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术中经食道心脏超声介导放置主动脉内球囊反搏泵

Positioning an Intraaortic Balloon Pump Using Intraoperative Transesophageal Echocardiogram Guidance

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Anesth Analg July 2011 113:40-43

一名射血分数 25% 的 72 岁老年男性计划在体外循环下择期行择期性冠状动脉搭桥术。由于手术的高风险性，外科医生想在体外循环开始前置入主动脉内球囊反搏泵 (IABP)。需要术中食道心脏超声 (TEE) 以确保放置在正确的位置。

(唐亮 译 马皓琳 李士通 校)

A 72-year-old man with an ejection fraction of 25% is scheduled to undergo elective coronary artery bypass graft using cardiopulmonary bypass. Because of the high-risk nature of the operation, the surgeon wants to insert an intraaortic balloon pump (IABP) before initiating cardiopulmonary bypass. An intraoperative transesophageal echocardiogram (TEE) is requested to ensure correct placement.

一项地氟烷与丙泊酚的对比：对超重病人术后早期肺功能的影响

A Comparison of Desflurane Versus Propofol: The Effects on Early Postoperative Lung Function in Overweight Patients

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背景：在这项研究中，我们评估并比较了丙泊酚与地氟烷麻醉对超重病人术后肺功能和脉搏血氧饱和度值的影响。

方法：我们前瞻性地研究了 134 名体重指数在 25 到 35 kg/m² 之间并正在进行持续 40 到 120 分钟的小型外周手术病人。病人被随机分配接受丙泊酚（全静脉麻醉）或经气管导管的地氟烷麻醉，控制脑电双频指数在 40 到 60 之间。术前用药、辅助药物使用和通气经过标准化。我们测定了术前（基线）和气管导管拔出后 10 分钟、0.5 小时、2 小时和 24 小时的血氧饱和度和肺功能。所有数值测定时病人均处于仰卧且头抬高 30° 体位。与术前基线数值比较的变化首先使用单变数方法分析体重指数和麻醉方式不同的影响，然后用线性回归和多元方差分析。

结果: 在术后 2 小时内, 丙泊酚组相对地氟烷组表现出较低的血氧饱和度 (2 小时, 平均值±标准差, 93.8% ± 2.0% 比 94.6% ± 2.1%; $P < 0.007$) 和肺功能 (用力肺活量、第一秒用力呼气量[FEV₁]、呼气峰流量、呼气中流量[MEF]、用力吸气肺活量和吸气峰流量; 在丙泊酚组相对基线有 11% 至 20% 的较大减少, 所有 $P < 0.001$)。甚至术后 24 小时, FEV₁、呼气峰流量、MEF、用力吸气肺活量和吸气峰流量在丙泊酚组也降低更多 (所有指标 $P < 0.01$)。在拔管后 2 小时, 肥胖程度加重使丙泊酚而非地氟烷麻醉的病人 FEV₁ 和 MEF 降低 ($P < 0.01$)。

结论: 我们推断, 对于最长达 120 分钟的表浅手术过程, 使用丙泊酚维持麻醉对术后早期肺功能和血氧饱和度的损害较使用地氟烷大。而且, 体重增加会降低丙泊酚麻醉术后 2 小时的肺功能, 但地氟烷麻醉不会。

(张怡译 马皓琳 李士通校)

BACKGROUND: In this study, we evaluated the influence of propofol versus desflurane anesthesia in overweight patients on postoperative lung function and pulse oximetry values.

METHODS: We prospectively studied 134 patients with body mass indices of 25 to 35 kg/m² undergoing minor peripheral surgery lasting 40 to 120 minutes. Patients were randomly assigned to receive propofol (total IV anesthesia) or desflurane anesthesia via a tracheal tube targeting bispectral index values of 40 to 60. Premedication, adjuvant drug usage, and ventilation were standardized. We measured oxyhemoglobin saturation and lung function preoperatively (baseline), and at 10 minutes, 0.5 hour, 2 hours, and 24 hours after tracheal extubation. All values were measured with the patient supine, in a 30° head-up position. Changes from preoperative baseline values were first analyzed for the impact of body mass index and type of anesthesia using univariate methods, followed by linear regression and multivariate analysis of variance.

RESULTS: Within the first 2 hours after surgery, the propofol group displayed lower oxyhemoglobin saturation (at 2 hours, mean ± SD, 93.8% ± 2.0% vs 94.6% ± 2.1%; $P < 0.007$) and lung function (forced vital capacity, forced expiratory volume exhaled in 1 second [FEV₁], peak expiratory flow, midexpiratory flow [MEF], forced inspiratory vital capacity, and peak inspiratory flow; between 11% and 20% larger reduction from baseline in the propofol group, all $P < 0.001$) compared with the desflurane group. Even 24 hours after surgery, FEV₁, peak expiratory flow, MEF, forced inspiratory vital capacity, and peak inspiratory flow were reduced more in the propofol group (all $P < 0.01$). At 2 hours after extubation, increasing obesity was associated with decreasing FEV₁ and MEF in patients anesthetized with propofol but not desflurane ($P < 0.01$).

CONCLUSION: We conclude that, for superficial surgical procedures of up to 120 minutes, maintenance of anesthesia with propofol impairs early postoperative lung function and pulse oximetry values more than with desflurane. Furthermore, increasing obesity decreases pulmonary function at 2 hours after propofol anesthesia but not after desflurane anesthesia.

麻醉前准备程序的疏漏步骤

Missed Steps in the Preanesthetic Set-Up

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背景：麻醉医师在诱导麻醉时快速完成许多工作。诱导准备的关键需要最大化患者的安全。考虑到手术室紧张的环境，准备步骤因为无意识或甚至可能有意为了节约时间而疏漏。我们做这研究来探究在手术室中诱导前即刻遗失步骤的发生率。

方法：在本研究中，我们用一个修正的麻醉前程序来随机核实 200 个外科手术在麻醉诱导前可能的疏漏步骤。另外记录多种其他手术房间/病例变量来探测疏漏步骤与某些变量（例如手术房间病例负荷和区域与全身麻醉比较）是否存在相关性。

结果：我们发现 23 个疏漏步骤。手动复苏装置可用性和一个处于工作状态的吸引器配备是最常见的疏漏步骤。计划的麻醉方法为区域麻醉的病例、在具有较多手术负荷（ ≥ 5 个计划手术）的手术房间中以及在主治医师完成配备的手术房间中疏漏步骤的发生率较高。

结论：疏漏步骤确实有显著且可测量的发生率。我们需要采取降低疏漏步骤数量的措施来改善患者的安全。

（刘朝辉译，马皓琳，李士通校）

BACKGROUND: Anesthesiologists accomplish many tasks rapidly during induction of an anesthetic. Key preparation for induction is needed to maximize patient safety. Given the intense environment of the operating room, preparatory steps may be missed either unintentionally or possibly even intentionally to save time. We conducted this study to determine the incidence of missed steps in the operating room immediately before induction.

METHODS: In this study, 200 surgical procedures were randomly checked for missed steps before induction of anesthesia using a “Revised Preanesthetic Set-Up.” Additionally, multiple other operating room/case variables were recorded to determine whether there was correlation between the missed steps and certain variables such as room case load and regional versus general anesthesia.

RESULTS: Twenty-three missed steps were discovered. Manual resuscitation device availability and a working suction set-up were the most frequently missed steps. A higher percentage of missed steps was found in cases in which regional was the planned anesthesia technique, in rooms with higher case loads (≥ 5 cases scheduled), and in rooms that attending anesthesiologists completed the set-up.

CONCLUSIONS: Missed steps do occur at a significant and measurable rate. Measures need to be taken to decrease the number of missed steps to improve patient safety.

用于直接喉镜检查的头颈部位置

Head and Neck Position for Direct Laryngoscopy

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嗅花位（SP）历来被认为是直接喉镜检查（DL）的最佳头位。但是它相对于其他头位的优势近十年来一直受到质疑。我们回顾了有关这一主题的稀有文献，来检查支持或者反对嗅花位常规使用的证据。为了避免对于什么是合适的嗅花位产生混淆以及便于比较从不同研究得到的结果，必须使用一个嗅花位的标准定义（如颈屈35°和头伸15°）。虽然有人提出一些理论来解释嗅花位优越性，但是三轴成一线理论仍然被认为是充分根据的解剖学解释。为了达到想得到的颈部前屈位，需要将头抬高，但是由于头颈部的解剖和胸廓的大小不同，每个人头部抬高的程度都不一样。比如，对于婴幼儿就不需要抬高头位，因为头的大小和形状的关系，在水平头位时三轴就很接近。胸骨与外耳道水平对齐可以作为肥胖以及非肥胖患者嗅花位的定位标记。对于所能获得的文献的分析是支持直接喉镜时采用嗅花位。在肥胖病人，为了达到合适的嗅花位，应该采用“斜坡”（或背部抬高）体位。嗅花位不能保证对于所有的患者都暴露充分，因为有很多其它解剖因素会影响暴露的最终分级。但是，嗅花位应该作为直接喉镜检查的初始头位，因为这个体位提供了暴露充分的最佳机会。为了达到合适的体位，必须要注意调整体位时的细节，避免小的技术失误。操作直接喉镜检查应该是不断修正的过程，在嗅花位遇到暴露困难的情况下应该调整体位。

(安光惠译 马皓琳 李士通校)

The sniffing position (SP) has traditionally been considered the optimal head position for direct laryngoscopy (DL). Its superiority over other head positions, however, has been questioned during the last decade. We reviewed the scarce literature on the subject to examine the evidence either in favor or against the routine use of the SP. A standard definition for the position should be used (e.g., 35° neck flexion and 15° head extension) to avoid confusion about what constitutes a proper SP and to compare the results from different studies. Although several theories were proposed to explain the superiority of the SP, the three axes alignment theory is still considered a valid anatomical explanation. Although head elevation is needed to achieve the desired neck flexion, the elevation height may vary from one patient to another depending on head and neck anatomy and size of the chest. In infants and small children, for example, no head elevation is needed because the size and shape of the head allow axes approximation in the head-flat position. Horizontal alignment of the external auditory meatus with the sternum, in both obese and non-obese patients, indicates, and can be used as a marker for, proper positioning. Analysis of the available literature supports the use of the SP for DL. To achieve a proper SP in obese patients, the “ramped” (or the back-up) position should be used. The SP does not guarantee adequate exposure in all patients, because many other anatomical factors control the final degree of visualization. However, it should be the starting head position for DL because it provides the best chance at adequate exposure. Attention to details during positioning and avoidance of minor technical errors are essential to achieve the proper position. DL should be a dynamic procedure and position adjustment should be instituted in case poor visualization is encountered in the SP.

在产科中用于硬膜外血斑的血量：一项随机、盲法临床试验

The Volume of Blood for Epidural Blood Patch in Obstetrics: A Randomized, Blinded Clinical Trial

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背景：此项多国、多中心、随机、盲法试验的目的在于确定用于硬膜外血斑的自体血 3 种容量中的最适容量。

方法：在硬膜外置管过程中非故意硬膜穿破后需行硬膜外血斑的产科患者，分别注入 15、20 或 30mL 血液，根据硬膜外血斑的时间和中心分组。随访受试者 5 天。主要研究指标为头痛持续或部分缓解的合成，次要指标包括头痛持续缓解、部分缓解、持续头痛的严重性以及操作过程中和操作后的腰痛。

结果：121 例女性患者完成了本试验。容量的中位数（四分位数间距）为 15（15-15）、20（20-20）和 30（22-30）mL，15、20 和 30mL 组分别有 98%、81% 和 54% 的患者接受了安排的容量。三组头痛持久或部分缓解率分别为 61%、73% 和 67%，头痛完全缓解率为 10%、32% 和 26%。15mL 组的 0-48 小时内头痛评分一时间曲线下面积最大。硬膜外血斑操作过程中和操作后的腰痛发生率各组相似，且程度较轻，但是 15mL 组操作后腰痛评分最高。未出现严重并发症。

结论：尽管硬膜外血斑的最适容量仍需要进一步确定，我们相信以上发现提示，在治疗产科患者硬膜穿破后头痛时，可尝试给予 20mL 自体血。

（陈彬彬 译 马皓琳 李士通 校）

BACKGROUND: Our aim in this multinational, multicenter, randomized, blinded trial was to determine the optimum of 3 volumes of autologous blood for an epidural blood patch.

METHODS: Obstetric patients requiring epidural blood patch after unintentional dural puncture during epidural catheter insertion were allocated to receive 15, 20, or 30 mL of blood, stratified for the timing of epidural blood patch and center. Participants were followed for 5 days. The primary study end point was a composite of permanent or partial relief of headache, and secondary end points included permanent relief, partial relief, persisting headache severity, and low back pain during or after the procedure.

RESULTS: One hundred twenty-one women completed the study. The median (interquartile range) volume administered was 15 (15–15), 20 (20–20), and 30 (22–30) mL, with 98%, 81%, and 54% of groups 15, 20, and 30 receiving the allocated volume. Among groups 15, 20, and 30, respectively, the incidence of permanent or partial relief of headache was 61%, 73%, and 67% and that of complete relief of headache was 10%, 32%, and 26%. The 0- to 48-hour area under the curve of headache score versus time was highest in group 15. The incidence of low back pain during or after the epidural blood patch was similar among groups and was of low intensity, although group 15 had the highest postprocedural back pain scores. Serious morbidity was not reported.

CONCLUSIONS: Although the optimum volume of blood remains to be determined, we believe these findings support an attempt to administer 20 mL of autologous blood when

treating postdural puncture headache in obstetric patients after unintentional dural puncture.

活性氧清除剂抑制大鼠短暂局灶性脑缺血-再灌注损伤后 STAT3 活化

Reactive Oxygen Species Scavenger Inhibits STAT3 Activation After Transient Focal Cerebral Ischemia-Reperfusion Injury in Rats

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背景：已证实信号传导子及转录激活子 3 (STAT3)在缺血性脑组织中被活化。然而，脑缺血-再灌注后 STAT3 活化的机制及其作用还不甚明了。本研究中，我们试图验证这一假设：脑缺血-再灌注后 STAT3 的活化与活性氧 (ROS) 的产生相关。

方法：采用阻断成年雄性 SD 大鼠大脑中动脉法建立局灶性脑缺血模型。用免疫组织化学和蛋白质免疫印迹法评估 STAT3 活化程度。通过大鼠持续性缺血或缺血-再灌注来明确 STAT3 活化的时间分布特性。给予 ROS 清除剂二甲叉三脲(DMTU)来评估 ROS 在诱导 STAT3 活化中起的作用。采用神经行为学评分和计算脑梗死体积法评估 DMTU 及 STAT3 活化抑制剂 AG490 对脑缺血损伤的影响。

结果：大脑中动脉阻断后缺血组织周围范围内神经元和星形胶质细胞 STAT3 的活化明显增加。STAT3 活化主要发生在再灌注时相而不是缺血相。此外，DMTU 以剂量依赖性方式抑制 STAT3 活化，提示 STAT3 活化或许是 ROS 产生后的继发性事件。DMTU 和 AG490 明显减少梗死面积且改善神经系统结果。

结论：相比缺血，再灌注能更强地刺激 STAT3 活化。ROS 清除与 STAT3 活化的抑制紧密相关。通过 ROS 的清除和 STAT3 活化的下调可达到神经保护作用。

(江继宏 译 马皓琳 李士通 校)

BACKGROUND: Signal transducer and activator of transcription 3 (STAT3) activation in ischemic brain has been verified. However, the mechanism and the role of STAT3 activation after cerebral ischemia-reperfusion are poorly elucidated. In the present study, we sought to test the hypothesis that STAT3 activation after cerebral ischemia-reperfusion was related to reactive oxygen species (ROS) production.

METHODS: Adult male Sprague-Dawley rats were subjected to focal cerebral ischemia induced by middle cerebral artery occlusion. STAT3 activation was evaluated by immunohistochemistry and Western blotting. Rats were subjected to permanent ischemia or ischemia-reperfusion to clarify the temporal profile of STAT3 activation. The role of ROS in inducing STAT3 activation was assessed by administration of the ROS scavenger dimethylthiourea (DMTU). The effects of DMTU and the STAT3 activation inhibitor AG490 administration on brain ischemic injuries were evaluated by neurologic behavior scores and brain infarct volumes.

RESULTS: The activation of STAT3 after middle cerebral artery occlusion was significantly increased within peri-ischemia neurons and astrocytes. STAT3 activation mainly occurred in the reperfusion phase rather than in the ischemia phase. In addition,

DMTU suppressed STAT3 activation in a dose-dependent manner, indicating that STAT3 activation may be a subsequent event after ROS production. DMTU and AG490 significantly reduced infarct sizes and improved neurologic outcomes.

CONCLUSION: In comparison with ischemia, reperfusion is a more powerful stimulus for STAT3 activation. ROS scavenging is closely correlated with an inhibition of STAT3 activation. Neuroprotective effects are achieved through ROS scavenging and down-regulation of STAT3 activation.

美金刚对大鼠浸润性皮肤镇痛的局部麻醉作用

The Local Anesthetic Effect of Memantine on Infiltrative Cutaneous Analgesia in the Rat

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背景：美金刚可阻滞 N-甲基-D-天冬氨酸受体以及 Na⁺离子流，这是局部麻醉的主要机制之一。迄今尚无研究提及美金刚有局部麻醉作用，因此我们研究了美金刚的局麻作用。

方法：在皮下注药阻滞表皮躯干肌肉反射后，我们评估了美金刚、利多卡因和地佐环平（MK-801）。将美金刚对大鼠的皮肤镇痛作用的剂量依赖性效应与利多卡因和 MK-801 进行比较。每种药物的作用时间通过等效基线（20%有效剂量 [ED₂₀], ED₅₀ 和 ED₈₀）来评估和比较。局麻药中频繁使用的利多卡因被视为对照组。

结果：我们证明了美金刚、利多卡因和 MK-801 在浸润性皮肤镇痛中产生剂量依赖性局麻作用。相对药效为 MK-801(10.4 [9.7–11.1]) > 美金刚(17.6 [15.2–20.4]) > 利多卡因(25.9 [23.8–28.1]) ($P < 0.01$)。在等效基线中，美金刚的作用时间较利多卡因($P = 0.012$)和 MK-801 ($P = 0.008$)长。联合给予美金刚(13.3 μmol/kg)和 MK-801(1.3 μmol/kg)的作用较单独给予美金刚(13.3 μmol/kg)或 MK-801 (1.3 μmol/kg)强，时间也较长。而局部注射生理盐水或腹腔内给予大剂量美金刚、利多卡因或 MK-801 均不产生皮肤镇痛作用（数据未显示）。

结论：本研究表明美金刚的效能弱于 MK-801，美金刚比利多卡因和 MK-801 可产生更长的镇痛时间。当与 MK-801 合用时，美金刚显示出皮肤镇痛的协同作用。我们的结论是美金刚比利多卡因提供更好的局部镇痛，而且 N-甲基-D-天冬氨酸受体同样促进了美金刚的镇痛作用。

（瞿亦枫 译 马皓琳 李士通 校）

BACKGROUND: Memantine blocks N-methyl-D-aspartate receptors and the Na⁺ current, one principal mechanism of local anesthesia. Until now, no study mentioned that memantine had a local anesthetic effect, and therefore we investigated the local anesthetic effect of memantine.

METHODS: After blockade of cutaneous trunci muscle reflex with subcutaneous injections, we evaluated the cutaneous analgesic effect of memantine, lidocaine, and dizocilpine (MK-801) in rats. The dose-dependent response of memantine on cutaneous analgesia was compared with lidocaine and MK-801 in rats. The duration of action for each drug was evaluated and compared on an equipotent basis (20% effective dose [ED₂₀], ED₅₀, and ED₈₀). Lidocaine, a frequently used local anesthetic, was used as control.

RESULTS: We demonstrated that memantine, lidocaine, and MK-801 produced dose-dependent local anesthetic effects as infiltrative cutaneous analgesia. The relative potency was MK-801 (10.4 [9.7–11.1]) > memantine (17.6 [15.2–20.4]) > lidocaine (25.9 [23.8–28.1]) ($P < 0.01$). On an equipotent basis, memantine showed longer duration than lidocaine ($P = 0.012$) and MK-801 ($P = 0.008$). Coadministration of memantine (13.3 $\mu\text{mol/kg}$) and MK-801 (1.3 $\mu\text{mol/kg}$) produced greater blockade and duration than memantine (13.3 $\mu\text{mol/kg}$) or MK-801 (1.3 $\mu\text{mol/kg}$) alone. Neither local injection of saline nor intraperitoneal administration of a large dose of memantine, lidocaine, or MK-801 produced cutaneous analgesia (data not shown).

CONCLUSIONS: This study indicated that memantine is less potent than MK-801, and that memantine elicits longer analgesic duration than both lidocaine and MK-801. When combined with MK-801, memantine demonstrates a synergistic effect of cutaneous analgesia. We conclude that memantine produces better local analgesia than lidocaine and that *N*-methyl-D-aspartate receptors also contribute to the analgesic effect of memantine.

围术期收缩压变异性是否能预测心脏手术后的死亡率？一项关于 ECLIPSE 试验的探索性分析

Does Perioperative Systolic Blood Pressure Variability Predict Mortality After Cardiac Surgery? An Exploratory Analysis of the ECLIPSE trials

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背景：对围术期血压稳定性与手术预后关系进行探讨的相关报道较罕见。本研究验证接受心脏手术患者收缩压（SBP）变异性与术后30天死亡率相关的假设。

方法：评估 ECLIPSE 试验中随机选取的 1512 名围术期高血压患者的围术期血压变异性。使用偏离设定收缩压范围所产生的压力幅度×持续时间（曲线下面积）来评

估血压变异度。以 10mmHg 为最小单位,将 SBP 下限逐步提高,在使术中设定 SBP 范围从 65-135 mmHg 升至 105-135 mmHg; 术前术后设定 SBP 范围从 75-145 mmHg 升至 105-135 mmHg 的过程中,进行各个设定下的变异度分析。采用多因素 Logistic 回归评估得出血压变异度与 ECLIPSE 试验得出的术后 30 天死亡率间关系。

结果: 当设定 SBP 范围为术中 75 - 135 mm Hg, 术前术后 85 - 145 mm Hg 时, 血压变异度与术后 30 天内死亡率显著相关。每增加收缩压 60 mm Hg × min/h, 30 天内死亡率比值比增加 1.16 (95% 可信区, 1.04-1.30)。如果曲线下面积从 0 提高至 300 mm Hg × min/h, 预计低风险患者的 30 天死亡率将从 0.2% 增至 0.5%, 而高风险患者将从 42.4% 增至 60.7%。

讨论: 围术期血压变异度与心脏手术患者 30 天死亡率相关, 术中偏离 75 to 135 mm Hg, 以及术前或术后偏离 85 to 145 mm Hg 范围的收缩压变异度与术后 30 天内死亡率显著相关。高风险患者预计死亡率大于低风险患者。

(陈毓雯 译 陈杰 校)

BACKGROUND: Few studies describe an association of perioperative blood pressure stability with postoperative outcome. We tested the hypothesis that systolic blood pressure (SBP) variability in patients undergoing cardiac surgery is associated with 30-day mortality.

METHODS: Perioperative blood pressure variability was evaluated in the 1512 patients who were randomized and had perioperative hypertension in the ECLIPSE trials. Blood pressure variability was assessed as the product of magnitude × duration of SBP excursions outside defined SBP ranges (area under the curve). SBP ranges were analyzed from 65 to 135 mm Hg intraoperatively and 75 to 145 mm Hg pre- or postoperatively, up to 105 to 135 mm Hg intraoperatively and 115 to 145 mm Hg pre- or postoperatively, with the narrower ranges defined by progressively increasing the lower SBP limit by 10 mm Hg increments. Multiple logistic regression was used to assess the association of blood pressure variability with 30-day mortality obtained from the primary ECLIPSE trial results.

RESULTS: Increased SBP variability outside a range of 75 to 135 mm Hg intraoperatively and 85 to 145 mm Hg pre- and postoperatively is significantly associated with 30-day mortality. The odds ratio was 1.16 (95% confidence interval, 1.04–1.30) for 30-day mortality risk per incremental SBP excursion of 60 mm Hg × min/h. The predicted probability of 30-day mortality increased for low-risk patients from 0.2% to 0.5%, and for high-risk patients from 42.4% to 60.7% if the area under the curve increased from 0 to 300 mm Hg × min/h.

CONCLUSIONS: Perioperative blood pressure variability is associated with 30-day mortality in cardiac surgical patients, proportionate to the extent of SBP excursions outside the range of 75 to 135 mm Hg intraoperatively and 85 to 145 mm Hg pre- and postoperatively. Predicted mortality was greater for high-risk patients than for low-risk patients.

麻醉恢复室中 CYP2D6-和 CYP3A-依赖的昂丹司琼血浆浓度具有对映体选择性
CYP2D6- and CYP3A-Dependent Enantioselective Plasma Concentrations of Ondansetron in Postanesthesia Care

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背景:细胞色素 P450 (CYP2D6)基因多态性会影响昂丹司琼的止吐作用,这一点已经被证实。然而, CYP3A 对于昂丹司琼代谢和药效影响的机制还不清楚。本研究的目的是评估基因型依赖的 CYP2D6 和 CYP3A 活性对昂丹司琼对映体血浆浓度的影响。另外,还评估了昂丹司琼加倍剂量对其基因型依赖的血浆浓度影响。

方法:病人麻醉前,静脉给予 4mg 或者 8mg 的昂丹司琼防止呕吐。CYP2D6 依赖活性评分包括 CYP2D6 酶活性无影响、降低、正常或增加,而 CYP3A 主要分为低表达(CYP3A5*3/*3)和高表达状态(CYP3A5 wt/wt or wt/*3)。使用液相质谱分析检测 R-昂丹司琼和 S-昂丹司琼对映体的血浆药物浓度。R-昂丹司琼和 S-昂丹司琼血浆浓度-时间曲线下面积(AUC)与 CYP2D6 和 CYP3A 基因型依赖的酶活性有关。

结果:共分析了 141 个完整数据。S-昂丹司琼的浓度随 CYP2D6 活性的不同而改变(P=0.01),没有 CYP2D6 活性组中浓度最高(95%CI: 362.5 [238.3/486.7] h·ng/mL),而 CYP2D6 活性增加组中,S-昂丹司琼的浓度则最低(95%CI: 149.6 [114.5/184.8] h·ng/mL),CYP2D6 活性减少和正常的基因型组中的 S-昂丹司琼的浓度分别为(263.6 [228.8/298.8], 255.4 [228.2/282.7] h·ng/mL),与 CYP3A5 高表达的基因型相比,低表达的 CYP3A5 基因型依赖的 R-昂丹司琼的 AUC 是其两倍多(281.5 [248.6/314.3] vs 142.5 [92.4/192.7] h·ng/mL; P = 0.003)。对于低活性 CYP3A 的个体,昂丹司琼剂量加倍会增加血浆药物浓度,而在高活性 CYP3A 的个体则无此现象(P<0.001)。

结论:昂丹司琼代谢是对映体选择性的。在麻醉恢复室中,CYP2D6 活性评分与 S-昂丹司琼的浓度相关联,而 CYP3A5 表达情况则主要影响 R-昂丹司琼的浓度。基因和环境决定了 CYP2D6 和 CYP3A 的酶活性,从而影响着昂丹司琼的止吐作用。

(张婷 译 陈杰 校)

BACKGROUND: An influence of polymorphic cytochromes P450 (CYP) 2D6 genetic variants on antiemetic efficacy of ondansetron has been suggested. However, the role of CYP3A in ondansetron metabolism and efficacy has been unclear. In this study, we evaluated the hypothesis that genotype-dependent CYP2D6 and CYP3A activity selectively influences plasma concentrations of ondansetron enantiomers. Additionally, the effects of doubling the ondansetron dose on genotype-dependent plasma concentrations were investigated.

METHODS: Patients received IV ondansetron 4 or 8 mg for emesis prophylaxis before emergence from anesthesia. The CYP2D6-dependent activity score representing no, decreased, normal, or increased CYP2D6 enzyme activity as well as CYP3A low (CYP3A5*3/*3) and high expressor status (CYP3A5 wt/wt or wt/*3) were determined. Plasma concentrations of R- and S-ondansetron enantiomers were measured by liquid

chromatography–tandem mass spectrometry. Area under the plasma concentration–time curves (AUCs) of *R*- and *S*-ondansetron were associated with CYP2D6 and CYP3A5 genotype-dependent enzyme activity.

RESULTS: Complete data of 141 subjects were analyzed. Concentrations of *S*-ondansetron differed between CYP2D6 activity groups ($P = 0.01$) with highest values in patients with no CYP2D6 activity (mean [95% confidence interval]: 362.5 [238.3/486.7] h · ng/mL) and lowest values in those with increased activity (149.6 [114.5/184.8] h · ng/mL) compared with subjects displaying genotypes resulting in reduced or normal CYP2D6 activity (263.6 [228.8/298.8], 255.4 [228.2/282.7] h · ng/mL). AUC of *R*-ondansetron was 2 times higher in CYP3A5 low expressors compared with high expressors (281.5 [248.6/314.3] vs 142.5 [92.4/192.7] h · ng/mL; $P = 0.003$). Doubling the ondansetron dose increased plasma concentrations only in individuals with low CYP3A activity, but not in individuals with high enzyme activity ($P < 0.001$).

CONCLUSIONS: The metabolism of ondansetron seems to be enantioselective. In this postoperative setting, CYP2D6 activity scores correlated with concentrations of *S*-ondansetron, whereas CYP3A5 expressor status mainly influenced concentrations of *R*-ondansetron. Genetically and environmentally determined CYP2D6 and CYP3A enzyme activity might have implications for antiemetic efficacy.

通过七氟醚浓度和脑电双频指数间滞后效应的测量证实肥胖不影响七氟起效和失效时间

Obesity Does Not Influence the Onset and Offset of Sevoflurane Effect as Measured by the Hysteresis Between Sevoflurane Concentration and Bispectral Index

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背景：在肥胖患者中，可能因患者的呼吸变化和气体交换改变而推迟麻醉气体的起效和失效的时间。这项研究评估了肥胖对于七氟醚显效滞后现象的影响。七氟醚的显效是通过脑电双频指数（BIS）测量来证实。由于呼气末正压（PEEP）可改善肥胖病人气体交换能力，作者还评估了 PEEP 对于滞后现象的影响。

方法：本研究对 15 名肥胖和 15 名体重正常，ASA 分级 I 级和 II 级，20 至 50 岁，接受全身麻醉的择期腹腔镜手术的患者进行前瞻性研究。使用异丙酚进行麻醉诱导，七氟醚和芬太尼进行麻醉维持。在手术结束后并使 BIS 值稳定在 60 至 65，增加七氟醚吸入浓度至 5% 维持 5 分钟后或直到 BIS 值 < 40 时降低吸入浓度。此项七氟醚的转换过程在体重正常的受试者（无 PEEP）进行一次，在肥胖患者中进行两次（PEEP 为 0 和 8cmH₂O）。使用 NONMEM 6 法建立人群药代学/药效动力学（PK / PD）相关的抑制 E_{max} 模型，应用此模型描述在转换过程中七氟醚呼气末浓

度和 BIS 值之间的迟滞效应。关于七氟醚吸入和呼出浓度、BIS 值以及达到不同 BIS 值终点的时间的描述性分析也用来比较 PK 和 PD 的特性。

结果：所有患者完成了研究。这些数据符合 PK / PD 模型。而体重指数或 PEEP ($P > 0.05$) 不会影响代表滞后效应的效应室消除速率常数。肥胖和 PEEP 不会对任何的 PK / PD 的描述性指标产生影响。

结论：此项研究结果并不支持以下假设：肥胖延长七氟醚-这一难溶麻醉剂的麻醉诱导时间或麻醉维持 90-120 分钟患者的麻醉恢复时间。

(孙晓琼 译 陈杰 校)

BACKGROUND: The onset and offset of action of anesthetic gases might be delayed by respiratory changes and gas exchange alterations present in obese patients. In this study, we assessed the influence of obesity on the hysteresis between sevoflurane and its effect as measured by the bispectral index (BIS). Because the use of positive end-expiratory pressure (PEEP) in obese patients has improved gas exchange, we also assessed the influence of PEEP on hysteresis.

METHODS: Fifteen obese and 15 normal-weight patients, ASA physical status I and II, 20 to 50 years old, scheduled to undergo general anesthesia for elective laparoscopic surgery, were prospectively studied. Anesthesia was induced with propofol and maintained with sevoflurane and fentanyl. At the end of surgery and after stable BIS values of 60 to 65, the inspired concentration of sevoflurane was increased to 5 vol% for 5 minutes or until BIS was <40 and then decreased. Sevoflurane transitions were performed once in normal-weight subjects (without PEEP) and twice in obese patients (one without PEEP and one with a PEEP of 8 cm H₂O). The hysteresis between sevoflurane end-tidal concentrations and BIS during these transition periods was modeled with an inhibitory Emax model using a population pharmacokinetic/ pharmacodynamic (PK/PD) approach with NONMEM VI. A descriptive analysis of sevoflurane inspired and expired concentrations, BIS values, and time to reach different BIS end points was also used to compare the PK and PD characteristics.

RESULTS: All patients completed the study. The data were adequately fit with the PK/PD model. The hysteresis expressed as the effect-site elimination rate constant was not influenced by body mass index or PEEP ($P > 0.05$). Neither obesity nor PEEP showed any influence on the PK/PD descriptors.

CONCLUSIONS: Our results do not support the hypothesis that obesity prolongs induction or recovery times when sevoflurane, a poorly soluble anesthetic, is used to maintain anesthesia from 90 to 120 minutes.

胃部超声检查在禁食外科患者中的应用：一项前瞻性描述性研究

Gastric Sonography in the Fasted Surgical Patient: A Prospective Descriptive Study

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背景：吸入性肺炎目前仍然是一项严重的麻醉相关并发症。目前缺少一种可靠的诊断工具来评估胃容量。不久前一项研究已经证实了在健康志愿者身上采用胃部超声检查可以提供可靠的关于胃容量和内容物的定性和定量信息。此项前瞻性研究将对 200 例接受择期手术的空腹患者的胃窦进行定性及定量分析。

方法：在全麻诱导前完成标准化胃部扫描程序。分别对仰卧位和右侧卧位患者进行胃窦超声的定性扫描后，采用三分制分级系统进行患者分类。

结果：86 例患者为 0 级（空胃窦），107 例为 1 级（仅在右侧卧位发现极少的液体体积），7 例为 2 级（在平卧位和右侧卧位均可清晰发现胃窦内液体伴有明显扩张）。3 分制分级系统与预先通过数学建模估计的全胃液体容量有相关性。0 级对应完全排空的胃，1 级对应可忽略不计的液体容量（ $16\pm 36\text{ml}$ ），在达到空腹要求的可接受范围内，2 级对应明显比预期大的胃液体容量（ $180\pm 83\text{ml}$ ），已经超过之前报道的“安全”限制。胃窦达到 2 级的一名患者在麻醉开始时发生了明显胃内容物返流。

结论：我们单独根据胃窦部超声结果定性分析，提出的 3 分制分级系统与预计的胃容量结果良好相关。此分级系统有望成为术前评估吸入风险的“生物标记”。在广泛运用于临床实践之前，这项诊断技术还需要进一步进行认证和设计。

（陆秉玮 译 陈杰 校）

BACKGROUND: Aspiration pneumonia remains a serious anesthetic-related complication. A reliable diagnostic tool to assess gastric volume is currently lacking. We recently demonstrated that gastric sonography can provide reliable qualitative and quantitative information about gastric content and volume in healthy volunteers. In the current study, we performed a prospective qualitative and quantitative analysis of the gastric antrum in 200 fasted patients undergoing elective surgery.

METHODS: A standardized gastric scanning protocol was applied before anesthetic induction. Patients were classified following a 3-point grading system based solely on qualitative sonographic assessment of the antrum in the supine and right lateral decubitus positions.

RESULTS: Eighty-six patients were classified as grade 0 (empty antrum); 107 patients as grade 1 (minimal fluid volume detected only in the right lateral decubitus position); and 7 patients were classified as grade 2 (antrum clearly distended with fluid visible in both supine and lateral positions). The 3-point grading system correlated with total gastric fluid volume as predicted by a previously reported mathematical model. Essentially grade 0 corresponds to a completely empty stomach, grade 1 corresponds to negligible fluid volumes ($16 \pm 36 \text{ mL}$) within normal ranges expected for fasted patients, and grade 2 correlates with significantly higher predicted gastric fluid volumes ($180 \pm 83 \text{ mL}$) beyond previously reported “safe” limits. One patient with a grade 2 antrum had an episode of significant regurgitation of gastric contents on emergence from anesthesia.

CONCLUSION: We propose a 3-point grading system based exclusively on qualitative sonographic assessment of the gastric antrum that correlates well with predicted gastric volume. This grading system could be a promising “biomarker” to assess perioperative aspiration risk. Before it can be applied widely to clinical practice, this diagnostic tool needs to be further validated and characterized.

羟乙基淀粉（130kD）抑制脂多糖激发的小鼠肺脏 Toll 样受体 4 信号转导通路

Hydroxyethyl Starch (130 kD) Inhibits Toll-Like Receptor 4 Signaling Pathways in Rat Lungs Challenged with Lipopolysaccharide

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背景：大量研究表明，羟乙基淀粉（HES）液体用于脓毒血症患者及其他严重炎症反应患者，能下调炎症介质的表达并抑制中性粒细胞介导的组织损伤。然而，我们对于潜在机制仍不甚了解。Toll样受体4（TLR4）信号在炎症反应中有着重要的作用。在此次实验中，笔者研究了TLR4信号在HES抗炎效应中的作用。

方法：选取雄性Sprague-Dawley大鼠，静脉注射脂多糖（LPS）10mg/kg。三组大鼠分别注射生理盐水（30 mL/kg）、HES 130/0.4（15及30 mL/kg）。当使用脂多糖激发后六小时，处死大鼠并提取其肺组织。通过苏木精-伊红染色测定大鼠肺损伤。通过定量聚合酶链式反应（PCR）技术和免疫印迹技术以及蛋白电泳迁移率变动分析法分别测定：大鼠肺组织中的TLR4 mRNA表达、p38丝裂原活化蛋白激酶（MAPK）、细胞外信号调节激酶1/2MAPK活性以及激活蛋白（AP-1）活性。

结果：与生理盐水组相比，两组不同给药量的HES均大大减少大鼠肺组织中由LPS引起的组织学改变。分子生物学分析表明，15及30 mL/kg的HES均显著减少脂多糖激发小鼠的TLR4 mRNA水平并抑制大鼠肺组织中p38 MAPK及AP-1，而两种剂量的HES均未对细胞外信号调节激酶1/2MAPK有所影响。

结论：这些研究结果表明HES 130/0.4至少部分通过TLR4/p38 MAPK/AP-1转导通路对脂多糖激发大鼠肺组织产生抗炎反应。

（赵嫣红 译 陈杰 校）

BACKGROUND: A number of studies have shown that hydroxyethyl starch (HES) solutions are able to down-regulate the expression of inflammatory mediators and inhibit neutrophil-mediated tissue injuries when they are used in patients with sepsis or other diseases with severe inflammatory responses. However, our knowledge about the underlying mechanisms is limited. Toll-like receptor 4 (TLR4) signaling has a pivotal 关键的 role in inflammatory processes. In this study, we examined the possible involvement of TLR4 signaling in the antiinflammatory effects of HES.

METHODS: Male Sprague-Dawley rats were exposed to lipopolysaccharide (LPS) (10 mg/kg, IV) and received IV saline (30 mL/kg) or HES 130/0.4 (15 or 30 mL/kg). Six hours after LPS challenge, rats were killed and their lungs harvested. Lung injury was examined by hematoxylin 苏木精 and eosin staining 伊红染色. TLR4 mRNA expression, p38 mitogen-activated protein kinase (MAPK) and extracellular signal-regulated kinases 1/2 MAPK activation, and activator protein 1 (AP-1) activity in the lungs were detected

with quantitative polymerase chain reaction, Western blotting, and electrophoretic mobility shift assay, respectively.

RESULTS: Compared with saline, HES profoundly attenuated the histological changes induced by LPS in the lungs at both dose levels. Molecular analysis showed that both 15 and 30 mL/kg HES significantly decreased TLR4 mRNA levels and inhibited activation of p38 MAPK and AP-1 in rats challenged with LPS, whereas activation of extracellular signal-regulated kinases 1/2 MAPK was not affected by either dose of HES.

CONCLUSIONS: These findings indicate that the beneficial effects of HES 130/0.4 on inflammation are mediated at least in part by inhibiting the TLR4/p38 MAPK/AP-1 pathway in lungs from rats challenged with LPS.

鸡蛋过敏的儿童对丙泊酚的过敏反应

Allergic Reactions to Propofol in Egg-Allergic Children

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背景：鸡蛋和/或豆类过敏通常是丙泊酚应用的禁忌症。本次研究的目的在于评估患有免疫球蛋白 E 介导的鸡蛋和/或豆类过敏症的儿童是否也在应用丙泊酚治疗后发生过敏反应。

方法：作者对悉尼 Westmead 儿童医院 1999 年至 2010 年间患有 IgE 介导的鸡蛋和/或豆类过敏症的儿童同时接受丙泊酚治疗的病例采取回顾性病例分析。

结果：研究共纳入 28 位鸡蛋过敏的患儿，他们共接受了 43 次丙泊酚治疗。没有患儿因为对豆类过敏并应用了丙泊酚而纳入研究。在被纳入的患儿中，21 位（75%）为男孩，患儿在接受麻醉时的平均年龄为 2.4 岁（范围为 1 至 15 岁），并且这些患儿通常合并有其它的过敏性疾病（61% 患有湿疹，32% 患有哮喘，43% 对花生过敏）。大多数患儿（n=19，68%）对鸡蛋发生过由 IgE 介导的临床反应，并且经蛋清皮肤点刺激试验（skin prick test, SPT）强阳性（≥7 mm）证实。其中，有两位患儿发生过对鸡蛋的过敏反应，其余的 9 位患儿由于 SPT 强阳性（≥7 mm）而从未进食过鸡蛋。所有对鸡蛋的 SPT 实验均在应用丙泊酚后 12 个月内进行。研究中有一位患儿在应用丙泊酚 15 分钟后发生了非过敏性休克性过敏反应（n=1，2%），该患儿为一位 7 岁的男孩，既往有鸡蛋过敏史，并对其它多种物质均有 IgE 介导的过敏症（如牛奶、坚果，和芝麻），患儿对丙泊酚的 SPT 为 3mm。其他对鸡蛋过敏的患儿应用丙泊酚后均无反应。

结论：尽管目前澳大利亚的标签上仍注明相关警告，丙泊酚还是被频繁应用于对鸡蛋过敏的患儿。对于大多数有鸡蛋过敏史但既往未发生过鸡蛋源性的过敏性休克的患儿来说，丙泊酚是可以安全使用的。

（周姝婧 译 陈杰 校）

BACKGROUND: Egg and/or soy allergy are often cited as contraindications to propofol administration. Our aim was to determine whether children with an immunoglobulin (Ig)E-mediated egg and/or soy allergy had an allergic reaction after propofol use.

METHODS: We performed a retrospective case review over an 11-year period (1999–2010) of children with IgE-mediated egg and/or soy allergy who had propofol administered to them at the Children's Hospital Westmead, Sydney.

RESULTS: Twenty-eight egg-allergic patients with 43 propofol administrations were identified. No child with a soy allergy who had propofol was identified. Twenty-one children (75%) were male, the median age at anesthesia was 2.4 years (range, 1–15 years), and the presence of other atopic disease was common (eczema 61%, asthma 32%, peanut allergy 43%). Most children ($n = 19$, 68%) had a history of an IgE-mediated clinical reaction to egg with evidence of a significantly positive egg white skin prick test (SPT) reaction (≥ 7 mm). Two of these had a history of egg anaphylaxis. The remaining children ($n = 9$, 32%) had never ingested egg because of significantly positive SPT (≥ 7 mm). All SPTs to egg were performed within 12 months of propofol administration. There was one nonanaphylactic immediate allergic reaction ($n = 1$ of 43, 2%) that occurred 15 minutes after propofol administration in a 7-year-old boy with a history of egg anaphylaxis and multiple other IgE-mediated food allergies (cow's milk, nut, and sesame). SPT to propofol was positive at 3 mm. No other egg-allergic child reacted to propofol.

CONCLUSIONS: Despite current Australian labeling warnings, propofol was frequently administered to egg-allergic children. Propofol is likely to be safe in the majority of egg-allergic children who do not have a history of egg anaphylaxis.

神经肽通过调节角质细胞白介素-1 β 的产生导致周围神经痛觉过敏

Neuropeptides Contribute to Peripheral Nociceptive Sensitization by Regulating Interleukin-1 β Production in Keratinocytes

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背景：越来越多的证据表明：对于复杂性区域疼痛综合症（CRPS）的患者，皮肤炎症细胞因子的产生与增高的神经肽信号表达有密切的关系。在此之前一项研究观察到在胫骨骨折的CRPS大鼠模型上，角质细胞产生白介素(IL)-1 β 需要包含NALP1炎性因子在内的蛋白酶-1的活化，且白介素-1受体拮抗剂（anakinra）的应用降低了骨折导致的后爪机械性痛觉过敏。因此，本研究假设神经肽通过提高炎症因子表达和蛋白酶-1的活性来激活皮肤的天然免疫系统从而导致痛觉过敏。

方法：考察向大鼠后爪皮肤注射神经肽P物质（SP）和降钙素基因相关肽（CGRP）后，出现的痛觉致敏是否有白介素-1 β 的参与。接着研究是否这些神经肽能够刺激角质细胞产生白介素-1 β ，并且可以增加包括NALP-1和蛋白酶-1在内的炎症因子蛋白质成分的表达。最后，确定神经肽刺激产生白介素-1 β 是否需要蛋白酶-1和组织蛋白酶B的激活。

结果：在大鼠足底注射P物质和降钙素基因相关肽导致痛觉过敏，降钙素基因相关肽的效应大约较前者小10倍。此外，静脉注射白介素-1受体拮抗剂阿那白滞素（anakinra），可预防神经肽产生的痛觉过敏。同样，局部应用神经肽后大鼠皮肤角质细胞白介素-1受体表达上调。体外实验数据证明，P物质和降钙素基因相关

肽都会剂量依赖性提高角质细胞内白介素-1 β 和蛋白的表达。此外，P物质能时间和剂量依赖性地上调角质细胞内NALP-1和蛋白酶1的mRNA和蛋白水平。相比之下，降钙素基因相关肽时间和剂量依赖性增加角质细胞内NALP-1和蛋白酶1的mRNA水平，但NALP-1和蛋白酶1的蛋白水平并没有显著改变。应用蛋白酶1选择性抑制剂Ac-YVAD-CHO可减少P物质和降钙素基因相关肽（效应较弱）引起的角质细胞内IL-1 β 产生增加。选择性组织蛋白酶B抑制剂CA-74Me也抑制角质细胞内神经肽刺激白介素-1 β 的产生。

结论：结果表明，神经肽通过增加角质细胞白介素-1 β 的产生诱发痛觉过敏。神经肽的增加角质细胞白介素-1 β 的产生是依赖蛋白酶-1和组织蛋白酶B。神经皮肤信号包括天然免疫神经肽的激活可能导致了复杂性区域疼痛综合症患者的疼痛。

（黄丹 译 陈杰 校）

BACKGROUND: It is increasingly evident that there is a close connection between the generation 产生 of cutaneous inflammatory cytokines and elevated neuropeptide signaling in complex regional pain syndrome (CRPS) patients. Previously, we observed in the rat tibia fracture model of CRPS that activation of caspase-1 containing NALP1 inflammasomes was required for interleukin (IL)-1 β production in keratinocytes, and that administration of an IL-1 receptor antagonist (anakinra) reduced the fracture-induced hindpaw mechanical allodynia. We therefore hypothesized that neuropeptides lead to nociceptive sensitization through activation of the skin's innate immune system by enhancing inflammasome expression and caspase-1 activity.

METHODS: We determined whether the neuropeptides substance P (SP) and calcitonin gene-related peptide (CGRP) require IL-1 β to support nociceptive sensitization when injected into mouse hindpaw skin by testing mechanical allodynia. We then investigated whether these neuropeptides could stimulate production of IL-1 β in a keratinocyte cell line (REKs), and could increase the expression of inflammasome component proteins including NALP1 and caspase-1. Finally, we determined whether neuropeptide-stimulated IL-1 β production required activation of caspase-1 and cathepsin.

RESULTS: Intraplantar injections of SP and CGRP lead to allodynia in mouse hindpaws but CGRP was approximately 10-fold less potent in causing this response. Moreover, systemic administration of the IL-1 receptor (IL-1R) antagonist anakinra prevented sensitization after neuropeptide injection. Also, mouse skin keratinocytes express IL-1R, which is up-regulated after local neuropeptide application. In vitro data demonstrated that both SP and CGRP increased IL-1 β gene and protein expression in REKs in a dose-dependent manner. Furthermore, SP time- and dose-dependently up-regulated NALP1 and caspase-1 mRNA and protein levels in REKs. In contrast, CGRP time- and dose-dependently enhanced NALP1 and caspase-1 mRNA levels without causing a significant change in NALP1 or caspase-1 protein expression in REKs. Inhibition of caspase-1 activity using the selective inhibitor Ac-YVAD-CHO reduced SP and, less effectively, CGRP induced increases in IL-1 β production in REK cells. The selective cathepsin B inhibitor CA-74Me inhibited neuropeptide induced IL-1 β production in REKs as well.

CONCLUSIONS: Collectively, these results demonstrate that neuropeptides induce nociceptive sensitization by enhancing IL-1 β production in keratinocytes. Neuropeptides rely on both caspase-1 and cathepsin B for this enhanced production. Neurocutaneous signaling involving neuropeptide activation of the innate immunity may contribute to pain in CRPS patients.

简报:蛛网膜下腔阻滞的评价：一项包括 175 篇文献以及改进意见的调查

Brief Reports: An Assessment of Subarachnoid Block: A Survey of 175 Articles and Recommendations for Improvement

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背景：蛛网膜下腔阻滞的评估，尤其是感觉部分，可能不完整并且会影响蛛网膜下腔阻滞麻醉研究的结论，以及在日常临床实践中的应用。

方法：作者手动搜索了出版时间在 2006 年至 2009 年之间的 8 本麻醉期刊，发现 175 篇关于蛛网膜下腔阻滞的文章，用来确定蛛网膜下腔麻醉过程记录的组成部分以及交感神经和运动阻滞的程度。

结果：86% 文章记录了蛛网膜下腔注射的部位，84% 记录局麻药配比，77% 记录局麻药浓度，75% 记录患者的体位，77% 记录穿刺针大小，以及 71% 记录穿刺针类型。69% 文章记录了用于评估感觉阻滞的刺激，17% 记录了阻滞是单侧或双侧，以及 11% 记录刺激应用的界限。运动和交感神经阻滞分别在 40% 和 18% 研究进行了评估。

结论：这些结果表明涉及蛛网膜下腔麻醉的研究，存在不完整的方法描述和感觉阻滞的评估。建议建立一份清单，以促进一个更加规范的有关蛛网膜下腔麻醉的评估。

(怀晓蓉 译 陈杰 校)

BACKGROUND: Assessment of subarachnoid block, particularly the sensory component, may be incomplete and influence the conclusions of studies involving subarachnoid anesthesia, as well as their application in routine clinical practice.

METHODS: We manually searched 175 articles concerning subarachnoid block published from 2006 to 2009 in 8 anesthesia journals to determine the components of the subarachnoid anesthetic procedure recorded as well as the extent of sympathetic and motor block.

RESULTS: The level of subarachnoid injection was reported in 86% of the articles, baricity in 84%, concentration of local anesthetic in 77%, patient's position in 75%, needle size in 77%, and needle type in 71%. The stimulus used for assessing sensory block was reported in 69% of the articles; 17% described the block as unilateral or bilateral, and 11% described the lines along which the stimulus was applied. Motor and sympathetic block were assessed in 40% and 18% of studies, respectively.

CONCLUSIONS: These results suggest incomplete description of tools and assessment of sensory block in studies involving subarachnoid anesthesia. We propose a checklist to facilitate a more standardized evaluation of the extent of subarachnoid anesthesia.

多重电极全血血小板聚集试验、血小板功能分析仪-100 及体内出血时间在阿司匹林介导的血小板功能障碍患者术前重点照护评估中的作用

Multiple Electrode Whole Blood Aggregometry, PFA-100, and In Vivo Bleeding Time for the Point-of-Care Assessment of Aspirin-Induced Platelet Dysfunction in the Preoperative Setting.

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背景：因服用阿司匹林引起的获得性血小板功能障碍可能导致围手术期出血倾向增加。因此，本研究旨在测定体内出血时间（BT）及另两项血小板功能试验在阿司匹林治疗患者术前残余抗血小板功能评估中的诊断精确度。

方法：陆续选取择期手术患者进入该前瞻性研究。“阿司匹林效应完全组”患者于血样采集前 48 小时最后服用阿司匹林；而“阿司匹林效应变动组”与“阿司匹林效应修复组”患者最后服用阿司匹林的时间分别为采血前 48-96 小时和 96 小时以上。对照组患者不服用阿司匹林。通过多重电极全血血小板聚集试验、血小板功能分析仪（PFA）-100 及体内出血时间对阿司匹林的效应进行评估。运用位列于因果多重比较程序（Dunn）中的单向方差分析对各组间的差异进行检测。使用 z 检验比较各分类数据。创建受试者工作特征（ROC）曲线对所研究的血小板功能试验的诊断精确度进行判定。分别计算 ROC 曲线下面积（AUC）及血小板功能试验的灵敏度和特异性。统计学显著性水平设定为 $P < 0.05$ 。

结果：共有 394 名患者纳入研究（其中包括 133 名对照组患者与 261 名阿司匹林治疗组患者）。所有 3 种方法均能检测出阿司匹林效应完全组患者阿司匹林的抗血小板作用。但在阿司匹林效应修复组与对照组，不论进行何种检测，两组的检测值均无统计学差异。在使用多重电极全血血小板聚集试验及 PFA-100 进行阿司匹林敏感患者鉴定试验与血小板闭锁功能试验时发现，阿司匹林效应变动组患者的测试值不同于对照组患者；但在 BT 测定中，两组并未显现差异。ROC 分析表明，在排除阿司匹林残余功能的试验中，阿司匹林敏感患者鉴定试验具有最高的诊断精确度（AUC 0.81， $P < 0.001$ ），其次分别为血小板闭锁功能试验（AUC 0.78， $P < 0.001$ ）与 BT（AUC 0.56， $P = 0.05$ ）。阿司匹林敏感患者鉴定试验排除阿司匹林残余功能的临界值为 53U，灵敏度和特异性分别为 88% 和 71%。

结论：在患者服用阿司匹林后 48 小时内，阿司匹林能充分发挥其抗血小板治疗效应。本研究发现，阿司匹林撤药 96 小时以上（大于 4 天），血小板功能即可修复；因此，对于这些患者，术前进行血小板功能试验是毫无帮助的。若要测定术前 48-96 小时内停用阿司匹林患者阿司匹林的残余效应，阿司匹林敏感患者鉴定试验可能具有最高的诊断精确度。

（范羽译 薛张纲校）

Background: Acquired platelet dysfunction due to aspirin ingestion may increase bleeding tendency during surgery. Thus, we examined the diagnostic accuracy of in vivo bleeding time (BT) and 2 platelet function assays for the preoperative assessment of a residual antiplatelet effect in patients treated with aspirin.

Methods: Consecutive patients scheduled for surgery were prospectively enrolled in this study. The patients' last aspirin ingestion had occurred within the previous 48 hours

before blood sampling in the "full aspirin effect" group, between 48 and 96 hours before in the "variable aspirin effect" group, and >96 hours before in the "recovered aspirin effect" group. The control group had not taken any aspirin. Multiple electrode aggregometry, platelet function analyzer (PFA)-100, and in vivo BT were performed to assess the effects of aspirin. One-way analysis of variance on ranks with a post hoc multiple-comparison procedure (Dunn) was used to detect differences among the groups. Categorical data were compared using the z test. Receiver operating characteristic (ROC) curves were created to determine the diagnostic accuracy of the platelet function assays investigated. The area under the ROC curve (AUC), sensitivity, and specificity of the assays were calculated. The level of statistical significance was set at $P < 0.05$.

Results: Three hundred ninety-four patients were included in the analysis (133 control and 261 aspirin-treated patients). All 3 methods were able to detect the antiplatelet effect of aspirin in the full aspirin effect group. Furthermore, no difference in the measurement values between the recovered aspirin effect and control group was found, irrespective of the assay performed. Measurement values in the variable aspirin effect group were different from those of the control group in the ASPItest using multiple electrode aggregometry and COL-EPI using PFA-100 but not in BT. ROC analysis showed the highest diagnostic accuracy in excluding the residual aspirin effect in the ASPItest (AUC 0.81, $P < 0.001$), followed by COL-EPI (AUC 0.78, $P < 0.001$) and BT (AUC 0.56, $P = 0.05$). The cutoff value of 53 U in the ASPItest excluded the effect of aspirin with a sensitivity of 88% and specificity of 71%.

Conclusions: The full therapeutic antiplatelet effects of aspirin can be expected within 48 hours of the patient's last aspirin ingestion. Platelet function recovered in our study if aspirin cessation occurred >96 hours (4 days) before; thus, in these patients, preoperative platelet function testing is not useful. To quantify any residual aspirin effect in patients who ceased their intake of aspirin between 48 and 96 hours before surgery, the ASPItest might have the highest diagnostic accuracy.

关于标准体重对于肥胖患者丙泊酚麻醉诱导剂量关系的研究

Lean Body Weight Scalar for the Anesthetic Induction Dose of Propofol in Morbidly Obese Subjects.

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背景: 病态肥胖相关的特殊的麻醉风险已经有所记录, 由于和肥胖有关的生理和人体的变化药物管理会有所改变。不幸的是, 对于极度肥胖的麻醉药效学的研究还很薄弱。尽管丙泊酚作为诱导药物频繁使用在肥胖病人身上, 但是适合这些患者的丙泊酚诱导剂量尚存争议。因此, 我们对肥胖病人丙泊酚麻醉诱导剂量的不同体重标量进行了对比。

方法: 选60名肥胖患者(体重指数 $\geq 40\text{kg/m}^2$)进行丙泊酚麻醉诱导, 他们随机接受以总体重或标准体重为标量的药物剂量。选30名正常体重的患者(体重指数 $\leq 25\text{kg/m}^2$)接受以总体重为基础的丙泊酚注射(100mg/kg/h), 注射器读数用于标

记意识丧失，在这一点上丙泊酚注射停止。丙泊酚的剂量需要记录意识丧失的注射读数和时时间。

结果：按标准体重给予丙泊酚，达到意识丧失的丙泊酚注射器读数和时时间所需的丙泊酚总量在正常体重和病态肥胖者中相似。按照标准体重注射丙泊酚，病态肥胖者达到意识丧失所需丙泊酚的剂量相当大且时时间相当短。三组中，标准体重与丙泊酚总剂量之间有很大相关性。

结论：在病态肥胖患者全麻诱导中，标准体重是丙泊酚诱导的体重基本标量。
(侯文婷译 薛张纲校)

Background: The unique anesthetic risks associated with the morbidly obese (MO) population have been documented. Pharmacologic management of these patients may be altered because of the physiologic and anthropometric changes associated with obesity. Unfortunately, studies examining the effects of extreme obesity on the pharmacology of anesthetics have been sparse. Although propofol is the induction drug most frequently used in these patients, the appropriate induction dosing scalar for propofol remains controversial in MO subjects. Therefore, we compared different weight-based scalars for dosing propofol for anesthetic induction in MO subjects.

Methods: Sixty MO subjects (body mass index ≥ 40 kg/m²) were randomized to receive a propofol infusion (100 mg kg⁻¹ h⁻¹) for induction of anesthesia based on total body weight (TBW) or lean body weight (LBW). Thirty control subjects (body mass index ≤ 25 kg/m²) received a propofol infusion (100 mg kg⁻¹ h⁻¹) based on TBW. Syringe drop was used as the marker for loss of consciousness (LOC), at which point the propofol infusion was stopped. The propofol dose required for syringe drop and time to LOC were recorded.

Results: Total propofol dose (mg/kg) required for syringe drop and time to LOC were similar between control subjects and MO subjects given propofol based on LBW. MO subjects receiving a propofol infusion based on TBW had a significantly larger propofol dose and significantly shorter time to LOC. There was a strong relationship between LBW and total propofol dose received in all 3 groups.

Conclusion: LBW is a more appropriate weight-based scalar for propofol infusion for induction of general anesthesia in MO subjects.

健康个体中交感神经阻断对手指光学体积描记图和手指温度的影响

The effects of sympathectomy on finger photoplethysmography and temperature measurements in healthy subjects

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背景：光学体积描记术是一种通过光线的传播情况来测量组织容量变化的技术。光学体积描记结果图像是由AC和DC两部分组成。关于血管舒张时对AC与DC的光

学体积描记信号的影响，目前所掌握的资料还很有限。我们的研究目的有两个，一是交感神经阻断对于光学体积描记图不同组件的影响；二是比较交感神经阻断所引起的变化与外周温度所引起的变化有何不同。

方法：在10名健康志愿者中，进行单侧腋路臂丛神经阻滞，从而使得交感神经阻断，血管扩张。未进行臂丛神经阻滞的一侧做为对照。使用光学体积描记法连续测量双侧的手指血容量和手指的温度。将手指的光学体积描记图像分离出AC和DC组分。并且计算AC与DC的比值(AC/DC)。所有数据从臂丛神经阻滞完成开始连续记录30分钟。使用邓尼特检验法重复测量分析各个变量以确定臂丛神经阻滞对手指光学体积描记图和手指温度的影响。

结果：臂丛神经阻滞2.7分钟开始，被阻滞的手臂血管扩张，手指光学体积描记图的DC部分明显减少($P < 0.0001$)。阻滞30分钟，DC减少的平均值为 $-51\% \pm 19\%$ (95%可信区间为 $-61\% \text{---} -42\%$)。光学体积描记图的其他组分与基线值相比，无明显变化。臂丛神经阻滞5.7分钟开始手指温度明显上升($P < 0.0001$)。阻滞30分钟，温度上升的平均值为 $7.1^\circ\text{C} \pm 3.8^\circ\text{C}$ (95%可信区间为 $5.1^\circ\text{C} \text{---} 9.0^\circ\text{C}$)。光学体积描记图中的DC组分对于预测神经阻滞的效果敏感性和特异性均为最优。

结论：本研究阐明了交感神经阻断所引起的手指光学体积描记图中AC和DC组分的变化情况。本次试验模型中，我们发现DC组分对于监测外周血管扩张情况最为敏感。

(黄剑译 薛张纲校)

BACKGROUND: Photoplethysmography uses light transmission to measure changes in tissue volume. The resulting photoplethysmogram is composed of AC and DC components. Limited data are available on the effects of vasodilation on the AC and the DC components of the photoplethysmograph signal. The aims of our study were (1) to investigate the effects of sympathectomy on different components of the photoplethysmogram, and (2) to compare sympathectomy-induced changes in the photoplethysmogram with changes in peripheral temperature.

METHODS: In 10 healthy subjects, sympathectomy-induced peripheral vasodilation was achieved using an axillary brachial plexus block. The nonblocked arm served as control. We obtained measurements of bilateral continuous measurements of finger blood volume (by photoplethysmography) and finger temperature. We separated the finger photoplethysmogram into its AC and DC components. In addition, we calculated the ratio of AC to DC (AC/DC). All data were recorded until 30 minutes after the end of brachial plexus block. Repeated-measures analysis of variance followed by the Dunnett post hoc test determined the effect of brachial plexus block on the finger photoplethysmogram and finger temperature.

RESULTS: The DC component of the finger photoplethysmogram decreased (vasodilation) significantly ($P < 0.0001$) after brachial plexus block in the blocked arm starting 2.7 minutes after the block. Average decrease in DC values was $-51\% \pm 19\%$ (95% confidence interval: -61% to -42%) at 30 minutes after the block. None of the other photoplethysmogram components changed significantly from preblock baseline values. On average, the finger temperature increased significantly ($P < 0.0001$) starting 5.7 minutes after brachial plexus block in the blocked arm. Average increase in temperature was $7.1^\circ\text{C} \pm 3.8^\circ\text{C}$ (95% confidence interval: $5.1^\circ\text{C} \text{---} 9.0^\circ\text{C}$) 30 minutes after the block.

The DC component of the photoplethysmogram had the highest sensitivity and specificity to predict a successful block.

CONCLUSIONS: This study characterizes sympathectomy-induced changes in the AC and DC components of the finger photoplethysmogram. In this experimental model, we found the DC component to be most sensitive in detecting peripheral vasodilation.

克-特二氏综合征患者行手术的麻醉管理：一项 136 例的综述

Anesthesia for Surgery Related to Klippel-Trenaunay Syndrome: A Review of 136 Anesthetics

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背景：克-特二氏综合征是一种很少见的先天的畸形以静脉曲张或静脉畸形，毛细血管畸形，其中包括神经血管的结构，在受影响的四肢有骨或软骨组织的肥大三联症。在躯干，结肠，膀胱，或脊髓也可能有。克-特二氏综合征不应当与克-费二氏综合征相混淆，克-费二氏综合征有椎骨或颈部的异常。对于有克-特二氏综合征的病人的麻醉方案中只有少数的案例报道需小心可能的困难气道但没有报道外科手术的大出血而需要输血的。

方法：我们在梅奥诊所的医学数据库内做了一个电子搜索，想找到进行 KTS 手术的麻醉的病人的数据。回顾了这类手术的医学记录，麻醉的设备，气道管理，药物的使用，手术中液体的管理，输液的设备，血管通路，术后的并发症。

结果：82 个少见的病人进行了与 KTS 相关的手术，共进行了 134 个一般的麻醉，2 个腰麻。外科手术前，27%的病人有周期性的出血，24%有周期性的蜂窝织炎，9%有深静脉血栓，2%有肺栓塞。主要进行手术的年龄是 21 ± 15 岁。主要的手术的步骤有激光抗凝，曲张静脉硬化疗法或剥脱，

结论：有 KTS 的患者都有复杂的相关的并存的疾病。相反于以前的报道，气道管理的困难并不是偶然遇到的。在严重的 KTS 的患者的手术中，尽管用了止血带，仍有大量的出血，麻醉医生应该配合需要进行适当的液体复苏。脊髓的麻醉只在神经血管的畸形的外伤被排除后才可以考虑使用。

(刘珏莹译 薛张纲校)

BACKGROUND: Klippel-Trenaunay syndrome (KTS) is a rare congenital malformation characterized by the triad of varicose veins or venous malformations, capillary malformations that may involve neurovascular structures, and bony or soft tissue hypertrophy in affected limbs. Areas such as the trunk, bowel, bladder, and spinal cord may be involved as well. KTS should not be confused with Klippel-Feil syndrome, which involves abnormalities of the cervical vertebrae. Anesthetic management for patients with KTS has only been described in limited case reports that caution about potential airway difficulty but do not report surgical hemorrhage requiring transfusion.

METHODS: We performed an electronic search of the Mayo Clinic medical record database to identify patients who had undergone an anesthetic for surgery related to KTS. Review of medical records was performed for type of surgery, anesthetic technique,

airway management and difficulty, medications used, intraoperative fluid administration, transfusion requirements, vascular access used, and postoperative complications.

RESULTS: Eighty-two unique patients were identified who underwent 134 general anesthetics and 2 lumbar neuraxial anesthetics for surgeries related to KTS. Preoperatively, 27% of patients had a history of recurrent bleeding, 24% recurrent cellulitis, 9% deep vein thrombosis, and 2% pulmonary embolism. The mean age at time of surgery was 21 ± 15 years. The majority of surgical procedures involved laser coagulation or varicose vein sclerotherapy or stripping. All of the 74 direct laryngoscopies and tracheal intubations were performed on the first attempt without difficulty. Mask ventilation was possible in all 131 patients for whom this was attempted, with only 1 requiring an oral airway. Documented estimated blood loss ranged from 20 to 18,000 mL, with a mean of 740 ± 2739 mL. Use of a tourniquet did not obviate the possibility of substantial blood loss. The only significant postoperative complication involved a calf hematoma after vein stripping and avulsion that required return to the operating room for evacuation.

CONCLUSIONS: Patients with KTS have multiple associated comorbidities relevant to perioperative management. In contrast to previous reports, difficulty with airway management was not encountered. Surgery related to severe KTS may be associated with massive hemorrhage despite tourniquet use, and the anesthesiologist should anticipate the need for appropriate fluid resuscitation. Neuraxial techniques may be considered only if the possibility of trauma to neurovascular malformations has been excluded with recent spine imaging.

毛细血管再充盈时间：这还是一个有用的临床标志？

Medical Intelligence Article: Capillary Refill Time: Is It Still a Useful Clinical Sign?

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毛细血管再充盈时间（CRT）作为对危重病人快速心肺评估的一部分被卫生保健工作者广泛运用。其测量包括血液回流到远端毛细血管的目视检查。据推测，CRT是对周围灌注改变的一个简单的测量方法。目前，麻醉状态下CRT的测量尚缺乏证据，尚需进一步研究。但可从其他领域的研究证据中得到借鉴。在这篇论文中，我们研究这方面的证据和影响CRT测量的影响因素。新的方法来评估的CRT正在研究中。在未来，CRT测量可能使用新技术，如数字录像或进化后的血氧饱和度探头，这些新的方法将消除与临床CRT显示器测量的限制，甚至可以提供一个自动化的CRT测量方法。

（陆丽虹译 薛张纲校）

Capillary refill time (CRT) is widely used by health care workers as part of the rapid, structured cardiopulmonary assessment of critically ill patients. Measurement involves the visual inspection of blood returning to distal capillaries after they have been emptied by pressure. It is hypothesized that CRT is a simple measure of alterations in peripheral

perfusion. Evidence for the use of CRT in anesthesia is lacking and further research is required, but understanding may be gained from evidence in other fields. In this report, we examine this evidence and factors affecting CRT measurement. Novel approaches to the assessment of CRT are under investigation. In the future, CRT measurement may be achieved using new technologies such as digital videography or modified oxygen saturation probes; these new methods would remove the limitations associated with clinical CRT measurement and may even be able to provide an automated CRT measurement.

麻醉药异氟醚对缺氧诱导的含半胱氨酸的天冬氨酸蛋白水解酶 3 激活和 β 位淀粉样前体蛋白裂解酶增加潜在的双重作用

The Potential Dual Effects of Anesthetic Isoflurane on Hypoxia-Induced Caspase-3 Activation and Increases in β -Site Amyloid Precursor Protein-Cleaving Enzyme Levels.

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背景： β 淀粉样蛋白(A β)积聚、含半胱氨酸的天冬氨酸蛋白水解酶激活、细胞凋亡和缺氧导致的神经毒性都被提出与阿尔茨海默病神经病理发生机制有关。 β 淀粉样蛋白是淀粉样前体蛋白由天冬氨酸蛋白水解酶 β 位淀粉样前体蛋白裂解酶(BACE)和 γ 分泌酶蛋白酶解加工产生。吸入麻醉药长久以来被认为有针对神经毒性的保护作用。但是，近期的研究提出吸入麻醉药异氟醚可能通过诱导含半胱氨酸的天冬氨酸蛋白水解酶激活和凋亡，以及增加 β 位淀粉样前体蛋白裂解酶和 β 淀粉样蛋白的水平来促进神经毒性。因此我们寻求明确异氟醚是否可诱导剂量相关性的双重作用：含半胱氨酸的天冬氨酸蛋白水解酶激活和 β 位淀粉样前体蛋白裂解酶水平增加，是神经保护作用还是促进神经毒性作用。

方法： 人类 H4 神经胶质瘤细胞由单纯缺氧(3% O₂)、不同浓度异氟醚 (0.5%和 2%)和缺氧联合 0.5%或 2%异氟醚处理。我们通过蛋白印迹分析测量含半胱氨酸的天冬氨酸蛋白水解酶 3 裂解(激活)、 β 位淀粉样前体蛋白裂解酶和 B 细胞淋巴瘤-2 基因水平。

结果： 结果显示初次经过 0.5%异氟醚处理 8 小时减弱了缺氧诱导的含半胱氨酸的天冬氨酸蛋白水解酶 3 激活和 β 位淀粉样前体蛋白裂解酶水平增加作用，而 2%异

氟醚处理 8 小时可增强这种作用。2%异氟醚处理也促进了缺氧诱导的 B 细胞淋巴瘤-2 基因水平降低。

结论：结果提示一种潜在性概念异氟醚有对缺氧诱导的毒性有双重作用（保护和助长作用），这可能通过 B 细胞淋巴瘤-2 基因家族蛋白作用产生。这些发现可引发更多系统性研究来确定麻醉药对阿尔茨海默病相关神经毒性的潜在双重作用。

（任云译 薛张纲校）

BACKGROUND: β -Amyloid protein ($A\beta$) accumulation, caspase activation, apoptosis, and hypoxia-induced neurotoxicity have been suggested to be involved in Alzheimer disease neuropathogenesis. $A\beta$ is produced from amyloid precursor protein through proteolytic processing by the aspartyl protease β -site amyloid precursor protein-cleaving enzyme (BACE) and γ -secretase. Inhaled anesthetics have long been considered to protect against neurotoxicity. However, recent studies have suggested that the inhaled anesthetic isoflurane may promote neurotoxicity by inducing caspase activation and apoptosis, and by increasing levels of BACE and $A\beta$. We therefore sought to determine whether isoflurane can induce concentration-dependent dual effectson hypoxia-induced caspase-3 activation and increases in BACE levels: protection versus promotion.

METHODS: H4 human neuroglioma cells were treated with hypoxia (3% O₂) alone, different concentrations of isoflurane (0.5% and 2%), and the combination of hypoxia and 0.5% or 2% isoflurane. The levels of caspase-3 cleavage (activation), BACE, and Bcl-2 were determined by Western blot analysis.

RESULTS: We show for the first time that treatment with 0.5% isoflurane for 8 hours attenuated, whereas treatment with 2% isoflurane for 8 hours enhanced, hypoxia-induced caspase-3 activation and increases in BACE levels. The 2% isofluranetreatment also enhanced a hypoxia-induced decrease in Bcl-2 levels.

CONCLUSIONS: These results suggest a potential concept that isoflurane has dual effects (protection versus promotion) on hypoxia-induced toxicity, which may act through Bcl-2 family proteins. These findings could lead to more systematic studies to determine the potential dual effects of anesthetics on Alzheimer disease-associated neurotoxicity.

对吗啡耐药的小鼠鞘内注射依那西普能减低谷氨酸能传递途径，从而部分恢复吗啡的抗伤害性刺激的作用。

Intrathecal Etanercept Partially Restores Morphine's Antinociception in Morphine-Tolerant Rats via Attenuation of the Glutamatergic Transmission

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背景：长期暴露于吗啡可以导致镇痛耐受。吗啡耐受除了阿片类受体的构型会受到改变，谷氨酸能传递途径增强也与之有关。肿瘤坏死因子 α 通过激活谷氨酸能传

递途径，与神经元的可塑性有关。我们检验了依那西普的作用，它是一种肿瘤坏死因子 α 能抑制小鼠身上的吗啡耐受。

方法：在雄性为 Wister 小鼠体内植入两根鞘内导管，一根导管连接一个微泵，用来注射吗啡(15 $\mu\text{g}/\text{h}$)或者生理盐水(1 $\mu\text{L}/\text{h}$)各 5 天。在第 5 天，吗啡停用后，给予注射依那西普(50 μg)或者生理盐水(10 μL)。3 个小时以后，给予急性的吗啡治疗(15 $\mu\text{g}/10 \mu\text{L}$, 静脉注射)，所有的小鼠之后都接受了伤害性的尾巴轻拍试验。

结果：结果显示对于吗啡耐受的小鼠，急性的依那西普(50 μg)治疗可以提高吗啡抗伤害性刺激的作用。对吗啡耐受的小鼠，蛋白电泳提示依那西普能降低细胞膜谷氨酸运载蛋白 GLT-1 和 GLAST 的下调。依那西普能抑制 AMP 受体和 N-methyl-d-aspartate 受体亚单位（包括 GluR1/GluR2 和 NR1/NR2A.）的上调。

结论：这些结果显示在吗啡耐受后，依那西普能部分恢复吗啡的抗伤害性刺激的作用。依那西普对减轻临床疼痛治疗有潜在价值，特别是对于长期接受阿片类药物治疗的患者，它能阻止耐受，更好地发挥阿片类药物的作用。

（翁梅琳译 薛张纲校）

BACKGROUND: Long-term exposure to morphine leads to analgesic tolerance. In addition to an opioid receptor conformational change, enhancing the glutamatergic signal transmission is also involved in morphine tolerance. Tumor necrosis factor- α has been demonstrated to correlate with neuronal plasticity via activation of glutamatergic transmission. We examined the effect of etanercept, a tumor necrosis factor- α inhibitor on morphine tolerance in rats.

METHODS: Male Wistar rats were implanted with 2 intrathecal (IT) catheters, and 1 IT catheter was connected to a mini-osmotic pump, used for either morphine infusion (15 $\mu\text{g}/\text{h}$) or saline (1 $\mu\text{L}/\text{h}$) infusion for 5 days. On day 5, either etanercept (50 μg) or saline (10 μL) was injected after discontinued morphine infusion. Three hours later, acute morphine (15 $\mu\text{g}/10 \mu\text{L}$, IT) treatment was given and all rats received a nociceptive tail-flick test.

RESULTS: The results showed that acute etanercept (50 μg) treatment caused a significant antinociceptive effect of morphine in morphine-tolerant rats. Western blotting indicated that etanercept attenuated the downregulation of membrane glutamate transporters GLT-1 and GLAST in morphine-tolerant rats. Etanercept also inhibited the upregulation of surface AMPA-receptor and N-methyl-d-aspartate-receptor subunits, including GluR1/GluR2 and NR1/NR2A.

CONCLUSIONS: These results demonstrate that etanercept partially restores the antinociceptive effect of morphine in morphine tolerance after a morphine challenge. Etanercept has potential for use in the clinical management of pain, particularly in patients who require long-term opioid treatment, and the effectiveness of which can be hampered by tolerance.

臂丛阻滞在术中对氧平衡的影响

Influence of Brachial Plexus Blockade on Oxygen Balance During Surgery

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有选择性地在四肢局部疾病手术中实施臂丛神经阻滞会产生一个集合麻醉、运动阻滞和药物性交感阻滞的有利的效果。为了在未来的治疗中更好地利用臂丛神经阻滞的持久效应，我们进行了一个健康病人择期手部手术的可控的前瞻性研究，研究中利用可靠的静脉血气监测技术，肯定了四肢阻滞区氧平衡的情况较非阻滞区地有改善。

（张玥琪译，薛张纲校）

The combined effects of anesthesia, motor blockade, and chemically induced sympathectomy after brachial plexus blockade can have a beneficial impact, when applied in selected, isolated diseased states of the upper limb. With the aim of using the prolonged effects of brachial plexus blockade for a future therapeutic application, we demonstrated a dependable methodology of venous blood gas monitoring and confirmed an improved oxygen balance of the blocked versus nonblocked upper extremity in a controlled, prospective study in healthy patients undergoing elective hand surgery.