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**多極血凝集監測儀 (Multiplate®) 測定體外迴圈患者低溫和魚精蛋白誘導的血小板功能障礙**

**Point-of-Care Assessment of Hypothermia and Protamine-Induced Platelet Dysfunction with Multiple Electrode Aggregometry (Multiplate®) in Patients Undergoing Cardiopulmonary Bypass**

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BACKGROUND: Coagulopathy is common after cardiopulmonary bypass (CPB), and platelet dysfunction is frequently considered to be a major contributor to excessive bleeding. Exposure to hypothermia may exacerbate the platelet function defect. We assessed platelet function during and after deep hypothermia with multiple electrode aggregometry (Multiplate®; Verum Diagnostica GmbH, Munich, Germany).

METHODS: Twenty adult patients undergoing pulmonary endarterectomy for chronic pulmonary hypertension were cooled on CPB to 20°C and deep hypothermic arrest was used to facilitate surgery. We analyzed platelet aggregation in whole blood samples at 12 measuring points during and after the procedure. Platelet aggregation was stimulated via the thrombin receptor (TRAPtest) at the patient’s actual body temperature (AUC-CT) and after rewarming the samples to 37°C (AUC-37). In addition, we tested samples at 2 time points after 2 minutes of in vitro incubation with 20 μg protamine (0.067 μg/μL). Results are expressed as area under the aggregation curve (AUC).

RESULTS: Low temperature caused platelet aggregation function to significantly decrease, and the AUC-CT also reached its lowest point at 20.5°C (95% CI 8.9-32.1). When the temperature reached 28°C, AUC-CT was significantly lower than the baseline (92.8, 95% CI 82.5-103.1, P < 0.001), and AUC-37 was also significantly lower than the baseline (59.4, 95% CI 41.3-77.4). When rewarming to 36°C, AUC-CT and AUC-37 were significantly lower than the baseline (67.6, 95% CI 53.9-81.3) and 71.1 (95% CI 52.5-90.8). From 28°C to 24°C, AUC-CT and AUC-37 were significantly lower than the baseline (38.2, 95% CI 27.9-48.5, P < 0.0001) and 44.5 (95% CI 38.5-50.5, P < 0.001). When protamine was added to the blood, the AUC significantly decreased (38.2, 95% CI 27.9-48.5, P < 0.0001) and 44.5 (95% CI 38.5-50.5, P < 0.001). The same was true for heparin and CPB end. Incubation with protamine in vitro led to a significant decrease in aggregation (35.1, 95% CI 27.1-43.1, P = 0.055) and 56.5 (95% CI 48.5-64.5, P = 0.005).

CONCLUSION: Using multiplate aggregometry, we assessed the effect of deep hypothermia on platelet aggregation and found that deep hypothermia significantly decreased platelet aggregation. Rewarming increased platelet aggregation, and the effect was different from CPB. This suggests that deep hypothermia may be a major contributor to excessive bleeding. Platelet aggregation was significantly lower in deep hypothermia than in normal temperature (AUC-CT).
RESULTS: Cooling resulted in a marked decrease of platelet aggregation to a minimum AUC-CT of 20.5 (95% confidence interval [CI] 8.9–32.1) at 20°C body temperature. AUC-CT was significantly different from baseline (92.8, 95% CI 82.5–103.1) for temperatures of ≤28°C (P < 0.001), whereas the change in AUC-37 only became significant at the lowest body temperature (59.4, 95% CI 41.3–77.4). After rewarming to 36°C, AUC-CT and AUC-37 had recovered to 67.6 (95% CI 53.9–81.3) and 71.7 (95% CI 52.5–90.8), respectively. The mean AUC-CT was significantly lower than the mean AUC-37 from cooling at 28°C to warming at 24°C inclusive, and the relationship with temperature during cooling was significantly different between AUC-CT and AUC-37 (regression coefficients 4.7 [95% CI 4.2–5.2] vs 1.3 [95% CI 0.7–1.9]; P < 0.0001). After administration of protamine, mean aggregation decreased significantly for both measurements by 38.2 (95% CI −27.9 to −48.5; P < 0.001) and 44.5 (95% CI −58.5 to −30.5; P < 0.001), respectively. Similarly, adding protamine in vitro resulted in a decrease of mean aggregation by 35.1 (95% CI −71.0 to 0.8; P = 0.055) when measured after administration of heparin, and 56.5 (95% CI −94.5 to −18.5; P = 0.005) at the end of CPB.

CONCLUSION: Platelet aggregation, assessed by multiple electrode aggregometry (Multiplate), was severely affected during deep, whole-body hypothermia. This effect was partially reversible after rewarming, and was distinct from a general decline of platelet aggregation during CPB. Protamine also caused a significant decrease in platelet aggregation in vivo and in vitro.

Technic交流：來自外科磁性手術單對心臟起搏器的磁性干擾

Technical Communication: Magnetic Interference of Cardiac Pacemakers from a Surgical Magnetic Drape

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無菌磁性手術單被頻繁用於需要在無菌區固定金屬器械的手術。磁性區域可能潛在影響心血管植入性電子儀器如起搏器和植入除顫儀的功能。本研究評估磁性手術單對起搏器功能的潛在磁性干擾。共 50 例患者在心臟門診就診時，將一塊含有 70 個磁鐵的手術單靠近心臟起搏器部位放置於他們的起搏器之上，在證實起搏器出現磁性干擾後，將手術單向尾側拉，每次 3cm 直至干擾消失。如果無干擾，則將手術單折疊置於起搏器上方。同時檢測維持對起搏器的磁性干擾所需要的磁鐵數量。在 47 例患者中觀察到存在對起搏器的磁性干擾。在 47 例患者中觀察到存在對起搏器的磁性干擾

(94%) ：35 例的手術單不需折疊而 12 例手術單經折疊。手術單未經折疊就發生磁干擾的患者體重比那些沒有磁干擾的患者小 (68±15 kg 和 81±19 kg; P = 0.016)。54%患者起搏器磁性干擾在手術單向尾側移 3cm 後消失。在向尾側移 15cm 後，沒有起搏器出現磁性干擾。磁性手術單可能導致心臓起搏器出現磁干擾，而干擾在手術單向尾側拉 15cm 後消失。磁干擾可能更容易在低體重病人中發生，在對裝有心血管植入性電子儀器的病人使用磁性手術單時應該仔細檢測心率和心電圖，注意有無非同步起搏的發生。

(瞿亦楓 譯 陳傑 校)
In this study, we evaluated the potential magnetic interference of magnetic drapes on pacemaker function. A magnetic drape with 70 magnets was placed with its approximate center over the pacemaker of 50 patients during their visit to the cardiology clinic. In those pacemakers that demonstrated magnetic interference, the drape was pulled caudally in 3-cm increments until the interference ceased. If there was no interference, the drape was folded in 2 over the pacemaker. The number of magnets necessary to maintain magnetic interference with the pacemaker was also tested. Magnetic interference was observed in the pacemakers of 47 (94%) patients: 35 with the unfolded drape and another 12 with the folded drape. Patients whose pacemakers had interference with the unfolded drape weighed less (68±15 kg vs 81±19 kg; P = 0.016) than those who had no interference. In 54% of patients, magnetic interference ceased when the drape was pulled 3 cm caudally and at 15 cm, no pacemaker had magnetic interference. Magnetic drapes may cause magnetic interference with cardiac pacemakers, and this interference ceases at a caudal distance of 15 cm. Magnetic interference seems more likely in patients with lower body weight. Careful monitoring of the pulse and electrocardiogram for asynchronous pacing activity should be considered when magnetic drapes are used in patients with cardiovascular implantable electronic devices.

在丙泊酚—瑞芬太尼麻醉過程中複合變異指數對標準化傷害刺激的反應

The Response of the Composite Variability Index to a Standardized Noxious Stimulus During Propofol-Remifentanil Anesthesia

Richard Klaus Ellerkmann, MD, Annekathrin Grass, Andreas Hoeft, MD, PhD and Martin Soehle, MD
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背景：最近複合變異指數（CVI）被用於對傷害進行量化研究。該指數衍生自腦電雙頻指數（sBIS）和肌電圖（SEMG）的標準差值。本研究主要目的為比較一個傷害性刺激前後CVI的變化。次要目的為考察瑞芬太尼對CVI的影響，並測試了在不同瑞芬太尼濃度情況下CVI預測傷害性刺激後病人體動的能力。此外在傷害性刺激後，比較CVI與其他臨床變數（BIS，sBIS，sEMG，心率[H]和收縮壓[BPsys]）的增幅差異。

方法：24名無心臟疾病史的患者納入研究。使用靶控輸注丙泊酚進行麻醉誘導。在增加或減少瑞芬太尼效應室濃度（Cerem）狀態下，對尺神經應用一個標準化的傷害性電刺激（50HZ，70mA，30s）。研究CVI，BIS，sBIS，HR和收縮壓的基線和受刺激後的變化。使用預測概率（PK）來評價傷害性刺激後各參數對體動的預測能力。

結果：在瑞芬太尼的效應室濃度為0.1,2或者3ng/ml時，給予一個傷害性刺激後所有參數（除了收縮壓）均顯著增加。刺激後最高參數值與體動之間的相關性表現如下：心率Pk=0.81，肌電圖Pk=0.78，複合變異指數Pk=0.72（複合變異指數兩兩差異不顯著）。Δ肌電或ΔCVI（刺激後參數值減去基線值）與體動之間的相關性（Pk分別=0.76和0.75）較ΔHR與體動間的相關性（Pk=0.53）更高（分別為：P=0.008和P=0.01）。ROC分析表明ΔCVI和ΔSEMG的體動閾值分別為>0.39（敏感度0.71，特異性0.74）和>0.31（敏感度0.68，特異性0.78）。

結論：在可接受的敏感度和特異性前提下，ΔsEMG和ΔCVI應用于癱瘓患者有助於識別鎮痛不足。神經阻滯對CVI的深遠影響有待進一步研究。
BACKGROUND: Recently the Composite Variability Index (CVI) was developed to quantify nociception. This index is derived from the standard deviations (s) of the Bispectral Index (sBIS) and the electromyogram (sEMG). The primary aim of our study was to compare CVI before and after a noxious stimulus. As secondary end points, we investigated the influence of remifentanil on the CVI and tested the ability of the CVI to indicate patient movement after a noxious stimulus under changing remifentanil concentrations. Furthermore, we measured the increase in CVI after a noxious stimulus in comparison to other clinical variables (BIS, sBIS, sEMG, heart rate [HR], and systolic blood pressure [BP_sys]).

METHODS: Twenty-four patients without a history of cardiac disease were investigated. Anesthesia was induced with propofol administered by target-controlled infusion. A standardized noxious electrical stimulus was applied (50 Hz, 70 mA, 30 seconds) to the ulnar nerve at increasing or decreasing remifentanil effect-compartment concentrations (Ce_remi). Changes in baseline and poststimulus CVI, BIS, sBIS, sEMG, HR, and BP_sys were investigated. Parameters’ ability to indicate movement after a noxious stimulus was evaluated with the prediction probability (P_K).

RESULTS: All investigated parameters (except BP_sys) increased significantly after a noxious stimulus at 0, 1, 2, or 3 ng·mL⁻¹ Ce_remi. The association between poststimulus maximal parameters and movement were P_K = 0.81 for HR, P_K = 0.78 for sEMG, and P_K = 0.72 for CVI (pairwise difference to CVI statistically nonsignificant). The association between ΔsEMG or ΔCVI (poststimulus value minus baseline value) and movement was significantly higher (P_K = 0.76 and 0.75, respectively) compared with ΔHR (P_K = 0.53) (P = 0.008 and P = 0.01, respectively). Receiver operating characteristic analysis revealed a threshold value for movement for ΔCVI of >0.39 (sensitivity of 0.71, specificity of 0.74) and for ΔsEMG of >0.31 (sensitivity of 0.68, specificity of 0.78).

CONCLUSION: In paralyzed patients, ΔsEMG and ΔCVI might help identify inadequately low levels of analgesia with an acceptable sensitivity and specificity. The impact of profound neuromuscular block on the CVI should be investigated in further studies.

通過 Fastrach 型喉罩使用 VivaSight Single Lumen™進行氣管插管的可行性研究：一項 50 例的初步報告

A Feasibility Study Using the VivaSight Single Lumen™ to Intubate the Trachea Through the Fastrach Laryngeal Mask Airway: A Preliminary Report of 50 Cases

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背景：VivaSight Single Lumen™(SL)是一種新型氣管導管，在其末端有攝像機和光源用於持續觀察氣道。此項研究驗證使用 VivaSight SL 通過 Fastrach 型喉罩(FT-LMA)進行氣管插管的可行性。
BACKGROUND: The VivaSight Single Lumen™ (SL) is new endotracheal tube with a video camera and a light source in the tip allowing continuous visual observation of the airway. In this study, we checked the feasibility of endotracheal intubation with a VivaSight-SL through the Fastrach Laryngeal Mask Airway® (FT-LMA).

METHODS: We studied 50 patients with normal airways, scheduled for elective surgery during general anesthesia requiring endotracheal intubation. The FT-LMA was inserted and once adequate ventilation was achieved, the VivaSight-SL was passed through the FT-LMA into the trachea under visual control. The following criteria were used to score the laryngeal view: grade 1: full view of the arytenoids and glottis; grade 2: epiglottis, arytenoids or glottic opening are partly visible, the structure of cords is difficult to see; grade 3: dark areas indicating an open space; and grade 4: no part of the larynx can be identified.

RESULTS: The FT-LMA was placed successfully in 49 patients at the first attempt. One patient was excluded from the study after 2 failed attempts to ventilate with the FT-LMA. All 49 patients were successfully intubated with the VivaSight-SL, (95% confidence interval [CI] 0.89–0.99), 47 patients at the first attempt (95% CI, 0.83–0.98) and 2 patients at the second attempt. (95% CI, 0.04–0.13). The time to achieve an effective airway with the FT-LMA was 15.4 ± 6 (mean ± SD) seconds. The time to achieve a laryngeal view with the VivaSight-SL was 28.8 ± 5 seconds. Correct position of the VivaSight-SL was confirmed with visualization of the carina. Time of successful intubation with VivaSight-SL from picking up the VivaSight-SL to observing a end-tidal CO₂ curve was 45 ± 7 seconds. After introducing the VivaSight-SL through the intubating channel of the FT-LMA, a grade 1 view was obtained in 18 patients, grade 2 in 18 patients, a grade 3 in 4 patients, and grade 4 in 9 patients.

CONCLUSION: The high first-attempt intubation success rate using the VivaSight-SL to intubate the trachea through a FT-LMA makes this technique an attractive and promising concept.
BACKGROUND: Softer endotracheal (ET) tubes are more difficult to navigate in the oropharynx than the stiffer polyvinyl chloride (PVC) tubes during nasotracheal intubation (NTI). Cuff inflation has been used to guide PVC tubes into the laryngeal inlet during blind NTI, but it has not been tested when performing NTI under direct laryngoscopic guidance. We assessed the role of cuff inflation in improving oropharyngeal navigation of 3 ET tubes of varying stiffness during direct laryngoscope-guided NTI. Simultaneously, we also assessed and compared the nasotracheal navigability and incidence of nasal injury with these ET tubes during cuff inflation-supplemented, laryngoscope-guided NTI.

METHODS: One hundred sixty-two adults were randomized to undergo NTI with either a conventional PVC (n = 54), wire reinforced (WR; n = 54) or a silicone-tipped WR (SWR; n = 54) ET tube. Ease of insertion of these tubes was assessed during passage from nose into oropharynx, from oropharynx into laryngeal inlet aided by cuff inflation if needed, and from laryngeal inlet into trachea. Nasal morbidity was assessed by a blinded observer.

RESULTS: All ET tubes could be inserted into the trachea. Seventy-one of 162 ET tubes could be inserted from the oropharynx into the laryngeal inlet without cuff inflation. Eighty-six of the remaining 91 tubes that did not enter the laryngeal inlet without cuff inflation could be inserted when using the cuff inflation technique. Thus, a total of 157 ET tubes could be inserted into the laryngeal inlet with cuff inflation (95% confidence interval of difference of proportions between
total number of tubes passed [157] and those without cuff inflation [71]: 53% [45%–61%]). The remaining 5 tubes had to be inserted with the help of Magill forceps. The incidence of epistaxis was lowest with the SWR tube (difference of proportions [95% confidence interval] SWR versus PVC 27% [8%–45%]; SWR versus WR 20% [1%–38%]; WR versus PVC 7% [−12% to 26%]).

**CONCLUSIONS:** The cuff inflation technique consistently improved the oropharyngeal insertion of the 3 ET tubes of varying stiffness during direct laryngoscope-guided NTI. Supplemented with the cuff inflation technique, the SWR ET tube seems to be better than the PVC and WR ET tubes in terms of complete nasotracheal navigability and less perioperative nasal injury.

Randomized Controlled Comparison of Epidural Analgesia and Combined Spinal-Epidural Analgesia in a Private Practice Setting: Pain Scores During First and Second Stages of Labor and at Delivery

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**BACKGROUND:** There has been no prospective evaluation of combined spinal-epidural (CSE) analgesia in a private practice setting and few studies have focused on pain relief during the
METHODS: Healthy, term parturients received epidural or CSE analgesia for labor pain upon request. Epidural analgesia was initiated with 0.125% bupivacaine plus 2 μg/mL fentanyl, 15 mL; CSE analgesia was initiated with intrathecal plain bupivacaine 3.125 mg plus 5 μg fentanyl. Thereafter, patient-controlled epidural analgesia with 0.125% bupivacaine plus 2 μg/mL fentanyl was used for maintenance analgesia in both groups. The primary outcome was an assessment of “typical” pain, using a verbal rating pain score from 0 to 10, made at the end of the first stage of labor and shortly after delivery.

RESULTS: Data from 398 epidural and 402 CSE subjects were analyzed. The typical verbal rating pain score during the first stage was lower in the CSE group (mean: 1.4 vs 1.9; \( P < 0.001 \); 99.5% confidence interval [CI] for difference: −0.92, −0.14). Pain scores during the second stage of labor (1.7 vs 1.9; \( P = 0.17 \); 99.5% CI for difference: −0.82, 0.28) and at delivery (2.0 vs 2.0; \( P = 0.77 \); 99.5% CI for difference: −0.73, 0.59) were the same between groups. Fewer patients received an epidural top-up dose in the CSE group (16.4% vs 25.6%; \( P = 0.002 \); 99.5% CI for difference: −17.0%, −1.0%). Epidural catheters were replaced in 1.2% CSE vs 2% in the epidural group (\( P = 0.39 \); 99.5% CI for difference: −3.3%, 1.8%).

CONCLUSIONS: Compared with traditional epidural labor analgesia, CSE analgesia provided better first-stage analgesia despite fewer epidural top-up injections by an anesthesiologist.

Detection of Tidal Recruitment/Overdistension in Lung-Healthy Mechanically Ventilated Patients Under General Anesthesia
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背景：容量依賴的單室模型（VDSCM）已用於鑒定接受機械通氣的急性肺損傷患者的肺過度膨脹。這項觀察性研究評估 VDSCM 在鑒定由潮氣量（VT）和呼氣末正壓（PEEP）引起的潮氣量複張/過度通氣方面的應用。

方法：15名（ASA I–II）接受全麻下行乳房整形手術的全麻患者，以容量控制通氣（VCV）的方式進行機械通氣，設置VT為 8 mL•kg\(^{-1}\)，PEEP為 0 cm H\(_2\)O。在這些設置下，通氣模式在 VCV 或壓力控制通氣模式（PCV）間隨機調換，PEEP相繼從 0cmH\(_2\)O 調整到 5cmH\(_2\)O，再到 10cmH\(_2\)O，每 5 分鐘調節一次。之後，PEEP 降至 0cmH\(_2\)O。VT 增加到 10 mL•kg\(^{-1}\)，並且保持分鍾潮氣量不變，PEEP 也相繼增加至 5cmH\(_2\)O 和 10cm H\(_2\)O。連續記錄氣道壓力和氣流量，並且在考慮或不考慮流量依賴情況下與 VDSCM 相匹配。用衍生自 VDSCM 的膨脹指數（%E\(_2\)）來評估潮氣量和 PEEP 引起的肺複張/過度膨脹。%E\(_2\)正負值分別提示潮氣量過度膨脹或補潮氣量複張。另外，計算線性呼吸系統順應性。將每個不同的 PEEP 值, VT 設置，通氣模式前提下的各參數間進行對比，考慮或者不考慮流量依賴的回歸模型採
用配對樣本的 Wilcoxon 符號秩和檢驗（P < 0.05）。使用 Bonferroni 方法校正多重比較。

結果：在幾乎所有的實驗條件下，包括流量依賴參數的 VDSCM 明顯改善預計嘈雜變數（11.2 to 71.4, 95%置信區間下限的最小值和上限的最高值）。在相似的 VT 和 PEEP 水準，當流量依賴包含在回歸模型中時，VCV 和 PCV 之間沒有發現%E₂差異。和 VCV 模式相比，忽略系統性的流量依賴參數導致了 PCV 的%E₂的低估（所有 P < 0.02）。在既定的 VT 下，PEEP 爲 0 cm H₂O 時%E₂為陰性，並且隨著 PEEP 的上升而明顯上升，在 PEEP 爲 5cm H₂O 時%E₂幾乎為 0。在既定的 PEEP 水準，%ET 明顯隨著 VT 的增加而增加。

結論：衍生自流量依賴的 VDSCM 的膨脹指數，似乎能確認由 VT 和 PEEP 引起的潮氣量複張/過度膨脹，且與擁有健康肺的麻醉患者的流量波形無關。

（馬霄雯 譯 陳傑 校）

BACKGROUND: The volume-dependent single compartment model (VDSCM) has been applied for identification of overdistension in mechanically ventilated patients with acute lung injury. In this observational study we evaluated the use of the VDSCM to identify tidal recruitment/overdistension induced by tidal volume (Vt) and positive end-expiratory pressure (PEEP) in lung-healthy anesthetized subjects.

METHODS: Fifteen patients (ASA physical status I–II) undergoing general anesthesia for elective plastic breast reconstruction surgery were mechanically ventilated in volume-controlled ventilation (VCV), with Vt of 8 mL•kg⁻¹ and PEEP of 0 cm H₂O. With these settings, ventilatory mode was randomly adjusted in VCV or pressure-controlled ventilation (PCV) and PEEP was sequentially increased from 0 to 5 and 10 cm H₂O, 5 min per step. Thereafter, PEEP was decreased to 0 cm H₂O, Vt increased to 10 mL•kg⁻¹ and, keeping minute ventilation constant, PEEP was similarly increased to 5 and 10 cm H₂O. Airway pressure and flow were continuously recorded and fitted to the VDSCM with or without considering flow-dependencies. A “distension index” (%E₂) derived from the VDSCM was used to assess Vt and PEEP-induced recruitment/overdistension. Positive and negative values of %E₂ suggest tidal overdistension or tidal recruitment, respectively. In addition, the linear respiratory system elastance was calculated. Comparisons among variables at each PEEP value, Vt setting, ventilatory mode, and regression model considering or not considering flow-dependencies were performed with the Wilcoxon-sign rank test for paired samples (P < 0.05). Multiple comparisons were corrected with the Bonferroni method. The relative change in the estimated noisy variance was used as an index of the goodness of fit of the models.

RESULTS: VDSCM including the flow-dependent parameter significantly improved estimated noisy variance in almost all experimental conditions (11.2 to 71.4, smallest of the lower and highest of the upper 95% confidence intervals). No differences in %E₂ were observed between VCV and PCV, at comparable Vt and PEEP levels, when flow-dependencies were included in the regression model. The negligence of the flow-dependent parameter systematically led to an underestimation of %E₂ in PCV compared to VCV mode (all P < 0.02). At a given Vt, %E₂ was negative at a PEEP of 0 cm H₂O and significantly increased with PEEP, being almost 0 at a PEEP of 5 cm H₂O. At a given level of PEEP, %E₂ significantly increased with Vt.

CONCLUSIONS: The distension index %E₂, derived from the VDSCM considering flow-dependencies, seems able to identify tidal recruitment/overdistension induced by Vt and PEEP independent of flow waveform in healthy lung-anesthetized patients.
有氧和阻力鍛煉誘導的抗傷害過程中中樞和外周 α2 腎上腺素受體的差異
Differential Involvement of Central and Peripheral α2 Adrenoreceptors in the Antinociception Induced by Aerobic and Resistance Exercise
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Anesth Analg March 2013 116:703-711

背景：數項研究已經驗證了鍛煉誘導抗傷害作用；然而，這種效果的詳細機理並沒有被很好的理解。因此，作者研究了大鼠和小鼠由鍛煉產生抗傷害作用的 α2 腎上腺素受體 (α2-ARs) 變化。

方法：雄性 Wistar 大鼠進行了急性有氧（AA）和急性阻力鍛煉，而 α2A/α2C-Ars 基因敲 除小鼠及其野生型小鼠也進行了 AA。

結果：在經過該方案鍛煉後，大鼠和野生型小鼠的疼痛閾值提高了（不包括基因敲除小鼠）。該效果可以被如下藥物逆轉：育亨賓，一種非選擇性 α2-Ars 拮抗劑（4 mg/kg, 皮下注射）；蘿芙素，一種選擇性（4 mg/kg, 皮下注射）；BRL 44408，一種選擇性（4 mg/kg, 皮下注射）；胍乙啶，一種選擇性腎上腺素傳導神經的傳導抑制劑（30 mg/kg, 腹腔注射）。此外，當鞘內注射或者側腦室注射給藥時，育亨賓不會改變鍛煉誘導的鎮痛效果。另外，AA 和急性阻力鍛煉後大鼠腦內的 α2-Ars 表達不會改變。

結論：這些結果暗示了有氧和阻力鍛煉誘導的抗傷害作用為外周 α2-Ars 效應。

BACKGROUND: Several studies have demonstrated antinociception induced by exercise; however, the specific mechanisms for this effect are not well understood. Thus, we investigated the involvement of α2-adrenergic receptors (α2-ARs) in the antinociceptive effect produced by exercise in rats and mice.

METHODS: Male Wistar rats performed acute aerobic (AA) and acute resistance exercise protocols, and male α2A/α2C-ARs knockout mice and their wild-type mice were also submitted to AA.

RESULTS: After the exercise protocols, the nociceptive threshold of rats and wild type was increased, (except in knockout mice). This effect was reversed by yohimbine, a nonselective α2-ARs antagonist (4 mg/kg, subcutaneously [s.c.]); rauwolscine, a selective α2C-ARs antagonist (4 mg/kg, s.c.); BRL 44408, a selective α2A-ARs antagonist (4 mg/kg, s.c.) and guanethidine, a selective inhibitor of transmission in adrenergic nerves (30 mg/kg, intraperitoneal). Furthermore, when given intrathecally or intracerebroventricularly, yohimbine did not alter antinociception induced by exercise protocols. In addition, α2-ARs expression in rat brains did not change after AA and acute resistance exercise.

CONCLUSION: These results suggest a peripheral involvement of α2-ARs in the antinociception induced by aerobic and resistance exercise.

背景：0.1% 羅呱卡因和 0.2% 羅呱卡因分別在肩部手術後連續肌間溝注射的隨機比較研究
Brief Report: A Randomized Comparison of Ropivacaine 0.1% and 0.2% for Continuous Interscalene Block After Shoulder Surgery
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BACKGROUND: The optimal concentration of ropivacaine for continuous interscalene block after shoulder surgery is currently unknown.

METHODS: Fifty-six patients received a perineural infusion of either ropivacaine 0.1% or 0.2% for 48 hours after shoulder surgery. We assessed pain scores as primary end points and supplemental analgesia, ropivacaine consumption, motor block, side effects, and patient satisfaction as secondary end points.

RESULTS: Pain scores were not statistically different during the infusion periods; however, supplemental analgesia consumption was higher in the group receiving ropivacaine 0.1% during the first 24 hours (64% vs 28%, P=0.022). Other secondary end points were statistically inconclusive.

CONCLUSIONS: These results suggest that ropivacaine 0.2% provides more effective analgesia than ropivacaine 0.1% during the first 24 hours for continuous interscalene block after shoulder surgery.
背景：一直以来，都有报告证实根据脑电双频谱指数（BIS）的提示拔管能缩短气管拔管时间。然而，目前还没有试验把通过 BIS 来提示拔管的作用与通过呼末麻醉浓度（ETAC）指示拔管的作用进行对比。我们假设在快速通道心胸手术患者中，通过 BIS 指导的拔管时间相比通过 ETAC 指导的拔管时间有明显的缩短。

方法：这项研究的患者来自单个机构，它是通过大量、多中心的“BIS 和麻醉气体减少重吸收”（BAG-RECALL）临床试验比较分别通过 BIS 和 ETAC 指导麻醉的患者术后意识这该项研究的副实验。接受心胸手术的患者被随机分为 BIS 组（n = 361）和 ETAC 组（n = 362）分别指导麻醉。挥发性麻醉剂滴定浓度，保持在 BIS 值在 40－60 之间（BIS 组）；或是根据年龄调整的最低肺泡浓度在 MAC0.7－1.3（ETAC 组）。在 ETAC 组中，麻醉医生接受 BIS 值的盲法。在这项副研究中，气管拔管时间在两组间相比较。Cox 回归曲线对可能的暂态拔管时间进行预测。

结果：两组患者气管拔管时间无明显差异（优势比为 1.04，95% 可信区间（0.88－1.23），P = 0.643）。此外，按此方法分组并没没有影响暂态拔管时间（P = 0.433）。降低暂态拔管几率的因素包括高体重指数（P = 0.001）、高 EuroSCORE（P = 0.015）、手术类型复杂（P = 0.034）以及手术在夜晚完成（P = 0.03）。

结论：与基于 ETAC 的麻醉管理相比，在接受快速通道心胸手术的患者中基于 BIS 的麻醉管理并不能明显提前气管拔管时间。患者的自身特点和围术特点相比较于 ETAC 和 BIS 监测来说更能决定拔管时间。

（郭晨跃译 薛张纲校）

BACKGROUND:Bispectral Index (BIS)-guided anesthesia administration has been reported to reduce the time to tracheal extubation. However, no trials have compared the ability of BIS guidance to promote earlier tracheal extubation relative to guidance by end-tidal anesthetic concentration (ETAC). We hypothesized that BIS-guided anesthesia would result in earlier tracheal extubation compared with ETAC-guided anesthesia in fast-track cardiac surgery patients.

METHODS:This study consisted of patients at a single institution who were enrolled in the larger, multicenter BIS or Anesthesia Gas to Reduce Explicit Recall (BAG-RECALL) clinical trial that compared rates of postoperative awareness for patient whose anesthetic was guided by BIS versus ETAC. Patients undergoing cardiac surgery were randomized to BIS (n = 361) or ETAC (n = 362) guided anesthesia. Volatile anesthetic was titrated either to maintain a BIS value of 40 to 60 (BIS group), or an age-adjusted minimum alveolar concentration of 0.7 to 1.3 (ETAC group). In the ETAC group, anesthesiologists were blinded to the BIS values. In this substudy, time to tracheal extubation was compared between groups. Cox regression identified predictors affecting the instantaneous probability of tracheal extubation.

RESULTS:Time to tracheal extubation was not significantly different between groups (odds ratio 1.04, 95% confidence interval, 0.88-1.23, P = 0.643). In addition, group assignment did not influence the instantaneous probability of tracheal extubation (P = 0.433). Predictors decreasing the instantaneous probability of tracheal extubation included higher body mass index (P = 0.001), higher logistic EuroSCORE (P = 0.015), complex surgery type (P = 0.034), and surgery completion in the evening (P = 0.03).
CONCLUSIONS: Compared with management based on ETAC, anesthetic management based on BIS guidance does not strongly increase the probability of earlier tracheal extubation in patients undergoing fast-track cardiac surgery. The decision to extubate the trachea is more influenced by patient characteristics and perioperative course than the assignment to BIS or ETAC monitoring.

BACKGROUND: Topical capsaicin and eutectic mixture of local anesthetics (EMLA) have been found to be equally effective in minimizing the pain of venipuncture. After the injection of capsaicin, both tertiary amine local anesthetics and their quaternary ammonium derivatives can elicit a prolonged and predominantly sensory/nociceptor selective block. We hypothesized that the combined application of capsaicin and ELMA will be more effective than their individual effect, and lower concentrations of individual drugs in this mixture may also be associated with reduced side effects.

METHODS: One hundred twenty patients were randomized into 4 equal groups. The control group received plain lubricant cream; the EMLA group received EMLA cream; the capsaicin group received Myolaxin ointment (containing oleoresin capsaicin equivalent to capsaicin 0.075% w/w, methylsalicylate IP 20% w/w, menthol IP 10% w/w, camphor USP 5% w/w, and eucalyptus oil IP 5% w/w); and the EMLA + capsaicin group received EMLA cream and Myolaxin ointment mixed in equal amounts. An anesthesiologist applied the cream to a 10-cm(2) area (site of venous cannulation) on the dorsum of the nondominant hand of the patient 1 hour before venipuncture.

Results: No significant pain was reported by any patient. A total of 8 patients in the control group, 6 in the EMLA group, 7 in the capsaicin group, and 9 in the EMLA + capsaicin group reported some pain (0-10 rating). The number of patients reporting pain was significantly higher in the EMLA + capsaicin group compared with the control group (P = 0.0031).

Conclusion: The addition of capsaicin to EMLA cream did not increase the effectiveness of the mixture in minimizing the pain of venipuncture. However, the combination of capsaicin and EMLA may be a useful approach for reducing the pain of venipuncture.
before venipuncture and covered the area with an occlusive transparent dressing. Venipuncture was performed with an 18-gauge cannula after removing the dressing. Venipuncture pain was graded by the patient on a 0 to 10 visual analog scale, where 0 means no pain and 10 means worst imaginable pain. P values (after correction for multiple comparisons) of <0.05 were considered significant.

RESULTS: The incidence of no pain on venous cannulation (primary end point) was 0% in the control group (0/30). The incidence of no pain were significantly higher in the EMLA group (32%, 9/28, 95% corrected confidence interval for the difference 12%-57%, P = 0.0025), capsaicin group (30%, 9/30, 10%-53%, P = 0.0031), and EMLA + capsaicin groups (47%, 14/30, 25%-69%, P < 0.0001). Severity of venipuncture pain as assessed by visual analog scale median (interquartile range) was lower in the EMLA + capsaicin group 1 (2) compared with other groups 3 (1), 1.5 (3), and 1.5 (3) for control, EMLA, and capsaicin, respectively (P < 0.001, P = 0.04, and P = 0.04, respectively).

CONCLUSION: We observed that the combination of capsaicin and EMLA in a low concentration is as effective in managing venous cannulation as when applied as an individual drug alone. Larger studies with varying concentration of capsaicin and EMLA are recommended to more fully evaluate the potential advantages.

異氟醚麻醉在體內基因調控的微陣列分析：一個新的方法來識別潛在的預處理機制。
Microarray analyses of genes regulated by isoflurane anesthesia in vivo: a novel approach to identifying potential preconditioning mechanisms.
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背景：雖然全身麻醉被確認為有潛力使患者在手術過程中意識消失，但是暴露也可導致細胞損傷和保護的長期結果。至於後者，延遲麻醉藥預處理是一種進化上保守的生理反應，它可能對許多組織缺血再灌注損傷具有保護作用。雖然我們知道延遲預處理需要蛋白質從頭合成，但是麻醉調節基因的知識是不完整的。在這項研究中，我們使用預處理的保守性質來分析 3 組不同的大鼠組織中差異表達的基因。我們假設，我們可以在多種組織中選擇那些調節基因，我們可以開發一個集中的候選基因，它們可能參與延遲麻醉藥預處理。

方法：用 2% 易氟烷與 98% 空氣混合物麻醉年輕的成年雄性大白鼠 90 分鐘。麻醉劑曝露後，立即將動物處死，取出肝，腎，心臟提取所有 RNA。用大鼠寡核苷酸基因序列決定基因表達差異。我們通過分析序列資料來選擇在多種組織中具有顯著調節作用的基因。

結果：一個臨床相關的暴露於異氟醚的所有 3 種組織顯示存在不同的調控基因。協調調控基因的分析產生了一個集中的 34 種潛在候選基因系列的一些本體論，包括調節炎症反應，調節細胞凋亡，調節離子梯度和維護能源途徑。

結論：對協同調控基因通過使用分析的方法，我們能夠產生一個可能與未來預處理研究有關的有趣的候選基因的集中列表。

BACKGROUND: Although general anesthetics are recognized for their potential to render patients unconscious during surgery, exposure can also lead to long-term outcomes of both
cellular damage and protection. As regards the latter, delayed anesthetic preconditioning is an evolutionarily conserved physiological response that has the potential for protecting against ischemic injury in a number of tissues. Although it is known that delayed preconditioning requires de novo protein synthesis, knowledge of anesthetic-regulated genes is incomplete. In this study, we used the conserved nature of preconditioning to analyze differentially regulated genes in 3 different rat tissues. We hypothesized that by selecting those genes regulated in multiple tissues, we could develop a focused list of gene candidates potentially involved in delayed anesthetic preconditioning.

METHODS: Young adult male Sprague-Dawley rats were anesthetized with a 2% isoflurane/98% air mixture for 90 minutes. Immediately after anesthetic exposure, animals were euthanized and liver, kidney, and heart were removed and total RNA was isolated. Differential gene expression was determined using rat oligonucleotide gene arrays. Array data were analyzed to select for genes that were significantly regulated in multiple tissues.

RESULTS: All 3 tissues showed differentially regulated genes in response to a clinically relevant exposure to isoflurane. Analysis of coordinately regulated genes yielded a focused list of 34 potential gene candidates with a range of ontologies including regulation of inflammation, modulation of apoptosis, regulation of ion gradients, and maintenance of energy pathways.

CONCLUSIONS: Through using an analysis approach focusing on coordinately regulated genes, we were able to generate a focused list of interesting gene candidates with potential to enable future preconditioning studies.


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技術交流：使用笑気時 TaperGuard™ 気管導管囊内圧力増加小於 Hi-Lo 導管：一項気管模型的研究。
BACKGROUND: Studies have compared sealing effects of the newly developed tapered endotracheal tube cuff with the conventional cylindrical cuff. In this study, we compared the difference between cuffs with regard to the increase in intracuff pressure during nitrous oxide (N(2)O) exposure.

METHODS: Two types of cuffs were studied using a model trachea connected to a mechanical test lung: high-volume, low-pressure cuff (Mallinckrodt Hi-Lo™, Covidien, Dublin, Ireland) and tapered cuff (Mallinckrodt TaperGuard™, Covidien). The intracuff pressure was set at 20 cm H(2)O, and the increase in pressure was measured during mechanical ventilation using 66% N(2)O. Intracuff pressures were recorded after 5, 10, 15, 30, 45, and 60 minutes of exposure to N(2)O.

RESULTS: The intracuff pressure recorded during the first 15 minutes of N(2)O exposure in high-volume, low-pressure cuffs was significantly higher than tapered cuffs (2-way repeated-measures analysis of variance, P < 0.0001 for internal diameters [IDs] 7.0 and 7.5 mm, P = 0.0004 for ID 8.0 mm, P = 0.0013 for ID 8.5 mm), and there were also statistically significant differences regarding interaction of time and cuff type (P < 0.0001 for IDs 7.0, 7.5, 8.0, and 8.5 mm). The difference in mean cuff pressures among groups after 10 minutes of N(2)O exposure was -18.5 (SE, 1.4; 99% confidence interval, -22.8 to -14.2; P < 0.0001) for ID 7.5 mm. Tapered endotracheal tube cuffs sealed the trachea with fewer dimples on the carina side of the cuff. Dimples on the cuff surface probably increase the surface for N(2)O diffusion. Therefore, fewer dimples result in a smaller surface area through which N(2)O can diffuse.

CONCLUSION: During general anesthesia with N(2)O, the intracuff pressure of tapered endotracheal tube cuffs did not increase as rapidly as it did in conventional high-volume, low-pressure cuffs. The pressure in both types of cuffs increased rapidly when exposed to 66% N(2)O, and hence continuous or frequent monitoring is recommended.

Volume-independent elastance: a useful parameter for open-lung positive end-expiratory pressure adjustment.

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BACKGROUND: A decremental positive end-expiratory pressure (PEEP) trial after full lung recruitment allows for the adjustment of the lowest PEEP that prevents end-expiratory collapse (open-lung PEEP). For a tidal volume (Vt) approaching zero, the PEEP of minimum respiratory system elastance (PEEP(minErs)) is theoretically equal to the pressure at the mathematical inflection point (MIP) of the pressure-volume curve, and seems to correspond to the open-lung PEEP in a decremental PEEP trial. Nevertheless, the PEEP(minErs) is dependent on Vt and decreases as Vt increases. To circumvent this dependency, we proposed the use of a second-order model in which the volume-independent elastance (E1) is used to set open-lung PEEP.

METHODS: Pressure-volume curves and a recruitment maneuver followed by decremental PEEP trials, with a Vt of 6 and 12 mL/kg, were performed in 24 Wistar rats with acute lung injury induced by intraperitoneally injected (n = 8) or intratracheally instilled (n = 8) Escherichia coli lipopolysaccharide. In 8 control animals, the anterior chest wall was surgically removed after PEEP trials, and the protocol was repeated. Airway pressure (Paw) and flow (F) were continuously acquired and fitted by the linear single-compartment model (Paw = Rrs·F + Ers·V + PEEP, where Rrs is the resistance of the respiratory system, and V is volume) and the volume-dependent elastance model (Paw = Rrs·F + E1 + E2·V·V + PEEP, where E2·V is the volume-dependent elastance). From each model, PEEP of minimum Ers and E1 (PEEP(minE1)) were identified and compared with each respective MIP. The accuracy of PEEPminE1 and PEEPminErs in estimating MIP was assessed by bias and precision plots. Comparisons among groups were performed with the unpaired t test whereas a paired t test was used between the control group before and after chest wall removal and within groups at different Vts. All P values were then corrected for multiple comparisons by the Bonferroni procedure.
RESULTS: In all experimental groups, PEEPminErs, but not PEEPminE1, tended to decrease as Vt increased. The difference between MIP and PEEPminE1 exhibited a lower bias compared with the difference between MIP and PEEPminErs (P < 0.001). The PEEPminE1 was always significantly higher than the PEEPminErs (7.7 vs 3.8, P < 0.001) and better approached MIP (7.7 vs 7.3 cm H2O with P = 0.04 at low Vt, and 7.8 vs 7.1 cm H2O with P < 0.001 at high Vt).

CONCLUSIONS: PEEPminE1 better identifies the open-lung PEEP independently of the adjusted Vt, and may be a practical, more individualized approach for PEEP titration.

Treatment with a Highly Selective β1 Antagonist Causes Dose-Dependent Impairment of Cerebral Perfusion After Hemodilution in Rats

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背景：急性 β 阻塞性休克与不良预后之间存在正向剂量依赖性，包括中风和死亡。急性失血增加这些不良事件的发生率。为了研究急性失血和 β 阻滞所致风险的相同时，动物实验研究显示，急性 β 阻滞剂减少血液稀释后的脑灌注。通过检验假设，我们扩展了这些结果，特异性 β1 阻滞剂（奈必洛尔）导致在血液稀释期间剂量依赖性脑缺氧。

方法：大鼠和小鼠麻醉后，在血液稀释至血红蛋白浓度 60 克/升前，随机接受安慰剂或奈必洛尔（1.25 或 2.5 毫克/公斤）静脉注射。血液稀释前后监测药物浓度、心率 (HR)、心输出量 (CO)、局部脑血流量 (rCBF)、脑微血管氧分压 (PBrO2)。Western blot 测定内皮型一氧化氮合酶 (NOS)，神经元型 NOS (nNOS)，诱导型 NOS，缺氧诱导因子 (HIF) - 1α。HIF-α 表达还使用 HIF-1ODD) 融合素酶小鼠模型评估。资料进行方差分析，P < 0.05 有意义，所有分析采用校正 P 值。

结果：奈必洛尔治疗导致剂量依赖的血药浓度。在安慰剂组，血液稀释后 CO 和 rCBF (P < 0.010) 增加，PBrO2 降低至 45.8 ± 18.7 mm Hg (校正 P < 0.001; 95% CI 29.4–69.7)。同剂量奈必洛尔降低 HR，而且减弱 CO 对血液稀释的反应 (P < 0.012)。低剂量奈必洛尔并未改善 rCBF 或在血液稀释后进一步降低 PBrO2。高剂量奈必洛尔减弱 rCBF 对血液稀释的反应，并引起 PBrO2 进一步降低至 28.4 ± 9.6 mm Hg (校正 P = 0.019; 95% CI 17.4–42.7)。所有剂量的奈必洛尔都增加 NOS 蛋白水準。血液稀释后高剂量奈必洛尔组中，脑组织 HIF-1α，诱导型一氧化氮合酶，和 nNOS 蛋白水準与脑缺氧诱导因子活性升高 (P < 0.032)。

结论：我们的数据表明：奈必洛尔导致脑组织氧分压下降和缺氧蛋白反应 (HIF-1α 和 nNOS) 增加，反应血液稀释后脑氧输送呈剂量依赖性下降。血液稀释后低剂量奈必洛尔
BACKGROUND: Acute β-blockade has been associated with a dose-dependent increase in adverse outcomes, including stroke and mortality. Acute blood loss contributes to the incidence of these adverse events. In an attempt to link the risks of acute blood loss and β-blockade, animal studies have demonstrated that acute β-blockade impairs cerebral perfusion after hemodilution. We expanded on these findings by testing the hypothesis that acute β-blockade with a highly β1-specific antagonist (nebivolol) causes dose-dependent cerebral hypoxia during hemodilution.

METHODS: Anesthetized rats and mice were randomized to receive vehicle or nebivolol (1.25 or 2.5 mg/kg) IV before hemodilution to a hemoglobin concentration near 60 g/L. Drug levels, heart rate (HR), cardiac output (CO), regional cerebral blood flow (rCBF, laser Doppler), and microvascular brain Po2 (PBrO2, G2 Oxyphor) were measured before and after hemodilution. Endothelial nitric oxide synthase (NOS), neuronal NOS (nNOS), inducible NOS, and hypoxia inducible factor (HIF)-1α were assessed by Western blot. HIF-α expression was also assessed using an HIF-(ODD)-luciferase mouse model. Data were analyzed using analysis of variance with significance assigned at \( P < 0.05 \), and corrected \( P \) values are reported for all post hoc analyses.

RESULTS: Nebivolol treatment resulted in dose-specific plasma drug levels. In vehicle-treated rats, hemodilution increased CO and rCBF (\( P < 0.010 \)) whereas PBrO2 decreased to 45.8 ± 18.7 mm Hg (corrected \( P < 0.001 ; 95\% \) CI 29.4–69.7). Both nebivolol doses comparably reduced HR and attenuated the CO response to hemodilution (\( P < 0.012 \)). Low-dose nebivolol did not impair rCBF or further reduce PBrO2 after hemodilution. High-dose nebivolol attenuated the rCBF response to hemodilution and caused a further reduction in PBrO2 to 28.4 ± 9.6 mm Hg (corrected \( P = 0.019 ; 95\% \) CI 17.4–42.7). Both nebivolol doses increased brain endothelial NOS protein levels. Brain HIF-1α, inducible NOS, and nNOS protein levels and brain HIF-luciferase activity were increased in the high-dose nebivolol group after hemodilution (\( P < 0.032 \)).

CONCLUSIONS: Our data demonstrate that nebivolol resulted in a dose-dependent decrease in cerebral oxygen delivery after hemodilution as reflected by a decrease in brain tissue Po2 and an increase in hypoxic protein responses (HIF-1α and nNOS). Low-dose nebivolol treatment did not result in worsened tissue hypoxia after hemodilution, despite comparable effects on HR and CO. These data support the hypothesis that acute β-blockade with a highly β1-specific antagonist causes a dose-dependent impairment in cerebral perfusion during hemodilution.

The effects of anesthetics on chronic pain after breast cancer surgery.
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泊酚麻醉對瑞芬太尼引起的痛覺過敏具有抗痛覺過敏作用，並且與七氟醚相比，它能減少急性疼痛。在這項研究中，我們假設，丙泊酚能防止乳腺癌術後的慢性疼痛及急性疼痛的發展和嚴重程度。

方法：我們對2007年3月至2008年12月間接受乳腺癌手術的175名女性（丙泊酚組n = 86，七氟醚組n = 89）進行回顧性研究。年齡分佈為20至65歲。2011年7月對患者進行電話隨訪。分析丙泊酚和七氟醚兩組之間慢性疼痛的發病率，嚴重程度和持續時間。嚴重程度分為輕度、中度和重度疼痛。慢性疼痛持續時間分為3組，各間隔1年時間。此外，還確定了與乳腺癌術後慢性疼痛的發病率及嚴重程度相關的危險因素。

結果：與丙泊酚組相比，乳腺癌術後的慢性疼痛更可能發生在七氟醚組（95%置信區間[CI] 1.146-1.809，P = 0.007）。在患有慢性疼痛的患者中，七氟醚和異丙酚兩組間的嚴重程度（95%CI 0.516-7.419）及持續時間（95%CI 0.106-1.007）無明顯差異。慢性疼痛發展的預測因素為年紀輕（95%CI 0.907-0.992，P = 0.021），行腋窩淋巴結清掃術（95%CI 1.204-1.898，P = 0.003），術後24小時嗎啡消費量（95%CI 1.004-1.116，P = 0.036）和七氟醚（95%CI 1.146-1.809，P = 0.007）。術後24小時嗎啡用量越多，慢性疼痛越是嚴重（95%CI 1.001-1.379，P = 0.049）。

結論：這項研究表明，與七氟醚麻醉相比，丙泊酚麻醉下的乳腺癌術後慢性疼痛的發病率較低。然而，在慢性疼痛的嚴重程度和持續時間上丙泊酚組與七氟醚組沒有顯著的差別。需要進一步的前瞻性研究來證實這些具有爭論的結果的真實性。

BACKGROUND: The incidence and predictive factors for chronic pain after breast cancer surgery have been widely studied. Because it negatively affects patients’ daily lives, methods to prevent and reduce chronic pain and its severity should be developed. Our previous study showed that propofol anesthesia has an antihyperalgesic effect under remifentanil-induced hyperalgesia and reduced acute pain compared with sevoflurane anesthesia. In this study, we investigated the hypothesis that propofol would prevent the development and severity of chronic pain after breast cancer surgery, as in acute pain.

METHODS: A retrospective study was conducted with 175 women (n = 86 in the propofol group and n = 89 in the sevoflurane group) aged 20 to 65 years who underwent breast cancer surgery between March 2007 and December 2008. Patients were followed up by telephone in July 2011. Analysis included incidence, severity, and duration of chronic pain between propofol and sevoflurane groups. Severity was categorized into mild, moderate, and severe pain. Duration of chronic pain was also divided into 3 categories by 1-year time interval. Risk factors associated with the incidence and severity of chronic pain after breast cancer surgery were also identified.

RESULTS: Chronic pain after breast cancer surgery was more likely to occur in the sevoflurane group compared with the propofol group (95% confidence interval [CI] 1.146-1.809, P = 0.007). Among patients with chronic pain, neither the severity (95% CI 0.516-7.419) nor duration (95% CI 0.106-1.007) differed between patients receiving sevoflurane and propofol. Younger age (95% CI 0.907-0.992, P = 0.021), axillary lymph node dissection (95% CI 1.204-1.898, P = 0.003), 24-hour postoperative morphine consumption (95% CI 1.004-1.116, P = 0.036), and sevoflurane (95% CI 1.146-1.809, P = 0.007) were predictive factors for the development of chronic pain. Higher 24-hour postoperative morphine consumption (95% CI 1.001-1.379, P = 0.049) increased the severity of chronic pain.

CONCLUSIONS: This study showed that propofol anesthesia was associated with a lower incidence of chronic pain after breast cancer surgery than sevoflurane anesthesia. However,
Propofol did not have a significant effect on severity and duration of chronic pain. Further prospective studies are needed to confirm the validity of these provocative findings.

Expression of Calcium/Calmodulin-Dependent Protein Kinase and Pain-Related Behavior in Rat Models of Type 1 and Type 2 Diabetes
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BACKGROUND: Abnormalities in peripheral nerves and dorsal root ganglia are noticed in the early stage of experimentally provoked diabetic neuropathy. Enzyme calcium/calmodulin-dependent protein kinase II (CaMKII) may have a modulating role in diabetic neuropathy because of its role in calcium homeostasis.

METHODS: A model of type 1 diabetes mellitus (DM1) was induced with 55 mg/kg streptozotocin and for DM2 induction a combination of high-fat diet and low-dose streptozotocin (35 mg/kg) was used. Pain-related behavior was analyzed using thermal and mechanical stimuli. Two weeks and 2 months after induction of diabetes rats were euthanized, and the expression of CaMKII and its isoforms in the dorsal root ganglia were analyzed using immunofluorescence.

RESULTS: Both types of diabetes were successfully induced, as confirmed by hyperglycemia. Increased pain-related behavior became evident in DM1 rats in 2 weeks after diabetes induction, but not in DM2 rats. The expression of total CaMKII and the phosphorylated α isoform of
CaMKII increased in DM1 animals concurrently with pain-related behavior. Expression of α, β, γ, and δ isoforms in DM1 animals and expression of total CaMKII and all of its analyzed isoforms in DM2 animals remained unchanged.

CONCLUSIONS: Our findings may indicate involvement of CaMKII in transmission of nociceptive input early in DM1, but not in DM2. CaMKII may be a suitable pharmacological target for diabetic neuropathy.

Single-Dose Application of Antithrombin as a Potential Alternative Anticoagulant During Continuous Renal Replacement Therapy in Critically Ill Patients with Advanced Liver Cirrhosis: A Retrospective Data Analysis
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BACKGROUND: Adequate anticoagulation is essential to achieve efficient and cost-effective continuous renal replacement therapy (CRRT). However, in critically ill patients with advanced liver cirrhosis, this goal is challenging because of the concomitant bleeding disorder. Therefore, the evaluation of alternative anticoagulants is necessary.

METHODS: In this retrospective study, we analyzed data of 37 CRRTs in 16 critically ill patients with advanced liver cirrhosis and acute kidney injury admitted to a medical intensive care unit between 2006 and 2008 and included patients undergoing CRRT with either single doses of antithrombin (AT) or continuous low-dose heparin as a sole anticoagulant. The primary outcome measure was lifetime of single CRRT filters.

RESULTS: Data were available for 13 CRRT filters for patients anticoagulated with single doses of AT (n = 6), and 24 CRRT filters for patients anticoagulated continuously with low-dose
heparin \((n = 10)\). Means of single-filter lifetimes were significantly higher in the AT group compared with the heparin group \((45 \pm 29\) hours [95\% confidence interval 27–62 hours] vs 26 \pm 23 hours [95\% confidence interval 16–36 hours]; \(P = 0.03\)), whereas mean filter lifetimes of individual patients were comparable (median [25th–75th percentile] 30 hours [21–59 hours] vs 28 hours [17–70 hours]; \(P = 0.79\)).

**CONCLUSIONS:** Our data suggest that anticoagulation with single doses of AT may be an alternative to continuously administered low-dose heparin in critically ill patients with advanced liver cirrhosis during CRRT. However, additional controlled trials are necessary to confirm our findings.

**A Transesophageal Echocardiography Technique to Locate the Kidney and Monitor Renal Perfusion**

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Monitoring the renal arterial Doppler flow velocity indices, the resistive index and pulsatility index, with ultrasound may help predict renal dysfunction. However, such monitoring has been done intermittently by transcutaneous ultrasound in the postoperative intensive care setting. In the operating room, transesophageal echocardiography (TEE) is an alternative to transcutaneous ultrasound for obtaining indices of renal perfusion. However, it is difficult to locate the right kidney using TEE. We propose a new technique to locate the left kidney that, in our experience, is simple and easy to perform. We believe, starting from a transgastric left ventricular short-axis view, turning left to locate the abdominal aorta, and following it to the origin of the left renal artery may help locate the left kidney faster than previously described techniques. We also propose a new technique to monitor these Doppler indices using TEE during the intraoperative period.

**The Pyrrole Etomidate Analog Carboetomidate Potently Inhibits Human 5-HT\(_{3A}\) Receptor Function: Comparisons with Etomidate and Potential Implications for Emetogenesis**

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BACKGROUND: 5-Hydroxytryptamine type 3 (5-HT\textsubscript{3}) receptors are excitatory ion channels belonging to the cys-loop family of ligand-gated ion channels. They are involved in nausea and vomiting and their antagonists are used clinically as antiemetic drugs. We previously reported the development of a novel pyrrole analog of etomidate, \((R)-\text{ethyl }1-(1\text{-phenylethyl})-1\text{H}-\text{pyrrole-2-carboxylate (carboetomidate), which retains etomidate’s desirable anesthetic and hemodynamic properties, but lacks its potent inhibitory effect on adrenocorticotropic hormone–stimulated steroid synthesis. Also in contrast to etomidate, carboetomidate potently inhibits nicotinic acetylcholine receptors. Because nicotinic acetylcholine and 5-HT\textsubscript{3} receptors are highly homologous, we hypothesized that carboetomidate might also potently inhibit 5-HT\textsubscript{3} receptors with potentially important implications for the drug’s emetogenic activity. In the current studies, we investigated and compared modulation of 5-HT\textsubscript{3A} receptors by carboetomidate and etomidate.}

METHODS: 5-HT\textsubscript{3} receptors were heterologously expressed in human embryonic kidney cells. Drugs were applied with a multichannel superfusion pipette coupled to piezoelectric elements, and currents were recorded from cells in either the whole-cell or excised outside-out patch configuration of patch-clamp recordings.

RESULTS: Carboetomidate and etomidate inhibited integrated 5-HT\textsubscript{3A} receptor–mediated currents with respective half-inhibitory concentrations of 1.9 \(\mu\text{M} (95\% \text{ confidence interval } [CI] = 1.4–2.7 \mu\text{M})\) and 25 \(\mu\text{M} (95\% \text{ CI} = 17–37 \mu\text{M})\). These values may be compared with respective hypnotic concentrations of 5.4 and 2.3 \(\mu\text{M}\). This inhibition reflected hypnotic effects
on peak current amplitudes and desensitization rates. Half-inhibitory concentrations for reducing peak current amplitudes were 34 μM (95% CI = 24–48 μM) for carboetomidate and 171 μM (95% CI = 128–228 μM) for etomidate. Half-inhibitory concentrations for reducing the desensitization time constant were 3.5 μM (95% CI = 2.4–5.1 μM) for carboetomidate and 36 μM (95% CI = 21–59 μM) for etomidate.

CONCLUSIONS: In contrast to etomidate, carboetomidate inhibits 5-HT₃A receptor–mediated currents at hypnotic concentrations. This inhibition is primarily the result of enhancing the rate of desensitization. Because carboetomidate potently inhibits 5-HT₃A receptors, it may be less emetogenic than etomidate.

有丁醯膽鹼酯酶基因 K 變異體的患者對琥珀醯膽鹼的反應
Response to Succinylcholine in Patients Carrying the K-Variant of the Butyrylcholinesterase Gene
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BACKGROUND: Succinylcholine is usually metabolized quickly by the butyrylcholinesterase enzyme (BChE) but genetic variants of BChE may prolong the duration of action. The Kalow (K) variant is the most common mutation in the butyrylcholinesterase gene (BCHE), being present in 25% of Caucasians. The significance of the K-variant for the duration of action of succinylcholine has not been well studied. Our hypothesis was that the duration of action of
succinylcholine would be prolonged in patients heterozygous for the K-variant genotype compared with the normal genotype (wild-type).

**METHODS:** We included 70 adult surgical patients who received succinylcholine 1 mg/kg for rapid sequence induction. Neuromuscular monitoring was performed using ulnar nerve stimulation and acceleromyography. Duration of action of succinylcholine was defined as the time to 90% recovery of first twitch in train-of-four (T1 90%), BChE activity was determined, and the presence of BCHE K and A (atypical) variants were determined using DNA analysis.

**RESULTS:** The wild-type BCHE was present in 38 patients, and 21 were heterozygous for the K-variant. Mean (SD) T1 90% in patients heterozygous for the K-variant, 11.6 (3.5) minutes, was longer than in patients with the wild-type genotype, 9.5 (2.7) minutes (P = 0.023), with a mean (95% confidence interval) difference of 2.1 (0.3–4.0) minutes. Patients heterozygous for the K-variant had a BChE activity of 5978 U/L compared with 7703 U/L in the wild-type group (P = 0.0045).

**CONCLUSION:** We conclude that the mean duration of action of succinylcholine is prolonged for the patient heterozygous for the K-variant allele by at most 4 minutes relative to the wild-type, but this difference is small relative to the wide variability and overlap in recovery times among all patients.

**重力驅動的微孔點滴靜脈輸注在“完全開放”流動過程中傳輸的藥物和液體容量**

Medication and Volume Delivery by Gravity-Driven Micro-Drip Intravenous Infusion: Potential Variations During “Wide-Open” Flow
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**背景：** 重力驅動的微孔點滴輸液裝置可以通過調節每分種滴數來控制給藥劑量。當滾輪調節器完全開放時，微孔點滴輸液器在遠端連接一個高流量的旋塞，旋塞再連接一個垂直方向的靜脈內導管（14-22 號）。鹽水袋的彎液面要高於出口 60—120cm。在所有試驗中輸液導管大小和液量高度的不同，其變化有 2.9 倍的差距（95% 的可信區間為 2.84—2.96）。帶旋塞和導管的微孔點滴輸液器的模型總阻力因流率不同而不同。背馱式微孔點滴輸液器的液體傳輸特性相似。
結論：通過實驗室模擬重力驅動的微孔點滴輸液器在完全開放下的臨床情況，我們得出：液體輸注率（藥物和/或容量輸入）的差距變化取決於導管的大小、液量的高度，以及載體流量等外在因素。多變的阻力意味著在微孔點滴輸注模型中液體的非層流流量很難做數學上的預測。這些發現支持以下觀點：使用機械泵取代重力驅動的微孔點滴法可以提高靜脈輸液尤其是血管活性藥輸注的精確性和安全性。

（王慧娟 譯  馬皓琳  李士通 校）

BACKGROUND: Gravity-driven micro-drip infusion sets allow control of medication dose delivery by adjusting drops per minute. When the roller clamp is fully open, flow in the drip chamber can be a continuous fluid column rather than discrete, countable, drops. We hypothesized that during this “wide-open” state, drug delivery becomes dependent on factors extrinsic to the micro-drip set and is therefore difficult to predict. We conducted laboratory experiments to characterize volume delivery under various clinically relevant conditions of wide-open flow in an in vitro laboratory model.

METHODS: A micro-drip infusion set, plugged into a bag of normal saline, was connected to a high-flow stopcock at the distal end. Vertically oriented IV catheters (gauges 14–22) were connected to the stopcock. The fluid meniscus height in the bag was fixed (60–120 cm) above the outflow point. The roller clamp on the infusion set was in fully open position for all experiments resulting in a continuous column of fluid in the drip chamber. Fluid volume delivered in 1 minute was measured 4 times with each condition. To model resistive effects of carrier flow, volumetric infusion pumps were used to deliver various flow rates of normal saline through a carrier IV set into which a micro-drip infusion was “piggybacked.” We also compared delivery by micro-drip infusion sets from 3 manufacturers.

RESULTS: The volume of fluid delivered by gravity-driven infusion under wide-open conditions (continuous fluid column in drip chamber) varied 2.9-fold (95% confidence interval, 2.84–2.96) depending on catheter size and fluid column height. Total model resistance of the micro-drip with stopcock and catheter varied with flow rate. Volume delivered by the piggybacked micro-drip decreased up to 29.7% ± 0.8% (mean ± SE) as the carrier flow increased from 0 to 1998 mL/min. Delivery characteristics of the micro-drip infusion sets from 3 different manufacturers were similar.

CONCLUSIONS: Laboratory simulation of clinical situations with gravity-driven micro-drip infusion sets under wide-open flow conditions revealed that infusion rate (drug and/or volume delivery) can vary widely depending on extrinsic factors including catheter size, fluid column height, and carrier flow. The variable resistance implies nonlaminar flow in the micro-drip model that cannot be easily predicted mathematically. These findings support the use of mechanical pumps instead of gravity-driven micro-drips to enhance the precision and safety of IV infusions, especially for vasoactive drugs.

剖腹產手術抗生素預防性應用中的不統一：一項麻醉醫師的全國調查

Unwarranted Variability in Antibiotic Prophylaxis for Cesarean Section Delivery: A National Survey of Anesthesiologists

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背景：美國婦產科協會最新的指南推薦在剖腹產手術切皮前即刻預防性使用抗生素。本研究的目的即以全美麻醉醫師為樣本來測試和描述此指南的執行相關情況。

方法：我們隨機邀請美國麻醉醫師協會的部分成員（n=1000）完成了一項網上調查。

結果：在1052名（10.5%）提供完整可供分析的資訊的應答者中，63.5%（95%CI 60.6%~66.3%，n=668）報告了切皮前預防性使用抗生素作爲監護標準應用於計畫剖腹產。28%（n=299）的醫師同意麻醉醫師必須對預防性使用抗生素的時機負主責。在多因素模型中，不同醫院類型（社區醫院比教學醫院，62%比 70%，P=0.004）、地域（西部比東南部，70%比 59%，P=0.01；西部比西南部，70%比 58%，P=0.02）以及應答者對於合適的切皮前使用時機的意見（80%的受試者主張常規切皮前給藥，17%主張常規在斷臍後給藥，47%主張隨從產科醫師的意願，43%認爲需要更多的資訊）（所有比較 P<0.001）對於切皮前預防性應用抗生素存在顯著差異。在該模型中，最大的區別因數為應答者關於合適的切皮前給藥時機的認識（受試者工作特徵曲線下面積變化=0.13 比其餘的≤0.02）。

結論：當前剖宮產預防性抗生素給藥指南的遵守不統一。教育的開展、監管的實施和過程的改進應針對不遵守當前指南的麻醉醫師所在地。

（王贇譯 馬皓琳 李士通 校）

BACKGROUND: Current guidelines from the American College of Obstetricians and Gynecologists recommend antibiotic prophylaxis for cesarean delivery immediately before incision. The purpose of this study was to measure and describe correlates of adherence to these guidelines in a sample of United States anesthesiologists.

METHODS: We invited a random sample of the membership of the American Society of Anesthesiologists (n = 10,000) to complete an online survey.

RESULTS: Of 1052 respondents (10.5%) with complete information for analysis, 63.5% (95% confidence interval 60.6%, 66.3%, n = 668) reported preincision prophylaxis as the standard of care for scheduled cesarean delivery. Twenty-eight percent (n = 299) agreed that the anesthesiologist should take primary responsibility for prophylaxis timing. In a multivariable model, significant variability in preincision prophylaxis was noted for hospital type (community versus teaching, 62% vs 70%, P = 0.004), region (West versus Southeast, 70% vs 59%, P = 0.01; West versus Southwest, 70% vs 58%, P = 0.02), and respondents’ belief in appropriate preincision timing (those endorsing routine preincision administration [80%], routine after cord clamp administration [17%], at the discretion of the obstetrician [47%], and the belief that more information was needed [43%]) (P < 0.001 all comparisons). Respondents’ belief about appropriate preincision timing was the strongest discriminator in the model (change in area under the receiver operating characteristic curve = 0.13 vs ≤0.02 for all others).

CONCLUSION: Adherence with current prophylactic antibiotic administration guidelines for cesarean delivery is not uniform. Education initiatives, regulatory maneuvers, and process improvement should be targeted at sites where anesthesiologists do not comply with current guidelines.

成人心臟手術患者中腦近紅外光譜監測與神經功能預後的關係：一篇系統性綜述

Cerebral Near-Infrared Spectroscopy Monitoring and Neurologic Outcomes in Adult Cardiac Surgery Patients: A Systematic Review
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BACKGROUND: Near-infrared spectroscopy is used during cardiac surgery to monitor the adequacy of cerebral perfusion. In this systematic review, we evaluated available data for adult patients to determine (1) whether decrements in cerebral oximetry during cardiac surgery are associated with stroke, postoperative cognitive dysfunction (POCD), or delirium; and (2) whether interventions aimed at correcting cerebral oximetry decrements improve neurologic outcomes.

METHODS: We searched PubMed, Cochrane, and Embase databases from inception until January 31, 2012, without restriction on languages. Each article was examined for additional references. A publication was excluded if it did not include original data (e.g., review, commentary) or if it was not published as a full-length article in a peer-reviewed journal (e.g., abstract only). The identified abstracts were screened first, and full texts of eligible articles were reviewed independently by 2 investigators. For eligible publications, we recorded the number of subjects, type of surgery, and criteria for diagnosis of neurologic end points.
RESULTS: We identified 13 case reports, 27 observational studies, and 2 prospectively randomized intervention trials that met our inclusion criteria. Case reports and 2 observational studies contained anecdotal evidence suggesting that regional cerebral \( O_2 \) saturation (rS\(\text{co}_2 \)) monitoring could be used to identify cardiopulmonary bypass cannula malposition. Six of 9 observational studies reported an association between acute rS\(\text{co}_2 \) desaturation and POCD based on the Mini-Mental State Examination \((n = 3 \) studies\) or more detailed cognitive testing \((n = 6 \) studies\). Two retrospective studies reported a relationship between rS\(\text{co}_2 \) desaturation and stroke or type I and II neurologic injury after surgery. The observational studies had many limitations, including small sample size, assessments only during the immediate postoperative period, and failure to perform risk adjustments. Two randomized studies evaluated the efficacy of interventions for treating rS\(\text{co}_2 \) desaturation during surgery, but adherence to the protocol was poor in one. In the other study, interventions for rS\(\text{co}_2 \) desaturation were associated with less major organ injury and shorter intensive care unit hospitalization compared with nonintervention.

CONCLUSIONS: Reductions in rS\(\text{co}_2 \) during cardiac surgery may identify cardiopulmonary bypass cannula malposition, particularly during aortic surgery. Only low-level evidence links low rS\(\text{co}_2 \) during cardiac surgery to postoperative neurologic complications, and data are insufficient to conclude that interventions to improve rS\(\text{co}_2 \) desaturation prevent stroke or POCD.

離體大鼠坐骨神經利多卡因吸收和清除動力學
Kinetics of Uptake and Washout of Lidocaine in Rat Sciatic Nerve In Vitro
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背景：臨床上用於周圍神經阻滯而注射的局部麻醉藥的效價和效能很大程度上取決於神經藥物吸收的速度。然而，因通過血管系統擴散到周圍組織以及去除是體內利多卡因總體分佈的重要因素，所以必須研究去除那些干擾因數的真正的藥物/神經組織相互作用的動力學。

方法：吸收：我們將有鞘或去鞘離體大鼠坐骨神經暴露於\[^{14}\text{C}\]-利多卡因 0 到 180 分鐘後取出，然後分析神經和鞘內的利多卡因含量。清除：我們將離體神經浸泡於\[^{14}\text{C}\]-利多卡因內 60 分鐘，然後置於無利多卡因的溶液內 0 到 30 分鐘，並評估在不同時間取出的樣本內藥物含量。實驗變數包括神經外膜鞘、利多卡因的濃度、pH、CO\(_2\)-碳酸氫鹽的存在以及培養持續時間的影響。

結果：利多卡因的平衡吸收隨培養時間、濃度以及非離子形式中的分子分數的增加而增加。雖然吸收率不受藥物濃度的影響，但因神經外膜鞘的存在而大約減半，同時清除率卻減慢得較少。使用碳酸氫鹽-CO\(_2\)緩衝液或非碳酸氫鹽緩衝液將pH從6.8到7.4的輕微鹼化能夠增強神經吸收，而且可到相同程度。利多卡因的清除在高濃度短時間培養後比低濃度長時間培養後吸收的等量利多卡因更快。

結論：利多卡因進入神經的過程不同于自由擴散，而是通過有輕微障礙的神經外膜鞘。考慮到在體外快速進入與在體內小得多且短暫的含量測量相比，利多卡因與神經在外周阻滯時達到平衡似乎不太可能。
BACKGROUND: The potency and efficacy of local anesthetics injected clinically for peripheral nerve block depends strongly on the rate of neural drug uptake. However, because diffusion into surrounding tissues and removal by the vascular system are major factors in the overall distribution of lidocaine in vivo, true kinetics of drug/neural tissue interactions must be studied in the absence of those confounding factors.

METHODS: Uptake: Ensheathed or desheathed isolated rat sciatic nerves were exposed to [14C]-lidocaine for 0 to 180 minutes and then removed and the lidocaine content of nerve and sheath analyzed. Washout: Isolated nerves were soaked in [14C]-lidocaine for 60 minutes and then placed in lidocaine-free solution for 0 to 30 minutes, with samples removed at different times to assess the drug content. Experimental variables included the effects of the ensheathing epineurium, lidocaine concentration, pH, presence of CO2-bicarbonate, and incubation duration.

RESULTS: The equilibrium uptake of lidocaine increased with incubation time, concentration, and the fraction of molecules in the nonionized form. The uptake rate was unaffected by drug concentration, but was about halved by the presence of the epineurial sheath, with the washout rate slowed less. Slight alkalinization, from pH 6.8 to pH 7.4, by bicarbonate-CO2 buffer or a nonbicarbonate buffer, enhanced the neural uptake, and to the same degree. The washout of lidocaine was faster after shorter incubations at high concentrations than when equal amounts of lidocaine were taken up after long incubations at low lidocaine concentrations.

CONCLUSION: Lidocaine enters a nerve by a process other than free diffusion, through an epineurial sheath that is a slight obstacle. Given the rapid entry in vitro compared with the much smaller and transient content measured in vivo, it seems highly unlikely that lidocaine equilibrates with the nerve during a peripheral blockade.

Association of Denervation Severity in the Dermis with the Development of Mechanical Allodynia and Hyperalgesia in a Murine Model of Postherpetic Neuralgia
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背景：帶狀皰疹後神經痛（PHN）是帶狀皰疹的一種常見併發症，而且會遺留神經病理性疼痛的具有挑戰性的情況。異常性疼痛作爲皰疹後神經痛的一個顯著特點，會擴散到最初的皮疹面積以外的區域。在本研究中，我們通過使用 PHN 的鼠類模型研究了皮膚去神經支配與異常性疼痛和痛覺過敏發展之間的聯繫。

方法：使用雌性 C57BL/6j 小鼠。將單純皰疹病毒 1 型(HSV1) 接種于單側小腿，這一區域主要是受 L3 背根神經節 (DRG) 神經元支配。在帶狀皰疹樣皮損癒合後，將小鼠按照在同側後肢足底方面的機械性異常性疼痛和痛覺過敏的表現來分類。用一種蛋白基因產物的抗體(PGP)9.5 將佈滿傷痕的腰（受 L2-4 DRG 神經元支配）和同側足底（受 L3-5 DRG 神經元支配）的表層皮膚去神經支配。
經元支配）的皮膚切片進行了免疫染色。分析在表皮和真皮中對 PGP9.5 有免疫反應（IR）的數量，用於皮膚神經支配的定量。

結果：在有疤痕的腰皮膚的表皮，有 PGP9.5-IR 特性的個體內平均數量在接種 HSV1 的小鼠中明顯減少。有疤痕皮膚的表皮中 PGP9.5-IR 的個體內最大和平均數量在有和沒有皰疹後異常性疼痛和痛覺過敏的小鼠之間沒有顯著差異。在有疤痕的腰皮膚的真皮層，有皰疹後異常性疼痛和痛覺過敏的小鼠的 PGP9.5-IR 個體內最大和平均數量顯著下降，但這不適用於沒有這些症狀的小鼠。HSV1 的接種使真皮和表皮中有 PGP9.5-IR 特性的個個內最低數量顯著減少。HSV1 接種使接種側表皮中有 PGP9.5-IR 特性的個個體內平均數量顯著減少，但真皮不受影響。

結論：本研究結果表明，有疤痕的皮膚真皮去神經支配的嚴重程度與皰疹後異常性疼痛和痛覺過敏的發展相關，它們的發展會超出最初的皮疹面積的邊緣。有疤痕的和刺激性皮膚的表皮神經密度的下降可能和皰疹後異常性疼痛和痛覺過敏沒有關聯。

(趙曉譯 馬皓琳 李士通校)

BACKGROUND: Postherpetic neuralgia (PHN) is a common complication of herpes zoster and remains a challenging condition of neuropathic pain. Allodynia, a prominent feature of PHN, extends beyond the margins of the initial rash area. In the present study, we investigated the association between cutaneous denervation and the development of postherpetic allodynia and hyperalgesia by using a murine model of PHN.

METHODS: Female C57BL/6j mice were used. Herpes simplex virus type-1 (HSV1) was inoculated on the unilateral shin, a region that is predominantly innervated by L3 dorsal root ganglion (DRG) neurons. After the zoster-like skin lesions healed, mice were classified by the presence of mechanical allodynia and hyperalgesia in the plantar aspect of the ipsilateral hindpaw. Scarred lumbar (innervated by L2-4 DRG neurons) and the ipsilateral plantar (innervated by L3-5 DRG neurons) skin sections were immunostained with an antibody against protein gene product (PGP)9.5. The number of PGP9.5-immunoreactive (IR) profiles in the epidermis and dermis were analyzed for quantification of cutaneous innervation.

RESULTS: In the epidermis of the scarred lumbar skin, the intraindividual mean number of PGP9.5-IR profiles was significantly decreased in mice inoculated with HSV1. The intraindividual maximum and mean numbers of PGP9.5-IR profiles in the epidermis of the scarred skin were not significantly different between mice with and without postherpetic allodynia and hyperalgesia. In the dermis of the scarred lumbar skin, the intraindividual maximum and mean numbers of PGP9.5-IR profiles were significantly decreased in mice with postherpetic allodynia and hyperalgesia, but not in mice without these symptoms. The intraindividual minimum number of PGP9.5-IR profiles in the dermis and epidermis was significantly decreased by HSV1 inoculation. HSV1 inoculation significantly decreased the intraindividual mean number of PGP9.5-IR profiles in the epidermis, but not dermis, of the plantar skin on the inoculated side.

CONCLUSIONS: The present results suggest that the severity of dermal denervation in the scarred skin is associated with the development of postherpetic allodynia and hyperalgesia that extend beyond the margins of the initial rash area. The decrease of epidermal nerve density in the scarred and stimulation skins may not be associated with postherpetic allodynia and hyperalgesia.