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*Anesth Analg April 2013 116:919-923; published ahead of print January 25, 2013*

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*Anesth Analg* April 2013 116:944-948; published ahead of print March 4, 2013

美國心血管麻醉醫師協會的一項隨機臨床試驗：主動脈縮窄修復術中血壓調節對使用近紅外光譜測量腦、腎和肌肉氧飽和度的影響

**Society of Cardiovascular Anesthesiologists: The Effect of Blood Pressure Regulation During Aortic Coarctation Repair on Brain, Kidney, and Muscle Oxygen Saturation Measured by Near-Infrared Spectroscopy: A Randomized, Clinical Trial**

Annelies Moerman, MD\*, Thierry Bové, MD†, Katrien François, MD, PhD†, Stefan Jacobs, MD\*, Isabel Deblaere, MD\*, Patrick Wouters, MD, PhD\* and Stefan De Hert, MD, PhD\*  
From the Departments of \*Anesthesiology and †Cardiac Surgery, Ghent University Hospital, Gent, Belgium.

*Anesth Analg* April 2013 116:760-766;

**背景：**這項研究比較 3 種常用藥物調節動脈血壓對在小兒主動脈縮窄修復術中對大腦 ( $rS_cO_2$ ), 腎臟 ( $S_rO_2$ ), 和肌肉 ( $S_mO_2$ ) 氧飽和度的影響。基於已有關於主動脈縮窄修復術中使用硝普鈉 (SNP) 對左側  $rS_cO_2$  會產生不良作用的報導, 本研究將驗證硝普鈉 (SNP), 而非七氟醚或硝酸甘油 (NTG), 會改變左側  $rS_cO_2$  的假設。此外還探討硝普鈉、硝酸甘油及七氟醚的血壓調節作用對右側  $rS_cO_2$ 、 $S_rO_2$ 、 $S_mO_2$  的影響。

**方法：**接受左側開胸路徑, 非體外迴圈下單純主動脈縮窄修復術的兒童被納入研究。在主動脈阻斷期間, 通過隨機方案, 使用硝普鈉、硝酸甘油或七氟醚控制右側肱動脈的平均動脈壓 (MAP) 限定於阻斷前數值的 120% -150%。採用近紅外光譜連續記錄雙側的  $rS_cO_2$ 、 $S_rO_2$  和  $S_mO_2$ 。作為主要終點, 比較各治療組間主動脈阻斷前後左側  $rS_cO_2$  相對變化的最大值。

**結果：**每組納入 10 例病人。觀察左側  $rS_cO_2$  相對變化的最大值, 治療組間無顯著差異 (硝普鈉與七氟醚相比, 平均差為 -0.7%, 99% 可信區間 [CI] 為 -31% to 29%,  $P = 1.0$ ; 硝普鈉與硝酸甘油相比: 平均差為 -1.8%, 99% CI 為 -32% 至 28%,  $P = 1.0$ ; 七氟醚與硝酸甘油相比: 平均差為 -1.1%, 99% CI 為 -31% 至 29%,  $P = 1.0$ )。各組間右側  $rS_cO_2$  的變化也無差異 ( $P = 0.4$ )。與硝酸甘油相比, 硝普鈉組的  $S_mO_2$  下降更為顯著 ( $-64\% \pm 17\%$  比  $-34\% \pm 25\%$ ,  $P = 0.01$ ), 發生更早 ( $-9 \pm 4\% \text{ min}^{-1}$  比  $-4 \pm 3\% \text{ min}^{-1}$ ,  $P = 0.004$ )。硝酸甘油組的右側  $rS_cO_2$  與平均動脈壓相關性較差 ( $r = -0.2$ ,  $P = 0.93$ ), 而七氟醚組 ( $r = 0.44$ ,  $P = 0.09$ ) 和硝普鈉組 ( $r = 0.56$ ,  $P = 0.04$ ) 的兩者關係處於臨界值。

**結論：**在主動脈阻斷期間分別使用硝普鈉、硝酸甘油或七氟醚處理近端高血壓, 三組間左側  $rS_cO_2$  的平均差不超過 32%。另外的分析報告顯示, 使用硝酸甘油時  $rS_cO_2$  的變化呈非 MAP 依賴性。由於硝酸甘油也可使外周組織氧飽和度的下降較少、較慢, 本研究建議在涉及主動脈阻斷的手術過程中使用硝酸甘油能更好地控制近端血壓。

(諸琳婕 譯 陳傑 校)

**BACKGROUND:** In this study, we compared the effects of 3 frequently used arterial blood pressure-regulating agents on brain ( $rS_cO_2$ ), renal ( $S_rO_2$ ), and muscle ( $S_mO_2$ ) oxygen saturation,

during aortic coarctation repair in children. Based on the reported adverse effect of sodium nitroprusside (SNP) on left-sided  $rS_cO_2$  during aortic coarctation repair, we tested the hypothesis that the alterations in left  $rS_cO_2$  occurring with SNP would not be present with sevoflurane and nitroglycerin (NTG). Additionally, we explored the effects of blood pressure regulation with SNP, NTG, or sevoflurane on right-sided  $rS_cO_2$ ,  $S_rO_2$ , and  $S_mO_2$ .

**METHODS:** Children with isolated aortic coarctation undergoing surgical repair through a left thoracotomy without the use of cardiopulmonary bypass were considered eligible for the study. During aortic cross-clamping, control of mean arterial blood pressure (MAP) was conducted according to randomization by the use of SNP, NTG, or sevoflurane to obtain a mean target right brachial blood pressure of 120% to 150% of the MAP value before cross-clamping. Bilateral  $rS_cO_2$ ,  $S_rO_2$ , and  $S_mO_2$  were recorded continuously with near-infrared spectroscopy. As a primary end point, the maximal relative change in left-sided  $rS_cO_2$  in response to aortic cross-clamping was compared among treatment groups.

**RESULTS:** Ten patients per group were included. No significant difference among treatment groups was observed in maximal relative change in left-sided  $rS_cO_2$  (SNP versus sevoflurane: mean difference  $-0.7\%$ , 99% confidence interval [CI]  $-31\%$  to  $29\%$ ,  $P = 1.0$ ; SNP versus NTG: mean difference  $-1.8\%$ , 99% CI  $-32\%$  to  $28\%$ ,  $P = 1.0$ ; sevoflurane versus NTG: mean difference  $-1.1\%$ , 99% CI  $-31\%$  to  $29\%$ ,  $P = 1.0$ ). Additional analyses also detected no difference between groups in right  $rS_cO_2$  ( $P = 0.4$ ). Compared with NTG, treatment with SNP resulted in a significantly larger ( $-64\% \pm 17\%$  vs  $-34\% \pm 25\%$ ,  $P = 0.01$ ) and faster ( $-9 \pm 4\% \text{ min}^{-1}$  vs  $-4 \pm 3\% \text{ min}^{-1}$ ,  $P = 0.004$ ) decrease in  $S_mO_2$ . Right-sided  $rS_cO_2$  and MAP showed a poor correlation for NTG ( $r = -0.2$ ,  $P = 0.93$ ), whereas borderline for sevoflurane ( $r = 0.44$ ,  $P = 0.09$ ) and SNP ( $r = 0.56$ ,  $P = 0.04$ ).

**CONCLUSIONS:** The mean differences in left-sided  $rS_cO_2$  among the patients treated with SNP, NTG, or sevoflurane for proximal hypertension during aortic cross-clamping were no more than 32%. Additional analysis demonstrated a low MAP- $rS_cO_2$  dependence with the use of NTG. Because NTG also resulted in a smaller and slower decrease of oxygen saturation in peripheral tissues, our data suggest that its use might be preferable for proximal blood pressure control during surgical procedures involving aortic cross-clamping.

### 局部麻醉藥聚合物微粒引起的局部毒性

#### Local Toxicity from Local Anesthetic Polymeric Microparticles

J. Brian McAlvin, MD\*†‡, Gally Reznor, BS, MBS†, Sahadev A. Shankarappa, MPH, MBBS, PhD†‡, Cristina F. Stefanescu, BS‡ and Daniel S. Kohane, MD, PhD†‡

From the \*Department of Medicine, Medicine Critical Care Program, Children's Hospital Boston, Harvard Medical School; †Laboratory for Biomaterials and Drug Delivery, Department of Anesthesiology, Division of Critical Care Medicine, Children's Hospital Boston, Harvard Medical School, Boston; and ‡Harvard-Massachusetts Institute of Technology Division of Health Sciences and Technology, Cambridge, Massachusetts.

Anesth Analg April 2013 116:794-803

**背景：**局部麻醉緩釋劑對局部組織損傷可能很嚴重。據報導此種損傷程度迥異。通過研究大鼠對膠囊型局部麻醉藥（低濃度利多卡因；高濃度布比卡因）的組織反應來驗證此種藥物的內在肌肉毒性。

**方法：**測量不同濃度的利多卡因和布比卡因對 C2C12 肌小管的細胞毒性，共 6 天。分別採用四種微粒配方的利多卡因和布比卡因對大鼠進行坐骨神經阻滯：10%（w/w）利多卡因（乳酸-乙醇酸）共聚體(PLGA)、10%（w/w）布比卡因 PLGA、50%（w/w）利多卡因

PLGA 和 50% (w/w) 布比卡因 PLGA。使用改良熱板實驗和負重測量來評估神經阻滯效果。通過對注射點的組織切片進行評分來評估肌肉毒性。同時檢測布比卡因和利多卡因微粒的釋放動力學參數。

**結果：**50% (w/w)利多卡因和 50% (w/w)布比卡因的感覺阻滯持續時間中位數分別為 255 (90-540) min、840 (277-1215) min ( $p=0.056$ )。所有微粒配方都可引起肌肉毒性。局部麻醉藥的選擇對肌肉毒性的嚴重程度並無影響。50% (w/w) 利多卡因與 50%(w/w)布比卡因相比，兩組 4 天和 14 天的肌肉毒性評分中位數分別為 3.4 (2.1-4.2) vs 3.3(2.9-3.5)( $p=0.44$ )；1.9 (1.8-2.4) vs 1.7 (1.3-1.9) ( $P = 0.23$ )。

**結論：**利多卡因和布比卡因 PLGA 微粒引起肌肉毒性的程度相似，而與劑量無關。內源性肌肉毒性並不能預測這些局麻藥持續釋放導致的組織損傷。在肌肉和神經附近注射此種製劑時需謹慎。

(馬霄雯 譯 陳傑 校)

**BACKGROUND:** Local tissue injury from sustained-release formulations for local anesthetics can be severe. There is considerable variability in reporting of that injury. We investigated the influence of the intrinsic myotoxicity of the encapsulated local anesthetic (lidocaine, low; bupivacaine, high) on tissue reaction in rats.

**METHODS:** Cytotoxicity from a range of lidocaine and bupivacaine concentrations was measured in C2C12 myotubes over 6 days. Rats were given sciatic nerve blocks with 4 microparticulate formulations of lidocaine and bupivacaine: 10% (w/w) lidocaine poly(lactic-co-glycolic) acid (PLGA), 10% (w/w) bupivacaine PLGA, 50% (w/w) lidocaine PLGA, and 50% (w/w) bupivacaine PLGA. Effectiveness of nerve blockade was assessed by a modified hotplate test and weightbearing measurements. Myotoxicity was scored in histologic sections of injection sites. Bupivacaine and lidocaine release kinetics from the particles were measured.

**RESULTS:** Median sensory blockade duration for 50% (w/w) lidocaine was 255 (90–540) minutes versus 840 (277–1215) minutes for 50% (w/w) bupivacaine ( $P = 0.056$ ). All microparticulate formulations resulted in myotoxicity. The choice of local anesthetic did not influence the severity of myotoxicity. Median myotoxicity scores for 50% (w/w) lidocaine compared with 50% (w/w) bupivacaine at 4 days were 3.4 (2.1–4.2) vs 3.3 (2.9–3.5) ( $P = 0.44$ ) and at 14 days 1.9 (1.8–2.4) vs 1.7 (1.3–1.9) ( $P = 0.23$ ), respectively.

**CONCLUSIONS:** Lidocaine and bupivacaine PLGA microspheres resulted in similar degrees of myotoxicity, irrespective of drug loading. Intrinsic myotoxicity did not predict tissue injury from sustained release of these anesthetics. Caution is warranted in the use of such devices near muscle and nerve.

### 俯臥位對於校準和未校準的脈衝波形衍生心臟指數測量值準確度的影響

#### The Influence of Prone Positioning on the Accuracy of Calibrated and Uncalibrated Pulse Contour-Derived Cardiac Index Measurements

Joern Grensemann, MD\*, Ulrike Bruecken, MD\*, András Treszl, MD, PhD, MSc†, Frank Wappler, MD, PhD\* and Samir G. Sakka, MD, PhD\*

From the \*Department of Anaesthesiology and Operative Intensive Care Medicine, University Hospital Witten/Herdecke, Koeln; and †Department of Medical Biometry and Epidemiology, University Medical Center, Hamburg-Eppendorf, Germany.

*Anesth Analg April 2013 116:820-826*

**背景：**因肺功能不全而處於俯臥體位元元患者常需要密切的血流動力學監護。採用肺熱稀釋法（TPTD）作為參考技術，本試驗考察此類患者中改良俯臥位（135°）對脈衝波形衍生的校準心臟指數（CI<sub>PC</sub>）和未校準的心臟指數（CI<sub>VIG</sub>）測量值精確度的影響。

**方法：**對 16 名併發急性肺損傷或者急性呼吸窘迫綜合征的重症機械通氣患者（11 位男性，5 位女性，年齡在 20 到 71 歲之間）進行研究。患者同時接受結合一個集成校準脈衝波形技術（PiCCO®）的 TPTD 監測和未校準的脈衝波形分析（FloTrac/Vigileo™）監測。在改變體位前，通過 TPTD 測量心臟指數（L·min<sup>-1</sup>·m<sup>-2</sup>）（CI<sub>TPTD</sub>）並對 CI<sub>PC</sub> 進行校準。俯臥位後，從監護儀上獲取 CI<sub>PC</sub> 和 CI<sub>VIG</sub> 值而 CI<sub>TPTD</sub> 值通過測量得到。在 8 到 10 小時之後結束俯臥位而再次測量相反的過程。使用基於一個隨機效應模型的 Bland-Altman 分析來計算一致性限度（LOA）和百分誤差。使用極座標圖來進行趨勢分析。

**結果：**仰臥位 CI<sub>TPTD</sub> 為 3.3 ± 0.9（平均值±標準差），而 CI<sub>VIG</sub> 為 3.1 ± 0.8。在俯臥後，CI<sub>PC</sub> 為 3.5 ± 0.8，CI<sub>VIG</sub> 為 3.3 ± 0.8，CI<sub>TPTD</sub> 為 3.6 ± 0.8。在恢復仰臥位前，CI<sub>TPTD</sub> 為 3.5 ± 0.7，CI<sub>VIG</sub> 為 3.3 ± 1.0。在恢復體位後，CI<sub>TPTD</sub> 為 3.1 ± 0.7，CI<sub>PC</sub> 為 3.3 ± 0.7，CI<sub>VIG</sub> 為 2.9 ± 0.6。CI<sub>PC</sub> 和 CI<sub>VIG</sub> 的俯臥位和復位匯總平均偏倚分別為 -0.1（LOA -0.7 至 0.6；百分誤差 19%），0.3（LOA -1.3 至 1.9；百分誤差 48%）。因 CI 變化過小而無法進行趨勢分析。

**結論：**根據 Critchley 標準，雖然俯臥位的改變對校準 CI 的測值影響輕微，但未校準的 CI 值顯示了一定程度的誤差，且因過高而無法被臨床接受。

（孫莉荔 譯 陳傑 校）

**BACKGROUND:** Patients with lung failure who undergo prone positioning often receive extended hemodynamic monitoring. We investigated the influence of modified prone positioning (135°) on the accuracy of pulse contour-derived calibrated cardiac index (CI<sub>PC</sub>) and uncalibrated cardiac index (CI<sub>VIG</sub>) in this patient population with transpulmonary thermodilution (TPTD) as reference technique.

**METHODS:** We studied 16 critically ill and mechanically ventilated patients (11 men, 5 women, aged 20–71 years) with acute lung injury or acute respiratory distress syndrome. Patients were monitored by TPTD with an integrated calibrated pulse contour technique (PiCCO®) and by uncalibrated pulse contour analysis (FloTrac/Vigileo™). Before prone positioning, cardiac index (given in L·min<sup>-1</sup>·m<sup>-2</sup>) was measured by TPTD (CI<sub>TPTD</sub>) and CI<sub>PC</sub> was calibrated. After positioning, CI<sub>PC</sub> and CI<sub>VIG</sub> were read from the monitor and CI<sub>TPTD</sub> was measured. After 8 to 10 hours, prone positioning was completed and measurements were performed analogously. Bland-Altman analysis based on a random-effects model was used to calculate limits of agreement (LOA) and percentage errors. Polar plots were used for trend analysis.

**RESULTS:** Supine CI<sub>TPTD</sub> was 3.3 ± 0.9 (mean ± SD) and CI<sub>VIG</sub> was 3.1 ± 0.8. After proning, CI<sub>PC</sub> was 3.5 ± 0.8, CI<sub>VIG</sub> 3.3 ± 0.8, and CI<sub>TPTD</sub> 3.6 ± 0.8. Before repositioning, CI<sub>TPTD</sub> was 3.5 ± 0.7 and CI<sub>VIG</sub> 3.3 ± 1.0. After repositioning, CI<sub>TPTD</sub> was 3.1 ± 0.7, CI<sub>PC</sub> 3.3 ± 0.7, and CI<sub>VIG</sub> 2.9 ± 0.6. Mean bias pooled for proning and repositioning was -0.1 (LOA -0.7 to 0.6) for CI<sub>PC</sub> (percentage error 19%) and 0.3 (LOA -1.3 to 1.9) for CI<sub>VIG</sub> (percentage error 48%). Changes in CI were too small for trending analysis.

**CONCLUSION:** Although calibrated CI measurements are only marginally influenced by prone positioning, according to the criteria of Critchley and Critchley, uncalibrated CI values show a degree of error, too high to be considered clinically acceptable.

異氟醚導致小鼠大腦皮層發育細胞凋亡的特徵和定量研究

## Characterization and Quantification of Isoflurane-Induced Developmental Apoptotic Cell Death in Mouse Cerebral Cortex

George K. Istaphanous, MD\*†, Christopher G. Ward, MD\*†, Xinyu Nan, BS\*, Elizabeth A. Hughes, BS\*, John C. McCann, BS\*, John J. McAuliffe, MD, MBA\*†, Steve C. Danzer, PhD\*† and Andreas W. Loepke, MD, PhD\*†

From the Departments of \*Anesthesia and †Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio.

Anesth Analg April 2013 116:845-854

**背景：**越來越多的證據表明：異氟醚和其他的麻醉藥一樣，對新生動物有神經毒性作用。但是，皮質細胞的瀕死特性和其消亡程度均未被充分描述。此項研究利用免疫組化方法識別瀕死的細胞，並定量分析新生小鼠皮質，及大腦影響區域的凋亡細胞比例。

**方法：**隨機分配七日齡同窩小鼠（每組 36 只），分別暴露於 1.5% 異氟醚或禁食狀態暴露於室內空氣共 6 小時。之後立即處死小鼠，用活化的半胱天冬酶 3 和以下的細胞標記物之一對大腦切片進行雙重染色：神經元的細胞核（NeuN）， $\gamma$ -氨基丁酸能細胞的谷氨酸脫羧酶（GAD）65 和 67，還有神經膠質纖維酸性蛋白和星形膠質細胞的 S100 $\beta$ 。

**結果：**活化的半胱天冬酶 3 免疫標記顯示：接受異氟醚暴露的七日齡小鼠較對照組，細胞凋亡普遍增加。對半胱天冬酶 3 標記的皮質板層 II/III 的細胞進行共聚焦分析表明：絕大多數細胞在神經元的有絲分裂後期，也有一些是星形膠質細胞。隨後對異氟醚誘導的視覺皮質（即實質損傷區）神經元凋亡進行量化。在非麻醉的對照組動物中， $0.08\% \pm 0.001\%$  NeuN 標記陽性的 II/III 板層皮質細胞對半胱天冬酶 3 有免疫反應。相反，異氟醚暴露後即刻，NeuN 標記陽性的神經元凋亡比例增加至少 11 倍（95% 可信區間的下限），達到  $2.0\% \pm 0.004\%$ （異氟醚組 vs 對照組， $P=0.0017$ ）。經異氟醚暴露的動物中，所有半胱天冬酶 3 標記陽性的淺表皮層神經元，其中  $2.9\% \pm 0.02\%$  也共同表達了谷氨酸脫羧酶 67（GAD67），表明抑制性神經元同樣受影響。然而，對  $\gamma$ -氨基丁酸能神經細胞的分析證明事實更為複雜。除了對一些 GAD67 免疫反應陽性的神經元誘導凋亡外，麻醉導致了谷氨酸脫羧酶 67（ $0.98$  vs  $1.84$  ng/mg 蛋白， $P < 0.00001$ ，麻醉組與對照組）和谷氨酸脫羧酶 65（ $2.25 \pm 0.74$  vs  $23.03 \pm 8.47$  ng/mg 蛋白， $P = 0.0008$ ，麻醉組與對照組）的蛋白水準戲劇性的降低。

**結論：**長期暴露在異氟醚中會增加 7 日齡小鼠神經元的凋亡率，喪失將近 2% 的皮質神經元，其中的一些被確定為  $\gamma$ -氨基丁酸能中間神經元。此外通過下調核心酶 GAD65 and GAD67 表達，異氟醚暴露也干擾了抑制性中樞神經系統。相反，在這個年齡組，只有少數退化的細胞被認定為星形膠質細胞。在動物身上的這些發現仍然有待進一步確定其臨床聯繫。

（鄭華容 譯 陳傑 校）

**BACKGROUND:** Accumulating evidence indicates that isoflurane and other, similarly acting anesthetics exert neurotoxic effects in neonatal animals. However, neither the identity of dying cortical cells nor the extent of cortical cell loss has been sufficiently characterized. We conducted the present study to immunohistochemically identify the dying cells and to quantify the fraction of cells undergoing apoptotic death in neonatal mouse cortex, a substantially affected brain region.

**METHODS:** Seven-day-old littermates ( $n = 36$ ) were randomly assigned to a 6-hour exposure to either 1.5% isoflurane or fasting in room air. Animals were euthanized immediately after

exposure and brain sections were double-stained for activated caspase 3 and one of the following cellular markers: Neuronal Nuclei (NeuN) for neurons, glutamic acid decarboxylase (GAD)65 and GAD67 for GABAergic cells, as well as GFAP (glial fibrillary acidic protein) and S100 $\beta$  for astrocytes.

**RESULTS:** In 7-day-old mice, isoflurane exposure led to widespread increases in apoptotic cell death relative to controls, as measured by activated caspase 3 immunolabeling. Confocal analyses of caspase 3–labeled cells in cortical layers II and III revealed that the overwhelming majority of cells were postmitotic neurons, but some were astrocytes. We then quantified isoflurane-induced neuronal apoptosis in visual cortex, an area of substantial injury. In unanesthetized control animals, 0.08%  $\pm$  0.001% of NeuN-positive layer II/III cortical neurons were immunoreactive for caspase 3. By contrast, the rate of apoptotic NeuN-positive neurons increased at least 11-fold (lower end of the 95% confidence interval [CI]) to 2.0%  $\pm$  0.004% of neurons immediately after isoflurane exposure ( $P = 0.0017$  isoflurane versus control). In isoflurane-treated animals, 2.9%  $\pm$  0.02% of all caspase 3–positive neurons in superficial cortex also coexpressed GAD67, indicating that inhibitory neurons may also be affected. Analysis of GABAergic neurons, however, proved unexpectedly complex. In addition to inducing apoptosis among some GAD67-immunoreactive neurons, anesthesia also coincided with a dramatic decrease in both GAD67 (0.98 vs 1.84 ng/mg protein,  $P < 0.00001$ , anesthesia versus control) and GAD65 (2.25  $\pm$  0.74 vs 23.03  $\pm$  8.47 ng/mg protein,  $P = 0.0008$ , anesthesia versus control) protein levels.

**CONCLUSIONS:** Prolonged exposure to isoflurane increased neuronal apoptotic cell death in 7-day-old mice, eliminating approximately 2% of cortical neurons, of which some were identified as GABAergic interneurons. Moreover, isoflurane exposure interfered with the inhibitory nervous system by downregulating the central enzymes GAD65 and GAD67. Conversely, at this age, only a minority of degenerating cells were identified as astrocytes. The clinical relevance of these findings in animals remains to be determined.

### 氬胺酮通過活性氧簇介導的線粒體途徑增強人神經幹細胞增殖和誘導神經元凋亡

#### **Ketamine Enhances Human Neural Stem Cell Proliferation and Induces Neuronal Apoptosis via Reactive Oxygen Species–Mediated Mitochondrial Pathway**

Xiaowen Bai, MD, PhD\*, Yasheng Yan, BS\*, Scott Canfield, BS\* $\dagger$ , Maria Y. Muravyeva, MD, PhD\*, Chika Kikuchi, MD\*, Ivan Zaja, MD\*, John A. Corbett, PhD $\ddagger$  and Zeljko J. Bosnjak, PhD\* $\dagger$

From the Departments of \*Anesthesiology,  $\dagger$ Physiology, and  $\ddagger$ Biochemistry, Medical College of Wisconsin, Milwaukee, Wisconsin.

Anesth Analg April 2013 116:869-880

**背景：**越來越多證據表明，氬胺酮在多種動物模型中引起神經毒性，導致關於兒科麻醉安全性的一系列顧慮。然而氬胺酮是否以及如何引起人類神經細胞毒性仍未知。人胚胎幹細胞 (hESCs) 神經的體外再現致氬胺酮對神經幹細胞 (NSCs) 以及發育中的神經元毒性效應的觀察成爲可能，而這些是無法在人類身上試驗的。此項研究評估氬胺酮對源於人胚胎細胞的神經幹細胞和神經元細胞的影響。

**方法：**人胚胎細胞通過神經幹細胞直接分化爲神經元。使用不同劑量的氬胺酮對神經幹細胞和生長 2 周的神經元進行不同時長的處理。用 Ki67 免疫螢光染色和溴去氧尿苷試驗分析神經幹細胞的增殖能力。用 TUNEL 染色和半胱天冬酶 3 活性測量分析神經凋亡。同

時研究線粒體相關的神經元凋亡途徑包括線粒體膜電位、細胞內細胞色素 C 分佈、線粒體分裂、活性氧簇產生。

**結果：**在 6 小時的接觸後，氯胺酮（100 $\mu$ M）增加神經幹細胞增殖。然而，顯著的神經元凋亡只發現於經氯胺酮處理 24 小時後。另外，氯胺酮降低線粒體膜電位，增加細胞色素 C 從線粒體到細胞液釋放。和對照組相比，氯胺酮也增強線粒體分裂和活性氧簇產生。重要的是，水溶性維生素 E，一種活性氧簇清除劑，顯著地減弱了氯胺酮引起的活性氧簇產生的增加和神經元凋亡。

**結論：**這些資料首次證實：（1）氯胺酮增加神經幹細胞增殖並導致神經元凋亡；（2）線粒體涉及氯胺酮相關的神經元毒性，可被水溶性維生素 E 拮抗；（3）幹細胞相關的神經形成系統可能為快速顯示麻醉的神經毒性，研究其潛在機制和為了避免這種毒性效應而研究預防策略提供一個簡單而有希望的離體模型。

（詹愷 譯 陳傑 校）

**BACKGROUND:** Growing evidence indicates that ketamine causes neurotoxicity in a variety of developing animal models, leading to a serious concern regarding the safety of pediatric anesthesia. However, if and how ketamine induces human neural cell toxicity is unknown. Recapitulation of neurogenesis from human embryonic stem cells (hESCs) in vitro allows investigation of the toxic effects of ketamine on neural stem cells (NSCs) and developing neurons, which is impossible to perform in humans. In the present study, we assessed the influence of ketamine on the hESC-derived NSCs and neurons.

**METHODS:** hESCs were directly differentiated into neurons via NSCs. NSCs and 2-week-old neurons were treated with varying doses of ketamine for different durations. NSC proliferation capacity was analyzed by Ki67 immunofluorescence staining and bromodeoxyuridine assay. Neuroapoptosis was analyzed by TUNEL staining and caspase 3 activity measurement. The mitochondria-related neuronal apoptosis pathway including mitochondrial membrane potential, cytochrome c distribution within cells, mitochondrial fission, and reactive oxygen species (ROS) production were also investigated.

**RESULTS:** Ketamine (100  $\mu$ M) increased NSC proliferation after 6-hour exposure. However, significant neuronal apoptosis was only observed after 24 hours of ketamine treatment. In addition, ketamine decreased mitochondrial membrane potential and increased cytochrome c release from mitochondria into cytosol. Ketamine also enhanced mitochondrial fission as well as ROS production compared with no-treatment control. Importantly, Trolox, a ROS scavenger, significantly attenuated the increase of ketamine-induced ROS production and neuronal apoptosis.

**CONCLUSIONS:** These data for the first time demonstrate that (1) ketamine increases NSC proliferation and causes neuronal apoptosis; (2) mitochondria are involved in ketamine-induced neuronal toxicity, which can be prevented by Trolox; and (3) the stem cell-associated neurogenesis system may provide a simple and promising in vitro model for rapidly screening anesthetic neurotoxicity and studying the underlying mechanisms as well as prevention strategies to avoid this toxic effect.

自報醫療差錯的頻率與麻醉培訓監督的關係：一項美國麻醉住院醫師培訓調查

**The Association Between Frequency of Self-Reported Medical Errors and Anesthesia Trainee Supervision: A Survey of United States Anesthesiology Residents-in-Training**

Gildasio S. De Oliveira Jr., MD, MSCI, Rod Rahmani, BS, Paul C. Fitzgerald, MS, Ray Chang, BS and Robert J. McCarthy, PharmD



From the Department of Anesthesiology, Northwestern University, Chicago, Illinois.  
Anesth Analg 2013;116:892-7

**背景：**對醫學實習生缺乏監管導致住院醫師教育與病人的護理和安全兩方面都受到損害。監管不力可導致接受低年資住院醫師治療的患者死亡率增加。本研究假設自報更多醫療差錯的住院醫師，較那些報導較低醫療差錯的，其受監督品質更低。這項研究主要目的是評估住院醫師自報醫療差錯的頻率和接受機構監督品質之間的關聯性。

**方法：**一項橫向的全國性調查隨機抽取美國麻醉培訓部門的 1000 名住院醫生。分別來自 122 住院醫師方案的住院醫師都被邀請參加此研究項目，每個機構人數的中位數（四分位間距）為 7（4-11）。參與者被要求完成一項關於人口學統計，對機構監督品質評價，對監督不利原因的調查。回復的陳述包括：“我實施的操作沒有得到適當的訓練”，“我犯的錯誤使病人產生不良後果”和“我在過去的一年有過錯誤用藥史（藥物種類或劑量錯誤）”用於評估錯誤發生率。根據 De Oliveira Filho 等人量表確定平均監督評分。使用 Kruskal-Wallis 檢驗比較自報差錯種類的發生頻率。

**結果：**640 名住院醫生對調查作出回答（60.4%）。45 名（7.5%）受訪者表示他們沒有得到適當的訓練，24 名（4%）受訪者報導，醫療差錯後患者產生不良後果，16 名（3%）受訪者在去年多次用藥錯誤或經常發生用錯藥。監督評分與這 3 個評估醫療差錯問題所報告的差錯頻率呈負相關。在臨界值為 3 時，用於預測這些問題的發生率，即操作未得到適當訓練，醫療差錯後患者產生不良後果及過去一年上報錯誤用藥，其監督評分整體精度（曲線下面積）（99% 置信區間）分別為 0.81（0.73-0.86），0.89（0.77-0.95）和 0.93（0.77-0.98）。

**結論：**對患者有不良後果和用藥錯誤相關醫療差錯發生率更高的麻醉實習生，其對機構監督的評分也較低。本研究結果表明，對監督和病人安全之間關係進行深入研究是必要的。

（孫曉瓊 譯 陳傑 校）

**BACKGROUND:** Poor supervision of physician trainees can be detrimental not only to resident education but also to patient care and safety. Inadequate supervision has been associated with more frequent deaths of patients under the care of junior residents. We hypothesized that residents reporting more medical errors would also report lower quality of supervision scores than the ones with lower reported medical errors. The primary objective of this study was to evaluate the association between the frequency of medical errors reported by residents and their perceived quality of faculty supervision.

**METHODS:** A cross-sectional nationwide survey was sent to 1000 residents randomly selected from anesthesiology training departments across the United States. Residents from 122 residency programs were invited to participate, the median (interquartile range) per institution was 7 (4–11). Participants were asked to complete a survey assessing demography, perceived quality of faculty supervision, and perceived causes of inadequate perceived supervision. Responses to the statements “I perform procedures for which I am not properly trained,” “I make mistakes that have negative consequences for the patient,” and “I have made a medication error (drug or incorrect dose) in the last year” were used to assess error rates. Average supervision scores were determined using the De Oliveira Filho et al. scale and compared among the frequency of self-reported error categories using the Kruskal-Wallis test.

**RESULTS:** Six hundred four residents responded to the survey (60.4%). Forty-five (7.5%) of the respondents reported performing procedures for which they were not properly trained, 24

(4%) reported having made mistakes with negative consequences to patients, and 16 (3%) reported medication errors in the last year having occurred multiple times or often. Supervision scores were inversely correlated with the frequency of reported errors for all 3 questions evaluating errors. At a cutoff value of 3, supervision scores demonstrated an overall accuracy (area under the curve) (99% confidence interval) of 0.81 (0.73–0.86), 0.89 (0.77–0.95), and 0.93 (0.77–0.98) for predicting a response of multiple times or often to the question of performing procedures for which they were not properly trained, reported mistakes with negative consequences to patients, and reported medication errors in the last year, respectively.

**CONCLUSIONS:** Anesthesiology trainees who reported a greater incidence of medical errors with negative consequences to patients and drug errors also reported lower scores for supervision by faculty. Our findings suggest that further studies of the association between supervision and patient safety are warranted. (Anesth Analg 2013;116:892–7)

### 適用於麻醉操作人員的時間關鍵的資訊：無線設備的通訊延遲

#### Communication Latencies of Wireless Devices Suitable for Time-Critical Messaging to Anesthesia Providers

Richard H. Epstein, MD, CPHIMS\*, Franklin Dexter, MD, PhD† and Brian Rothman, MD‡  
From the \*Department of Anesthesiology, Jefferson Medical College, Philadelphia, Pennsylvania; †Division of Management Consulting, Department of Anesthesia, University of Iowa, Iowa City, Iowa; and ‡Division of Multispecialty Adult Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee.

Anesth Analg April 2013 116:911-918;

**背景：**負責麻醉操作的流動工作人員之間擁有快速可靠的文本資訊通訊對於患者的護理及有效的手術室管理是重要的。麻醉部門正在實施發送文本資訊到移動設備的自動方法，這些文本資訊包括：反常的生命體征，臨床建議，護理品質，依從性或計費問題。通訊系統最關鍵的執行時間決定了可接受的最長延遲限度。為確定一個最適合通訊系統，我們對一些數位通信系統的可靠性進行了研究。

**方法：**作者測量了三個數位尋呼設備數周內的文本資訊發送及傳遞延遲程度。其中兩種設備使用的是醫院局域網外的互聯網途徑與外部的尋呼通訊 (SkyTel)。第三種設備僅使用了醫院內部的網路 (Zetron)。相繼的手機文本資訊延遲通 Lag1 的自相關函數測定，按照小時和天分級的結果。延遲的消息隨後被分批到連續 1 周的箱子中去計算平均值以及延遲的第 99 位百分位。驗收標準定義為：平均延遲小於 30 秒並且 200 個傳呼機中不超過 1 個 (0.5%) 具有的延遲超過 100 秒。手機文本被用來做陽性對照，以確保分析是恰當的，因為上述裝備 (已知的) 在高強度網路活動中的可靠性是差的。

**結果：**當按照小時分級時，延遲與手機文本資訊的次序有重大的相關性 ( $P < 0.0001$ )，按照天分級時則沒有 ( $P = 0.61$ )。運用醫院局域網外的互聯網途徑的兩種設備則展示了讓人不能接受的表現，超過 100 秒的延遲率分別為 1.3% 與 33%。依賴醫院內部網路的設備具有平均 8 秒的延遲，測試的 40200 個尋呼機均為小於 100 秒的延遲。這些發現說明何種網路的使用成為延遲的決定因素。

**結論：**麻醉通訊系統的開發需要評估預計通訊路徑的延遲時間，以及評估用於傳送緊急資訊給流動人員的設備。類似的評價與文本傳呼機相關，用於臨時想法的時間關鍵資訊傳遞。超過數小時至數天的測試僅能用於發現不合格的候選傳呼系統，因為這個結果並不一定預示長期的表現。相反，數周的測試是必要，將傳呼機適當分批進行分析。

(王苑 譯 陳傑 校)

**BACKGROUND:** Rapid and reliable methods of text communication to mobile anesthesia care providers are important to patient care and to efficient operating room management. Anesthesia departments are implementing automated methods to send text messages to mobile devices for abnormal vital signs, clinical recommendations, quality of care, and compliance or billing issues. The most time-critical communications determine maximum acceptable latencies. We studied the reliability of several alphanumeric messaging systems to identify an appropriate technology for such use.

**METHODS:** Latencies between message initiation and delivery to 3 alphanumeric paging devices were measured over weeks. Two devices used Internet pathways outside the hospital's local network with an external paging vendor (SkyTel). The third device used only the internal hospital network (Zetron). Sequential cell phone text page latencies were examined for lag-1 autocorrelation using the runs test, with results binned by hour and by day. Message latencies subsequently were batched in successive 1-week bins for calculation of the mean and 99th percentiles of latencies. We defined acceptance criteria as a mean latency <30 seconds and no more than 1 in 200 pages (0.5%) having a latency longer than 100 seconds. Cell phone texting was used as a positive control to assure that the analysis was appropriate, because such devices have (known) poor reliability during high network activity.

**RESULTS:** There was substantial correlation among latencies for sequential cell phone text messages when binned by hours ( $P < 0.0001$ ), but not by days ( $P = 0.61$ ). The 2 devices using Internet pathways outside the hospital's network demonstrated unacceptable performance, with 1.3% and 33% of latencies exceeding 100 seconds, respectively. The device dependent only on the internal network had a mean latency of 8 seconds, with 100% of 40,200 pages having latencies <100 seconds. The findings suggest that the network used was the deciding factor.

**CONCLUSIONS:** Developers of anesthesia communication systems need to measure latencies of proposed communication pathways and devices used to deliver urgent messages to mobile users. Similar evaluation is relevant for text pagers used on an ad hoc basis for delivery of time-critical notifications. Testing over a period of hours to days is adequate only for disqualification of a candidate paging system, because acceptable results are not necessarily indicative of long-term performance. Rather, weeks of testing are required, with appropriate batching of pages for analysis.

### 在大鼠脊髓背角神經元局部注射異丙酚的抗傷害及抗痛覺過敏效應

#### The Antinociceptive and Antihyperalgesic Effects of Topical Propofol on Dorsal Horn Neurons in the Rat

Kenichi Takechi, MD\*, Mirela Iodi Carstens, BA†, Amanda H. Klein, PhD† and E. Carstens, PhD†

From the \*Department of Anesthesiology and Resuscitology, Ehime University Medical School, Matsuyama, Japan; and †Department of Neurobiology, Physiology and Behavior, University of California, Davis, Davis, California.

Anesth Analg April 2013 116:932-938

**背景：**異丙酚（2,6-二異丙基苯酚）是用於全身麻醉的一種靜脈麻醉藥物。最近有證據表明接受異丙酚麻醉的病人術後疼痛較輕，異丙酚在局部注射時具有鎮痛的作用。本研究通過行為學方法和電生理學方法對大鼠局部注射異丙酚的抗傷害效應進行研究。

**方法：**在對大鼠的行為學實驗中，評估在後足局部注射不同濃度異丙酚（1%-25%）後對熱刺激以及機械刺激產生的縮足反應。在電生理實驗中，記錄被戊巴比妥麻醉的大鼠從腰段脊髓背角的廣動力閾（WDR）型神經元相關資料。評估局部注射異丙酚後同側後足對傷害性熱刺激、冷刺激及機械性刺激的神經元反應。同時檢測異丙酚是否阻斷縮足的熱敏化以及局部應用異硫氰酸烯丙酯（AITC）誘導的 WDR 神經元反應。

**結果：**局部注射異丙酚（1%-25%）顯著增加了處理側（而非對側）溫度刺激產生的縮足反射平均潛伏期，呈濃度相關性，對機械性刺激產生的縮足反射的閾值無效應。異丙酚還避免了 AITC 誘導的縮足反射潛伏期縮短。在電生理實驗中，在同側後足局部注射 10%-25% 異丙酚，而非 1% 異丙酚或賦形劑，使後足無毛區域的皮膚對傷害性熱刺激的 WDR 神經元反應程度顯著降低，而對溫度的反應閾值無顯著變化。對傷害性熱刺激產生的反應在注射異丙酚後 15min 達到最大抑制，在之後 30min 內恢復至異丙酚應用前水準。各濃度的異丙酚對皮膚冷刺激或分級機械刺激無顯著影響。局部注射 AITC 可顯著增加脊髓背角神經元對傷害性熱刺激產生的反應。這種在注射 AITC 後對熱刺激反應的增加在局部注射 10% 異丙酚時被抑制。

**結論：**這些結果證明局部注射異丙酚可以抑制 WDR 神經元對傷害性熱刺激的反應，產生鎮痛效應，同時減少了注射 AITC 後的 WDR 神經元致敏，具有抗痛覺過敏作用。這些結果與證明接受異丙酚麻醉的外科病人可減少術後疼痛的臨床研究結果一致。局部注射異丙酚減少疼痛的機制尚不明確，但可能與表達于外周傷害性神經末梢的 TRPV1 or TRPA1 受體的去敏感化

有關，同時有內源性大麻酚類的參與或外周  $\gamma$ -氨基丁酸 A 受體的啟動相關。

（瞿亦楓 譯 陳傑 校）

**BACKGROUND:** Propofol (2,6-diisopropylphenol) is an IV anesthetic used for general anesthesia. Recent evidence suggests that propofol-anesthetized patients experience less postoperative pain, and that propofol has analgesic properties when applied topically. We presently investigated the antinociceptive effects of topical propofol using behavioral and single-unit electrophysiological methods in rats.

**METHODS:** In behavioral experiments with rats, we assessed the effect of topical hindpaw application of propofol (1%–25%) on heat and mechanically evoked paw withdrawals. In electrophysiological experiments, we recorded from lumbar dorsal horn wide dynamic range (WDR)-type neurons in pentobarbital-anesthetized rats. We assessed the effect of topical application of propofol to the ipsilateral hindpaw on neuronal responses elicited by noxious heat, cold, and mechanical stimuli. We additionally tested whether propofol blocks heat sensitization of paw withdrawals and WDR neuronal responses induced by topical application of allyl isothiocyanate (AITC; mustard oil).

**RESULTS:** Topical application of propofol (1%–25%) significantly increased the mean latency of the thermally evoked hindpaw withdrawal reflex on the treated (but not opposite) side in a concentration-dependent manner, with no effect on mechanically evoked hindpaw withdrawal thresholds. Propofol also prevented shortening of paw withdrawal latency induced by AITC. In electrophysiological experiments, topical application of 10% and 25% propofol, but not 1% propofol or vehicle (10% intralipid), to the ipsilateral hindpaw significantly attenuated the magnitude of responses of WDR neurons to noxious heating of glabrous hindpaw skin with no significant change in thermal thresholds. Maximal suppression of noxious heat-evoked responses was achieved 15 minutes after application followed by recovery to the pre-propofol baseline by 30 minutes. Responses to skin cooling or graded mechanical stimuli were not significantly

affected by any concentration of propofol. Topical application of AITC enhanced the noxious heat-evoked response of dorsal horn neurons. This enhancement of heat-evoked responses was attenuated when 10% propofol was applied topically after application of AITC.

**CONCLUSIONS:** The results indicate that topical propofol inhibits responses of WDR neurons to noxious heat consistent with analgesia, and reduced AITC sensitization of WDR neurons consistent with an antihyperalgesic effect. These results are consistent with clinical studies demonstrating reduced postoperative pain in surgical patients anesthetized with propofol. The mechanism of analgesic action of topical propofol is not clear, but may involve desensitization of TRPV1 or TRPA1 receptors expressed in peripheral nociceptive nerve endings, engagement of endocannabinoids, or activation of peripheral  $\gamma$ -aminobutyric acid A receptors

### 丙泊酚能增強長期使用血管緊張素轉換酶抑制劑卡托普利治療的衰老大鼠血管舒張 Propofol Increases Vascular Relaxation in Aging Rats Chronically Treated with the Angiotensin-Converting Enzyme Inhibitor Captopril

Ferrante S. Gragasin, MD, FRCPC\*†‡§ ||, Stephane L. Bourque, PhD‡§ || ¶ and Sandra T. Davidge, PhD†‡§ || ¶

From the Departments of \*Anesthesiology and Pain Medicine, †Physiology, and ¶Obstetrics & Gynecology, University of Alberta; ‡Women and Children's Health Research Institute, §Cardiovascular Research Centre, and ||Mazinkowski Alberta Heart Institute, University of Alberta, Edmonton, Alberta, Canada.

Anesth Analg April 2013 116:775-783;

**背景：**丙泊酚的使用以及高齡都是術中低血壓的預測因數。以前，我們證明瞭丙泊酚能增強老齡大鼠腸系膜動脈的血管舒張，在一定程度上是歸因於增加了一氧化氮（NO）的生物利用度。長期使用血管緊張素轉換酶（ACE）抑制劑的患者可能在全麻下出現難治性低血壓。我們假設丙泊酚對取自於長期使用 ACE 抑制劑治療的老齡大鼠動脈增強了 NO 介導的血管舒張效應。

**方法：**12 到 13 月齡的 SD 大鼠給予或不給予卡托普利治療 7 到 8 周，在實驗的時候產生最後的 14 至 15 月齡。在安樂死前，通過頸動脈置管獲得動脈血壓。用丙泊酚（0.1–100  $\mu$ M）或醋甲膽鹼（MCh）（0.01–3  $\mu$ M）的量效曲線評估取自於治療組（卡托普利）和對照組大鼠的腸系膜動脈（100–200  $\mu$ m 直徑）的離體阻力。在丙泊酚預處理（1 和 10  $\mu$ M）後也評估 MCh 舒張效應。用左旋硝基精氨酸甲酯（1-NAME）（100  $\mu$ M）以及甲氧基的結合域（10  $\mu$ M）分別抑制 NO 和前列腺素的合成。量效資料歸納為 50% 最大鬆弛反應或曲線下面積。

**結果：**卡托普利治療組大鼠的平均動脈壓低於未治療組大鼠（ $P = 0.049$ ）。在比較卡托普利治療組和未治療組大鼠的動脈舒張時，量效曲線表明卡托普利治療組大鼠顯示出更加直接的丙泊酚舒張效應（ $P = 0.018$ ）。然而，缺少丙泊酚的 MCh 舒張在卡托普利治療組和未治療組大鼠中沒有區別（ $P = 0.80$ ）。卡托普利治療組和未治療組大鼠相比，丙泊酚預處理增強了 MCh 的動脈舒張效應（1  $\mu$ M 時  $P = 0.029$  和 10  $\mu$ M 時  $P = 0.020$ ）。在這個反應中甲氧基的結合域沒有作用（ $P = 0.22$ ）。然而，和卡托普利治療組大鼠相比較，對照組對動脈中 MCh 舒張效應的 1-NAME 依賴性抑制作用較大（ $P = 0.0077$ ）。然而在兩組中，相對於丙泊酚增加的對 MCh 的 NO 依賴性血管舒張比例是相似的。這表明在卡托普利治療組大鼠中存在丙泊酚時，對 MCh 的不同效應涉及了其他血管舒張途徑。

**結論：**我們的結果顯示，丙泊酚產生的腸系膜動脈舒張效應是直接刺激和通過內皮依賴性機制的調節的結果，其在一定程度上是 NO 依賴性的。在卡托普利治療組大鼠中，丙泊酚通過非 NO 依賴性血管舒張途徑（例如內皮衍生超極化因數）進一步增強了動脈舒張效應，這可能能解釋對用 ACE 抑制劑治療的病人給予丙泊酚時血管舒張效應增強。

（唐瑩譯 馬皓琳 李士通校）

**BACKGROUND:** Both propofol use and advanced age are predictors of intraoperative hypotension. We previously demonstrated that propofol enhances vasodilation in mesenteric arteries from aged rats, partly due to increased nitric oxide (NO) bioavailability. Patients chronically treated with angiotensin-converting enzyme (ACE) inhibitors may exhibit refractory hypotension under general anesthesia. We hypothesized that propofol enhances NO-mediated vasodilation in arteries from aged rats chronically treated with ACE inhibitors.

**METHODS:** Sprague-Dawley rats aged 12 to 13 months were treated with or without captopril for 7 to 8 weeks, yielding a final age of 14 to 15 months at the time of experimentation. Before euthanasia, arterial blood pressures were obtained through carotid artery cannulation.

Concentration-response curves to propofol (0.1–100  $\mu\text{M}$ ) or methacholine (MCh) (0.01–3  $\mu\text{M}$ ) were then assessed on isolated resistance mesenteric arteries (100–200  $\mu\text{m}$  diameter) from both treatment (captopril) and control rats. MCh relaxation was also assessed after propofol pretreatment (1 and 10  $\mu\text{M}$ ).  $N^G$ -nitro-L-arginine methyl ester (L-NAME) (100  $\mu\text{M}$ ) and meclofenamate (10  $\mu\text{M}$ ) were used to inhibit NO and prostaglandin synthesis, respectively. Concentration-response data were summarized as 50% of the maximum relaxation response or area under the curve.

**RESULTS:** Mean arterial blood pressure in the captopril-treated rats was lower than in untreated rats ( $P = 0.049$ ). When comparing relaxation in arteries from captopril-treated versus untreated rats, concentration-response curves revealed that captopril-treated rats display greater direct propofol relaxation ( $P = 0.018$ ). MCh relaxation in the absence of propofol, however, was not different between captopril-treated and untreated rats ( $P = 0.80$ ). Propofol pretreatment increased MCh relaxation in arteries from captopril-treated compared with untreated rats ( $P = 0.029$  for 1  $\mu\text{M}$  and  $P = 0.020$  for 10  $\mu\text{M}$ ). Meclofenamate did not have an effect in this response ( $P = 0.22$ ). L-NAME-dependent inhibition of MCh relaxation, however, was greater in arteries from control compared with captopril-treated rats ( $P = 0.0077$ ). However, propofol increased the proportion of NO-dependent vasodilation to MCh similarly in both groups. This suggests that other vasodilatory pathways are involved in the differential response to MCh in the presence of propofol in captopril-treated rats.

**CONCLUSIONS:** Our results show that mesenteric arterial relaxation in response to propofol, both by direct stimulation and through modulation of endothelium-dependent mechanisms, is, in part, NO-dependent. In captopril-treated rats, propofol further increased arterial relaxation through a non-NO-dependent vasodilating pathway (e.g., endothelium-derived hyperpolarizing factor), which may account for enhanced vasodilation during propofol exposure in patients treated with ACE inhibitors.

**TASK-1 (KCNK3) 和 TASK-3 (KCNK9) 雙孔鉀離子通道拮抗劑對異氟醚麻醉大鼠的呼吸刺激作用**

**TASK-1 (KCNK3) and TASK-3 (KCNK9) Tandem Pore Potassium Channel Antagonists Stimulate Breathing in Isoflurane-Anesthetized Rats**

Joseph F. Cotten, MD, PhD

From the Department of Anesthesia, Critical Care, and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts.  
Anesth Analg April 2013 116:810-816;

**背景：**TASK-1 和 TASK-3 雙孔鉀離子通道亞單位在結構上產生酸性 pH 值和缺氧抑制性鉀電導。TASK 通道在許多參與呼吸調節的組織上均有表達，且 TASK-1/TASK-3 異源二聚體在頸動脈體 1 型血管球化學感受細胞上產生缺氧敏感佔優勢的鉀電導。頸動脈體在呼吸調節中起重要作用。多沙普侖是一種強效的 TASK-1 和 TASK-3 鉀通道拮抗劑，也是頸動脈體和呼吸興奮劑。PK-THPP 和 A1899 是強效選擇性的 TASK-1 和 TASK-3 拮抗劑。本研究提出如下假說：PK-THPP 和 A1899 是與多沙普侖類似的呼吸興奮劑。

**方法：**利用 Fisher 大鼠甲狀腺單層細胞，通過尤斯灌流室研究大鼠 TASK-3 鉀通道功能。並通過無創體積描記法和動脈血氣分析，研究雄性 SD 大鼠在室內空氣中自主呼吸 1.5% 異氟醚的情況，以定量呼吸效應。

**結果：**PK-THPP、A1899 和多沙普侖可抑制大鼠 TASK-3 鉀通道的功能，半抑制濃度分別為 42 nM (33–52)、1.6 μM (0.8–3.3) 和 22 μM (18–28) ( $n = 4–6$ ；95% 可信區間)。體積描記術顯示，靜脈注射 PK-THPP、A1899 和多沙普侖產生的呼吸刺激使每分鐘通氣量出現峰值變化，與基線相比分別為  $84\% \pm 19\%$  和  $226\% \pm 56\%$  (PK-THPP 為 0.5 和 5 mg/kg 時；均值±標準誤； $n = 3–4$ ；與空白溶劑對照相比分別  $P < 0.05$  和  $P < 0.001$ )； $46\% \pm 2\%$  和  $236\% \pm 48\%$  (A1899 為 5 和 25 mg/kg 時； $n = 3–4$ ；分別  $P > 0.05$  和  $P < 0.001$ )； $103\% \pm 20\%$  (多沙普侖 25 mg/kg； $n = 4$ )，以及  $33\% \pm 9\%$  (二甲亞砒溶劑 1 mL/kg； $n = 4$ )。血氣分析顯示，與多沙普侖不同，PK-THPP 和 A1899 產生強大且持久的呼吸性碱中毒。靜脈給藥 30 分鐘後，發現動脈 pH 值和 PaCO<sub>2</sub> 分別為  $7.62 \pm 0.02$  和  $23 \pm 0.8$  mm Hg (PK-THPP 5 mg/kg 後； $n = 4$ ；與溶劑相比  $P$  均  $< 0.001$ )、 $7.49 \pm 0.02$  和  $31 \pm 2$  mm Hg (A1899 25 mg/kg 後； $n = 6$ ； $P$  分別  $< 0.05$  和  $0.001$ )、 $7.43 \pm 0.03$  和  $39 \pm 4$  mm Hg (多沙普侖 25 mg/kg 後； $n = 4$ ；兩者  $P > 0.05$ ) 以及  $7.38 \pm 0.03$  和  $48 \pm 4$  mm Hg (二甲亞砒溶劑 1 mL/kg 後； $n = 3$ )。

**結論：**PK-THPP 和 A1899 是強效的大鼠 TASK-3 拮抗劑和有效的呼吸興奮劑。PK-THPP 和 A1899 對呼吸影響的強度和/或持續時間均大於多沙普侖。PK-THPP 和 A1899 或相關化合物可能具有治療呼吸系統疾病的潛力。

(陳彬彬 譯，馬皓琳、李士通 校)

**BACKGROUND:** TASK-1 and TASK-3 tandem pore potassium channel subunits provide a constitutive acidic pH- and hypoxia-inhibited potassium conductance. TASK channels are expressed in a number of tissues involved in regulation of breathing, and the TASK-1/TASK-3 heterodimer provides the predominant hypoxia-sensitive potassium conductance in carotid body type 1 glomus chemosensing cells. The carotid bodies have an important role in regulation of breathing. Doxapram is a potent TASK-1 and TASK-3 potassium channel antagonist and a carotid body and breathing stimulant. PK-THPP and A1899 are potent and selective TASK-1 and TASK-3 antagonists. I hypothesized PK-THPP and A1899 are, like doxapram, breathing stimulants.

**METHODS:** I studied rat TASK-3 potassium channel function by Ussing chamber using Fischer rat thyroid monolayers. To quantify breathing effects, I studied male Sprague–Dawley rats spontaneously breathing 1.5% isoflurane in room air by noninvasive plethysmography and by arterial blood gas analysis.

**RESULTS:** PK-THPP, A1899, and doxapram inhibit rat TASK-3 potassium channel function with  $IC_{50}$ s of 42 nM (33–52), 1.6  $\mu$ M (0.8–3.3), and 22  $\mu$ M (18–28) ( $n = 4–6$ ; 95% confidence limits). IV PK-THPP, A1899, and doxapram stimulated breathing by plethysmography with a peak change in minute ventilation relative to baseline of  $84\% \pm 19\%$  and  $226\% \pm 56\%$  (for PK-THPP at 0.5 and 5 mg/kg; mean  $\pm$  SEM;  $n = 3–4$ ;  $P < 0.05$  and  $P < 0.001$ , respectively, relative to vehicle);  $46\% \pm 2\%$  and  $236\% \pm 48\%$  (for A1899 at 5 and 25 mg/kg;  $n = 3–4$ ;  $P > 0.05$  and  $P < 0.001$ , respectively);  $103\% \pm 20\%$  (for doxapram at 25 mg/kg;  $n = 4$ ), and  $33\% \pm 9\%$  (for dimethylsulfoxide vehicle at 1 mL/kg;  $n = 4$ ). PK-THPP and A1899, unlike doxapram, induced a profound and lasting respiratory alkalosis by arterial blood gas analysis. Thirty minutes after IV drug administration, I observed an arterial pH and carbon dioxide partial pressure of  $7.62 \pm 0.02$  and  $23 \pm 0.8$  mm Hg (for PK-THPP after 5 mg/kg;  $n = 4$ ;  $P < 0.001$  for both relative to vehicle),  $7.49 \pm 0.02$  and  $31 \pm 2$  mm Hg (for A1899 at 25 mg/kg;  $n = 6$ ;  $P < 0.05$  and  $0.001$ , respectively),  $7.43 \pm 0.03$  and  $39 \pm 4$  mm Hg (for doxapram after 25 mg/kg;  $n = 4$ ;  $P > 0.05$  for both), and  $7.38 \pm 0.03$  and  $48 \pm 4$  mm Hg (for dimethylsulfoxide vehicle after 1 mL/kg;  $n = 3$ ).

**CONCLUSIONS:** PK-THPP and A1899 are potent rat TASK-3 antagonists and effective breathing stimulants. PK-THPP and A1899 effects on breathing were of greater magnitude and/or duration relative to that of doxapram. PK-THPP and A1899 or related compounds may have therapeutic potential for treating breathing disorders.

### 麻醉對幼豬模型中血管加壓素調節腦血流作用的影響

#### The Anesthetic Effects on Vasopressor Modulation of Cerebral Blood Flow in an Immature Swine Model

Benjamin Bruins, MD\*, Todd J. Kilbaugh, MD\*, Susan S. Margulies, PhD† and Stuart H. Friess, MD‡

From the \*Department of Anesthesiology and Critical Care Medicine, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; †Department of Bioengineering, University of Pennsylvania, Philadelphia, Pennsylvania; and ‡Department of Pediatrics, Washington University in St. Louis School of Medicine, St. Louis, Missouri.

Anesth Analg April 2013 116:838-844

**背景：**各種鎮靜劑和麻醉藥對兒童腦血流（CBF）的升壓調節作用的影響目前還不清楚。在成人中，已經描述了異氟醚降低 CBF 的程度比芬太尼和咪達唑侖小。大多數神經重症監護的大型動物模型使用吸入麻醉藥麻醉。涉及 CBF 調節的調查將改善模型的可譯性：更接近於目前兒科重症監護病房的常例。

**方法：**15 只 4 周齡仔豬採用 2 個麻醉方案中的一個：全憑靜脈麻醉（TIVA）（咪達唑侖 1mg/kg/h 和芬太尼 100 $\mu$ g/kg/h,  $n = 8$ ）或 ISO（異氟醚 1.5%-2 %和芬太尼 100 $\mu$ g/kg/h 中,  $n = 7$ ）。當給予仔豬劑量逐步增大的精氨酸加壓素、去甲腎上腺素（NE）和去氧腎上腺素（PE）時，連續監測平均動脈血壓、顱內壓（ICP）、CBF 和腦組織氧分壓。

**結果：**儘管 ISO 組的基線腦灌注壓較低（ $45 \pm 11$  比  $71 \pm 11$  mmHg;  $P < 0.0005$ ），兩組的基線 CBF 相似（ISO  $38 \pm 10$  比 TIVA  $35 \pm 26$  mL/100g/min）。結果顯示 PE 和 NE 使 ISO 組仔豬的 ICP 升高（ $11 \pm 4$  比  $16 \pm 4$  mmHg 和  $11 \pm 8$  比  $18 \pm 5$  mmHg,  $P < 0.05$ ）。但在 TIVA 組，只有當最大劑量值與基線資料比較時 PE 才使 ICP 升高（ $11 \pm 4$  和  $15 \pm 5$  mmHg,  $P < 0.05$ ）。當給予仔豬 NE 和 PE（ $P < 0.05$ ）時，標準化的 CBF 顯示出與麻醉組和血管加



壓素劑量有關的統計學上的顯著增加 ( $P < 0.05$ )，提示 ISO 會損害腦血流的自動調節，但 TIVA 不會。

**結論：**與吸入麻醉藥相比較，使用以麻醉性鎮痛藥—苯二氮卓類藥物為基礎的麻醉方案時，升壓藥對 CBF 的影響是有限的，這與自動調節機制的保持是一致的。麻醉藥物的選擇，對於調查腦血管血液動力學機制和在實驗室和臨床床旁之間轉化重症監護調查研究是至關重要的。

(方斌 譯 馬皓琳 李士通 校)

**BACKGROUND:** The effect of various sedatives and anesthetics on vasopressor modulation of cerebral blood flow (CBF) in children is unclear. In adults, isoflurane has been described to decrease CBF to a lesser extent than fentanyl and midazolam. Most large-animal models of neurocritical care use inhaled anesthetics for anesthesia. Investigations involving modulations of CBF would have improved translatability within a model that more closely approximates the current practice in the pediatric intensive care unit.

**METHODS:** Fifteen 4-week-old piglets were given 1 of 2 anesthetic protocols: total IV anesthesia (TIVA) (midazolam 1 mg/kg/h and fentanyl 100  $\mu$ g/kg/h,  $n = 8$ ) or ISO (isoflurane 1.5%–2% and fentanyl 100  $\mu$ g/kg/h,  $n = 7$ ). Mean arterial blood pressure, intracranial pressure (ICP), CBF, and brain tissue oxygen tension were measured continuously as piglets were exposed to escalating doses of arginine vasopressin, norepinephrine (NE), and phenylephrine (PE).

**RESULTS:** Baseline CBF was similar in the 2 groups (ISO  $38 \pm 10$  vs TIVA  $35 \pm 26$  mL/100 g/min) despite lower baseline cerebral perfusion pressure in the ISO group ( $45 \pm 11$  vs  $71 \pm 11$  mm Hg;  $P < 0.0005$ ). Piglets in the ISO group displayed increases in ICP with PE and NE ( $11 \pm 4$  vs  $16 \pm 4$  mm Hg and  $11 \pm 8$  vs  $18 \pm 5$  mm Hg;  $P < 0.05$ ), but in the TIVA group, only exposure to PE resulted in increases in ICP when comparing maximal dose values with baseline data ( $11 \pm 4$  vs  $15 \pm 5$  mm Hg;  $P < 0.05$ ). Normalized CBF displayed statistically significant increases regarding anesthetic group and vasopressor dose when piglets were exposed to NE and PE ( $P < 0.05$ ), suggesting an impairment of autoregulation within ISO, but not TIVA.

**CONCLUSION:** The vasopressor effect on CBF was limited when using a narcotic-benzodiazepine-based anesthetic protocol compared with volatile anesthetics, consistent with a preservation of autoregulation. Selection of anesthetic drugs is critical to investigate mechanisms of cerebrovascular hemodynamics, and in translating critical care investigations between the laboratory and bedside.

**一個隨機試驗：開顱幕上腦腫瘤切除術中兩種不同劑量的甘露醇降顱壓效果的比較**

### **A Comparison of Two Doses of Mannitol on Brain Relaxation During Supratentorial Brain Tumor Craniotomy: A Randomized Trial**

Charlotte Quentin, MD\*, Sonia Charbonneau, MD\*, Robert Moundjian, MD†, Alexandre Lallo, MD\*, Alain Bouthilier, MD†, Marie-Pierre Fournier-Gosselin, MD†, Michel Bojanowski, MD†, Monique Ruel, RN\*, Marie-Pierre Sylvestre, PhD‡ and Francois Girard, MD\*

From the Departments of \*Anesthesiology and †Surgery, Montreal University Medical Center; and ‡Research Center, Montreal University Medical Centre, Montreal, Quebec, Canada.

Anesth Analg April 2013 116:862-868

**背景：**雖然 20% 的甘露醇已廣泛用來減少腦容積以便於顱內手術的手術操作，但是還沒有建立量效關係。在這個研究中，我們比較了擇期幕上腦腫瘤切除術中  $0.7$  和  $1.4 \text{ g kg}^{-1}$  的甘露醇降顱壓的效果。

**方法：**在這個前瞻性、隨機、雙盲研究中我們挑選了 80 個行開顱幕上腦腫瘤切除術的病人。病人分成了兩組：在手術劃皮時分別給予 20% 甘露醇  $0.7 \text{ g kg}^{-1}$  (L 組) 和  $1.4 \text{ g kg}^{-1}$  (H 組)。在劃開硬腦膜後立即評估腦鬆弛水準，並分為 1 到 4 四個等級 (1：完美的鬆弛，2：滿意的鬆弛，3：腦硬，4：腦膨脹)。

**結果：**兩組間病人的性別、年齡、體重指數、腫瘤位置和大小沒有明顯差異。有 52.5% 的 L 組病人和 77.5% 的 H 組病人有中線偏移 ( $P = 0.03$ )。L 組和 H 組病人腦鬆弛狀態的得分中位數 (四分位數間距) 分別是 2.0 (1.75—3) 和 2.0 (1—3) ( $P = 0.16$ )。然後我們用一種比例比數模型來調整這種偏態分佈並評估分組 (低劑量比高劑量甘露醇) 對腦鬆弛得分的影響。在調整中線偏移的時候，更大劑量的甘露醇的使用導致了一個 2.5 ( $P = 0.03$ ) 的比值比。這就說明：在糾正了中線偏移的影響以後，在高劑量甘露醇組中腦鬆弛評分達到 1 分水準的改善的可能性是低劑量組的 2.5 倍。中線偏移的比值比為 0.29 ( $P = 0.007$ )，說明其發生使得到較低的平均鬆弛評分的可能性更高。

**結論：**在這個研究中我們發現：在開顱幕上腦腫瘤切除術中的患者， $1.4 \text{ g kg}^{-1}$  的 20% 甘露醇降顱壓的效果和  $0.7 \text{ g kg}^{-1}$  甘露醇是相同的。在糾正了中線偏移的影響以後，這個研究顯示高劑量甘露醇組的病人比低劑量組達到更好的腦鬆弛評分的機會顯著更大。

(王慧娟 譯 馬皓琳 李士通 校)

**BACKGROUND:** Twenty percent mannitol is widely used to reduce brain bulk and facilitate the surgical approach in intracranial surgery. However, a dose-response relationship has not yet been established. In this study, we compared the effects of  $0.7$  and  $1.4 \text{ g kg}^{-1}$  mannitol on brain relaxation during elective supratentorial brain tumor surgery.

**METHODS:** In this prospective, randomized, double-blind study, we enrolled 80 patients undergoing supratentorial craniotomy for tumor resection. Patients were assigned to receive  $0.7 \text{ g kg}^{-1}$  (group L) or  $1.4 \text{ g kg}^{-1}$  (group H) of 20% mannitol at surgical incision. Brain relaxation was assessed immediately after opening of the dura on a scale ranging from 1 to 4 (1 = perfectly relaxed, 2 = satisfactorily relaxed, 3 = firm brain, 4 = bulging brain).

**RESULTS:** There was no significant difference between the 2 groups regarding age, sex, body mass index, and brain tumor localization or size. In group L 52.5% of patients and in group H 77.5% of patients presented a midline shift ( $P = 0.03$ ). The median scores of brain relaxation (interquartile range) were 2.0 (1.75–3) and 2.0 (1–3) ( $P = 0.16$  for patients in group L and H, respectively). We then used a proportional odds model to adjust for this unbalanced distribution and to assess the group effect (low-dose versus high-dose mannitol) on brain relaxation scores. When adjusted for the presence of midline shift, the use of a higher dose of mannitol resulted in an odds ratio of 2.5 ( $P = 0.03$ ). This indicates that, considering the effect of a midline shift, the odds of having a 1-level improvement in relaxation score in patients who received a higher dose of mannitol (group H) was 2.5 times as large as the odds for the low-dose group. The odds ratio of 0.29 ( $P = 0.007$ ) for the midline shift indicates that its occurrence was associated with a higher probability of a lower relaxation score, on average.

**CONCLUSION:** In this study, we show that  $1.4 \text{ g kg}^{-1}$  of 20% mannitol results in equivalent brain relaxation scores as  $0.7 \text{ g kg}^{-1}$  in patients undergoing craniotomy for supratentorial brain tumor. When corrected for the presence of midline shift, this study reveals that patients in the

high-dose group had significantly more chances of obtaining a better relaxation score compared with the lower-dose group.

### 用明確的回憶評估術中知曉:兩種方法的比較

#### **Assessment of Intraoperative Awareness with Explicit Recall: A Comparison of 2 Methods**

George A. Mashour, MD, PhD\*, Christopher Kent, MD†, Paul Picton, MB, ChB, MRCP, FRCA\*, Satya Krishna Ramachandran, MD, FRCA\*, Kevin K. Tremper, PhD, MD\*, Christopher R. Turner, MD, PhD, MBA‡, Amy Shanks, MS\* and Michael S. Avidan, MBBCh§  
From the \*Department of Anesthesiology, University of Michigan, Ann Arbor, Michigan; †Department of Anesthesiology and Pain Medicine, University of Washington, Seattle, Washington; ‡Department of Anesthesiology, Bay Area Medical Center, Marinette, Wisconsin; and §Department of Anesthesiology, Washington University, St. Louis, Missouri.  
Anesth Analg April 2013 116:889-891

背景:對於用明確的回憶發現術中知曉,修改的 Brice 訪視與品質保障技術相比的優越性還未被明確證明。

方法:我們研究了一個患者群來比較用一個修改的 Brice 訪視(術後 28-30 天)和品質保障資料(術後 1 天)對明確知曉的發現。

結果:以修訂的 Brice 訪視為基礎的知曉發生率為 19/18847 或 0.1%。更少的意識情況(發生率 0.02%)由品質保障方法發現的知曉例數較少(發生率 0.02%)( $P < 0.0001$ )。

結論:對於用明確的回憶評估術中知曉,修訂的 Brice 訪視是較適合的方法。

(王曉莉 譯 馬皓琳 李士通 校)

**BACKGROUND:** Superiority of the modified Brice interview over quality assurance techniques in detecting intraoperative awareness with explicit recall has not been demonstrated definitively.

**METHODS:** We studied a single patient cohort to compare the detection of definite awareness using a single modified Brice interview (postoperative day 28–30) versus quality assurance data (postoperative day 1).

**RESULTS:** The incidence of awareness based on the modified Brice interview was 19 per 18,847 or 0.1%. Fewer awareness cases (incidence 0.02%) were detected by the quality assurance approach ( $P < 0.0001$ ).

**CONCLUSION:** The modified Brice interview is the preferred modality for assessing intraoperative awareness with explicit recall.

### 一個三級醫療中心成人及兒童手術期間用基於電腦的麻醉呼叫系統緊急呼叫的特點

#### **Characteristics of Emergency Pages Using a Computer-Based Anesthesiology Paging System in Children and Adults Undergoing Procedures at a Tertiary Care Medical Center**

Toby N. Weingarten, MD\*, John P. Abenstein, MD, MSEET†, Claire H. Dutton, SRNA‡, Melinda A. Kohn, SRNA‡, Elizabeth A. Lee, SRNA‡, Tami E. Mullenbach, SRNA‡, Bradley J. Narr, MD\*, Darrell R. Schroeder, MS§ and Juraj Sprung, MD, PhD\*  
From the \*Division of Multispecialty Anesthesia, †Division of Cardiovascular/Thoracic Anesthesia, ‡Mayo School of Health Sciences, and §Division of Biomedical Statistics and Informatics, Mayo Clinic, Rochester, Minnesota.  
Anesth Analg April 2013 116:904-910

**背景：**在我們的大型學術監督實踐中，主治麻醉醫師同時要看顧幾個患者。爲了管理手術室裡的通訊，我們使用的是專門的基於電子電腦麻醉可視呼叫系統。該系統在需要緊急說明時會發出一個緊急呼叫來警示主治麻醉醫師及其他可用人員。我們對成人及兒童的術中緊急呼叫的特點進行了分析。

**方法：**我們選取了在總手術室內的從 2005 年 1 月 1 日到 2010 年 7 月 31 日的全部緊急呼叫啓動情況。對電子醫療記錄中的呼叫發生率和特點（諸如原發病、進行的幹預及預後）進行了回顧。

**結果：**在研究期間，共實施 258,135 例麻醉（兒童  $n=32103$ ，年齡小於 18 歲），其中有 370 次緊急呼叫記錄（成人  $n=309$ ，兒童  $n=61$ ）（1.4‰；95% 可信區間，1.3-1.6）。對於嬰兒的緊急呼叫啓動的發生率最高（9.4‰，95% 可信區間，5.7-14.4）（與其他年齡組相比  $P < 0.001$ ）。在成人，最常見的原因爲血流動力學事件（55%），在兒童則爲呼吸及氣道事件（60.7%）。

**結論：**在年齡大於 2 歲的患者中緊急呼叫較少。儘管嬰兒和 1-2 歲兒童兩個年齡組均由接受過嬰幼兒麻醉專業訓練的麻醉醫師看顧，嬰兒較 1-2 歲的小兒仍更易出現緊急呼叫啓動。

（王贊 譯 馬皓琳 李士通 校）

**BACKGROUND:** In our large academic supervisory practice, attending anesthesiologists concomitantly care for multiple patients. To manage communications within the procedural environment, we use a proprietary electronic computer-based anesthesiology visual paging system. This system can send an emergency page that instantly alerts the attending anesthesiologist and other available personnel that immediate help is needed. We analyzed the characteristics of intraoperative emergency pages in children and adults.

**METHODS:** We identified all emergency page activations between January 1, 2005 and July 31, 2010 in our main operating rooms. Electronic medical records were reviewed for rates and characteristics of pages such as primary etiology, performed interventions, and outcomes.

**RESULTS:** During the study period, 258,135 anesthetics were performed ( $n = 32,103$  children, younger than 18 years) and 370 emergency pages ( $n = 309$  adults,  $n = 61$  children) were recorded (1.4 per 1000 cases; 95% confidence interval, 1.3–1.6). Infants had the highest rates (9.4 per 1000; 95% confidence interval, 5.7–14.4) of emergency page activations ( $P < 0.001$  compared with each other age group). In adults, the most frequent causes were hemodynamic (55%), and in children respiratory and airway (60.7%) events.

**CONCLUSION:** Emergency pages were rare in patients older than 2 years. Infants were more likely than children 1 to 2 years of age to have emergency page activation, despite both groups being cared for by pediatric fellowship trained anesthesiologists.

### 一篇關於麻醉醫生面對腫瘤細胞減滅術和熱灌注腹腔化療的概述

#### **An Overview of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion for the Anesthesiologist**

Christopher Allen-John Webb, MD, Paul David Weyker, MD, Vivek K. Moitra, MD and Richard K. Raker, MD

From the Department of Anesthesiology, Columbia University College of Physicians & Surgeons, Columbia University Medical Center, New York, New York.

Anesth Analg April 2013 116:924-931

當病人需要進行腫瘤細胞減滅術和熱灌注腹腔化療時，對麻醉醫生來講是一種圍術期挑戰。爲了更好的管理這類病人，麻醉醫生不但需要掌握常用化療藥物的基本知識，還必須瞭解手術治療要達到的目標和目的。對於進行腫瘤細胞減滅術和熱灌注腹腔化療病人的最優化麻醉管理需要控制一系列生理機制間複雜的相互作用，包括高溫、腹內高壓、電解質紊亂、凝血異常、心指數增大、氧耗量增加和全身血管阻力降低。由於這類手術繼續在腫瘤外科醫生間得到普及，需要實施明確闡述化學、藥代動力學、藥效動力學和效應終點的進一步研究來闡明最優化圍術期管理。

(張怡 譯 馬皓琳 李士通 校)

Anesthesiologists face several perioperative challenges when patients need cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion. To adequately care for these patients, anesthesiologists must understand the goals and objectives of the operation in addition to having a basic knowledge of the chemotherapeutic drugs that are frequently used. Optimal anesthetic management of patients treated with cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion requires control of a complex interplay of physiologic mechanisms, including hyperthermia, abdominal hypertension, electrolyte abnormalities, coagulopathies, increased cardiac index, oxygen consumption, and decreased systemic vascular resistance. As this surgery continues to gain popularity among oncologic surgeons, further studies that clearly define the chemistry, pharmacokinetics, pharmacodynamics, and end points of efficacy need to be performed to elucidate optimal perioperative management.

### 在大鼠模型中麻黃素和布比卡因或利多卡因聯合用於脊麻顯示有協同性的運動阻滯 **Ephedrine Shows Synergistic Motor Blockade When Combined with Bupivacaine or Lidocaine for Spinal Anesthesia in a Rat Model**

Alimorad G. Djalali, MD, PhD\*, Jeffrey Chi-Fei Wang, MD†, Jose Ramon Perez-Valdivieso, MD, PhD‡, Thomas Danninger, MD§, Gerhard Fritsch, MD§, David Zurakowski, PhD || ¶ and Peter Gerner, MD§

From the \*Department of Anesthesia, Stanford University School of Medicine, Stanford, California; †Pain Research Center, Department of Anesthesia, Perioperative and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts; ‡Department of Anesthesia and Critical Care, Clinica Universidad de Navarra, University of Navarra, Spain; §Department of Anesthesiology, Perioperative Medicine and Critical Care Medicine, Paracelsus Medical University, Salzburg, Austria; and Departments of ||Anesthesia and ¶Surgery, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts.

Anesth Analg April 2013 116:944-948;

**背景：**麻黃素是一種直接/間接血管活性藥物。此外，麻黃素還有內在的局部麻醉作用，主要是因其對鈉離子通道的阻滯作用。本文旨在研究麻黃素與布比卡因或利多卡因通過脊髓導管注射入大鼠的脊髓腔時的協同作用。

**方法：**通過手術置入脊髓導管到 47 個大鼠身上（每組 8 個，7 個排除）。定容 60μL 不同濃度的麻黃素、布比卡因、利多卡因通過脊髓導管注射以測定每種藥物的均等勢。然後麻黃素與布比卡因或利多卡因組合注射入脊髓導管。

**結果：**麻黃素和布比卡因或利多卡因在固定的配比下均有顯著的協同作用。對於麻黃素

和布比卡因有顯著協同作用的合用指數為 0.792（95% 置信區間為：0.665-0.919），而麻黃素和利多卡因的合用指數為 0.663（95% 置信區間為：0.532-0.794）。

**結論：**麻黃素和布比卡因或利多卡因聯合應用均能協同阻滯運動機能，這可能會減少脊髓所需要的局部麻醉藥用量。麻黃素與局部麻醉劑的協同作用是一個有趣的藥理學現象，需要進一步的臨床評價。

（趙曉 譯 馬皓琳 李士通 校）

**BACKGROUND:** Ephedrine is a direct/indirect vasoactive drug. In addition, it also possesses intrinsic local anesthetic properties, mainly due to its sodium-channel blockage. We investigated whether ephedrine demonstrates a synergistic effect with bupivacaine and lidocaine when injected via a spinal catheter into the spinal space of rats.

**METHODS:** Spinal catheters were surgically placed in 47 rats ( $n = 8$  per group; 7 rats were excluded.) Bupivacaine, lidocaine, and ephedrine in various concentrations and constant volumes (60  $\mu$ L) were injected into the spinal catheters to determine the equipotency of each drug. Ephedrine in combination with either bupivacaine or lidocaine was then injected into the spinal catheters.

**RESULTS:** Ephedrine demonstrated statistically significant synergistic effects with bupivacaine as well as with lidocaine in fixed combinations. The combination index reflecting a synergistic effect was 0.792 (95% confidence interval: 0.665–0.919) for ephedrine + bupivacaine and 0.663 (95% confidence interval: 0.532–0.794) for ephedrine + lidocaine.

**CONCLUSION:** Ephedrine combined with either bupivacaine or lidocaine acted synergistically to block motor function and has the potential to reduce the amount of local anesthetic needed for spinal block. The synergistic effect of ephedrine in combination with local anesthetics is an interesting pharmacological phenomenon that warrants further clinical evaluation.

### 在健康人中，用七氟醚實施全身麻醉能夠減少心臟容量及充血時血流速度

#### General Anesthesia with Sevoflurane Decreases Myocardial Blood Volume and Hyperemic Blood Flow in Healthy Humans

Carolien S. E. Bulte, MD\*, Jeroen Slikkerveer, MD†, Otto Kamp, MD, PhD†, Martijn W. Heymans, PhD‡, Stephan A. Loer, MD, PhD\*, Stefano F. de Marchi, MD§, Rolf Vogel, MD, PhD ||, Christa Boer, PhD\* and R. Arthur Bouwman, MD, PhD\*

+Author Affiliations

From the Departments of \*Anesthesiology, †Cardiology, and ‡Epidemiology and Biostatistics, Institute for Cardiovascular Research, VU University Medical Center, Amsterdam, The Netherlands; §Department of Cardiology, Bern University Hospital, Bern; and || Department of Cardiology and ARTORG Cardiovascular Engineering, Bern University Hospital and University of Bern, Bern, Switzerland.

Anesth Analg April 2013 116:767-774

**背景：**全身麻醉時心肌灌注保護措施對於圍術期引起心臟併發症風險方面很重要。有關全身麻醉在正常心肌迴圈影響的資料有限。在這項研究中，應用七氟醚實施全身麻醉，並在外科手術前，我們研究了心肌迴圈對藥物擴張血管及交感刺激後的反應。

**方法：**六位女性和七位男性（平均年齡 43 歲，在 28~61 歲之間）參與了該項研究，並記錄清醒時的基本資料及給予七氟醚 1 個最小肺泡有效溶度後的資料，應用心肌造影超聲心動圖，評估靜息狀態、腺苷誘導的心臟充血狀態及冷加壓實驗所致的交感刺激時心肌血流

速度計微循環的變化。心臟血流量等於相對心臟血容量乘以其頻率在除以心肌組織密度 ( $1.5\text{g}\cdot\text{mL}^{-1}$ )。

**結果：**在七氟醚麻醉中，心臟血流量在靜息時與基礎值相近 ( $1.05 \pm 0.28$  vs  $1.05 \pm 0.32$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.98$ ; 95% 可信區間 [CI],  $-0.18$  to  $0.18$ )，對比基線時，當心率增加時心臟血容量減少( $P = 0.0044$ ; 95% CI,  $0.01$ – $0.04$ )。相反，心臟充血時，心臟血容量是減少的( $2.25 \pm 0.5$  vs  $3.53 \pm 0.7$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.0003$ ; 95% CI,  $0.72$ – $1.84$ )。給予一定的交感刺激時心臟血流量變化不大( $1.53 \pm 0.53$  and  $1.55 \pm 0.49$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.74$ ; 95% CI,  $-0.47$  to  $0.35$ )。

**結論：**在七氟醚實施的麻醉中，儘管血容量是減少的,但在沒有外科刺激的情況下，心臟血流量在靜息及交感刺激後的是代償的，然而，在一些減少心臟充血情況下，心臟血流量也是代償的。

(鄧利兵譯 薛張綱校)

**BACKGROUND:** Preservation of myocardial perfusion during general anesthesia is likely important in patients at risk for perioperative cardiac complications. Data related to the influence of general anesthesia on the normal myocardial circulation are limited. In this study, we investigated myocardial microcirculatory responses to pharmacological vasodilation and sympathetic stimulation during general anesthesia with sevoflurane in healthy humans immediately before surgical stimulation.

**METHODS:** Six female and 7 male subjects (mean age 43 years, range 28–61) were studied at baseline while awake and during the administration of 1 minimum alveolar concentration sevoflurane. Using myocardial contrast echocardiography, myocardial blood flow (MBF) and microcirculatory variables were assessed at rest, during adenosine-induced hyperemia, and after cold pressor test-induced sympathetic stimulation. MBF was calculated from the relative myocardial blood volume multiplied by its exchange frequency ( $\beta$ ) divided by myocardial tissue density ( $\rho_T$ ), which was set at  $1.05\text{g}\cdot\text{mL}^{-1}$ .

**RESULTS:** During sevoflurane anesthesia, MBF at rest was similar to baseline values ( $1.05 \pm 0.28$  vs  $1.05 \pm 0.32$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.98$ ; 95% confidence interval [CI],  $-0.18$  to  $0.18$ ). Myocardial blood volume decreased ( $P = 0.0044$ ; 95% CI,  $0.01$ – $0.04$ ) while its exchange frequency ( $\beta$ ) increased under sevoflurane anesthesia when compared with baseline. In contrast, hyperemic MBF was reduced during anesthesia compared with baseline ( $2.25 \pm 0.5$  vs  $3.53 \pm 0.7$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.0003$ ; 95% CI,  $0.72$ – $1.84$ ). Sympathetic stimulation during sevoflurane anesthesia resulted in a similar MBF compared to baseline ( $1.53 \pm 0.53$  and  $1.55 \pm 0.49$   $\text{mL}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ ;  $P = 0.74$ ; 95% CI,  $-0.47$  to  $0.35$ ).

**CONCLUSIONS:** In otherwise healthy subjects who are not subjected to surgical stimulation, MBF at rest and after sympathetic stimulation is preserved during sevoflurane anesthesia despite a decrease in myocardial blood volume. However, sevoflurane anesthesia reduces hyperemic MBF, and thus MBF reserve, in these subjects.

### 脂肪乳劑對布比卡因在小鼠中藥代動力學和組織分佈的影響

#### The Effect of Lipid Emulsion on Pharmacokinetics and Tissue Distribution of Bupivacaine in Rats

Kejian Shi, MD\*, Yun Xia, MD, PhD†, Quanguang Wang, MD\*, Yiquan Wu, MD\*, Xiaoxi Dong, MD‡, Chanjuan Chen, BS\*, Wan Tang, BS\*, Yujian Zhang, MD\*, Mengxu Luo, BS\*, Xianqin Wang, PhD ||, Thomas J. Papadimos, MD, MPH† and Xuzhong Xu, MD

**背景：**雖然脂肪乳劑可能逆轉布比卡因的全身毒性作用，但在注射脂肪乳劑後布比卡因的藥代動力學和組織分佈並不清楚。在這項研究中，我們評估了注射脂肪乳劑對布比卡因藥代動力學和組織分佈的影響。

**方法：**脂肪乳劑組小鼠以  $2 \text{ mg kg}^{-1} \text{ 分鐘}^{-1}$  到  $4 \text{ 分鐘}$  的速度靜脈注射布比卡因，然後分別以  $3 \text{ mL kg}^{-1} \text{ 分鐘}^{-1}$  到  $5 \text{ 分鐘}$  的速度注射 30% 的脂肪乳劑；在對照組用生理鹽水取代（ $n=6$  的藥代動力學）。然後我們隨機分配 100 只小鼠到脂肪乳劑組和對照組（以  $n=50$  分配）。這個毒性模型和治療與其藥代動力學部分相同。採集的血漿和組織包括腦、心、肝、脾、肺、腎、大網膜和肌肉。通過液相色譜-串聯質譜法測定布比卡因的血藥濃度和組織含量。一個 2-房室模型分析計算布比卡因的藥代動力學。

**結果：**所有資料都以平均值±標準差顯示。在經過脂肪乳劑治療後，在脂肪乳劑組布比卡因的  $t_{1/2\beta}$  明顯縮短（ $110 \pm 25 \text{ 分鐘}$  比上  $199 \pm 38 \text{ 分鐘}$ ,  $P = 0.001$ ），清除較高（ $14 \pm 4 \text{ mL mg}^{-1} \text{ kg}^{-1}$  比上  $9 \pm 4 \text{ mL mg}^{-1} \text{ kg}^{-1}$ ,  $P = 0.038$ ），並且  $t_{1/2\alpha}$  比對照組延長（ $4 \pm 1 \text{ 分鐘}$  比上  $2 \pm 1 \text{ 分鐘}$ ,  $P = 0.014$ ）；K12 在脂肪乳劑組比對照組少（ $0.13 \pm 0.04$  比上  $0.32 \pm 0.13$ ,  $P = 0.011$ ）。在脂肪乳劑組，布比卡因在心、腦、肺、腎和脾的含量比對照組少，但在 20、30 和 45 分鐘時在肝臟中含量較對照組高。

**結論：**在本研究中觀察到脂質沉積現象。脂肪乳劑的應用能加速布比卡因的清除。  
（方昕譯 薛張綱校）

**BACKGROUND:** While lipid emulsion may reverse the systemic toxicity of bupivacaine, the pharmacokinetics and tissue distribution of bupivacaine after lipid emulsion infusion are not clear. In this study, we assessed the influence of lipid emulsion administration on the pharmacokinetics and tissue distribution of bupivacaine.

**METHODS:** Rats in the lipid group were administered IV bupivacaine at the rate of  $2 \text{ mg kg}^{-1} \text{ min}^{-1}$  for 4 minutes, and then were treated with an infusion of 30% lipid emulsion at the rate of  $3 \text{ mL kg}^{-1} \text{ min}^{-1}$  for 5 minutes; saline was substituted in the control group ( $n = 6$  for pharmacokinetics). We then randomly assigned 100 rats into the lipid group and control group ( $n = 50$  for distribution). The toxicity model and treatment were the same as the pharmacokinetic portion. Plasma and tissues including brain, heart, liver, spleen, lung, kidney, omentum, and muscle were collected. The plasma concentration and tissue content of bupivacaine were measured by a liquid chromatography-tandem mass spectrometric method. A 2-compartmental analysis was performed to calculate the pharmacokinetics of bupivacaine.

**RESULTS:** All data are shown as mean  $\pm$  SD. After treatment with the lipid emulsion,  $t_{1/2\beta}$  of bupivacaine in the lipid group was significantly shorter ( $110 \pm 25 \text{ minutes}$  vs  $199 \pm 38 \text{ minutes}$ ,  $P = 0.001$ ), the clearance was higher ( $14 \pm 4 \text{ mL mg}^{-1} \text{ kg}^{-1}$  vs  $9 \pm 4 \text{ mL mg}^{-1} \text{ kg}^{-1}$ ,  $P = 0.038$ ), and the  $t_{1/2\alpha}$  was longer than that of the control group ( $4 \pm 1 \text{ minutes}$  vs  $2 \pm 1 \text{ minutes}$ ,  $P = 0.014$ ); the K12 in the lipid group was less than that of the control group ( $0.13 \pm 0.04$  vs  $0.32 \pm 0.13$ ,  $P = 0.011$ ). In the lipid group, the bupivacaine content in heart, brain, lung, kidney, and spleen was lower than that in the control group, but higher in the liver at 20, 30, and 45 minutes.

**CONCLUSION:** The lipid sink phenomenon was observed in this study. The use of a lipid emulsion accelerated the elimination of bupivacaine.



超聲用於輔助定位肥胖產婦的硬膜外穿刺中點：旁正中斜入路與橫向正中橫向入路的比較。

**Ultrasound estimates for midline epidural punctures in the obese parturient: paramedian sagittal oblique is comparable to transverse median plane.**

Jagpaul S. Sahota, MD, Jose C. A. Carvalho, MD, PhD, Mrinalini Balki, MBBS, MD, Niall Fanning, MD and Cristian Arzola, MD, MSc

From the Department of Anesthesia and Pain Management, Mount Sinai Hospital, and University of Toronto, Toronto, Ontario, Canada.

Anesth Analg April 2013 116:829-835

**背景：**臨床使用脊髓超聲（US）多使用橫向中線（TM）平面觀察，在肥胖孕婦中，通常由於彌補因皮下組織過後引起的低能見度，向下擠壓皮下組織來觀察，這樣會低估肥胖孕婦皮膚至硬膜外間隙的距離。我們試驗了在這類人群中使用旁正中斜入路平面（PSO）是否比 TM 平面測量皮膚-硬膜外下腔的實際距離更為精確。

**方法：**我們招募了要求硬膜外鎮痛或行腰硬聯合麻醉剖宮產的肥胖產婦人群（世界衛生組織分級 I、II 和 III）。超聲使用 5-2MHz 探頭定位進針點並分別用 PSO 平面或 TM 平面估算皮膚至硬膜外下腔的距離（超聲估計距離，UD）。測量時盡可能用探頭下壓皮膚及皮下組織，測量最短距離。所有的進針方式都是中線進針。麻醉醫生使用腰硬組合針在預先定位的穿刺點進針，標記實際進針距離（進針深度，ND）。我們用 Bland-Altman 分析法確定 UD 和 ND 之間的差異以及 95% 可信區間。

**結果：**我們研究了 60 名女性患者，平均 BMI 值為 39.6 ( $\pm 7.9$ ) kg/m<sup>2</sup> (範圍 30.4-66.2kg/m<sup>2</sup>)。超聲在 PSO 和 TM 平面上的估計值與實際 ND 分別為 6.5 ( $\pm 1.2$ ) cm，6.5( $\pm 1.1$ )cm 以及 6.6 ( $\pm 1.3$ ) cm。Bland-Altman 分析表明兩者之間的差異為 0.05cm，95% 可信區間為  $\pm 1$ cm。在 PSO 平面與 TM 平面成像品質優良的比例分別為 86.7% 和 68.3% (P=0.028)。

**結論：**使用 PSO 平面行超聲測量硬膜外間隙與皮膚之間的距離和 TM 平面之間是可比的。在那些使用 TM 平面能見度低的患者中使用兩平面聯合評估可能對結果有一定提升作用。

（郭晨躍譯 薛張綱校）

**BACKGROUND:** Spinal ultrasound (US) in the transverse median (TM) plane underestimates the distance to the epidural space in obese pregnant women, most likely because of compression of the subcutaneous tissue during the assessment, often required to compensate for poor visibility. We tested whether scanning in the paramedian sagittal oblique (PSO) plane compared with the TM plane resulted in a more precise estimate of the actual skin-epidural space measurement in this population.

**METHODS:** We recruited obese (World Health Organization classes I, II, and III) pregnant women at term requesting labor epidural analgesia or combined spinal-epidural anesthesia for cesarean delivery. US imaging was performed with a 5-2 MHz curved array probe to identify the insertion point and to estimate the distance from the skin to the epidural space (US-estimated depth, UD) in the PSO and TM planes. The measurements were performed with the least possible compression of the subcutaneous tissue by the US probe. All punctures were performed via the midline approach. An anesthesiologist performed the epidural/combined spinal-epidural procedure at the predetermined insertion point, and marked the actual needle distance from the

skin to the epidural space (needle depth, ND). Bland-Altman analysis was used to determine the differences and 95% limits of agreement between US depth and ND.

**RESULTS:** We studied 60 women. The mean (SD) body mass index was 39.6 (7.9) kg/m<sup>2</sup> (range 30.4-66.2 kg/m<sup>2</sup>). The US estimate in the PSO and TM planes, and the actual ND were 6.5 (1.2) cm, 6.5 (1.1) cm, and 6.6 (1.3) cm, respectively. The Bland-Altman analysis showed a mean difference of 0.05 cm and 95% limits of agreement of  $\pm 1$  cm. The quality of imaging was rated as good in the PSO and TM planes in 86.7% and 68.3%, respectively (P = 0.028).

**CONCLUSION:** The estimates of the US-determined distance to the epidural space in the PSO are comparable to those in the TM plane. The ability to use both estimates interchangeably for midline punctures may prove useful in patients presenting with poor visibility in the TM plane.

### 非創傷性腦出血患者的神經源性肺水腫：預測因數與相關結果。

#### Neurogenic pulmonary edema in patients with nontraumatic intracerebral hemorrhage: predictors and association with outcome.

Eija Junttila, MD\*, Tero Ala-Kokko, MD, PhD\*, Pasi Ohtonen, MSc†, Anne Vaarala, MD‡, Ari Karttunen, MD, PhD‡, Olli Vuolteenaho, MD, PhD§, Tuula Salo, DDS, PhD ||, Meeri Sutinen, PhD ||, Toni Karhu, MSc§, Karl-Heinz Herzig, MD, PhD§¶ and Juha Koskenkari, MD, PhD\*

From the Departments of \*Anesthesiology and Intensive Care, †Anesthesiology and Surgery, and ‡Radiology, Oulu University Hospital; §Department of Physiology, Oulu University Hospital, Oulu University, Biocenter of Oulu; || Department of Diagnostics and Oral Medicine, Oulu University Hospital, Oulu University, Institute of Dentistry, Oulu; and ¶Department of Psychiatry, Kuopio University Hospital, Kuopio, Finland.

Anesth Analg April 2013 116:855-861

**背景：**神經源性肺水腫（NPE）是顱內出血後出現的一個公認的現象。在這項研究中，我們評估了在重症監護病房治療的非創傷性腦出血患者出現 NPE 的預測因數與相關結果。

**方法：**這是一個在校級水準的重症監護病房進行的一項前瞻性，觀察性臨床試驗。入院時記錄患者的臨床表現，意識水準，以及急性生理和慢性健康評估（APACHE）II 評分和評估患者主要頭部電腦斷層掃描結果。連續隨訪患者胸片和動脈血氣分析結果，NPE 在胸片上表現為急性雙肺浸潤和低氧血症。我們記錄 NPE 患者超聲心動圖，心臟和炎症標誌物，使用格拉斯哥結局量表評估 1 年結果。

**結果：**108 例患者中有 38 例（35%）發展為 NPE。NPE 預測因數均高於 APACHE II 評分（ $\geq 20$ ，比值比為 6.17，P = 0.003）和較高的白介素-6 的血漿濃度（ $>40$  皮克/毫升，比值比為 5.62，P = 0.003）。患者有上述 0，1 或 2 的預測因數，分別有 4%，37%，和 65% 的患有 NPE。NPE 具有較高的 1 年死亡率（37% 對 14%，P = 0.007），但 1 年後的功能結局不變（格拉斯哥預後評分 1-3 分，53% 與 51%，P > 0.9）。

**結論：**APACHE II 評分系統預測 NPE 疾病的嚴重程度和更高水準的全身性炎症介質。NPE 與較高的 1 年死亡率相關，但與較差的 1 年的功能結局無關。

（賀盼譯 薛張綱校）

**BACKGROUND:** Neurogenic pulmonary edema (NPE) is a well-recognized phenomenon after intracranial insult. In this study, we evaluated the predictors for NPE and

its association with outcome in patients with intensive care unit-treated nontraumatic intracranial hemorrhage.

**METHODS:**This was a prospective, observational clinical study in a university-level intensive care unit. Clinical characteristics, level of consciousness, and Acute Physiology and Chronic Health Evaluation (APACHE) II score were recorded on admission and the findings of primary head computed tomography were reviewed. A chest radiograph and arterial blood gas analysis were taken serially and NPE was determined as acute bilateral infiltrates in chest radiograph and hypoxemia. Echocardiography and cardiac and inflammatory markers were recorded. The 1-year outcome was assessed using the Glasgow Outcome Scale.

**RESULTS:**NPE developed in 38 (35%) of the 108 patients included. Predictors for NPE were higher APACHE II score ( $\geq 20$ , odds ratio 6.17,  $P = 0.003$ ) and higher interleukin-6 plasma concentration ( $>40$  pg/mL, odds ratio 5.62,  $P = 0.003$ ). Of patients with 0, 1, or 2 predictors mentioned above, 4%, 37%, and 65% had NPE, respectively. NPE was associated with a higher 1-year mortality (37% vs 14%,  $P = 0.007$ , respectively), but with an unchanged functional outcome after 1 year (Glasgow Outcome Scale score 1-3, 53% vs 51%,  $P > 0.9$ ).

**CONCLUSIONS:**Predictors for NPE are the severity of disease defined by APACHE II scores and higher levels of systemic inflammatory mediators. NPE is associated with a higher 1-year mortality, but not with a poorer 1-year functional outcome.

### 癲癇患者的術前評估：麻醉醫生的職責

#### **Review article: presurgical evaluation of patients with epilepsy: the role of the anesthesiologist.**

Jason Chui, MBChB, FANZCA, FHKCA, Lashmi Venkatraghavan, MD, FRCA, FRCPC and Pirjo Manninen, MD, FRCPC

From the Department of Anesthesia, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada.

Anesth Analg April 2013 116:881-888

藥物難治性癲癇患者擬行外科手術治療通常需要更好的術前評估，以此來判斷萬科手術是否可行。手術的可行性取決於與癲癇發作相關的中樞病變部位及癲癇發作的頻率。良好的手術效果取決於完整地切除與癲癇相關的病變部位且不損傷有功能的正常組織。多種有創或無創的檢查用於術前評估，包括影像學檢查、腦電圖檢查以判斷功能區域。瞭解癲癇定位診斷及藥物的作用對於該類患者的術前處理是有必要地。在這篇綜述中，我們討論了麻醉醫生在這類患者處理中的作用，麻醉藥物對於協助癲癇定位診斷及腦功能判斷的作用。

(李麗紅譯 薛張綱校)

Patients with medically refractory epilepsy when referred for surgical treatment often undergo extensive investigations to determine whether surgical treatment is feasible. Surgical feasibility is determined by identifying the location and number of seizure foci and their relationship to eloquent areas of the brain. Good surgical outcome depends on complete resection of seizure foci without any damage to eloquent brain function. Various noninvasive and invasive techniques are used in the presurgical evaluation of patients with epilepsy that include imaging techniques, electrophysiologic studies, and tests to determine functional areas. Understanding of the principles of seizure localization and of the effects of anesthetic drugs on the various preoperative investigations is essential for patient management. In this review article, we discuss

the role of the anesthesiologist in patient management during many of these investigations and the role of anesthetic drugs to aid in the localization of the seizure focus and of determining eloquent brain function.

### 手術室外監督協調麻醉醫生活動的通信系統的作用

#### **Role of communication systems in coordinating supervising anesthesiologists' activities outside of operating rooms.**

Bettina Smallman, Dr Med\*, Franklin Dexter, MD, PhD†, Danielle Masursky, PhD\*, Fenghua Li, MD\*, Reza Gorji, MD\*, Dave George, MBA‡ and Richard H. Epstein, MD, CPHIMS§  
From the \*Department of Anesthesiology, State University of New York Upstate, Syracuse, New York; †Department of Anesthesia, Division of Management Consulting, University of Iowa, Iowa City, Iowa; ‡Department of Telecommunications, Division of Information Management & Technology, State University of New York Upstate, Syracuse, New York; and §Department of Anesthesiology, Jefferson Medical College, Philadelphia, Pennsylvania.  
Anesth Analg April 2013 116:898-903

**背景：**從理論上說，通信系統可能促進指導了麻醉。我們最大評價了通信系統在手術室中通過對麻醉協調管理的促進作用。

**方法：**在 A 醫院，一份 13368 例的資料從內部字母數位元文本分頁系統中獲得。蘇醒室的資料是從數位尋呼系統中獲取的並不包含所有的。B 醫院中，在美國的不同洲，3 名作者分別用內部無線音訊系統分類 898 通電話。上下 95% 置信區間為百分比報告的值。

**結果：**至少 45% 例來源於 A 醫院的手術室外和至少 56% 通電話來自 B 醫院。相比較，A 醫院中手術室外麻醉的緊急請求最多為 0.2% 例，B 醫院為 1.8% 通電話。

**結論：**接近一半的消息是為監督麻醉師在手術室的活動。為了手術當天用通信工具幫助麻醉，他們的作用應該包括一個專注於手術室外的護理如等候區和手術室外如控制台。  
(孫莉萍譯 薛張綱校)

**BACKGROUND:** Theoretically, communication systems have the potential to increase the productivity of anesthesiologists supervising anesthesia providers. We evaluated the maximal potential of communication systems to increase the productivity of anesthesia care by enhancing anesthesiologists' coordination of care (activities) among operating rooms (ORs).

**METHODS:** At hospital A, data for 13,368 pages were obtained from files recorded in the internal alphanumeric text paging system. Pages from the postanesthesia care unit were processed through a numeric paging system and thus not included. At hospital B, in a different US state, 3 of the authors categorized each of 898 calls received using the internal wireless audio system (Vocera®). Lower and upper 95% confidence limits for percentages are the values reported.

**RESULTS:** At least 45% of pages originated from outside the ORs (e.g., 20% from holding area) at hospital A and at least 56% of calls (e.g., 30% administrative) at hospital B. In contrast, requests from ORs for urgent presence of the anesthesiologist were at most 0.2% of pages at hospital A and 1.8% of calls at hospital B.

**CONCLUSIONS:** Approximately half of messages to supervising anesthesiologists are for activity originating outside the ORs being supervised. To use communication tools to increase anesthesia productivity on the day of surgery, their use should include a focus on care coordination outside ORs (e.g., holding area) and among ORs (e.g., at the control desk).

## 選擇哪一位執業者對下一位麻醉前評估患者進行評估取決於執業者的相對速度

### Choosing which practitioner sees the next patient in the preanesthesia evaluation clinic based on the relative speeds of the practitioner.

Franklin Dexter, MD, PhD\*, Hyun-Soo Ahn, PhD† and Richard H. Epstein, MD, CPHIMS‡  
From the \*Department of Anesthesia, Division of Management Consulting, University of Iowa, Iowa City, Iowa; †Department of Operations and Management Science, University of Michigan, Ann Arbor, Michigan; and ‡Department of Anesthesiology, Jefferson Medical College, Philadelphia, Pennsylvania.

Anesth Analg April 2013 116:919-923

**背景：**臨床上麻醉前評估通常不是評估患者，因為病人不會等著被評估，執業者更多時間是用來複習患者的病史。執業者完整評估的時間是不同的，針對評估較慢的，我們需要不同的方案以縮短患者等候的時間（至少有 2 名患者在等候）。

**方法：**通過研究明確如何優化等候隊伍的狀況（如最快平均評估一名患者的時間比最慢的少一半）。我們比較了隊伍狀況與診所內註冊護士完成評估的時間的關係。計算平均評估時間按的 99.9% 置信區間。

**結果：**最快的執業者比第二快的速度快 1.23 倍(CI 1.22-1.23)，比最慢的三個執業者快 1.61 倍 (1.59-1.61)。上述差別可以明顯加快 3 倍和 2 倍等候時間，從而保證等候隊伍的秩序。速度較慢的執業者評估所占時間較長 (Kendall  $\tau_b = 0.56$ ,  $P = 0.0001$ )，因此優先將患者安排給速度較快的人。

**結論：**執業者評估患者的速度沒有顯著改變資訊系統常規選擇下一名患者。臨床是降低患者等候的時間應該著眼於減少總體評估時間（如複習病史的時間），合適的安排患者和有適當的輔助護士和執業者的人數。

（郁玲玲譯 薛張綱校）

**BACKGROUND:** When a practitioner in a preanesthesia evaluation clinic is not evaluating a patient because no patient is waiting to be seen, the practitioner often has other responsibilities such as reviewing charts of patients. When practitioners differ in how quickly they complete evaluations, multiple scenarios can be created wherein the slowest practitioner would only evaluate patients when the number of patients waiting exceeds a threshold (e.g., at least 2 patients are waiting).

**METHODS:** Review of operations research studies identified conditions for which such management of the queue can be beneficial (e.g., mean evaluation time of the fastest practitioner is less than half that of the slowest practitioner). These conditions were compared with the actual completion rates of certified registered nurse practitioners at a hospital's clinic. The 99.9% confidence intervals (CI) were calculated for ratios of mean evaluation times.

**RESULTS:** The fastest practitioner was typically 1.23 times faster than the second fastest practitioner (CI 1.22-1.23) and 1.61 times faster than the slowest of three practitioners (1.59-1.61). These are significantly less than the 3 times and 2 times faster, respectively, that would be sufficiently large to warrant managing queue discipline. Practitioners with longer mean evaluation times had larger percentage utilizations of working time (Kendall  $\tau_b = 0.56$ ,  $P = 0.0001$ ), inconsistent with preferential assignment of patients to the fastest practitioner(s) available.

**CONCLUSIONS:** Practitioners' speeds in evaluating patients do not differ sufficiently for information systems to be used routinely to choose who evaluates the next patient (i.e., state-dependent assignment policy). Clinics aiming to reduce patient waiting should focus on reducing the overall mean evaluation time (e.g., by chart review ahead), appropriately scheduling patients, and having the right numbers of nursing assistants and practitioners

### 區域麻醉下手術後出現快速眼動睡眠剝奪

#### Occurrence of rapid eye movement sleep deprivation after surgery under regional anesthesia.

Frank Dette, MD\*, Werner Cassel, MSc†, Friederike Urban‡, Martin Zoremba, MD‡, Ulrich Koehler, MD†, Hinnerk Wulf, MD‡, Jürgen Graf, MD‡ and Thorsten Steinfeldt, MD‡

From the \*Department of Anesthesiology, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz; and †Department of Internal Medicine, Division of Pneumology, and ‡Department of Anesthesiology and Intensive Care, Philipps-University Marburg, Marburg, Germany.

Anesth Analg April 2013 116:939-943

**背景：**普外科手術後出現睡眠障礙已經被描述過了。在這項研究中，我們評估患者在區域麻醉下行膝關節置換術後快速眼動睡眠（REM）的情況。

**方法：**在3個晚上進行動態多導睡眠監測（PSG）：手術前一天晚上（PSG1），手術後的第1天晚上（PSG2），術後第5天的晚上（PSG3）。術後鎮痛前3天採用外周神經置管，隨後口服阿片類藥物。此外，還可給予非甾體類抗炎藥物。採用視覺類比評分法評價術後疼痛程度。

**結果：**在12名患者中實行了PSG，其中6名男性和6名女性，平均年齡為61（±12）歲。從PSG1（中位數為16.4%）到PSG2（中位數為6.3%， $P=0.02$ ）提示REM睡眠減少。利用Hodges-Lehmann法估計中位數減少-7.8%（95%置信區間為-14.8%至-0.7%）。在PSG3階段，與PSG2相比，監測到顯著的REM睡眠（中位數為15.4%）（ $P=0.01$ ）。利用Hodges-Lehmann法估計中位數增加為10.0%（95%置信區間為1.7%至25.3%）。

**結論：**在手術及區域麻醉後，會出現REM睡眠的減少。

（周玲譯 薛張綱校）

**BACKGROUND:** Sleep disturbances after general surgery have been described. In this study, we assessed rapid eye movement (REM) sleep in patients undergoing knee replacement surgery using a regional anesthetic technique.

**METHODS:** Ambulatory polysomnography (PSG) was performed on 3 nights: the night before surgery (PSG1), the first night after surgery (PSG2), and the fifth postoperative night (PSG3). Postoperative analgesia was maintained with peripheral nerve catheters for the first 3 days and with oral opioids thereafter. In addition, nonsteroidal antiinflammatory drugs were administered. Postoperative pain was monitored using a visual analog scale.

**RESULTS:** PSG was performed in 12 patients, 6 men and 6 women, with a mean age of 61 (±12) years. REM sleep was reduced from PSG1 (median 16.4%) to PSG2 (median 6.3%;  $P=0.02$ ). The Hodges-Lehmann estimate for the median reduction is -7.8% (95% confidence interval -14.8% to -0.7%). During PSG3, significantly more REM sleep was detected (median 15.4%)

compared with PSG2 ( $P = 0.01$ ). The Hodges-Lehmann estimate for this median increase is 10.0% (95% confidence interval 1.7%-25.3%).