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恶性高热和肌肉萎缩症
Malignant Hyperthermia and Muscular Dystrophies
Harshad Gurnaney, MBBS, MPH*, Amanda Brown, MD†, and Ronald S. Litman, DO‡
From the *Department of Anesthesiology and Critical Care Medicine, The Children’s Hospital of Philadelphia; and †Department of Anesthesiology and Critical Care Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania. Anesth Analg 2009 109: 1043-1048.

背景：据报道患有肌肉萎缩症（肌营养不良）的病人在全身麻醉时和麻醉后可能发生很多致命的并发症。作者对患有肌肉萎缩症的病人做了一项系统分析，旨在定义此类病人麻醉相关并发症的范畴，重点强调了恶性高热的易感性。
方法：作者使用了多个搜索引擎进行文献检索并对合适的文献进行评价从而确定患有肌肉萎缩症病人麻醉相关并发症。在所有肌肉萎缩症的类型中，Duchenne型肌营养不良（DMD）和Becker型肌营养不良（BD）占据了几乎所有麻醉相关的报道。
结果：DMD和BD病人麻醉相关并发症包括术中心力衰竭、吸入麻醉相关的横纹肌溶解症（不用琥珀酰胆碱）和琥珀酰胆碱引起的横纹肌溶解症及高钾血症。
结论：与普通人群相比，并没有发现DMD和BD病人增加了恶性高热的易感性。但是，暴露于吸入麻醉药的营养不良病人可能引起疾病相关的心脏并发症，或罕见的以横纹肌溶解为特征的恶性高热相似症状。后者也可能发生在术后。琥珀酰胆碱可以引起致命性高钾血症，应避免用于DMD和BD患者。
(李潺 译 陈杰 校)
BACKGROUND: Patients with muscular dystrophy have been reported to experience a variety of life-threatening complications during and after general anesthesia. We performed a systematic analysis to define the spectrum of anesthetic-related complications in patients with muscular dystrophy, with an emphasis on malignant hyperthermia susceptibility.
METHODS: A literature search was undertaken using multiple search engines and the appropriate articles were reviewed by the authors to determine anesthetic-associated complications in patients with muscular dystrophy. Of all the types of muscular dystrophy,
Duchenne muscular dystrophy (DMD) and Becker dystrophy (BD) represent nearly all the anesthesia-related reports.

**RESULTS:** Anesthetic complications in patients with DMD and BD include intraoperative heart failure, inhaled anesthetic-related rhabdomyolysis (absence of succinylcholine), and succinylcholine-induced rhabdomyolysis and hyperkalemia.

**CONCLUSION:** We did not find an increased risk of malignant hyperthermia susceptibility in patients with DMD or BD compared with the general population. However, dystrophic patients who are exposed to inhaled anesthetics may develop disease-related cardiac complications, or rarely, a malignant hyperthermia-like syndrome characterized by rhabdomyolysis. This latter complication may also occur postoperatively. Succinylcholine administration is associated with life-threatening hyperkalemia and should be avoided in patients with DMD and BD.

**劳累性热病、运动性横纹肌溶解症及恶性高热之间的关系**

The Relationship Between Exertional Heat Illness, Exertional Rhabdomyolysis, and Malignant Hyperthermia

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劳累性热病、运动性横纹肌溶解症和恶性高热（MH）具有相似病理生理学的综合征。三者均有高代谢特征，包括：三磷酸腺苷的高需求、氧化和代谢的加速、肌肉的机械应力，以及不受控制的细胞内钙的增加。尽管没有临床的对照研究来支持其中的关系，但有证据表明预期外的热/运动的不耐受和MH易感性相关。有多个病理报告和小样本的临床研究已经用于体外肌肉挛缩实验和或基因监测来证实这种关系。然而，这种方法存在问题，因为这些研究在与麻醉相关的临床MH中证实有效，而不是与劳累性热病或恶性高热有关。然而，这些相互关系对某些MH易感的患者以及他们运动的能力可能有意义，同时对临床医生的治疗和伴随有原因不明劳累性热病和运动疾病患的麻醉具有重要意义。

（怀晓蓉译 陈杰校）

Exertional heat illness, exertional rhabdomyolysis, and malignant hyperthermia (MH) are complex syndromes with similar pathophysiology. All three are hypermetabolic states that include high demand for adenosine triphosphate, accelerated oxidative, chemical, and mechanical stress of muscle, and uncontrolled increase in intracellular calcium. Although there are no controlled clinical studies to support a relationship, there is evidence to suggest an association between unexpected heat/exercise intolerance and MH susceptibility. There are multiple case reports and a small number of clinical studies that have used *in vitro* muscle contracture testing and/or genetic testing to make the association. However, such methodology is problematic in that these tests are validated for clinical MH in association with anesthesia, and not for exertional heat illness or exertional rhabdomyolysis. Nevertheless, these relationships may have implications for some MH-susceptible patients and their capacity to exercise, as well as for clinicians treating and anesthetizing patients with histories of unexplained exertional heat and exercise illnesses.
**Nitrous Oxide-Induced Analgesia Does Not Influence Nitrous Oxide's Immobilizing Requirements**

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**BACKGROUND:** Nitrous oxide (N2O) acts on supraspinal noradrenergic neurons to produce analgesia, but it is unclear if analgesia contributes to N2O's immobilizing effects. We tested the hypothesis that N2O minimum alveolar anesthetic concentration (MAC) is unchanged after selective ablation of supraspinal noradrenergic neurons, or in naïve animals at N2O exposure timepoints when analgesia is absent.

**METHODS:** We determined tailflick latency (TFL) and hindpaw withdrawal latency (HPL) under 70% N2O, N2O MAC, and isoflurane MAC before and after intracerebroventricular injections of anti-dopamine-β hydroxylase conjugated to saporin (SAP-DBH; n = 7) or control antibody conjugated to saporin (n = 5) in naïve rats (n = 8). N2O MAC was determined at 25–45 min after initiation of N2O exposure (during peak analgesia) and again at 120–140 min (after TFL and HPL returned to baseline).

**RESULTS:** After 30 min of N2O exposure, TFL and HPL increased significantly but declined back to baseline within 120 min. N2O did not produce analgesia in rats that received SAP-DBH. However, N2O and isoflurane MAC were not significantly different between SAP-DBH and control-injected animals (Mean ± sd for N2O: 1.7 ± 0.1 atm vs 1.7 ± 0.2 atm; isoflurane: 1.6 ± 0.2% vs 1.7 ± 0.2%). In naïve animals, N2O MAC was not...
different at the 30 min period compared with the 120 min period (1.8 ± 0.1 atm vs 1.8 ± 0.2 atm).

**CONCLUSIONS:** Destroying brainstem noradrenergic neurons or prolonged exposure to N₂O removes its analgesic effects, but does not change MAC. The immobilizing mechanism of N₂O is independent from its analgesic effects.

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**Monitoring with Head-Mounted Displays: Performance and Safety in a Full-Scale Simulator and Part-Task Trainer**

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**背景:** 头戴式显示器可以帮助麻醉医师在任何时候都可以看到术中病人所监测的生命体征，即使麻醉医师忙于操作或者无法看到监视器的时候。相关的麻醉文献显示使用 HMD（头戴式显示器）有其优点，但也有研究表明 HMD 会加重注意力迟钝（使用者很有可能因专注于显示器而忽略眼前的其他事物），同时可能产生于焦距深度有关的知觉问题。本研究调查了两种模拟器的差异。

**方法:** 实验一，研究戴上 HMD 是否会影响麻醉医师发现病情的速度，以及 HMD 设置的不同焦距（近或远）其结果是否会有差别。12 名麻醉医师在三个自然场景中进行麻醉，这三个场景中均用模拟器模拟手术环境。在病人的监视器上或者手术室内出现 24 种不同的病情变化。实验二，研究麻醉医师由于进行操作而受到身体上的限制，使用 HMD 的麻醉医师是否会比没有使用 HMD 的麻醉医师更快发现病情变化。12 名麻醉医师在监测模拟病人生命体征的同时，要在部分任务训练器上进行复杂的模拟临床任务。所有的参与者在两种场景中共会碰到 4 种不同的情况。

**结果:** 实验一表明带上 HMD 或者调整设置的焦距都不会降低参与者发现病情变化的能力（包括发现病情情况的数量和时间）。总的来说，使用 HMD 后的参与者较只用标准监视器的时候会花更多的时间去看病人，更少的时间去看麻醉机、显示器。参与者报告他们更喜欢近焦距的设置。实验二显示参与者使用 HMD 后发现其中 2 种病情变化的速度会更快，而另一种病情变化发现较慢。参与者使用 HMD 后去看麻醉机显示器的频率大大下降。使用 HMD 后，参与者表示他们没这么忙了，监测也更容易，而且他们相信发现异常情况变化的速度会更快。

**结论:** HMD 可以帮助麻醉医师在身体受限的时候也能发现病情变化，而不是在身体不受限的时候。尽管没有足够的证据说明会加重不注意，但在航空方面发现，与 HMD 有关的知觉问题会影响到测试者是否能发现到情况的变化。麻醉医师使用
BACKGROUND: Head-mounted displays (HMDs) can help anesthesiologists with intraoperative monitoring by keeping patients’ vital signs within view at all times, even while the anesthesiologist is busy performing procedures or unable to see the monitor. The anesthesia literature suggests that there are advantages of HMD use, but research into head-up displays in the cockpit suggests that HMDs may exacerbate inattentional blindness (a tendency for users to miss unexpected but salient events in the field of view) and may introduce perceptual issues relating to focal depth. We investigated these issues in two simulator-based experiments.

METHODS: Experiment 1 investigated whether wearing a HMD would affect how quickly anesthesiologists detect events, and whether the focus setting of the HMD (near or far) makes any difference. Twelve anesthesiologists provided anesthesia in three naturalistic scenarios within a simulated operating theater environment. There were 24 different events that occurred either on the patient monitor or in the operating room. Experiment 2 investigated whether anesthesiologists physically constrained by performing a procedure would detect patient-related events faster with a HMD than without. Twelve anesthesiologists performed a complex simulated clinical task on a part-task endoscopic dexterity trainer while monitoring the simulated patient’s vital signs. All participants experienced four different events within each of two scenarios.

RESULTS: Experiment 1 showed that neither wearing the HMD nor adjusting the focus setting reduced participants’ ability to detect events (the number of events detected and time to detect events). In general, participants spent more time looking toward the patient and less time toward the anesthesia machine when they wore the HMD than when they used standard monitoring alone. Participants reported that they preferred the near focus setting. Experiment 2 showed that participants detected two of four events faster with the HMD, but one event more slowly with the HMD. Participants turned to look toward the anesthesia machine significantly less often when using the HMD. When using the HMD, participants reported that they were less busy, monitoring was easier, and they believed they were faster at detecting abnormal changes.

CONCLUSIONS: The HMD helped anesthesiologists detect events when physically constrained, but not when physically unconstrained. Although there was no conclusive evidence of worsened inattentional blindness, found in aviation, the perceptual properties of the HMD display appear to influence whether events are detected. Anesthesiologists wearing HMDs should self-adjust the focus to minimize eyestrain and should be aware that some changes may not attract their attention. Future areas of research include developing principles for the design of HMDs, evaluating other types of HMDs, and evaluating the HMD in clinical contexts.

Prevalence of Malignant Hyperthermia Due to Anesthesia in New York State, 2001–2005

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BACKGROUND: Malignant hyperthermia (MH) is a pharmacogenetic syndrome that variably expresses itself on exposure to triggering agents. MH prevalence in the United States is not well documented. In this study, we assessed the prevalence of MH in New York State hospitals.

METHODS: Using New York hospital discharge data for the years 2001 through 2005, we identified all patients with a diagnosis of MH due to anesthesia using International Classification of Diseases, Ninth Revision, Clinical Modification code 995.86. MH prevalence was evaluated by demographic and clinical characteristics.

RESULTS: Of the 12,749,125 discharges from New York hospitals during the study period, 73 patients had a recorded diagnosis of MH due to anesthesia. Nearly three quarters of the MH patients were male and 71% were patients from emergency/urgent admissions. The estimated prevalence rate of MH was 0.96 (95% confidence interval [CI] 0.67–1.24) per 100,000 surgical discharges and 1.08 (95% CI 0.75–1.41) per 100,000 discharges in which there was any indication of exposure to anesthesia. The estimated prevalence of MH for males was 2.5 to 4.5 times the rate for females.

CONCLUSION: The prevalence of MH due to anesthesia in surgical patients treated in New York State hospitals is approximately 1 per 100,000. MH risk in males is significantly higher than in females.
BACKGROUND: Morbid obesity (MO), obstructive sleep apnea (OSA), and neck circumference (NC) are widely believed to be independent risk factors for difficult tracheal intubation. In this study, we sought to determine whether these factors were associated with increased risk of difficult intubation in patients undergoing bariatric surgery. The predictive factors tested were OSA and its severity, as determined by apnea-hypopnea index (AHI), gender, NC, and body mass index (BMI).

METHODS: All sequentially enrolled MO patients underwent preoperative polysomnography. Severity of OSA was quantified using AHI and the American Society of Anesthesiologists’ OSA severity scale. All patients had a standardized anesthetic that included positioning in the "ramped position" for direct laryngoscopy.

RESULTS: One hundred eighty consecutive patients were recruited, 140 women and 40 men. The incidence of OSA was 68%. The mean BMI was 49.4 kg/m². The mean AHI was 31.3 (range, 0-135). All the patients’ tracheas were intubated successfully without the aid of rescue airways by anesthesia residents. Six patients required three or more
intubation attempts, a difficult intubation rate of 3.3%. There was an 8.3% incidence of difficult laryngoscopy, defined as a Cormack and Lehane Grade 3 or 4 view. There was no relationship between NC and difficult intubation (odds ratio 1.02, 95% confidence interval 0.93-1.1), between the diagnosis of OSA and difficult intubation ($P = 0.09$), or between BMI and difficult intubation (odds ratio 0.99, 95% confidence interval 0.92-1.06, $P = 0.8$). There was no relationship between number of intubation attempts and BMI ($P = 0.8$), AHI ($P = 0.82$), or NC ($P = 0.3$). Mallampati Grade III or more predicted difficult intubation ($P = 0.02$), as did male gender ($P = 0.02$). Finally, there was no relationship between Cormack and Lehane grade and BMI ($P = 0.88$), AHI ($P = 0.93$), or OSA ($P = 0.6$). Increasing NC was associated with difficult laryngoscopy but not difficult intubation ($P = 0.02$).

**CONCLUSIONS:** In MO patients undergoing bariatric surgery in the "ramped position," there was no relationship between the presence and severity of OSA, BMI, or NC and difficulty of intubation or laryngoscopy grade. Only a Mallampati score of 3 or 4 or male gender predicted difficult intubation.

**PEEP 提高使用大剂量肾上腺素 CPR 大鼠模型的存活率**

Positive End-Expiratory Pressure Improves Survival in a Rodent Model of Cardiopulmonary Resuscitation Using High-Dose Epinephrine

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**背景：**多种干预措施用于心肺复苏（CPR）的研究，以优化药物的使用、胸外按压和通气功能。没有研究显示呼气末正压（PEEP）对于 CPR 结果的作用。作者推测，由于呼气末正压可扭转肺不张，降低肺血管阻力，并有可能改善心输出量，因此，CPR 中使用 PEEP 将提高存活率。

**方法：**麻醉的 Sprague-Dawley 大鼠暴露于 1 分钟窒息心脏骤停。复苏程序为标准化的胸外按压、吸氧（FiO2 1.0）和静脉注射肾上腺素 30µg/kg（组 1）和 10µg/kg（组 2）。使用超声心动图评估左心功能（组 1），大鼠在 CPR 开始阶段或者是整个复苏过程中随机接受 5cm H2O PEEP 或 0 PEEP。存活定义为初步复苏后，自主循环恢复正常并持续 60min 或者 120min（组 2）。

**结果：**组间基础情况无差异。在组 1，与 0 PEEP 相比较，接受 5 cm H2O PEEP (FiO2 1.0 and 0.21) 可提升其存活率（7/9 和 6/6 vs 0/9, $P < 0.01$ and <0.001）。应用 5 cm H2O PEEP (FiO2 1.0) 能够增加左室舒张末容积，全身氧供和功能残气量。呼气末正压的使用并没有影响左室收缩功能或动脉血压。其结果差异不是因为氧合的增加，因为其存活率依次为 5 cm H2O PEEP (FiO2 1.0) < 5 cm H2O PEEP (FiO2 0.21) >
zero PEEP (Fio\textsubscript{2} 1.0),然而其动脉血氧分压的排序依次为 5 cm H\textsubscript{2}O PEEP (Fio\textsubscript{2} 0.21) > 5 cm H\textsubscript{2}O PEEP (Fio\textsubscript{2} 1.0) > zero PEEP (Fio\textsubscript{2} 1.0)。在另外一个组中，使用 10 µg/kg 肾上腺素，即使其存活率为 100%，PEEP 的益处仍有限。

结论：啮齿动物窒息心跳骤停模型，在 CPR 期间和之后持续呼气末正压通气（5 cm H\textsubscript{2}O），对于存活率有多方面的有益作用，但与吸入氧浓度无关，且无不良心血管效应。

（张蕾 译 陈杰 校）

**BACKGROUND:** Multiple interventions have been tested in models of cardiopulmonary resuscitation (CPR) to optimize drug use, chest compressions, and ventilation. None has studied the effects of positive end-expiratory pressure (PEEP) on outcome. We hypothesized that because PEEP can reverse pulmonary atelectasis, lower pulmonary vascular resistance, and potentially improve cardiac output, its use during CPR would increase survival.

**METHODS:** Anesthetized Sprague-Dawley rats were exposed to 1 min of asphyxial cardiac arrest. Resuscitation was standardized and consisted of chest compressions, oxygen (Fio\textsubscript{2} 1.0), and IV epinephrine 30 µg/kg (Series 1) and 10 µg/kg (Series 2). Left ventricular function was assessed by echocardiography (Series 1), and animals were randomized to receive either 5 cm H\textsubscript{2}O PEEP or zero PEEP at commencement of CPR and throughout resuscitation. Survival was defined as the presence of a spontaneous circulation 60 or 120 min (Series 2) after initial resuscitation.

**RESULTS:** There were no baseline differences between the groups. In Series 1, administration of 5 cm H\textsubscript{2}O PEEP (Fio\textsubscript{2} 1.0 and 0.21) was associated with improved survival compared with zero PEEP (7/9 and 6/6 vs 0/9, \( P < 0.01 \) and <0.001, respectively). Application of 5 cm H\textsubscript{2}O PEEP (Fio\textsubscript{2} 1.0) increased left ventricular end-diastolic area, systemic oxygenation, and functional residual capacity. Use of PEEP during CPR did not adversely affect left ventricular systolic function or arterial blood pressure. The outcome differences were not due to increased oxygenation because the rank order of survival was 5 cm H\textsubscript{2}O PEEP (Fio\textsubscript{2} 1.0) > 5 cm H\textsubscript{2}O PEEP (Fio\textsubscript{2} 0.21) > zero PEEP (Fio\textsubscript{2} 1.0), whereas the rank order of Pa\textsubscript{o}\textsubscript{2} was 5 cm H\textsubscript{2}O PEEP (Fio\textsubscript{2} 1.0) > 5 cm H\textsubscript{2}O PEEP (Fio\textsubscript{2} 0.21) > zero PEEP (Fio\textsubscript{2} 1.0). In an additional series in which epinephrine 10 µg/kg was used (Series 2), the survival was 100% with no beneficial effects of PEEP.

**CONCLUSION:** In asphyxial cardiac arrest in a small rodent model, continuous application of PEEP (5 cm H\textsubscript{2}O) during and after CPR had beneficial effects on survival that were independent of oxygenation and without adverse cardiovascular effects.

**The Effect of Obesity on Neuraxial Technique Difficulty in Pregnant Patients: A Prospective, Observational Study**

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BACKGROUND: Practitioners often presuppose that obesity will increase neuraxial technique difficulty in pregnant patients, but few investigators have systematically examined this population for risk factors associated with difficult epidural or spinal needle placement. We designed this study to prospectively identify factors that predict neuraxial technique difficulty in pregnant patients.

METHODS: Using a prospective, observational format, pregnant patients were examined for multiple potential risk factors for neuraxial technique difficulty, including current body mass index, ability to palpate spinous processes, maximum back flexion, scoliosis, and experience of the practitioner. Neuraxial technique difficulty was then assessed using two measures: 1) the number of needle passes needed to reach the desired space, and 2) the placement time from skin infiltration to either spinal injection or epidural catheter threading. Predictors of total needle passes were determined by fitting the data to a generalized linear model with negative binomial error. Predictors of neuraxial anesthetic time were determined by fitting a linear model to the log of neuraxial anesthetic placement time. A survival model was used to account for bias introduced when attending physicians intervened in resident physician procedures.

RESULTS: Neuraxial procedures in 427 pregnant patients were studied. For both the number of needle passes and the neuraxial anesthetic placement time, the significant predictors of difficulty were the practitioner’s ability to palpate the patient’s bony landmarks and the patient’s ability to flex her back. Obesity, as measured by body mass index, was not an independent predictor of either end point. Obesity did, however, strongly predict both the ability to palpate landmarks and flex the back.
CONCLUSIONS: Despite concerns that obesity may cause difficulty with neuraxial technique, some obese patients have surprisingly easy neuraxial block placements. When approaching any neuraxial anesthetic in a pregnant patient, and especially in the obese parturient, back flexion and landmark palpation predict neuraxial technique difficulty.

羟考酮与吗啡在腹腔镜下切除术后的病人静脉自控镇痛之比较

A Comparison of Intravenous Oxycodone and Intravenous Morphine in Patient-Controlled Postoperative Analgesia After Laparoscopic Hysterectomy

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背景：在这项研究中，作者研究了术后有内脏疼痛患者所需羟考酮和吗啡的剂量，缓解疼痛的程度以及副作用。

方法：91 位行腹腔镜子宫切除术的女患者在手术结束前接受羟考酮或吗啡静脉注射，并在术后 24 小时给予病人自控镇痛。

结果：羟考酮的累积消耗量比吗啡少（13.3 ± 10.4 mg 比 22.0 ± 13.1 mg, \( P = 0.001 \)）。使用羟考酮，术后第一小时的视觉模拟量表评分显著低，但术后 24 小时的镇静效果差，\( P=0.006 \)。

结论：与吗啡相比，羟考酮更适于缓解内脏疼痛，但不适用于镇静。

（邹巧群 译 陈杰 校）

INTRODUCTION: In this study, we investigated the dose requirements, pain relief, and side effects of oxycodone versus morphine after surgery with visceral pain.

METHODS: Ninety-one women received IV oxycodone or morphine before the end of laparoscopic hysterectomy and then continued with patient-controlled analgesia for 24 h postoperatively.

RESULTS: The accumulated oxycodone consumption was less (13.3 ± 10.4 mg vs 22.0 ± 13.1 mg, \( P = 0.001 \)) than morphine. With oxycodone, the visual analog scale scores were significantly lower in the first hour postoperatively and sedation was less during the 24-h postoperative period, \( P = 0.006 \).

CONCLUSIONS: Oxycodone was more potent than morphine for visceral pain relief but not for sedation.
背景：大量数据显示，吗啡和 n-甲基-d-天冬氨酸（NMDA）受体都位于外周水平，而作用于这些受体的药物经局部给药后，均可产生抗伤害作用，但是这些受体的内源性配体的抗伤害效应目前仍不明确。本次研究的目的在于确定内源性阿片肽，即内啡肽-1（EM1）和内源性 NMDA 受体拮抗剂犬尿喹啉酸（KYNA）的抗伤害效能，并在大鼠验证关节模型中研究两者在外周水平的相互作用。

方法：在大鼠右后足胫骨跗骨关节内注射角叉菜聚糖（300 µg/20 µL）以产生机械性超敏反应。用 von Frey 细丝（0.064-110 g）评估其机械痛阈。将 EM1（30, 100 和 200µg）、KYNA（30, 100, 200 和 400µg）以及以 1:1 的比例相混的两者的混合液分别注入受感染的关节，并在给药后 75min 时再次测定痛阈。


结论：外周给予内源性阿片类激动剂和 NMDA 受体拮抗剂的配体可能可以对抗炎症性疼痛。由于这两种药物很少越过血脑屏障，因此局部使用不会产生中枢性的副作用。

（周姝婧 译 陈杰 校）

BACKGROUND: Several data suggest that both opioid and N-methyl-d-aspartate (NMDA) receptors are localized at the peripheral level, and drugs acting on these receptors may produce antinociception after topical administration; however, the antinociceptive effect of endogenous ligands at these receptors is poorly clarified. Our goal in this study was to determine the antinociceptive potency of the endogenous opioid peptide, endomorphin-1 (EM1), and the endogenous NMDA receptor antagonist, kynurenic acid (KYNA), and their interaction at the peripheral level in the rat inflamed joint model.

METHODS: Mechanical hypersensitivity was produced by injection of carrageenan (300 µg/20 µL) into the tibiotarsal joint of the right hind leg. The mechanical pain threshold was assessed by von Frey filaments (0.064-110 g). EM1 (30, 100, and 200 µg), KYNA (30, 100, 200, and 400 µg), and their combinations in a fixed-dose ratio (1:1) were injected into the inflamed joint, and the pain threshold was determined repeatedly for 75 min after the drug administrations.

RESULTS: Neither EM1 nor KYNA administered to the inflamed joint influenced the pain threshold at the noninflamed side. Both ligands produced dose-dependent antihyperalgesia, and the highest doses caused a prolonged effect. EM1 had higher potency (30% effective dose [ED30] and 50% effective dose [ED50] values were 112 µg [confidence interval {CI}：80-146] and 167 µg [CI：135-220], respectively) compared
with KYNA (ED₃₀ and ED₅₀ values were 204 µg [CI: 160-251] and 330 µg [CI: 280-407], respectively). The antinociceptive effect of EM1 was prevented by subcutaneous naltrexone pretreatment. The coadministration of EM1 with KYNA caused an enhanced and/or prolonged antinociceptive effect. The ED₃₀ and ED₅₀ values of the combination were 141 µg [CI: 83-182] and 231 µg [CI: 190-293], respectively, which did not differ significantly from the theoretically additive values (ED₃₀ and ED₅₀ values were 145 µg [CI: 68-237] and 220 µg [CI: 144-230], respectively), thus the interaction between these ligands is additive. None of the treatments caused any sign of side effects.

**CONCLUSION:** Peripherally administered endogenous opioid agonist and NMDA receptor antagonist ligands might be beneficial in inflammatory pain. Because both drugs barely cross the blood-brain barrier, their local administration causes no central side effects.

**BACKGROUND:** Nociceptive behaviors might attenuate pain sensation. Phosphorylation of extracellular signal-regulated kinase (pERK) was recently reported to be induced by noxious stimuli in dorsal horn neurons. We investigated, in a formalin test, whether pERK of the dorsal horn is affected by licking.

**METHODS:** Twenty-four adult male rats were divided into four groups: control, formalin test, restricted control, and restricted formalin test. Ten percent formalin was applied to the hindpaw and licking was prevented by placing the animals in a modified restraint tube. After 25 minutes, the rats were sacrificed, and the lumbar spinal cord was collected. Immunohistochemistry was performed to detect pERK levels in the dorsal horn.

**RESULTS:** In the restricted formalin test group, the number of pERK-positive cells in the dorsal horn was significantly higher than in the other groups (P < 0.05). There was no significant difference in pERK expression between the formalin test and restricted control groups.

**CONCLUSION:** Licking decreases phosphorylation of extracellular signal-regulated kinase in the dorsal horn of the spinal cord after a formalin test.
injected subcutaneously into the left rear paw of the formalin test and restricted formalin test groups. The control and formalin test group rats were kept in a clear plastic chamber, whereas the restricted control and restricted formalin test group rats were kept in a modified-restraint, pipe-shaped chamber. All rats were killed after 25 min. Twelve sections of the lumbar spinal cord were processed for p-ERK immunohistochemistry using the avidin-biotin peroxidase method.

**RESULTS:** The number of p-ERK positive cells in the restricted formalin test group was significantly higher than in the other three groups in the ipsilateral-side superficial dorsal horn ($P < 0.05$). However, there was no significant difference between the formalin test group and the two control groups in pERK expression.

**CONCLUSION:** Licking decreased pERK of the spinal cord of the formalin test group. The findings suggested that licking attenuated the pain of the formalin test.
BACKGROUND: Intrathecal anesthesia is commonly used for lower limb surgery. Bupivacaine, levobupivacaine, and ropivacaine have all been used as intrathecal drugs, but their relative potency in this context has not been fully determined. In this study, we determined the median effective dose (ED_{50}) of these three local anesthetics for intrathecal anesthesia in lower limb surgery and hence their relative potencies.

METHODS: Seventy-five patients scheduled for lower limb surgery under combined spinal-epidural anesthesia were randomly allocated to one of three groups receiving intrathecal bupivacaine, levobupivacaine, or ropivacaine. The dose of local anesthetic was varied using up-down sequential allocation technique. The dose for the first patient in each group was 8 mg, and the dosing increment was set at 1 mg. Subsequent doses in each group were determined by the outcome in the previous patient using success or failure of the spinal anesthesia as the primary end point. A success was recorded if a bilateral T12 sensory block to cold was attained within 20 min after intrathecal injection, and the surgery proceeded successfully until at least 50 min after the intrathecal injection without supplementary epidural injection. The ED_{50} was calculated using the method of Dixon and Massey.

RESULTS: The ED_{50}s were 5.50 mg for bupivacaine (95% confidence interval [CI]: 4.90–6.10 mg), 5.68 mg for levobupivacaine (95% CI: 4.92–6.44 mg), and 8.41 mg for ropivacaine (95% CI: 7.15–9.67 mg) in intrathecal anesthesia. The relative anesthetic potency ratios are 0.97 (95% CI: 0.81–1.17) for levobupivacaine/bupivacaine, 0.65 (95% CI: 0.54–0.80) for ropivacaine/bupivacaine, and 0.68 (95% CI: 0.55–0.84) for ropivacaine/levobupivacaine.

CONCLUSION: This study suggests that in intrathecal anesthesia for lower limb surgery, ropivacaine is less potent than levobupivacaine and bupivacaine, whereas the potency is similar between levobupivacaine and bupivacaine.

In Vitro Inhibition of Factor XIII Retards Clot Formation, Reduces Clot Firmness, and Increases Fibrinolytic Effects in Whole Blood.
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背景: 在围术期进行血栓弹力图的检查又重新引起了人们的兴趣。血栓弹力图检查结果的主要决定因素包括凝血因子浓度（各种酶原和纤维原）和血小板计数，因此血小板抑制剂会使得主要受凝血因子影响的检测指标变得无意义。从而使得合并应用血小板抑制剂与否的检测结果逐渐被用于评估和检测血液制品替代治疗的效果。在本次研究中，我们评估了 XIII 因子抑制剂配伍应用糖蛋白 (GP) IIb/IIIa（血小板抑制）在全血血栓弹力图中的效应，以及应用 XIII 因子抗体对常规检测做一改进是否可用于检测 XIII 因子缺乏症。

方法: 正常全血会随着非特异性抗体、抗 GP IIb/IIIa 抗体或者中性抗 XIII 因子抗体数量的增加而被孵化改变。样本在经过组织因子激活和血小板抑制的处理后进行分
BACKGROUND: Thrombelastography has received renewed interest in the perioperative setting. The main determinants of thrombelastographic results are coagulation factor concentrations (various zymogens and fibrinogen) and platelet count; thus, platelet inhibition renders these assays mainly coagulation factor dependent. Assays with and without platelet inhibition are thus increasingly used to trigger and monitor replacement therapy with blood products. In this study, we evaluated the effect of factor XIII inhibition and additional glycoprotein (GP) IIb/IIIa blockade on (platelet-inhibited) whole blood thrombelastography and whether a modified routine assay (using factor XIII antibody) can be used to detect factor XIII deficiency.

METHODS: Normal whole blood was incubated with increasing amounts of a nonspecific antibody, an anti-GPIIb/IIIa antibody, or a neutralizing anti-factor XIII antibody; samples were analyzed with a tissue factor-activated and platelet-inhibited whole blood thrombelastographic assay. Clotting time, clot formation time, maximum clot firmness, and clot lysis at 60 min were evaluated in triplicate. Also, 25 whole blood routine samples were evaluated for factor XIII deficiency using a new thrombelastographic assay incorporating a factor XIII antibody and using a standard factor XIII assay for comparison.

RESULTS: Although GPIIb/IIIa inhibition did not alter the results of the platelet-inhibited whole blood thrombelastography, factor XIII inhibition significantly reduced maximum clot firmness (P = 0.020) and increased clot formation time (P = 0.025) and clot lysis (P = 0.007), leaving clotting time unchanged; a ceiling effect seemed to be present with increasing antibody concentrations in whole blood (but not plasma). The thrombelastographic assay for factor XIII deficiency (<70% activity) had a 90% sensitivity and negative predictive value (area under receiver operating characteristic curve 0.803, P = 0.0015); for a deficiency <60%, sensitivity and negative predictive value were 100% (area under receiver operating characteristic curve 0.84, P = 0.0037).
CONCLUSION: Factor XIII has significant impact on platelet-inhibited activated whole blood thrombelastography. This phenomenon should be considered when interpreting thrombelastographic results in the bleeding patient, especially when the results trigger procoagulant therapy. Antibody-mediated factor XIII inhibition can be used to establish thrombelastography-based assays to detect factor XIII deficiency.

The Myotonias and Susceptibility to Malignant Hyperthermia
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Malignant hyperthermia (MH) is a pharmacogenetic disorder of skeletal muscle in which volatile anesthetics trigger a sustained increase in intramyoplasmic Ca^{2+} via release from sarcoplasmic reticulum and, possibly, entry from the extracellular milieu that leads to hypermetabolism, muscle rigidity, rhabdomyolysis, and death. Myotonias are a class of myopathies that result from gene mutations in various channels involved in skeletal muscle excitation-contraction coupling and sarcolemmal excitability, and unusual DNA sequence repeats that result in the inability of many proteins, including skeletal muscle channels that affect excitability, to undergo proper splicing. The suggestion has often been made that myotonic patients have an increased risk of developing MH. In this article, we review the physiology of muscle excitability and excitation-contraction coupling, the pathophysiology of MH and the myotonias, and review the clinical literature upon which the claims of MH susceptibility are based. We conclude that patients with these myopathies have a risk of developing MH that is equivalent to that of the general population with one potential exception, hypokalemic periodic paralysis. Despite the fact that there are no clinical reports of MH developing in patients with hypokalemic periodic paralysis, for theoretical reasons we cannot be as certain in estimating their risk of developing MH, even though we believe it is low.
Prolonged propofol anesthesia is not associated with an increase in blood lactate.

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BACKGROUND: Lactic acidosis is considered an early sign of propofol infusion syndrome. In this study, we investigated the changes in lactate and pH with propofol versus volatile anesthesia (VA) of long duration.

METHODS: Demographic and intraoperative data were recorded retrospectively from the anesthesia records of patients who underwent elective spine surgery longer than 8 h. Propofol patients were matched 1:2 to VA patients, based on anesthesia time (AT) (±30 min) and blood loss (BL) (±500 mL).

RESULTS: Of 246 patients identified, 50 received propofol (AT = 10 ± 2 h, BL = 1955 ± 1409 mL) and were matched to 100 VA cases (AT = 10 ± 1 h, BL = 1801 ± 1543 mL), and of those, 40 and 72 patients, respectively, had complete lactate data at baseline and at 8 h after anesthesia and were included in the main analysis. The propofol group received 8.8 ± 2 mg · kg⁻¹ · h⁻¹ of propofol. The VA group age was older than the propofol group (58 ± 12 vs 51 ± 15 yr, respectively, P = 0.002), but there was no difference between the groups in gender, ASA grade, intraoperative hemodynamic variables, and use of vasopressors. After 8 h, the VA group had a larger increase in arterial lactate from baseline compared with the propofol group (change from baseline: propofol, 0.48 ± 0.72 mmol/L; VA, 1.2 ± 1.2 mmol/L, P = 0.001).
CONCLUSIONS: During prolonged spine surgery >8 h, VA was associated with higher serum lactate, when compared with propofol infusion. Prospective studies are needed to elucidate the exact mechanisms and clinical implications of this finding.

异氟烷抑制SH-SY5Y细胞的环磷酸腺苷反应元件结合蛋白磷酸化以及钙调蛋白易位至细胞核

Isoflurane inhibits cyclic adenosine monophosphate response element-binding protein phosphorylation and calmodulin translocation to the nucleus of SH-SY5Y cells.


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BACKGROUND: Calmodulin (CaM) activation by Ca(2+), its translocation to the nucleus, and stimulation of phosphorylation of cyclic adenosine monophosphate response element-binding protein (CREB) (P-CREB) are necessary for new gene expression and have been linked to long-term potentiation, a process important in memory formation. Because isoflurane affects memory, we tested whether isoflurane interfered with the translocation of CaM to the neuronal cell nucleus and attenuated the formation P-CREB.

METHODS: SH-SY5Y cells, a human neuroblastoma cell line, were cultured. Cells were depolarized with KCl and the phosphorylation of CREB examined by Western blotting, enzyme-linked immunosorbant assay, and immunocytochemistry. The translocation of CaM from the cytosol to the nucleus was also examined after
depolarization. Cells were depolarized and lysed and fractionated by centrifugation to determine the amount of CaM translocated to the nucleus. CaM was localized by immunocytochemistry and quantitated by Western blotting and imaging. Before and during KCl depolarization, cells were exposed to isoflurane, isoflurane plus BΩay K 8644, nitrendipine, and Ω-conotoxin GV1a, respectively.

RESULTS: P-CREB increased after KCl depolarization. The increase of P-CREB peaked at depolarization duration of 30 s. The increase in P-CREB formation was inhibited by nitrendipine, but not omega-conotoxin, and by isoflurane in a concentration-dependent fashion. Pretreatment with the L-type Ca(2+) channel agonist, Bay K 8644, attenuated the inhibition of P-CREB formation by isoflurane. CaM presence in the nucleus occurred after KCl depolarization. CaM translocation was inhibited by nitrendipine and attenuated by isoflurane. Bay K 8644 pretreatment decreased the isoflurane inhibition of CaM translocation to the nucleus.

CONCLUSIONS: Our data demonstrate that isoflurane inhibits CaM translocation and P-CREB formation. This most likely occurs through isoflurane inhibition of Ca(2+)entry through L-type Ca(2+) channels.
BACKGROUND: Pediatric patients frequently receive continuous infusions of drugs via central venous catheters in the intensive care unit and the operating room. This study characterized drug delivery profiles in a quantitative laboratory model of a standard pediatric central venous infusion system.

METHODS: We evaluated drug delivery via a standard pediatric 8-cm, 4-F double-lumen catheter. One syringe pump infused normal saline as the carrier fluid through a limb of a Y-piece connected to the catheter's 22-gauge distal lumen. Through the other limb of the Y-piece, a second syringe pump infused methylene blue, the model drug, at a constant rate of 0.5 mL/h. The volume delivered was collected every minute for quantitative analysis. We compared 2 mL/h and 12 mL/h total flow rates to mimic volume delivery to a 3-kg infant, and priming of the Y-piece with the model drug, to mimic resumption of a stopped drug infusion, versus no priming, to mimic a new infusion. Drug pump system start-up performance was measured to estimate this factor's contribution to infusion onset profiles.

RESULTS: When initiating a new infusion of the model drug, the time to steady-state delivery at the catheter's end varied significantly among the studied scenarios as measured by the time to reach half of the targeted dose (t(50)). Onset of delivery with a low total flow was much slower (t(50) = 23.5 +/- 2.1 min) than with the high flow rate (t(50) = 15.7 +/- 2.9 min). Priming the drug limb of the connecting Y-piece with methylene blue substantially shortened the time to steady state (low flow t(50) = 12.7 +/- 0.6 min, high flow t(50) = 5.2 +/- 0.8 min). Time to cessation of drug delivery to the end of the catheter after stopping the drug pump was substantially shorter using the high carrier flow rate (t(50) = 3 +/- 0.5 min) compared with the low carrier flow rate (t(50) = 11.6 +/- 0.8 min). Drug pump system start-up performance contributed to onset delay.

CONCLUSIONS: Current infusion techniques in the pediatric care setting can result in significant, unrecognized, and potentially hazardous delays in achieving delivery of intended drug doses to the patient. Total flow rate, priming of the infusion system, the dead volume of the fluid path, and the start-up performance of the infusion pump system contribute to delays in achieving targeted rates of drug delivery.

背景：镇痛分娩过程中麻醉相关的并发症的流行病学研究

Epidemiology of Anesthesia-Related Complications in Labor and Delivery, New York State, 2002-2005

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背景：镇痛分娩过程中麻醉相关的并发症的流行病学资料对于评估产科麻醉的安全性及有效性是非常有必要的，但是这方面的数据是缺乏的。在我们的这项研究中，我们对纽约医院中产妇进行大规模的研究，旨在调查麻醉相关的并发症的流行病学情况。
方法：使用医疗保健的费用，并应用国家住院病人数据库资料，我们收集了纽约各大医院从 2002 年至 2005 年产科病人的资料。根据第九版国际疾病分类法修订版，我们收集了分娩镇痛过程中出现麻醉相关并发症的病人信息。我们统计了麻醉相关并发症发生的人口特征及临床特征。并使用多因素回归分析的方法评估了麻醉相关并发症的危险因素。

结果：总共调查了 957,471 名产妇，其中 4438 (0.46%) 名至少出现一项麻醉相关并发症。其中并发症主要是椎管内麻醉相关的并发症（占 55%），其次是系统性症状（占 43%），药物过量及药物副作用占 2%。多因素回归分析揭示了五个麻醉相关并发症的危险因素：剖宫产(优势比[OR] 2.51, 95%置信区间[CI] 2.36-2.68), 农村地区(OR 1.33, 95% CI 1.21-1.46), Charlson-Deyo 同病指数≥1 (OR 1.47, 95% CI 1.28-1.69), 高加索人种(OR 1.37, 95% CI 1.24-1.52), 及择期入院(OR 1.10, 95% CI 1.03-1.18)。麻醉相关并发症与平均住院天数增加天相关（3.89 ± 3.69 [均数±标准差]天 vs 2.92 ± 2.38 天，分娩过程中没有麻醉相关并发症, P < 0.0001），增加了孕产妇死亡率 22 倍(OR 22.26, 95% CI 11.20-44.24)。

结论：尽管分娩镇痛过程中麻醉相关并发症的发生率较低，但是仍应引起重视，特别是那些行剖宫产的，生活在农村或有合并症的产妇。

（陈珺珺译 薛张纲校）

BACKGROUND: Epidemiologic data on anesthesia-related complications occurring during labor and delivery are essential for measuring and evaluating the safety and quality of obstetric anesthesia care but are lacking. We aimed to fill this research gap by exploring the epidemiologic patterns and risk factors of anesthesia-related complications in a large sample of women giving birth in New York hospitals.

METHODS: Using the Healthcare Cost and Utilization Project State Inpatient Databases files, we identified all discharge records for labor and delivery from New York hospitals between 2002 and 2005. We then identified women who experienced any recorded anesthesia-related complication during labor and delivery as determined by International Classification of Diseases, Ninth Revision, Clinical Modification codes. The incidence of anesthesia-related complications was calculated by demographic and clinical characteristics. Multivariate logistic regression was performed to assess risk factors of anesthesia-related complications.

RESULTS: Of the 957,471 deliveries studied, 4438 (0.46%) had at least one anesthesia-related complication. The majority (55%) of anesthesia-related events occurring during labor and delivery were spinal complications, followed by systemic complications (43%) and overdose or adverse effects (2%). Multivariate logistic regression revealed five risk factors of anesthesia-related complications: cesarean delivery (odds ratio [OR] 2.51, 95% confidence interval [CI] 2.36-2.68), rural area (OR 1.33, 95% CI 1.21-1.46), Charlson-Deyo Comorbidity Index ≥1 (OR 1.47, 95% CI 1.28-1.69), Caucasian race (OR 1.37, 95% CI 1.24-1.52), and scheduled admission (OR 1.10, 95% CI 1.03-1.18). Anesthesia-related complications were associated with about a one-day increase in the average length of stay (3.89 ± 3.69 [mean ± sd] days vs 2.92 ± 2.38 days for deliveries without anesthesia-related complications, P < 0.0001) and a 22-fold increased risk of maternal mortality (OR 22.26, 95% CI 11.20-44.24).

CONCLUSION: The incidence of anesthesia-related complications during labor and delivery seems to be low but remains a cause of concern, particularly in women
undergoing cesarean delivery, living in rural areas, or having preexisting medical conditions.

**A Prediction Model for Out-of-Hospital Cardiopulmonary Resuscitation**

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**BACKGROUND:** We created a prediction model to be used in cardiopulmonary resuscitation (CPR) attempts as a decision tool to omit futile CPR attempts and to save resources.

**METHODS:** In this post hoc analysis, we assessed predictive parameters for neurological recovery after successful CPR. The original study was designed as a blinded, randomized, prospective, controlled, multicenter clinical trial.

**RESULTS:** We identified 1166 prehospital cardiac arrest patients being treated with advanced cardiac life support. Seven hundred eighty-six of 1166 patients (67.4%) died at the scene and 380 of 1166 (32.6%) were brought to the hospital. Two hundred sixty-five of 1166 patients (22.7%) died in the hospital. One hundred fifteen of 1166 (9.8%) were discharged from the hospital and 92 of the 115 patients (80%) could be followed-up. Good cerebral performance was regained by 54% of discharged patients (50 of 92 patients). In 46% of patients (42/92), unconsciousness or severe disability remained. Ventricular fibrillation was more likely to have occurred in patients with good neurological recovery (42/50 = 84.0%), whereas asystole was more likely in patients with...
poor neurological recovery (9/42 = 21.4%). A score was developed to predict the probability of death using logistic regression analysis. Predicting death in the hospital revealed a sensitivity of 99.8% (953/955), but only a specificity of 2.9% (3/104; threshold 0.5). Predicting survival until discharge from the hospital revealed a sensitivity of 99% (103/104), but only a specificity of 8% (72/955; threshold 0.99). A receiver operating characteristic curve yielded an area under the curve of 0.795 (0.751-0.839) at a confidence interval of 95%.

CONCLUSION: For out-of-hospital patients with cardiac arrest, parameters documented in the field did not allow accurate prediction of hospital survival.

A Randomized Trial Comparing Colloid Preload to Coload During Spinal Anesthesia for Elective Cesarean Delivery
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BACKGROUND: Hypotension after spinal anesthesia for cesarean delivery is common. Previous studies have demonstrated that a crystalloid fluid "coload" (rapid administration of a fluid bolus starting at the time of intrathecal injection) is superior to the conventional crystalloid preload (fluid
administered before the intrathecal injection) for preventing hypotension. Colloid preload provides a sustained increase in central blood volume. We hypothesized that, in contrast to crystalloid, a colloid preload may be more effective than colloid coload for reducing the incidence of spinal anesthesia-induced hypotension.

METHODS: In this double-blind study, 178 patients were randomly assigned to receive a preload of 500 mL of hydroxyethyl starch over a period of 15–20 min before initiation of spinal anesthesia (n = 90) or an identical fluid bolus of hydroxyethyl starch starting at the time of identification of cerebrospinal fluid (n = 88). Vasopressors (ephedrine or phenylephrine) were administered if systolic arterial blood pressure decreased less than 80% of the baseline pressure and <100 mm Hg, or with smaller decreases in blood pressure if accompanied by nausea, vomiting, or dizziness. The primary outcome was the incidence of hypotension (defined as the administration of at least one dose of vasopressor).

RESULTS: There was no significant difference between the groups in the incidence of hypotension (68% in preload group and 75% in coload group, 95% confidence interval of difference –6%–20%; P = 0.28), doses of ephedrine and phenylephrine, and number of vasopressor unit doses. The incidence of severe hypotension (systolic blood pressure <80 mm Hg) was 16% in the preload group and 22% in the coload group (P = 0.30). There were no differences in the incidence of nausea and/or vomiting, or neonatal outcome between the groups.

CONCLUSION: There was no difference in the incidence of hypotension in women who received colloid administration before the initiation of spinal anesthesia compared with at the time of initiation of anesthesia. Both modalities are inefficient as single interventions to prevent hypotension.

Sevoflurane Preconditioning Induces Rapid Ischemic Tolerance Against Spinal Cord Ischemia/Reperfusion Through Activation of Extracellular Signal-Regulated Kinase in Rabbits
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背景：七氟醚预处理对脊髓缺血/再灌注（I/R）保护作用是不清楚的。我们设计这个研究，调查是否七氟醚预处理可在短暂兔脊髓缺血模型中诱导快速缺血耐受，以及细胞外信号调节激酶（ERK）如何作用的。
方法：新西兰白色雄性家兔随机分为三组来测试七氟醚预处理是否诱导快速缺血耐受。七氟醚组动物预处理吸入3.7%七氟醚（1.0最低肺泡麻醉浓度）混合96%氧气30分钟，而氧气组动物仅控制性吸入96%氧气30分钟。假手术组接受了同样的麻醉和手术的准备，但没有预处理或脊髓的缺血/再灌注。评估ERK的激活在七氟醚预处理中作用，兔随机分为4组。U0126，ERK的抑制剂，于预处理前20分钟注入U0126+O2组和U0126+七氟醚组。同时在媒介物+O2组和媒介物+七氟醚组中静脉注入二甲基亚砜。预处理后1小时，动物通过腹主动脉阻断来导致脊髓
BACKGROUND: The protective effect of sevoflurane preconditioning against spinal cord ischemia/reperfusion (I/R) is unclear. We designed this study to investigate whether sevoflurane preconditioning could induce rapid ischemic tolerance to the spinal cord in a rabbit model of transient spinal cord ischemia and how the role of extracellular signal-regulated kinase (ERK) is involved.

METHODS: To test whether preconditioning with sevoflurane induces rapid ischemic tolerance, New Zealand White male rabbits were randomly assigned to three groups. Animals in the Sev group received preconditioning with 3.7% sevoflurane (1.0 minimum alveolar anesthetic concentration) in 96% oxygen for 30 min, whereas animals in the O2 group serving as controls inhaled only 96% oxygen for 30 min. The Sham group received the same anesthesia and surgical preparation but no preconditioning or spinal cord I/R. To evaluate the role of ERK activation in sevoflurane preconditioning, rabbits were randomly assigned to four groups. U0126, an ERK inhibitor, was administered IV 20 min before the beginning of preconditioning in the U0126 + O2 and U0126 + Sev groups. Dimethylsulfoxide was administered IV at the same time in the vehicle + O2 and vehicle + Sev groups. At 1 h after preconditioning, the animals were subjected to spinal cord I/R induced by infrarenal aorta occlusion. All animals were assessed at 48 h after reperfusion with modified Tarlov criteria, and the spinal cord segments (L5) were harvested for histopathological examination, TUNEL staining, and Western blot of phosphor-ERK1/2.

RESULTS: The animals in the Sev group had higher neurological scores and more normal motor neurons than those in the O2 group (P < 0.01 for each comparison). Compared with vehicle + Sev group, the U0126 + Sev group had worse neurological outcomes, fewer viable neurons, more apoptotic neurons, and significantly decreased ERK1/2 phosphorylation (P ≤0.01 for each comparison). There were no significant differences in the outcomes among vehicle + O2, U0126 + O2, and U0126 + Sev groups.

CONCLUSIONS: This study demonstrates that sevoflurane preconditioning induces rapid tolerance to spinal cord I/R in rabbits, and the tolerance is possibly mediated through the activation of ERK. These data suggest that sevoflurane preconditioning might provide a new practical method for protecting perioperative spinal cord I/R.

弗罗因德式完全佐剂诱发椎间盘炎的椎间盘源性下腰痛的动物模型
Complete Freund's adjuvant-induced intervertebral discitis as an animal model for discogenic low back pain.
BACKGROUND: Although numerous animal models for low back pain associated with intervertebral disk (IVD) degeneration have been proposed, insufficient data have been provided to make any conclusions regarding pain. Our aim in this study was to determine the reliability of complete Freund's adjuvant (CFA) injection into the rat spine as an animal model representing human discogenic pain.

METHODS: We studied IVD degenerative changes with pain development after a 10-microL CFA injection into the L5-6 IVD of adult rats using behavioral, histologic, and biochemical studies. Serial histologic changes were analyzed to detect degenerative changes. Expression of calcitonin gene-related peptide (CGRP), prostaglandin E (PGE), and inducible nitric oxide synthase (iNOS) were determined using immunohistochemistry or real-time polymerase chain reaction as support data for pain development. In addition, CGRP immunoreactivity (ir) at the IVD was considered indirect evidence of neural ingrowth into the IVD.

RESULTS: There was a significant increase of the hindpaw withdrawal response in the CFA group until 7 wk postoperatively (P < 0.05). Histologic analyses revealed progressive degenerative changes of the disks without any damage in adjacent structures, including nerve roots. In the CGRP-ir staining study, the bilateral dorsal horns and IVD had positive ir after intradiscal CFA injection. CGRP mRNA expression was increased in the dorsal root ganglion (DRG) at 2 and 4 wk, whereas PGE and iNOS mRNAs were markedly increased at 2 wk. The increment of CGRP expression was higher in allodynic rats compared with nonallodynic rats.
CONCLUSION: Intradiscal CFA injection led to chronic disk degeneration with allodynia, which was suggested by pain behavior and expression of pain-related mediators. The increment of CGRP, PGE, and iNOS also suggest pain-related signal processing between the IVD and the neural pathway in this animal model. This animal model may be useful for future research related to the pathophysiology and development of novel treatment for spine-related pain.

大鼠鞘内注射吗啡与马普替林的协同效应
The Synergistic Interaction Between Morphine and Maprotiline After Intrathecal Injection in Rats

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BACKGROUND: Antidepressant drugs act as potent inhibitors of norepinephrine and/or serotonin reuptake and are widely used with opioids for the treatment of chronic pain. The mechanism of this increased analgesic action is unclear. We compared the anti-nociceptive effects of the intrathecal administration of morphine with that of a nonselective (amitriptyline) or selective (maprotiline or citalopram) antidepressant drug
using the thermal withdrawal test in rats. We also investigated the possible mechanisms involved in the interactions of these drugs.

**METHODS:** Male Wistar rats were anesthetized with sevoflurane and administered morphine and antidepressant drugs, or saline, through intrathecal injection. The antinociceptive effect was evaluated using the thermal withdrawal test before and after drug administration. The time for the withdrawal reaction was expressed as percentage of maximum possible effect (MPE). Animals were also pretreated with yohimbine (a nonselective alpha2-adrenergic antagonist) and naloxone (a nonselective opioid antagonist) for mechanism of action studies. Pharmacologic interaction was evaluated using isobolographic analysis of simultaneous administration of fixed proportions of maprotiline and morphine.

**RESULTS:** Single intrathecal administration of morphine (2 µg), amitriptyline (125 µg), citalopram (144 µg), and maprotiline (1.25 µg) produced 51.6% ± 8.9%, 10.3% ± 3.2%, 33.8% ± 5.2%, and 48.5% ± 9.2% MPE, respectively. The antinociceptive effect of morphine was increased when combined with amitriptyline (91.3% ± 4.6% MPE) and maprotiline (86.9% ± 9.2% MPE) but not with citalopram (40.6% ± 4.6% MPE). Coadministration of maprotiline increased the antinociceptive duration of morphine by 4-fold (from 120 to 480 min), which was reversed by pretreatment with the α2-adrenoceptor inhibitor, yohimbine, and the mu-type opioid receptor antagonist, naloxone. Isobolographic analysis demonstrated a synergistic interaction between morphine and maprotiline.

**CONCLUSIONS:** Selective norepinephrine reuptake inhibitors can significantly increase the intensity and duration of morphine antinociceptive activity via both α2-adrenergic and opioid receptors. This interaction was not observed with the selective serotonin inhibitor, citalopram.
BACKGROUND: In this study, we evaluated the effect of paracetamol on sensory and motor block onset time, tourniquet pain, and postoperative analgesia, when added to lidocaine in IV regional anesthesia (IVRA).

METHODS: Sixty patients undergoing hand surgery were randomly and blindly divided into three groups. All groups received IVRA lidocaine (3 mg/kg) diluted with saline to a total volume of 40 mL. Group 1 received IVRA lidocaine plus IV saline, Group 2 received IVRA lidocaine and paracetamol (300 mg) admixture plus IV saline, and Group 3 received IVRA lidocaine plus IV paracetamol (300 mg). Sensory and motor block onset time, tourniquet pain, and analgesic use were assessed during operation. After tourniquet deflation, visual analog scale (VAS) scores at 1, 2, 4, 6, 12, and 24 h, the time to first analgesic requirement, total analgesic consumption in first 24 h, and side effects were noted.

RESULTS: Onset of motor block was shorter and recovery of motor and sensory block was significantly longer in Group 2 ($P < 0.05$). Intraoperative VAS scores at intraoperative 20, 30, and 40 min were significantly lower in Group 2 ($P < 0.05$). Intraoperative fentanyl consumption (78 ± 12, 58 ± 14, 78 ± 11 µg, respectively) and the number of patients who required fentanyl for tourniquet pain (13 patients, 3 patients, 9 patients, respectively) were significantly less in Group 2 ($P < 0.05$). Time to postoperative fentanyl administration was also prolonged (15 ± 6, 25 ± 5, 15 ± 4 min, respectively) in Group 2 ($P < 0.05$). The quality of surgical anesthesia was better in Group 2 ($P < 0.05$). Postoperative VAS scores and time of initial analgesic requirement were similar among groups; however, the total amount of diclofenac use was less in Group 2 ($P < 0.05$).

CONCLUSION: The addition of paracetamol during IVRA with lidocaine decreased tourniquet pain, increased anesthesia quality, and decreased postoperative analgesic consumption.

The Effects of Cardiopulmonary Bypass on the Number of Cerebral Microemboli and the Incidence of Cognitive Dysfunction After Coronary Artery Bypass Graft Surgery

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BACKGROUND: Postoperative cognitive dysfunction (POCD) can be a debilitating complication after coronary artery bypass graft (CABG) surgery. Cerebral microemboli during cardiopulmonary bypass (CPB) are believed to be an important etiologic factor of POCD. In this study, we examined whether avoidance of CPB with "off-pump" surgery reduces the number of cerebral microemboli and the incidence of POCD after CABG surgery in Chinese population.

METHODS: Two hundred twenty-seven patients were enrolled in this prospective cohort study. Fifty-nine patients underwent CABG surgery with CPB and 168 underwent off-pump surgery. Cerebral microemboli were measured continuously with bilateral transcranial Doppler ultrasonography of the middle cerebral arteries. A neuropsychological test battery that included seven tests with nine subscales was administered at baseline, as well as at 1 wk and 3 mo after surgery. POCD was defined using the international study of POCD1 definition.

RESULTS: The median total number of cerebral microemboli for the case was 430 (range: 155–2088) in patients undergoing surgery with CPB and 2 (0–66) in the off-pump patients (P < 0.001). There were no differences in the incidence of POCD between the patients having surgery with or without CPB either at 1 wk (55.2% or 32/58 [95% confidence interval: 41.5%–68.3%] vs 47.0% or 78/166 [39.2%–54.9%], P = 0.283) and 3 mo (6.4% or 3/47 [1.3%–17.5%] vs 13.1% or 16/122 [7.7%–20.4%], P = 0.214), for patients with or without CPB. Age at intervention and shorter postoperative length of stay were independently associated with POCD at 1 wk. Age at intervention and diabetes were associated with POCD at 3 mo. CPB and cerebral microemboli were not associated with POCD in both groups.
patients [7.7%–20.4%, P = 0.214) after surgery. Increasing age and shorter duration of postoperative hospital stay were independently associated with cognitive dysfunction at 1 wk after surgery. Increasing age and a history of diabetes mellitus were independently associated with cognitive dysfunction 3 mo after surgery. CPB or cerebral microemboli were not significantly related to the occurrence of POCD.

CONCLUSIONS: In Chinese population, avoidance of CPB during CABG surgery significantly decreased the number of cerebral microemboli, but it did not decrease the incidence of POCD at either 1 wk or 3 mo after CABG. Neither CPB nor cerebral microemboli was independently associated with the risk of POCD.

恶性高热、共存失调和酶病：风险和管理选择
Malignant Hyperthermia, Coexisting Disorders, and Enzymopathies: Risks and Management Options
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已观察到患多种综合症、酶病和两者共存的病人出现与诊断恶性高热一致的临床症状和异常实验室试验，因此提高了有相同诊断的其他病人的病因相关的可能性和已增高的围术期风险。在本综述中，我们检查了被其他医生认定为潜在易患恶性高热患者的可得到的已发表系列、病例报道和挛缩试验的结果。对多数情况下，与恶性高热易感性有病因相关的证据是很少的。本综述总结了当支持或不支持相关性的证据不确定时的临床管理的建议。

Clinical episodes and abnormal laboratory tests compatible with a diagnosis of malignant hyperthermia have been observed in patients with a diversity of syndromes, enzymopathies, and coexisting disorders thereby raising the likelihood of causal associations and heightened perioperative risk in others carrying a shared diagnosis. In the present review, we survey available published series, case reports, and the results of contracture testing in patients identified by others to be potentially predisposed to malignant hyperthermia. For most conditions, evidence for a causal relationship with malignant hyperthermia susceptibility is weak. The review concludes with suggestions for clinical management when evidence for or against an association is uncertain.

神经肌肉阻滞不同程度地影响近最低肺泡有效浓度麻醉下的体动抑制和皮层活性
Neuromuscular Block Differentially Affects Immobility and Cortical Activation at Near–Minimum Alveolar Concentration Anesthesia
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BACKGROUND: Anesthesia-induced immobility and cortical suppression are governed by anatomically separate, but interacting, areas of the central nervous system. Consequently, larger volatile anesthetic concentrations are required to suppress cortical activation than to abolish movement in response to noxious stimulation. We examined the effect of decreased afferent input, as produced by neuromuscular block (NMB), on immobility and cortical activation, as measured by Bispectral index (BIS) of the electrocardiogram, in the presence of noxious stimulation during approximately minimum alveolar concentrations (MACs) of desflurane anesthesia.

METHODS: The effect of NMB on the median effective end-tidal concentration of desflurane (EtDes50, or MACtetanus) for immobility was estimated using the up-and-down method and isolated forearm technique in 24 healthy volunteers. Each volunteer sequentially received saline, mivacurium, and succinylcholine in a randomized order, while EtDes concentration during each of the treatments was determined based on the
movement response of the previous volunteer on the same treatment. Nonlinear mixed-effects modeling was used to evaluate the effect of NMB on BIS versus EtDes concentration relationship at baseline and after noxious stimulation, while the frontal electromyogram (EMG_{BIS}) effect on BIS was also modeled as a covariate. Cardiovascular responses to noxious stimulation were compared across treatments.

RESULTS: Succinylcholine and mivacurium significantly reduced MAC_{tetanus} (95% confidence interval) from 5.00% (4.85%–5.13%), during saline, to 4.05% (3.81%–4.29%) and 3.84% (3.60%–4.08%), respectively. Noxious stimulation significantly, although minimally, increased BIS response during all treatments. Succinylcholine increased BIS independently of an effect on EMG_{BIS}. Succinylcholine administration increased cardiovascular activity. Interestingly, although cardiovascular reaction to the noxious event was ablated by mivacurium, cortical response, as determined by BIS, was retained.

CONCLUSIONS: Both succinylcholine and mivacurium enhanced immobility during near-MAC anesthesia. All treatments were associated with a small, although significant, BIS increase in response to noxious stimulation, whereas succinylcholine increased BIS independently of noxious stimulation or EMG_{BIS}. Mivacurium suppressed autonomic response to a noxious event.

短暂接触七氟烷后，干细胞样人内皮祖细胞显示集落形成能力增强：吸入麻醉药对血管生成细胞的预处理
Stem Cell-Like Human Endothelial Progenitors Show Enhanced Colony-Forming Capacity After Brief Sevoflurane Exposure: Preconditioning of Angiogenic Cells by Volatile Anesthetics
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背景：内皮祖细胞在组织修复中起关键作用，因此在“再生医学”中被用于细胞的替代治疗。我们检验麻醉药七氟烷是否会调制这些血管生成细胞的生长或动员。
方法：在离体模型中，从健康捐献者的外周血中分离出来的单核细胞用七氟烷预处理（2 vol%, 30 min 3 次，间隔于 30 min 空气）。9 天后在培养中测定集落形成单位，并与同期配对的未处理对照进行比较。使用磁性细胞分选法，从人脐带血中富集 CD133+/CD34+ 的内皮祖细胞，并用实时逆转录多聚酶链式反应对七氟烷处理或未处理细胞内血管内皮生长因子（VEGF）、VEGFR2（KDR）、粒细胞集落刺激因子（G-CSF）、STAT3、c-kit 以及 CXCR4 的表达进行测定。在一个采用交叉试验设计的志愿者研究中，我们使用外周血样流式细胞仪，检验吸入七氟烷（呼气
末浓度<1 vol%）是否动员内皮祖细胞从骨髓生态位区进入循环。同时测定血浆中VEGF 和 G-CSF 的水平。

结果：单核细胞体外接触七氟烷增强 CD133+/CD34+ 脐带血细胞的集落形成能力并增加 VEGF mRNA 水平（P = 0.017）。健康志愿者吸入七氟烷并不改变循环中 CD133+/CD34+ 或 KDR+/CD34+ 内皮祖细胞的数量，但增加了集落形成单位的数量（P = 0.034），而血浆中 VEGF 和 G-CSF 的水平保持不变。

结论：七氟烷预处理促进了干细胞样人类内皮祖细胞的生长和增殖，因此可能用于促进围手术期血管愈合并支持细胞替代治疗。

（黄施伟 译，马皓琳 李士通 校）

BACKGROUND: Endothelial progenitor cells play a pivotal role in tissue repair, and thus are used for cell replacement therapies in "regenerative medicine." We tested whether the anesthetic sevoflurane would modulate growth or mobilization of these angiogenic cells.

METHODS: In an in vitro model, mononuclear cells isolated from peripheral blood of healthy donors were preconditioned with sevoflurane (3 times 30 min at 2 vol% interspersed by 30 min of air). Colony-forming units were determined after 9 days in culture and compared with time-matched untreated control. Using magnetic cell sorting, CD133+/CD34+ endothelial progenitors were enriched from human umbilical cord blood, and vascular endothelial growth factor (VEGF), VEGFR2 (KDR), granulocyte colony-stimulating factor (G-CSF), STAT3, c-kit, and CXCR4 expressions were determined in sevoflurane-treated and untreated cells by real-time reverse transcriptase polymerase chain reaction. In a volunteer study with crossover design, we tested whether sevoflurane inhalation (<1 vol% end-tidal concentration) would mobilize endothelial progenitor cells from the bone marrow niche into the circulation using flow cytometry of peripheral blood samples. VEGF and G-CSF plasma levels were also measured.

RESULTS: In vitro sevoflurane exposure of mononuclear cells enhanced colony-forming capacity and increased VEGF mRNA levels in CD133+/CD34+ cord blood cells (P = 0.017). Sevoflurane inhalation in healthy volunteers did not alter the number of CD133+/CD34+ or KDR+/CD34+ endothelial progenitors in the circulation, but increased the number of colony-forming units (P = 0.034), whereas VEGF and G-CSF plasma levels remained unchanged.

CONCLUSIONS: Sevoflurane preconditioning promotes growth and proliferation of stem cell-like human endothelial progenitors. Hence, it may be used to promote perioperative vascular healing and to support cell replacement therapies.

Impact of Multiaccess Infusion Devices on In Vitro Drug Delivery During Multi-Infusion Therapy

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BACKGROUND: Multiaccess infusion sets allow multiple simultaneous infusions but may induce interference in drug delivery resulting from large variations in the delivery rate of potent drugs. In this study, we sought to understand the influence of multiaccess infusion device properties (dead space volume and antireflux valve [ARV]) on drug delivery during multi-infusion therapy.

METHODS: Infusion sets differing in length, dead space volume, and presence of an ARV were assessed. Three drugs were infused simultaneously through different access points, and their concentrations were obtained using UV spectrophotometric analysis of the effluent. Different infusion configurations were compared by assessing (1) the amount of drug delivered to the patient per unit of time, (2) the mean amount of drug delivered to the patient per unit of time during the steady-state infusion (mass flow rate plateau), and (3) flow change efficiency calculated from the ratio of the area under the experimental instant mass flow rate curve to the area corresponding to theoretical instant mass flow rate curve.

RESULTS: Infusion sets with lower dead space volumes offered significantly higher flow change efficiency (53.0% ± 15.4% with a dead space volume equal to 0.046 mL 5 min after the start of infusion) than infusion sets with higher dead space volume (5.6% ± 8.2% with a dead space volume equal to 6.16 mL), whatever the flow rate changes. Even in case of large dead space volumes, the presence of an ARV significantly increased the mass flow rate plateau (from 92.4% to 99.3% of the theoretical plateau without and with the presence of an ARV, respectively).
CONCLUSIONS: Multi-infusion therapy induces perturbation in drug delivery. These perturbations (lag time, backflow, and bolus) could be reduced by using infusion sets including very low dead space volume and an ARV.

Core Myopathies and Risk of Malignant Hyperthermia
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In this article, we analyze myopathies with cores, for which an association to malignant hyperthermia (MH) has been suggested. We discuss the clinical features, the underlying genetic defects, subsequent effects on cellular calcium metabolism, and in vitro muscle responses to MH triggers. We describe in detail central core disease, multimimicore disease, and nemaline rod myopathy. We categorize the diseases according to the affected proteins and discuss the risk for MH, which is high or theoretically possible when the calcium-conducting proteins are affected.

The Relative Exposure of the Operating Room Staff to Sevoflurane During Intracerebral Surgery
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The background of this study is to investigate whether the exposure of anesthesiologists and neurosurgeons to sevoflurane is higher than that of other medical staff during intracerebral surgery. The study was conducted at the University Hospital of Debrecen, Hungary, and included 35 consecutive patients who underwent intracerebral surgery. The study measured the exposure levels of sevoflurane in the operating room, and compared them to those of other medical staff. The results showed that the exposure levels of sevoflurane were significantly higher for the anesthesiologists and neurosurgeons, with a peak of 1.8 times higher than that of the other medical staff. The study concluded that the exposure levels of sevoflurane during intracerebral surgery are significantly higher for anesthesiologists and neurosurgeons, and that proper precautions should be taken to minimize the exposure levels.
BACKGROUND: Our primary aim in this study was to investigate whether escape of the volatile anesthetic sevoflurane from the surgical site during craniotomy for tumor resection increases the exposure of the neurosurgeon to the anesthetic when compared with the anesthesiologist.

METHODS: Initially, the release of sevoflurane from the surgical site was measured during 35 tumorectomies starting from opening to closure of the dura. Volatile anesthetic absorbers were placed at three detection sites: 1) the surgeon’s breathing zone, 2) the anesthesiologist’s breathing zone, and 3) the farthest corner of the operation room. In the second sampling series that included 16 patients, the detector that had been in the corner of the operating room in the first series was now placed in the vicinity of the patient’s mouth (within 5 cm). Sevoflurane captured by the absorbers was quantified by an independent chemist using chromatography.

RESULTS: Absorbers in the surgeon’s breathing zone (0.24 ± 0.04 ppm) captured a significantly lower amount of sevoflurane compared with absorbers in the anesthesiologist’s breathing zone (1.40 ± 0.37 ppm) and comparable with that in the farthest corner of the operation room (0.25 ± 0.07 ppm). There was no correlation between the amount of absorbed sevoflurane and the size of craniotomy window, even when adjusting for the variation in duration of surgery. In the second series of sampling, absorbers in the proximity of the patient’s mouth captured the highest amount of sevoflurane (1.54 ± 0.55 ppm), followed by the anesthesiologist’s (1.14 ± 0.43 ppm) and the surgeon’s (0.15 ± 0.05 ppm) breathing zones.

CONCLUSIONS: The close proximity of the surgeon’s breathing zone to the craniotomy window does not appear to be a source of increased exposure to sevoflurane. The observed higher exposure of the anesthesiologist to sevoflurane in the operating room environment warrants further exploration.

The Effect of Gender on Compensatory Neuromuscular Response to Upper Airway Obstruction in Normal Subjects Under Midazolam General Anesthesia

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BACKGROUND: Upper airway patency may be compromised during sleep and anesthesia by either anatomical alterations (mechanical properties) or disturbances in the neural control (compensatory neuromuscular responses). The pathophysiology of upper airway obstruction during anesthesia may differ between men and women. Recently, we reported that the upper airway mechanical properties were comparable with those found during natural nonrapid eye movement sleep, as evaluated by measurements of passive critical closing pressure ($P_{CRIT}$) and upstream resistance ($R_{US}$) during midazolam sedation. In this study, we compared the effects of gender on compensatory neuromuscular responses to upper airway obstruction during midazolam general anesthesia.

METHOD: Thirty-two subjects (14 men and 18 women) were studied. We constructed pressure-flow relationships to evaluate $P_{CRIT}$ and $R_{US}$ during midazolam anesthesia. The midazolam anesthesia was induced with an initial dose of midazolam (0.07–0.08 mg/kg bolus) and maintained by midazolam infusion (0.3–0.4 µg · kg$^{-1}$ · min$^{-1}$), and the level of anesthesia was assessed by Ramsay score (Level 5) and Observer’s Assessment of Alertness/Sedation score (Level 2). Polysomnographic and hemodynamic variables were monitored while nasal pressure (via mask), inspiratory air flow (via pneumotachograph), and genioglossal electromyograph (EMGGG) were recorded. $P_{CRIT}$ was obtained in both
the passive condition, under conditions of decreased EMG (passive $P_{CRIT}$), and in an active condition, whereas EMG was increased (active $P_{CRIT}$). The difference between the active $P_{CRIT}$ and passive $P_{CRIT}$ ($\Delta P_{CRIT A-P}$) was calculated in each subject to determine the compensatory neuromuscular response.

**RESULTS:** The difference between the active $P_{CRIT}$ and passive $P_{CRIT}$ ($\Delta P_{CRIT A-P}$) was significantly greater in women than in men (4.6 ± 2.8 cm H2O and 2.2 ± 1.7 cm H2O, respectively; $P < 0.01$), suggesting greater compensatory neuromuscular response to upper airway obstruction independent of arousal.

**CONCLUSION:** We demonstrate that the arousal-independent compensatory neuromuscular responses to upper airway obstruction during midazolam anesthesia were partially maintained in women, and that gender may be a major determinant of the strength of compensatory responses during anesthesia.

从实验室及理论角度分析安氟醚的皮质电效应

**The Electrocortical Effects of Enflurane: Experiment and Theory**

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**背景：**高浓度的安氟醚能引起典型的脑电图：包括周期性抑制与大而短的突发性癫痫样放电(PEDs)交替。在本研究中，我们比较了这种活性的理论性计算机模型与从麻醉大鼠中获得的真实局部场电位(LFP)数据。

**方法：**将 $8 \times 8$ 高密度电极植入视皮层后，记录大鼠在0.5、1.0、1.5及2.0倍最小肺泡麻醉浓度(MAC)的安氟醚麻醉时LFP及多元峰活性。将来自于新皮层动力学平均场模型的电脑模拟与这些记录进行比较。通过延长抑制性突触后电位(IPSP)衰减时间常数模拟增加安氟醚浓度所产生的神经元效应。与新皮层的激发率相反，我们调整了兴奋性突触后电位(EPSP)的振幅。

**结果：**在麻醉大鼠中，安氟醚浓度的持续增加会始终引起LFP记录中表现出抑制波型(>1.5 MAC)。多元峰电位的平均速率从2.54/s(0.5 MAC)下降到0.19/s(2.0 MAC)。在高MAC时，大多数的多元运动电位事件变得与PED同步。在理论模型中，IPSP衰减时间的延长及活性依赖EPSP的调整所导致的输出结果与从实验数据中所获得的形态相似。通过分析方程的本征值来测定模型中节律性暴发样活动的倾向。

**结论：**使用新皮层动力的平均场理论来复制安氟醚麻醉大鼠LFP中所观察到的PED图型是可能的。该图型需要作一些综合调整：适当增加IPSP下的总面积，延长IPSP衰减时间，及对EPSP的振幅进行活性依赖的调整。

(裘毅敏译，马皓琳、李士通校)
BACKGROUND: High concentrations of enflurane will induce a characteristic electroencephalogram pattern consisting of periods of suppression alternating with large short paroxysmal epileptiform discharges (PEDs). In this study, we compared a theoretical computer model of this activity with real local field potential (LFP) data obtained from anesthetized rats.

METHODS: After implantation of a high-density 8 x 8 electrode array in the visual cortex, the patterns of LFP and multiunit spike activity were recorded in rats during 0.5, 1.0, 1.5, and 2.0 minimum alveolar anesthetic concentration (MAC) enflurane anesthesia. These recordings were compared with computer simulations from a mean field model of neocortical dynamics. The neuronal effect of increasing enflurane concentration was simulated by prolonging the decay time constant of the inhibitory postsynaptic potential (IPSP). The amplitude of the excitatory postsynaptic potential (EPSP) was modulated, inverse to the neocortical firing rate.

RESULTS: In the anesthetized rats, increasing enflurane concentrations consistently caused the appearance of suppression pattern (>1.5 MAC) in the LFP recordings. The mean rate of multiunit spike activity decreased from 2.54/s (0.5 MAC) to 0.19/s (2.0 MAC). At high MAC, the majority of the multiunit action potential events became synchronous with the PED. In the theoretical model, prolongation of the IPSP decay time and activity-dependent EPSP modulation resulted in output that was similar in morphology to that obtained from the experimental data. The propensity for rhythmic seizure-like activity in the model could be determined by analysis of the eigenvalues of the equations.

CONCLUSION: It is possible to use a mean field theory of neocortical dynamics to replicate the PED pattern observed in LFPs in rats under enflurane anesthesia. This pattern requires a combination of a moderately increased total area under the IPSP, prolonged IPSP decay time, and also activity-dependent modulation of EPSP amplitude.
pregabalin 300 mg 12 h apart for preventing and attenuating PLSP after laparoscopic cholecystectomy. The frequency and severity of PLSP, need for postoperative rescue analgesia, and side effect profiles were assessed for 48 h postoperatively. In both groups, the overall incidence of PLSP did not differ significantly, and the pain score for PLSP, time to first rescue analgesia, and cumulative ketorolac consumption were similar at each timepoint. However, the 2-h postoperative incidence of oversedation was higher with pregabalin.

Activation of Extracellular Signal-Regulated Kinase in Sciatic Nerve Contributes to Neuropathic Pain After Partial Sciatic Nerve Ligation in Mice
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BACKGROUND: The mitogen-activated protein kinase family plays an important role in several types of pain. However, the detailed role of phosphorylated extracellular signal-regulated kinase (pERK) in the region of injured peripheral nerve is poorly understood. In this study, we investigated whether pERK in injured sciatic nerve contributes to neuropathic pain induced by partial sciatic nerve ligation (PSL) in mice.

METHODS: Mice received PSL; pERK1/2 (p44/42) in sciatic nerve was measured by both Western blotting and immunohistochemistry. U0126 (an ERK kinase inhibitor) was
injected twice, an intraneural injection (20 nmol/2 µL) 30 min before PSL, and a perineural injection (20 nmol/10 µL) on Day 1 after PSL. Thermal hyperalgesia and tactile allodynia induced by PSL were evaluated by the thermal paw withdrawal test and the von Frey test, respectively.

RESULTS: As measured by Western blotting, in sham-operated mice, the levels of pERK1/2 in sciatic nerve were constant and the same as those in naive mice across Days 1-14. In PSL-operated mice, a significant increase in pERK1/2 was observed on Day 1 after PSL and persisted until Day 3. As measured by immunohistochemistry, immunoreactivity of pERK1/2 in PSL-operated sciatic nerve was markedly increased in comparison with that in sham-operated sciatic nerve on Day 1 after PSL. In the sciatic nerve on Day 1 after PSL, as indicated by double immunostaining, the increased immunoreactivity of pERK1/2 was colocalized with glial fibrillary acidic protein (GFAP), a marker of Schwann cells, but not F4/80, a marker of macrophages. PSL-induced thermal hyperalgesia was significantly attenuated by treatment with U0126 on Days 3, 7, and 14 after PSL. The PSL-induced tactile allodynia was also significantly attenuated by treatment with U0126 on Days 7 and 14 after PSL.

CONCLUSION: Activation of ERK in Schwann cells of the injured peripheral nervous system may play an important role in the development of neuropathic pain. Our results suggest that pERK itself and ERK-related mediators are potential therapeutic targets for the treatment of neuropathic pain.
BACKGROUND: Cardiac toxicity significantly correlates with the lipophilicity of local anesthetics (LAs). Recently, the infusion of lipid emulsions has been shown to be a promising approach to treat LA-induced cardiac arrest. As the postulated mechanism of action, the so-called "lipid sink" effect may depend on the lipophilicity of LAs. In this study, we investigated whether lipid effects differ with regard to the administered LAs.

METHODS: In the isolated rat heart, cardiac arrest was induced by administration of equipotent doses of bupivacaine, ropivacaine, and mepivacaine, respectively, followed by cardiac perfusion with or without lipid emulsion (0.25 mL · kg⁻¹ · min⁻¹). Subsequently, the times from the start of perfusion to return of first heart activity and to recovery of heart rate and rate-pressure product (to 90% of baseline values) were assessed.

RESULTS: In all groups, lipid infusion had no effects on the time to the return of any cardiac activity. However, recovery times of heart rate and rate-pressure product (to 90% of baseline values) were significantly shorter with the administration of lipids in bupivacaine-induced cardiac toxicity, but not in ropivacaine- or mepivacaine-induced cardiac toxicity.

CONCLUSIONS: These data show that the effects of lipid infusion on LA-induced cardiac arrest are strongly dependent on the administered LAs itself. We conclude that lipophilicity of LAs has a marked impact on the efficacy of lipid infusions to treat cardiac arrest induced by these drugs.

星状神经节阻滞后分形心血管动力和压力反射敏感性的状态
Fractal Cardiovascular Dynamics and Baroreflex Sensitivity After Stellate Ganglion Block
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背景：研究现实星状神经节阻滞可降低压力反射的敏感性。本研究主要目的为确定心率和收缩压变异性分形动力学（自体相似波动模式的动态改变）是否均参与了星状神经节阻滞后压力反射敏感性降低的机制。

方法：16 名健康年轻志愿者参与了本次研究。采用 1% 甲哌卡因 6mL 间隔 1~1.5 月对志愿者行左或右星状神经节阻滞。阻滞前、阻滞后 30、60、90 和 120 分钟进行心率和收缩压变异性频谱分析。每次频谱分析后即刻采用直立倾斜试验评估压力反射敏感性。

结果：经直立倾斜试验评估，右侧或左侧星状神经节阻滞后 30 分钟压力反射敏感性显著降低（分别为 1.26 ± 0.18 到 0.46 ± 0.08 bpm/mm Hg, P < 0.05 和 1.17 ± 0.35 到 0.51 ± 0.13 bpm/min, P < 0.01）。显示波动自体相似性程度的分形斜率在右侧或左侧星状神经节阻滞后 30 分钟显著增加（右星状神经节阻滞一心率：-1.08 ± 0.31
到\(-1.62 \pm 0.22, P < 0.01\); 右星状神经节阻滞—收缩压；\(-1.30 \pm 0.80\) 到 \(-2.40 \pm 0.80, P < 0.05\); 左星状神经节阻滞—收缩压；\(-1.20 \pm 0.40\) 到 \(-2.13 \pm 0.50, P < 0.05\)。心率变异性分析显示分形斜率在左星状神经节阻滞后没有改变。

结论：分形斜率的增加提示心率和收缩压变异性复杂性的复杂性消失（保持复杂行为的状态），这是星状神经节阻滞后压力反射敏感性降低的机制之一。

（周雅春 译 马皓琳 李士通 校）

BACKGROUND: It has been shown that stellate ganglion block can attenuate baroreflex sensitivity. Our primary purpose in this study was to determine whether fractal dynamics (dynamic change of self-similar fluctuation patterns) of not only heart rate but also systolic blood pressure variability are involved in attenuation of baroreflex sensitivity after stellate ganglion block.

METHODS: Sixteen young, healthy volunteers entered the study. Spectral analysis of heart rate and systolic blood pressure variability was performed before and 30, 60, 90, and 120 min after either right or left stellate ganglion block, separated by a 1 to 1 interval, with 6 mL of 1% mepivacaine. Shortly after each spectral analysis, baroreflex sensitivity was assessed with the head-up tilt test.

RESULTS: Baroreflex sensitivity, assessed by the head-up tilt test, was significantly attenuated at 30 min after either right or left stellate ganglion block (1.26 ± 0.18 to 0.46 ± 0.08 bpm/mm Hg, \(P < 0.05\) and 1.17 ± 0.35 to 0.51 ± 0.13 bpm/min, \(P < 0.01\), respectively). Fractal slopes reflecting the degree of self-similarity of fluctuations were significantly increased at 30 min after either right or left stellate ganglion block (right stellate ganglion block—heart rate; \(-1.08 \pm 0.30\) to \(-1.62 \pm 0.22, P < 0.01\); right stellate ganglion block—systolic blood pressure; \(-1.30 \pm 0.80\) to \(-2.40 \pm 0.80, P < 0.05\); left stellate ganglion block—systolic blood pressure; \(-1.20 \pm 0.40\) to \(-2.13 \pm 0.50, P < 0.05\)). Fractal slope did not change after left stellate ganglion block with heart rate variability analysis.

CONCLUSIONS: Loss of complexity (status of being complex behavior) of both heart rate and systolic blood pressure variability, indicated by increased fractal slopes, is one mechanism in attenuating baroreflex sensitivity after stellate ganglion block.