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**經旋轉血栓彈性測定法 (ROTEM(R)) 證實纖溶亢進的嚴重創傷患者其死亡率較高**

**Hyperfibrinolysis Diagnosed by Rotational Thromboelastometry (ROTEM(R)) Is Associated with Higher Mortality in Patients with Severe Trauma.**

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此項研究旨在探究纖溶亢進及其嚴重程度與創傷或非創傷患者結局間的相互關係。2008年4月至2010年4月間所有經診斷證實為纖溶亢進的急診患者均納入該項研究。根據有無軀體創傷將上述纖溶亢進患者分為創傷組（創傷纖溶亢進組）與非創傷組（非創傷纖溶亢進組）。另將24位無纖溶亢進的多發傷患者（創傷配對組）與創傷纖溶亢進患者相配對。採集旋轉血栓彈性測定法的測量結果、血氣分析（代謝狀態）、實驗室檢查、創傷嚴重度評分以及30天死亡率等相關資料以供分析。經鑒定共有35名患者被診斷為纖溶亢進（其中創傷患者13名，非創傷患者22名）。纖溶亢進的總體死亡率為54%。創傷纖溶亢進組患者的死亡率（77%

±12%) 明顯高於非創傷纖維溶亢進組 (41%±10%; P=0.001, 95%CI 5%-67%) 與創傷配對組 (33% ±10%; P=0.009, 95%CI 13%-74%) 患者。纖維溶亢進與創傷患者的死亡率間存在顯著相關性 (P=0.017)。比較血氣分析所回饋的代謝狀態, 創傷纖維溶亢進組患者僅在 pH 值 (P=0.02) 與鉀離子濃度 (P=0.01) 兩方面較非創傷纖維溶亢進組患者明顯降低。基於創傷纖維溶亢進患者的死亡率顯著高於創傷患者與非創傷纖維溶亢進患者, 因此可將纖維溶亢進作為預測創傷患者死亡的獨立危險因素。旋轉血栓彈性測定法所提供的纖維溶亢進即時診斷為早期治療創造了條件。

(范羽譯 薛張綱校)

We investigated whether hyperfibrinolysis and its severity was associated with outcome of traumatized and nontraumatized patients. From April 2008 to April 2010, all emergency patients with hyperfibrinolysis were enrolled in this study. Hyperfibrinolysis patients were divided into traumatized (trauma hyperfibrinolysis group) and nontraumatized (nontrauma hyperfibrinolysis group). The trauma hyperfibrinolysis group was matched with 24 polytrauma patients without hyperfibrinolysis (matched trauma group). Data from rotational thromboelastometry measurements, blood gas analysis (metabolic state), laboratory analysis, injury severity score, and 30-day mortality were collected. Thirty-five patients with hyperfibrinolysis were identified (13 traumatized, 22 nontraumatized). Overall mortality for hyperfibrinolysis was 54%. Mortality in the trauma hyperfibrinolysis group (77% ± 12%) was significantly higher than in the nontrauma hyperfibrinolysis group (41% ± 10%; P = 0.001, 95% CI 5%-67%) and the matched trauma group (33% ± 10%; P = 0.009, 95% CI 13%-74%). Hyperfibrinolysis is significantly (P = 0.017) associated with mortality in trauma patients. In the blood gas analysis representing the metabolic state, only pH (P = 0.02) and potassium (P = 0.01) were significantly lower in the trauma hyperfibrinolysis group compared to the nontrauma hyperfibrinolysis group. Mortality from hyperfibrinolysis is significantly higher in trauma compared with nontrauma patients, and hyperfibrinolysis is an independent factor predicting mortality in trauma patients. Rotational thromboelastometry provides real-time recognition of hyperfibrinolysis allowing early treatment.

### 關於驗證和觀察麻醉藥物作於早期脊神經網路 (離體八目鰻脊髓) 的研究

#### Validation and insights of anesthetic action in an early vertebrate network: the isolated lamprey spinal cord

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**背景:** 八目鰻脊髓是一種典型的脊椎網路便於我們理解麻醉劑的作用。我們檢測了一系列關於八目鰻的麻醉臨床應用及麻醉劑作用位點和機制的假設。

**方法:** 離體的八目鰻脊髓, 在 d-谷氨酸鹽介導的虛擬的遊動或者毒物刺激尾部時, 應用氟烷、異氟醚、七氟醚、地氟醚、丙泊酚或者非制動劑 f6 (1、2-六氟環乙烷), 來確定這些麻醉劑使受體不動的最低濃度即(MICs)。檢驗存在和不存在土的甯和或印防己毒時異氟醚和丙泊酚對虛擬遊動的影響。

**結果：**揮發性麻醉劑的最低制動濃度是客觀的可以進行比較的。異氟醚對虛擬遊動和毒素刺激誘發的活動的 MIC 是相同的。F6不能制動，但是會降低虛擬遊動的幅度和滯相。異氟醚降低虛擬遊動的頻率，幅度，自動校正，首尾滯相和連貫性。在異氟醚作用下土的甯和印防己毒僅僅誘導出不規律的體動，且在 MIC 濃度時引起小幅度降低。丙泊酚的效果不同於異氟醚，因為所有運動器官除了振幅以外的節律各不相同。相比哺乳動物，八目鰻的丙泊酚 MIC 要大得多。然而，印防己毒通過再調節運動器官的活動和增加 MIC(>8倍) 來拮抗丙泊酚的抗體動作用。

**結論：**八目鰻脊髓是一種研究麻醉劑作用的確切的易於處理的脊椎網路模型。異氟醚擾亂神經元間的運動網路。γ-氨基丁酸 A 和甘氨酸受體對異氟醚抑制八目鰻體動也有微弱的作用。丙泊酚選擇性的 GABA 受體介導的抑制體動機制在八目鰻身上被保留。異氟醚和丙泊酚相比，不同的抑制運動的機制在哺乳動物中反應出來，並且進一步提示存在不同的抑制運動的神經網路模型。

(侯文婷譯 薛張綱校)

**BACKGROUND:**The lamprey spinal cord is a well-characterized vertebrate network that could facilitate our understanding of anesthetic action. We tested several hypotheses concerning the lamprey's clinical application to anesthesia, and the sites/mechanisms of anesthetic action.

**METHODS:**In isolated lamprey spinal cords, minimum immobilizing concentrations (MICs) were determined for halothane, isoflurane, sevoflurane, desflurane, propofol, or the nonimmobilizer F6 (1,2-dichlorohexafluorocyclobutane), applied during d-glutamate-induced fictive swimming or noxious tail stimulation. Isoflurane and propofol effects on fictive swimming were tested in the presence and absence of strychnine and/or picrotoxin.

**RESULTS:**Volatile anesthetic MICs were clinically comparable. Isoflurane MIC for fictive swimming and noxious stimulus-evoked movement were the same. F6 did not produce immobility, but decreased the amplitude and phase lag of fictive swimming. Isoflurane decreased fictive swimming cycle frequency, amplitude, autocorrelation, rostrocaudal phase lag, and coherence. Strychnine and picrotoxin elicited only disorganized motor activity under isoflurane and caused small increases in MIC. The effects of propofol differed from isoflurane for all locomotor rhythm variables except amplitude. The propofol MIC was much larger in lampreys compared with mammals. However, picrotoxin reversed propofol-induced immobility by reinitiating coordinated locomotor activity and increasing MIC >8-fold.

**CONCLUSIONS:**The lamprey spinal cord is a relevant and tractable vertebrate network model for anesthetic action. Isoflurane disrupts interneuronal locomotor networks. γ-Aminobutyric acid A and glycine receptors have marginal roles in isoflurane-induced immobility in lampreys. Propofol's selective γ-aminobutyric acid A receptor-mediated 介導 immobilizing mechanism is conserved in lampreys. The differential immobilizing mechanisms of isoflurane versus propofol reflect those in mammals, and further suggest different network modes of immobilizing action.

### 結直腸手術中脈氧變異指數對液體治療反應性的預測價值

#### **Pleth variability index to predict fluid responsiveness in colorectal surgery.**

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**背景：**腹部手術時，目標導向性的液體治療可以減少術後併發症。脈氧變異指數 (PVI) 是由脈氧波型得出的一種數值。已經有研究表明它可以在多種手術中預測液體治療的反應。本次研究選擇了低危的結直腸癌根治手術，採用食道超聲多普勒測量每搏輸出量為標準，測試脈氧變異指數是否能夠準確預測液體治療的反應。

**方法：**研究選取了25名全麻下行結直腸癌根治術的患者。經食道超聲多普勒測量患者每搏輸出量的基礎值，指尖和耳垂測量患者脈氧變異指數的基礎值。麻醉誘導氣管插管後，手術開始前立即給予500ml液體負荷量，然後記錄此時每搏輸出量和脈氧變異指數為靜息時的最終值。術中監測經食道超聲多普勒，當每搏輸出量降低超過10%時則給予250ml的追加劑量。此為每搏輸出量和脈氧變異指數的動態最終值。根據每搏輸出量的增加量是否超過10%將研究物件分為有反應組和無反應組。

**結果：**不論是靜息狀態還是術中的情況下，對液體治療有反應組的指尖脈氧變異指數基礎值均顯著較高。在靜息狀態下，指尖和耳垂的脈氧變異指數均可以預測每搏輸出量的增加：指尖脈氧變異指數的曲線下面積AUC=0.96 95%可信區間為0.88-1, P=0.011；耳垂脈氧變異指數的曲線下面積AUC=0.98 95%可信區間為0.93-1, P=0.008。術中動態情況下，指尖脈氧變異指數可以預測每搏輸出量的增加，其曲線下面積為AUC=0.71 95%可信區間為0.57-0.85, P=0.006，然而耳垂脈氧變異指數則不具有此預測價值。

**結論：**指尖脈氧變異指數可以預測手術中行機械通氣下的患者對於液體治療的反應性。

(黃劍譯 薛張綱校)

**BACKGROUND:** Goal-directed fluid therapy during major abdominal surgery may reduce postoperative morbidity. The Pleth Variability Index (PVI), derived from the pulse oximeter waveform, has been shown to be able to predict fluid responsiveness in a number of surgical circumstances. In the present study, we sought to determine whether PVI could predict fluid responsiveness in low-risk colorectal surgery patients who had fluid therapy guided by esophageal Doppler stroke volume measurements.

**METHODS:** Twenty-five low-risk patients undergoing colorectal resection under general anesthesia were studied. Baseline values for esophageal Doppler stroke volume and PVI taken from finger and ear probes were compared with final values after (a) a 500-mL fluid bolus immediately after induction (steady state) and tracheal intubation before the start of the surgery, and (b) 250-mL boluses given in response to a decrease in stroke volume of 10% during surgery as measured by esophageal Doppler (dynamic). Patients were classified into responders and nonresponders based on a stroke volume increase of >10%.

**RESULTS:** Baseline PVI at the finger was significantly higher in responders in both steady-state and intraoperative conditions. In steady state, PVI at both finger and earlobe had significant predictive ability of an increase in stroke volume: area under the curve for finger 0.96 (95% confidence interval [CI], 0.88-1.00; P = 0.011) and for earlobe 0.98 (95% CI, 0.93-1.00; P = 0.008). In dynamic intraoperative conditions, PVI at the finger predicted increases in stroke volume, area under the curve 0.71 (95% CI, 0.57-0.85; P = 0.006), but PVI at the earlobe had no predictive value.



**CONCLUSIONS:** PVI measured at the finger may be able to predict fluid responsiveness during surgery in ventilated patients.

### 在開腹手術中使用 PerfectTemp 和熱風加溫法的隨機比較

#### A Randomized Comparison of Intraoperative PerfectTemp and Forced-Air Warming During Open Abdominal Surgery

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**背景：** PerfectTemp 是在身體下面放置可以加溫並有緩衝壓力作用的彈性海綿，從而控制溫度的加溫系統。這個系統的臨床效果有待正式評估。因此我們該假設進行驗證：在全身麻醉下行開腹手術患者，通過測定術中遠端食管（核心）的溫度比較 PerfectTemp（身體下面控溫）加溫系統和上半身吹熱風的效果。

**方法：** 在全身麻醉下進行擇期開腹大手術（肝、胰、婦科和結腸手術）的成年患者被分到兩個中心。患者被隨機分為兩組：身體下面控溫和上半身吹熱風組。身體下面控溫組當患者被轉運至手術室床上系統開始加熱；上半身吹熱風組在患者鋪巾後開始加熱。主要結果為在手術時間及體重平均的情況下，身體下面加溫的效果不比上半身吹熱風差，調整基線特徵並使用 0.5°C 的緩衝。

**結果：** 36 例患者被隨機安排到身體下面控溫組，34 例患者被安排到上半身吹熱風組。兩組患者的基線溫度和手術特點大體相似。我們有足夠的證據得出結論 ( $P = 0.018$ )：在手術時間及體重相似的情況下，身體下面控溫組的效果不比上半身吹熱風組差，他們只有 -0.12°C 的微小差別（95% 的置信區間為 -0.37 到 0.14）。手術結束時的核心溫度在身體下面控溫組組為 36.3°C（95% CI 為 36 到 36.5），在上半身吹熱風組組為 36.6（95% CI 為 36.4 到 36.8），兩者之間的平均差別為 -0.34°C（95% CI 為 -0.69 到 0.01）。

**結論：** 手術時間及體重平均的情況下，身體下面控溫組的保溫效果不比上半身吹熱風組差。身體下面加溫裝置可能是上半身吹熱風的一種替換的選擇。

（劉珏瑩譯 薛張綱校）

**BACKGROUND:** The PerfectTemp is an underbody resistive warming system that combines servocontrolled underbody warming with viscoelastic foam pressure relief. Clinical efficacy of the system has yet to be formally evaluated. We therefore tested the hypothesis that intraoperative distal esophageal (core) temperatures with the PerfectTemp (underbody resistive) warming system are noninferior to upper-body forced-air warming in patients undergoing major open abdominal surgery under general anesthesia.

**METHODS:** Adults scheduled for elective major open abdominal surgery (liver, pancreas, gynecological, and colorectal surgery) under general anesthesia were enrolled at 2 centers. Patients were randomly assigned to underbody resistive or forced-air warming. Resistive heating started when patients were transferred to the operating room table; forced-air warming started after patients were draped. The primary outcome was

noninferiority of intraoperative time-weighted average core temperature, adjusted for baseline characteristics and using a buffer of 0.5°C.

**RESULTS:** Thirty-six patients were randomly assigned to underbody resistive heating and 34 to forced-air warming. Baseline and surgical characteristics were generally similar. We had sufficient evidence ( $P = 0.018$ ) to conclude that underbody resistive warming is not worse than (i.e., noninferior to) upper-body forced-air warming in the time-weighted average intraoperative temperature, with a mean difference of  $-0.12^{\circ}\text{C}$  [95% confidence interval (CI)  $-0.37$  to  $0.14$ ]. Core temperatures at the end of surgery averaged  $36.3^{\circ}\text{C}$  [95% CI  $36$  to  $36.5$ ] in the resistive warming patients and  $36.6^{\circ}\text{C}$  [95% CI  $36.4$  to  $36.8$ ] in those assigned to forced-air warming for a mean difference of  $-0.34^{\circ}\text{C}$  [95% CI  $-0.69$  to  $0.01$ ].

**CONCLUSIONS:** Mean intraoperative time-weighted average core temperatures were no different, and significantly noninferior, with underbody resistive heating in comparison with upper-body forced-air warming. Underbody resistive heating may be an alternative to forced-air warming.

### 一項比較頭上抬 30 度和仰臥位兩種體位下，對於臨產婦肺功能殘氣量 (FRC) 的影響差別隨機對照試驗研究

#### A Randomized Crossover Study to Determine the Effect of a 30° Head-Up Versus a Supine Position on the Functional Residual Capacity of Term Parturients

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**背景：**產科的氣道管理對於麻醉科醫生來講一直是一項挑戰。作為氧氣的儲存庫，功能殘氣量在妊娠的 6 個月之後減少，而在仰臥位的時候減少更加明顯。在呼吸暫停之後，增加 FRC 可能會延遲低氧血症的開始。目前尚未可知半直立位的體位對於臨產婦 FRC 改變的價值是怎麼樣的。我們假設認為，與仰臥位相比較，頭上抬 30 度對於健康臨產婦的 FRC 的增加是有幫助的。

**方法：**22 位健康臨產婦納入我們的研究。早期進行的肺功能的檢查是用以除外原先是否有肺的基礎疾病。通過氦稀釋的方法來測定平臥位、頭上抬 30 度、坐位三種體位 FRC 的量。受測者隨機被安排不同的體位進行測定。另外，在每個測試體位下，進行無創血壓、心率以及氧飽和度的測量。

**結果：**分析 20 位受測者的測量結果。每位受測者基礎肺功能的檢查均在正常範圍內。不同體位下 FRC 的測定結果則意義顯著 ( $p < 0.001$ )。從平臥位到頭上抬 30

度，FRC 平均增加了 188ml ( $p=0.03$ ，95% 置信區間是 18-358ml)。其他生命體征上各種體位下的比較並沒有差異 ( $p>0.16$ )。

**結論：**經過我們的研究認為，健康臨產婦的 FRC 在頭上抬 30 度的體位下要比平臥位明顯要多。

(陸麗虹譯 薛張綱校)

**BACKGROUND:** Airway management continues to pose challenges to the obstetric anesthesiologist. Functional residual capacity (FRC), which acts as an oxygen reservoir, is reduced from the second trimester onwards and is exacerbated in the supine position. Mechanisms to increase FRC may delay the onset of hypoxemia during periods of apnea. Values for changes in FRC in term parturients in semierect positions are unknown. We hypothesized that the FRC of healthy term parturients would increase significantly in the 30° head-up position in comparison with the supine position.

**METHODS:** Twenty-two healthy term parturients were recruited. Initial screening spirometry was performed to exclude undiagnosed respiratory disease. FRC was measured using the helium dilution technique in the supine, 30° head-up, and sitting erect positions. Subjects were randomized to sequence of position testing order. Noninvasive systolic blood pressure, heart rate, and oxygen saturation were measured twice in each testing position.

**RESULTS:** Results from 20 subjects were analyzed. The spirometry results for all subjects were within predicted normal reference intervals. FRC measurements differed significantly ( $P < 0.001$ ) among all positions. FRC increased by a mean of 188 mL (95% confidence interval 18 to 358 mL) from the supine to the 30° head-up position ( $P = 0.03$ ). There were no significant differences in vital signs among testing positions ( $P > 0.16$ ).

**CONCLUSIONS:** We have demonstrated that the FRC of healthy term parturients increases significantly in the 30° head-up position in comparison with supine.

### 綜述：右旋美托嘧啶在兒童中的應用：現狀與展望

#### Reviewarticle: dexmedetomidine in children: current knowledge and future applications.

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**摘要：**關於右旋美托嘧啶在嬰兒和兒童中的應用目前已有 200 多個研究和報導發表。我們回顧了其中的英文文獻，總結了實踐麻醉學家對於此藥在兒科應用目前的認識。右旋美托嘧啶對於嬰兒和兒童來說是一種有效的鎮靜劑，其幾乎不抑制呼吸系統，保持了呼吸道開放。但是右旋美托嘧啶抑制了心血管系統。特別是心動過緩、低血壓和高血壓根據兒童年齡不同程度的發生。低血壓更易發生於使用大劑量右旋美托嘧啶後的嬰兒。與其 2 小時的消除半衰期相一致，使用右旋美托嘧啶後蘇醒期較其他鎮靜藥延長。右旋美托嘧啶產生和增強鎮痛作用，並且減少了術後寒戰

和躁動。在有適當監護和干預來管理心血管結局的情況下，右旋美托嘧啶使用的安全記錄提示該藥可安全有效用於兒童。

（任雲譯 薛張綱校）

**Abstract:** More than 200 studies and reports have been published regarding the use of dexmedetomidine in infants and children. We reviewed the English literature to summarize the current state of knowledge of this drug in children for the practicing anesthesiologist. Dexmedetomidine is an effective sedative for infants and children that only minimally depresses the respiratory system while maintaining a patent airway. However, dexmedetomidine does depress the cardiovascular system. Specifically, bradycardia, hypotension, and hypertension occur to varying degrees depending on the age of the child. Hypertension is more prevalent when larger doses of dexmedetomidine are given to infants. Consistent with its 2-hour elimination half-life, recovery after dexmedetomidine may be protracted in comparison with other sedatives. Dexmedetomidine provides and augments analgesia and diminishes shivering as well as agitation postoperatively. The safety record of dexmedetomidine suggests that it can be used effectively and safely in children, with appropriate monitoring and interventions to manage cardiovascular sequelae.

**S 型氯胺酮在體外通過抑制神經元  $Ca^{2+}$  的振盪，從而在發揮其分化神經元的毒性作用**

### **The Toxic Effects of S(+)-Ketamine on Differentiating Neurons In Vitro as a Consequence of Suppressed Neuronal $Ca^{2+}$ Oscillations**

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**背景：**在未成熟的大腦中，在一段高度塑型期中，神經元的  $Ca^{2+}$  振盪會出現，並調節神經元的分化和突觸發生。在這項研究中，我們研究了長期阻斷海馬的  $Ca^{2+}$  振盪，它是 NMDA 受體的重要角色，並影響了 S 型氯胺酮在神經元突觸蛋白的表達。

**方法：**海馬的神經元被放在有特殊 NMDA 受體拮抗劑地佐環平中培養15天或者 S 型氯胺酮中培養24小時。末端去氧核苷酸轉移酶（TUNEL）和活化的半胱天冬酶用來檢測凋亡的神經元。給神經元染色後檢測  $Ca^{2+}$  振盪，並用雙波長螢光顯微鏡觀察。用 western 印跡來測量  $Ca^{2+}$ /鈣調節蛋白激酶 II。用共焦點抗突觸蛋白免疫螢光法來鑒定突觸蛋白。

**結果：**用 MK801 或者 S 型氯胺酮去阻滯 NMDA 受體會引起神經元凋亡增加。MK801 導致細胞溶質中  $Ca^{2+}$  濃度顯著增加，並減少  $Ca^{2+}$  振盪的幅度和頻率。和 MK801 相似，長期使用 S 型氯胺酮可導致沖洗後24小時內細胞溶質中  $Ca^{2+}$  濃度顯著增加。這與下調了  $Ca^{2+}$ /鈣調節蛋白激酶 II 並降低沖洗後24小時內突觸蛋白有關係。

**結論：**神經元  $\text{Ca}^{2+}$  振盪通過啓動  $\text{Ca}^{2+}$ /鈣調節蛋白激酶 II，介導了神經元的分化和突觸發生。通過作用於 NMDA 受體，S 型氫胺酮通過抑制神經元  $\text{Ca}^{2+}$  振盪，下調  $\text{Ca}^{2+}$ /鈣調節蛋白激酶 II，連續地減低突觸的完整性，從而來發揮其毒性作用。

(翁梅琳譯 薛張綱校)

**Background:** In the immature brain, neuronal  $\text{Ca}^{2+}$  oscillations are present during a time period of high plasticity and regulate neuronal differentiation and synaptogenesis. In this study we examined the long-term blockade of hippocampal  $\text{Ca}^{2+}$  oscillations, the role of the *N*-methyl-d-aspartate (NMDA) receptors and the effects of S(+)-ketamine on neuronal synapsin expression.

**Methods:** Hippocampal neurons were incubated at day 15 in culture with the specific NMDA receptor antagonists dizocilpine (MK 801, 100  $\mu\text{M}$ ) or S(+)-ketamine (3  $\mu\text{M}$  to 25  $\mu\text{M}$ ) for 24 hours. Terminal-deoxynucleotidyl-transferase (TUNEL) and activated caspase3 were used to detect apoptotic neurons.  $\text{Ca}^{2+}$  oscillations were detected after loading the neurons with the  $\text{Ca}^{2+}$ -sensitive dye fura-2AM, and dual wavelength excitation fluorescence microscopy was performed.  $\text{Ca}^{2+}$ /calmodulin kinase II (CaMKII) was measured using Western blots. Synapsin was identified with confocal antisynapsin immunofluorescence.

**Results:** Blocking the NMDA receptor with MK 801 or 25  $\mu\text{M}$  S(+)-ketamine resulted in a significant increase in apoptotic neurons. MK 801 led to a significant increase in cytosolic  $\text{Ca}^{2+}$  concentration and reduction of the amplitude and frequency of the  $\text{Ca}^{2+}$  oscillations. Similar to MK 801, the long-term application of S(+)-ketamine resulted in a significant increase in cytosolic  $\text{Ca}^{2+}$  concentration 24 hours after washout. This was associated with a down-regulation of the CaMKII and a reduction of the synapsin 24 hours after washout.

**Conclusion:** Neuronal  $\text{Ca}^{2+}$  oscillations mediate neuronal differentiation and synaptogenesis via activating CaMKII. By acting via the NMDA receptor, S(+)-ketamine exerts its toxic effect through the suppression of neuronal  $\text{Ca}^{2+}$  oscillations, down-regulation of the CaMKII, and consecutively reduced synaptic integrity.

### 在一個三級轉診中心麻醉過程中的過敏反應

**Allergic Reactions During Anesthesia at a Large United States Referral Center**  
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**背景:**能引起術中過敏反應的藥物根據報導不盡相同，且在美國近期沒有相關報導。在本回顧性研究中，我們回顧了一個大型三級轉診中心的圍術期過敏反應。**方法:**爲了明確與過敏反應相關的圍術期過敏原，我們回顧了 1992 年至 2010 年 Mayo 臨床中心的過敏性皮膚測試資訊。回顧內容包括了所有接受圍術期及麻醉藥物過敏原檢測的病人。過敏專家處獲得的詳細病史，皮膚檢測結果和類胰蛋白酶檢測均記錄入病歷。

**結果:**38 名病人在麻醉時發生過敏反應，其中有 18 例為 IgE 介導的過敏反應（根據皮膚檢測確定的疑似藥物），6 例為非 IgE 介導的過敏反應（類胰蛋白酶水準升高，皮膚測試陰性），14 例可能是非 IgE 介導的過敏反應（類胰蛋白酶水準正常或者未獲得，皮膚測試陰性）。在所有 IgE 介導的過敏反應中，抗生素是最常見的過敏原（50%），而神經肌肉阻滯藥物占了 11%。

**結論:**抗生素是 IgE 介導的過敏反應中最常見的過敏原；然而，52.6%的過敏反應中，並不能明確過敏原，提示其為非 IgE 介導的過敏反應。未明確過敏原的過敏反應使得病人可能持續暴露于同一過敏原，也可能導致本來安全的藥物治療。

（姚敏敏譯 薛張綱校）

**BACKGROUND:** The types of agents implicated to trigger intraoperative anaphylactic reactions vary among reports, and there are no recent series from the United States. In this retrospective study, we examined perioperative anaphylactic reactions that occurred at a major tertiary referral academic center.

**METHODS:** To characterize perioperative allergens associated with anaphylactic reactions, we reviewed the Mayo Clinic Division of Allergic Diseases skin test database between 1992 to 2010. The records of all patients who were tested for perioperative and anesthetic medications were reviewed. Charts that included a detailed history obtained by an allergist, skin test results, and tryptase measurements when available were reviewed and categorized.

**RESULTS:** Thirty-eight patients were found to have an anaphylactic reaction during anesthesia, of which 18 were immunoglobulin (Ig)E-mediated anaphylactic reactions (likely causative agent identified by skin test), 6 were non-IgE-mediated anaphylactic reactions (elevated tryptase levels and negative skin test), and 14 were probable non-IgE-mediated anaphylactic reactions (tryptase levels normal or not obtained and negative skin test). Of the IgE-mediated anaphylactic reactions, antibiotics were the most prevalent likely causative agent (50%) whereas neuromuscular blocking drugs were implicated as a likely causative agent in 11% of reactions.

**CONCLUSION:** Antibiotics were the most common likely causative agent associated with IgE-mediated anaphylactic reactions; however, for 52.6% of reactions, a causative agent could not be determined, suggesting a non-IgE-mediated anaphylactic reaction. The undiagnosed allergic reactions place patients at risk of a subsequent reexposure to the same allergen, or lead to unnecessary avoidance of needed medications.

胸段硬膜外使用布比卡因減輕炎症反應，腸脂質過氧化，氧化損傷，腸系膜缺血/再灌注誘導的胃黏膜上皮細胞凋亡

**Thoracic epidural bupivacaine attenuates inflammatory response, intestinal lipid peroxidation, oxidative injury, and mucosal apoptosis induced by mesenteric ischemia/reperfusion.**

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**背景：**我們進行這項研究，以評估胸段硬膜外麻醉（TEA）對大鼠腸系膜缺血/再灌注（I/R）模型的炎症反應、脂質過氧化和氧化應激的影響。

**方法：**大鼠分為4組：假手術組（N=6，深水剖腹手術），對照組（N=6，I/R），布比卡因組（N=6；腸系膜 I/R，20  $\mu$ L/h 的 0.5% 布比卡因）和生理鹽水組（N=6，腸系膜 I/R，20  $\mu$ L/h 的 0.9% 生理鹽水）。I/R 損傷由腸系膜上動脈夾閉 1 小時、12 小時後再灌注誘發。檢測血氣，腫瘤壞死因數- $\alpha$ ，白細胞介素-6，白細胞介素-1 $\beta$ ，谷胱甘肽 peroxidase，超氧化物歧化酶，catalase，髓過氧化物酶濃度，免疫組化考試（細胞間黏附分子-1），細胞凋亡和腸道水腫的幹/濕比例。

**結果：**布比卡因顯著減低細胞因數，丙二醛，髓過氧化物酶水準而增加抗氧化酶的水準。濕/幹比比比較顯示，布比卡因組（2.88 $\pm$ 0.17）相較與對照組（5.45 $\pm$ 0.67）和生理鹽水組（5.87 $\pm$ 0.17）顯著降低。在，硬膜外布比卡因（2[1-2]）輸注組與對照組（3[2-3]）和生理鹽水（3[2-4]）組相比大鼠腸道損傷評分顯著下降。布比卡因（63%）僅比對照組細胞凋亡的百分比（85%）有明顯的下降。布比卡因（27.4 $\pm$ 7.1）組與對照組（12.3 $\pm$ 7.4）和生理鹽水組（24.9 $\pm$ 3.2）比較，ICAM-1 水準下降。

**結論：**這項研究表明，硬膜外布比卡因減少了腸系膜 I/R-相關的炎症反應和腸道損傷。

（張玥琪譯，薛張綱校）

**BACKGROUND:** We conducted this study to evaluate the effects of thoracic epidural anesthesia (TEA) on inflammatory response, lipid peroxidation, and oxidative stress in a rat model of mesenteric ischemia/reperfusion (I/R).

**METHOD:** Rats were divided into 4 groups: sham group (n = 6; sham laparotomy), control group (n = 6; I/R), bupivacaine group (n = 6; mesenteric I/R and 20  $\mu$ L/h 0.5% bupivacaine), and saline group (n = 6, mesenteric I/R and 20  $\mu$ L/h 0.9% saline). I/R injury was established by occluding the superior mesenteric artery for 1 hour followed by 12 hours reperfusion. Blood gas, tumor necrosis factor- $\alpha$ , interleukin-6, interleukin-1 $\beta$ , glutathione peroxidase, superoxide dismutase, catalase, myeloperoxidase concentrations, immunohistochemical examinations (intracellular adhesion molecule-1), apoptosis determination, and wet/dry ratio of intestinal edema were determined.

**RESULTS:** Bupivacaine significantly decreased the cytokine, malondialdehyde, and myeloperoxidase levels and increased the antioxidant enzyme levels. Wet/dry ratio comparison showed a significant decrease in the bupivacaine (2.88  $\pm$  0.17) group in comparison with control (5.45  $\pm$  0.67) and saline (5.87  $\pm$  0.17) groups. The intestinal injury score was significantly decreased in rats in the epidural bupivacaine (2 [1-2]) infusion group in comparison with rats in the control (3 [2-3]) and saline (3 [2-4]) groups. Bupivacaine (63%) caused a significant decrease in the percentage of apoptotic cells in comparison with control (85%) only. ICAM-1 levels in the bupivacaine (27.4  $\pm$  7.1) group decreased in comparison with control (12.3  $\pm$  7.4) and saline (24.9  $\pm$  3.2) groups.

**CONCLUSION:** This study demonstrated that epidural bupivacaine attenuates the mesenteric I/R-related inflammatory response and intestinal damage.

**氯胺酮通過啓動 L-精氨酸/一氧化氮/cGMP 通路導致大鼠外周鎮痛作用**

**Ketamine Activates the L-Arginine/Nitric Oxide/Cyclic Guanosine Monophosphate Pathway to Induce Peripheral Antinociception in Rats**

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**背景：**許多鎮痛藥物通過作用於 L-精氨酸/一氧化氮/cGMP 通路達到鎮痛作用，包括  $\mu$ 、 $\kappa$  或  $\delta$  阿片受體激動劑、非甾體類抗炎藥、膽鹼能受體激動劑和  $\alpha_{2C}$  腎上腺能受體激動劑。在我們的這項研究中，我們研究了氯胺酮——一種分離性麻醉藥物 NMDA 受體拮抗劑，是否也是通過 L-精氨酸/一氧化氮/cGMP 通路導致外周鎮痛作用。

**方法：**在大鼠足底注射前列腺素 E2 誘導痛覺，並測定腳爪壓力。所有的藥物均局部注射入雄性 Wistar 大鼠的後爪。

**結果：**氯胺酮 (10, 20, 40, 80  $\mu\text{g}/\text{爪}$ ) 所致的局部鎮痛作用可以被非選擇性 NOS 抑制劑 L-NOARG (12, 18, 和 24  $\mu\text{g}/\text{爪}$ ) 或選擇性 NOS 抑制劑 L-NPA (12, 18, 和 24  $\mu\text{g}/\text{爪}$ ) 拮抗。在另一項實驗中，我們使用抑制劑 L-NIO 和 L-NIL (24  $\mu\text{g}/\text{爪}$ ) 分別選擇性地抑制內皮及誘導的 NOS。這兩種藥物都不能有效的阻斷外周使用氯胺酮的作用。此外爪均質的亞硝酸鹽的水準提示外源性氯胺酮可以增加 NO 的釋放。可溶性的鳥苷醯環化酶抑制劑 ODQ (25, 50 和 100  $\mu\text{g}/\text{爪}$ ) 可以阻斷氯胺酮的作用，cGMP-磷酸二酯酶抑制劑 敏喘寧 (50  $\mu\text{g}/\text{爪}$ ) 可以增強低劑量氯胺酮 (10  $\mu\text{g}/\text{爪}$ ) 的鎮痛作用。

**結論：**我們的結果提示氯胺酮通過 NO 合酶刺激 L-精氨酸/NO/cGMP 通路，從而產生外周抗傷害性刺激的作用。

(陳珺珺譯 薛張綱校)

**Background:** The involvement of the L-arginine/nitric oxide (NO)/cyclic guanosine monophosphate (cGMP) pathway in antinociception has been implicated as a molecular mechanism of antinociception produced by several antinociceptive agents, including  $\mu$ -,  $\kappa$ -, or  $\delta$ -opioid receptor agonists, nonsteroidal analgesics, cholinergic agonist, and  $\alpha_{2C}$  adrenoceptor agonist. In this study, we investigated whether ketamine, a dissociative anesthetic N-methyl-D-aspartate receptor antagonist, was also capable of activating the L-arginine/NO/cGMP pathway and eliciting peripheral antinociception.

**Methods:** The rat paw pressure test was used, with hyperalgesia induced by intraplantar injection of prostaglandin E<sub>2</sub>. All drugs were locally administered into the right hindpaw of male Wistar rats.

**Results:** Ketamine (10, 20, 40, 80  $\mu\text{g}/\text{paw}$ ) elicited a local antinociceptive effect that was antagonized by the nonselective NOS inhibitor L-NOARG (12, 18, and 24  $\mu\text{g}/\text{paw}$ ) and by the selective neuronal NOS inhibitor L-NPA (12, 18, and 24  $\mu\text{g}/\text{paw}$ ). In another experiment, we used the inhibitors L-NIO and L-NIL (24  $\mu\text{g}/\text{paw}$ ) to selectively inhibit endothelial and inducible NOS, respectively. These 2 drugs were ineffective at blocking the effects of the peripheral ketamine injection. In addition, the level of nitrite in the homogenized paw indicated that exogenous ketamine is able to induce NO release. The soluble guanylyl cyclase inhibitor ODQ (25, 50, and 100  $\mu\text{g}/\text{paw}$ ) blocked the action of ketamine, and the cGMP-phosphodiesterase inhibitor zaprinast (50  $\mu\text{g}/\text{paw}$ ) enhanced the antinociceptive effects of low-dose ketamine (10  $\mu\text{g}/\text{paw}$ ).



**Conclusions:** Our results suggest that ketamine stimulates the L-arginine/NO/cyclic GMP pathway via neuronal NO synthase to induce peripheral antinociceptive effects

一項關於行膝關節鏡手術的隨機、雙盲研究：腰麻時在布比卡因中加入小劑量利多卡因不能縮短麻醉持續時間

### **The Addition of Lidocaine to Bupivacaine Does Not Shorten the Duration of Spinal Anesthesia : A Randomized, Double-Blinded Study of Patients Undergoing Knee Arthroscopy**

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**背景：**對於日間手術，使用布比卡因行腰麻的作用時間通常過長。最近一項研究提示行經尿道手術患者行腰麻時，在重比重布比卡因中加入小劑量的利多卡因可以縮短運動擊感覺阻滯的時間。在這項前瞻性、隨機、雙盲試驗中，我們對行單側膝關節鏡患者進一步研究上述發現。

**方法：**五十名患者隨機分為兩組：分別接受 2ml 重比重 0.5% 布比卡因加 0.6ml 1% 利多卡因（利多卡因組）或 0.6ml 生理鹽水（對照組）。分別監測感覺擊運動功能直到患者完全恢復直至準備出院。術後第二天及第 7 天分別隨訪有無任何副反應及短暫神經綜合症的任何症狀。

**結果：**總共獲得 45 名患者的資料並對其分析（利多卡因組有 24 例）。兩組在以下幾方面沒有統計學差異：可以滿足手術起效時間、最大程度感覺阻滯或運動阻滯的起效時間及持續時間及離開復蘇室的時間。對照組中的 2 名患者及試驗組中的 1 名患者在術後 24 小時內出現了短暫神經綜合症。一名患者出現排尿困難並持續三天。所有症狀都自行緩解。沒有患者出現背痛或頭痛。

**結論：**我們尚不能確定行膝關節鏡患者進行腰麻時，在重比重布比卡因中加入小劑量的利多卡因是否可以縮短感覺或運動阻滯持續時間，以及是否可以縮短離開復蘇室的時間。

（陳珺珺譯 薛張綱校）

**BACKGROUND:** The duration of spinal anesthesia with bupivacaine is often too long for day surgery. A recent study of patients presenting for transurethral surgery suggested that the addition of a small amount of lidocaine to intrathecal hyperbaric bupivacaine could shorten the duration of the sensory and motor blocks. In this prospective, randomized double-blind study we investigated these findings in patients undergoing unilateral knee arthroscopy.

**METHODS:** Fifty patients were randomized to receive 2 mL hyperbaric 0.5% bupivacaine plus either 0.6 mL 1% lidocaine (lidocaine group) or 0.6 mL saline (control group). The sensory and motor blocks were monitored until complete regression and the patient was ready for discharge. The patients were interviewed 2 and 7 days after the operation about any side effects and any signs of transient neurologic syndrome.

**RESULTS:** Data on 45 patients were available for analysis (24 in the lidocaine group). There was no statistically significant difference between the groups regarding time to readiness for surgery, maximum level of sensory block, total duration of sensory, and motor blocks or time to discharge from the postoperative care unit. Two patients in the control group and 1 patient in the study group had symptoms of transient neurologic syndrome for <24 hours after the operation. One patient had voiding difficulties for 3 days. All symptoms resolved spontaneously. No patient had spinal headache or backache. **CONCLUSION:** We did not confirm, in patients undergoing knee arthroscopy, that the addition of a small dose of lidocaine to intrathecal hyperbaric bupivacaine could shorten the duration of sensory or motor blocks or time to readiness for discharge from the postanesthesia care unit.

### 心臟手術中使用肺動脈導管缺乏有效性

#### Lack of Effectiveness of the Pulmonary Artery Catheter in Cardiac Surgery

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**背景：**儘管肺動脈導管（PAC）的安全性和有效性的關注度在提高，其仍然一直廣泛用於心臟搭橋術中的血流動力學監測。考慮到冠脈搭橋病人使用 PAC 的資料相對缺乏以及臨床實踐的不易改變，作者在不同的醫學中心評估了致命、非致命冠脈搭橋病人使用 PAC 的效果。

**方法：**設計前瞻性觀察實驗：一共收錄了從 1996 年 11 月到 2000 年 6 月間，70 個中心共 5065 個病人。用傾向性因數配對分析來調整置入肺動脈導管時不同的可能性。如果出現以下結果，則預定試驗結束：死亡（不論原因），心功能異常（心梗或充血性心衰），腦功能障礙（腦梗或腦病），腎功能障礙（異常或腎衰），肺功能異常（ARDS），第二變數包括治療（強心藥的使用，液體管理），術後插管時間，ICU 入住時間。分類基礎是 PAC 和經食管超聲心動圖的使用（都使用，都不使用，僅使用 PAC 及僅使用經食管超聲心動圖）。作者對比了僅使用 PAC 和都不用的患者（共 3321 例病人），共產生 1273 組配對。

**結果：**有 271 例 PAC 病人和 196 例未使用 PAC 病人試驗終止 (21.3% vs.15.4%; 調整優勢比[AOR]：1.68; 95% 可信區間 [CI], 1.24 to 2.26;  $P < 0.001$ )。PAC 組死亡率 3.5% 對 1.7% (AOR, 2.08; 95% CI, 1.11 to 3.88;  $P = 0.02$ )，心功能異常 (AOR, 1.58; 95% CI, 1.14 to 2.20;  $P = 0.007$ )，腦功能異常 (AOR, 2.02; 95% CI, 1.08 to 3.77;  $P = 0.03$ )，腎功能異常 (AOR, 2.47; 95% CI, 1.68 to 3.62;  $P < 0.001$ )。PAC 病人使用更多的強心藥 (57.8% vs 50.0%;  $P < 0.001$ )，更多的靜脈補液 (3220 mL vs 3022 mL;  $P = 0.003$ )，以及更長的拔管時間 (15.40 hours [11.28/20.80] 對 13.18 hours [9.58/19.33], 中位數加 Q1/Q3 四分位間距;  $P < 0.0001$ )，使用 PAC 也與入 ICU 時間延長有關 (14.5% vs 10.1%; AOR, 1.55; 95% CI, 1.06 to 2.27;  $P = 0.02$ )。**結論：**在這個匹配觀察實驗中，心臟搭橋術中使用肺動脈導管與高死亡率和終末器官併發症有關。理想的是今後以血流動力學目標的隨機對照研究以證實或否定這一觀察結果。

(範逸辰 譯 陳傑 校)

**BACKGROUND:** The pulmonary artery catheter (PAC) continues to be used for monitoring of hemodynamics in patients undergoing coronary artery bypass graft (CABG) surgery despite concerns raised in other settings regarding both effectiveness and safety. Given the relative paucity of data regarding its use in CABG patients, and given entrenched practice patterns, we assessed the impact of PAC use on fatal and nonfatal CABG outcomes as practiced at a diverse set of medical centers.

**METHODS:** Using a formal prospective observational study design, 5065 CABG patients from 70 centers were enrolled between November 1996 and June 2000 using a systemic sampling protocol. Propensity score matched-pair analysis was used to adjust for differences in likelihood of PAC insertion. The predefined composite endpoint was the occurrence of any of the following: death (any cause), cardiac dysfunction (myocardial infarction or congestive heart failure), cerebral dysfunction (stroke or encephalopathy), renal dysfunction (dysfunction or failure), or pulmonary dysfunction (acute respiratory distress syndrome). Secondary variables included treatment indices (inotrope use, fluid administration), duration of postoperative intubation, and intensive care unit length of stay. After categorization based on PAC and transesophageal echocardiography use (both, neither, PAC only, transesophageal echocardiography only), we performed the primary analysis contrasting PAC only and neither (total, 3321 patients), from which propensity pairing yielded 1273 matched pairs.

**RESULTS:** The primary endpoint occurred in 271 PAC patients versus 196 without PAC (21.3% vs.15.4%; adjusted odds ratio [AOR], 1.68; 95% confidence interval [CI], 1.24 to 2.26;  $P < 0.001$ ). The PAC group had an increased risk of all-cause mortality, 3.5% vs 1.7% (AOR, 2.08; 95% CI, 1.11 to 3.88;  $P = 0.02$ ) and an increased risk of cardiac (AOR, 1.58; 95% CI, 1.14 to 2.20;  $P = 0.007$ ), cerebral (AOR, 2.02; 95% CI, 1.08 to 3.77;  $P = 0.03$ ) and renal (AOR, 2.47; 95% CI, 1.68 to 3.62;  $P < 0.001$ ) morbid outcomes. PAC patients received inotropic drugs more frequently (57.8% vs 50.0%;  $P < 0.001$ ), had a larger positive IV fluid balance after surgery (3220 mL vs 3022 mL;  $P = 0.003$ ), and experienced longer time to tracheal extubation (15.40 hours [11.28/20.80] versus 13.18 hours [9.58/19.33], median plus Q1/Q3 interquartile range;  $P < 0.0001$ ). Use of PAC was also associated with prolonged intensive care unit stay (14.5% vs 10.1%; AOR, 1.55; 95% CI, 1.06 to 2.27;  $P = 0.02$ ).

**CONCLUSIONS:** Use of a PAC during CABG surgery was associated with increased mortality and a higher risk of severe end-organ complications in this propensity-matched observational study. A randomized controlled trial with defined hemodynamic goals would be ideal to either confirm or refute our findings.

### 梗阻性黃疸患者其依託咪酯的需要量減少

#### The Etomidate Requirement Is Decreased in Patients with Obstructive Jaundice

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**背景:** 梗阻性黃疸患者對吸入麻醉藥的敏感性升高。在鼠類動物的大腦中，膽紅素能增強  $\gamma$ -氨基丁酸的 A/甘氨酸突觸傳遞。依託咪酯是一類非巴比妥類靜脈催眠藥，可以通過中樞神經系統的  $\gamma$ -氨基丁酸 A 受體產生鎮靜作用。作者假設梗阻性黃疸患者對依託咪酯的敏感性有所改變並就此研究。

**方法:** 本研究比較了梗阻性黃疸患者與膽紅素正常的慢性膽石症患者腦電雙頻指數達到 50 的依託咪酯的需要量。在達到預期值之前依託咪酯以 30  $\mu\text{g}/\text{kg}/\text{min}$  輸注。

**結果:** 梗阻性黃疸患者依託咪酯的需要量較對照組顯著減少 ( $150 \pm 46 \mu\text{g}/\text{kg}$  與  $206 \pm 74 \mu\text{g}/\text{kg}$ ,  $P = 0.007$ )，平均減少量為 56  $\mu\text{g}/\text{kg}$  (95% 置信區間: 16–96  $\mu\text{g}/\text{kg}$ )。另外，作者發現血清總膽紅素和依託咪酯需要量有顯著的負相關，Pearson  $r$  值為 -0.545，而  $r$  值的 95% 置信區間為 -0.791 到 -0.148。所有受試者在實驗中血流動力學穩定。

**結論:** 梗阻性黃疸患者依託咪酯麻醉達到腦電雙頻指數 50 時的需要量減少。

(俞劼晶 譯 陳傑 校)

**BACKGROUND:** Patients with obstructive jaundice have increased sensitivity to inhaled anesthetics. In rodent brain, bilirubin can enhance  $\gamma$ -aminobutyric acid A/glycinergic synaptic transmission. Etomidate is a nonbarbiturate hypnotic that induces sedation through  $\gamma$ -aminobutyric acid A receptors in the central nervous system. We tested the hypothesis that patients with obstructive jaundice have an altered sensitivity to etomidate.

**METHODS:** The study design was a comparison of etomidate requirements to reach a Bispectral Index of 50 in patients with obstructive jaundice versus patients with chronic cholelithiasis and normal bilirubin levels. Etomidate was infused at 30  $\mu\text{g}/\text{kg}/\text{min}$  until this end point was reached.

**RESULTS:** The etomidate requirement in the obstructive jaundice group was lower than that in the control group ( $150 \pm 46 \mu\text{g}/\text{kg}$  vs  $206 \pm 74 \mu\text{g}/\text{kg}$ ,  $P = 0.007$ ). The average decrease in etomidate requirement was 56  $\mu\text{g}/\text{kg}$  (95% confidence interval: 16–96  $\mu\text{g}/\text{kg}$ ). In addition, we found a significant negative correlation between serum total bilirubin and etomidate requirement with Pearson  $r$  of -0.545, and 95% confidence interval for  $r$  value (-0.791 to -0.148). All subjects were hemodynamically stable during the study.

**CONCLUSIONS:** Etomidate requirements to reach a level of anesthesia defined by a Bispectral Index of 50 are reduced in patients with obstructive jaundice.

### 心臟手術後無創多波長脈搏血氧飽和度測量血紅蛋白的準確度

#### The Accuracy of Noninvasive Hemoglobin Measurement by Multiwavelength Pulse Oximetry After Cardiac Surgery

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**背景：**2008年3月，Radical Masimo (Rad7; Masimo Corp., Irvine, CA) 公司開發提供了一種無創血紅蛋白監測儀。它的準確度已經在健康成人和一些外科手術病人中得到證實，但對於心臟術後重症監護的有術後出血和貧血事件高風險的人群的早期診斷，它的準確度還未得到證實。

**方法：**一項在心血管重症監護室進行的前瞻性觀察研究，作者比較使用 Rad7 監測出的血紅蛋白值和使用 XE-2100 血細胞分析儀 (羅氏，塞納河，法國) 檢測出的動脈血紅蛋白值。Rad7 的兩個軟體版本 (V 7.3.0.1, 14 個病人中 42 點比較；升級版本 V7.3.1.1, 27 個病人中 61 點比較) 在兩個為一周的周期間研究。偏差定義為這兩種方法 (Masimo SpHb 和 XE-2100 測得血紅蛋白) 之間的差異。負偏差定義為 Masimo 測得血紅蛋白值低於實驗室分析儀的測量值。Rad7 的灌注指數和血紅蛋白偏差值之間的相關性也進行的研究。

**結果：**Rad 和 XE-2100 之間的相關性很小，兩個版本 V 7.3.0.1 和 V 7.3.1.1 的相關性分別為 0.11 和 0.27。V 7.3.0.1 和 V 7.3.1.1 版本的平均偏差分別為 -1.3g/dl 和 -1.7g/dl，95% 預測區間分別為 -4.6-2.1g/dl 和 -5.7-2.3 g/dl。隨著灌注指數的下降血紅蛋白偏差的絕對值增加。V 7.3.0.1 版本，當灌注指數 <2 時和 >2 時的平均偏差絕對值分別為 1.9 g/dL 和 0.8g/dL ( $P = 0.03$ )。V 7.3.1.1 版本，當灌注指數 <2 時和 >2 時的平均偏差絕對值分別為 2.1g/dL 和 1.6g/dL ( $P = 0.26$ )。

**結論：**作者的研究表明多波長脈搏血氧飽和度測量的無創血紅蛋白和實驗室血液分析儀測量出的血紅蛋白值之間相關性較差。當脈搏灌注指數較小時兩者差異較大，如在發生休克、體溫過低或血管收縮的病人。多波長血氧飽和度監測血紅蛋白在心血管重症監護室中的臨床應用並不精確。

(滕凌雅 譯 陳傑 校)

**BACKGROUND:** In March 2008, a new multiwavelength pulse oximeter, the Radical 7 (Rad7; Masimo Corp., Irvine, CA), was developed that offers noninvasive measurement of hemoglobin concentration. Accuracy has been established in healthy adults and some surgical patients, but not in cardiac surgery intensive care patients, a group at high risk of postoperative bleeding events and anemia in whom early diagnosis could improve management.

**METHODS:** In this prospective, observational study conducted in a cardiovascular intensive care unit, we compared hemoglobin concentrations shown by the Rad7 with

arterial hemoglobin concentrations determined by an automated hematology analyzer, XE-2100 (Roche, Neuilly sur Seine, France). Two software versions of Rad7 (V 7.3.0.1 [42 points of comparison in 14 patients] and the updated V 7.3.1.1 [61 points of comparison in 27 patients]) were studied during two 1-week periods. Bias, defined as the difference between the 2 methods (Masimo SpHb – XE-2100 laboratory hemoglobin), was calculated. A negative bias indicated that the Masimo underestimated hemoglobin compared with the laboratory analyzer. Correlation between the perfusion index given by Rad7 and the hemoglobin bias was also studied.

**RESULTS:** Correlations between Rad7 and XE-2100 were weak for both software versions ( $R^2 = 0.11$  for V 7.3.0.1 and  $R^2 = 0.27$  for V 7.3.1.1). Mean bias was  $-1.3$  g/dL for V 7.3.0.1 and  $-1.7$  g/dL for V 7.3.1.1, with wide 95% prediction intervals for the bias (respectively,  $-4.6$  to  $2.1$  g/dL and  $-5.7$  to  $2.3$  g/dL). The absolute hemoglobin bias tended to increase when the perfusion index decreased. For the V 7.3.0.1 software, the average absolute bias was  $1.9$  g/dL for perfusion index  $<2$  and  $0.8$  g/dL for perfusion index  $>2$  ( $P = 0.03$ ). For V 7.3.1.1, the mean absolute bias was  $2.1$  g/dL when the perfusion index was  $<2$ , and  $1.6$  g/dL when the perfusion index was  $>2$  ( $P = 0.26$ ).

**CONCLUSIONS:** Our study demonstrates poor correlation between hemoglobin measured noninvasively by multiwavelength pulse oximetry and a laboratory hematology analyzer. The difference was greater when the pulse oximetry perfusion index was low, as may occur in shock, hypothermia, or vasoconstriction patients. The multiwavelength pulse oximetry is not sufficiently accurate for clinical use in a cardiovascular intensive care unit.

#### 45°特倫德倫伯格臥位下機器人協助腹腔鏡前列腺癌根治術時血流動力學的變化 Hemodynamic Perturbations During Robot-Assisted Laparoscopic Radical Prostatectomy in 45° Trendelenburg Position

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**背景：**機器人協助的腹腔鏡下前列腺癌根治術已被廣泛應用。然而當患者置於完全的特倫德倫伯格臥位(45°)時的血流動力學變化尚未闡明。

**方法：**作者研究了 16 例平均年齡為 59 歲 (ASA 分級為 I-II)，擇期行機器人協助的腹腔鏡下前列腺癌根治術的患者 (45°頭低位，腹腔內壓力位 11–12 mm Hg)。採集氣腹前以及氣腹期間、擺置特倫德倫伯格臥位時以及手術後的血流動力學參數、超聲心動圖、氣體交換以及肺通氣-灌注係數等各種資料，

**結果：**在 45°頭低位時，中心靜脈壓力較基礎值升高了 3 倍，平均肺動脈壓力以及肺毛細血管楔壓增加 2 倍 ( $P < 0.01$ )。平均動脈壓力增加 35%。心率，每搏輸出量，心排量以及混合靜脈血氧飽和度以及超聲心動圖下心臟大小在術中並未改變。麻醉誘導後，等容舒張期延長，在術中並未有進一步改變。減速時間是正常的並且穩定。氣腹放氣置於平臥位時，充盈壓已經平均動脈呀恢復至基礎水準。氣腹

減少了肺順應性 40% ( $P < 0.01$ )。增加了 45°頭低位時引起了進一步減少( $P < 0.05$ )。動脈血氣酸堿平衡在術中是正常的。肺通氣量不改變的情況下呼氣末二氧化碳壓力增加的同時動脈血二氧化碳分壓並未受影響。氣腹增加了 PaO<sub>2</sub> ( $P < 0.05$ )。通氣-灌注比例，以及死腔通氣在術中保持不變。

**結論：**氣腹以及 45°頭低位引起了 2-3 倍充盈壓的增加，心功能並未受影響。充盈壓在術後馬上回復至基礎值。肺順應性減少，氣體交換並未受影響。手術期間心血管併發症並未出現。

(龔寅 譯 陳傑 校)

**BACKGROUND:** Robot-assisted laparoscopic radical prostatectomy has gained widespread use. However, circulatory effects in patients subjected to an extreme Trendelenburg position (45°) are not well characterized.

**METHODS:** We studied 16 patients (ASA physical status I–II) with a mean age of 59 years scheduled for robot-assisted laparoscopic radical prostatectomy (45° head-down tilt, with an intraabdominal pressure of 11–12 mm Hg). Hemodynamics, echocardiography, gas exchange, and ventilation-perfusion distribution were investigated before and during pneumoperitoneum, in the Trendelenburg position and, in 8 of the patients, also after the conclusion of surgery.

**RESULTS:** In the 45° Trendelenburg position, central venous pressure increased almost 3-fold compared with the initial value, with an associated 2-fold increase in mean pulmonary artery pressure and pulmonary capillary wedge pressure ( $P < 0.01$ ). Mean arterial blood pressure increased by 35%. Heart rate, stroke volume, cardiac output, and mixed venous oxygen saturation were unaffected during surgery, as were echocardiographic heart dimensions. After induction of anesthesia, isovolumic relaxation time was prolonged, with no further change during the study. Deceleration time was normal and stable. In the horizontal position after pneumoperitoneum exsufflation, filling pressures and mean arterial blood pressure returned to baseline levels.

Pneumoperitoneum reduced lung compliance by 40% ( $P < 0.01$ ). Addition of the Trendelenburg position caused a further decrease ( $P < 0.05$ ). Arterial blood acid-base balance was normal. End-tidal carbon dioxide tension increased whereas arterial carbon dioxide was unaffected with unchanged ventilation settings. Pneumoperitoneum increased PaO<sub>2</sub> ( $P < 0.05$ ). Ventilation-perfusion distribution, shunt, and dead space were unaltered during the study.

**CONCLUSIONS:** Pneumoperitoneum and 45° Trendelenburg position caused 2- to 3-fold increases in filling pressures, without effects on cardiac performance. Filling pressures were normalized immediately after surgery. Lung compliance was halved. Gas exchange was unaffected. No perioperative cardiovascular complications occurred.

在肺萎陷程度相同的情況下，自主呼吸比控制通氣更能改善肺內分流和氧合

### Spontaneous Breathing Improves Shunt Fraction and Oxygenation in Comparison with Controlled Ventilation at a Similar Amount of Lung Collapse

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**背景：**在不同的急性肺損傷的模型中，機械通氣(MV)時允許自主呼吸(SB)能改善氧合。然而，在機械通氣不支持SB時是否能改善氧合尚不明確。因此，在豬萎陷肺的模型中，作者比較了不使用任何支持的SB與用相同的潮氣量( $V_T$ )和呼吸頻率(RR)不使用呼吸末正壓MV的呼吸情況。

**方法：**在25例麻醉的豬中，通過使用負壓肺萎陷模型，並隨機分組至SB組或者MV組，相同的 $V_T$  (5 mL/kg; 95% 可信區間: 3.8 至 6.4) 且RR (65 每分鐘[57-73])，在SB初始階段開始記錄。記錄血氣中的氧分壓( $n = 15$ )，此外，可能的肺複張通過X線表現 ( $n=10$ )

**結果：**在肺萎陷後， $PaO_2/FIO_2$  下降至 90 mm Hg (76 至 103)。使用SB， $PaO_2/FIO_2$  在15min中增加至 235 mm Hg (177 至 93)，而MV並沒有改善氧合。肺萎陷後45min，SB組中肺內分流較低(SB: 27% [24 至 30] vs MV: 41% [28 至 55];  $P = 0.017$ )。SB和MV都不能減少減少肺萎陷的面積。

**結論：**與相同呼吸參數下MV相比，無任何支持的SB能改善氧合，減少肺內分流。這可能有益於促進肺複張。

(丁佳 譯 陳傑 校)

**BACKGROUND:** Spontaneous breathing (SB), when allowed during mechanical ventilation (MV), improves oxygenation in different models of acute lung injury. However, it is not known whether oxygenation is improved during mechanically unsupported SB. Therefore, we compared SB without any support with controlled MV at identical tidal volume ( $V_T$ ) and respiratory rate (RR) without positive end-expiratory pressure in a porcine lung collapse model.

**METHODS:** In 25 anesthetized piglets, stable lung collapse was induced by application of negative pressure, and animals were randomized to either resume SB or to be kept on MV at identical  $V_T$  (5 mL/kg; 95% confidence interval: 3.8 to 6.4) and RR (65 per minute [57 to 73]) as had been measured during an initial SB period. Oxygenation was assessed by blood gas analysis ( $n = 15$ ) completed by multiple inert gas elimination technique ( $n = 8$  of the 15) for shunt measurement. In addition, possible lung recruitment was studied with computed tomography of the chest ( $n = 10$ ).

**RESULTS:** After induction of lung collapse,  $PaO_2/FIO_2$  decreased to 90 mm Hg (76 to 103). With SB,  $PaO_2/FIO_2$  increased to 235 mm Hg (177 to 293) within 15 minutes, whereas MV at identical  $V_T$  and RR did not cause any improvement in oxygenation. Intrapulmonary shunt by 45 minutes after induction of lung collapse was lower during SB (SB: 27% [24 to 30] versus MV: 41% [28 to 55];  $P = 0.017$ ). Neither SB nor MV reduced collapsed lung areas on computed tomography.

**CONCLUSIONS:** SB without any support improves oxygenation and reduces shunt in comparison with MV at identical settings. This seems to be achieved without any major signs of recruitment of collapsed lung regions.

高解析度熔解曲線分析蘭尼城惡性高熱致病突變基因 1 的篩選



## Screening of the Ryanodine 1 Gene for Malignant Hyperthermia Causative Mutations by High Resolution Melt Curve Analysis

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**背景：**惡性高熱（MH）的診斷可在體外肌肉攣縮測試（IVCT）執行中被確定或確定一個已知的蘭尼城惡性高熱致病突變基因 1 (*RYR1*)。基因診斷優於 IVCT，因為它創傷小。直接測序非常大的 *RYR1* 的編碼區（15.117 碱基），是一個艱苦的和昂貴的任務。在這項研究中，作者採用高解析度熔解曲線（HRM）分析篩查基因編碼的整個區域。

**方法：**在 16 個 MH 易感經 IVCT 確診的患者佇列中從外周血標本中提取基因組 DNA。*RYR1* 總的編碼區通過在 131 個 DNA 片段的聚合酶鏈反應被劃分和擴增並將融化型與對照樣本作比較。轉基因 Q 軟體和外觀檢驗用於評估高解析度熔解曲線。對表現出異常的融化型的片段進行測序，以確定基本的序列變異。

**結果：**520/2520（21%）的 DNA 片段，呈顯著異常的融化型。經測序，131 個已知的多態性與 17 個已知或懷疑有突變在 16 例 MH 易感患者中有 13 例（81%）。因此，測序的工作量減少了 79%。

**結論：**高解析度熔解曲線分析是複雜的基因（如 *RYR1* 基因）核苷酸序列變異識別的一個敏感和具成本效益的工具。

(孫曉瓊 譯 陳傑 校)

**BACKGROUND:** A diagnosis of malignant hyperthermia (MH) can be determined by performing an in vitro (muscle) contracture test (IVCT) or by identifying a known MH causative mutation in the ryanodine receptor 1 gene (*RYR1*). Genetic diagnosis has an advantage over IVCT because it is less invasive. Direct sequencing of the very large *RYR1* coding region (15.117 bases) is a laborious and expensive task. In this study, we applied the High Resolution Melting (HRM) curve analysis as a tool to screen the entire coding region of the gene.

**METHODS:** Genomic DNA was extracted from peripheral blood samples in a cohort of 16 MH-susceptible patients diagnosed by the IVCT. The total coding region of *RYR1* was divided and amplified by polymerase chain reaction in 131 DNA fragments and the melting profiles were compared with those of control samples. HRM curves were evaluated by Rotor-Gene Q software and visual inspection. Fragments showing aberrant melting profiles were sequenced to identify the underlying sequence variation.

**RESULTS:** A subset of 520 of 2520 DNA fragments (21%) showed significantly aberrant melting profiles. Upon sequencing, 131 known polymorphisms and 17 known or

suspected mutations were found in 13 of 16 MH-susceptible patients (81%). Thus, the workload of sequencing was reduced by 79%.

**CONCLUSION:** HRM curve analysis is a sensitive and cost-effective tool for the identification of nucleotide sequence variants in complex genes such as the *RYR1* gene.

### 異氟醚對未成熟海馬椎體神經元細胞產生 $\gamma$ -氨基丁酸興奮性毒性損傷

#### GABAergic Excitotoxicity Injury of the Immature Hippocampal Pyramidal Neurons' Exposure to Isoflurane

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**背景：**某些麻醉藥物會對未成熟大腦造成神經損傷而對成熟大腦無損傷作用。 $\gamma$ -氨基丁酸 (GABA) 是成年大腦中主要的抑制性神經遞質，而對非成熟神經細胞具興奮作用，通過與 A 型 GABA 受體結合產生作用，逆轉膜內外的氯離子濃度，使膜電位去極化，引起胞內鈣離子濃度升高。目前幾類齧齒類動物的實驗資料顯示早期接觸異氟醚可以導致神經元細胞的興奮性中毒和凋亡。A 型 GABA 受體介導的突觸電壓依賴鈣離子通道的過度活化和鈣湧入參與了這些神經改變。

**方法：**作者採用 Fluo-4 AM 螢光成像監測  $[Ca^{2+}]_i$  濃度。採用全細胞膜片鉗技術，記錄原代小鼠海馬神經元細胞（培養 5 天）暴露於異氟醚後的  $I_{VDCC}$ （電壓依賴鈣離子通道電流）。為更深一步探究劑量依賴和時間依賴兩種不同異氟醚暴露方法導致的胞質內高濃度游離鈣對神經細胞的損傷，通過 western blot 技術和即時定量-聚合酶鏈式反應 (RTQ-PCR) 評估 caspase-3 水準升高的可能性。資料顯著性通過團體 t 檢驗或者單因素方差分析後進行 Tukey 顯著性差異比較來評價。

**結果：**在控制條件下，異氟醚能劑量依賴增強 GABA 誘導的  $[Ca^{2+}]_i$  升高。丹曲林和尼卡地平能顯著抑制這種由異氟醚介導的增強效應。同時，在無鈣離子的介質中，採用異氟醚預處理後並未發現其對咖啡因誘導的  $[Ca^{2+}]_i$  濃度升高產生影響。同樣的，採用全細胞膜片鉗記錄後發現，異氟醚能使培養的小鼠海馬神經元的  $I_{VDCC}$  的去極化峰值幅度升高。不同濃度的異氟醚 (0.25, 0.5, 0.75, and 1 最小肺泡濃度 [MAC]) 加強  $I_{VDCC}$  峰電流的幅度分別為  $109.11\% \pm 9.03\%$ ,  $120.56\% \pm 11.46\%$ ,  $141.33\% \pm 13.87\%$ , and  $146.78\% \pm 15.87\%$ 。從蛋白水準方面分析，異氟醚引起 caspase-3 既有劑量依賴也有時間依賴，1MAC 的異氟醚暴露 6 小時可到達最大 caspase-3 活動 ( $P < 0.001$ )。但是，在 mRNA 水準，發育中的海馬神經元的 caspase-3 mRNA 水準是在暴露於 0.25MAC 6 小時後開始顯著升高。

**結論：**異氟醚介導的 GABA 觸發  $[Ca^{2+}]_i$  釋放增強作用是由於膜去極化和繼發的 VDCC 啟動，進一步導致鈣誘導阿諾城敏感的鈣池中的鈣釋放。A 型 GABA 受體啟動和 VDCC 的開放導致  $[Ca^{2+}]_i$  增加是異氟醚誘導非成熟小鼠海馬神經元產生鈣超載所必須的，這可能是異氟醚造成發育中的齧齒類動物大腦產生神經毒性效應的機制的一部分。

(陸秉璋 譯 陳傑 校)

**BACKGROUND:** Certain anesthetics exhibit neurotoxicity in the brains of immature but not mature animals.  $\gamma$ -Aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the adult brain, is excitatory on immature neurons via its action at the GABA<sub>A</sub> receptor, depolarizing the membrane potential and inducing a cytosolic Ca<sup>2+</sup> increase ([Ca<sup>2+</sup>]<sub>i</sub>), because of a reversed transmembrane chloride gradient. Recent experimental data from several rodent studies have demonstrated that exposure to isoflurane during an initial phase causes neuronal excitotoxicity and apoptosis. GABA<sub>A</sub> receptor-mediated synaptic voltage-dependent calcium channels' (VDCCs) overactivation and Ca<sup>2+</sup> influx are involved in these neural changes.

**METHODS:** We monitored [Ca<sup>2+</sup>]<sub>i</sub> using Fluo-4 AM fluorescence imaging. Using whole-cell patch clamp techniques, I<sub>VDCC</sub> (voltage-dependent calcium channel currents) were recorded from primary cultures of rat hippocampal neurons (5-day culture) exposed to isoflurane. To further investigate the neurotoxicity of high cytosolic-free calcium after isoflurane in a dose- and time-dependent manner, the possibility of increased caspase-3 levels was evaluated by Western blot and quantitative real-time polymerase chain reaction. Statistical significance was assessed using the Student *t* test or 1-way analysis of variance followed by the Tukey post hoc test.

**RESULTS:** Under control conditions, isoflurane enhanced the GABA-induced [Ca<sup>2+</sup>]<sub>i</sub> increase in a dose-dependent manner. Dantrolene and nifedipine markedly inhibited this enhancement mediated by isoflurane. Moreover, in Ca<sup>2+</sup>-free media, pretreatment with isoflurane did not show any influence on the caffeine-induced increase of [Ca<sup>2+</sup>]<sub>i</sub>. Similarly, using whole-cell recording, isoflurane increased the peak amplitude of I<sub>VDCC</sub> in the cultured neurons from rat hippocampus by depolarization pulses. Isoflurane (0.25, 0.5, 0.75, and 1 minimum alveolar concentration [MAC]) potentiated I<sub>VDCC</sub> peak current amplitude by 109.11% ± 9.03%, 120.56% ± 11.46%, 141.33% ± 13.87%, and 146.78% ± 15.87%, respectively. To analyze variation in protein levels, the effect of treatments with isoflurane on caspase-3 activity was dose- and time-dependent, reaching a maximal caspase-3 activity after exposure to 1 MAC for 6 hours (*P* < 0.001). However, in the mRNA levels, hippocampal caspase-3 mRNA levels began to be significantly increased in isoflurane-treated developing rat hippocampal neurons after 6 hours of exposure to 0.25 MAC isoflurane (*P* < 0.001).

**CONCLUSIONS:** Isoflurane-mediated enhancement of GABA-triggered [Ca<sup>2+</sup>]<sub>i</sub> release results from membrane depolarization with subsequent activation of VDCCs and further Ca<sup>2+</sup>-induced Ca<sup>2+</sup> release from the ryanodine-sensitizing Ca<sup>2+</sup> store. An increase in [Ca<sup>2+</sup>]<sub>i</sub>, caused by activation of the GABA<sub>A</sub> receptor and opening of VDCCs, is necessary for isoflurane-induced calcium overload of immature rat hippocampal neurons, which may be involved in the mechanism of an isoflurane-induced neurotoxic effect in the developing rodent brain.

在大鼠中，遠端肢體後處理可以通過  $\delta$  蛋白激酶 C 的活性氧調節抑制劑降低大腦再灌注損傷

**Limb Remote Postconditioning Alleviates Cerebral Reperfusion Injury Through Reactive Oxygen Species-Mediated Inhibition of Delta Protein Kinase C in Rats**

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**背景：**現在認為，遠隔缺血後處理對於腦梗死的保護有一定作用，但是其機制尚不清楚。本研究的目的是證實在大鼠腦缺血模型中活性氧和  $\delta$  蛋白激酶 C 對於實現遠隔缺血後處理的腦保護作用以及兩者之間的聯繫。

**方法：**在雄性大鼠中通過夾閉大腦中動脈來建立大鼠腦缺血模型。大腦中動脈再灌注時通過反復夾閉/再灌注右側大腿股動脈來實行遠隔缺血後處理，3-10 分鐘一個週期。研究中分別只進行遠隔缺血後處理或者事先給予 N-乙醯半胱氨酸（一種活性氧的清除劑）。在各組中，再灌注開始時分別給予 TAT- $\delta$ V1-1，一種  $\delta$  蛋白激酶 C 的選擇性肽抑制劑。大腦缺血損傷程度由神經病學評分，梗死面積以及 TUNEL 染色來判定。在缺血半影區  $\delta$  蛋白激酶 C 被啟動，再灌注後可以被蛋白質印跡發現。

**結果：**遠隔缺血後處理提高了神經疾病的預後，減少梗死面積，抑制神經細胞凋亡以及再灌注後  $\delta$  蛋白激酶 C 的啟動。另外，給予 TAT- $\delta$ V1-1 後可以抑制再灌注損傷，從而保護大腦。再灌注後， $\delta$  蛋白激酶 C 啟動，若事先給予 N-乙醯半胱氨酸不僅完全抑制了遠隔缺血後處理的腦保護作用，而且逆轉了遠隔缺血後處理引起的抑制  $\delta$  蛋白激酶 C 啟動的作用。

**結論：**結果顯示大鼠模型局部腦缺血後，通過  $\delta$  蛋白激酶 C 的活性氧調節抑制劑，遠隔缺血後處理可以減少再灌注損傷。

(張婷 譯 陳傑 校)

**BACKGROUND:** Remote ischemic postconditioning (RPostC) is an emerging concept for cerebral infarction protection, and its potential protective mechanisms have not been well established. We attempted to investigate the implications of reactive oxygen species (ROS) and  $\delta$  protein kinase C ( $\delta$ PKC) in neuroprotection induced by RPostC in a rat model of focal cerebral ischemia, and also to explore a possible relationship between ROS and  $\delta$ PKC.

**METHODS:** Focal cerebral ischemia was induced by middle cerebral artery occlusion using the intraluminal filament technique in male rats. RPostC was generated by 3 10-minute cycles of femoral artery occlusion/reperfusion on the right limb at the onset of middle cerebral artery reperfusion. RPostC was performed alone or with pretreatment of N-acetylcysteine, a ROS scavenger. In separate group, TAT- $\delta$ V1-1, a  $\delta$ PKC-selective peptide inhibitor, was administered at the onset of reperfusion. Brain ischemic injury was evaluated by neurologic scores, infarction volumes, and TUNEL staining. Moreover, the activation of  $\delta$ PKC in the ischemic penumbra was investigated by Western blot after reperfusion.

**RESULTS:** RPostC improved neurologic outcome, reduced infarct size, and inhibited neuronal apoptosis as well as suppressed the activation of  $\delta$ PKC after reperfusion. Moreover, systemic delivery of TAT- $\delta$ V1-1 conferred neuroprotection against cerebral reperfusion injury at the onset of reperfusion. Pretreatment with N-acetylcysteine not only completely prevented all aspects of RPostC-induced neuroprotection, but also reversed RPostC-induced inhibition of  $\delta$ PKC activation after reperfusion.

**CONCLUSION:** These findings suggested that RPostC performed in one limb alleviated reperfusion injury after focal cerebral ischemia through ROS-mediated inhibition of endogenous  $\delta$ PKC activation signaling cascade in an in vivo rat model of focal cerebral ischemia.

### 一項門診腹腔鏡後腹橫肌阻滯對術後恢復品質及鎮痛影響的劑量研究

#### **A Dose-Ranging Study of the Effect of Transversus Abdominis Block on Postoperative Quality of Recovery and Analgesia After Outpatient Laparoscopy**

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**背景:** 術後疼痛可延緩門診術後功能恢復。多管道鎮痛可改善術後疼痛並提高復蘇品質。該研究中,作者利用復蘇品質(QoR-40)問卷調查,來評估婦科腹腔鏡手術腹橫肌平面(TAP)阻滯的劑量效果反應。QoR-40分數從40至200,分別代表非常差至復蘇品質高。

**方法:** 門診婦科腹腔鏡手術患者隨機術前給予生理鹽水、0.25%羅呱卡因或0.5%羅呱卡因進行TAP阻滯。由一名不知情的研究者在超聲引導下雙側TAP阻滯局麻藥或生理鹽水15 mL)。術後24小時內進行QoR-40評分來評估鎮痛效果。主要結果為術後24小時為QoR-40評分。資料分析採用Kruskal-Wallis檢驗。6對事後成對比較採用Dunn檢驗P值和Bonferroni校正95%可信區間。

**結果:** 75例患者入組,其中70名受試者完成了這項研究。TAP阻滯後,生理鹽水組、0.25%羅呱卡因組、0.5%羅呱卡因組QoR-40評分分別為157(127-193),173(133-195),和172(130-196)。0.5%羅呱卡因組、0.25%羅呱卡因組QoR-40評分的平均差(99.2%可信區間)分別為17[2-31], $P=0.01$ ;16[1-30], $P=0.03$ ,均高於生理鹽水組(-1[-16 to 12], $P=1.0$ ),但兩者無明顯差異。QoR-40評分增加對應減少麻醉後恢復過程中疼痛時間區域曲線( $\rho=-0.56$ ,99.2%上限(UCL)=0.28),24小時阿片類藥物使用( $\rho=-0.61$ ,99.2%UCL=-0.34)、24小時內疼痛評分(0-10分),( $\rho=-0.53$ ,99.2%UCL=-0.25),及出院時間( $\rho=-0.65$ ,99.2%UCL=0.42)。上述變數在羅呱卡因組均低於生理鹽水組。

**結論:** TAP阻滯是腹腔鏡術後多模式鎮痛中一種有效的輔助鎮痛方法。使用0.5%羅呱卡因或0.25%羅呱卡因可減少疼痛及阿片類藥物使用,並提供更好的恢復品質並促使儘早出院。

(陳毓雯 譯 陳傑 校)

**BACKGROUND:** Postoperative pain can delay functional recovery after outpatient surgery. Multimodal analgesia can improve pain and possibly improve quality of recovery. In this study, we evaluated the dose-dependent effects of a preoperative transversus abdominis plane (TAP) block on patient recovery using the Quality of Recovery 40 (QoR-40) questionnaire after ambulatory gynecological laparoscopic surgery. Global QoR-40 scores range from 40 to 200, representing very poor to outstanding quality of recovery, respectively.

**METHODS:** Healthy women undergoing outpatient gynecological laparoscopy were randomly allocated to receive a preoperative TAP block using saline, ropivacaine 0.25%, or ropivacaine 0.5%. Needle placement for the TAP blocks was performed using ultrasound guidance and 15 mL of the study solution was injected bilaterally by a blinded investigator. QoR-40 score and analgesic use were assessed 24 hours postoperatively. The primary outcome was global QoR-40 score at 24 hours after surgery. Data were analyzed using the Kruskal-Wallis test. Post hoc pairwise comparisons were made using the Dunn test with *P* values and 95% confidence intervals Bonferroni corrected for 6 comparisons.

**RESULTS:** Seventy-five subjects were enrolled and 70 subjects completed the study. The median (range) for the QoR-40 score after the TAP block was 157 (127–193), 173 (133–195), and 172 (130–196) for the saline group and 0.25% and 0.5% ropivacaine groups, respectively. The median difference (99.2% confidence interval) in QoR-40 score for 0.5% bupivacaine (16 [1–30], *P* = 0.03) and 0.25% bupivacaine (17 [2–31], *P* = 0.01) was more than saline but not significantly different between ropivacaine groups (–1 [–16 to 12], *P* = 1.0). Increased global QoR-40 scores correlated with decreased area under the pain score time curve during postanesthesia recovery room stay ( $\rho$  = –0.56, 99.2% upper confidence limit [UCL] = –0.28), 24-hour opioid consumption ( $\rho$  = –0.61, 99.2% UCL = –0.34), pain score (0–10 scale) at 24 hours ( $\rho$  = –0.53, 99.2% UCL = –0.25), and time to discharge readiness ( $\rho$  = –0.65, 99.2% UCL = –0.42). The aforementioned variables were lower in the TAP block groups receiving ropivacaine compared with saline.

**CONCLUSIONS:** The TAP block is an effective adjunct in a multimodal analgesic strategy for ambulatory laparoscopic procedures. TAP blocks with ropivacaine 0.25% and 0.5% reduced pain, decreased opioid consumption, and provided earlier discharge readiness that was associated with better quality of recovery.

### 超前鎮痛：何去何從？

#### Review Article: Preventive Analgesia: Quo Vadimus?

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傳統對超前鎮痛的界定需要兩組患者在術前或術後接受相同治療。兩組患者唯一的不同點是給藥的時間點不同。手術後給藥這組的實驗結果往往是令人感興趣的，這是由於產生了陽性結果，這一結果為我們提供了在哪個時間段內給藥能觀察到效果這一“時間窗”，其可能的機制如下所示：傳統觀點假設術中傷害性刺激所導致的術後疼痛遠遠大於術後傷害性刺激對術後疼痛的影響。然而，這一觀點過於狹隘，因為眾所周知，致敏作用由很多因素影響包括切皮及術中相關有害因素引起的外周傷害性刺激。預防術後疼痛的方法可以主要概括為最小化的減少手術期間直接有害因素及長效有害因素的產生。對於超前鎮痛，我們不應該聚焦在鎮痛藥物及鎮靜麻醉藥物的給藥時間上，而是應該聚焦在儘量減少術前術中及術後外周傷害性刺激。這些有害刺激包括外周致敏及中樞致敏，這會增加術後疼痛強度並且增加鎮痛藥物

的需要量。保護致敏現象能減少疼痛及減少鎮痛藥物用量。當術後疼痛及術後鎮痛藥減少量超過了藥物的持續時間則證實產生疼痛保護。這一結果表明，我們觀察到的鎮痛現象並不是鎮痛藥物的直接作用。在這篇文章中，筆者簡要回顧了超前鎮痛的歷史及鎮痛保護的廣義定義，筆者特別強調了一些超前鎮痛及疼痛保護的設計實驗及文獻，並為其進來的研究作一展望。

(趙嫣紅 譯 陳傑 校)

The classic definition of preemptive analgesia requires 2 groups of patients to receive identical treatment before or after incision or surgery. The only difference between the 2 groups is the timing of administration of the drug relative to incision. The constraint to include a postincision or postsurgical treatment group is methodologically appealing, because in the presence of a positive result, it provides a window of time within which the observed effect occurred, and thus points to possible mechanisms underlying the effect: the classic view assumes that the intraoperative nociceptive barrage contributes to a greater extent to postoperative pain than does the postoperative nociceptive barrage. However, this view is too restrictive and narrow, in part because we know that sensitization is induced by factors other than the peripheral nociceptive barrage associated with incision and subsequent noxious intraoperative events. A broader approach to the prevention of postoperative pain has evolved that aims to minimize the deleterious immediate and long-term effects of noxious perioperative afferent input. The focus of preventive analgesia is not on the relative timing of analgesic or anesthetic interventions, but on attenuating the impact of the peripheral nociceptive barrage associated with noxious preoperative, intraoperative, and/or postoperative stimuli. These stimuli induce peripheral and central sensitization, which increase postoperative pain intensity and analgesic requirements. Preventing sensitization will reduce pain and analgesic requirements. Preventive analgesia is demonstrated when postoperative pain and/or analgesic use are reduced beyond the duration of action of the target drug, which we have defined as 5.5 half-lives of the target drug. This requirement ensures that the observed effects are not direct analgesic effects. In this article, we briefly review the history of preemptive analgesia and relate it to the broader concept of preventive analgesia. We highlight clinical trial designs and examples from the literature that distinguish preventive analgesia from preemptive analgesia and conclude with suggestions for future research.

腹腔內羅呱卡因霧化療法用於腹腔鏡膽囊切除術後鎮痛：與腹腔內灌注療法的比較研究

### **Intraperitoneal Ropivacaine Nebulization for Pain Management After Laparoscopic Cholecystectomy: A Comparison with Intraperitoneal Instillation**

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**背景：**關於腹腔內灌注局部麻醉藥用於腹腔鏡術後疼痛緩解治療的研究結果目前仍存在爭議。在本次隨機、雙盲研究中，作者評估了腹腔內霧化噴射局部麻醉藥對腹腔鏡膽囊切除術後疼痛的緩解作用。

**方法：**將接受擇期腹腔鏡膽囊切除術的患者隨機分為兩組：一組患者在氣腹後即刻在腹腔內管著 0.5% 羅呱卡因 20ml，另一組患者在術前以及術後在腹腔內霧化噴射 1% 羅呱卡因各 3ml。所有的患者均採用標準化的麻醉和手術方案。在術後第 6、24 和 48 小時評估患者的靜息及深呼吸時疼痛程度、肩部痛的發生率、嗎啡的消耗量、無需借助外力步行的時間以及術後噁心嘔吐的發生情況。

**結果：**在 60 位納入研究的患者中，3 位因手術中轉開腹而剔除。兩組患者的疼痛評分或嗎啡消耗量沒有明顯的差異。霧化治療組的患者中無一例發生肩部痛，而灌注治療組的患者中有 83% 發生了肩部疼痛（絕對風險減少-83，95% 置信區間-70 至 -90， $p < 0.001$ ）。霧化治療組的患者中，有 19 位（70%）在術後 12 小時即可不借助外力步行，在灌注治療組該資料為 14 位元（47%）（絕對風險減少-24，95% 置信區間-48 至 1， $p = 0.04$ ）。術後發生嘔吐的患者數在灌注治療組和霧化治療組分別為 1 位（3%）和 6 位（22%）。

**結論：**腹腔內羅呱卡因霧化療法可減少腹腔鏡膽囊切除術後肩部疼痛，並可使患者提早下床自主活動，但其術後嘔吐的發生率較高。

(周姝婧 譯 陳傑 校)

**BACKGROUND:** Studies evaluating intraperitoneal local anesthetic instillation for pain relief after laparoscopic procedures have reported conflicting results. In this randomized, double-blind study we assessed the effects of intraperitoneal local anesthetic nebulization on pain relief after laparoscopic cholecystectomy.

**METHODS:** Patients undergoing elective laparoscopic cholecystectomy were randomly assigned to receive either instillation of ropivacaine 0.5%, 20 mL after induction of the pneumoperitoneum, or nebulization of ropivacaine 1%, 3 mL before and after surgery. Anesthetic and surgical techniques were standardized. Degree of pain at rest and on deep breathing, incidence of shoulder pain, morphine consumption, unassisted walking time, and postoperative nausea and vomiting were evaluated at 6, 24, and 48 hours after surgery.

**RESULTS:** Of the 60 patients included, 3 exclusions occurred for conversion to open surgery. There were no differences between groups in pain scores or in morphine consumption. No patients in the nebulization group presented significant shoulder pain in comparison with 83% of patients in the instillation group (absolute risk reduction -83, 95% CI -97 to -70,  $P < 0.001$ ). Nineteen (70%) patients receiving nebulization walked without assistance within 12 hours after surgery in comparison with 14 (47%) patients receiving instillation (absolute risk reduction -24, 95% CI -48 to 1,  $P = 0.04$ ). One (3%) patient in the instillation group vomited in comparison with 6 (22%) patients in the nebulization group (absolute risk reduction -19%, 95% CI -36 to -2,  $P = 0.03$ ).



**CONCLUSIONS:** Intraperitoneal ropivacaine nebulization was associated with reduced shoulder pain and unassisted walking time but with an increased incidence of postoperative vomiting after laparoscopic cholecystectomy.

### 在麻醉科術前評估門診使用 BATHE 法

#### Use of the BATHE Method in the Preanesthetic Clinic Visit

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**背景：**在最初的術前訪視過程中，使用 BATHE 法（詢問背景、干預措施、發現問題、解決方法、移情作用）對病人進行問診可以增加病人的滿意度。此方法是一項可以發現病人身心疾病的簡明的心理學療法。目前並沒有對 BATHE 法作為提高病人術前滿意度的一種方法進行評價。在本次研究中，我們希望瞭解麻醉醫生在術前評估病人時使用 BATHE 法是否能增加手術病人術前的滿意度。

**方法：**我們在一家學術性醫院的麻醉前門診訪視了 50 名心外科手術病人和 50 名普外科手術病人。所有病人隨機分到 BATHE 組和對照組，並被要求在訪視後完成一項不記名的滿意度調查。這個調查是從近期研究加工後制定的，但並未在其他研究中驗證過。與訪視過程、病人滿意度及病人對 BATHE 各項的報告相關的可能影響 BATHE 結果的相關因素我們同樣都進行了調查。

**結果：**研究小組訪視的病人中有 92% 自願加入本次研究中。用 BATHE 方法訪視的病人報告較對照組顯著更頻繁地被詢問所有的 BATHE 問題： $t(98) = 19.10, P = 0.001$  (95% 置信區間 [CI] = 2.59, 3.20)。在麻醉科術前評估門診中，BATHE 組病人較對照組滿意度更高： $t(98) = 5.37, P = 0.001$  (95% CI = 0.19, 0.41)。使用 BATHE 法並沒有顯著增加醫生評估病人所花的時間： $t(98) = 0.110, P = 0.912$  (95% CI = -1.519, 1.359)。

**結論：**本次初步研究顯示在學術性醫療中心的心外科和普外科麻醉前門診使用 BATHE 法進行訪視，結果是有希望的。在我們能夠令人信服地得出結論認定 BATHE 法是增加患者滿意度的有效手段之前，我們還需要更加有效和完善的調查方法進行研究。

（劉伍 譯 馬皓琳 李士通 校）

**BACKGROUND:** In the primary care setting, use of the BATHE (Background, Affect, Trouble, Handling, and Empathy) method of interviewing has been shown to increase patient satisfaction. This technique is a brief psychotherapeutic method used to address patients' physical and psychosocial problems. The BATHE technique has not been evaluated in the perioperative setting as a way of improving patient satisfaction. In this study, we sought to determine whether satisfaction could be enhanced by use of the BATHE technique during the preoperative evaluation by anesthesiologists.

**METHODS:** Fifty cardiac and 50 general surgery patients were interviewed in the preanesthesia clinic (PAC) of an academic hospital. They were randomly enrolled in the

BATHE group or the control group and asked to complete an anonymous satisfaction survey after their visit. This survey was modified from current studies and not validated elsewhere. The relative influence of the BATHE condition was examined as it pertained to interview duration, patient satisfaction, and patient report of the BATHE items being asked.

**RESULTS:** Ninety-two percent of patients approached by the study group voluntarily enrolled. Patients interviewed using the BATHE method reported being asked about all BATHE questions significantly more often than control patients:  $t(98) = 19.10$ ,  $P = 0.001$  (95% confidence interval [CI] = 2.59, 3.20). Patients in the BATHE group were more satisfied with their visit to the PAC than those in the control group:  $t(98) = 5.37$ ,  $P = 0.001$  (95% CI = 0.19, 0.41). The use of the BATHE method did not significantly increase the amount of time physicians spent evaluating patients:  $t(98) = 0.110$ ,  $P = 0.912$  (95% CI = -1.519, 1.359).

**CONCLUSIONS:** Use of the BATHE method in an academic medical center's cardiac and general PAC showed promising results in this preliminary study. A validated and fully developed survey instrument is needed before we can convincingly conclude that the BATHE method is an effective way of improving patient satisfaction.

### 新型水溶性鎮靜催眠藥 JM-1232(-)對小鼠海馬 CA1 區長時程增強效應的影響

#### The Effect of a New Water-Soluble Sedative-Hypnotic Drug, JM-1232(-), on Long-Term Potentiation in the CA1 Region of the Mouse Hippocampus

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**背景：** JM-1232(-) {(-)-3-[2-(4-甲基-1-吡嗪基)-2-氧代乙基]-2-苯-3,5,6,7-四氫環戊二烯並 a[f]異吲哚-1(2H)-酮} 是一種對  $\gamma$ -氨基丁酸 A 受體上苯二氮卓結合位點具有親和力的新型水溶性鎮靜催眠藥物。JM-1232(-) 對大腦突觸傳遞的效應還不甚明瞭。我們在本實驗中研究了 JM-1232(-) 對小鼠海馬切片 CA1 區錐體細胞突觸傳遞、突觸可塑性(如長時程增強效應[LTP]和成對脈衝易化)以及興奮性/抑制性突觸後電流(EPSCs/IPSCs)的影響。

**方法：** 在小鼠海馬腦片 CA1 區，我們採用全細胞膜片鉗技術記錄了 Schaffer 側枝刺激誘發的區域興奮性突觸後電位和錐體細胞的 EPSCs 和 IPSCs。

**結果：** JM-1232(-) 對區域興奮性突觸後電位無明顯影響。在  $\theta$  短陣快速脈衝刺激前，JM-1232(-) 處理腦片 20min 能夠劑量依賴性地損傷 LTP。JM-1232(-) 也損傷成對脈衝易化。苯二氮卓激動劑氟馬西尼抵消了 JM-1232(-) 對 LTP 和成對脈衝易化的抑制作用。JM-1232(-) 對 Schaffer 側枝刺激誘發的 EPSCs 無影響，反而能增加 CA1 區錐體細胞中誘發的 IPSCs 的振幅，並延長其衰退。氟馬西尼阻斷 JM-1232(-) 對誘發的 IPSCs 振幅和衰退的影響。JM-1232(-) 抑制  $\theta$  短陣快速脈衝刺激過程中 CA1 區錐體細胞動作電位放電，且此作用可被氟馬西尼逆轉。

**結論：** JM-1232(-)增強小鼠海馬 CA1 區神經元的突觸抑制，並損傷 LTP 和成對脈衝易化。這些作用是通過  $\gamma$ -氨基丁酸 A 受體上苯二氮卓類結合位點介導的。  
(江繼宏 譯 馬皓琳 李士通 校)

**BACKGROUND:**

JM-1232(-){(-)-3-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-2-phenyl-3,5,6,7-tetrahydrocyclopenta[*f*]isoindol-1(2*H*)-one} is a new water-soluble sedative-hypnotic drug with affinity for the benzodiazepine binding site on  $\gamma$ -aminobutyric acid A receptors. The effects of JM-1232(-) on synaptic transmission in the brain are not known. In the present study, we investigated the effects of JM-1232(-) on synaptic transmission, synaptic plasticity (i.e., long-term potentiation [LTP] and paired-pulse facilitation), and excitatory/inhibitory postsynaptic currents (EPSCs/IPSCs) of pyramidal neurons in the CA1 region of mouse hippocampal slices.

**METHODS:** We recorded Schaffer collateral-evoked field excitatory postsynaptic potentials and EPSCs and IPSCs of pyramidal neurons using whole-cell patch-clamp techniques in the CA1 region of mouse hippocampal slices.

**RESULTS:** JM-1232(-) had no significant effect on the field excitatory postsynaptic potentials. Application of JM-1232(-) for 20 minutes before theta-burst stimulation dose dependently impaired LTP. JM-1232(-) impaired paired-pulse facilitation. The benzodiazepine antagonist flumazenil abolished the inhibitory effect of JM-1232(-) on LTP and paired-pulse facilitation. JM-1232(-) had no effect on Schaffer collateral stimulation-evoked EPSCs, whereas it potentiated the amplitude and prolonged the decay of evoked IPSCs in CA1 pyramidal neurons. Flumazenil blocked the effect of JM-1232(-) on the amplitude and decay of evoked IPSCs. JM-1232(-) suppressed the action potential discharge in the CA1 pyramidal neurons during theta-burst stimulation, which was reversed by flumazenil.

**CONCLUSION:** JM-1232(-) enhances synaptic inhibition and impairs LTP and paired-pulse facilitation in area CA1 of the mouse hippocampus. These effects were mediated by benzodiazepine binding sites on  $\gamma$ -aminobutyric acid A receptors.

**對一種新型麻醉藥物清除介面的初步評估**

**An Initial Evaluation of a Novel Anesthetic Scavenging Interface**

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在過去的 30 年間麻醉廢氣清除技術沒有發生一點變化。開放式貯氣系統產生高容量的室內空氣並且在排入大氣前稀釋廢氣。這個過程需要一個大的真空泵，它需要昂貴的安裝並且即使效率非常高也需要連續運轉，並且接近滿負荷生產。在一個能源成本和環保意識日益增長的時代，減少碳足跡是一個優先選項，並且安全清除麻醉廢氣的更加高效的系統是非常可取的。我們測試了一個低流量清除介面來評估成本和能源的節省潛力。這種介面應用在一排 4 個術間使每台麻醉機的清除流量從恒定的 37L/min 降低到等於新鮮氣流量的值（通常是 2L/min）。應用通氣機增加了

這種流量約 6 L/min，是因為通氣機驅動氣體排出到清除環路。中央真空泵的日常工作負荷從 92% 降到 12%（表達為工作期）。新系統節約了能源並且可能增加了真空泵壽命。

（劉朝輝譯，馬皓琳，李士通校）

Waste anesthetic gas scavenging technology has not changed appreciably in the past 30 years. Open reservoir systems entrain high volumes of room air and dilute waste gases before emission into the atmosphere. This process requires a large vacuum pump, which is both costly to install and, although efficient, operates continuously and at near-full capacity. In an era of increasing energy costs and environmental awareness, carbon footprint reduction is a priority and a more efficient system of safely scavenging waste anesthetic gases is desirable. We tested a low-flow scavenger interface to evaluate the potential for cost and energy savings. The use of this interface in a suite of 4 operating rooms reduced scavenging flow from a constant 37 L/min to a value equal to the fresh gas flow (usually 2 L/min) for each anesthesia machine. Using the ventilator increased this flow by approximately 6 L/min because of the exhaust of ventilator drive gas into the scavenging circuit. Daytime workload of the central vacuum pump decreased from 92% to 12% (expressed as duty cycle). The new system produces energy savings and may increase vacuum pump lifespan.

### **Pentax-AWS 視頻喉鏡與 Macintosh 喉鏡用於病態肥胖患者的隨機對照研究**

#### **A Randomized Comparison Between the Pentax AWS Video Laryngoscope and the Macintosh Laryngoscope in Morbidly Obese Patients**

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**背景：**Pentax-AWS 是一種新型視頻喉鏡，通過提供喉入口的間接視覺化影像以便於氣管插管。本試驗旨在比較 Pentax-AWS 喉鏡與經典的 Macintosh 喉鏡的插管成功率以及插管時間。我們還特別檢驗了以下假說：在肥胖患者中使用 Pentax-AWS 喉鏡插管比標準的 Macintosh #4 喉鏡片更快、更方便。

**方法：**105 名需經口氣管插管行擇期手術的肥胖患者（體重指數 30~50 kg/m<sup>2</sup>）隨機分配到 Macintosh（用 #4 喉鏡片）插管或 Pentax-AWS 喉鏡插管組。由兩名經驗豐富的麻醉醫師作為喉鏡檢查專家。記錄插管成功率、插管時間、插管難度和併發症發生率。

**結果：**使用 Macintosh 喉鏡和 #4 喉鏡片插管明顯快於使用 Pentax-AWS 裝置：半數使用 Macintosh #4 喉鏡片的患者成功在 26 秒內完成氣管插管，而使用 AWS 喉鏡達到同樣比例需要 38 秒。使用 Pentax-AWS 喉鏡首次嘗試的成功率為 86%，二次嘗試的成功率增加到 90%。相比之下，所有使用 Macintosh #4 喉鏡片的患者均成功完成氣管插管，首次嘗試的成功率為 92%，二次嘗試的成功率增加到 100%。

**結論：**使用 Pentax-AWS 喉鏡行氣管插管所需時間長於 Macintosh 喉鏡和 #4 喉鏡片。在病態肥胖患者中不應該常規用 AWS 喉鏡替代傳統的 Macintosh #4 喉鏡片。

(陳彬彬譯 馬皓琳 李士通校)

**BACKGROUND:** The Pentax AWS is a novel video laryngoscope designed to facilitate tracheal intubation by providing indirect visualization of the laryngeal inlet. We sought to compare the intubation success rate and time to intubation for the Pentax AWS and the classic Macintosh laryngoscope. Specifically, we tested the hypothesis that intubation with the Pentax AWS would be easier and faster than with a standard Macintosh #4 blade in obese patients.

**METHODS:** One hundred five obese patients (body mass index between 30 and 50 kg/m<sup>2</sup>) requiring orotracheal intubation for elective surgery were allocated randomly to tracheal intubation with either the Macintosh (using a #4 blade) or the Pentax AWS laryngoscope. Two experienced anesthesiologists served as laryngoscopists. Intubation success rate, time to intubation, ease of intubation, and occurrence of complications were recorded.

**RESULTS:** Intubations using the Macintosh laryngoscope and #4 blade were significantly faster than with the Pentax AWS device: half of the patients' tracheas were intubated successfully within 26 seconds with the Macintosh #4 blade, whereas the same fraction required 38 seconds with the AWS. The first-attempt success rate with the Pentax AWS was 86%; the rate increased to 90% with a second attempt. In contrast, all patients' tracheas were intubated successfully with the Macintosh #4 blade, with a first-attempt success rate of 92%, which increased to 100% by the second attempt.

**CONCLUSION:** The time required for tracheal intubation using the Pentax AWS was longer than for the Macintosh laryngoscope and #4 blade. The AWS should not routinely be substituted for a conventional Macintosh #4 blade in morbidly obese patients.

### 惡性高熱研究及患者監護的未來方向

#### Future Directions in Malignant Hyperthermia Research and Patient Care

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惡性高熱 (MH) 是一個複雜的肌肉代謝的遺傳性藥理學紊亂疾病。為了更進一步調查 MH 以及其他相關肌肉紊亂疾病的複雜性，美國惡性高熱協會 (MHAUS) 最近發起了一項科學會議，在會上不同學科組的專家聚集一堂，分享新資訊及新觀念。在這篇專文中，我們著重於會議提出的在 MH 研究及患者護理方面的關鍵概念及理論，同時還有令人欣喜的新的趨勢和挑戰。

(瞿亦楓 譯 馬皓琳 李士通 校)

Malignant hyperthermia (MH) is a complex pharmacogenetic disorder of muscle metabolism. To more closely examine the complexities of MH and other related muscle disorders, the Malignant Hyperthermia Association of the United States (MHAUS) recently sponsored a scientific conference at which an interdisciplinary group of experts gathered to share new information and ideas. In this Special Article, we highlight key concepts and theories presented at the conference along with exciting new trends and challenges in MH research and patient care.

### 同胞出生群組中孩童時期早期麻醉暴露及發育和行為失常的風險

#### Early Childhood Exposure to Anesthesia and Risk of Developmental and Behavioral Disorders in a Sibling Birth Cohort

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**背景：**在體內和體外實驗中，麻醉藥的研究已經證實對發育中的大腦有嚴重的神經毒性反應。然而，這些發現對於進行麻醉的兒童的臨床相關性尚不清晰。應用從同胞出生群組得到的資料，我們評價了低於 3 歲手術病人的麻醉暴露與發育和行為失常風險之間的關係。

**方法：**我們組建了一個回顧性研究的佇列，包括出生於 1999 年至 2005 年之間並且登記入紐約州醫療援助計畫的 10450 名同胞兒童。暴露組為 304 名無發育和行為失常病史並在小於 3 歲時接受了外科手術的兒童。非暴露組為 10146 名在 3 歲以前沒有接受任何外科手術的兒童。暴露組患兒在手術之日進入資料分析。非暴露組在 10 月齡（暴露組進行手術的平均年齡）進入資料分析。隨訪暴露組和非暴露組兒童，直到診斷為發育或行為異常、失隨訪或 2005 年底。用比例危險度模型以及配對檢驗分析評價麻醉暴露與隨後的發育和行為失常之間的關係。

**結果：**在暴露組群中，發育和行為失常的發生率為每 1000 人一年中 128.2 例診斷。而在非暴露組群中，為每 1000 人一年中 56.3 例診斷。通過調整性別和分娩相關的醫學併發症史以及同胞情況的聚集，3 歲以前暴露於麻醉相關的發育和行為失常的估計危害比為 1.6（95% 可信區間 [CI] 為 1.4, 1.8）。手術次數增加，危險度增加：1 次手術的危險度為 1.1（95% CI: 0.8, 1.4），而 2 次手術的危險度為 2.9（94% CI: 2.5, 3.1），大於等於 3 次手術的危險度為 4.0（95% CI: 3.5, 4.5）。138 對同胞之間進行配對分析，相對危險度為 0.9（95% CI: 0.6, 1.4）。

**結論：**進入州醫療援助計畫且小於 3 歲時曾經進行手術的患兒隨後診斷為發育和行為失常的風險比未接受過外科手術的同胞兒童的相近組群風險高 60%。更為嚴謹的配對分析提示過分危險的程度歸因於麻醉或由待確定的不可測的因素介導。

（黃麗娜 譯 馬皓琳 李士通 校）

**BACKGROUND:** In vitro and in vivo studies of anesthetics have demonstrated serious neurotoxic effects on the developing brain. However, the clinical relevance of these findings to children undergoing anesthesia remains unclear. Using data from a sibling birth cohort, we assessed the association between exposure to anesthesia in the setting of

surgery in patients younger than 3 years and the risk of developmental and behavioral disorders.

**METHODS:** We constructed a retrospective cohort of 10,450 siblings who were born between 1999 and 2005 and who were enrolled in the New York State Medicaid program. The exposed group was 304 children without a history of developmental or behavioral disorders who underwent surgery when they were younger than 3 years. The unexposed group was 10,146 children who did not receive any surgical procedures when they were younger than 3 years. Exposed children were entered into analysis at the date of surgery. Unexposed children were entered into analysis at age 10 months (the mean age at which exposed children underwent surgery). Both exposed and unexposed children were followed until diagnosis with a developmental or behavioral disorder, loss to follow-up, or the end of 2005. The association of exposure to anesthesia with subsequent developmental and behavioral disorders was assessed with both proportional hazards modeling, and pair-matched analysis.

**RESULTS:** The incidence of developmental and behavioral disorders was 128.2 diagnoses per 1000 person-years for the exposed cohort and 56.3 diagnoses per 1000 person-years for the unexposed cohort. With adjustment for sex and history of birth-related medical complications, and clustering by sibling status, the estimated hazard ratio of developmental or behavioral disorders associated with any exposure to anesthesia when they were younger than 3 years was 1.6 (95% confidence interval [CI]: 1.4, 1.8). The risk increased from 1.1 (95% CI: 0.8, 1.4) for 1 operation to 2.9 (94% CI: 2.5, 3.1) for 2 operations and 4.0 (95% CI: 3.5, 4.5) for  $\geq 3$  operations. The relative risk in a matched analysis of 138 sibling pairs was 0.9 (95% CI: 0.6, 1.4).

**CONCLUSION:** The risk of being subsequently diagnosed with developmental and behavioral disorders in children who were enrolled in a state Medicaid program and who had surgery when they were younger than 3 years was 60% greater than that of a similar group of siblings who did not undergo surgery. More tightly matched pairwise analyses indicate that the extent to which the excess risk is causally attributable to anesthesia or mediated by unmeasured factors remains to be determined.

### 麻醉藥品對發育中大腦的神經毒性

#### Neurotoxicity of Anesthetic Drugs in the Developing Brain

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麻醉會導致嬰兒期動物（包括靈長類動物）的腦部神經元死亡，並可導致永久性和進行性神經認知水準下降。麻醉界和監管當局同樣關心人類是否也是這樣。在本綜述中，我總結了我們目前瞭解的小兒麻醉對於長期認知功能的風險。如果在人類中發現麻醉導致認知能力的下降，我們需要知道如何預防和治療。預防需要瞭解麻醉引起的認知能力下降的機制。本綜述概述了一些已經被提出的麻醉引起認知能力下降的機制，並討論了可能的治療選擇。如果在人類中麻醉導致認知能力的下降，我們需要知道什麼類型麻醉和多長的麻醉是安全的，並且如果有的話，什麼是不安全的。本綜述討論了關於動物麻醉的神經毒性的比較性研究的早期結果。在我們知道

兒科麻醉是否影響人類的認知和如何影響之前，改變麻醉實踐還為時過早，沒有更好的供選方案的證據可以遵循，因此還有潛在的危險。由國際麻醉研究學會及食品和藥物管理局共同自發支援的 SmartTots 的目的是，為設計來揭示這些麻醉界和公眾同樣高度重視的問題的研究提供經費，因此值得這些感興趣的群體的全力支持。

（唐亮 譯 馬皓琳 李士通 校）

Anesthesia kills neurons in the brain of infantile animals, including primates, and causes permanent and progressive neurocognitive decline. The anesthesia community and regulatory authorities alike are concerned that is also true in humans. In this review, I summarize what we currently know about the risks of pediatric anesthesia to long-term cognitive function. If anesthesia is discovered to cause cognitive decline in humans, we need to know how to prevent and treat it. Prevention requires knowledge of the mechanisms of anesthesia-induced cognitive decline. This review gives an overview of some of the mechanisms that have been proposed for anesthesia-induced cognitive decline and discusses possible treatment options. If anesthesia induces cognitive decline in humans, we need to know what type and duration of anesthetic is safe, and which, if any, is not safe. This review discusses early results of comparative animal studies of anesthetic neurotoxicity. Until we know if and how pediatric anesthesia affects cognition in humans, a change in anesthetic practice would be premature, not guided by evidence of better alternatives, and therefore potentially dangerous. The SmartTots initiative jointly supported by the International Anesthesia Research Society and the Food and Drug Administration aims to fund research designed to shed light on these issues that are of high priority to the anesthesia community and the public alike and therefore deserves the full support of these interest groups.

**一項全髖關節置換術後病人自控硬膜外布比卡因和可樂定鎮痛的前瞻性調查：  
1000 名患者用布比卡因和氫嗎啡酮改變前後的比較**

**A Prospective Survey of Patient-Controlled Epidural Analgesia with Bupivacaine and Clonidine After Total Hip Replacement: A Pre- and Postchange Comparison with Bupivacaine and Hydromorphone in 1,000 Patients**

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**背景和目的：**用布比卡因和氫嗎啡酮的病人自控硬膜外鎮痛（PCEA）可以提供矯形外科手術後高品質的鎮痛效果，但是同時伴隨著阿片類藥物相關副作用的高發生率（15%–30%）。硬膜外可樂定有不同的副作用，但是沒有記錄其使用的大樣本調查。我們進行了此項前瞻性調查，以評估全髖置換術後將 PCEA 從用布比卡因/氫嗎啡酮改為布比卡因/可樂定前後的鎮痛和副作用的情況。

**方法：**五百名接受 0.06% 布比卡因和氫嗎啡酮（10 mcg/mL）PCEA 的連續患者作為之前描述的改變前的對照組。該標準鎮痛方案隨後系統性地改為 0.06% 布比卡因和可樂定（1mcg/mL），PCEA 設置和圍術期醫護均不變，五百名連續病人作為改變後組。前瞻性輸入所有資料，然後從電子醫療記錄中提取。採集的資料包括每日



口頭疼痛評分（VPS）、瘙癢、噁心、低血壓、靜脈注射液體的需要、鎮靜和呼吸抑制。測定對改變的員工滿意程度的線上調查表發給所有參與的外科醫生、麻醉醫師、理療醫生以及醫師助理。

**結果：**2組病人的特徵類似。大部分病人採用椎管內麻醉（99%）。術後當天，可樂定組病人靜息VPS評分更低（2.3比3.7， $P < 0.001$ ，差值的95%可信區間[CI]為1.4[1.1,1.7]）。可樂定組噁心的發生率為10%-11%，氫嗎啡酮組為13%-15%。可樂定組瘙癢的發生率更低（1%比10%， $P < 0.01$ ，差值的95%可信區間為9%[6,12]）。然而，可樂定組低血壓發生率（20%比11%， $P < 0.001$ ，差值的95%CI為9%[5, 14]）以及靜脈需要注射液體的發生率較高（36比19%， $P < 0.001$ ，差值的95%可信區間為16[11,12]）。65%的員工完成了線上調查問卷，70%認為可樂定比氫嗎啡酮差。

**結論：**從硬膜外氫嗎啡酮系統性地換成硬膜外可樂定產生了混合的結果，並且沒有明顯的優越性。靜息時VPS評分僅僅在術後當天降低，瘙癢減少了，但是低血壓增多了。根據醫務人員的偏愛，我們中止了系統性的更換藥物，並且回復到我們原本用於全髖置換術後PCEA的布比卡因和氫嗎啡酮的標準溶液。

（安光惠 譯 馬皓琳 李士通 校）

**BACKGROUND AND OBJECTIVES:** Patient-controlled epidural analgesia (PCEA) with bupivacaine and hydromorphone provides high quality analgesia after orthopedic surgery but is associated with a frequent incidence of opioid-related side effects (15%–30%). Epidural clonidine has a different side effect profile, but there are no large surveys documenting its use. We performed this prospective survey to evaluate analgesia and the side effect profile in total hip replacement patients before and after a systematic change from PCEA with bupivacaine/hydromorphone to bupivacaine/clonidine.

**METHODS:** Five hundred consecutive patients received PCEA with 0.06% bupivacaine and hydromorphone (10 mcg/mL) as a previously described prechange control group. The standard analgesic regimen was then systematically changed to 0.06% bupivacaine and clonidine (1 mcg/mL) without changing the PCEA settings or other aspects of perioperative care, and 500 consecutive patients were included as a postchange group. All data were prospectively entered and then abstracted from the electronic medical record. Data collection included daily verbal pain scores (VPS), pruritus, nausea, hypotension, need for IV fluid boluses, sedation, and respiratory depression. An online survey to measure staff satisfaction with the changeover was sent to all participating surgeons, anesthesiologists, physical therapists, and physician's assistants.

**RESULTS:** Patient characteristics were similar between groups. Most patients received central neuraxial anesthesia (99%). The clonidine group had lower VPS at rest (2.3 vs 3.7,  $P < 0.001$  with 95% confidence interval [CI] of difference of 1.4 [1.1, 1.7]) on POD0. The incidence of nausea was 10%–11% for clonidine and 13%–15% for hydromorphone. The incidence of pruritus was less with clonidine (1 vs 10%,  $P < 0.01$  with 95% CI of difference of 9% [6, 12]). However, the incidence of hypotension (20 vs 11%,  $P < 0.001$  with 95% CI of differences 9% [5, 14]) and IV fluid boluses was more frequent with clonidine (36 vs 19%,  $P < 0.001$  with 95% CI of differences of 16 [11, 12]). Sixty-five percent of staff completed the online survey, and 70% considered clonidine worse than hydromorphone.

**CONCLUSION:** The systematic changeover from epidural hydromorphone to clonidine produced mixed results without obvious superiority. The VPS at rest was reduced only on postoperative day 0; pruritus was reduced, but hypotension was increased. On the basis of medical staff preference, we discontinued the systematic change and returned to our previous standard solution of bupivacaine and hydromorphone for PCEA after total hip replacement.

感覺刺激閾值會影響腰椎平面射頻去神經化結果嗎？一項前瞻性臨床相關性研究

### **Does Sensory Stimulation Threshold Affect Lumbar Facet Radiofrequency Denervation Outcomes? A Prospective Clinical Correlational Study**

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**背景：**射頻平面去神經化在用於慢性腰背痛治療的最常用方法之一。儘管感覺刺激常被當做一種替代方法來指示電極與神經足夠接近，但是沒有研究闡明刺激閾值是否對結果有影響。

**方法：**我們前瞻性地記錄了 61 個進行了腰椎平面射頻去神經化並在內側分支阻滯後有明顯疼痛減輕的連續病人的資料。對每例神經損傷，均進行了多次嘗試以使感覺刺激閾值(SST)達到最大。根據用於每例內側支以 0.1 V 的增量察覺到的最小刺激來計算平均的 SST。陽性結果定義為背痛感減輕大於等於 50%加上陽性的滿意評分持續大於等於三個月。通過受試者工作特徵曲線 (ROC) 和不同截斷值基礎上的分層結果來評估平均 SST 與去神經化結果之間的關係。

**結果：**平均 SST 與疼痛減輕之間沒有顯著關聯，無論在靜息(皮爾森檢驗的  $r = -0.01$ , 95% 可信區間[CI]:  $-0.24$  到  $0.23$ ,  $P = 0.97$ )或活動( $r = -0.17$ , 95% CI:  $-0.40$  到  $0.07$ ,  $P = 0.20$ )狀態下，都沒有成功的結果。無法定義最佳 SST。

**結論：**在腰椎平面射頻去神經化過程中的平均 SST 和治療結果之間沒有顯著關係，可能是由於個人的感知覺有差異。由於對每個病人的刺激閾值進行了最優化，因此這些資料並不能作為建議取消感覺測試或可取地採納首次嘗試取得的高感覺刺激閾值的依據。

(張怡譯 馬皓琳 李士通校)

**BACKGROUND:** Radiofrequency facet denervation is one of the most frequently performed procedures for chronic low back pain. Although sensory stimulation is

generally used as a surrogate measure to denote sufficient proximity of the electrode to the nerve, no study has examined whether stimulation threshold influences outcome.

**METHODS:** We prospectively recorded data in 61 consecutive patients undergoing lumbar facet radiofrequency denervation who experienced significant pain relief after medial branch blocks. For each nerve lesioned, multiple attempts were made to maximize sensory stimulation threshold (SST). Mean SST was calculated on the basis of the lowest stimulation perceived at 0.1-V increments for each medial branch. A positive outcome was defined as a  $\geq 50\%$  reduction in back pain coupled with a positive satisfaction score lasting  $\geq 3$  months. The relationship between mean SST and denervation outcomes was evaluated via a receiver's operating characteristic (ROC) curve, and stratifying outcomes on the basis of various cutoff values.

**RESULTS:** No correlation was noted between mean SST and pain relief at rest (Pearson's  $r = -0.01$ , 95% confidence interval [CI]:  $-0.24$  to  $0.23$ ,  $P = 0.97$ ), with activity ( $r = -0.17$ , 95% CI:  $-0.40$  to  $0.07$ ,  $P = 0.20$ ), or a successful outcome. No optimal SST could be identified.

**CONCLUSIONS:** There is no significant relationship between mean SST during lumbar facet radiofrequency denervation and treatment outcome, which may be due to differences in general sensory perception. Because stimulation threshold was optimized for each patient, these data cannot be interpreted to suggest that sensory testing should not be performed, or that high sensory stimulation thresholds obtained on the first attempt should be deemed acceptable.

### 大鼠神經病模型中抗抑鬱藥和脊髓刺激的疼痛緩解作用之間的相互作用

#### The Interaction Between Antidepressant Drugs and the Pain-Relieving Effect of Spinal Cord Stimulation in a Rat Model of Neuropathy

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**背景：**脊髓刺激（SCS）已被證明為治療神經痛的有效方法。基於我們先前關於 SCS 作用模式的研究，鞘內注射亞效應劑量的特定藥物可增強 SCS 病人的疼痛緩解作用。目前認為抗抑鬱藥對於神經痛有有益的作用。我們進行本研究來檢驗抗抑鬱藥阿米替林（三環類抗抑鬱藥）、氟西汀（選擇性 5-羥色胺再攝取抑制劑）及米那普侖（選擇性 5-羥色胺/去甲腎上腺素再攝取抑制劑）與 SCS 潛在的協同或拮抗作用。

**方法：**我們評估了在清醒、可自由活動的大鼠在外周神經損傷後，SCS 對於機械超敏反應的作用。通過鞘內給予抗抑鬱藥。

**結果：**當 SCS 與亞效應劑量的阿米替林或米那普侖聯合應用時，SCS 對於機械超敏反應的抑制作用較單獨應用 SCS 有所增強。而氟西汀則未發現此作用。沒有發現任何藥物對 SCS 的作用有拮抗作用。

**結論：**這些發現表明 SCS 與三環類抗抑鬱藥或選擇性 5-羥色胺/去甲腎上腺素再攝取抑制劑的聯合應用在臨床上可能可應用於已證實 SCS 本身無效的病例。

（毛祖旻 譯 馬皓琳 李士通 校）

**BACKGROUND:** Spinal cord stimulation (SCS) has proven to be a valuable treatment in neuropathic pain. On the basis of our previous studies on the mode of action of SCS, intrathecal administration of subeffective doses of certain drugs has been shown to enhance the pain-relieving effect in patients with SCS. Antidepressants have a well-established beneficial effect in neuropathic pain. We performed the present study to examine potential synergistic or antagonistic effects on SCS of antidepressants: amitriptyline (tricyclic antidepressant), fluoxetine (selective serotonin reuptake inhibitor), and milnacipran (selective serotonin/noradrenaline reuptake inhibitor).

**METHODS:** In rats, the effect of SCS on mechanical hypersensitivity after peripheral nerve injury was assessed in awake, freely moving animals. Antidepressants were administered intrathecally.

**RESULTS:** When combining SCS with subeffective doses of amitriptyline or milnacipran, the suppressive effect of SCS on the mechanical hypersensitivity was enhanced in comparison with that obtained with SCS alone. There was no detectable effect of fluoxetine. No signs of an antagonistic effect of the drugs on the SCS effect were observed.

**CONCLUSIONS:** These findings suggest a possible clinical application with a combination of SCS and a tricyclic antidepressant or selective serotonin/noradrenaline reuptake inhibitor drug in cases in which SCS per se has proven inefficient.

超聲引導下以刺激型導管行股神經阻滯過程中用於監測導管-神經接觸的運動反應的敏感度

### The Sensitivity of Motor Responses for Detecting Catheter-Nerve Contact During Ultrasound-Guided Femoral Nerve Blocks with Stimulating Catheters

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**背景：**以超聲檢查作為參考，我們測定了確定導管-神經發生接觸時刺激型導管誘發的運動反應的敏感度。

**方法：**用刺激型導管在超聲掃描下與 25 例患者的股神經產生接觸。輸出電流從最小值開始增加，直到股四頭肌發生收縮。以 0.5 mA 作為閾電流計算確定導管-神經接觸時運動反應的靈敏度。

**結果：**用來激發運動反應的導管刺激所需要電流範圍為 0.18 到 2.0 mA。25 例患者中有 16 例對 0.5 mA 電流刺激產生了肌肉收縮反應。運動反應對神經刺激的敏感度為 64%(95%可信區間：0.43, 0.82)。

**結論：**當刺激電流 $\leq 0.5$  mA 而肌肉無反應時，並不一定代表導管-神經未發生接觸。

(瞿亦楓 譯 馬皓琳 李士通 校)

**BACKGROUND:** We determined the sensitivity of motor responses evoked by stimulating catheters in determining catheter-nerve contact using ultrasonography as reference.

**METHODS:** Femoral nerves were contacted using stimulating catheters under ultrasonography scanning in 25 patients. The output current was increased from its minimum until quadriceps muscle contraction occurred. The sensitivity of the motor response in determining catheter-nerve contact was calculated using 0.5 mA as current threshold.

**RESULTS:** The current required for catheter stimulation to evoke a motor response ranged between 0.18 and 2.0 mA. Muscle contraction in response to 0.5 mA occurred in 16 of 25 subjects. The sensitivity of motor response for nerve stimulation was 64% (95% confidence interval: 0.43, 0.82).

**CONCLUSIONS:** The absence of muscle responses at a stimulating current  $\leq 0.5$  mA does not necessarily indicate the absence of catheter-nerve contact.