortical activation (low amplitude—fast wave electroencephalogram) with (wakefulness) or without (REM sleep) behavioral arousal, and correlated with cortical acetylcholine concentrations. Coherence and frontal-parietal directed connectivity in high gamma band were not mediated by cholinergic mechanisms. See the accompanying Editorial View on page 832. (Summary: M. J. Avram. Illustration: A. Johnson, Vivo Visuals.)



861 Neural Correlates of Sevoflurane-induced Unconsciousness Identified by Simultaneous Functional Magnetic Resonance Imaging and Electroencephalography

Resting-state functional magnetic resonance imaging (fMRI) and electroencephalography were recorded simultaneously in 16 volunteers while awake and during sevoflurane anesthesia at burst suppression, 3 vol% and suppression and 3 and 2 vol% steady-state concentrations to test the hypothesis that, like propofol, sevoflurane would reduce frontal information processing (measured by permutation entropy [PE_n]) and disrupt frontoparietal connectivity, resulting in decreased frontal-to-parietal directed connectivity (DC, measured by symbolic transfer entropy [STEn]). Sevoflurane at 2 and 3 vol% profoundly decreased fMRI-based measures of functional connectivity in frontal networks, especially ventral parts of the frontoparietal attention networks. Thalamocortical functional connectivity was decreased in all stages of anesthesia. Electroencephalographic analyses findings of a pronounced decrease in surrogates of information processing (PE_n) in the frontal cortex and reversal of DC (STEn) between frontoparietal electrode pairs were consistent with those of fMRI. See the accompanying Editorial View on page 827. (Summary: M. J. Avram. Image: ImagePower Productions, John Ursino.)



873 Resting-state Network-specific Breakdown of Functional Connectivity during Ketamine Alteration of Consciousness in Volunteers

The hypnotic effects of ketamine are largely mediated by blockade of N-methyl-D-aspartate receptors and HCNI channels. A functional magnetic resonance imaging study was conducted in eight volunteers submitted to stepwise increments in plasma ketamine concentrations, up to loss of responsiveness to verbal command, to explore the effects of ketamine on within and between resting-state consciousness networks connectivities. Ketamine-induced unresponsiveness has features in common with that induced by GABAergic drugs, including breakdown of frontal-parietal connectivity and of anticorrelated activity between the Default-Mode network (DMn) and other brain regions. Ketamine preserved subcortical input to the cortex in addition to sensory and motor processing. Alteration of higher-order integration networks (such as the DMn) and their anticorrelation with other networks as well as breakdown of Salience network connectivity are responsible for mental content perturbation under ketamine sedation. See the accompanying Editorial View on page 830. (Summary: M. J. Avram. Image: iStock.)



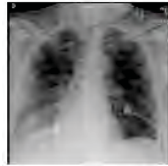
952 Exposure of Stored Packed Erythrocytes to Nitric Oxide Prevents Transfusion-associated Pulmonary Hypertension

The viability of erythrocytes is reduced by extended storage, leading to release of hemoglobin into the red blood cell (RBC) unit supernatant. Circulating cell-free hemoglobin and hemoglobin-containing microvesicles scavenge nitric oxide generated by endothelial cells, which may be the cause of pulmonary vasoconstriction after transfusion of stored blood. Nitric oxide consumption by ovine RBC supernatant fluid was reduced when stored RBC units were treated with either nitric oxide gas or a short-lived nitric oxide donor, due to conversion of extracellular oxyhemoglobin to methemoglobin, which is unable to scavenge nitric oxide. Nitric oxide treatment of stored RBCs by either method prevented pulmonary vasoconstriction and hypertension in lambs during and after transfusion of autologous erythrocytes stored for either 2 days or 40 days. Washing stored RBCs before transfusion did not prevent pulmonary hypertension. (Summary: M. J. Avram. Photo: J. P. Rathmell.)



889 Distinct Cortical Signatures Associated with Sedation and Respiratory Rate Depression by Morphine in a Pediatric Population

An observational study was conducted in pediatric patients to identify cortical signatures of morphine-induced sedation and to determine how these are associated with respiratory changes. The effect of morphine on cortical activity, as measured by electroencephalogram spectral content, topography, and coherence, was determined in young patients given morphine for pain relief after elective surgery as were its effects on respiratory activity. Morphine reduced high-frequency (β_1 and β_2 band powers, 13.5 to 30 Hz) cortical activity in the central and frontal lobes, without changing low-frequency activity or affecting occipital lobe activities. These results were characteristic of morphine-induced sedation and distinct from the changes induced by non-rapid eye movement sleep. Morphine decreased frontal-occipital coherence in the β_2 electroencephalographic frequency band. Morphine-induced changes in respiratory rate were related to the reduction in β_1 frequency cortical activity and frontal-occipital coherence. (Summary: M. J. Avram. Photo: J. P. Rathmell.)



992 Lung Metabolic Activation as an Early Biomarker of Acute Respiratory Distress Syndrome and Local Gene Expression Heterogeneity

Acute respiratory distress syndrome (ARDS) is conceived to be an acute, diffuse, inflammatory lung injury with increased pulmonary vascular permeability and lung density. The hypothesis that lung cellular metabolism and gene expression manifest spatial and temporal heterogeneity in response to distinct regional injury mechanisms and precede density changes detectable with conventional radiography was tested in sheep subjected to endotoxemia and mechanical ventilation over 20 h, which reprises the "two-hit" injury often seen in patients. Multitracer positron emission tomography and gene expression techniques were used to study molecular processes during early ARDS development. Increased *in vivo* whole-lung and regional metabolic activation were observed within the first 20 h of lung injury, which preceded lung density increases used routinely for ARDS diagnosis. Temporal trajectories of metabolic activation were spatially heterogeneous and co-registered with topographical heterogeneity in gene expression. See the accompanying Editorial View on page 838. (Summary: M. J. Avram. Image: J. P. Rathmell.)



1046 Association between Participation in an Intensive Longitudinal Assessment Program and Performance on a Cognitive Examination in the Maintenance of Certification in Anesthesiology Program®

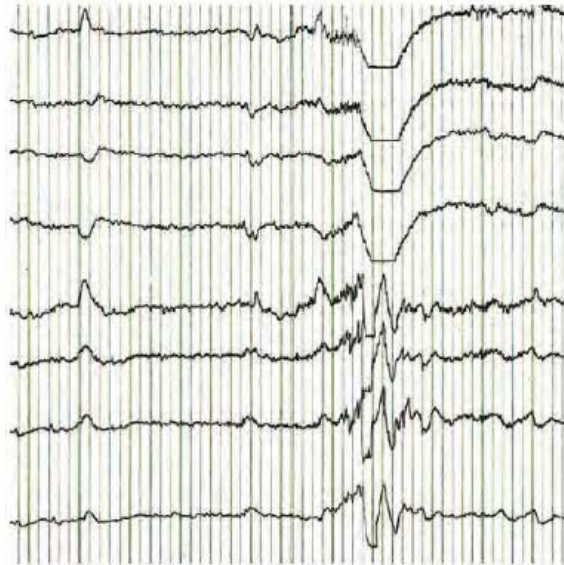
The American Board of Anesthesiology (ABA) requires diplomates with time-limited certificates to participate in a Maintenance of Certification in Anesthesiology Program® (MOCA®). The Assessment of Knowledge, Judgment, and Skills by the MOCA Cognitive Examination has to be passed every ten years. The ABA launched the pilot MOCA Minute program, a web-based longitudinal assessment involving weekly questions with immediate feedback and links to learning resources, in 2014 to help diplomates master topics included in the Cognitive Examination. The hypothesis that voluntary enrollment and participation in the MOCA Minute program is associated with improved performance on the Cognitive Examination was tested in an observational study. When other factors were taken into account, participation in MOCA Minute was associated with a modest but significant improvement in performance for items querying topics covered by MOCA Minute questions and those in other topic areas. See the accompanying Editorial View on page 844. (Summary: M. J. Avram. Image: The MOCA Minute® logo is a trademark of the American Board of Anesthesiology.)



846 Preclinical Pain Research: Can We Do Better?

The ability of modern medicine to control both acute and chronic pain is limited despite extensive pain research. Clinical trials of newly designed drugs that were effective in changing pain-related behavior in preclinical models have often failed. This special article reviews reasons for these failures and makes recommendations for how to improve the process. Reasons for failure include poor preclinical pain models, preclinical pain measures, and reporting practices. Recommendations include selecting models closely resembling their targeted clinical conditions, studying animals under conditions relevant to clinical pain, and using pain measures involving more informative behaviors as alternatives to, or in addition to, evoked responses largely involving spinal reflexes. A final recommendation is that reports should be written clearly and accurately, key experimental details should be included, and sources of potential bias should be disclosed. (Summary: M. J. Avram. Photo: @ThinkStock.)

Hudson AE, Pryor KO:
Integration and Information: Anesthetic
Unconsciousness Finds a New Bandwidth
Anesthesiology 2016;125:827-9



“How might disruption of the functional connection between cortical modules... be so crucial to inducing a state of unconsciousness?”

Hudson AE, Pryor KO

Integration and Information: Anesthetic
Unconsciousness Finds a New Bandwidth
Anesthesiology 2016;125:827-9

Just as the early 20th century astronomers exploring the solar system and local star clusters before relativity could have no comprehension of the questions facing modern cosmologists, the current models of human consciousness will inevitably evolve. Any plausible theory must be consistent with what is observed in experimental studies of anesthetic unconsciousness, and in this regard, the work presented by Pal *et al.*¹ contributes to the critical evaluation of models such as the IIT. But its impact in the anesthesia literature is greater. It adds important evidence to support the theory that the common, essential cause of anesthetic unconsciousness is related to the functional disruption of feedback systems and challenges the field to now seek bridges between systems- and cellular-level models.

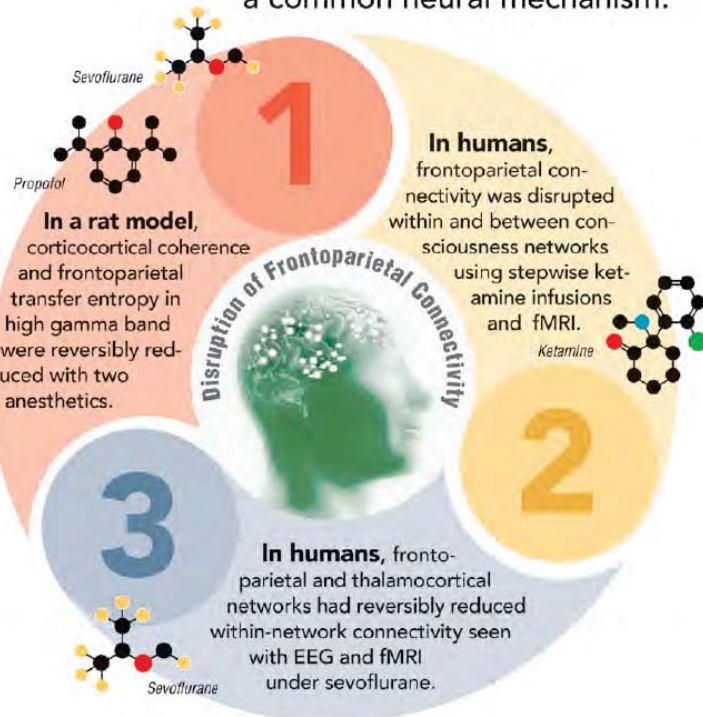
INFOGRAPHICS IN ANESTHESIOLOGY

Complex Information for Anesthesiologists Presented Quickly and Clearly

Created by: James P. Rathmell, M.D.

Functional Breakdown of Cortical Networks: A Tale of Three Anesthetics

Results from three research groups,^{1,2,3} with three anesthetics and three research paradigms, suggest a common neural mechanism:



“An ounce of replication is worth a ton of small *P* values.”⁴

Anesthesiology

November 2016, Volume 125, Issue 5

Editor-in-Chief's Podcast

Evan D. Kharasch, M.D., Ph.D.

Overview of November issue original studies.

Duration 19 minutes 07 seconds



Anesthesiology

November 2016 Author Podcast

Wakefulness and Unconsciousness

Moderator: James P. Rathmell, M.D.

Participants: George A. Mashour, M.D., Ph.D.,
and Andrew E. Hudson, M.D., Ph.D.

Duration: 21 minutes 16 seconds

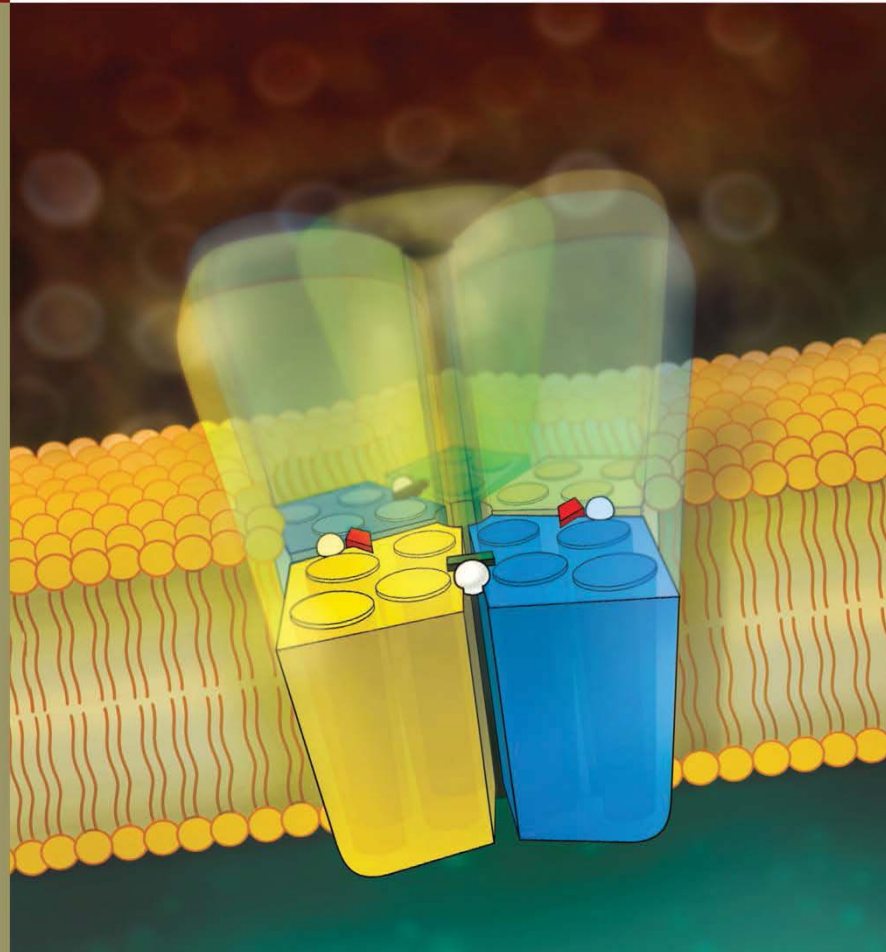


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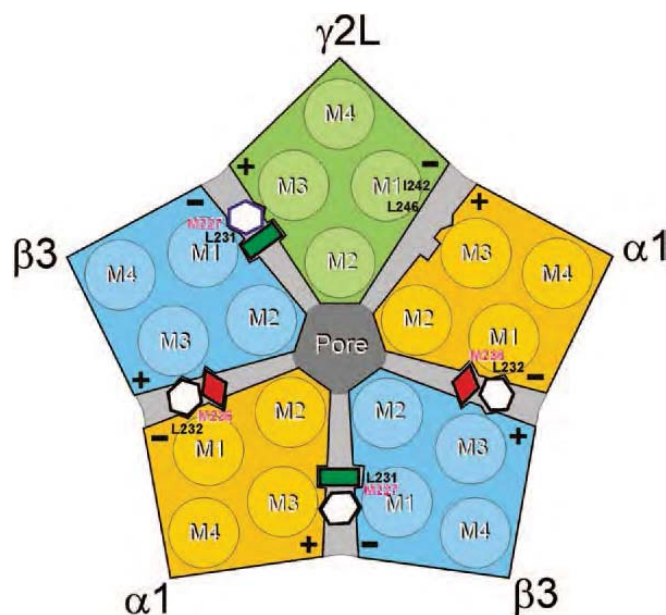


Intravenous General Anesthetic Binding to GABA_A Receptors

Nourmahnad A, Stern AT, Hotta M, Stewart DS,
Ziemba AM, Szabo A, Forman SA:

**Tryptophan and Cysteine Mutations in M1 Helices
of $\alpha 1\beta 3\gamma 2L$ γ -Aminobutyric Acid Type A Receptors
Indicate Distinct Intersubunit Sites for Four
Intravenous Anesthetics and One Orphan Site.**

Anesthesiology 2016;125:1144-1158.



Jenkins MA, Jenkins A:
Anesthetic-Receptor Relationship Status:
It's Complicated
Anesthesiology 2016;125:1088-1089

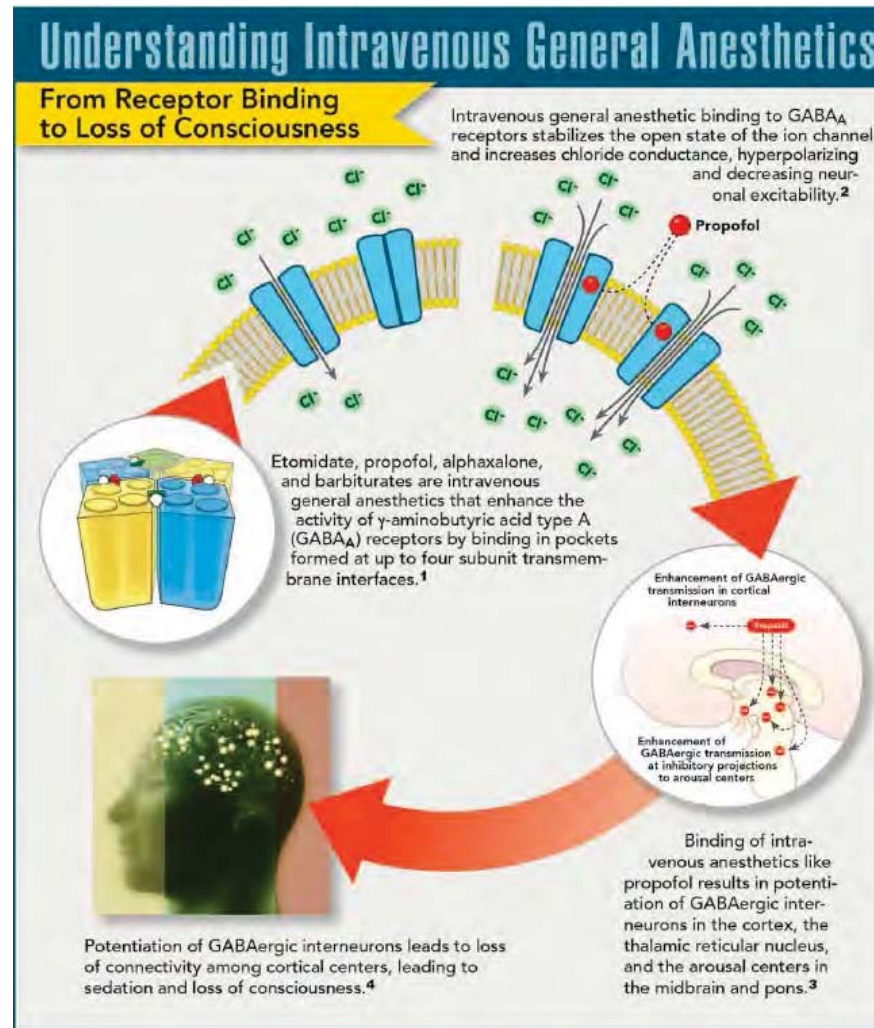


“...an enormous leap forward in our understanding of how anesthetics work.”

INFOGRAPHICS IN ANESTHESIOLOGY

Complex Information for Anesthesiologists Presented Quickly and Clearly

Created by: James P. Rathmell, M.D.



Mapping where general anesthetics bind

Duration 3:23



New Section Being Rolled Out



**METHODOLOGIES
EXPLAINED**

Propensity Score Matching – Principles, Uses, and Controversies

Author Names

A Few Words about Statistical Analysis



Timothy Houle, Ph.D.

ANESTHESIOLOGY



Jean Mantz, M.D., Ph.D., Editor

**Spinal cord reconstitution with homologous neural grafts enables robust corticospinal regeneration. Nat Med 2016; 22:479–90.**

Traumatic spinal cord injury is a devastating disease associated with severe sequelae. Despite recent progress in promoting the regeneration of many classes of central nervous system axons after spinal cord injury (SCI), the corticospinal projection remains largely refractory to regeneration. Using a combination of sophisticated experimental approaches in murine models of SCI, the authors demonstrated robust corticospinal axon regeneration, functional synapse formation, and improved skilled forelimb function after grafting multipotent neural progenitor cells into sites of SCI. Corticospinal regeneration requires grafts to be driven toward caudalized (spinal cord), rather than rostralized, fates. Corticospinal axons can also emerge from neural grafts and regenerate beyond the lesion, a process that is potentially related to the attenuation of the glial scar. These findings will be essential for advancing corticospinal regeneration in future translational efforts. (Summary: J. Mantz. Illustration: J. P. Rathmell.)

Take home message: Corticospinal axon regeneration, functional synapse formation, and improved skilled forelimb function have been shown after grafting multipotent neural progenitor cells into sites of spinal cord injury in murine models.

**Effects of aspirin on risk and severity of early recurrent stroke after transient ischaemic attack and ischaemic stroke: Time-course analysis of randomised trials. Lancet 2016; 388:365–75.**

Aspirin is recommended for secondary prevention after transient ischemic attack (TIA) or ischemic stroke on the basis of trials showing a 13% reduction in long-term risk of recurrent stroke, but short-term effects may have been underestimated. In this time-course analysis of aspirin effects after TIA, 15,778 participants from 12 trials of aspirin versus control in secondary prevention were pooled. The severity of early recurrent strokes between treatment groups was analyzed with shift analysis of the modified Rankin Scale score. Aspirin reduced the 6-week risk of recurrent ischemic stroke by about 60% (84 of 8,452 participants in the aspirin group had an ischemic stroke vs. 175 of 7,326; hazard ratio 0.42; 95% CI, 0.32 to 0.55; $P < 0.0001$) and disabling or fatal ischemic stroke by about 70% (36 of 8,452 vs. 110 of 7,326; hazard ratio 0.29; 95% CI, 0.20 to 0.42; $P < 0.0001$), with greatest benefit noted in patients presenting with TIA or minor stroke. The effect of aspirin on early recurrent ischemic stroke was due partly to a substantial reduction in severity of the primary event. (Summary: J. Mantz. Illustration: J. P. Rathmell.)

Take home message: Medical treatment substantially reduces the risk of early recurrent stroke after transient ischemic attack and minor stroke and aspirin is identified as the key intervention.

**Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: Early outcomes from a randomised controlled phase 3 study. Lancet 2016; 388:1057–66.**

The absence of trial data comparing robot-assisted laparoscopic prostatectomy and open radical retropubic prostatectomy is a crucial knowledge gap in urologic oncology. In this prospective randomized controlled trial, the authors aimed at comparing urinary function (urinary domain of the Expanded Prostate Cancer Index Composite [EPIC]) and sexual function (sexual domain of EPIC and International Index of Erectile Function Questionnaire) at 6 weeks, 12 weeks, and 24 months, and oncological outcome (positive surgical margin status and biochemical and imaging evidence of progression at 24 months) in men undergoing either robot-assisted laparoscopic prostatectomy or radical retropubic prostatectomy. Early outcomes at 6 weeks and 12 weeks were reported in 326 patients. The two techniques yield similar functional outcomes at 12 weeks; examination of the longer-term follow-up data in this trial will help guide future patient and practitioner decisions. (Summary: J. Mantz. Photo: ©ThinkStock.)

Take home message: In this randomized controlled trial, robotic versus conventional laparoscopic prostatectomy did not reveal significant differences in functional outcomes at 12 weeks after surgery.

**Adaptive Designs for Clinical Trials. N Engl J Med 2016; 375:65–74.**

Randomized clinical trials (RCTs) serve as the standard for clinical research and have contributed to major advances in patient care, yet they have several shortcomings. Adaptive trial design has been proposed as a means to increase the efficiency of RCTs, potentially benefiting trial participants and future patients while reducing costs and enhancing the likelihood of finding a true benefit of the therapy being studied. Adaptive trials apply to both exploratory trials aimed at finding a safe and efficient dose range and confirmatory trials aimed at testing the clinical benefit of a therapy/intervention. In this review, the authors focus on adaptive designs of confirmatory clinical trials and discuss the benefits and limitations of such designs, using four case studies that highlight the statistical and operational considerations for a successful trial. Readers will find here robust and easy-to-read information on how to identify patients who are most likely to derive benefit from a given therapy. (Summary: J. Mantz. Illustration: J. P. Rathmell.)

Take home message: Adaptive design applied to confirmatory clinical trials may help identify those patients who are most likely to derive benefit from a therapy.



Effect of a primary care management intervention on mental health–related quality of life among survivors of sepsis: A randomized clinical trial. JAMA 2016; 315:2703–11.

This randomized clinical trial examined if a primary care–based intervention improves mental health–related quality of life among survivors of sepsis. Two hundred ninety-one patients 18 yr or older who survived sepsis, including septic shock, were recruited from nine intensive care units (ICUs) across Germany. Participants were randomized to usual care (n = 143) or to a 12-month intervention (n = 148). Usual care was provided by their primary care physician (PCP) and included periodic contacts, referrals to specialists, and prescription of medication, other treatment, or both. The intervention included PCP and patient training, case management provided by trained nurses, and clinical decision support for PCPs by consulting physicians. The primary outcome was change in mental health–related quality of life between ICU discharge and 6 months after ICU discharge using the Mental Component Summary of the 36-Item Short-Form Health Survey. It was found that among survivors of sepsis and septic shock, the use of a primary care–focused team–based intervention, compared with usual care, did not improve mental health–related quality of life 6 months after ICU discharge. (Summary: J. Mantz. Photo: ©ThinkStock.)

Take home message: In this randomized controlled trial, a targeted, primary care intervention versus standard care did not improve mental health–related quality of life among sepsis survivors.



Standardized rehabilitation and hospital length of stay among patients with acute respiratory failure: A randomized clinical trial. JAMA 2016; 315:2694–702.

Physical rehabilitation in the intensive care unit (ICU) may improve the outcomes of patients with acute respiratory failure. The objective of this single-center randomized clinical trial was to compare the effect of standardized rehabilitation therapy (SRT) to usual ICU care in acute respiratory failure on hospital length of stay (LOS; primary outcome). Patients in the SRT group received daily therapy until hospital discharge, consisting of passive range of motion, physical therapy, and progressive resistance exercise. The usual care group received weekday physical therapy when ordered by the clinical team. Of the 300 randomized patients, the median hospital LOS was 10 days (interquartile range, 6 to 17) for the SRT group and 10 days (interquartile range, 7 to 16) for the usual care group (median difference, 0 [95% CI, -15 to 3], P = 0.41). No significant difference was observed between groups in most of the secondary outcomes (handgrip and dynamometer strength, 36-item Short-Form Health Surveys and Mini-Mental State Evaluation Score performed at 2, 4, and 6 months). (Summary: J. Mantz. Photo: J. P. Rathmell.)

Take home message: Among patients hospitalized with acute respiratory failure, standardized rehabilitation therapy compared with usual care did not decrease hospital length of stay.



Effect of buprenorphine implants on illicit opioid use among abstinent adults with opioid dependence treated with sublingual buprenorphine: A randomized clinical trial. JAMA 2016; 316:282–90.

Rates of opioid addiction and deaths related to abuse have risen in parallel to liberalized prescribing practices over the past 15 yr. Opioid maintenance therapy with buprenorphine or methadone represents an important treatment option, although adherence to therapy is often problematic. To address this issue, a 6-month implantable form of buprenorphine was tested against a conventional sublingual formulation of the drug. Using a randomized, active-control, 24-week, double-blind study design involving 177 patients, the investigators found that the implantable formulation was noninferior to sublingual buprenorphine, and slightly better at promoting opioid abstinence (85.7 vs. 71.9%; P = 0.03 at 24 weeks). An important limitation of the generalizability of the study is that the patient population was predominantly educated and employed, characteristics associated with high rates of treatment response. Nonetheless, this trial suggests that use of implantable buprenorphine in the treatment of opioid addiction is promising. (Summary: David J. Clark. Photo: J. P. Rathmell.)

Take home message: This randomized controlled trial shows promising results for implantable buprenorphine in the treatment of opioid addiction.



Measuring moral courage for interns and residents: Scale development and initial psychometrics. Acad Med 2016 Jul 5. [Epub ahead of print.]

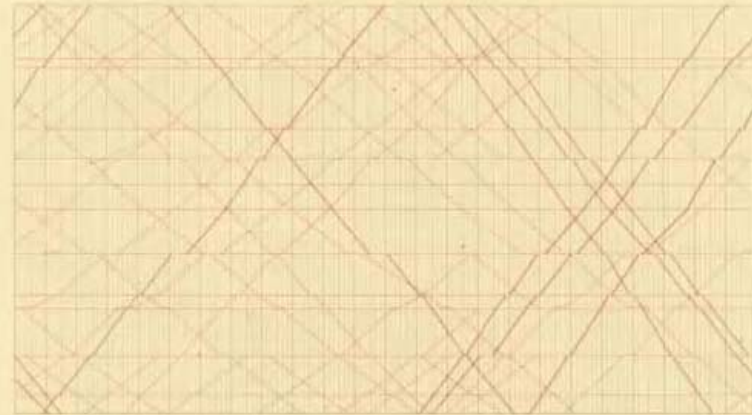
Moral courage, willingness to do the right thing even when it is not in your personal best interest, such as reporting an error or speaking up to authority, is a desirable quality to develop in resident physicians. Can it be taught? Can it be measured? These authors developed and provide initial validation of a method that can be used to measure and potentially track the development of moral courage in the context of clinical care. Three hundred fifty-two interns and residents in medicine and surgical specialties at two academic medical centers completed the Moral Courage Scale for Physicians as part of a voluntary safety culture survey. The 12-question survey tool addresses the five aspects that define moral courage. Correlation to established measures of empathy assessed validity. Perhaps this simple survey tool could be used to track effectiveness of educational interventions in professionalism, a competency that is challenging to measure. (Summary: Cathleen Peterson-Layne. Photo: J. P. Rathmell.)

Take home message: The authors developed a 12-question survey tool to assess moral courage of residents such as reporting an error or speaking up to authority.

Novack GD:
How Should We Display Our Data?
What Is the Best Number?
The Occular Surface 212:10:193-7



Gary D. Novack, Ph.D.

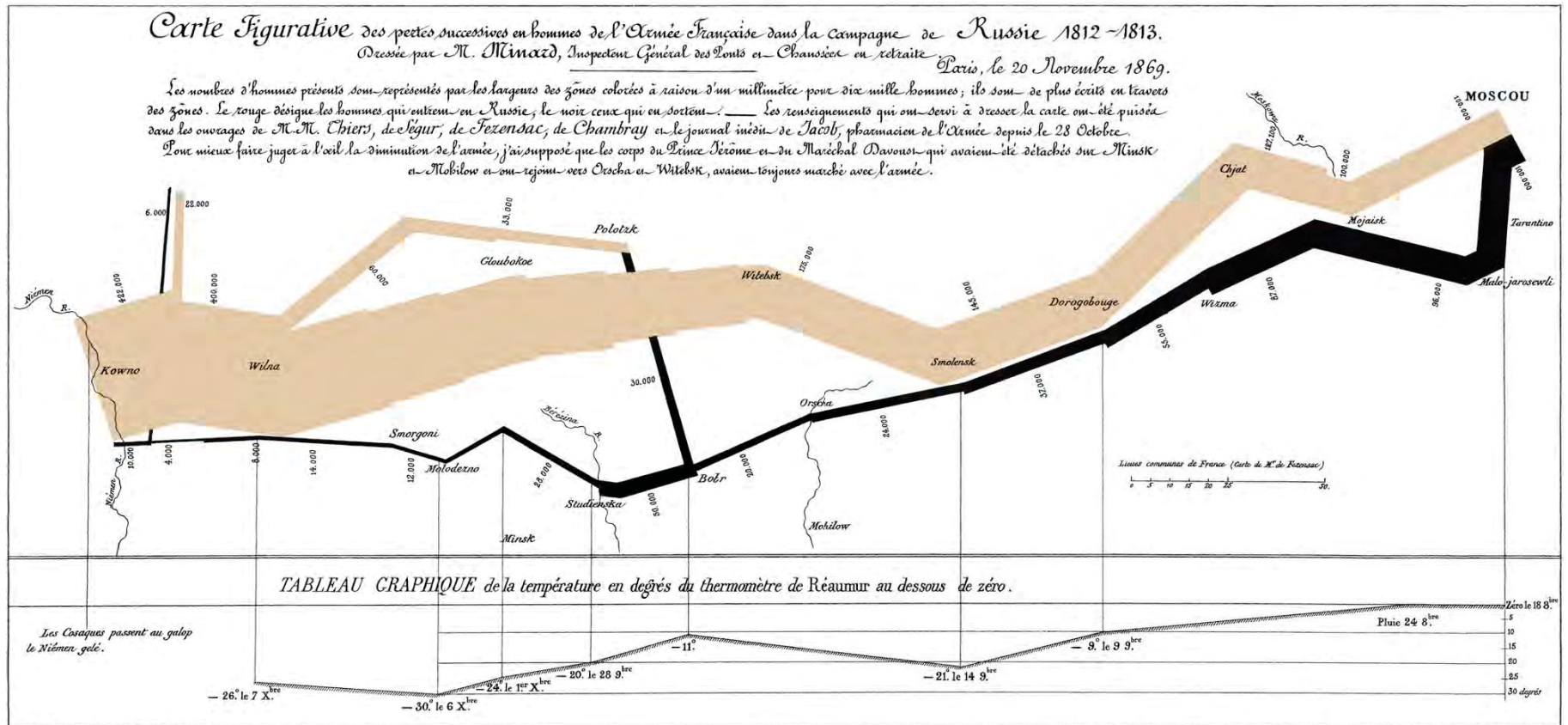


The Visual Display
of Quantitative Information

EDWARD R. TUFTE

Charles-Joseph Minard

Napoleon's March to Moscow in 1812 & Subsequent Retreat



Thank you!