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一项关于瑞芬太尼--丙泊酚联合应用引起对食道检查仪器的反应丧失、应答反应丧失、和/或发生重度呼吸抑制的研究

An Exploration of Remifentanil-Propofol Combinations That Lead to a Loss of Response to Esophageal Instrumentation, a Loss of Responsiveness, and/or Onset of Intolerable Ventilatory Depression

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背景：瑞芬太尼和丙泊酚被越来越多应用于保留自主呼吸病人的短时操作过程。在此情况，最好可以消除中度刺激引起的反应同时避免应答反应丧失（LOR）和重度呼吸抑制（IVD）。在这项研究中，我们探索了瑞芬太尼-丙泊酚复合应用时引起对食道检查仪器（EI）的反应丧失、LOR、和/或发生 IVD 的效应部位浓度（Ces）。研究的次要目标是用这些数据来建立每种反应测量的响应面模型。我们假设（1）在大多数志愿者中，选择性的瑞芬太尼和丙泊酚效应部位浓度将会允许 EI 但会避免 LOR 和 IVD，并且（2）对这些反应的药物相互作用是协同作用。
方法：24 名志愿者接受了剂量逐步提高的的芬太尼和丙泊酚靶控注射，注射剂量范围分别是 0 至 6.4 ng ·mL^{-1} 和 0 至 4.3 μg · mL^{-1}。在每个设置的靶浓度，记录对插入钝性探头到食道中部（40cm）的反应、应答反应等级、呼吸频率。通过这些数据，建立对 EI 反应的丧失和 IVD 的响应面模型并定性为协同作用、相加作用或拮抗作用。应用一个之前已发表的 LOR 模型。
结果：在可能的 384 项评估中，志愿者在 105 个预测的瑞芬太尼-丙泊酚效应部位浓度下对 EI 无反应；其中 30 个浓度时，志愿者没有 IVD；其中 30 个浓度，志愿者没有 LOR；其中 9 个浓度，志愿者均没有 IVD 和 LOR。但是，许多其他在相同浓度范围以上的评估发生了 LOR 和/或 IVD。允许 EI 并避免 IVD 和/或 LOR 的瑞芬太尼-丙泊酚的效应部位浓度大约分别是 0.8 至 1.6 ng ·mL^{-1} 和 1.5 至 2.7 μg · mL^{-1} ，较小的范围大约分别是 3.0 至 4.0 ng ·mL^{-1} 和 0.0 to 1.1 μg · mL^{-1}。EI 反应丧失和 IVD 的模型都表明瑞芬太尼和丙泊酚之间有协同作用。
结论：选择性的瑞芬太尼-丙泊芬浓度组，尤其是高浓度的丙泊酚和低浓度的瑞芬太尼组，在保留自护呼吸的志愿者中能够消除对 EI 的反应同时避免 IVD。然而要同时消除对 EI 的反应并避免 LOR 和 IVD 是很难做到的。也许我们有必要承受一些钝性探头的不适感而不是一味的追求消除对 EI 的反应以避免 LOR 和 IVD。
（张怡译 马皓琳 李士通校）

BACKGROUND: Remifentanil and propofol are increasingly used for short-duration procedures in spontaneously breathing patients. In this setting, it is preferable to block the response to moderate stimuli while avoiding loss of responsiveness (LOR) and intolerable ventilatory depression (IVD). In this study, we explored selected effects of combinations of remifentanil-propofol effect-site concentrations (Ces) that lead to a loss of response to esophageal instrumentation (EI), LOR, and/or onset of IVD. A secondary aim was to use these observations to create response surface models for each effect measure. We hypothesized that (1) in a large percentage of volunteers, selected

remifentanil and propofol Ces would allow EI but avoid LOR and IVD, and (2) the drug interaction for these effects would be synergistic.
METHODS: Twenty-four volunteers received escalating target-controlled remifentanil and propofol infusions over ranges of 0 to 6.4 ng $\cdot mL^{-1}$ and 0 to 4.3 μg $\cdot mL^{-1}$, respectively. At each set of target concentrations, responses to insertion of a blunt end bougie into the midesophagus (40 cm), level of responsiveness, and respiratory rate were recorded. From these data, response surface models of loss of response to EI and IVD were built and characterized as synergistic, additive, or antagonistic. A previously published model of LOR was used.
RESULTS: Of the possible 384 assessments, volunteers were unresponsive to EI at 105 predicted remifentanil-propofol Ces; in 30 of these, volunteers had no IVD; in 30, volunteers had no LOR; and in 9, volunteers had no IVD or LOR. Many other assessments over the same concentration ranges, however, did have LOR and/or IVD. The combinations that allowed EI and avoided IVD and/or LOR primarily clustered around remifentanil-propofol Ces ranging from 0.8 to 1.6 ng $\cdot mL^{-1}$ and 1.5 to 2.7 μg $\cdot mL^{-1}$, respectively, and to a lesser extent approximately 3.0 to 4.0 ng $\cdot mL^{-1}$ and 0.0 to 1.1 μg $\cdot mL^{-1}$, respectively. Models of loss of response to EI and IVD both demonstrated a synergistic interaction between remifentanil and propofol.
CONCLUSION: Selected remifentanil-propofol concentration pairs, especially higher propofol-lower remifentanil concentration pairs, can block the response to EI while avoiding IVD in spontaneously breathing volunteers. It is, however, difficult to block the response to EI and avoid both LOR and IVD. It may be necessary to accept some discomfort and blunt rather than block the response to EI to consistently avoid LOR and IVD.

评估 Flotrac/vigileo 新的软件版本（3.02 版）并和以往肝硬化患者肝移植手术中的数据比较

Evaluation of a New Software Version of the FloTrac/Vigileo (Version 3.02) and a Comparison with Previous Data in Cirrhotic Patients Undergoing Liver Transplant Surgery

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背景：在肝硬化患者进行肝移植手术时，可靠的心输出量监测是非常有用的，因为肝硬化合并有血管扩张和高心输出状态，称为肝硬化心肌病，这就会挑战脉搏轮廓线心输出量监测技术可靠性。尽管射血分数和心输出量的升高是由于外周血管阻力低，但是长期耐受的肝硬化患者的心室收缩力还是会受损的。然而，肝硬化患者在手术时由于生理变化与手术应激可以代偿。最近，我们发现 Flotrac/vigileo™无法在肝硬化患者移植手术中使用。对此，公司升级了他们的软件。因此，我们需要

在同一环境中评估这一新的第三代（3.02 版）Flotrac/vigileo 计算软件的准确性和可靠性。
方法：同时使用肺动脉导管进行快速灌注热稀释法和 Flotrac/vigileo(CI_V)进行脉搏轮廓线分析来监测心脏指数。在 21 例肝移植手术中，读了移植期间和移植后共 10 个时间点的数据。将其与我们 2009 年使用第二代（1.10 版）软件的研究数据进行了比较。
结果：我们的新数据表明 3.02 版软件显著减少了在低外周阻力状态时对脉搏轮廓心输出读数偏差的不利影响，从而提高系统的整体精度和趋势能力。回归分析表明 CI_{TD} 和 CI_V 之间呈现中等相关性（r =0.67，95%置信区间为 0.40－0.86）。Bland 和 Altman 分析表明，偏差为 0.4 $L.min^{-1} \cdot m^{-2}$，百分比误差为 52%（95%置信区间为 49%－55%）。新软件的趋势能力也得到了改进，但仍远远低于目前的基准。
结论：新版软件（3.02 版）与以前的版本比较有了重大的改进，整体精度和趋势能力更好。进一步的计算改进将会增加这一技术的可靠性，使其广泛应用在高度复杂环境的肝硬化患者肝移植手术中。
（唐亮 译 马皓琳 李士通 校）

BACKGROUND: Reliable cardiac output monitoring is particularly useful in the cirrhotic patient undergoing liver transplant surgery, because cirrhosis of the liver is associated with a vasodilated and high output state, known as *cirrhotic cardiomyopathy*, that challenges the reliability of pulse contour cardiac output technology. The contractility of the ventricle in cirrhosis is impaired, which is tolerated even though the ejection fraction and cardiac output are elevated because of the low peripheral resistance. However, during surgery the cirrhotic patient can decompensate because of the physiological changes and stress of surgery. Recently, we showed that the FloTrac/Vigileo™ failed to perform in cirrhotic patients undergoing transplant surgery. In response, the company upgraded their software. Therefore, we have assessed the accuracy and reliability of this new third-generation (version 3.02) FloTrac/Vigileo algorithm software in the same setting.
METHODS: The cardiac index was measured simultaneously by single-bolus thermodilution (CI_{TD}), using a pulmonary artery catheter, and pulse contour analysis, using the FloTrac/Vigileo (CI_V). Readings were made at 10 time points during and after liver transplant surgery in 21 patients. Comparisons with data from our 2009 study, which used second-generation (version 01.10) software, were also made.
RESULTS: Our new data show that version 3.02 software significantly reduced the adverse effect on pulse contour cardiac output reading bias in low peripheral resistance states, and thus improves the overall precision and trending ability of the system. Regression analysis between CI_{TD} and CI_V showed that the correlation was moderate (r =0.67, 95% confidence interval, 0.40 to 0.86). The Bland and Altman analysis showed that bias was 0.4 $L.min^{-1} \cdot m^{-2}$, and the percentage error was 52% (95% confidence interval, 49% to 55%). Trending ability of the new software also was improved but was still well below the current benchmarks.
CONCLUSION: The new software (version 3.02) provided substantial improvements over the previous versions with better overall precision and trending ability. Further algorithm refinements will increase this technology's reliability to be extensively used in the highly complex setting of cirrhotic patients undergoing liver transplantation.

低流量麻醉工作站有无湿热交换器对温度和湿度的影响

The Temperature and Humidity in a Low-Flow Anesthesia Workstation With and Without a Heat and Moisture Exchanger

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背景：Dräger Primus 麻醉工作站有一个内置的加热器用来加热病人呼出的气流。加热后的呼出气流经过钠石灰罐的同时与新鲜气流混合。一个湿热交换器（HME）可用于进一步加热和湿化吸入的气体。在本研究中，我们测量了安装或未安装湿热交换器的 Dräger Primus 麻醉工作站的吸入气体温度和湿度。

方法：30 名女性患者随机分为 2 组，分别由安装或未安装 HME 的 Dräger Primus 麻醉工作站辅助通气。在患者与呼吸环路连接后 15、30、60、90 和 120 分钟测量吸入气体的温度和湿度。

结果：经过 120 分钟低流量辅助通气后，安装或未安装 HME 的吸入气体温度分别为 30℃ ± 2℃ 和 25℃ ± 1℃，组间差异具有统计学意义(P < 0.001)，95%置信区间(CI)为 3.80℃ 至 6.40℃。安装或未安装 HME 的吸入气体的绝对湿度分别为 30 ± 2 $mgH_2O \cdot L^{-1}$ 和 20.5 ± 3.6 $mgH_2O \cdot L^{-1}$，组间差异具有统计学意义(P < 0.001)，95%置信区间(CI)为 7.37℃ 至 13.03℃。

结论：当使用低流量新鲜气体时，Primus 麻醉工作站可将吸入气体部分湿化。插入一个 HME 可提高吸入气体的湿度，使其接近生理值。

（刘伍 译 马皓琳 李士通 校）

BACKGROUND: The Dräger Primus anesthesia workstation has a built-in hotplate to heat the patient's exhaled gas. The fresh gas flow is mixed with the heated exhaled gas as they pass through the soda lime canister. A heat and moisture exchanger (HME) may also be used to further heat and humidify the inhaled gas. In this study we measured the temperature and humidity of the inhaled gas coming from the Dräger Primus with or without a HME.

METHODS: Thirty female patients were randomly divided into 2 groups and their lungs ventilated by the Primus Dräger anesthesia workstation with or without a HME. The humidity and temperature of the inhaled gas were measured 15, 30, 60, 90, and 120 minutes after connecting the patient to the breathing circuit.

RESULTS: After 120 minutes of ventilation with a low-flow breathing circuit, the temperatures of inhaled gas were 25℃ ± 1℃ and 30℃ ± 2℃ without and with HME, respectively, with a statistically significant difference between groups ($P < 0.001$) with 95% confidence interval (CI) of 3.80℃ to 6.40℃; and the absolute humidity values of the inhaled gas were 20.5 ± 3.6 $mgH_2O \cdot L^{-1}$ and 30 ± 2 $mgH_2O \cdot L^{-1}$ without and with HME, respectively, with a statistically significant difference between groups ($P < 0.001$) with 95% CI of 7.37℃ to 13.03℃.

CONCLUSIONS: The Primus anesthesia workstation partially humidifies the inspired gas when a low fresh gas flow is used. Insertion of an HME increases the humidity in inhaled gas, bringing it close to physiological values.

超声评估妊娠期髂嵴线的脊椎水平

Ultrasound Assessment of the Vertebral Level of the Intercristal Line in Pregnancy

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背景：众所周知髂嵴线最常穿过腰 4 脊柱棘突或者腰 4-5 间隙；然而据推测在妊娠期间由于过度腰椎前凸髂嵴线位置较高。已有研究显示临床上依赖于应用髂嵴线来估计脊椎水平常常是不准确的。我们假设，按照触诊的方法决定妊娠妇女髂嵴线的脊椎水平高于超声测得的水平。
方法：51 名足月妊娠患者入组。两位有经验的麻醉医师按照触诊的方法对髂嵴线的位置进行估计。另一个麻醉医师在对临床估计不知情的条件下应用超声确定髂嵴上缘在横向和纵向平面的位置，然后识别腰椎水平。记录临床估计髂嵴线穿过脊柱的脊椎水平，并且与超声测得的髂嵴上缘水平相比较。
结果：临床估计髂嵴线脊椎水平与超声测量的一致率只有 14%（101 次中有 14 次，95%置信区间 8%，22%）。临床估计高于超声测量一个节段的比率为 23%（101 次中有 23 次，95%置信区间 16%，32%），超过 1 个节段的比率为 25%（101 次中有 25 次，单侧 95%置信区间，＞18%）。临床估计的分布发现临床医生定位髂嵴线在腰 3 或腰 3-4 间隙的比率为 54%(101 次中有 54 次，95%置信区间 44%，63%)，在腰 2-3 或更高节段的比率为 27%(101 次中有 27 次，单尾 95%置信区间＞20%)。
结论：应用超声发现至少有 6%的足月产妇定位髂嵴线解剖位置在腰 3 或更高。研究发现临床估测比超声探测的解剖学位置高大于等于 1 个节段的比率至少为 40%。这种差异可能导致椎管内麻醉期间错误定位腰椎间隙，并增加神经损伤的风险。
（刘朝辉译，马皓琳，李士通校）

BACKGROUND: The intercristal line is known to most frequently cross the L4 spinous process or L4-5 interspace; however, it is speculated to be positioned higher during pregnancy because of the exaggerated lumbar lordosis. Clinical estimation of vertebral levels relying on the use of the intercristal line has been shown to often be inaccurate. We hypothesized that the vertebral level of the intercristal line determined by palpation would be higher than the level determined by ultrasound in pregnant women.
METHODS: Fifty-one term pregnant patients were recruited. Two experienced anesthesiologists performed estimates of the position of the intercristal line by palpation. Using ultrasound, another anesthesiologist who was blinded to the clinical estimates, determined the position of the superior border of the iliac crest in the transverse and

longitudinal planes and then identified the lumbar vertebral levels. The vertebral level at which the clinical estimates of the intercristal line crossed the spine was recorded and compared with the ultrasound-determined level of the superior border of the iliac crest. **RESULTS:** The clinical estimates of the spinal level of the intercristal line agreed with the ultrasound measurement 14% of the time (14 of 101; 95% confidence interval [CI]: 8%, 22%). The clinical estimates were 1 level higher than the ultrasound measurement 23% of the time (23 of 101; 95% CI: 16%, 32%) and >1 level higher 25% of the time (25 of 101; 1-tailed 95% CI: >18%). The distribution of the clinical estimates found clinicians locating the intercristal line at L3 or L3-4 54% of the time (54 of 101; 95% CI: 44%, 63%) and at L2-3 or higher 27% of the time (27 of 101; 1-tailed 95% CI: >20%). **CONCLUSION:** The anatomical position of the intercristal line was at L3 or higher in at least 6% of term pregnant patients using ultrasound. Clinical estimates were found to be ≥1 vertebral level higher than the anatomical position determined by ultrasound at least 40% of the time. This disparity may contribute to misidentification of lumbar interspaces and increased risk of neurologic injury during neuraxial anesthesia.

超声引导对疼痛干预管理是否有优势？一篇关于急性疼痛结果的综述

Is Ultrasound Guidance Advantageous for Interventional Pain Management? A Review of Acute Pain Outcomes

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背景：超声（US）引导下周围神经阻滞已在全球范围内得到广泛应用。关于实时超声可视化技术较传统的神经定位技术的优势的报导大多是关于操作和技术阻滞相关的结果，而关于急性疼痛治疗的相关结果则明显较少报导。在本综述中，我们比较了 US 引导与传统神经定位技术对于急性疼痛干预管理和急性疼痛相关结果的作用。
方法：我们对 1990 年 1 月至 2011 年 1 月期间的 MEDLINE、EMBASE、循证医学中心登记的对照临床试验做了系统检索，检索出关于比较评估 US 引导和传统神经定位技术对急性疼痛及其相关结果的作用的随机对照试验。排除标准包括：纳入实验未报告以下至少一项急性疼痛的结果——疼痛程度、阿片类药物使用量、感觉阻滞持续时间、首次需要止痛药的时间。相关结果分类如下：患者相关结果（阿片类药物相关副作用、患者满意度、术后认知功能障碍）、麻醉相关结果（不必要的运动阻滞、周围神经置管失败、患病率、慢性疼痛的发生）、手术相关结果（再次入院、行走的能力），住院相关结果（住院时间、花费）。我们对于 US 引导治疗急性疼痛的有前景的新颖应用也予以了讨论。
结果：我们纳入了比较 US 引导与或不与外周神经刺激器联用、单用外周神经刺激器和应用解剖标志技术的 23 项随机对照试验，共 1674 名患者。在 16 项评估了疼痛程度的研究中， 8 项报道了 US 引导带来的改善，但是仅 1 项研究报道了 US 引导与对照组有大于 1 个区间的数值分级疼痛评分的差异性。8 项研究评估了感觉阻滞的持续时间，其中 3 项报道了 US 引导的阻滞持续时间延长。7 项研究评估了阿

片类药物的使用量，其中 3 项报道了 US 引导组的使用量减少。3 项研究评估了首次需用镇痛药的时间，其中 2 项支持 US 引导技术。我们未发现 US 引导和传统神经定位技术在其他相关结果上的差异性。我们未发现在任何结果上显示 US 引导次于传统的神经定位技术。非随机的数据显示 US 引导的腹横肌平面的阻滞可能提供多于标准镇痛治疗的益处，但未与解剖学标志定位阻滞技术相比。
结论：目前根据同时期的文献报导没有足够的证据可用于定义 US 引导用于急性疼痛干预管理时与传统神经定位技术比较对于急性疼痛及其相关结果的作用。
（毛祖旻 译 马皓琳 李士通 校）

BACKGROUND: Ultrasound (US) guidance for peripheral nerve blockade has gained popularity worldwide. The reported benefits of real-time sonographic visualization compared with traditional nerve localization techniques generally apply to procedural and technical block-related outcomes whereas acute pain–related outcomes are featured less prominently. In this review, we evaluated the effect of US guidance compared with traditional nerve localization techniques for interventional management of acute pain and acute pain–related outcomes.
METHODS: We performed a systematic search of MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Clinical Trials (from January 1990 to January 2011) to identify randomized controlled trials evaluating the effects of US guidance on acute pain and related outcomes compared with traditional nerve localization techniques. Studies were excluded if they did not report at least one of the following acute pain outcomes: pain severity, opioid consumption, sensory block duration, and time to first analgesic request. Related outcomes were classified as follows: patient related (opioid-related adverse effects, patient satisfaction, postoperative cognitive deficit); anesthesia related (unwanted motor block, perineural catheter failure, morbidity, development of chronic pain); surgery related (hospital readmission, ability to ambulate); and hospital related (length of stay, cost). Promising novel applications of US guidance for acute pain management were also sought for discussion purposes.
RESULTS: We identified 23 randomized controlled trials, including 1674 patients, that compared US guidance with and without peripheral nerve stimulation with peripheral nerve stimulation alone or anatomical landmark techniques. Of the 16 studies that evaluated pain severity, 8 reported improvement with US guidance; however, only 1 study reported a difference between US guidance and the comparator of >1 interval on the numeric rating pain scale. Eight studies evaluated sensory block duration and 3 of these reported prolonged block duration with US guidance. Seven studies evaluated opioid consumption, of which 3 reported a reduction with US guidance. Three studies evaluated time to first analgesic request, of which 2 favored US guidance. We uncovered no significant differences between US guidance and traditional nerve localization techniques for any other related outcome. US guidance was not found to be inferior compared with traditional nerve localization techniques for any outcome. Nonrandomized data suggest that US-guided transversus abdominis plane blocks may offer analgesic benefit over standard analgesic therapy, but has not been compared with an anatomical landmark technique.
CONCLUSIONS: At present, there is insufficient evidence in the contemporary literature to define the effect of US guidance on acute pain and related outcomes

compared with traditional nerve localization techniques for interventional acute pain management.

大鼠剖腹手术后持续腹膜外输注和全身给予不同剂量罗哌卡因的比较

A Comparison of Different Dosages of a Continuous Preperitoneal Infusion and Systemic Administration of Ropivacaine After Laparotomy in Rats

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介绍：为了进一步解释局麻药伤口输注的镇痛作用中所涉及的作用机制，我们评估了开腹手术后和给予局麻药后的体壁和内脏的敏感度以及炎症指数。不同剂量的罗哌卡因通过多孔的腹膜外导管或者全身连续输注给大鼠。
方法：9 组接受剖腹手术或者模拟手术的大鼠接受 2 种注射：（1）通过腹膜外导管单次注射（罗哌卡因或者盐水）或（2）肌肉注射（罗哌卡因或者盐水）。接下来，腹膜外导管持续 24h 输注（罗哌卡因或者盐水），肌注每 8 小时一次。机械和内脏刺激后阈值在术后 48 小时内评估 3 次。用酶联免疫吸附法测量全血培养中刺激产生的肿瘤坏死因子 α 和白细胞介素 1β。采用气相色谱法测量血浆罗哌卡因浓度。
结果：腹膜外输注高剂量罗哌卡因和全身性使用罗哌卡因同样可防止对机械痛和内脏痛的敏感性改变，并导致更好的功能恢复。全身使用的镇痛作用与抗炎作用相关。
结论：本研究表明，通过腹膜外输注和全身性间断注射给予高剂量罗哌卡因对于开腹手术后的机械痛和内脏痛的敏感性作用效果相近。而且，全身的使用与抗炎作用相关。关于腹膜外输注高剂量罗哌卡因和全身性使用的优越性比较还需进一步的研究。
（安光惠译 马皓琳 李士通校）

INTRODUCTION: To further explain the mechanisms of action involved in the analgesic effect of a local anesthetic wound infusion, we evaluated parietal and visceral sensitivity as well as indices of inflammation after laparotomy and administration of a local anesthetic. Ropivacaine was administered at different dosages by a continuous infusion using a multiholed catheter in the preperitoneal position or systemically in rats.
METHODS: Nine groups of rats received 2 injections after laparotomy or sham surgery: (1) a bolus injection (ropivacaine or saline) via a preperitoneal catheter and (2) an IM injection (IM) (ropivacaine or saline). These injections were followed by a continuous infusion (ropivacaine or saline) in the preperitoneal catheter for 24 hours and 1 IM injection every 8 hours. Mechanical and visceral thresholds after stimulation were evaluated 3 times during the 48 hours after surgery. Stimulated production of tumor necrosis factor α, and interleukin 1β in whole-blood cultures were measured by enzyme-

linked immunosorbent assay. The ropivacaine plasma concentration was measured by gas chromatography.
RESULTS: Preperitoneal infusion of high doses of ropivacaine and systemic ropivacaine similarly prevented mechanical and visceral sensitivity alterations and led to a better functional recovery. The analgesic effect of systemic administration was associated with an anti-inflammatory effect.
CONCLUSION: In the current study, high-dose ropivacaine administered via a preperitoneal infusion or systemic boluses had the same effect on mechanical and visceral sensitivity after laparotomy. Moreover, systemic administration was associated with an anti-inflammatory effect. The merits of the comparable benefit of systemic and high-dose preperitoneal infusion of ropivacaine need to be confirmed with further studies.

吗啡和芬太尼在大鼠嗅上皮的优先分布后增强的镇痛效应

Enhanced Analgesic Responses After Preferential Delivery of Morphine and Fentanyl to the Olfactory Epithelium in Rats

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背景：中枢性阿片类镇痛药（如吗啡和芬太尼）是有效的，但药物到达脑和中枢神经系统前的首过消除会产生延迟反应和副作用，从而常使其效应受限。通常认为，经鼻腔给药可直接进入脑和中枢神经系统，在治疗学上有诸如起效快、全身浓度低等优点。鼻腔的嗅区涉及促进这一鼻到中枢神经系统直接转移。如果能改善经嗅区给予的阿片类药物的成分，那么便可有更多药物直接进入中枢神经系统，产生更好的疗效。
方法：我们开发了一个加压嗅觉投放（POD）装置对 S-D 大鼠鼻腔嗅区进行连续、非侵袭性大量给药。通过甩尾潜伏期试验和血浆及中枢神经组织的药物浓度分析，我们比较了阿片类药物吗啡和芬太尼在不同给药途径下（鼻腔嗅区 POD 装置给药、鼻腔呼吸区滴鼻给药和经腹腔内注射全身性给药）的分布和效应。
结果：与滴鼻剂相比，通过 POD 给予吗啡产生显著更高的总体疗效（效应-时间曲线下面积[$AUC_{效应}$]），且血浆药物浓度（$AUC_{血浆}$）无显著升高。POD 给予吗啡产生 38%到 55%的鼻到中枢神经系统直接转移。与鼻腔呼吸区给药相比，POD 给予芬太尼产生更快（5 比 10 分钟）且更强的镇痛作用。与腹腔内注射和滴鼻给药不同，通过 POD 装置对鼻腔嗅上皮给予吗啡和芬太尼后，均显示出相应的顺时针（血浆）比效应滞后现象，与鼻到中枢神经系统直接药物转移机制相一致。
结论：阿片类药物在鼻腔嗅区的沉积可对药物的分布和药效学作用产生显著影响，因此在未来应该考虑经鼻给予阿片类药物。
（陈彬彬译 马皓琳 李士通校）
BACKGROUND: Centrally acting opioid analgesics such as morphine and fentanyl are effective, but their efficacy is often limited by a delayed response or side effects resulting from systemic first pass before reaching the brain and the central nervous system (CNS). It is generally accepted that drugs applied to the nasal cavity can directly access the brain and the CNS, which could provide therapeutic advantages such as rapid onset and lower systemic exposure. The olfactory region of the nasal cavity has been implicated in

facilitating this direct nose-to-CNS transfer. If the fraction of opioid administered to the olfactory region could be improved, there could be a larger fraction of drug directly delivered to the CNS, mediating greater therapeutic benefit.
METHODS: We have developed a pressurized olfactory delivery (POD) device to consistently and noninvasively deposit a majority of drug on the olfactory region of the nasal cavity in Sprague-Dawley rats. Using the tail-flick latency test and analysis of plasma and CNS tissue drug exposure, we compared distribution and efficacy of the opioids morphine and fentanyl administered to the nasal olfactory region with the POD device or the nasal respiratory region with nose drops or systemically via intraperitoneal injection.
RESULTS: Compared with nose drop administration, POD administration of morphine resulted in a significantly higher overall therapeutic effect (area under the curve [over the time course] $[AUC]_{effect}$) without a significant increase in plasma drug exposure (AUC_{plasma}). POD of morphine resulted in a nose-to-CNS direct transport percentage of 38% to 55%. POD of fentanyl led to a faster (5 vs 10 minutes) and more intense analgesic effect compared with nasal respiratory administration. Unlike intraperitoneal injection or nose drop administration, both morphine and fentanyl given by the POD device to olfactory nasal epithelium exhibited clockwise (plasma) versus effect hysteresis after nasal POD administration, consistent with a direct nose-to-CNS drug transport mechanism.
CONCLUSIONS: Deposition of opioids to the olfactory region within the nasal cavity could have a significant impact on drug distribution and pharmacodynamic effect, and thus should be considered in future nasally administered opioid studies.

综述：围术期心脏舒张功能不全的评估

Review Article: Perioperative Assessment of Diastolic Dysfunction

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心脏的舒张功能是围术期经食道超声心动图对心脏进行综合评估的一部分。50%以上的接受心脏手术或高风险非心脏手术的患者会出现心脏舒张功能的异常，这也是发生术后不良预后的独立预测因素。舒张功能不全可能是 50%心脏收缩功能正常的充血性心力衰竭患者的病因。对舒张功能的综合评估需要全方位的、负荷依赖的多普勒技术。体液丢失及麻醉药物可以对心肌舒张和顺应性产生影响，使得多普勒评估心肌功能变得更为复杂。更高端的多普勒技术，比如组织多普勒成像和血流传播速度，能够更精密的检测左室舒张功能，分析舒张期各个特殊阶段，鉴别异常来自心肌舒张还是顺应性。此外，不同的多普勒推导比率可以估计左室充盈压。当麻

醉状态下接受手术的病人需要在经食道超声心动图评估左室舒张功能时，因其在手术室时与非卧床状态时的血流动力学环境不同，故要求对诊断程序进行修正。（陆秉玮　译　陈杰　校）

Assessment of diastolic function should be a component of a comprehensive perioperative transesophageal echocardiographic examination. Abnormal diastolic function exists in >50% of patients presenting for cardiac and high-risk noncardiac surgery, and has been shown to be an independent predictor of adverse postoperative outcome. Normalcy of systolic function in 50% of patients with congestive heart failure implicates diastolic dysfunction as the probable etiology. Comprehensive evaluation of diastolic function requires the use of various, load-dependent Doppler techniques This is further complicated by the additional effects of dehydration and anesthetic drugs on myocardial relaxation and compliance as assessed by these Doppler measures. The availability of more sophisticated Doppler techniques, e.g., Doppler tissue imaging and flow propagation velocity, makes it possible to interrogate left ventricular diastolic function with greater precision, analyze specific stages of diastole, and to differentiate abnormalities of relaxation from compliance. Additionally, various Doppler-derived ratios can be used to estimate left ventricular filling pressures. The varying hemodynamic environment of the operating room mandates modification of the diagnostic algorithms used for ambulatory cardiac patients when left ventricular diastolic function is evaluated with transesophageal echocardiography in anesthetized surgical patients.

前脑特定的 γ-氨基丁酸 A 型受体 β3 亚基的基因敲除小鼠对异氟醚的遗忘效应有抵抗作用

Gamma-Aminobutyric Acid Type A Receptor β3 Subunit Forebrain-Specific Knockout Mice Are Resistant to the Amnestic Effect of Isoflurane

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背景：包括 γ -氨基的丁酸 A 型受体（$GABA_A$-Rs）的 β3 介导静脉麻醉药的作用，如制动和催眠。前脑目标区域敲除了 $GABA_A$-Rs 的 β3 亚基的实验鼠对依托咪酯的催眠效果敏感性降低，表现为测量时翻正反射消失。在这种条件性敲除下，由吸入麻醉药产生的遗忘和制动作用尚未评估。

方法：作者通过对前脑选择性 β3 条件敲除的实验鼠及作为对照的同窝出生鼠条件性恐惧的测试，来评估组间吸入性麻醉药对伤害性刺激产生不动性的遗忘和最小肺泡浓度的差异，即不动性方面的差异。评估依托咪酯和异氟醚对条件恐惧的抑制，评估异氟醚的 MAC。

结果：依托咪酯对两种基因型产生同样的条件恐惧抑制。相对于同窝出生鼠，被敲除的实验鼠表现出了对由异氟醚产生的条件恐惧抑制的抵抗力。在异氟醚 MAC 值方面，对照组和试验组没有不同。
结论：这些结果表明异氟醚而不是依托咪酯能抑制前脑与记忆相关的海马区包含 $GABA_A$-Rs 的 β3 作用。
（孙晓琼　译　陈杰　校）

BACKGROUND: β3 containing γ–aminobutyric acid type A receptors ($GABA_A$-Rs) mediate behavioral end points of IV anesthetics such as immobility and hypnosis. A knockout mouse with targeted forebrain deletion of the β3 subunit of the $GABA_A$-R shows reduced sensitivity to the hypnotic effect of etomidate, as measured by the loss of righting reflex. The end points of amnesia and immobility produced by an inhaled anesthetic have yet to be evaluated in this conditional knockout.
METHODS: We assessed forebrain selective β3 conditional knockout mice and their littermate controls for conditional fear to evaluate amnesia and MAC, the minimum alveolar concentration of inhaled anesthetic necessary to produce immobility in response to noxious stimulation, to assess immobility. Suppression of conditional fear was assessed for etomidate and isoflurane, and MAC was assessed for isoflurane.
RESULTS: Etomidate equally suppressed conditional fear for both genotypes. The knockout showed resistance to the suppression of conditional fear produced by isoflurane in comparison with control littermates. Controls and knockouts did not differ in isoflurane MAC values.
CONCLUSIONS: These results suggest that β3 containing $GABA_A$-Rs in the forebrain contribute to hippocampal-dependent memory suppressed by isoflurane, but not etomidate.

CNAP™测得的脉压变异率对患者术中补液反应性的预测能力

The Ability of Pulse Pressure Variations Obtained with CNAP™ Device to Predict Fluid Responsiveness in the Operating Room

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背景：机械通气患者呼吸相关脉压（动脉压力）变异率(ΔPP_{ART})能提示液体治疗反应。 Infinity ® CNAP™SmartPod ® (Dräger Medical AG & Co., Lübeck, 德国) 系统提供无创连续动脉压测量和近乎实时的压力波形。本研究推测，CNAP 系统来源的呼吸相关脉压变异率(ΔPP_{CNAP}) 和ΔPP_{ART}一样，能预测全麻机械通气患者的液体治疗反应性。
方法： 35 例行血管手术全身麻醉诱导后的患者使用 6%羟乙基淀粉 130/0.4（500 毫升）进行扩容（VE），扩容前后记录由 Vigileo™/ FloTrac™（Edwards Lifesciences, Irvine, CA）测量每搏输出量（SV）、ΔPP_{ART}和ΔPP_{CNAP}数据。如 SV 扩容后增加≥15%，则受试者被认定为有反应。

结果： 20 例患者有扩容反应，15 例无扩容反应。扩容前 ΔPP_{ART} and ΔPP_{CNAP} 之间的相关系数为 R = 0.90（95%可信区间[CI] = 0.84-0.96，P <0.0001）。有扩容反应者的 ΔPP_{ART} and ΔPP_{CNAP} 数值在扩容之前显著高于无反应患者($P < 0.0001$)。扩容前 ΔPP_{ART} and ΔPP_{CNAP} 数值与扩容后 SV 增加百分比之间有显著关系（分别为，$r^2 = 0.50$; $P < 0.0001$ and $r^2 = 0.57$; $P < 0.0001$）。扩容前，ΔPP_{ART} 数值>10%区分有扩容反应患者与无扩容反应患者，灵敏度为 90%（95%CI = 69%-99%），特异性为 87%（95%CI = 60%-98%）。ΔPP_{AR} 受试者特征（ROC）曲线下面积为 0.957 ± 0.035。扩容前，ΔPP_{CNAP} 数值> 11%区分有扩容反应患者与无扩容反应患者，灵敏度为 85%（95%CI = 62%-97%），特异性为 100%（95%CI = 78%-100%）。ΔPP_{CNAP}ROC 曲线下面积为 0.942 ± 0.040。ΔPP_{ART} 和 ΔPP_{CNAP}ROC 曲线面积间无显著差异。

结论：用 ΔPP_{CNAP} > 11%预测全麻下前负荷依赖的机械通气患者有无扩容反应，其敏感性至少有 62%。

（陈毓雯　译　陈杰　校）

BACKGROUND: Respiratory-induced pulse pressure variations obtained with an arterial line (ΔPP_{ART}) indicate fluid responsiveness in mechanically ventilated patients. The Infinity® CNAP™ SmartPod® (Dräger Medical AG & Co. KG, Lübeck, Germany) provides noninvasive continuous beat-to-beat arterial blood pressure measurements and a near real-time pressure waveform. We hypothesized that respiratory-induced pulse pressure variations obtained with the CNAP system (ΔPP_{CNAP}) predict fluid responsiveness as well as ΔPP_{ART} predicts fluid responsiveness in mechanically ventilated patients during general anesthesia.

METHODS: Thirty-five patients undergoing vascular surgery were studied after induction of general anesthesia. Stroke volume (SV) measured with the Vigileo™/FloTrac™ (Edwards Lifesciences, Irvine, CA), ΔPP_{ART}, and ΔPP_{CNAP} were recorded before and after intravascular volume expansion (VE) (500 mL of 6% hydroxyethyl starch 130/0.4). Subjects were defined as responders if SV increased by ≥15% after VE.

RESULTS: Twenty patients responded to VE and 15 did not. The correlation coefficient between ΔPP_{ART} and ΔPP_{CNAP} before VE was $r = 0.90$ (95% confidence interval [CI] = 0.84–0.96; $P < 0.0001$). Before VE, ΔPP_{ART} and ΔPP_{CNAP} were significantly higher in responders than in nonresponders ($P < 0.0001$). The values of ΔPP_{ART} and ΔPP_{CNAP} before VE were significantly correlated with the percent increase in SV induced by VE (respectively, $r^2 = 0.50$; $P < 0.0001$ and $r^2 = 0.57$; $P < 0.0001$). Before VE, a ΔPP_{ART} >10% discriminated between responders and nonresponders with a sensitivity of 90% (95% CI = 69%–99%) and a specificity of 87% (95% CI = 60%–98%). The area under the receiver operating characteristic (ROC) curve was 0.957 ± 0.035 for ΔPP_{ART}. Before VE, a ΔPP_{CNAP} >11% discriminated between responders and nonresponders with a sensitivity of 85% (95% CI = 62%–97%) and a specificity of 100% (95% CI = 78%–100%). The area under the ROC curve was 0.942 ± 0.040 for ΔPP_{CNAP}. There was no significant difference between the area under the ROC curve for ΔPP_{ART} and ΔPP_{CNAP}.

CONCLUSIONS: A value of ΔPP_{CNAP} >11% has a sensitivity of at least 62% in predicting preload-dependent responders to VE in mechanically ventilated patients during general anesthesia.

改变体表降温的速度对于血管收缩和寒战阈值的影响

The Effect of Altering Skin-Surface Cooling Speeds on Vasoconstriction and Shivering Thresholds

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背景：体核温度和体表温度对稳态体温调节控制都有影响。动态体温调节反应触发对快速热变化的强力的防御反应。这些反应可能使体温调节研究变得更加复杂，同时减慢了对低体温治疗的实施。本研究假设在较高的体表温度水平，快速降温比慢速或者中速降温更容易引起血管收缩和寒战。

方法：11 位健康志愿者用加压气流或/和传导冷却的方法，随机地以 3 种不同速度降低体表温度。其中一天志愿者接受慢速降温 (≈2°C/h)，另外一天同时接受中速(≈4°C/h)和快速(≈6℃/h)降温。血管内热交换导管测量体核温度。指尖血流速度≤ 0.25ml/min 定义为血管收缩发生；氧耗持续增加≥25%定义为寒战发生。数据结果使用重复测量的方差分析方法，P< 0.05 表示差异显著。

结果：志愿者的平均年龄为 25 ± 5 岁，身高为 175 ± 7 cm，体重为 63 ± 10 kg。实验中体核温度维持在 37 度左右。血管收缩时，慢速、中速以及快速降温时其平均体表温度分别为 33.2℃ (95% CI: 32.0℃, 34.4℃), 33.5℃ (95% CI: 32.3℃, 34.7℃), and 33.0℃ (95% CI: 31.4℃, 34.6℃)。寒战时，其体表温度则分别为 31.4℃ (95% CI: 30.3℃, 32.5℃), 31.5℃ (95% CI: 30.2℃, 32.8℃), and 30.7℃ (95% CI: 28.9℃, 32.5℃)。

结论：对于 3 种不同的降温速度，开始发生血管收缩或寒战时，其体表温度相似。积极地体表降温可以用于体温调节研究以及指导治疗性低体温而没有引起令人难以接受的体温调节的防御反应。

（张婷　译　陈杰　校）

BACKGROUND: Both core and skin temperatures contribute to steady-state thermoregulatory control. Dynamic thermoregulatory responses trigger aggressive defenses against rapid thermal perturbations. These responses potentially complicate interpretation of thermoregulatory studies and could slow induction of therapeutic hypothermia. We thus tested the hypothesis that rapid external skin-cooling triggers vasoconstriction and shivering at higher mean skin temperatures than slow or moderate rates of skin cooling.

METHODS: Eleven healthy volunteers were cooled at 3 skin-cooling rates using forced air or/and conductive cooling in random order. One day volunteers received slow (≈2°C/h) skin cooling, and on another day, they received both medium (≈4°C/h) and fast (≈6°C/h) skin cooling. An endovascular heat-exchanging catheter maintained core temperature. Fingertip blood flow ≤0.25 mL/min defined onset of vasoconstriction; sustained ≥25% increase in oxygen consumption defined onset of shivering. Results were evaluated with repeated-measures analysis of variance, with $P < 0.05$ representing statistical significance.

RESULTS: Volunteers were 25 ± 5 years of age (mean ± SD), 175 ± 7 cm tall, and weighed 63 ± 10 kg. Core temperature remained constant (≈37°C) throughout each study day. At vasoconstriction, mean skin temperatures were 33.2℃ (95% confidence interval [CI]: 32.0℃, 34.4℃), 33.5℃ (95% CI: 32.3℃, 34.7℃), and 33.0℃ (95% CI: 31.4℃, 34.6℃) at slow, medium, and fast skin-cooling rates, respectively. Mean skin temperatures at shivering were also comparable: 31.4℃ (95% CI: 30.3℃, 32.5℃), 31.5℃ (95% CI: 30.2℃, 32.8℃), and 30.7℃ (95% CI: 28.9℃, 32.5℃), respectively.
CONCLUSIONS: Onset of vasoconstriction and shivering occurred at similar mean skin temperatures with all 3 cooling rates. Aggressive surface cooling can thus be used in thermoregulatory studies and for induction of therapeutic hypothermia without provoking dynamic thermoregulatory defenses.

应用辛伐他丁能减少大鼠的脊髓缺血再灌注损伤

Reduction of Spinal Cord Ischemia/Reperfusion Injury with Simvastatin in Rats

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背景：胸或胸腹主动脉手术会导致脊髓缺血及并发截瘫。然而，预防脊髓缺血引起截瘫的常规方法并不能提供全面的预防作用并可能导致其他副作用。作者假设辛伐他丁——近期已被证实对大脑缺血再损伤有神经保护作用的一种药物，应用于脊髓缺血再损伤的大鼠模型同样有神经保护作用。
方法：实验大鼠随机分为三组：辛伐他丁组、对照组、假手术组，每组 6 只大鼠。在主动脉球囊阻断前，对大鼠每日皮下注射辛伐他丁 10mg/kg 或对照药物，并在再灌注后 24 小时再次注射辛伐他丁或对照药物。对置入胸主动脉的 2F 大小 Fogarty 导管球囊充气后引起大鼠脊髓缺血，并在 12 分钟内维持近端平均动脉压大约 40mmHg。假手术组同样进行手术但不进行球囊充气的操作。在缺血再灌注后 6-48 小时应用运动缺陷指数对大鼠后肢运动功能进行缺血损伤的评估。在缺血再灌注后 48 小时进行脊髓组织学评估。
结果：与对照组相比，辛伐他丁组在再灌注后 24 小时和 48 小时的运动缺陷指数有显著改善。(P = 0.021 ，P = 0.023)。此外，辛伐他丁组的正常运动神经元要显著多于对照组(P = 0.037)。辛伐他丁组的白质空泡形成体积也显著小于对照组(P = 0.030)。
结论：应用辛伐他丁能减轻脊髓缺血再灌注大鼠的下肢运动功能障碍和组织病理学变化。
（赵嫣红　译　陈杰　校）
BACKGROUND: Surgery of the thoracic or thoracoabdominal aorta may cause spinal cord ischemia and subsequent paraplegia. However, conventional strategies for preventing paraplegia due to spinal cord ischemia provide insufficient protection and cause additional side effects. We hypothesized that simvastatin, a drug recently shown to

be neuroprotective against brain ischemia/reperfusion, would be neuroprotective in a rat spinal cord ischemia/reperfusion model.
METHODS: Rats were randomly assigned to simvastatin, vehicle, or sham-surgery (sham) groups (n = 6 per group). Simvastatin (10 mg/kg) or vehicle was administered subcutaneously once daily for 7 days before aortic balloon occlusion, and once at 24 hours after reperfusion. Spinal cord ischemia was induced by balloon inflation of a 2F Fogarty catheter in the thoracic aorta, and the proximal mean arterial blood pressure was maintained at 40 mm Hg for 12 minutes. The sham group received the same operation without inflation of the balloon. Ischemic injury was assessed by hindlimb motor function using the Motor Deficit Index score at 6 to 48 hours after ischemic reperfusion, and histological assessment of the spinal cord was performed 48 hours after reperfusion.
RESULTS: The Motor Deficit Index scores at 24 and 48 hours after reperfusion were significantly improved in the simvastatin group compared with the vehicle group (P = 0.021 and P = 0.023, respectively). Furthermore, there were significantly more normal motor neurons in the simvastatin group than in the vehicle group (P = 0.037). The percentage area of white matter vacuolation was significantly smaller in the simvastatin group than in the vehicle group (P = 0.030).
CONCLUSIONS: Simvastatin treatment can attenuate hindlimb motor dysfunction and histopathological changes in spinal cord ischemia/reperfusion injury in rats.

早期胸交感神经阻滞提高上肢神经病理性疼痛的疗效

Early Thoracic Sympathetic Block Improves the Treatment Effect for Upper Extremity Neuropathic Pain

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背景：交感神经系统在介导多种神经病理性疼痛中发挥重要的作用。胸交感神经阻滞（thoracic sympathetic block，TSB）对上肢和胸部的神经病理性疼痛具有良好的治疗作用。然而，未有研究评估过促进 TSB 治疗作用的相关因素。本次研究评估了 TSB 产生良好预后作用的影响因素，并确定临床上重要的影响预后的因素。
方法：对 51 位患者在 X 线引导下实施经皮 TSB，并采集每位患者的年龄、性别、体重指数、诊断、疼痛强度和症状的持续时间。用 logistic 回归计算每个变量的调整后的比值比和 95%置信区间。
结果：相比于症状持续时间长于 1 年的患者，TSB 对持续时间小于或者等于 1 年的患者的疗效更好（P=0.006，比值比，8.037，95%置信区间为 1.808-35.729）。患者的年龄、性别、体重指数、诊断和 TSB 前患者的疼痛强度与 TSB 疗效不相关。

结论：研究结果显示，对于慢性疼痛综合征的患者，早期 TSB 的疗效更好。由此，早期 TSB 可应用于患有上肢慢性疼痛的患者。
(周姝婧　译　陈杰　校)

BACKGROUND: The sympathetic nervous system has important roles in mediating many neuropathic pain conditions. A thoracic sympathetic block (TSB) is a useful therapeutic procedure for neuropathic pain in the upper extremities and thorax. However, no studies have examined the factors related to an improved therapeutic effect of TSB. In this study, we evaluated the influence of potential prognostic factors for a better TSB effect and identified clinically important prognostic factors.
METHODS: Percutaneous TSB was performed in 51 patients, under fluoroscopic guidance. Data collected for each patient included age, gender, body mass index, diagnosis, pain intensity, and symptom duration. The adjusted odds ratios and 95% confidence intervals for each variable were calculated by logistic regression.
RESULTS: TSB was more effective in patients with symptom durations of ≤1 year compared with >1 year (P = 0.006; odds ratio, 8.037; 95% confidence interval, 1.808–35.729). Patient age, gender, body mass index, diagnosis, and intensity of pre-TSB pain were not associated with TSB effectiveness.
CONCLUSION: The results showed that an earlier TSB produced a better outcome for patients with chronic pain syndrome. Thus, early TSB should be performed in patients with chronic pain in the upper extremities.

高压氧疗缓解慢性压迫性损伤所致神经性疼痛，并减少肿瘤坏死因子α产生

Hyperbaric Oxygenation Therapy Alleviates Chronic Constrictive Injury–Induced Neuropathic Pain and Reduces Tumor Necrosis Factor-Alpha Production

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背景：慢性压迫性损伤（CCI）后的痛觉过敏和痛觉异常的发展与肿瘤坏死因子（TNF）-α和白细胞介素（IL）-1β显着增加有关。从理论上说，如果可以减少 TNF -α和/或 IL -1β的产生，就可以缓解神经性疼痛综合征。最近，有建议表明高压氧治疗(HBOT)对于疼痛疾病中有治疗作用。本研究旨在探讨以下假说（1）CCI 诱导的神经性疼痛可能与 TNF -α和 IL -1β产生增加有关，（2）高压氧治疗可能能够缓解 CCI 引起的神经性疼痛，以及（3）神经性疼痛的缓解可能与 TNF -α和/或 IL -1β产生减少相关。
方法：对雄性大鼠（体重 250-300 克）用氯胺酮和甲苯噻嗪行麻醉诱导。从股二头肌暴露坐骨神经。手术组，在坐骨神经三个分叉部近端，4 根结扎线松散地系在神经周围。在假手术组，同样暴露坐骨神经但不进行结扎。通过 von Frey 细丝刺激

和丙酮传播分别测试机械性痛觉异常和冷痛觉异常。 HBO 的大鼠（N = 18）每天一次暴露于 2.4 个大气压的纯氧 1 小时。非 HBO（N = 18）和假手术大鼠（N = 6）被放置在高压氧治疗室呼吸空气。用 ELISA 法检测坐骨神经中的 TNF - α 和 IL -1 β 。用 Western blot 分析验证组织匀浆中肿瘤坏死因子- α 蛋白的存在。
结果：CCI 后第 4 和第 7 天测量 CCI 诱发的显著冷和机械性痛觉异常。HBO 大鼠中冷痛觉异常出现频率显着低于非 HBO 组。第 4 天和第 7 天的的比值分别为 20％± 1.6％比 50％± 4.5％，和 40％± 4.6％比 70％±4.5％（F = 87.42，置信区间[HBO 和非 HBO 的差异] = 29.612 ± 8.781， 第 4 和第 7 天的 P <0.05）。与非 HBO 的大鼠相比，HBO 大鼠机械性痛觉异常的阈值显着增加。第 4 天和第 7 天的比值分别为 6.20 ± 0.9 VS 4.1 ± 1.0g 和 3.8.2 ± 0.5 VS 2.3 ± 0.4 g（F = 18.8，置信区间[HBO 和非 HBO 的差异] = 1.806 ± 1.171，第 4 和第 7 天的 P <0.05）。非 HBO 组大鼠 TNF - α 含量显着高于假手术组大鼠，第 4 天（17.89 ± 0.83 比 10.66 ± 1.1 pg / mg 蛋白，P <0.05）和第 7 天（18.97 ± 1.57 比 9.09 ± 1.5 pg/mg 蛋白，P <0.05）。高压氧治疗后 TNF - α 含量显著降低到的假手术大鼠组水平左右，第 4 天和第 7 天分别为 10.94 ± 2.78 和 11.32 ± 2.98 pg / mg 蛋白水平（与非 HBO 组相比 P <0.05）。Western blot 分析证实大鼠坐骨神经匀浆中存在分子量为 51 kDa 的蛋白质。于假手术组相比，非 HBO 的大鼠中 IL -1 β 含量也显著增高，第 4 天和第 7 天分别为（636 ± 74 VS 256 ± 31pg / mg 蛋白质，P <0.05）（687 ± 89 VS 288 ± 35pg / mg 蛋白，P <0.05）。在 HBO 大鼠中，高压氧治疗对 IL -1 β 含量没有影响，第 4 天和第 7 天分别为 671 ± 85pg / mg 蛋白和 672± 75pg / mg 蛋白（与非 HBO 的大鼠相比 P 不显着）。
结论：这些数据表明，高压氧治疗能够缓解 CCI 引起的神经性疼痛，并且抑制期间内源性肿瘤坏死因子- α 的产生，但对 IL -1 β 的产生没有影响。肿瘤坏死因子- α 产生的减少，可能至少部分对于高压氧治疗的治疗作用有一定作用。
(怀晓蓉　译　陈杰　校)
BACKGROUND: The development of hyperalgesia and allodynia after chronic constrictive injury (CCI) is associated with significantly increased tumor necrosis factor (TNF)-α and interleukin (IL)-1β. Theoretically, if the production of TNF-α and/or IL-1β could be reduced, neuropathic pain syndrome may be alleviated. Recently, a beneficial effect of hyperbaric oxygenation therapy (HBOT) in the treatment of pain disorders has been suggested. Our present study was designed to examine the hypotheses that (1) CCI-induced neuropathic pain may be associated with increased production of TNF-α and IL-1β, (2) HBOT may alleviate CCI-induced neuropathic pain, and (3) the alleviated neuropathic pain may be associated with reduced production of TNF-α and/or IL-1β.
METHODS: Male rats (weighing 250–300 g) were anesthetized with ketamine and xylazine. The common sciatic nerve was exposed through the biceps femoris. Proximal to the sciatic's trifurcation, 4 ligatures were loosely tied around the nerve. In the sham group, an identical dissection was performed without ligation of the sciatic nerve. Mechanical allodynia and cold allodynia were tested by von Frey filament stimulation and the spread of acetone, respectively. HBO rats (*n* =18) were exposed to pure oxygen for 1 hour at 2.4 atm once a day. Non-HBO (*n* =18) and sham rats (*n* =6) were placed in the HBOT chamber breathing air. TNF-α and IL-1β in the sciatic nerve were assayed with ELISA. The presence of TNF-α protein in homogenates was verified by Western blot analysis.

RESULTS: CCI induced significant cold and mechanical allodynia as measured after CCI on days 4 and 7. The cold allodynia response frequency was significantly lower in HBO rats than in non-HBO rats. The values were 20% ± 1.6% vs 50% ± 4.5% on day 4 and 40% ± 4.6% vs 70% ± 4.5% on day 7 (F =87.42, confidence interval [for the difference between HBO and non-HBO]=29.612 ± 8.781, $P < 0.05$ for day 4 and day 7). The threshold of mechanical allodynia significantly increased in HBO rats compared with non-HBO rats. The values were 6.20 ± 0.9 vs 4.1 ± 1.0 g on day 4 and 3.8.2 ± 0.5 vs 2.3 ± 0.4 g on day 7 (F =18.8, confidence interval [for the difference between HBO and non-HBO]=1.806 ± 1.171, $P < 0.05$ for day 4 and day 7). TNF-α content was significantly higher in non-HBO rats than in sham rats on day 4 (17.89 ± 0.83 vs 10.66 ± 1.1 pg/mg protein, $P < 0.05$) and day 7 (18.97 ± 1.57 vs 9.09 ± 1.5 pg/mg protein, $P < 0.05$). HBOT significantly reduced TNF-α content to near the level in sham rats, which was 10.94 ± 2.78 and 11.32 ± 2.98 pg/mg protein on day 4 ($P < 0.05$ versus non-HBO) and 7 ($P < 0.05$ versus non-HBO), respectively. Western blot analysis confirmed the presence of proteins with molecular weights of 51 kDa in the rat sciatic nerve homogenates. IL-1β content was also significantly higher in non-HBO rats than in sham rats on day 4 (636 ± 74 vs 256 ± 31 pg/mg protein, $P < 0.05$) and on day 7 (687 ± 89 vs 288 ± 35 pg/mg protein, $P < 0.05$). HBOT had no effect on IL-1β content, which was 671 ± 85 pg/mg protein on day 4 and 672 ± 75 pg/mg protein on day 7 in HBO rats (P =not significant versus non-HBO rats).
CONCLUSION: These data show that HBOT alleviates CCI-induced neuropathic pain and inhibits endoneuronal TNF-α production, but not IL-1β in CCI-induced neuropathic pain. Reduced TNF-α production may, at least in part, contribute to the beneficial effect of HBOT.

新的三叉神经痛动物模型：大鼠眶下神经注入克痛宁

A New Animal Model of Trigeminal Neuralgia Produced by Administration of Cobra Venom to the Infraorbital Nerve in the Rat

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背景：建立严格模拟三叉神经痛的特定类型特征的实验室动物模型可阐明三叉神经痛的机制。作者已经建立了注射克痛宁至眶下神经（ION）主干的三叉神经痛实验动物模型。
方法：选择雄性 SD 大鼠，在眶下神经主干注射克痛宁或者生理盐水。手术后连续几天都在眶下神经主干区域进行机械性刺激。在双侧面部区域测量 90 天得到机械阈值。用伊文思蓝染料测定眶下神经区域的血管通透性。

结果：克痛宁组大鼠在术后三天同侧发生机械性疼痛，并在术后持续 60 天。对侧眶下神经区域的机械阈值显著下降，但术后只持续了约 30 天。对照组的机械阈值没有变化。克痛宁组大鼠和对照组相比，伊文思蓝染料渗出皮肤显著增加（$P<0.05$）。

结论：克痛宁模型可以提供一个合理的模型来研究三叉神经痛的机制。

(黄丹　译　陈杰　校)

BACKGROUND: Understanding the mechanism of trigeminal neuralgia may be elucidated by developing laboratory animal models that closely mimic the features of this specific type of neuropathic pain. We have developed an experimental animal model for trigeminal neuralgia using a technique of injecting cobra venom into the infraorbital nerve (ION) trunk.

METHODS: Male Sprague-Dawley rats were subjected to the administration of cobra venom or saline into the ION trunk. Mechanical stimuli were applied to the ION territory in consecutive days after surgery. Mechanical thresholds were measured over a 90-day period on the bilateral facial region. Vascular permeability in the ION territory was measured using Evans blue dye.

RESULTS: The cobra venom–treated rats developed mechanical allodynia 3 days after surgery that lasted for 60 days postoperatively at the ipsilateral side. The mechanical thresholds of the contralateral ION territory also showed a profound decrease but were sustained for only approximately 30 days. There was no change of mechanical thresholds in the control groups. The extravasation of Evans blue increased significantly in the skin after administration of cobra venom to the ION compared with control rats ($P < 0.05$).

CONCLUSION: The cobra venom model may provide a reasonable model for investigating the mechanism of trigeminal neuropathic pain.

简报：术中小剂量氯胺酮可预防瑞芬太尼引起的麻醉后寒战

Brief report: an intraoperative small dose of ketamine prevents remifentanil-induced postanesthetic shivering.

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将接受妇科开腹手术的患者随机分成两组，一组于麻醉诱导时给予 0.5mg/kg 氯胺酮，并以 0.3mg/kg/h 的速率持续输注氯胺酮至手术结束（氯胺酮组，n=32），另一组则接受同等容量的生理盐水（对照组，n=32）。通过静脉注射异丙酚、恒速输注瑞芬太尼（0.25ug/kg/min）及硬膜外给予罗哌卡因维持麻醉。对苏醒后 30 分钟内的麻醉后寒战（PAS）进行评估。研究显示，两组患者的术中体温较为接近。但较对照组（n=12.38%，P=0.005）而言，氯胺酮组患者发生麻醉后寒战的几率明显减少（n=2.6%）。故本研究推断，在术后恢复早期，术中使用氯胺酮可预防瑞芬太尼引起的麻醉后寒战

（范羽译 薛张纲校）

Patients undergoing gynecological laparotomy were randomized to receive either 0.5 mg/kg ketamine at induction of anesthesia followed by an infusion of 0.3 mg/kg/h until

the end of surgery (ketamine group, n = 32), or an equivalent volume of normal saline (control group, n = 32). Anesthesia was maintained with IV propofol, a fixed infusion rate of remifentanil (0.25 μg/kg/min), and epidural ropivacaine. Postanesthetic shivering (PAS) was evaluated for 30 minutes after emergence. Intraoperative temperatures were similar between the 2 groups. The incidence of PAS was less frequent in the ketamine group (n = 2, 6%) compared with the control group (n = 12, 38%, P = 0.005). We conclude that, during the early recovery phase, intraoperative ketamine reduces remifentanil-induced PAS.

研究氯胺酮和瑞芬太尼与小鼠七氟醚麻醉的最低肺泡有效浓度及小鼠急性阿片耐受的相互影响

Ketamine and remifentanil interactions on the sevoflurane minimum alveolar concentration and acute opioid tolerance in the rat.

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背景：小剂量氯胺酮具有镇痛和抗痛觉过敏的性质，被用来同阿片类药物合用但也用于出现阿片类所致的痛觉过敏及阿片类耐受时。我们对氯胺酮及瑞芬太尼同小鼠七氟醚麻醉的 MAC 值的相互影响，以及氯胺酮是否可以阻断急性阿片耐受进行了研究。

方法：用七氟醚麻醉大鼠，监测单独给氯胺酮前后（10、20、40及80mgmg kg(-1)）或氯胺酮联合瑞芬太尼(120 及 240 μg kg(-1) h(-1), 分别小剂量及大剂量)时七氟醚的 MAC 值.另有一组在开始瑞芬太尼注射后给予最低剂量氯胺酮。最后，用纳洛酮检测氯胺酮是否潜在作用于阿片受体。监测气管内气体样本获得 MAC 值，并钳夹老鼠尾部产生超强刺激。通过侧流气体分析仪监测呼气末麻醉气体浓度。并应用方差分析进行统计分析。

结果：氯胺酮及瑞芬太尼呈剂量依赖性降低小鼠七氟醚麻醉的 MAC 值。此外对氯胺酮加用小剂量瑞芬太尼并不有助于 MAC 值的降低。然而大剂量瑞芬太尼通过次加性形式来加强氯胺酮降低 MAC 值的作用。然而，任何一种剂量的氯胺酮都不能阻断瑞芬太尼的急性阿片类耐受的作用。最后，纳洛酮阻断了氯胺酮降低 MAC 值的作用。

结论：

发现对于降低老鼠七氟醚麻醉的 MAC 值，氯胺酮及瑞芬太尼彼此存在有次加作用。此外。氯胺酮不能阻断阿片类耐受。这个结果的临床意义在于减少未来的麻醉研究。

（侯文婷译 薛张纲校）

BACKGROUND: Ketamine is used at low doses for its analgesic and antihyperalgesic properties when combined with opioids but also when opioid-induced hyperalgesia and tolerance appear. In this study we determined the interaction of ketamine and remifentanil on the minimum alveolar concentration (MAC) of sevoflurane in rats and to determine whether ketamine may block acute opioid tolerance (AOT).
METHODS: Male Wistar rats were anesthetized with sevoflurane, and the MAC was determined before and after ketamine administration (10, 20, 40, and 80 mg kg(-1) or saline) alone or combined with remifentanil (120 and 240 μg kg(-1) h(-1), low and high doses, respectively). One additional group received the lowest ketamine dose after starting a remifentanil infusion. Finally, naloxone was administered to determine the potential action of ketamine on opioid receptors. MAC was determined from intratracheal gas samples, and tail clamping was used as a supramaximal stimulus. End-tidal anesthetic concentrations were assayed using a side stream gas analyzer. Statistical analysis was performed with an analysis of variance.
RESULTS: Ketamine and remifentanil dose-dependently reduced the MAC. Adding the low dose of remifentanil to ketamine did not improve the MAC reduction, whereas the high dose of remifentanil enhanced ketamine reduction in a subadditive fashion. Nevertheless, ketamine was unable to block the development of AOT to remifentanil at either dose. Finally, naloxone blocked the MAC reduction produced by ketamine.
CONCLUSIONS:A subadditive effect between ketamine and remifentanil was found on the sevoflurane MAC reduction rats. In addition, ketamine was unable to block AOT. The clinical relevance of these findings should be elucidated in future studies to reduce anesthetic requirements.

机械通气装置对于压力控制性通气的影响：一项模肺研究

The effect of ventilator performance on airway pressure release ventilation: a model lung study.

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背景：将模肺连接在六种不同的机械通气装置上，每一种机械通气装置均采用不同的压力控制模式进行机械通气。我们测量了各种模式下呼气相时的固有呼气末正压力间的差异，计算出吸气及呼气时的压力时间乘积(PTP)作为吸气相时的呼吸做功指数。
方法：我们比较了六种不同的通气装置: Puritan-Bennett 840, Evita XL, Servo i, Avea, Hamilton G5 以及 Engström。设置持续25cm H2O正压通气和0cm H2O的呼气压力。呼气时间从1秒开始以0.1秒的幅度递减直至0.2秒，测量这一过程中的PEEPi。在吸气相给予刺激诱发自主呼吸，潮气量为300ml，呼吸频率为30次每分钟，而呼气流速分别为0.5升每秒，1升每秒以及1.5升每秒，此时测量和计算呼吸时的压力时间乘积。

结果：在所有的通气装置中，随着呼吸时间的一步步缩短，PEEPi值显著升高(P<0.001)。在呼气时间为0.2秒时，Servo i的PEEPi数值为9.4± 0.07 cm H(2)O 而Avea的PEEPi值为15.7± 0.04 cm H(2)O。Servo i的吸气压力时间乘积显著小于其他几种通气装置(P<0.001)。当呼气流速为0.5升每秒和1升每秒时，Servo i和 Evita XL的呼气压力时间乘积小于其他几种通气装置(P<0.001)。
结论：不同机械通气装置之间 PEEPi的值变化很大。在机械通气装置的吸气相发生了自主呼吸时，不同的通气装置吸气和呼气所做的呼吸功也不同。
（黄剑译 薛张纲校）

BACKGROUND: Using a model lung connected to six different ventilators, with each ventilator in the airway pressure release ventilation mode, we measured differences in intrinsic positive end-expiratory pressure (PEEPi) during the expiratory phase and calculated the inspiratory and expiratory pressure time product (PTP) as an index of work of breathing during the inspiratory phase.
METHODS: We compared 6 ventilators: Puritan-Bennett 840, Evita XL, Servo i, Avea, Hamilton G5, and Engström. With a constant inspiratory pressure level of 25 cm H(2)O and expiratory pressure level of 0 cm H(2)O, PEEPi was measured as the expiratory time was decremented from 1.0 second to 0.2 second in steps of 0.1 second. The inspiratory and expiratory PTPs were measured during the ventilator's inspiratory phase by simulating spontaneous breathing with a tidal volume of 300 mL, with a respiratory rate of 30 breaths/min and with expiratory flow rates of 0.5 L/s, 1.0 L/s, and 1.5 L/s.
RESULTS: In all ventilators, the progressive diminution of the expiratory time caused a significant increase in PEEPi (P< 0.001). With a 0.2-second expiratory time, PEEPi ranged from 9.4± 0.07 cm H(2)O for the Servo i to 15.7± 0.04 cm H(2)O for the Avea. The Servo i had a significantly lower inspiratory PTP than did the other ventilators (P< 0.001). When the expiratory flow rate was 0.5 L/s and 1.0 L/s, the expiratory PTP was lower with the Servo i and Evita XL than with the other ventilators (P< 0.001).
CONCLUSIONS: PEEPi varied significantly among ventilators. Inspiratory and expiratory work of breathing varied between ventilators when spontaneous breathing occurred during the ventilator's inspiratory phase.

一项随机、开放性研究：关于磷异丙酚应用于重症监护病房行机械通气患者的安全性及有效性研究

A Randomized, Open-Label Study of the Safety and Tolerability of Fospropofol for Patients Requiring Intubation and Mechanical Ventilation in the Intensive Care Unit

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背景：在重症监护病房，现有的用于机械通气患者镇静诱导和维护的药物有局限性。磷丙泊酚，异丙酚前体药物，还没有研究作为一个在 ICU 设置的镇静。
方法：在这项随机，开放性的试验研究中，患者接受 3 个方案中的一个，最终镇静的目的是 Ramsay 镇静评分为 2 至 5：（1）给予磷丙泊酚注射液负荷剂量，在病人出现烦躁时增加持续输注速度（持续输注/负荷剂量）（2）在病人出现烦躁时增加磷丙泊酚注射液持续输注的速度（只持续输注）（3）在病人出现烦躁时增加丙泊酚输注液持续输注的速度。
结果：60 名患者参与该药物研究，包括在安全性和有效性分析。由于不良事件的发生率在两组磷丙泊酚组相似，同时因为这项研究并不能证明治疗组间安全性方面是否有显著差异，因此对两个磷丙泊酚组的不良事件合并进行研究。在磷丙泊酚组，38 例中有 28 例（74％）出现了需要紧急治疗的副作用，而异丙酚组的该事件为 22 例中的 14 例（64％）。最常见的治疗过程中出现的不良事件为注射磷丙泊酚过程中出现的注射痛（21.1％）和恶心（13.2％）。两名患者（在磷丙泊酚持续输注/负荷剂量组及异丙酚组分别有一例）在研究期间出现低血压，并将该事件解释为潜在的镇静相关的不良事件。不同试验组在平均血浆甲酸水平方面没有显著差异。三组患者均有大于 90％的时间，保持 Ramsay 镇静分数 2 至 5。
结论：本试验研究表明，磷丙泊酚，无论是持续输注/负荷剂量或只持续输注，患者都是能够耐受的，并且对于重症监护病房中行机械通气患者的短期诱导或维持镇静均为有效的。
（刘珏莹译 薛张纲校）

Background: Current drugs for induction and maintenance of sedation in mechanically ventilated patients in the intensive care unit have limitations. Fospropofol, a prodrug of propofol, has not been studied as a sedative in the ICU setting.
Methods: In this randomized, open-label pilot study, patients received 1 of 3 regimens with a goal of maintaining a Ramsay Sedation Score of 2 to 5: (1) fospropofol IV infusion with a bolus and increased infusion rate for agitation events (infusion/bolus); (2) fospropofol IV infusion with an increased infusion rate for agitation events (infusion only); or (3) propofol IV infusion with an increased infusion rate for agitation events.
Results: Sixty patients received study drug and were included in the safety and efficacy analyses. Because incidence rates for adverse events were similar between fospropofol groups, and because the study was not powered to determine significant differences between treatment groups for safety variables, adverse events for both fospropofol groups were combined. In the fospropofol groups, 28 out of 38 patients (74%) experienced treatment-emergent adverse events in comparison with 14 out of 22 patients (64%) in the propofol group. The most common treatment-emergent adverse events with fospropofol were procedural pain (21.1%) and nausea (13.2%). Two patients (1 each in the fospropofol infusion/bolus and the propofol groups) experienced hypotension during the study as a potential sedation-related adverse event. Mean plasma formate levels were not significantly different among groups. Patients in all 3 treatment groups maintained Ramsay Sedation Scores of 2 to 5 for >90% of the time they were sedated.
Conclusion: This pilot study suggests that fospropofol, administered in either an infusion/bolus or infusion-only regimen, is tolerable and effective for short-term

induction and maintenance of sedation in mechanically ventilated intensive care unit patients.

全麻下开颅手术期间免疫细胞数量下降

Immune Cell Populations Decrease During Craniotomy Under General Anesthesia

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背景： 术后感染是神经外科重症监护医学中常见和潜在致命的并发症。免疫损害是中枢神经系统手术后的感染和术后并发症的高危因素。我们研究的目的是探讨开颅手术的患者在麻醉和手术中的免疫细胞的变化情况。
方法： 选取接受吸入全麻的开颅手术患者。收集麻醉前 30min，45min，60min，120min，血液样本， 测定血液中性粒细胞，单核细胞和淋巴细胞计数、淋巴细胞亚群（T 细胞，诱导和辅助性 T 细胞，抑制和细胞毒性 T 淋巴细胞，自然杀伤细胞，细胞和 B 细胞）。随着肿瘤坏死因子-α 和干扰素 γ 白细胞介素（IL）-2，IL - 4，IL - 6 和 IL - 10 的血浆浓度进行了测定。使用重复测量方差分析，由 Bonferroni 校正用 SPSS 13.0 软件进行数据分析。
结果： 18 例患者，在这项研究中。神经麻醉过程中的免疫细胞计数的比较，我们发现，在麻醉诱导后 30 分钟，中性粒细胞，单核细胞和淋巴细胞减少 18％（95％可信区间[CI]：11.0％-24.6％），34％（95 ％CI：16.2％-51.1％），和 39％（95％ CI：29.0％-48.9％）相比，麻醉前的水平。在拔管的中性粒细胞返回到基本水平。它还表明，自然杀伤细胞在麻醉期间显著下降。外周血细胞因子的浓度没有显著改变。
结论： 我们的研究结果表明，麻醉和手术，打乱了开颅手术过程中的免疫系统的平衡，免疫细胞数量显著减少在全身麻醉诱导后出现的。
（陆丽虹译 薛张纲校）

BACKGROUND: Postoperative infections are common and potentially fatal complications in neurosurgical intensive care medicine. An impairment of immune function after central nervous system surgery is associated with higher risk of infection and postoperative complications. The aim of our study was to investigate how the immune cell population changes during the anesthesia process in patients undergoing craniotomy surgery.
METHODS: Patients undergoing craniotomy who had an inhaled general anesthetic were studied. Blood samples were collected before anesthesia and 30, 45, 60, 120, and 240 minutes after anesthesia began. Blood counts for neutrophils, monocytes, and lymphocytes were determined along with lymphocyte subpopulations (T cells, inducer and helper T cells, suppressor and cytotoxic T cells, natural killer cells, and B cells). Plasma concentrations of interleukin (IL)-2, IL-4, IL-6, and IL-10 were also measured along with tumor necrosis factor-α and interferon-γ. Data were analyzed by SPSS 13.0

software using repeated-measures analysis of variance followed by a Bonferroni correction.
RESULTS: Eighteen patients were enrolled in this study. In the comparison of the immune cell counts during neuroanesthesia, we found that at 30 minutes after anesthesia induction, neutrophils, monocytes, and lymphocytes decreased 18% (95% confidence interval [CI]: 11.0%-24.6%), 34% (95% CI: 16.2%-51.1%), and 39% (95% CI: 29.0%-48.9%) compared with their levels before anesthesia. At extubation the neutrophils returned to the base level. It also showed that natural killer cells decreased significantly during anesthesia. The concentration of cytokines in peripheral blood did not change significantly.
CONCLUSION: Our results showed that anesthesia and surgery upset the balance of the immune system during craniotomy, and a significant decrease in immune cell populations emerged after induction under general anesthesia.

对大鼠背根神经节应用脉冲射频电流可调节神经损伤导致的触痛觉过敏

Application of pulsed radiofrequency currents to rat dorsal root Ganglia modulates nerve injury-induced tactile allodynia.

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背景：报道称对背根神经节(DRG)应用脉冲射频(PRF)电流对明确的疼痛有缓解作用而不导致热烧灼。在本实验中，我们研究了对脊神经损伤相关的背根神经节(DRG)应用脉冲射频(PRF)和在大鼠神经性疼痛模型中损伤诱导的行为超敏反应的直接联系。
方法：神经损伤通过结扎成年雄性斯普拉格-道利鼠的 L5 左脊神经实施。当受伤大鼠发生触痛觉过敏时，一组被指定对 L5 背根神经节(DRG)进行脉冲射频(PRF)电流处理，另一组被指定对 L5 背根神经节(DRG)进行伪处理。在术前和指定的天数对试验组和对照组使用 von Frey 纤毛测试对大鼠进行行为测试。结果数据由线性混合模型进行分析来评价治疗组间的总体差异和实验天数间的总体差异。对治疗后的 14 个实验天中每天的配对基线差异得分计算出 Cohen's d 统计值，这些度量出的作用程度被用来描述性对比每组中随着时间变化的恢复模式。
结果：脊神经损伤导致了左侧(损伤侧)足对 von Frey 纤毛刺激产生了行为超敏反应(痛觉过敏)。混合线性模型显示在处理后组间对照有显著差异(P = 0.0079)，并且随着时间过去，所有 12 个动物爪逃避阈值平均值均有显著改变(P = 0.0006)。Cohen's d 评估显示了脉冲射频(PRF)治疗后的动物展示了更好的恢复，相对于伪治疗组在

脉冲射频(PRF)治疗后 14 天内有 10 天记录到了更大的作用程度，且在第 8 到 10 天和 32 天后显示了中到强效的治疗后效果。
结论：研究结果支持对背根神经节(DRG)行脉冲射频(PRF)可对大鼠神经损伤(脊神经结扎)诱导的触痛觉过敏产生逆转作用。这种痛觉过敏的逆转提示非烧灼性脉冲射频(PRF)通过调节背根神经节(DRG)可加速神经顺上损伤诱导疼痛的恢复。
（任云译 薛张纲校）

BACKGROUND: Application of pulsed radiofrequency (PRF) currents to the dorsal root ganglia (DRG) has been reported to produce relief from certain pain states without causing thermal ablation. In this study, we examined the direct correlation between PRF application to DRG associated with spinal nerve injury and reversal of injury-induced behavioral hypersensitivity in a rat neuropathic pain model.
METHODS: Neuropathic lesioning was performed via left L5 spinal nerve ligation on male adult Sprague-Dawley rats. Once the injured rats had developed tactile allodynia, one group was then assigned to PRF treatment of the L5 DRG and another group was assigned to the sham treatment to the DRG. Behavioral testing was performed on both the control and treated paws using the von Frey filament test before the surgery and at indicated days. The resulting data were analyzed using a linear mixed model to assess the overall difference between the treatment groups and the overall difference among the study days. Cohen's d statistic was computed from paired difference-from-baseline scores for each of the 14 study days after treatment and these measures of effect size were then used to descriptively compare the recovery patterns over time for each study group.
RESULTS: Spinal nerve injury resulted in the development of behavioral hypersensitivity to von Frey filament stimulation (allodynia) in the hindpaw of the left (injury) side. Mixed linear modeling showed a significant difference between the treatment groups ($P = 0.0079$) and a significant change of paw withdrawal threshold means over time ($P = 0.0006$) for all 12 animals. Evaluation of Cohen's d (effect size) revealed that the PRF-treated animals exhibited better recovery and recorded larger effect sizes than the sham-treated animals on 10 of the 14 post-PRF treatment days and exhibited moderate-to-strong effects posttreatment at days 8 to 10 and at and beyond day 32.
CONCLUSION: Findings from this study support that PRF of the DRG causes reversal of nerve injury (spinal nerve ligation)-induced tactile allodynia in rats. This allodynia reversal indicates that nonablative PRF acting via modulation of the DRG can speed recovery in nerve injury-induced pain.

氯胺酮和加巴喷丁对于阿片类诱导的大鼠痛觉超敏的中位有效剂量: 一项它们相互作用的等辐射分析

The Median Effective Dose of Ketamine and Gabapentin in Opioid-Induced Hyperalgesia in Rats: An Isobolographic Analysis of Their Interaction

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背景:氯胺酮和加巴喷丁被认为对于短期全身性应用阿片类药物诱导的延迟性痛觉超敏具有预防作用。这种预防作用的机制被认为在脊髓水平，通过氯胺酮对于NMDA 受体的拮抗作用和加巴喷丁对于一个特殊结合部位的作用而发挥作用。本研究中，我们试图找出这两种药理学机制上相距甚远的抗痛觉超敏药物在阿片类诱导大鼠痛觉超敏模型中相互作用的机制。首先计算出这两种药物和其相互作用的中位有效剂量，运用单辐射分析来评价它们相互作用的本质。
方法：SD 大鼠中皮下注射芬太尼总量为 240ug/kg（4 次，间隔 15 分钟，每次 60ug/kg）诱导长时间的痛觉超敏。在首剂皮下注射芬太尼之前 30 分钟皮下注射氯胺酮，或腹膜周围注射加巴喷丁，或同时注射这两种药物。试验日和注射后的第一天分别测试大鼠对于伤害性刺激的敏感度。给予每只特定大鼠的氯胺酮或加巴喷丁的剂量取决于同组的前一只大鼠对于伤害性刺激的反应，运用来回技术。氯胺酮组和加巴喷丁组的首剂分别为 10 mg/kg 和 300 mg/kg，调节的剂量为每次 1 mg/kg 和 30 mg/kg。氯胺酮和加巴喷丁结合组的首剂剂量为 5 mg/kg 和 150 mg/kg，调节的剂量不变。抗痛觉超敏的效能定义为注射药物后的第一天能完全抑制痛觉超敏。
结果：氯胺酮和加巴喷丁的中位有效剂量（中位数和 95%置信区间）分别为 12.4 mg/kg (11.7–13.1 mg/kg) 和 296.3 mg/kg (283.5–309.1 mg/kg)。两药组合后的氯胺酮和加巴喷丁的中位有效剂量和 95%置信区间分别为 4.3 mg/kg (3.7–4.6 mg/kg) 和 123.9 mg/kg (111.1–136.7 mg/kg)。
结论：单辐射分析法显示氯胺酮和加巴喷丁结合使用对于抗痛觉超敏具有叠加（协同）作用。
（姚敏敏译，薛张纲校）

BACKGROUND: Ketamine and gabapentin have been shown to prevent the delayed hyperalgesia induced by short-term use of systemic opioids. The mechanism of this action is believed to be likely at the spinal level, through an antagonism of the *N*-methyl-d-aspartate receptors for ketamine, and through a specific binding site for gabapentin. In this study, we sought to determine the nature of the interaction of these 2 mechanistically distinct antihyperalgesic drugs in a model of opioid-induced hyperalgesia in rats. The median effective antihyperalgesic doses of each drug and of their combination were first defined, to assess the nature of the interaction using an isobolographic analysis.
METHODS: Long-lasting hyperalgesia was induced in male Sprague Dawley rats with subcutaneous fentanyl (4 injections, 60 μg/kg per injection at 15-minute intervals) resulting in a total dose of 240 μg/kg. Subcutaneous ketamine, or intraperitoneal gabapentin, or their combination was administered 30 minutes before the first subcutaneous fentanyl injection. Sensitivity to nociceptive stimuli (von Frey filaments) was assessed on the day of the experiment and on the day after injections. The dose of ketamine and gabapentin received by a particular animal was determined by the response of the previous animal of the same group, using an up-and-down technique. Initial doses were 10 mg/kg and 300 mg/kg, with dose adjustment intervals of 1 mg/kg and 30 mg/kg, in the ketamine and gabapentin groups, respectively. The initial doses of ketamine and gabapentin were 5 mg/kg and 150 mg/kg, respectively, in the ketamine-gabapentin group, with the same dose adjustment intervals. Antihyperalgesic efficacy was defined as complete prevention of hyperalgesia on the day after drug injections.

RESULTS: The median effective antihyperalgesic doses (median value and 95% confidence interval) of ketamine and gabapentin were 12.4 mg/kg (11.7–13.1 mg/kg) and 296.3 mg/kg (283.5–309.1 mg/kg), respectively. The median effective antihyperalgesic dose of the combination was 4.3 mg/kg (3.7–4.6 mg/kg) for ketamine and 123.9 mg/kg (111.1–136.7 mg/kg) for gabapentin.
CONCLUSION: The isobolographic analysis demonstrated that the combination of the 2 drugs produces effective antihyperalgesia with a supraadditive (synergistic) action.

简要报道：超声的螯合剂与神经接触：一项动物组织学研究

Brief report: ultrasound gel-nerve contact: an experimental animal histologic study.

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背景：超声（US）引导下行神经阻滞需要使用螯合剂。在之后穿刺针进行穿刺时，有一部分螯合剂会粘附在针表面或进入针内，并将其带入神经周围组织或进入神经内。我们在动物身上进行这项实验，目的是研究超声使用的螯合剂接触神经组织结构的影响因素。
方法：我们研究了九只雄性比格犬。1 到 3 号犬为对照组，4 到 9 号犬为试验组。对照组对双侧胫后神经进行解剖。伤口关闭后即刻对第一条狗的标本进行组织学检查，24 小时后对第二条狗，48 小时后对第三条狗的标本进行检查。对于试验组，暴露双侧胫后神经，神经局部给予 2ml US 螯合剂，然后关闭伤口。24 小时时对一侧的神经标本进行检测，48 小时后检测另一侧。神经病理学家检测神经标本，从而获得神经炎症反应的证据。
结果：对照组的神经标本并没有显著的病理改变。试验组 24 小时末的神经标本显示神经周围有轻度炎症改变并伴有多核白细胞的聚集。在 48 小时神经周围有中度炎症改变，在 2 条狗身上发现淋巴细胞和巨噬细胞。所有的动物都出现了长期的神经功能缺陷，表现为跛行。
结论：周围神经接触 US 螯合剂后的组织学改变均为非特异性改变。然而关于 US 螯合剂对神经组织的影响尚有待于进一步研究。
（张月琪译 薛张纲校）

BACKGROUND: Ultrasound (US) regional nerve block requires the use of gel applied over the skin. With subsequent needle insertion, some of the gel may adhere either on the shaft or within the needle lumen and may be carried to the perineural structures or intraneurally. We performed this experimental animal study to investigate the effects of US gel contact on the nerve histologic structure.
METHODS: Nine male beagle dogs were studied. Dogs 1 to 3 were the control group and dogs 4 to 9 were the study group. Bilateral posterior tibial nerves were dissected and exposed for the control group. Nerve specimens were obtained for histologic examination immediately for the first dog, at 24 hours for the second dog, and at 48 hours for the third

dog followed by wound closure. For the study group, bilateral posterior tibial nerves were exposed, and 2 mL US gel was applied locally directly on the nerve, followed by wound closure. Nerve specimens were excised at 24 hours from one side and at 48 hours from the other side. Nerve specimens were examined by a neuropathologist for evidence of nerve inflammation.
RESULTS: The control nerve specimens showed no significant pathology. Nerve specimens of the study group at the end of 24 hours of gel-nerve contact showed mild focal perineural inflammatory changes with clusters of polymorph leukocytes. At 48 hours, perineural moderate inflammatory changes with clusters of lymphocytes and macrophages were demonstrated in 2 animals. Long-term neurologic deficit in the form of limping was observed for all dogs.
CONCLUSION: Histologic features after perineural exposure to US gel are rather nonspecific and likely of no clinical significance. However, further studies are needed to determine the effect of US gel injection on intraneural tissues.