

# Table of Contents

April, 2013

## Cardiovascular Anesthesiology

[美国心血管麻醉医师协会的一项随机临床试验：主动脉缩窄修复术中血压调节对使用近红外光谱测量脑、肾和肌肉氧饱和度的影响](#)

(诸琳婕译 陈杰校)

**The Effect of Blood Pressure Regulation During Aortic Coarctation Repair on Brain, Kidney, and Muscle Oxygen Saturation Measured by Near-Infrared Spectroscopy: A Randomized, Clinical Trial**

- Annelies Moerman,
- Thierry Bové,
- Katrien François,
- Stefan Jacobs,
- Isabel Deblaere,
- Patrick Wouters,
- and Stefan De Hert

*Anesth Analg April 2013 116:760-766; published ahead of print March 4, 2013*

[在健康人中，用七氟醚实施全身麻醉能够减少心脏容量及充血时血流速度](#)

(邓利兵译 薛张纲校)

**General Anesthesia with Sevoflurane Decreases Myocardial Blood Volume and Hyperemic Blood Flow in Healthy Humans**

- Carolien S. E. Bulte,
- Jeroen Slikkerveer,
- Otto Kamp,
- Martijn W. Heymans,
- Stephan A. Loer,
- Stefano F. de Marchi,
- Rolf Vogel,
- Christa Boer,
- and R. Arthur Bouwman

*Anesth Analg April 2013 116:767-774; published ahead of print February 5, 2013*

[丙泊酚能增强长期使用血管紧张素转换酶抑制剂卡托普利治疗的衰老大鼠血管舒张](#)

(唐莹译 马皓琳 李士通校)

### **Propofol Increases Vascular Relaxation in Aging Rats Chronically Treated with the Angiotensin-Converting Enzyme Inhibitor Captopril**

- Ferrante S. Gragasin,
- Stephane L. Bourque,
- and Sandra T. Davidge

*Anesth Analg April 2013 116:775-783; published ahead of print February 21, 2013*

## **Anesthetic Pharmacology**

### 局部麻醉药聚合物微粒引起的局部毒性

(马霄雯译 陈杰校)

### **Local Toxicity from Local Anesthetic Polymeric Microparticles**

- J. Brian McAlvin,
- Gally Reznor,
- Sahadev A. Shankarappa,
- Cristina F. Stefanescu,
- and Daniel S. Kohane

*Anesth Analg April 2013 116:794-803; published ahead of print March 4, 2013*

### 脂肪乳剂对布比卡因在小鼠中药代动力学和组织分布的影响

(方昕译 薛张纲校)

### **The Effect of Lipid Emulsion on Pharmacokinetics and Tissue Distribution of Bupivacaine in Rats**

- Kejian Shi,
- Yun Xia,
- Quanguang Wang,
- Yiquan Wu,
- Xiaoxi Dong,
- Chanjuan Chen,
- Wan Tang,
- Yujian Zhang,
- Mengxu Luo,
- Xianqin Wang,
- Thomas J. Papadimos,

- and Xuzhong Xu

*Anesth Analg April 2013 116:804-809; published ahead of print March 4, 2013*

[TASK-1 \(KCNK3\) 和 TASK-3 \(KCNK9\) 双孔钾离子通道拮抗剂对异氟醚麻醉大鼠的呼吸刺激作用](#)

(陈彬彬译, 马皓琳、李士通校)

**TASK-1 (KCNK3) and TASK-3 (KCNK9) Tandem Pore Potassium Channel Antagonists Stimulate Breathing in Isoflurane-Anesthetized Rats**

- Joseph F. Cotten

*Anesth Analg April 2013 116:810-816; published ahead of print March 4, 2013*

## Technology, Computing, and Simulation

[俯卧位对于校准和未校准的脉冲波形衍生心脏指数测量值准确度的影响](#)

(孙莉荔译 陈杰校)

**The Influence of Prone Positioning on the Accuracy of Calibrated and Uncalibrated Pulse Contour-Derived Cardiac Index Measurements**

- Joern Grensemann,
- Ulrike Bruecken,
- András Treszl,
- Frank Wappler,
- and Samir G. Sakka

*Anesth Analg April 2013 116:820-826; published ahead of print March 4, 2013*

## Obstetric Anesthesiology

[超声用于辅助定位肥胖产妇的硬膜外穿刺中点：旁正中斜入路与横向正中横向入路的比较。](#)

(郭晨跃译 薛张纲校)

**Ultrasound Estimates for Midline Epidural Punctures in the Obese Parturient: Paramedian Sagittal Oblique Is Comparable to Transverse Median Plane**

- Jagpaul S. Sahota,
- Jose C. A. Carvalho,
- Mrinalini Balki,
- Niall Fanning,

- and Cristian Arzola

*Anesth Analg April 2013 116:829-835; published ahead of print February 5, 2013*

## **Pediatric Anesthesiology**

[麻醉对幼猪模型中血管加压素调节脑血流作用的影响](#)

(方斌译 马皓琳 李士通校)

**The Anesthetic Effects on Vasopressor Modulation of Cerebral Blood Flow in an Immature Swine Model**

- Benjamin Bruins,
- Todd J. Kilbaugh,
- Susan S. Margulies,
- and Stuart H. Friess

*Anesth Analg April 2013 116:838-844; published ahead of print March 4, 2013*

## **Pediatric Neuroscience**

[异氟醚导致小鼠大脑皮层发育细胞凋亡的特征和定量研究](#)

(郑华容译 陈杰校)

**Characterization and Quantification of Isoflurane-Induced Developmental Apoptotic Cell Death in Mouse Cerebral Cortex**

- George K. Istaphanous,
- Christopher G. Ward,
- Xinyu Nan,
- Elizabeth A. Hughes,
- John C. McCann,
- John J. McAuliffe,
- Steve C. Danzer,
- and Andreas W. Loepke

*Anesth Analg April 2013 116:845-854; published ahead of print March 4, 2013*

## **Neuroscience in Anesthesiology and Perioperative Medicine**

[非创伤性脑出血患者的神经源性肺水肿：预测因子与相关结果。](#)

(贺盼译 薛张纲校)

**Neurogenic Pulmonary Edema in Patients with Nontraumatic Intracerebral Hemorrhage: Predictors and Association with Outcome**

- Eija Junttila,
- Tero Ala-Kokko,
- Pasi Ohtonen,
- Anne Vaarala,
- Ari Karttunen,
- Olli Vuolteenaho,
- Tuula Salo,
- Meeri Sutinen,
- Toni Karhu,
- Karl-Heinz Herzig,
- and Juha Koskenkari

*Anesth Analg April 2013 116:855-861; published ahead of print February 21, 2013*

[一个随机试验：开颅幕上脑肿瘤切除术中两种不同剂量的甘露醇降颅压效果的比较](#)

(王慧娟译 马皓琳 李士通校)

**A Comparison of Two Doses of Mannitol on Brain Relaxation During Supratentorial Brain Tumor Craniotomy: A Randomized Trial**

- Charlotte Quentin,
- Sonia Charbonneau,
- Robert Moumdjian,
- Alexandre Lallo,
- Alain Bouthilier,
- Marie-Pierre Fournier-Gosselin,
- Michel Bojanowski,
- Monique Ruel,
- Marie-Pierre Sylvestre,
- and Francois Girard

*Anesth Analg April 2013 116:862-868; published ahead of print January 25, 2013*

[氯胺酮通过活性氧簇介导的线粒体途径增强人神经干细胞增殖和诱导神经元凋亡](#)

(詹恺诞译 陈杰校)

**Ketamine Enhances Human Neural Stem Cell Proliferation and Induces Neuronal Apoptosis via Reactive Oxygen Species-Mediated Mitochondrial Pathway**

- Xiaowen Bai,
- Yasheng Yan,
- Scott Canfield,
- Maria Y. Muravyeva,
- Chika Kikuchi,
- Ivan Zaja,
- John A. Corbett,
- and Zeljko J. Bosnjak

*Anesth Analg April 2013 116:869-880; published ahead of print March 4, 2013*

### [癫痫患者的术前评估：麻醉医生的职责](#)

(李丽红译 薛张纲校)

#### **Review Article: Presurgical Evaluation of Patients with Epilepsy: The Role of the Anesthesiologist**

- Jason Chui,
- Lashmi Venkatraghavan,
- and Pirjo Manninen

*Anesth Analg April 2013 116:881-888; published ahead of print February 21, 2013*

### [用明确的回忆评估术中知晓:两种方法的比较](#)

(王晓莉译 马皓琳 李士通校)

#### **Brief Report: Assessment of Intraoperative Awareness with Explicit Recall: A Comparison of 2 Methods**

- George A. Mashour,
- Christopher Kent,
- Paul Picton,
- Satya Krishna Ramachandran,
- Kevin K. Tremper,
- Christopher R. Turner,
- Amy Shanks,
- and Michael S. Avidan

*Anesth Analg April 2013 116:889-891; published ahead of print March 4, 2013*

## **Economics, Education, and Policy**

[自报医疗差错的频率与麻醉培训监督的关系：一项美国麻醉住院医师培训调查](#)

(孙晓琼译 陈杰校)

**The Association Between Frequency of Self-Reported Medical Errors and Anesthesia Trainee Supervision: A Survey of United States Anesthesiology Residents-in-Training**

- Gildasio S. De Oliveira, Jr.,
- Rod Rahmani,
- Paul C. Fitzgerald,
- Ray Chang,
- and Robert J. McCarthy

*Anesth Analg April 2013 116:892-897; published ahead of print February 5, 2013*

[手术室外监督协调麻醉医生活动的通信系统的作用](#)

(孙莉萍译 薛张纲校)

**Role of Communication Systems in Coordinating Supervising Anesthesiologists' Activities Outside of Operating Rooms**

- Bettina Smallman,
- Franklin Dexter,
- Danielle Masursky,
- Fenghua Li,
- Reza Gorji,
- Dave George,
- and Richard H. Epstein

*Anesth Analg April 2013 116:898-903; published ahead of print February 5, 2013*

[一个三级医疗中心成人及儿童手术期间用基于计算机的麻醉呼叫系统紧急呼叫的特点](#)

(王赞译 马皓琳 李士通校)

**Characteristics of Emergency Pages Using a Computer-Based Anesthesiology Paging System in Children and Adults Undergoing Procedures at a Tertiary Care Medical Center**

- Toby N. Weingarten,
- John P. Abenstein,
- Claire H. Dutton,
- Melinda A. Kohn,
- Elizabeth A. Lee,
- Tami E. Mullenbach,
- Bradley J. Narr,
- Darrell R. Schroeder,
- and Juraj Sprung

*Anesth Analg April 2013 116:904-910; published ahead of print January 25, 2013*

[适用于麻醉操作人员的时间关键的信息：无线设备的通讯延迟](#)

(王苑译 陈杰校)

**Communication Latencies of Wireless Devices Suitable for Time-Critical Messaging to Anesthesia Providers**

- Richard H. Epstein,
- Franklin Dexter,
- and Brian Rothman

*Anesth Analg April 2013 116:911-918; published ahead of print February 5, 2013*

[选择哪一位执业者对下一位麻醉前评估患者进行评估取决于执业者的相对速度](#)

(郁玲玲译 薛张纲校)

**Choosing Which Practitioner Sees the Next Patient in the Preanesthesia Evaluation Clinic Based on the Relative Speeds of the Practitioner**

- Franklin Dexter,
- Hyun-Soo Ahn,
- and Richard H. Epstein

*Anesth Analg April 2013 116:919-923; published ahead of print January 25, 2013*

## General Articles

[一篇关于麻醉医生面对肿瘤细胞减灭术和热灌注腹腔化疗的概述](#)

(张怡译 马皓琳 李士通校)

**Special Article: An Overview of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion for the Anesthesiologist**

- Christopher Allen-John Webb,
- Paul David Weyker,
- Vivek K. Moitra,
- and Richard K. Raker

*Anesth Analg April 2013 116:924-931; published ahead of print March 4, 2013*

## Analgesia



# Pain and Analgesic Mechanisms

[在大鼠脊髓背角神经元局部注射异丙酚的抗伤害及抗痛觉过敏效应](#)

(瞿亦枫译 陈杰校)

## **The Antinociceptive and Antihyperalgesic Effects of Topical Propofol on Dorsal Horn Neurons in the Rat**

- Kenichi Takechi,
- Mirela Iodi Carstens,
- Amanda H. Klein,
- and E. Carstens

*Anesth Analg April 2013 116:932-938; published ahead of print January 21, 2013*

# Regional Anesthesia

[区域麻醉下手术后出现快速眼动睡眠剥夺](#)

(周玲译 薛张纲校)

## **Occurrence of Rapid Eye Movement Sleep Deprivation After Surgery Under Regional Anesthesia**

- Frank Dette,
- Werner Cassel,
- Friederike Urban,
- Martin Zoremba,
- Ulrich Koehler,
- Hinnerk Wulf,
- Jürgen Graf,
- and Thorsten Steinfeldt

*Anesth Analg April 2013 116:939-943; published ahead of print March 4, 2013*

[在大鼠模型中麻黄素和布比卡因或利多卡因联合用于脊麻显示有协同性的运动阻滞](#)

(赵晓译 马皓琳 李士通校)

## **Ephedrine Shows Synergistic Motor Blockade When Combined with Bupivacaine or Lidocaine for Spinal Anesthesia in a Rat Model**

- Alimorad G. Djalali,
- Jeffrey Chi-Fei Wang,
- Jose Ramon Perez-Valdivieso,
- Thomas Danninger,

- Gerhard Fritsch,
- David Zurakowski,
- and Peter Gerner

*Anesth Analg* April 2013 116:944-948; published ahead of print March 4, 2013

美国心血管麻醉医师协会的一项随机临床试验：主动脉缩窄修复术中血压调节对使用近红外光谱测量脑、肾和肌肉氧饱和度的影响

**Society of Cardiovascular Anesthesiologists: The Effect of Blood Pressure Regulation During Aortic Coarctation Repair on Brain, Kidney, and Muscle Oxygen Saturation Measured by Near-Infrared Spectroscopy: A Randomized, Clinical Trial**

Annelies Moerman, MD\*, Thierry Bové, MD†, Katrien François, MD, PhD†, Stefan Jacobs, MD\*, Isabel Deblaere, MD\*, Patrick Wouters, MD, PhD\* and Stefan De Hert, MD, PhD\*  
From the Departments of \*Anesthesiology and †Cardiac Surgery, Ghent University Hospital, Gent, Belgium.

*Anesth Analg* April 2013 116:760-766;

**背景：**这项研究比较3种常用药物调节动脉血压对在小儿主动脉缩窄修复术中对大脑( $rS_cO_2$ )、肾脏( $S_rO_2$ )和肌肉( $S_mO_2$ )

氧饱和度的影响。基于已有关于主动脉缩窄修复术中使用硝普钠(SNP)对左侧 $rS_cO_2$ 会产生不良作用的报道,本研究将验证硝普钠(SNP),而非七氟醚或硝酸甘油(NTG),会改变左侧 $rS_cO_2$ 的假设。此外还探讨硝普钠、硝酸甘油及七氟醚的血压调节作用对右侧 $S_cO_2$ 、 $S_rO_2$ 、 $S_mO_2$ 的影响。

**方法：**接受左侧开胸路径,非体外循环下单纯主动脉缩窄修复术的儿童被纳入研究。在主动脉阻断期间,通过随机方案,使用硝普钠、硝酸甘油或七氟醚控制右侧肱动脉的平均动脉压(MAP)限定于阻断前数值的120% -150%。采用近红外光谱连续记录双侧的 $rS_cO_2$ 、 $S_rO_2$ 和

$S_mO_2$ 。作为主要终点,比较各治疗组间主动脉阻断前后左侧 $rS_cO_2$ 相对变化的最大值。

**结果：**每组纳入10例病人。观察左侧 $rS_cO_2$ 相对变化的最大值,治疗组间无显著差异(硝普钠与七氟醚相比,平均差为-0.7%,99%可信区间[CI]为-31% to 29%, $P = 1.0$ ;

硝普钠与硝酸甘油相比:平均差为-1.8%,99% CI为-32%至28%, $P =$

1.0;七氟醚与硝酸甘油相比:平均差为-1.1%,99% CI为-31%至29%, $P =$

1.0)。各组间右侧 $rS_cO_2$ 的变化也无差异( $P = 0.4$ )。与硝酸甘油相比,硝普钠组的 $S_mO_2$ 下降更为显著( $-64\% \pm 17\%$ 比 $-34\% \pm 25\%$ , $P = 0.01$ ),发生更早( $-9 \pm 4\% \cdot \text{min}^{-1}$ 比 $-4 \pm 3\% \cdot \text{min}^{-1}$ , $P = 0.004$ )。硝酸甘油组的右侧 $rS_cO_2$ 与平均动脉压相关性较差( $r = -0.2$ , $P =$

0.93),而七氟醚组( $r = 0.44$ , $P = 0.09$ )和硝普钠组( $r = 0.56$ , $P =$

0.04)的两者关系处于临界值。

**结论：**在主动脉阻断期间分别使用硝普钠、硝酸甘油或七氟醚处理近端高血压,三组间左侧 $rS_cO_2$ 的平均差不超过32%。另外的分析报告显示,使用硝酸甘油时 $rS_cO_2$ 的变化呈非MAP依赖性。由于硝酸甘油也可使外周组织氧饱和度的下降较少、较慢,本研究建议在涉及主动脉阻断的手术过程中使用硝酸甘油能更好地控制近端血压。

(诸琳婕 译 陈杰 校)

**BACKGROUND:** In this study, we compared the effects of 3 frequently used arterial blood pressure-regulating agents on brain ( $rS_cO_2$ ), renal ( $S_rO_2$ ), and muscle ( $S_mO_2$ ) oxygen saturation, during aortic coarctation repair in children. Based on the reported adverse effect of sodium nitroprusside (SNP) on left-sided  $rS_cO_2$  during aortic coarctation repair, we tested the hypothesis that the alterations in left  $rS_cO_2$  occurring with SNP would not be present with sevoflurane and nitroglycerin (NTG). Additionally, we explored the effects of blood pressure regulation with SNP, NTG, or sevoflurane on right-sided  $rS_cO_2$ ,  $S_rO_2$ , and  $S_mO_2$ .

**METHODS:** Children with isolated aortic coarctation undergoing surgical repair through a left thoracotomy without the use of cardiopulmonary bypass were considered eligible for the study. During aortic cross-clamping, control of mean arterial blood pressure (MAP) was conducted according to randomization by the use of SNP, NTG, or sevoflurane to obtain a mean target right brachial blood pressure of 120% to 150% of the MAP value before cross-clamping. Bilateral  $rS_cO_2$ ,  $S_rO_2$ , and  $S_mO_2$  were recorded continuously with near-infrared spectroscopy. As a primary end point, the maximal relative change in left-sided  $rS_cO_2$  in response to aortic cross-clamping was compared among treatment groups.

**RESULTS:** Ten patients per group were included. No significant difference among treatment groups was observed in maximal relative change in left-sided  $rS_cO_2$  (SNP versus sevoflurane: mean difference  $-0.7\%$ , 99% confidence interval [CI]  $-31\%$  to  $29\%$ ,  $P = 1.0$ ; SNP versus NTG: mean difference  $-1.8\%$ , 99% CI  $-32\%$  to  $28\%$ ,  $P = 1.0$ ; sevoflurane versus NTG: mean difference  $-1.1\%$ , 99% CI  $-31\%$  to  $29\%$ ,  $P = 1.0$ ). Additional analyses also detected no difference between groups in right  $rS_cO_2$  ( $P = 0.4$ ). Compared with NTG, treatment with SNP resulted in a significantly larger ( $-64\% \pm 17\%$  vs  $-34\% \pm 25\%$ ,  $P = 0.01$ ) and faster ( $-9 \pm 4\% \cdot \text{min}^{-1}$  vs  $-4 \pm 3\% \cdot \text{min}^{-1}$ ,  $P = 0.004$ ) decrease in  $S_mO_2$ . Right-sided  $rS_cO_2$  and MAP showed a poor correlation for NTG ( $r = -0.2$ ,  $P = 0.93$ ), whereas borderline for sevoflurane ( $r = 0.44$ ,  $P = 0.09$ ) and SNP ( $r = 0.56$ ,  $P = 0.04$ ).

**CONCLUSIONS:** The mean differences in left-sided  $rS_cO_2$  among the patients treated with SNP, NTG, or sevoflurane for proximal hypertension during aortic cross-clamping were no more than 32%. Additional analysis demonstrated a low MAP- $rS_cO_2$  dependence with the use of NTG. Because NTG also resulted in a smaller and slower decrease of oxygen saturation in peripheral tissues, our data suggest that its use might be preferable for proximal blood pressure control during surgical procedures involving aortic cross-clamping.

## 局部麻醉药聚合物微粒引起的局部毒性

### Local Toxicity from Local Anesthetic Polymeric Microparticles

J. Brian McAlvin, MD\*†‡, Gally Reznor, BS, MBS†, Sahadev A. Shankarappa, MPH, MBBS, PhD†‡, Cristina F. Stefanescu, BS‡ and Daniel S. Kohane, MD, PhD†‡

From the \*Department of Medicine, Medicine Critical Care Program, Children's Hospital Boston, Harvard Medical School; †Laboratory for Biomaterials and Drug Delivery, Department of Anesthesiology, Division of Critical Care Medicine, Children's Hospital Boston, Harvard Medical School, Boston; and ‡Harvard-Massachusetts Institute of Technology Division of Health Sciences and Technology, Cambridge, Massachusetts.

Anesth Analg April 2013 116:794-803

**背景：**局部麻醉缓释剂对局部组织损伤可能很严重。据报道此种损伤程度迥异。通过研究大鼠对胶囊型局部麻醉药（低浓度利多卡因；高浓度布比卡因）的组织反应来验证此种药物的内在肌肉毒性。

**方法：**测量不同浓度的利多卡因和布比卡因对C2C12肌小管的细胞毒性，共6天。分别采用四种微粒配方的利多卡因和布比卡因对大鼠进行坐骨神经阻滞：10%（w/w）利多卡因（乳酸-乙醇酸）共聚体(PLGA)、10%（w/w）布比卡因PLGA、50%（w/w）利多卡因PLGA和50%（w/w）布比卡因PLGA。使用改良热板实验和负重测量来评估神经阻滞效果。通过对注射点的组织切片进行评分来评估肌肉毒性。同时检测布比卡因和利多卡因微粒的释放动力学参数。

**结果：**50% (w/w)利多卡因和50% (w/w)布比卡因的感觉阻滞持续时间中位数分别为255（90-540）min、840（277-1215）min（ $p=0.056$ ）。所有微粒配方都可引起肌肉毒性。局部麻醉药的选择对肌肉毒性的严重程度并无影响。50%（w/w）利多卡因与50% (w/w)布比卡因相比，两组4天和14天的肌肉毒性评分中位数分别为3.4（2.1-4.2）vs 3.3(2.9-3.5)( $p=0.44$ )；1.9 (1.8–2.4) vs 1.7 (1.3–1.9) ( $P = 0.23$ )。

**结论：**利多卡因和布比卡因PLGA微粒引起肌肉毒性的程度相似，而与剂量无关。内源性肌肉毒性并不能预测这些局麻药持续释放导致的组织损伤。在肌肉和神经附近注射此种制剂时需谨慎。

（马霄雯 译 陈杰 校）

**BACKGROUND:** Local tissue injury from sustained-release formulations for local anesthetics can be severe. There is considerable variability in reporting of that injury. We investigated the influence of the intrinsic myotoxicity of the encapsulated local anesthetic (lidocaine, low; bupivacaine, high) on tissue reaction in rats.

**METHODS:** Cytotoxicity from a range of lidocaine and bupivacaine concentrations was measured in C2C12 myotubes over 6 days. Rats were given sciatic nerve blocks with 4 microparticulate formulations of lidocaine and bupivacaine: 10% (w/w) lidocaine poly(lactic-co-glycolic) acid (PLGA), 10% (w/w) bupivacaine PLGA, 50% (w/w) lidocaine PLGA, and 50% (w/w) bupivacaine PLGA. Effectiveness of nerve blockade was assessed by a modified hotplate test and weightbearing measurements. Myotoxicity was scored in histologic sections of injection sites. Bupivacaine and lidocaine release kinetics from the particles were measured.

**RESULTS:** Median sensory blockade duration for 50% (w/w) lidocaine was 255 (90–540) minutes versus 840 (277–1215) minutes for 50% (w/w) bupivacaine ( $P = 0.056$ ). All microparticulate formulations resulted in myotoxicity. The choice of local anesthetic did not influence the severity of myotoxicity. Median myotoxicity scores for 50% (w/w) lidocaine compared with 50% (w/w) bupivacaine at 4 days were 3.4 (2.1–4.2) vs 3.3 (2.9–3.5) ( $P = 0.44$ ) and at 14 days 1.9 (1.8–2.4) vs 1.7 (1.3–1.9) ( $P = 0.23$ ), respectively.

**CONCLUSIONS:** Lidocaine and bupivacaine PLGA microspheres resulted in similar degrees of myotoxicity, irrespective of drug loading. Intrinsic myotoxicity did not predict tissue injury from sustained release of these anesthetics. Caution is warranted in the use of such devices near muscle and nerve.

### 俯卧位对于校准和未校准的脉冲波形衍生心脏指数测量值准确度的影响

#### The Influence of Prone Positioning on the Accuracy of Calibrated and Uncalibrated Pulse Contour-Derived Cardiac Index Measurements

Joern Grensemann, MD\*, Ulrike Bruecken, MD\*, András Treszl, MD, PhD, MSc†, Frank Wappler, MD, PhD\* and Samir G. Sakka, MD, PhD\*

From the \*Department of Anaesthesiology and Operative Intensive Care Medicine, University Hospital Witten/Herdecke, Koeln; and †Department of Medical Biometry and Epidemiology, University Medical Center, Hamburg-Eppendorf, Germany.

*Anesth Analg* April 2013 116:820-826

**背景：**因肺功能不全而处于俯卧体位患者常需要密切的血流动力学监护。采用肺热稀释法（TPTD）作为参考技术，本试验考察此类患者中改良俯卧位（135°）对脉冲波形衍生的校准心脏指数（CI<sub>PC</sub>）和未校准的心脏指数（CI<sub>VIG</sub>）测量值精确度的影响。

**方法：**对16名并发急性肺损伤或者急性呼吸窘迫综合征的重症机械通气患者（11位男性，5位女性，年龄在20到71岁之间）进行研究。患者同时接受结合一个集成校准脉冲波形技术（PiCCO®）的TPTD监测和未校准的脉冲波形分析（FloTrac/Vigileo™）监测。在改变体位前，通过TPTD测量心脏指数（L min<sup>-1</sup> m<sup>-2</sup>）（CI<sub>TPTD</sub>）并对CI<sub>PC</sub>进行校准。俯卧位后，从监护仪上获取CI<sub>PC</sub>和CI<sub>VIG</sub>值而CI<sub>TPTD</sub>

值通过测量得到。在8到10小时之后结束俯卧位而再次测量相反的过程。使用基于一个随机效应模型的Bland-

Altman分析来计算一致性限度（LOA）和百分误差。使用极坐标图来进行趋势分析。

**结果：**仰卧位CI<sub>TPTD</sub>为3.3 ± 0.9（平均值±标准差），而CI<sub>VIG</sub>为3.1 ±

0.8。在俯卧后，CI<sub>PC</sub>为3.5 ± 0.8，CI<sub>VIG</sub>为3.3 ± 0.8，CI<sub>TPTD</sub>为3.6 ±

0.8。在恢复仰卧位前，CI<sub>TPTD</sub>为3.5 ± 0.7，CI<sub>VIG</sub>为3.3 ± 1.0。在恢复体位后，CI<sub>TPTD</sub>为3.1 ± 0.7，CI<sub>PC</sub>为3.3 ± 0.7，CI<sub>VIG</sub>为2.9 ± 0.6。CI<sub>PC</sub>

和CI<sub>VIG</sub>的俯卧位和复位汇总平均偏倚分别为-0.1（LOA -0.7至0.6；百分误差19%），0.3（LOA -1.3至1.9；百分误差48%）。因CI变化过小而无法进行趋势分析。

**结论：**根据Critchley标准，虽然俯卧位的改变对校准CI的测值影响轻微，但未校准的CI值显示了一定程度的误差，且因过高而无法被临床接受。

（孙莉荔 译 陈杰 校）

**BACKGROUND:** Patients with lung failure who undergo prone positioning often receive extended hemodynamic monitoring. We investigated the influence of modified prone positioning (135°) on the accuracy of pulse contour-derived calibrated cardiac index (CI<sub>PC</sub>) and uncalibrated cardiac index (CI<sub>VIG</sub>) in this patient population with transpulmonary thermodilution (TPTD) as reference technique.

**METHODS:** We studied 16 critically ill and mechanically ventilated patients (11 men, 5 women, aged 20–71 years) with acute lung injury or acute respiratory distress syndrome. Patients were monitored by TPTD with an integrated calibrated pulse contour technique (PiCCO®) and by uncalibrated pulse contour analysis (FloTrac/Vigileo™). Before prone positioning, cardiac index (given in L min<sup>-1</sup> m<sup>-2</sup>) was measured by TPTD (CI<sub>TPTD</sub>) and CI<sub>PC</sub> was calibrated. After positioning, CI<sub>PC</sub> and CI<sub>VIG</sub> were read from the monitor and CI<sub>TPTD</sub> was measured. After 8 to 10 hours, prone positioning was completed and measurements were performed analogously. Bland-Altman analysis based on a random-effects model was used to calculate limits of agreement (LOA) and percentage errors. Polar plots were used for trend analysis.

**RESULTS:** Supine CI<sub>TPTD</sub> was 3.3 ± 0.9 (mean ± SD) and CI<sub>VIG</sub> was 3.1 ± 0.8. After proning, CI<sub>PC</sub> was 3.5 ± 0.8, CI<sub>VIG</sub> 3.3 ± 0.8, and CI<sub>TPTD</sub> 3.6 ± 0.8. Before repositioning, CI<sub>TPTD</sub> was 3.5 ± 0.7 and CI<sub>VIG</sub> 3.3 ± 1.0. After repositioning, CI<sub>TPTD</sub> was 3.1 ± 0.7, CI<sub>PC</sub> 3.3 ± 0.7, and CI<sub>VIG</sub> 2.9 ± 0.6. Mean bias pooled for proning and repositioning was -0.1 (LOA -0.7 to 0.6) for CI<sub>PC</sub>

(percentage error 19%) and 0.3 (LOA -1.3 to 1.9) for CI<sub>VIG</sub> (percentage error 48%). Changes in CI were too small for trending analysis.

**CONCLUSION:** Although calibrated CI measurements are only marginally influenced by prone positioning, according to the criteria of Critchley and Critchley, uncalibrated CI values show a degree of error, too high to be considered clinically acceptable.

## 异氟醚导致小鼠大脑皮层发育细胞凋亡的特征和定量研究

### Characterization and Quantification of Isoflurane-Induced Developmental Apoptotic Cell Death in Mouse Cerebral Cortex

George K. Istaphanous, MD\*†, Christopher G. Ward, MD\*†, Xinyu Nan, BS\*, Elizabeth A. Hughes, BS\*, John C. McCann, BS\*, John J. McAuliffe, MD, MBA\*†, Steve C. Danzer, PhD\*† and Andreas W. Loepke, MD, PhD\*†

From the Departments of \*Anesthesia and †Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.

Anesth Analg April 2013 116:845-854

**背景:** 越来越多的证据表明: 异氟醚和其他的麻醉药一样, 对新生动物有神经毒性作用。但是, 皮质细胞的濒死特性和其消亡程度均未被充分描述。此项研究利用免疫组化方法识别濒死的细胞, 并定量分析新生小鼠皮质, 及大脑影响区域的凋亡细胞比例。

**方法:** 随机分配七日龄同窝小鼠 (每组36只), 分别暴露于1.5%异氟醚或禁食状态暴露于室内空气共6小时。之后立即处死小鼠, 用活化的半胱天冬酶3和以下的细胞标记物之一对大脑切片进行双重染色: 神经元的细胞核 (NeuN),  $\gamma$ -氨基丁酸能细胞的谷氨酸脱羧酶 (GAD) 65和67, 还有神经胶质纤维酸性蛋白和星形胶质细胞的S100 $\beta$ 。

#### 结果:

活化的半胱天冬酶3免疫标记显示: 接受异氟醚暴露的七日龄小鼠较对照组, 细胞凋亡普遍增加。对半胱天冬酶3标记的皮质板层 II/III 的细胞进行共聚焦分析表明: 绝大多数细胞在神经元的有丝分裂后期, 也有一些是星形胶质细胞。随后对异氟醚诱导的视觉皮质 (即实质损伤区) 神经元凋亡进行量化。在非麻醉的对照组动物中, 0.08%  $\pm$  0.001%

NeuN标记阳性的 II/III 板层皮质细胞对半胱天冬酶3有免疫反应。相反, 异氟醚暴露后即刻, NeuN标记阳性的神经元凋亡比例增加至少11倍 (95%可信区间的下限), 达到2.0%  $\pm$

0.004% (异氟醚组vs对照组,  $P=0.0017$ )。经异氟醚暴露的动物中, 所有半胱天冬酶3标记阳性的浅表皮层神经元, 其中2.9%  $\pm$  0.02%也共同表达了谷氨酸脱羧酶67

(GAD67), 表明抑制性神经元同样受影响。然而, 对 $\gamma$ -氨基丁酸能神经细胞的分析证明事实更为复杂。除了对一些GAD67免疫反应阳性的神经元诱导凋亡外, 麻醉导致了谷氨酸脱羧酶67 (0.98 vs 1.84 ng/mg 蛋白,  $P < 0.00001$ , 麻醉组与对照组) 和谷氨酸脱羧酶65 (2.25  $\pm$  0.74 vs 23.03  $\pm$  8.47 ng/mg 蛋白,  $P = 0.0008$ , 麻醉组与对照组) 的蛋白水平戏剧性的降低。

**结论:** 长期暴露在异氟醚中会增加7日龄小鼠神经元的凋亡率, 丧失将近2%的皮质神经元, 其中的一些被确定为 $\gamma$ -氨基丁酸能中间神经元。此外通过下调核心酶GAD65 and GAD67表达, 异氟醚暴露也干扰了抑制性中枢神经系统。相反, 在这个年龄组, 只有少

数退化的细胞被认定为星形胶质细胞。在动物身上的这些发现仍然有待进一步确定其临床联系。

(郑华容 译 陈杰 校)

**BACKGROUND:** Accumulating evidence indicates that isoflurane and other, similarly acting anesthetics exert neurotoxic effects in neonatal animals. However, neither the identity of dying cortical cells nor the extent of cortical cell loss has been sufficiently characterized. We conducted the present study to immunohistochemically identify the dying cells and to quantify the fraction of cells undergoing apoptotic death in neonatal mouse cortex, a substantially affected brain region.

**METHODS:** Seven-day-old littermates ( $n = 36$ ) were randomly assigned to a 6-hour exposure to either 1.5% isoflurane or fasting in room air. Animals were euthanized immediately after exposure and brain sections were double-stained for activated caspase 3 and one of the following cellular markers: Neuronal Nuclei (NeuN) for neurons, glutamic acid decarboxylase (GAD)65 and GAD67 for GABAergic cells, as well as GFAP (glial fibrillary acidic protein) and S100 $\beta$  for astrocytes.

**RESULTS:** In 7-day-old mice, isoflurane exposure led to widespread increases in apoptotic cell death relative to controls, as measured by activated caspase 3 immunolabeling. Confocal analyses of caspase 3–labeled cells in cortical layers II and III revealed that the overwhelming majority of cells were postmitotic neurons, but some were astrocytes. We then quantified isoflurane-induced neuronal apoptosis in visual cortex, an area of substantial injury. In unanesthetized control animals,  $0.08\% \pm 0.001\%$  of NeuN-positive layer II/III cortical neurons were immunoreactive for caspase 3. By contrast, the rate of apoptotic NeuN-positive neurons increased at least 11-fold (lower end of the 95% confidence interval [CI]) to  $2.0\% \pm 0.004\%$  of neurons immediately after isoflurane exposure ( $P = 0.0017$  isoflurane versus control). In isoflurane-treated animals,  $2.9\% \pm 0.02\%$  of all caspase 3–positive neurons in superficial cortex also coexpressed GAD67, indicating that inhibitory neurons may also be affected. Analysis of GABAergic neurons, however, proved unexpectedly complex. In addition to inducing apoptosis among some GAD67-immunoreactive neurons, anesthesia also coincided with a dramatic decrease in both GAD67 ( $0.98$  vs  $1.84$  ng/mg protein,  $P < 0.00001$ , anesthesia versus control) and GAD65 ( $2.25 \pm 0.74$  vs  $23.03 \pm 8.47$  ng/mg protein,  $P = 0.0008$ , anesthesia versus control) protein levels.

**CONCLUSIONS:** Prolonged exposure to isoflurane increased neuronal apoptotic cell death in 7-day-old mice, eliminating approximately 2% of cortical neurons, of which some were identified as GABAergic interneurons. Moreover, isoflurane exposure interfered with the inhibitory nervous system by downregulating the central enzymes GAD65 and GAD67. Conversely, at this age, only a minority of degenerating cells were identified as astrocytes. The clinical relevance of these findings in animals remains to be determined.

氯胺酮通过活性氧簇介导的线粒体途径增强人神经干细胞增殖和诱导神经元凋亡

**Ketamine Enhances Human Neural Stem Cell Proliferation and Induces Neuronal Apoptosis via Reactive Oxygen Species–Mediated Mitochondrial Pathway**

Xiaowen Bai, MD, PhD\*, Yasheng Yan, BS\*, Scott Canfield, BS\*†, Maria Y. Muravyeva, MD, PhD\*, Chika Kikuchi, MD\*, Ivan Zaja, MD\*, John A. Corbett, PhD‡ and Zeljko J. Bosnjak, PhD\*†

From the Departments of \*Anesthesiology, †Physiology, and ‡Biochemistry, Medical College of Wisconsin, Milwaukee, Wisconsin.

**背景：**越来越多证据表明，氯胺酮在多种动物模型中引起神经毒性，导致关于儿科麻醉安全性的一系列顾虑。然而氯胺酮是否以及如何引起人类神经细胞毒性仍未知。人胚胎干细胞

(hESCs)神经的体外再现致氯胺酮对神经干细胞(NSCs)以及发育中的神经元毒性效应的观察成为可能，而这些是无法在人类身上试验的。此项研究评估氯胺酮对源于人胚胎细胞的神经干细胞和神经元细胞的影响。

**方法：**人胚胎细胞通过神经干细胞直接分化为神经元。使用不同剂量的氯胺酮对神经干细胞和生长2周的神经元进行不同时间的处理。用Ki67免疫荧光染色和溴脱氧尿苷试验分析神经干细胞的增殖能力。用TUNEL染色和半胱天冬酶3活性测量分析神经凋亡。同时研究线粒体相关的神经元凋亡途径包括线粒体膜电位、细胞内细胞色素C分布、线粒体分裂、活性氧簇产生。

**结果：**在6小时的接触后，氯胺酮(100 $\mu$ M)增加神经干细胞增殖。然而，显著的神经元凋亡只发现于经氯胺酮处理24小时后。另外，氯胺酮降低线粒体膜电位，增加细胞色素C从线粒体到细胞液释放。和对照组相比，氯胺酮也增强线粒体分裂和活性氧簇产生。重要的是，水溶性维生素E，一种活性氧簇清除剂，显著地减弱了氯胺酮引起的活性氧簇产生的增加和神经元凋亡。

**结论：**这些数据首次证实：(1)氯胺酮增加神经干细胞增殖并导致神经元凋亡；(2)线粒体涉及氯胺酮相关的神经元毒性，可被水溶性维生素E拮抗；(3)干细胞相关的神经形成系统可能为快速显示麻醉的神经毒性，研究其潜在机制和为了避免这种毒性效应而研究预防策略提供一个简单而有希望的离体模型。

(詹恺诞 译 陈杰 校)

**BACKGROUND:** Growing evidence indicates that ketamine causes neurotoxicity in a variety of developing animal models, leading to a serious concern regarding the safety of pediatric anesthesia. However, if and how ketamine induces human neural cell toxicity is unknown. Recapitulation of neurogenesis from human embryonic stem cells (hESCs) in vitro allows investigation of the toxic effects of ketamine on neural stem cells (NSCs) and developing neurons, which is impossible to perform in humans. In the present study, we assessed the influence of ketamine on the hESC-derived NSCs and neurons.

**METHODS:** hESCs were directly differentiated into neurons via NSCs. NSCs and 2-week-old neurons were treated with varying doses of ketamine for different durations. NSC proliferation capacity was analyzed by Ki67 immunofluorescence staining and bromodeoxyuridine assay. Neuroapoptosis was analyzed by TUNEL staining and caspase 3 activity measurement. The mitochondria-related neuronal apoptosis pathway including mitochondrial membrane potential, cytochrome c distribution within cells, mitochondrial fission, and reactive oxygen species (ROS) production were also investigated.

**RESULTS:** Ketamine (100  $\mu$ M) increased NSC proliferation after 6-hour exposure. However, significant neuronal apoptosis was only observed after 24 hours of ketamine treatment. In addition, ketamine decreased mitochondrial membrane potential and increased cytochrome c release from mitochondria into cytosol. Ketamine also enhanced mitochondrial fission as well as ROS production compared with no-treatment control. Importantly, Trolox, a ROS scavenger, significantly attenuated the increase of ketamine-induced ROS production and neuronal apoptosis.



**CONCLUSIONS:** These data for the first time demonstrate that (1) ketamine increases NSC proliferation and causes neuronal apoptosis; (2) mitochondria are involved in ketamine-induced neuronal toxicity, which can be prevented by Trolox; and (3) the stem cell-associated neurogenesis system may provide a simple and promising in vitro model for rapidly screening anesthetic neurotoxicity and studying the underlying mechanisms as well as prevention strategies to avoid this toxic effect.

### 自报医疗差错的频率与麻醉培训监督的关系：一项美国麻醉住院医师培训调查

#### **The Association Between Frequency of Self-Reported Medical Errors and Anesthesia Trainee Supervision: A Survey of United States Anesthesiology Residents-in-Training**

Gildasio S. De Oliveira Jr., MD, MSCI, Rod Rahmani, BS, Paul C. Fitzgerald, MS, Ray Chang, BS and Robert J. McCarthy, PharmD

From the Department of Anesthesiology, Northwestern University, Chicago, Illinois.

Anesth Analg 2013;116:892-7

**背景：**对医学实习生缺乏监管导致住院医师教育与病人的护理和安全两方面都受到损害。监管不力可导致接受低年资住院医师治疗的患者死亡率增加。本研究假设自报更多医疗差错的住院医师，较那些报道较低医疗差错的，其受监督质量更低。这项研究主要目的是评估住院医师自报医疗差错的频率和接受机构监督质量之间的关联性。

**方法：**一项横向的全国性调查随机抽取美国麻醉培训部门的1000名住院医师。分别来自122住院医师方案的住院医师都被邀请参加此研究项目，每个机构人数的中位数（四分位间距）为7（4-

11）。参与者被要求完成一项关于人口学统计，对机构监督质量评价，对监督不利原因的调查。回复的陈述包括：“我实施的操作没有得到适当的训练”，“我犯的错误使病人产生不良后果”和“我在过去的一年有过错误用药史（药物种类或剂量错误）”用于评估错误发生率。根据De Oliveira Filho等人量表确定平均监督评分。使用Kruskal-Wallis检验比较自报差错种类的发生频率。

**结果：**640名住院医师对调查作出回答（60.4%）。45名（7.5%）受访者表示他们没有得到适当的训练，24名（4%）受访者报道，医疗差错后患者产生不良后果，16名（3%）受访者在去年多次用药错误或经常发生用错药。监督评分与这3个评估医疗差错问题所报告的差错频率呈负相关。在临界值为3时，用于预测这些问题的发生率，即操作未得到适当训练，医疗差错后患者产生不良后果及过去一年上报错误用药，其监督评分整体精度（曲线下面积）（99%置信区间）分别为0.81（0.73-0.86），0.89（0.77-0.95）和0.93（0.77-0.98）。

**结论：**对患者有不良后果和用药错误相关医疗差错发生率更高的麻醉实习生，其对机构监督的评分也较低。本研究结果表明，对监督和病人安全之间关系进行深入研究是必要的。

（孙晓琼 译 陈杰 校）

**BACKGROUND:** Poor supervision of physician trainees can be detrimental not only to resident education but also to patient care and safety. Inadequate supervision has been associated with more frequent deaths of patients under the care of junior residents. We hypothesized that residents reporting more medical errors would also report lower quality of supervision scores than the ones with lower reported medical errors. The primary objective of this study was to

evaluate the association between the frequency of medical errors reported by residents and their perceived quality of faculty supervision.

**METHODS:** A cross-sectional nationwide survey was sent to 1000 residents randomly selected from anesthesiology training departments across the United States. Residents from 122 residency programs were invited to participate, the median (interquartile range) per institution was 7 (4–11). Participants were asked to complete a survey assessing demography, perceived quality of faculty supervision, and perceived causes of inadequate perceived supervision. Responses to the statements “I perform procedures for which I am not properly trained,” “I make mistakes that have negative consequences for the patient,” and “I have made a medication error (drug or incorrect dose) in the last year” were used to assess error rates. Average supervision scores were determined using the De Oliveira Filho et al. scale and compared among the frequency of self-reported error categories using the Kruskal-Wallis test.

**RESULTS:** Six hundred four residents responded to the survey (60.4%). Forty-five (7.5%) of the respondents reported performing procedures for which they were not properly trained, 24 (4%) reported having made mistakes with negative consequences to patients, and 16 (3%) reported medication errors in the last year having occurred multiple times or often. Supervision scores were inversely correlated with the frequency of reported errors for all 3 questions evaluating errors. At a cutoff value of 3, supervision scores demonstrated an overall accuracy (area under the curve) (99% confidence interval) of 0.81 (0.73–0.86), 0.89 (0.77–0.95), and 0.93 (0.77–0.98) for predicting a response of multiple times or often to the question of performing procedures for which they were not properly trained, reported mistakes with negative consequences to patients, and reported medication errors in the last year, respectively.

**CONCLUSIONS:** Anesthesiology trainees who reported a greater incidence of medical errors with negative consequences to patients and drug errors also reported lower scores for supervision by faculty. Our findings suggest that further studies of the association between supervision and patient safety are warranted. (*Anesth Analg* 2013;116:892–7)

### 适用于麻醉操作人员的时间关键的信息：无线设备的通讯延迟

#### Communication Latencies of Wireless Devices Suitable for Time-Critical Messaging to Anesthesia Providers

Richard H. Epstein, MD, CPHIMS\*, Franklin Dexter, MD, PhD† and Brian Rothman, MD‡

From the \*Department of Anesthesiology, Jefferson Medical College, Philadelphia, Pennsylvania; †Division of Management Consulting, Department of Anesthesia, University of Iowa, Iowa City, Iowa; and ‡Division of Multispecialty Adult Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee.

*Anesth Analg* April 2013 116:911-918;

**背景：**负责麻醉操作的流动工作人员之间拥有快速可靠的文本信息通讯对于患者的护理及有效的手术室管理是重要的。麻醉部门正在实施发送文本信息到移动设备的自动方法，这些文本信息包括：反常的生命体征，临床建议，护理质量，依从性或计费问题。通讯系统最关键的运行时间决定了可接受的最长延迟限度。为确定一个最适合通讯系统，我们对一些数字通信系统的可靠性进行了研究。

**方法：**作者测量了三个数字寻呼设备数周内的文本信息发送及传递延迟程度。其中两种设备使用的是医院局域网外的互联网途径与外部的寻呼通讯（SkyTel）。第三种设备仅使用了医院内部的网络（Zetron）。相继的手机文本信息延迟通Lag1的自相关函数测定，按

照小时和天分级的结果。延迟的消息随后被分批到连续1周的箱子中去计算平均值以及延迟的第99位百分位。验收标准定义为：平均延迟小于30秒并且200个传呼机中不超过1个（0.5%）具有的延迟超过100秒。手机文本被用来做阳性对照，以确保分析是恰当的，因为上述装备（已知的）在高强度网络活动中的可靠性是差的。

**结果：**当按照小时分级时，延迟与手机文本信息的次序有重大的相关性( $P < 0.0001$ )，按照天分级时则没有( $P =$

0.61)。运用医院局域网外的互联网途径的两种设备则展示了让人不能接受的表现，超过100秒的延迟率分别为1.3%与33%。依赖医院内部网络的设备具有平均8秒的延迟，测试的40200个寻呼机均为小于100秒的延迟。这些发现说明何种网络的使用成为延迟的决定因素。

**结论：**麻醉通讯系统的开发需要评估预计通讯路径的延迟时间，以及评估用于传送紧急信息给流动人员的设备。类似的评价与文本传呼机相关，用于临时想法的时间关键信息传递。

超过数小时至数天的测试仅能用于发现不合格的候选传呼系统，因为这个结果并不一定预示长期的表现。相反，数周的测试是必要，将传呼机适当分批进行分析。

（王苑 译 陈杰 校）

**BACKGROUND:** Rapid and reliable methods of text communication to mobile anesthesia care providers are important to patient care and to efficient operating room management. Anesthesia departments are implementing automated methods to send text messages to mobile devices for abnormal vital signs, clinical recommendations, quality of care, and compliance or billing issues. The most time-critical communications determine maximum acceptable latencies. We studied the reliability of several alphanumeric messaging systems to identify an appropriate technology for such use.

**METHODS:** Latencies between message initiation and delivery to 3 alphanumeric paging devices were measured over weeks. Two devices used Internet pathways outside the hospital's local network with an external paging vendor (SkyTel). The third device used only the internal hospital network (Zetron). Sequential cell phone text page latencies were examined for lag-1 autocorrelation using the runs test, with results binned by hour and by day. Message latencies subsequently were batched in successive 1-week bins for calculation of the mean and 99th percentiles of latencies. We defined acceptance criteria as a mean latency  $<30$  seconds and no more than 1 in 200 pages (0.5%) having a latency longer than 100 seconds. Cell phone texting was used as a positive control to assure that the analysis was appropriate, because such devices have (known) poor reliability during high network activity.

**RESULTS:** There was substantial correlation among latencies for sequential cell phone text messages when binned by hours ( $P < 0.0001$ ), but not by days ( $P = 0.61$ ). The 2 devices using Internet pathways outside the hospital's network demonstrated unacceptable performance, with 1.3% and 33% of latencies exceeding 100 seconds, respectively. The device dependent only on the internal network had a mean latency of 8 seconds, with 100% of 40,200 pages having latencies  $<100$  seconds. The findings suggest that the network used was the deciding factor.

**CONCLUSIONS:** Developers of anesthesia communication systems need to measure latencies of proposed communication pathways and devices used to deliver urgent messages to mobile users. Similar evaluation is relevant for text pagers used on an ad hoc basis for delivery of time-critical notifications. Testing over a period of hours to days is adequate only for disqualification of a candidate paging system, because acceptable results are not necessarily indicative of long-

term performance. Rather, weeks of testing are required, with appropriate batching of pages for analysis.

### 在大鼠脊髓背角神经元局部注射异丙酚的抗伤害及抗痛觉过敏效应

#### The Antinociceptive and Antihyperalgesic Effects of Topical Propofol on Dorsal Horn Neurons in the Rat

Kenichi Takechi, MD\*, Mirela Iodi Carstens, BA†, Amanda H. Klein, PhD† and E. Carstens, PhD†

From the \*Department of Anesthesiology and Resuscitology, Ehime University Medical School, Matsuyama, Japan; and †Department of Neurobiology, Physiology and Behavior, University of California, Davis, Davis, California.

Anesth Analg April 2013 116:932-938

**背景：**异丙酚（2,6-

二异丙基苯酚）是用于全身麻醉的一种静脉麻醉药物。最近有证据表明接受异丙酚麻醉的病人术后疼痛较轻，异丙酚在局部注射时具有镇痛的作用。本研究通过行为学方法和电生理学方法对大鼠局部注射异丙酚的抗伤害效应进行研究。

**方法：**在对大鼠的行为学实验中，评估在后足局部注射不同浓度异丙酚（1%-25%）后对热刺激以及机械刺激产生的缩足反应。在电生理实验中，记录被戊巴比妥麻醉的大鼠从腰段脊髓背角的广动力阈（WDR）型神经元相关数据。评估局部注射异丙酚后同侧后足对伤害性热刺激、冷刺激及机械性刺激的神经元反应。同时检测异丙酚是否阻断缩足的热敏化以及局部应用异硫氰酸烯丙酯（AITC）诱导的WDR神经元反应。

**结果：**局部注射异丙酚（1%-25%）显著增加了处理侧（而非对侧）温度刺激产生的缩足反射平均潜伏期，呈浓度相关性，对机械性刺激产生的缩足反射的阈值无效应。异丙酚还避免了AITC诱导的缩足反射潜伏期缩短。在电生理实验中，在同侧后足局部注射10%-25%异丙酚，而非1%异丙酚或赋形剂，使后足无毛区域的皮肤对伤害性热刺激的WDR神经元反应程度显著降低，而对温度的反应阈值无显著变化。对伤害性热刺激产生的反应在注射异丙酚后15min达到最大抑制，在之后30min内恢复至异丙酚应用前水平。各浓度的异丙酚对皮肤冷刺激或分级机械刺激无显著影响。局部注射AITC可显著增加脊髓背角神经元对伤害性热刺激产生的反应。这种在注射AITC后对热刺激反应的增加在局部注射10%异丙酚时被抑制。

**结论：**这些结果证明局部注射异丙酚可以抑制WDR神经元对伤害性热刺激的反应，产生镇痛效应，同时减少了注射AITC后的WDR神经元致敏，具有抗痛觉过敏作用。这些结果与证明接受异丙酚麻醉的外科病人可减少术后疼痛的临床研究结果一致。局部注射异丙酚减少疼痛的机制尚不明确，但可能与表达于外周伤害性神经末梢的TRPV1 or TRPA1受体的去敏感化

有关，同时有内源性大麻酚类的参与或外周γ-氨基丁酸A受体的激活相关。

（瞿亦枫 译 陈杰 校）

**BACKGROUND:** Propofol (2,6-diisopropylphenol) is an IV anesthetic used for general anesthesia. Recent evidence suggests that propofol-anesthetized patients experience less postoperative pain, and that propofol has analgesic properties when applied topically. We

presently investigated the antinociceptive effects of topical propofol using behavioral and single-unit electrophysiological methods in rats.

**METHODS:** In behavioral experiments with rats, we assessed the effect of topical hindpaw application of propofol (1%–25%) on heat and mechanically evoked paw withdrawals. In electrophysiological experiments, we recorded from lumbar dorsal horn wide dynamic range (WDR)-type neurons in pentobarbital-anesthetized rats. We assessed the effect of topical application of propofol to the ipsilateral hindpaw on neuronal responses elicited by noxious heat, cold, and mechanical stimuli. We additionally tested whether propofol blocks heat sensitization of paw withdrawals and WDR neuronal responses induced by topical application of allyl isothiocyanate (AITC; mustard oil).

**RESULTS:** Topical application of propofol (1%–25%) significantly increased the mean latency of the thermally evoked hindpaw withdrawal reflex on the treated (but not opposite) side in a concentration-dependent manner, with no effect on mechanically evoked hindpaw withdrawal thresholds. Propofol also prevented shortening of paw withdrawal latency induced by AITC. In electrophysiological experiments, topical application of 10% and 25% propofol, but not 1% propofol or vehicle (10% intralipid), to the ipsilateral hindpaw significantly attenuated the magnitude of responses of WDR neurons to noxious heating of glabrous hindpaw skin with no significant change in thermal thresholds. Maximal suppression of noxious heat-evoked responses was achieved 15 minutes after application followed by recovery to the pre-propofol baseline by 30 minutes. Responses to skin cooling or graded mechanical stimuli were not significantly affected by any concentration of propofol. Topical application of AITC enhanced the noxious heat-evoked response of dorsal horn neurons. This enhancement of heat-evoked responses was attenuated when 10% propofol was applied topically after application of AITC.

**CONCLUSIONS:** The results indicate that topical propofol inhibits responses of WDR neurons to noxious heat consistent with analgesia, and reduced AITC sensitization of WDR neurons consistent with an antihyperalgesic effect. These results are consistent with clinical studies demonstrating reduced postoperative pain in surgical patients anesthetized with propofol. The mechanism of analgesic action of topical propofol is not clear, but may involve desensitization of TRPV1 or TRPA1 receptors expressed in peripheral nociceptive nerve endings, engagement of endocannabinoids, or activation of peripheral  $\gamma$ -aminobutyric acid A receptors

### 丙泊酚能增强长期使用血管紧张素转换酶抑制剂卡托普利治疗的衰老大鼠血管舒张 Propofol Increases Vascular Relaxation in Aging Rats Chronically Treated with the Angiotensin-Converting Enzyme Inhibitor Captopril

Ferrante S. Gragasin, MD, FRCPC\*†‡§|| , Stephane L. Bourque, PhD‡§|| ¶ and Sandra T. Davidge, PhD†‡§|| ¶

From the Departments of \*Anesthesiology and Pain Medicine, †Physiology, and ¶Obstetrics & Gynecology, University of Alberta; ‡Women and Children's Health Research Institute, §Cardiovascular Research Centre, and || Mazinkowski Alberta Heart Institute, University of Alberta, Edmonton, Alberta, Canada.

Anesth Analg April 2013 116:775-783;

**背景：**丙泊酚的使用以及高龄都是术中低血压的预测因子。以前，我们证明了丙泊酚能增强老龄大鼠肠系膜动脉的血管舒张，在一定程度上是归因于增加了一氧化氮（NO）的生物利用度。长期使用血管紧张素转换酶（ACE）抑制剂的患者可能在全麻下出现难治性

低血压。我们假设丙泊酚对取自于长期使用ACE抑制剂治疗的老鼠动脉增强了NO介导的血管舒张效应。

**方法：**12到13月龄的SD大鼠给予或不给予卡托普利治疗7到8周，在实验的时候产生最后的14至15月龄。在安乐死前，通过颈动脉置管获得动脉血压。用丙泊酚（0.1–100  $\mu\text{M}$ ）或醋甲胆碱（MCh）（0.01–3  $\mu\text{M}$ ）的量效曲线评估取自于治疗组（卡托普利）和对照组大鼠的肠系膜动脉（100–200  $\mu\text{m}$ 直径）的离体阻力。在丙泊酚预处理（1和10  $\mu\text{M}$ ）后也评估MCh舒张效应。用左旋硝基精氨酸甲酯（l-NAME）（100  $\mu\text{M}$ ）以及甲氧基灭酸的结合碱（10  $\mu\text{M}$ ）分别抑制NO和前列腺素的合成。量效数据归纳为50%最大松弛反应或曲线下面积。

**结果：**卡托普利治疗组大鼠的平均动脉压低于未治疗组大鼠（ $P = 0.049$ ）。在比较卡托普利治疗组和未治疗组大鼠的动脉舒张时，量效曲线表明卡托普利治疗组大鼠显示出更加直接的丙泊酚舒张效应（ $P = 0.018$ ）。然而，缺少丙泊酚的MCh舒张在卡托普利治疗组和未治疗组大鼠中没有区别（ $P = 0.80$ ）。卡托普利治疗组和未治疗组大鼠相比，丙泊酚预处理增强了MCh的动脉舒张效应（1  $\mu\text{M}$ 时 $P = 0.029$ 和10  $\mu\text{M}$ 时 $P = 0.020$ ）。在这个反应中甲氧基灭酸的结合碱没有作用（ $P = 0.22$ ）。然而，和卡托普利治疗组大鼠相比较，对照组对动脉中MCh舒张效应的l-NAME依赖性抑制作用较大（ $P = 0.0077$ ）。然而在两组中，相对于丙泊酚增加的对MCh的NO依赖性血管舒张比例是相似的。这表明在卡托普利治疗组大鼠中存在丙泊酚时，对MCh的不同效应涉及了其他血管舒张途径。

**结论：**我们的结果显示，丙泊酚产生的肠系膜动脉舒张效应是直接刺激和通过内皮依赖性机制的调节的结果，其在一定程度上是NO依赖性的。在卡托普利治疗组大鼠中，丙泊酚通过非NO依赖性血管舒张途径（例如内皮衍生超极化因子）进一步增强了动脉舒张效应，这可能能解释对用ACE抑制剂治疗的病人给予丙泊酚时血管舒张效应增强。

（唐莹译 马皓琳 李士通校）

**BACKGROUND:** Both propofol use and advanced age are predictors of intraoperative hypotension. We previously demonstrated that propofol enhances vasodilation in mesenteric arteries from aged rats, partly due to increased nitric oxide (NO) bioavailability. Patients chronically treated with angiotensin-converting enzyme (ACE) inhibitors may exhibit refractory hypotension under general anesthesia. We hypothesized that propofol enhances NO-mediated vasodilation in arteries from aged rats chronically treated with ACE inhibitors.

**METHODS:** Sprague-Dawley rats aged 12 to 13 months were treated with or without captopril for 7 to 8 weeks, yielding a final age of 14 to 15 months at the time of experimentation. Before euthanasia, arterial blood pressures were obtained through carotid artery cannulation.

Concentration-response curves to propofol (0.1–100  $\mu\text{M}$ ) or methacholine (MCh) (0.01–3  $\mu\text{M}$ ) were then assessed on isolated resistance mesenteric arteries (100–200  $\mu\text{m}$  diameter) from both treatment (captopril) and control rats. MCh relaxation was also assessed after propofol pretreatment (1 and 10  $\mu\text{M}$ ).  $N^G$ -nitro-l-arginine methyl ester (l-NAME) (100  $\mu\text{M}$ ) and meclofenamate (10  $\mu\text{M}$ ) were used to inhibit NO and prostaglandin synthesis, respectively. Concentration-response data were summarized as 50% of the maximum relaxation response or area under the curve.

**RESULTS:** Mean arterial blood pressure in the captopril-treated rats was lower than in untreated rats ( $P = 0.049$ ). When comparing relaxation in arteries from captopril-treated versus untreated rats, concentration-response curves revealed that captopril-treated rats display greater direct propofol relaxation ( $P = 0.018$ ). MCh relaxation in the absence of propofol, however, was not different between captopril-treated and untreated rats ( $P = 0.80$ ). Propofol pretreatment increased MCh relaxation in arteries from captopril-treated compared with untreated rats ( $P = 0.029$  for 1  $\mu\text{M}$  and  $P = 0.020$  for 10  $\mu\text{M}$ ). Meclofenamate did not have an effect in this response ( $P = 0.22$ ). l-NAME-dependent inhibition of MCh relaxation, however, was greater in arteries from control compared with captopril-treated rats ( $P = 0.0077$ ). However, propofol increased the proportion of NO-dependent vasodilation to MCh similarly in both groups. This suggests that other vasodilatory pathways are involved in the differential response to MCh in the presence of propofol in captopril-treated rats.

**CONCLUSIONS:** Our results show that mesenteric arterial relaxation in response to propofol, both by direct stimulation and through modulation of endothelium-dependent mechanisms, is, in part, NO-dependent. In captopril-treated rats, propofol further increased arterial relaxation through a non-NO-dependent vasodilating pathway (e.g., endothelium-derived hyperpolarizing factor), which may account for enhanced vasodilation during propofol exposure in patients treated with ACE inhibitors.

### **TASK-1 (KCNK3) 和 TASK-3 (KCNK9) 双孔钾离子通道拮抗剂对异氟醚麻醉大鼠的呼吸刺激作用**

#### **TASK-1 (KCNK3) and TASK-3 (KCNK9) Tandem Pore Potassium Channel Antagonists Stimulate Breathing in Isoflurane-Anesthetized Rats**

Joseph F. Cotten, MD, PhD

From the Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts.

Anesth Analg April 2013 116:810-816;

**背景：**TASK-1和TASK-

3双孔钾离子通道亚单位在结构上产生酸性pH值和缺氧抑制性钾电导。TASK通道在许多参与呼吸调节的组织上均有表达，且TASK-1/TASK-

3异源二聚体在颈动脉体1型血管球化学感受细胞上产生缺氧敏感占优势的钾电导。颈动脉体在呼吸调节中起重要作用。多沙普仑是一种强效的TASK-1和TASK-

3钾通道拮抗剂，也是颈动脉体和呼吸兴奋剂。PK-THPP和A1899是强效选择性的TASK-1和TASK-3拮抗剂。本研究提出如下假说：PK-

THPP和A1899是与多沙普仑类似的呼吸兴奋剂。

**方法：**利用Fisher大鼠甲状腺单层细胞，通过尤斯灌流室研究大鼠TASK-

3钾通道功能。并通过无创体积描记法和动脉血气分析，研究雄性SD大鼠在室内空气中自主呼吸1.5%异氟醚的情况，以定量呼吸效应。

**结果：**PK-THPP、A1899和多沙普仑可抑制大鼠TASK-

3钾通道的功能，半抑制浓度分别为42 nM (33–52)、1.6  $\mu\text{M}$  (0.8–3.3)和22  $\mu\text{M}$  (18–28) ( $n = 4–6$ ；95%可信区间)。体积描记术显示，静脉注射PK-

THPP、A1899和多沙普仑产生的呼吸刺激使每分钟通气量出现峰值变化，与基线相比分

别为 $84\% \pm 19\%$ 和 $226\% \pm 56\%$  (PK-THPP为0.5和5 mg/kg时；均值 $\pm$ 标准误； $n = 3-4$ ；与空白溶剂对照相比分别 $P < 0.05$ 和 $P < 0.001$ )； $46\% \pm 2\%$ 和 $236\% \pm 48\%$  (A1899为5和25 mg/kg时； $n = 3-4$ ；分别 $P > 0.05$  and  $P < 0.001$ )； $103\% \pm 20\%$  (多沙普仑25 mg/kg； $n = 4$ )，以及 $33\% \pm 9\%$  (二甲亚砷溶剂1 mL/kg； $n = 4$ )。血气分析显示，与多沙普仑不同，PK-THPP和A1899产生强大且持久的呼吸性碱中毒。静脉给药30分钟后，发现动脉pH值和PaCO<sub>2</sub>分别为 $7.62 \pm 0.02$ 和 $23 \pm 0.8$  mm Hg (PK-THPP 5 mg/kg后； $n = 4$ ；与溶剂相比 $P$ 均 $< 0.001$ )、 $7.49 \pm 0.02$ 和 $31 \pm 2$  mm Hg (A1899 25 mg/kg后； $n = 6$ ； $P$ 分别 $< 0.05$ 和 $0.001$ )、 $7.43 \pm 0.03$ 和 $39 \pm 4$  mm Hg (多沙普仑25 mg/kg后； $n = 4$ ；两者 $P > 0.05$ )以及 $7.38 \pm 0.03$ 和 $48 \pm 4$  mm Hg (二甲亚砷溶剂1 mL/kg后； $n = 3$ )。

**结论：**PK-THPP和A1899是强效的大鼠TASK-3拮抗剂和有效的呼吸兴奋剂。PK-THPP和A1899对呼吸影响的强度和/或持续时间均大于多沙普仑。PK-THPP和A1899或相关化合物可能具有治疗呼吸系统疾病的潜力。

(陈彬彬 译，马皓琳、李士通 校)

**BACKGROUND:** TASK-1 and TASK-3 tandem pore potassium channel subunits provide a constitutive acidic pH- and hypoxia-inhibited potassium conductance. TASK channels are expressed in a number of tissues involved in regulation of breathing, and the TASK-1/TASK-3 heterodimer provides the predominant hypoxia-sensitive potassium conductance in carotid body type 1 glomus chemosensing cells. The carotid bodies have an important role in regulation of breathing. Doxapram is a potent TASK-1 and TASK-3 potassium channel antagonist and a carotid body and breathing stimulant. PK-THPP and A1899 are potent and selective TASK-1 and TASK-3 antagonists. I hypothesized PK-THPP and A1899 are, like doxapram, breathing stimulants.

**METHODS:** I studied rat TASK-3 potassium channel function by Ussing chamber using Fischer rat thyroid monolayers. To quantify breathing effects, I studied male Sprague–Dawley rats spontaneously breathing 1.5% isoflurane in room air by noninvasive plethysmography and by arterial blood gas analysis.

**RESULTS:** PK-THPP, A1899, and doxapram inhibit rat TASK-3 potassium channel function with IC<sub>50</sub>s of 42 nM (33–52), 1.6  $\mu$ M (0.8–3.3), and 22  $\mu$ M (18–28) ( $n = 4-6$ ; 95% confidence limits). IV PK-THPP, A1899, and doxapram stimulated breathing by plethysmography with a peak change in minute ventilation relative to baseline of  $84\% \pm 19\%$  and  $226\% \pm 56\%$  (for PK-THPP at 0.5 and 5 mg/kg; mean  $\pm$  SEM;  $n = 3-4$ ;  $P < 0.05$  and  $P < 0.001$ , respectively, relative to vehicle);  $46\% \pm 2\%$  and  $236\% \pm 48\%$  (for A1899 at 5 and 25 mg/kg;  $n = 3-4$ ;  $P > 0.05$  and  $P < 0.001$ , respectively);  $103\% \pm 20\%$  (for doxapram at 25 mg/kg;  $n = 4$ ), and  $33\% \pm 9\%$  (for dimethylsulfoxide vehicle at 1 mL/kg;  $n = 4$ ). PK-THPP and A1899, unlike doxapram, induced a profound and lasting respiratory alkalosis by arterial blood gas analysis. Thirty minutes after IV drug administration, I observed an arterial pH and carbon dioxide partial pressure of  $7.62 \pm 0.02$  and  $23 \pm 0.8$  mm Hg (for PK-THPP after 5 mg/kg;  $n = 4$ ;  $P < 0.001$  for both relative to vehicle),  $7.49 \pm 0.02$  and  $31 \pm 2$  mm Hg (for A1899 at 25 mg/kg;  $n = 6$ ;  $P < 0.05$  and  $0.001$ , respectively),  $7.43 \pm 0.03$  and  $39 \pm 4$  mm Hg (for doxapram after 25 mg/kg;  $n = 4$ ;  $P > 0.05$  for both), and  $7.38 \pm 0.03$  and  $48 \pm 4$  mm Hg (for dimethylsulfoxide vehicle after 1 mL/kg;  $n = 3$ ).

**CONCLUSIONS:** PK-THPP and A1899 are potent rat TASK-3 antagonists and effective breathing stimulants. PK-THPP and A1899 effects on breathing were of greater magnitude and/or duration relative to that of doxapram. PK-THPP and A1899 or related compounds may have therapeutic potential for treating breathing disorders.



## 麻醉对幼猪模型中血管加压素调节脑血流作用的影响

### The Anesthetic Effects on Vasopressor Modulation of Cerebral Blood Flow in an Immature Swine Model

Benjamin Bruins, MD\*, Todd J. Kilbaugh, MD\*, Susan S. Margulies, PhD† and Stuart H. Friess, MD‡

From the \*Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; †Department of Bioengineering, University of Pennsylvania, Philadelphia, Pennsylvania; and ‡Department of Pediatrics, Washington University in St. Louis School of Medicine, St. Louis, Missouri.

Anesth Analg April 2013 116:838-844

**背景：**各种镇静剂和麻醉药对儿童脑血流（CBF）的升压调节作用的影响目前还不清楚。在成人中，已经描述了异氟醚降低CBF的程度比芬太尼和咪达唑仑小。大多数神经重症监护的大型动物模型使用吸入麻醉药麻醉。涉及CBF调节的调查将改善模型的可译性：更接近于目前儿科重症监护病房的常例。

**方法：**

15只4周龄仔猪采用2个麻醉方案中的一个：全凭静脉麻醉（TIVA）（咪达唑仑1mg/kg/h和芬太尼100μg/kg/h， $n = 8$ ）或ISO（异氟醚1.5%-2%和芬太尼100μg/kg/h中， $n = 7$ ）。当给予仔猪剂量逐步增大的精氨酸加压素、去甲肾上腺素（NE）和去氧肾上腺素（PE）时，连续监测平均动脉血压、颅内压（ICP）、CBF和脑组织氧分压。

**结果：**尽管ISO组的基线脑灌注压较低（ $45 \pm 11$ 比 $71 \pm 11$  mmHg;  $P$

$< 0.0005$ ），两组的基线CBF相似（ISO  $38 \pm 10$ 比TIVA

$35 \pm 26$  mL/100g/min）。结果显示PE和NE使ISO组仔猪的ICP升高（ $11 \pm 4$ 比 $16 \pm 4$  mmHg和 $11 \pm 8$ 比 $18 \pm 5$  mmHg， $P$

$< 0.05$ ）。但在TIVA组，只有当最大剂量值与基线数据比较时PE才使ICP升高（ $11 \pm 4$ 和 $15 \pm 5$  mmHg， $P < 0.05$ ）。当给予仔猪NE和PE（ $P$

$< 0.05$ ）时，标准化的CBF显示出与麻醉组和血管加压素剂量有关的统计学上的显著增加（ $P < 0.05$ ），提示ISO会损害脑血流的自动调节，但TIVA不会。

**结论：**与吸入麻醉药相比较，使用以麻醉性镇痛药—苯二氮卓类药物为基础的麻醉方案时，升压药对CBF的影响是有限的，这与自动调节机制的保持是一致的。麻醉药物的选择，对于调查脑血管血液动力学机制和在实验室和临床床旁之间转化重症监护调查研究是至关重要的。

（方斌 译 马皓琳 李士通 校）

**BACKGROUND:** The effect of various sedatives and anesthetics on vasopressor modulation of cerebral blood flow (CBF) in children is unclear. In adults, isoflurane has been described to decrease CBF to a lesser extent than fentanyl and midazolam. Most large-animal models of neurocritical care use inhaled anesthetics for anesthesia. Investigations involving modulations of CBF would have improved translatability within a model that more closely approximates the current practice in the pediatric intensive care unit.

**METHODS:** Fifteen 4-week-old piglets were given 1 of 2 anesthetic protocols: total IV anesthesia (TIVA) (midazolam 1 mg/kg/h and fentanyl 100 μg/kg/h,  $n = 8$ ) or ISO (isoflurane 1.5%–2% and fentanyl 100 μg/kg/h,  $n = 7$ ). Mean arterial blood pressure, intracranial pressure

(ICP), CBF, and brain tissue oxygen tension were measured continuously as piglets were exposed to escalating doses of arginine vasopressin, norepinephrine (NE), and phenylephrine (PE).

**RESULTS:** Baseline CBF was similar in the 2 groups (ISO  $38 \pm 10$  vs TIVA  $35 \pm 26$  mL/100 g/min) despite lower baseline cerebral perfusion pressure in the ISO group ( $45 \pm 11$  vs  $71 \pm 11$  mm Hg;  $P < 0.0005$ ). Piglets in the ISO group displayed increases in ICP with PE and NE ( $11 \pm 4$  vs  $16 \pm 4$  mm Hg and  $11 \pm 8$  vs  $18 \pm 5$  mm Hg;  $P < 0.05$ ), but in the TIVA group, only exposure to PE resulted in increases in ICP when comparing maximal dose values with baseline data ( $11 \pm 4$  vs  $15 \pm 5$  mm Hg;  $P < 0.05$ ). Normalized CBF displayed statistically significant increases regarding anesthetic group and vasopressor dose when piglets were exposed to NE and PE ( $P < 0.05$ ), suggesting an impairment of autoregulation within ISO, but not TIVA.

**CONCLUSION:** The vasopressor effect on CBF was limited when using a narcotic-benzodiazepine-based anesthetic protocol compared with volatile anesthetics, consistent with a preservation of autoregulation. Selection of anesthetic drugs is critical to investigate mechanisms of cerebrovascular hemodynamics, and in translating critical care investigations between the laboratory and bedside.

### 一个随机试验：开颅幕上脑肿瘤切除术中两种不同剂量的甘露醇降颅压效果的比较

#### A Comparison of Two Doses of Mannitol on Brain Relaxation During Supratentorial Brain Tumor Craniotomy: A Randomized Trial

Charlotte Quentin, MD\*, Sonia Charbonneau, MD\*, Robert Moundjian, MD†, Alexandre Lallo, MD\*, Alain Bouthilier, MD†, Marie-Pierre Fournier-Gosselin, MD†, Michel Bojanowski, MD†, Monique Ruel, RN\*, Marie-Pierre Sylvestre, PhD‡ and Francois Girard, MD\*

From the Departments of \*Anesthesiology and †Surgery, Montreal University Medical Center; and ‡Research Center, Montreal University Medical Centre, Montreal, Quebec, Canada.

Anesth Analg April 2013 116:862-868

**背景：**虽然20%的甘露醇已广泛用来减少脑容积以便于颅内手术的手术操作，但是还没有建立量效关系。在这个研究中，我们比较了择期幕上脑肿瘤切除术中0.7和1.4 g kg<sup>-1</sup>的甘露醇降颅压的效果。

**方法：**在这个前瞻性、随机、双盲研究中我们挑选了80个行开颅幕上脑肿瘤切除术的病人。病人分成了两组：在手术划皮时分别给予20%甘露醇0.7 g kg<sup>-1</sup> (L组)和1.4 g kg<sup>-1</sup> (H组)

。在划开硬脑膜后立即评估脑松弛水平，并分为1到4四个等级（1：完美的松弛，2：满意的松弛，3：脑硬，4：脑膨胀）。

**结果：**两组间病人的性别、年龄、体重指数、肿瘤位置和大小没有明显差异。有52.5%的L组病人和77.5%的H组病人有中线偏移( $P = 0.03$ )。L组和H组病人脑松弛状态的得分中位数（四分位数间距）分别是2.0（1.75—3）和2.0（1—3）（ $P = 0.16$ ）。然后我们用一种比例比数模型来调整这种偏态分布并评估分组（低剂量比高剂量甘露醇）对脑松弛得分的影响。在调整中线偏移的时候，更大剂量的甘露醇的使用导致了一个2.5 ( $P =$

0.03)的比值比。这就说明：在纠正了中线偏移的影响以后，在高剂量甘露醇组中脑松弛

评分达到1分水平的改善的可能性是低剂量组的2.5倍。中线偏移的比值比为0.29( $P = 0.007$ )，说明其发生使得到较低的平均松弛评分的可能性更高。

**结论：**在这个研究中我们发现：在开颅幕上脑肿瘤切除术中的患者，1.4

$\text{g kg}^{-1}$ 的20%甘露醇降颅压的效果和0.7

$\text{g kg}^{-1}$ 甘露醇是相同的。在纠正了中线偏移的影响以后，这个研究显示高剂量甘露醇组的病人比低剂量组达到更好的脑松弛评分的机会显著更大。

(王慧娟 译 马皓琳 李士通 校)

**BACKGROUND:** Twenty percent mannitol is widely used to reduce brain bulk and facilitate the surgical approach in intracranial surgery. However, a dose-response relationship has not yet been established. In this study, we compared the effects of 0.7 and 1.4  $\text{g kg}^{-1}$  mannitol on brain relaxation during elective supratentorial brain tumor surgery.

**METHODS:** In this prospective, randomized, double-blind study, we enrolled 80 patients undergoing supratentorial craniotomy for tumor resection. Patients were assigned to receive 0.7  $\text{g kg}^{-1}$  (group L) or 1.4  $\text{g kg}^{-1}$  (group H) of 20% mannitol at surgical incision. Brain relaxation was assessed immediately after opening of the dura on a scale ranging from 1 to 4 (1 = perfectly relaxed, 2 = satisfactorily relaxed, 3 = firm brain, 4 = bulging brain).

**RESULTS:** There was no significant difference between the 2 groups regarding age, sex, body mass index, and brain tumor localization or size. In group L 52.5% of patients and in group H 77.5% of patients presented a midline shift ( $P = 0.03$ ). The median scores of brain relaxation (interquartile range) were 2.0 (1.75–3) and 2.0 (1–3) ( $P = 0.16$  for patients in group L and H, respectively). We then used a proportional odds model to adjust for this unbalanced distribution and to assess the group effect (low-dose versus high-dose mannitol) on brain relaxation scores. When adjusted for the presence of midline shift, the use of a higher dose of mannitol resulted in an odds ratio of 2.5 ( $P = 0.03$ ). This indicates that, considering the effect of a midline shift, the odds of having a 1-level improvement in relaxation score in patients who received a higher dose of mannitol (group H) was 2.5 times as large as the odds for the low-dose group. The odds ratio of 0.29 ( $P = 0.007$ ) for the midline shift indicates that its occurrence was associated with a higher probability of a lower relaxation score, on average.

**CONCLUSION:** In this study, we show that 1.4  $\text{g kg}^{-1}$  of 20% mannitol results in equivalent brain relaxation scores as 0.7  $\text{g kg}^{-1}$  in patients undergoing craniotomy for supratentorial brain tumor. When corrected for the presence of midline shift, this study reveals that patients in the high-dose group had significantly more chances of obtaining a better relaxation score compared with the lower-dose group.

### 用明确的回忆评估术中知晓:两种方法的比较

#### Assessment of Intraoperative Awareness with Explicit Recall: A Comparison of 2 Methods

George A. Mashour, MD, PhD\*, Christopher Kent, MD†, Paul Picton, MB, ChB, MRCP,

FRCA\*, Satya Krishna Ramachandran, MD, FRCA\*, Kevin K. Tremper, PhD, MD\*,

Christopher R. Turner, MD, PhD, MBA‡, Amy Shanks, MS\* and Michael S. Avidan, MBBCh§

From the \*Department of Anesthesiology, University of Michigan, Ann Arbor, Michigan;

†Department of Anesthesiology and Pain Medicine, University of Washington, Seattle,

Washington; ‡Department of Anesthesiology, Bay Area Medical Center, Marinette, Wisconsin;

and §Department of Anesthesiology, Washington University, St. Louis, Missouri.

Anesth Analg April 2013 116:889-891

背景:对于用明确的回忆发现术中知晓,修改的Brice访视与质量保障技术相比的优越性还未被明确证明。

方法:我们研究了一个患者群来比较用一个修改的Brice访视(术后28-30天)和质量保障数据(术后1天)对明确知晓的发现。

结果:以修订的Brice访视为基础的知晓发生率为19/18847或0.1%。更少的意识情况(发生率0.02%)由质量保障方法发现的知晓例数较少(发生率0.02%)( $P < 0.0001$ )。

结论:对于用明确的回忆评估术中知晓,修订的Brice访视是较适合的方法。

(王晓莉译 马皓琳 李士通校)

**BACKGROUND:** Superiority of the modified Brice interview over quality assurance techniques in detecting intraoperative awareness with explicit recall has not been demonstrated definitively.

**METHODS:** We studied a single patient cohort to compare the detection of definite awareness using a single modified Brice interview (postoperative day 28–30) versus quality assurance data (postoperative day 1).

**RESULTS:** The incidence of awareness based on the modified Brice interview was 19 per 18,847 or 0.1%. Fewer awareness cases (incidence 0.02%) were detected by the quality assurance approach ( $P < 0.0001$ ).

**CONCLUSION:** The modified Brice interview is the preferred modality for assessing intraoperative awareness with explicit recall.

### 一个三级医疗中心成人及儿童手术期间用基于计算机的麻醉呼叫系统紧急呼叫的特点

#### Characteristics of Emergency Pages Using a Computer-Based Anesthesiology Paging System in Children and Adults Undergoing Procedures at a Tertiary Care Medical Center

Toby N. Weingarten, MD\*, John P. Abenstein, MD, MSEE†, Claire H. Dutton, SRNA‡, Melinda A. Kohn, SRNA‡, Elizabeth A. Lee, SRNA‡, Tami E. Mullenbach, SRNA‡, Bradley J. Narr, MD\*, Darrell R. Schroeder, MS§ and Juraj Sprung, MD, PhD\*

From the \*Division of Multispecialty Anesthesia, †Division of Cardiovascular/Thoracic Anesthesia, ‡Mayo School of Health Sciences, and §Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, Minnesota.

Anesth Analg April 2013 116:904-910

**背景:** 在我们的大型学术监督实践中,主治麻醉医师同时要看顾几个患者。为了管理手术室里的通讯,我们使用的是专门的基于电子计算机麻醉可视呼叫系统。该系统在需要紧急帮助时会发出一个紧急呼叫来警示主治麻醉医师及其他可用人员。我们对成人及儿童的术中紧急呼叫的特点进行了分析。

**方法:** 我们选取了在总手术室内的从2005年1月1日到2010年7月31日的全部紧急呼叫激活情况。对电子医疗记录中的呼叫发生率和特点(诸如原发病、进行的干预及预后)进行了回顾。

**结果:** 在研究期间,共实施258,135例麻醉(儿童 $n=32103$ ,年龄小于18岁),其中有370次紧急呼叫记录(成人 $n=309$ ,儿童 $n=61$ )(1.4‰;95%可信区间,1.3-1.6)。对于婴儿的紧急呼叫激活的发生率最高(9.4‰,95%可信区间,5.7-14.4)(与其他年龄组相比 $P < 0.001$ )。在成人,最常见的原因因为血流动力学事件(55%),在儿童则为呼吸及气道事件(60.7%)。

**结论：**在年龄大于2岁的患者中紧急呼叫较少。尽管婴儿和1-2岁儿童两个年龄组均由接受过婴幼儿麻醉专业训练的麻醉医师看顾，婴儿较1-2岁的小儿仍更易出现紧急呼叫激活。

（王赞 译 马皓琳 李士通 校）

**BACKGROUND:** In our large academic supervisory practice, attending anesthesiologists concomitantly care for multiple patients. To manage communications within the procedural environment, we use a proprietary electronic computer-based anesthesiology visual paging system. This system can send an emergency page that instantly alerts the attending anesthesiologist and other available personnel that immediate help is needed. We analyzed the characteristics of intraoperative emergency pages in children and adults.

**METHODS:** We identified all emergency page activations between January 1, 2005 and July 31, 2010 in our main operating rooms. Electronic medical records were reviewed for rates and characteristics of pages such as primary etiology, performed interventions, and outcomes.

**RESULTS:** During the study period, 258,135 anesthetics were performed ( $n = 32,103$  children, younger than 18 years) and 370 emergency pages ( $n = 309$  adults,  $n = 61$  children) were recorded (1.4 per 1000 cases; 95% confidence interval, 1.3–1.6). Infants had the highest rates (9.4 per 1000; 95% confidence interval, 5.7–14.4) of emergency page activations ( $P < 0.001$  compared with each other age group). In adults, the most frequent causes were hemodynamic (55%), and in children respiratory and airway (60.7%) events.

**CONCLUSION:** Emergency pages were rare in patients older than 2 years. Infants were more likely than children 1 to 2 years of age to have emergency page activation, despite both groups being cared for by pediatric fellowship trained anesthesiologists.

### 一篇关于麻醉医生面对肿瘤细胞减灭术和热灌注腹腔化疗的概述

#### **An Overview of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion for the Anesthesiologist**

Christopher Allen-John Webb, MD, Paul David Weyker, MD, Vivek K. Moitra, MD and Richard K. Raker, MD

From the Department of Anesthesiology, Columbia University College of Physicians & Surgeons, Columbia University Medical Center, New York, New York.

Anesth Analg April 2013 116:924-931

当病人需要进行肿瘤细胞减灭术和热灌注腹腔化疗时，对麻醉医生来讲是一种围术期挑战。为了更好的管理这类病人，麻醉医生不但需要掌握常用化疗药物的基本知识，还必须了解手术治疗要达到的目标和目的。对于进行肿瘤细胞减灭术和热灌注腹腔化疗病人的最优化麻醉管理需要控制一系列生理机制间复杂的相互作用，包括高温、腹内高压、电解质紊乱、凝血异常、心指数增大、氧耗量增加和全身血管阻力降低。由于这类手术继续在肿瘤外科医生间得到普及，需要实施明确阐述化学、药代动力学、药效动力学和效应终点的进一步研究来阐明最优化围术期管理。

（张怡 译 马皓琳 李士通 校）

Anesthesiologists face several perioperative challenges when patients need cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion. To adequately care for these patients, anesthesiologists must understand the goals and objectives of the operation in addition to having a basic knowledge of the chemotherapeutic drugs that are frequently used. Optimal anesthetic management of patients treated with cytoreductive surgery and hyperthermic intraperitoneal

chemoperfusion requires control of a complex interplay of physiologic mechanisms, including hyperthermia, abdominal hypertension, electrolyte abnormalities, coagulopathies, increased cardiac index, oxygen consumption, and decreased systemic vascular resistance. As this surgery continues to gain popularity among oncologic surgeons, further studies that clearly define the chemistry, pharmacokinetics, pharmacodynamics, and end points of efficacy need to be performed to elucidate optimal perioperative management.

### 在大鼠模型中麻黄素和布比卡因或利多卡因联合用于脊麻显示有协同性的运动阻滞 **Ephedrine Shows Synergistic Motor Blockade When Combined with Bupivacaine or Lidocaine for Spinal Anesthesia in a Rat Model**

Alimorad G. Djalali, MD, PhD\*, Jeffrey Chi-Fei Wang, MD†, Jose Ramon Perez-Valdivieso, MD, PhD‡, Thomas Danninger, MD§, Gerhard Fritsch, MD§, David Zurakowski, PhD|| ¶ and Peter Gerner, MD§

From the \*Department of Anesthesia, Stanford University School of Medicine, Stanford, California; †Pain Research Center, Department of Anesthesia, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts; ‡Department of Anesthesia and Critical Care, Clinica Universidad de Navarra, University of Navarra, Spain; §Department of Anesthesiology, Perioperative Medicine and Critical Care Medicine, Paracelsus Medical University, Salzburg, Austria; and Departments of || Anesthesia and ¶Surgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts.

Anesth Analg April 2013 116:944-948;

**背景：**麻黄素是一种直接/间接血管活性药物。此外，麻黄素还有内在的局部麻醉作用，主要是因其对钠离子通道的阻滞作用。本文旨在研究麻黄素与布比卡因或利多卡因通过脊髓导管注射入大鼠的脊髓腔时的协同作用。

**方法：**通过手术置入脊髓导管到47个大鼠身上（每组8个，7个排除）。定容60μL不同浓度的麻黄素、布比卡因、利多卡因通过脊髓导管注射以测定每种药物的均等势。然后麻黄素与布比卡因或利多卡因组合注射入脊髓导管。

**结果：**麻黄素和布比卡因或利多卡因在固定的配比下均有显著的协同作用。对于麻黄素和布比卡因有显著协同作用的合用指数为0.792（95%置信区间为：0.665-0.919），而麻黄素和利多卡因的合用指数为0.663（95%置信区间为：0.532-0.794）。

**结论：**麻黄素和布比卡因或利多卡因联合应用均能协同阻滞运动机能，这可能会减少脊麻所需要的局部麻醉药用量。麻黄素与局部麻醉剂的协同作用是一个有趣的药理学现象，需要进一步的临床评价。

（赵晓译 马皓琳 李士通 校）

**BACKGROUND:** Ephedrine is a direct/indirect vasoactive drug. In addition, it also possesses intrinsic local anesthetic properties, mainly due to its sodium-channel blockage. We investigated whether ephedrine demonstrates a synergistic effect with bupivacaine and lidocaine when injected via a spinal catheter into the spinal space of rats.

**METHODS:** Spinal catheters were surgically placed in 47 rats ( $n = 8$  per group; 7 rats were excluded.) Bupivacaine, lidocaine, and ephedrine in various concentrations and constant volumes (60 μL) were injected into the spinal catheters to determine the equipotency of each drug. Ephedrine in combination with either bupivacaine or lidocaine was then injected into the spinal catheters.

**RESULTS:** Ephedrine demonstrated statistically significant synergistic effects with bupivacaine as well as with lidocaine in fixed combinations. The combination index reflecting a synergistic effect was 0.792 (95% confidence interval: 0.665–0.919) for ephedrine + bupivacaine and 0.663 (95% confidence interval: 0.532–0.794) for ephedrine + lidocaine.

**CONCLUSION:** Ephedrine combined with either bupivacaine or lidocaine acted synergistically to block motor function and has the potential to reduce the amount of local anesthetic needed for spinal block. The synergistic effect of ephedrine in combination with local anesthetics is an interesting pharmacological phenomenon that warrants further clinical evaluation.

### 在健康人中，用七氟醚实施全身麻醉能够减少心脏容量及充血时血流速度

#### General Anesthesia with Sevoflurane Decreases Myocardial Blood Volume and Hyperemic Blood Flow in Healthy Humans

Carolien S. E. Bulte, MD\*, Jeroen Slikkerveer, MD†, Otto Kamp, MD, PhD†, Martijn W. Heymans, PhD‡, Stephan A. Loer, MD, PhD\*, Stefano F. de Marchi, MD§, Rolf Vogel, MD, PhD||, Christa Boer, PhD\* and R. Arthur Bouwman, MD, PhD\*

+Author Affiliations

From the Departments of \*Anesthesiology, †Cardiology, and ‡Epidemiology and Biostatistics, Institute for Cardiovascular Research, VU University Medical Center, Amsterdam, The Netherlands; §Department of Cardiology, Bern University Hospital, Bern; and || Department of Cardiology and ARTORG Cardiovascular Engineering, Bern University Hospital and University of Bern, Bern, Switzerland.

Anesth Analg April 2013 116:767-774

**背景：**全身麻醉时心肌灌注保护措施对于围术期引起心脏并发症风险方面很重要。有关全身麻醉在正常心肌循环影响的数据有限。在这项研究中，应用七氟醚实施全身麻醉，并在外科手术前，我们研究了心肌循环对药物扩张血管及交感刺激后的反应。

**方法：**六位女性和七位男性（平均年龄43岁，在28~61岁之间）参与了该项研究，并记录清醒时的基本数据及给予七氟醚1个最小肺泡有效溶度后的数据，应用心肌造影超声心动图，评估静息状态、腺苷诱导的心脏充血状态及冷加压实验所致的交感刺激时心肌血流速度计微循环的变化。心脏血流量等于相对心脏血容量乘以其频率在除以心肌组织密度（ $1.5\text{g mL}^{-1}$ ）。

**结果：**在七氟醚麻醉中，心脏血流量在静息时与基础值相近（ $1.05 \pm 0.28$  vs  $1.05 \pm 0.32$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.98$ ; 95% 可信区间 [CI],  $-0.18$  to  $0.18$ ），对比基线时，当心率增加时心脏血容量减少（ $P = 0.0044$ ; 95% CI,  $0.01$ – $0.04$ ）。相反，心脏充血时，心脏血容量是减少的（ $2.25 \pm 0.5$  vs  $3.53 \pm 0.7$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.0003$ ; 95% CI,  $0.72$ – $1.84$ ）。给予一定的交感刺激时心脏血流量变化不大（ $1.53 \pm 0.53$  and  $1.55 \pm 0.49$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.74$ ; 95% CI,  $-0.47$  to  $0.35$ ）。

**结论：**在七氟醚实施的麻醉中，尽管血容量是减少的，但在没有外科刺激的情况下，心脏血流量在静息及交感刺激后的是代偿的，然而，在一些减少心脏充血情况下，心脏血流量也是代偿的。

（邓利兵译 薛张纲校）

**BACKGROUND:** Preservation of myocardial perfusion during general anesthesia is likely important in patients at risk for perioperative cardiac complications. Data related to the influence of general anesthesia on the normal myocardial circulation are limited. In this study, we

investigated myocardial microcirculatory responses to pharmacological vasodilation and sympathetic stimulation during general anesthesia with sevoflurane in healthy humans immediately before surgical stimulation.

**METHODS:** Six female and 7 male subjects (mean age 43 years, range 28–61) were studied at baseline while awake and during the administration of 1 minimum alveolar concentration sevoflurane. Using myocardial contrast echocardiography, myocardial blood flow (MBF) and microcirculatory variables were assessed at rest, during adenosine-induced hyperemia, and after cold pressor test-induced sympathetic stimulation. MBF was calculated from the relative myocardial blood volume multiplied by its exchange frequency ( $\beta$ ) divided by myocardial tissue density ( $\rho_T$ ), which was set at  $1.05 \text{ g}\cdot\text{mL}^{-1}$ .

**RESULTS:** During sevoflurane anesthesia, MBF at rest was similar to baseline values ( $1.05 \pm 0.28$  vs  $1.05 \pm 0.32 \text{ mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.98$ ; 95% confidence interval [CI],  $-0.18$  to  $0.18$ ). Myocardial blood volume decreased ( $P = 0.0044$ ; 95% CI,  $0.01$ – $0.04$ ) while its exchange frequency ( $\beta$ ) increased under sevoflurane anesthesia when compared with baseline. In contrast, hyperemic MBF was reduced during anesthesia compared with baseline ( $2.25 \pm 0.5$  vs  $3.53 \pm 0.7 \text{ mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.0003$ ; 95% CI,  $0.72$ – $1.84$ ). Sympathetic stimulation during sevoflurane anesthesia resulted in a similar MBF compared to baseline ( $1.53 \pm 0.53$  and  $1.55 \pm 0.49 \text{ mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.74$ ; 95% CI,  $-0.47$  to  $0.35$ ).

**CONCLUSIONS:** In otherwise healthy subjects who are not subjected to surgical stimulation, MBF at rest and after sympathetic stimulation is preserved during sevoflurane anesthesia despite a decrease in myocardial blood volume. However, sevoflurane anesthesia reduces hyperemic MBF, and thus MBF reserve, in these subjects.

### 脂肪乳剂对布比卡因在小鼠中药代动力学和组织分布的影响

#### The Effect of Lipid Emulsion on Pharmacokinetics and Tissue Distribution of Bupivacaine in Rats

Kejian Shi, MD\*, Yun Xia, MD, PhD†, Quanguang Wang, MD\*, Yiquan Wu, MD\*, Xiaoxi Dong, MD‡, Chanjuan Chen, BS\*, Wan Tang, BS\*, Yujian Zhang, MD\*, Mengxu Luo, BS\*, Xianqin Wang, PhD||, Thomas J. Papadimos, MD, MPH† and Xuzhong Xu, MD  
Anesth Analg April 2013 116:804-809

**背景:** 虽然脂肪乳剂可能逆转布比卡因的全身毒性作用,但在注射脂肪乳剂后布比卡因的药代动力学和组织分布并不清楚。在这项研究中,我们评估了注射脂肪乳剂对布比卡因药代动力学和组织分布的影响。

**方法:** 脂肪乳剂组小鼠以  $2 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{分钟}^{-1}$  到4分钟的速度静脉注射布比卡因,然后分别以  $3 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{分钟}^{-1}$  到5分钟的速度注射30%的脂肪乳剂;在对照组用生理盐水取代 ( $n=6$ 的 药代动力学)。然后我们随机分配100只小鼠到脂肪乳剂组和对照组 (以  $n=50$  分配)。这个毒性模型和治疗与其药代动力学部分相同。采集的血浆和组织包括脑、心、肝、脾、肺、肾、大网膜和肌肉。通过液相色谱-串联质谱法测定布比卡因的血药浓度和组织含量。一个2-房室模型分析计算布比卡因的药代动力学。

**结果:** 所有数据都以平均值 $\pm$ 标准差显示。在经过脂肪乳剂治疗后,在脂肪乳剂组布比卡因的  $t_{1/2\beta}$  明显缩短 ( $110 \pm 25$  分钟比上  $199 \pm 38$  分钟,  $P = 0.001$ ),清除较高 ( $14 \pm 4 \text{ mL}\cdot\text{mg}^{-1}\cdot\text{kg}^{-1}$  比上  $9 \pm 4 \text{ mL}\cdot\text{mg}^{-1}\cdot\text{kg}^{-1}$ ,  $P = 0.038$ ),并且  $t_{1/2\alpha}$  比对照组延长 ( $4 \pm 1$



分钟比上 $2 \pm 1$ 分钟,  $P = 0.014$ ) ; K12在脂肪乳剂组比对照组少 ( $0.13 \pm 0.04$  比上 $0.32 \pm 0.13$ ,  $P = 0.011$ ) 。在脂肪乳剂组, 布比卡因在心、脑、肺、肾和脾的含量比对照组少, 但在20、30和45分钟时在肝脏中含量较对照组高。

**结论:** 在本研究中观察到脂质沉积现象。脂肪乳剂的应用能加速布比卡因的清除。

(方昕译 薛张纲校)

**BACKGROUND:** While lipid emulsion may reverse the systemic toxicity of bupivacaine, the pharmacokinetics and tissue distribution of bupivacaine after lipid emulsion infusion are not clear. In this study, we assessed the influence of lipid emulsion administration on the pharmacokinetics and tissue distribution of bupivacaine.

**METHODS:** Rats in the lipid group were administered IV bupivacaine at the rate of  $2 \text{ mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  for 4 minutes, and then were treated with an infusion of 30% lipid emulsion at the rate of  $3 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$  for 5 minutes; saline was substituted in the control group ( $n = 6$  for pharmacokinetics). We then randomly assigned 100 rats into the lipid group and control group ( $n = 50$  for distribution). The toxicity model and treatment were the same as the pharmacokinetic portion. Plasma and tissues including brain, heart, liver, spleen, lung, kidney, omentum, and muscle were collected. The plasma concentration and tissue content of bupivacaine were measured by a liquid chromatography-tandem mass spectrometric method. A 2-compartmental analysis was performed to calculate the pharmacokinetics of bupivacaine.

**RESULTS:** All data are shown as mean  $\pm$  SD. After treatment with the lipid emulsion,  $t_{1/2\beta}$  of bupivacaine in the lipid group was significantly shorter ( $110 \pm 25$  minutes vs  $199 \pm 38$  minutes,  $P = 0.001$ ), the clearance was higher ( $14 \pm 4 \text{ mL}\cdot\text{mg}^{-1}\cdot\text{kg}^{-1}$  vs  $9 \pm 4 \text{ mL}\cdot\text{mg}^{-1}\cdot\text{kg}^{-1}$ ,  $P = 0.038$ ), and the  $t_{1/2\alpha}$  was longer than that of the control group ( $4 \pm 1$  minutes vs  $2 \pm 1$  minutes,  $P = 0.014$ ); the K12 in the lipid group was less than that of the control group ( $0.13 \pm 0.04$  vs  $0.32 \pm 0.13$ ,  $P = 0.011$ ). In the lipid group, the bupivacaine content in heart, brain, lung, kidney, and spleen was lower than that in the control group, but higher in the liver at 20, 30, and 45 minutes.

**CONCLUSION:** The lipid sink phenomenon was observed in this study. The use of a lipid emulsion accelerated the elimination of bupivacaine.

**超声用于辅助定位肥胖产妇的硬膜外穿刺中点：旁正中斜入路与横向正中横向入路的比较。**

**Ultrasound estimates for midline epidural punctures in the obese parturient: paramedian sagittal oblique is comparable to transverse median plane.**

Jagpaul S. Sahota, MD, Jose C. A. Carvalho, MD, PhD, Mrinalini Balki, MBBS, MD, Niall Fanning, MD and Cristian Arzola, MD, MSc

From the Department of Anesthesia and Pain Management, Mount Sinai Hospital, and University of Toronto, Toronto, Ontario, Canada.

Anesth Analg April 2013 116:829-835

**背景:** 临床使用脊髓超声 (US) 多使用横向中线 (TM) 平面观察, 在肥胖孕妇中, 通常由于弥补因皮下组织过后引起的低能见度, 向下挤压皮下组织来观察, 这样会低估肥胖孕妇皮肤至硬膜外间隙的距离。我们试验了在这类人群中使用旁正中斜入路平面 (PSO) 是否比TM平面测量皮肤-硬膜外下腔的实际距离更为精确。

**方法：**我们招募了要求硬膜外镇痛或行腰硬联合麻醉剖宫产的肥胖产妇人群（世界卫生组织分级I、II和III）。超声使用5-2MHz探头定位进针点并分别用PSO平面或TM平面估算皮肤至硬膜外下腔的距离（超声估计距离，UD）。测量时尽可能用探头下压皮肤及皮下组织，测量最短距离。所有的进针方式都是中线进针。麻醉医生使用腰硬组合针在预先定位的穿刺点进针，标记实际进针距离（进针深度，ND）。我们用Bland-Altman分析法确定UD和ND之间的差异以及95%可信区间。

**结果：**我们研究了60名女性患者，平均BMI值为39.6（±7.9）kg/m<sup>2</sup>（范围30.4-66.2kg/m<sup>2</sup>）。超声在PSO和TM平面上的估计值与实际ND分别为6.5（±1.2）cm，6.5（±1.1）cm以及6.6（±1.3）cm。Bland-Altman分析表明两者之间的差异为0.05cm，95%可信区间为±1cm。在PSO平面与TM平面成像质量优良的比例分别为86.7%和68.3%（P=0.028）。

**结论：**使用PSO平面行超声测量硬膜外间隙与皮肤之间的距离和TM平面之间是可比的。在那些使用TM平面能见度低的患者中使用两平面联合评估可能对结果有一定提升作用。（郭晨跃译 薛张纲校）

**BACKGROUND:** Spinal ultrasound (US) in the transverse median (TM) plane underestimates the distance to the epidural space in obese pregnant women, most likely because of compression of the subcutaneous tissue during the assessment, often required to compensate for poor visibility. We tested whether scanning in the paramedian sagittal oblique (PSO) plane compared with the TM plane resulted in a more precise estimate of the actual skin-epidural space measurement in this population.

**METHODS:** We recruited obese (World Health Organization classes I, II, and III) pregnant women at term requesting labor epidural analgesia or combined spinal-epidural anesthesia for cesarean delivery. US imaging was performed with a 5-2 MHz curved array probe to identify the insertion point and to estimate the distance from the skin to the epidural space (US-estimated depth, UD) in the PSO and TM planes. The measurements were performed with the least possible compression of the subcutaneous tissue by the US probe. All punctures were performed via the midline approach. An anesthesiologist performed the epidural/combined spinal-epidural procedure at the predetermined insertion point, and marked the actual needle distance from the skin to the epidural space (needle depth, ND). Bland-Altman analysis was used to determine the differences and 95% limits of agreement between US depth and ND.

**RESULTS:** We studied 60 women. The mean (SD) body mass index was 39.6 (7.9) kg/m<sup>2</sup> (range 30.4-66.2 kg/m<sup>2</sup>). The US estimate in the PSO and TM planes, and the actual ND were 6.5 (1.2) cm, 6.5 (1.1) cm, and 6.6 (1.3) cm, respectively. The Bland-Altman analysis showed a mean difference of 0.05 cm and 95% limits of agreement of ±1 cm. The quality of imaging was rated as good in the PSO and TM planes in 86.7% and 68.3%, respectively (P = 0.028).

**CONCLUSION:** The estimates of the US-determined distance to the epidural space in the PSO are comparable to those in the TM plane. The ability to use both estimates interchangeably for midline punctures may prove useful in patients presenting with poor visibility in the TM plane.

**非创伤性脑出血患者的神经源性肺水肿：预测因子与相关结果。**

**Neurogenic pulmonary edema in patients with nontraumatic intracerebral hemorrhage: predictors and association with outcome.**

Eija Junttila, MD\*, Tero Ala-Kokko, MD, PhD\*, Pasi Ohtonen, MSc†, Anne Vaarala, MD‡, Ari Karttunen, MD, PhD‡, Olli Vuolteenaho, MD, PhD§, Tuula Salo, DDS, PhD||, Meeri Sutinen, PhD||, Toni Karhu, MSc§, Karl-Heinz Herzig, MD, PhD§¶ and Juha Koskenkari, MD, PhD\*

From the Departments of \*Anesthesiology and Intensive Care, †Anesthesiology and Surgery, and ‡Radiology, Oulu University Hospital; §Department of Physiology, Oulu University Hospital, Oulu University, Biocenter of Oulu; || Department of Diagnostics and Oral Medicine, Oulu University Hospital, Oulu University, Institute of Dentistry, Oulu; and ¶Department of Psychiatry, Kuopio University Hospital, Kuopio, Finland.

Anesth Analg April 2013 116:855-861

**背景：**神经源性肺水肿（NPE）是颅内出血后出现的一个公认的现象。在这项研究中，我们评估了在重症监护病房治疗的非创伤性脑出血患者出现NPE的预测因子与相关结果。

**方法：**这是一个在校级水平的重症监护病房进行的一项前瞻性，观察性临床试验。入院时记录患者的临床表现，意识水平，以及急性生理和慢性健康评估（APACHE）II评分和评估患者主要头部电脑断层扫描结果。连续随访患者胸片和动脉血气分析结果，NPE在胸片上表现为急性双肺浸润和低氧血症。我们记录NPE患者超声心动图，心脏和炎症标志物，使用格拉斯哥结局量表评估1年结果。

**结果：**108例患者中有38例（35%）发展为NPE。NPE预测因子均高于APACHE II评分（ $\geq 20$ ，比值为6.17， $P = 0.003$ ）和较高的白介素-

6的血浆浓度（ $>40$ 皮克/毫升，比值为5.62， $P = 0.003$ ）。

患者有上述0，1或2的预测因子，分别有4%，37%，和65%的患有NPE。

NPE具有较高的1年死亡率（37%对14%， $P=0.007$ ），但1年后的功能结局不变（格拉斯哥预后评分1-3分，53%与51%， $P>0.9$ ）。

**结论：**APACHE II评分系统预测NPE疾病的严重程度和更高水平的全身性炎症介质。

NPE与较高的1年死亡率相关，但与较差的1年的功能结局无关。

（贺盼译 薛张纲校）

**BACKGROUND:** Neurogenic pulmonary edema (NPE) is a well-recognized phenomenon after intracranial insult. In this study, we evaluated the predictors for NPE and its association with outcome in patients with intensive care unit-treated nontraumatic intracranial hemorrhage.

**METHODS:** This was a prospective, observational clinical study in a university-level intensive care unit. Clinical characteristics, level of consciousness, and Acute Physiology and Chronic Health Evaluation (APACHE) II score were recorded on admission and the findings of primary head computed tomography were reviewed. A chest radiograph and arterial blood gas analysis were taken serially and NPE was determined as acute bilateral infiltrates in chest radiograph and hypoxemia. Echocardiography and cardiac and inflammatory markers were recorded. The 1-year outcome was assessed using the Glasgow Outcome Scale.

**RESULTS:** NPE developed in 38 (35%) of the 108 patients included. Predictors for NPE were higher APACHE II score ( $\geq 20$ , odds ratio 6.17,  $P = 0.003$ ) and higher interleukin-6 plasma concentration ( $>40$  pg/mL, odds ratio 5.62,  $P = 0.003$ ). Of patients with 0, 1, or 2 predictors mentioned above, 4%, 37%, and 65% had NPE, respectively. NPE was associated with a higher 1-year mortality (37% vs 14%,  $P = 0.007$ , respectively), but with an unchanged functional outcome after 1 year (Glasgow Outcome Scale score 1-3, 53% vs 51%,  $P > 0.9$ ).

**CONCLUSIONS:** Predictors for NPE are the severity of disease defined by APACHE II scores and higher levels of systemic inflammatory mediators. NPE is associated with a higher 1-year mortality, but not with a poorer 1-year functional outcome.

### 癫痫患者的术前评估：麻醉医生的职责

#### **Review article: presurgical evaluation of patients with epilepsy: the role of the anesthesiologist.**

Jason Chui, MBChB, FANZCA, FHKCA, Lashmi Venkatraghavan, MD, FRCA, FRCPC and Pirjo Manninen, MD, FRCPC

From the Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada.

Anesth Analg April 2013 116:881-888

药物难治性癫痫患者拟行外科手术治疗通常需要更好的术前评估，以此来判断外科手术是否可行。手术的可行性取决于与癫痫发作相关的中枢病变部位及癫痫发作的频率。良好的手术效果取决于完整地切除与癫痫相关的病变部位且不损伤有功能的正常组织。多种有创或无创的检查用于术前评估，包括影像学检查、脑电图检查以判断功能区域。了解癫痫定位诊断及药物的作用对于该类患者的术前处理是有必要地。在这篇综述中，我们讨论了麻醉医生在这类患者处理中的作用，麻醉药物对于协助癫痫定位诊断及脑功能判断的作用。

（李丽红译 薛张纲校）

Patients with medically refractory epilepsy when referred for surgical treatment often undergo extensive investigations to determine whether surgical treatment is feasible. Surgical feasibility is determined by identifying the location and number of seizure foci and their relationship to eloquent areas of the brain. Good surgical outcome depends on complete resection of seizure foci without any damage to eloquent brain function. Various noninvasive and invasive techniques are used in the presurgical evaluation of patients with epilepsy that include imaging techniques, electrophysiologic studies, and tests to determine functional areas. Understanding of the principles of seizure localization and of the effects of anesthetic drugs on the various preoperative investigations is essential for patient management. In this review article, we discuss the role of the anesthesiologist in patient management during many of these investigations and the role of anesthetic drugs to aid in the localization of the seizure focus and of determining eloquent brain function.

### 手术室外监督协调麻醉医生活动的通信系统的作用

#### **Role of communication systems in coordinating supervising anesthesiologists' activities outside of operating rooms.**

Bettina Smallman, Dr Med\*, Franklin Dexter, MD, PhD†, Danielle Masursky, PhD\*, Fenghua Li, MD\*, Reza Gorji, MD\*, Dave George, MBA‡ and Richard H. Epstein, MD, CPHIMS§  
From the \*Department of Anesthesiology, State University of New York Upstate, Syracuse, New York; †Department of Anesthesia, Division of Management Consulting, University of Iowa, Iowa City, Iowa; ‡Department of Telecommunications, Division of Information Management & Technology, State University of New York Upstate, Syracuse, New York; and §Department of Anesthesiology, Jefferson Medical College, Philadelphia, Pennsylvania.

**背景：**从理论上说，通信系统可能促进指导了麻醉。我们最大评价了通信系统在手术室中通过对麻醉协调管理的促进作用。

**方法：**在A医院，一份13368例的数据从内部字母数字文本分页系统中获得。苏醒室的资料是从数字寻呼系统中获取的并不包含所有的。B医院中，在美国的不同洲，3名作者分别用内部无线音频系统分类898通电话。上下95%置信区间为百分比报告的值。

**结果：**至少45%例来源于A医院的手术室外和至少56%通电话来自B医院。相比较，A医院中手术室外麻醉的紧急请求最多为0.2%例，B医院为1.8%通电话。

**结论：**接近一半的消息是为监督麻醉师在手术室的活动。为了手术当天用通信工具帮助麻醉，他们的作用应该包括一个专注于手术室外的护理如等候区和手术室外如控制台。(孙莉萍译 薛张纲校)

**BACKGROUND:** Theoretically, communication systems have the potential to increase the productivity of anesthesiologists supervising anesthesia providers. We evaluated the maximal potential of communication systems to increase the productivity of anesthesia care by enhancing anesthesiologists' coordination of care (activities) among operating rooms (ORs).

**METHODS:** At hospital A, data for 13,368 pages were obtained from files recorded in the internal alphanumeric text paging system. Pages from the postanesthesia care unit were processed through a numeric paging system and thus not included. At hospital B, in a different US state, 3 of the authors categorized each of 898 calls received using the internal wireless audio system (Vocera®). Lower and upper 95% confidence limits for percentages are the values reported.

**RESULTS:** At least 45% of pages originated from outside the ORs (e.g., 20% from holding area) at hospital A and at least 56% of calls (e.g., 30% administrative) at hospital B. In contrast, requests from ORs for urgent presence of the anesthesiologist were at most 0.2% of pages at hospital A and 1.8% of calls at hospital B.

**CONCLUSIONS:** Approximately half of messages to supervising anesthesiologists are for activity originating outside the ORs being supervised. To use communication tools to increase anesthesia productivity on the day of surgery, their use should include a focus on care coordination outside ORs (e.g., holding area) and among ORs (e.g., at the control desk).

### 选择哪一位执业者对下一位麻醉前评估患者进行评估取决于执业者的相对速度

#### Choosing which practitioner sees the next patient in the preanesthesia evaluation clinic based on the relative speeds of the practitioner.

Franklin Dexter, MD, PhD\*, Hyun-Soo Ahn, PhD† and Richard H. Epstein, MD, CPHIMS‡  
From the \*Department of Anesthesia, Division of Management Consulting, University of Iowa, Iowa City, Iowa; †Department of Operations and Management Science, University of Michigan, Ann Arbor, Michigan; and ‡Department of Anesthesiology, Jefferson Medical College, Philadelphia, Pennsylvania.

**背景：**临床上麻醉前评估通常不是评估患者，因为病人不会等着被评估，执业者更多时间是用来复习患者的病史。执业者完整评估的时间是不同的，针对评估较慢的，我们需要不同的方案以缩短患者等候的时间（至少有2名患者在等候）。

**方法：**通过研究明确如何优化等候队伍的状况（如最快平均评估一名患者的时间比最慢的少一半）。

我们比较了队伍状况与诊所内注册护士完成评估的时间的关系。计算平均评估时间按的99.9%置信区间。

**结果：**最快的执业者比第二快的速度快1.23倍(CI 1.22-1.23)，比最慢的三个执业者快1.61倍（1.59-

1.61）。上述差别可以明显加快3倍和2倍等候时间，从而保证等候队伍的秩序。速度较慢的执业者评估所占时间较长 (Kendall  $\tau_b = 0.56$ ,  $P = 0.0001$ )，因此优先将患者安排给速度较快的人。

**结论：**执业者评估患者的速度没有显著改变信息系统常规选择下一名患者。临床是降低患者等候的时间应该着眼于减少总体评估时间（如复习病史的时间），合适的安排患者和有适当的辅助护士和执业者的人数。

（郁玲玲译 薛张纲校）

**BACKGROUND:** When a practitioner in a preanesthesia evaluation clinic is not evaluating a patient because no patient is waiting to be seen, the practitioner often has other responsibilities such as reviewing charts of patients. When practitioners differ in how quickly they complete evaluations, multiple scenarios can be created wherein the slowest practitioner would only evaluate patients when the number of patients waiting exceeds a threshold (e.g., at least 2 patients are waiting).

**METHODS:** Review of operations research studies identified conditions for which such management of the queue can be beneficial (e.g., mean evaluation time of the fastest practitioner is less than half that of the slowest practitioner). These conditions were compared with the actual completion rates of certified registered nurse practitioners at a hospital's clinic. The 99.9% confidence intervals (CI) were calculated for ratios of mean evaluation times.

**RESULTS:** The fastest practitioner was typically 1.23 times faster than the second fastest practitioner (CI 1.22-1.23) and 1.61 times faster than the slowest of three practitioners (1.59-1.61). These are significantly less than the 3 times and 2 times faster, respectively, that would be sufficiently large to warrant managing queue discipline. Practitioners with longer mean evaluation times had larger percentage utilizations of working time (Kendall  $\tau_b = 0.56$ ,  $P = 0.0001$ ), inconsistent with preferential assignment of patients to the fastest practitioner(s) available.

**CONCLUSIONS:** Practitioners' speeds in evaluating patients do not differ sufficiently for information systems to be used routinely to choose who evaluates the next patient (i.e., state-dependent assignment policy). Clinics aiming to reduce patient waiting should focus on reducing the overall mean evaluation time (e.g., by chart review ahead), appropriately scheduling patients, and having the right numbers of nursing assistants and practitioners

### 区域麻醉下手术后出现快速眼动睡眠剥夺

#### Occurrence of rapid eye movement sleep deprivation after surgery under regional anesthesia.

Frank Dette, MD\*, Werner Cassel, MSc†, Friederike Urban‡, Martin Zoremba, MD‡, Ulrich Koehler, MD†, Hinnerk Wulf, MD‡, Jürgen Graf, MD‡ and Thorsten Steinfeldt, MD‡

From the \*Department of Anesthesiology, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz; and †Department of Internal Medicine, Division of Pneumology, and

‡Department of Anesthesiology and Intensive Care, Philipps-University Marburg, Marburg, Germany.  
Anesth Analg April 2013 116:939-943

**背景：**普外科手术中出现睡眠障碍已经被描述过了。在这项研究中，我们评估患者在区域麻醉下行膝关节置换术后快速眼动睡眠（REM）的情况。

**方法：**在3个晚上进行动态多导睡眠监测（PSG）：手术前一天晚上（PSG1），手术后的第1天晚上（PSG2），术后第5天的晚上（PSG3）。术后镇痛前3天采用外周神经置管，随后口服阿片类药物。此外，还可给予非甾体类抗炎药物。采用视觉模拟评分法评价术后疼痛程度。

**结果：**在12名患者中实行了PSG，其中6名男性和6名女性，平均年龄为61（±12）岁。从PSG1（中位数为16.4%）到PSG2（中位数为6.3%， $P = 0.02$ ）提示REM睡眠减少。利用Hodges-Lehmann法估计中位数减少-7.8%（95%置信区间为-14.8%至-0.7%）。在PSG3阶段，与PSG2相比，监测到显著的REM睡眠（中位数为15.4%）（ $P = 0.01$ ）。利用Hodges-Lehmann法估计中位数增加为10.0%（95%置信区间为1.7%至25.3%）。

**结论：**在手术及区域麻醉后，会出现REM睡眠的减少。

（周玲译 薛张纲校）

**BACKGROUND:** Sleep disturbances after general surgery have been described. In this study, we assessed rapid eye movement (REM) sleep in patients undergoing knee replacement surgery using a regional anesthetic technique.

**METHODS:** Ambulatory polysomnography (PSG) was performed on 3 nights: the night before surgery (PSG1), the first night after surgery (PSG2), and the fifth postoperative night (PSG3). Postoperative analgesia was maintained with peripheral nerve catheters for the first 3 days and with oral opioids thereafter. In addition, nonsteroidal antiinflammatory drugs were administered. Postoperative pain was monitored using a visual analog scale.

**RESULTS:** PSG was performed in 12 patients, 6 men and 6 women, with a mean age of 61 (±12) years. REM sleep was reduced from PSG1 (median 16.4%) to PSG2 (median 6.3%;  $P = 0.02$ ). The Hodges-Lehmann estimate for the median reduction is -7.8% (95% confidence interval -14.8% to -0.7%). During PSG3, significantly more REM sleep was detected (median 15.4%) compared with PSG2 ( $P = 0.01$ ). The Hodges-Lehmann estimate for this median increase is 10.0% (95% confidence interval 1.7%-25.3%).