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在旋轉式血栓彈力計與血栓彈力圖中評估血小板對血凝塊（血小板成分）強度影響的計算方法

Assessing the Methodology for Calculating Platelet Contribution to Clot Strength (Platelet Component) in Thromboelastometry and Thrombelastography.

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Anesthesia & Analgesia 2015 121 868–878

研究血栓的粘彈性性質最常使用血栓彈力圖（TEG®）和旋轉式血栓彈力計（ROTEM®）。基於 ROTEM®的出血治療演算法推薦，一旦血栓的 ROTEM®纖維強度試驗(FIBTEM) 得到修正，給予低運轉血凝塊強度的患者使用血小板（例如，凝塊幅度在 10 分鐘[A10] < 40 毫米）。基於 TEG®演算法通常使用最大振幅的低值（例如，<50 毫米）作爲給藥的一個觸發。然而，這個參數反映了各種血液成分的血凝塊，包括血小板和纖維蛋白/纖維蛋白原的影響。相較全血血栓振幅 TEG®或 Rotem®法測定，血栓強度的血小板組分可對血小板缺乏提供更爲敏感的指示。已形成血栓的血小板成分是來自 TEG®/Rotem®試驗和血小板有無抑制的結果。在本文中,我們審查了爲什麼這個計算應該基於血栓彈性（例如，TEG®的 E 參數和 ROTEM®的 CE 參數）相對於血栓振幅（例如，TEG®或 Rotem®的 A 參數）的依據。這是因爲血栓的彈性，不同於血栓的振幅，反映了在設備內的血液凝塊抵抗旋轉的力量，且血栓振幅（變數 X）和血栓彈性（變數 Y）之間的關係是非線性的。根據不同的初始值，一個特定的增量 X（ΔX）將與不同的 Y 增量（ΔY）相關。當正確時計算，使用血栓彈性資料，該血凝塊的血小板成分可以對急性出血時的血小板缺乏給出有價值的提示。

（黃堯卿 譯，李士通 審校）

The viscoelastic properties of blood clot have been studied most commonly using thrombelastography (TEG®) and thromboelastometry (ROTEM®). ROTEM® -based bleeding treatment algorithms recommend administering platelets to patients with low EXTEM clot strength (e.g., clot amplitude at 10 minutes [A10] <40 mm) once clot strength of the ROTEM® fibrin-based test (FIBTEM) is corrected. Algorithms based on TEG® typically use a low value of maximum amplitude (e.g., <50 mm) as a trigger for administering platelets. However, this parameter reflects the contributions of various blood components to the clot, including platelets and fibrin/fibrinogen. The platelet component of clot strength may provide a more sensitive indication of platelet deficiency than clot amplitude from a whole blood TEG® or ROTEM® assay. The platelet component of the formed clot is derived from the results of TEG® /ROTEM® tests performed with and without platelet inhibition. In this article, we review the basis for why this calculation should be based on clot elasticity (e.g., the E parameter with TEG® and the CE parameter with ROTEM®) as opposed to clot amplitude (e.g., the A parameter with TEG® or ROTEM®). This is because clot elasticity, unlike clot amplitude, reflects the force with which the blood clot resists rotation within the device, and the relationship between clot amplitude (variable X) and clot elasticity (variable Y) is nonlinear. A specific increment of X (ΔX) will be associated with different increments of Y (ΔY), depending on the initial value of X. When calculated correctly, using clot elasticity data, the platelet component of the clot can provide a valuable insight into platelet deficiency in emergency bleeding.

在健康志願者中靜脈輸注鎮靜麻醉藥物 azd3043 後一個對藥代動力學和對腦電雙頻指數的影響的迴圈模型

A Recirculatory Model for Pharmacokinetics and the Effects on Bispectral Index After Intravenous Infusion of the Sedative and Anesthetic AZD3043 in Healthy Volunteers

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Anesthesia & Analgesia 2015 121 904–913

背景：AZD3043 是一種 γ-氨基丁酸 A 型受體陽性變構調節劑，具有鎮靜和麻醉作用。我們描述一個在健康志願者中動靜脈 azd3043 的濃度和藥效學效應對腦電雙頻指數（BIS）的作用的群體藥代動力學（PK）模型。

方法：在 2 個臨床研究 125 名健康志願者中測量動脈和靜脈 AZD3043 血漿濃度

和 BIS 值，AZD3043 給予一個 1 分鐘的單次劑量（1-6 毫克/公斤），一個 30 分鐘的輸注（1-81 毫克/公斤/小時），或 0.8 + 10，1 + 15，3 + 30，4 + 40（毫克/千克單次劑量+毫克/公斤/小時 30 分鐘輸注）。群體藥代動力學 /藥效學分析，使用 NONMEM。

結果：一個迴圈模型，包括一系列的 5 個室用於靜脈和動脈血漿藥物之間的運輸，2 個周圍分佈室，和 1 個爲從動脈到靜脈血漿藥物的非分配運輸室，描述了 AZD3043 的藥代動力學。全身清除率高（2.2 升/分鐘；95%置信區間，2.12-2.25），表觀分佈容積低，導致一個短的消除半衰期。動脈和外周室分佈的表觀體積隨劑量的增加而增加，總的表觀體積爲最低劑量後的 15 升和最大劑量後的 37 升。乙狀結腸最大效應（Emax），15.6 克/毫升的 EC50 和 1.7 的 γ 描述了 AZD3043 效應部位濃度 EC50 和 BIS 之間的關係模型。個體間變異的 EC50 爲 37%。效應室模型半衰期平衡速率常數 ke0 爲 1.1 分鐘，描述了有關的動脈血漿濃度效果的延遲。

結論：AZD3043 具有較高的清除和較低的分佈容積，導致半衰期減短。而表觀體積分佈呈劑量依賴性（P<0.001），導致半衰期與劑量的增加。效應位置的分佈快速且同步於短血漿半衰期導致的快速起效和失效作用。

（黃堯卿 譯，李士通 審校）

BACKGROUND: AZD3043 is a positive allosteric modulator of the gamma-aminobutyric acid type A receptor, with sedative and anesthetic properties. We describe a population pharmacokinetic (PK) model of arterial and venous concentrations of AZD3043 and the pharmacodynamic effects on bispectral index (BIS) in healthy volunteers.

METHODS: Arterial and venous plasma concentrations of AZD3043 and BIS were measured in 2 clinical studies in 125 healthy volunteers, where AZD3043 was given as a 1-minute bolus (1-6 mg/kg), a 30-minute infusion (1-81 mg/kg/h), or 0.8 + 10, 1 + 15, 3 + 30, and 4 + 40 (mg/kg bolus + mg/kg/h infusion for 30 minutes). Population PK/pharmacodynamic analysis was performed with NONMEM.

RESULTS: A recirculatory model, comprising a series of 5 compartments for the transit of drug between venous and arterial plasma, 2 peripheral distribution compartments, and 1 compartment for the nondistributive transit of drug from arterial to venous plasma, described the PK of AZD3043. Systemic clearance was high (2.2 L/min; 95% confidence interval, 2.12-2.25), and apparent volumes of distribution were low, leading to a short elimination half-life. The apparent volumes of distribution of the arterial and peripheral compartments increased with increasing administered dose, giving a total apparent volume of distribution of 15 L after the lowest dose and 37 L after the greatest dose. A sigmoid maximum effect (Emax) model with an EC50 of 15.6 g/mL and a gamma of 1.7 described the relationship between AZD3043 effect-site concentrations and BIS. The between-subject variability in EC50 was 37%. An effect compartment model, with a half-life of the equilibration rate constant ke0 of 1.1 min, described the delay in effect in relation to the arterial plasma concentrations.

CONCLUSIONS: AZD3043 had a high clearance and a low apparent volume of distribution, leading to a short half-life. However, the apparent volume of distribution was dose dependent ($P < 0.001$), leading to an increased half-life with increasing dose. The distribution to the effect site was fast and together with the short plasma half-life led to a fast onset and offset of effects.

對比術中胸骨上及食管多普勒，上腹部大手術改變心臟生物電抗輸出讀數，NICOM

Major Upper Abdominal Surgery Alters the Calibration of Bioreactance Cardiac Output Readings, the NICOM, When Comparisons Are Made Against Suprasternal and Esophageal Doppler Intraoperatively

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Anesthesia & Analgesia 2015 121 936–945

背景：在麻醉過程中，建議使用微創連續心輸出量測量來指導液體治療，但這種測量必需可靠的趨勢變化。NICOM（Cheetah 公司），一種生物電抗檢測儀，正在被推薦用於術中使用。爲了驗證它的使用方法，多普勒，胸骨上 USCOM 及食管 CardiQ 串聯使用，可提供可靠的估計心輸出量的變化趨勢。初步比較表明，上腹部手術引起的 NICOM 校準偏移。本研究的目的是確認和測量這些校準偏移。

方法：大手術的患者，年齡在 58 歲（32~78），12 個男性和 15 個女性，分爲 4 組：（a 組）對照組下腹部或外周手術（9 例）；（b 組）氣腹腹腔鏡手術（6 例）；（C 組）放置大的多葉牽開器的開放上腹部手術（6 例）和（d 組）頭頸機器人手術（6 例）。NICOM 和多普勒每 15 到 30 分鐘同時讀數。在個別時間繪製圖表，對 NICOM-USCOM 和 CardioQ-USCOM 讀數進行回歸分析。同時進行 Bland-Altman 分析和趨勢（一致性）分析。

結果：390 例 NICOM 對照被收集。手術時間爲 4（1 至 11）小時，每例 7 至 22 組。平均（SD）USCOM 心臟指數爲 3.5（1.0）L/min/m。個別時間圖顯示外科手術期間心臟指數在 NICOM 校準相對多普勒（USCOM）的變化爲±0.9 (0.6-1.4) L/min/m 。18 例中 13 例（72%），變化呈下降趨勢，但上升變化也有發現。在個體之間的相關性顯示出良好的趨勢 CardioQ-USCOM R = 0.87（範圍，0.60-0.97）。在對照組中，NICOM-USCOM 也表現出良好的趨勢 R = 0.89（0.69-0.97）。然而，趨勢是在干預組不明顯，R = 0.43（0.03-0.71；P＜0.0001）。Bland-Altman 分析的誤差百分比在 NICOM-USCOM 之間（57 [54-60] %）大於 CardioQ-USCOM 之間（42 [40-44]%）（P＜0.0001）。一致率分別爲 101 個資料對的 82（77-88）% 和 72 個數據對的 95 (90-99)% 。

結論：多普勒監測串聯使用，提供了對心輸出量的變化有效的趨勢線與 NICOM 讀數可以相比較。術中，可靠地跟蹤的 NICOM 被證明在大多數情況下顯示心輸出量的變化。然而，上腹部外科手術引起的讀數改變 >1 L/min/m，且方向的變化是不可預測的。每當術中應用 NICOM，麻醉醫生需要知道這些校準變化並且預見其發生。

（黃堯卿 譯，李士通 審校）

BACKGROUND: Minimally invasive continuous cardiac output measurements are recommended for use during anesthesia to guide fluid therapy, but such measurements must trend changes reliably. The NICOM Cheetah, a BioReactance monitor, is being recommended for intraoperative use. To validate its use, Doppler methods, suprasternal USCOM and esophageal CardioQ, were used in tandem to provide reliable estimates of changing trends in cardiac output. Preliminary comparisons showed that upper abdominal surgical interventions caused shifts in the calibration of the NICOM. The purpose of this study was to confirm and measure these calibration shifts.

METHODS: Major surgery patients, aged 58 (32-78) years, 12 males and 15 females, were divided into 4 study groups: (a) controls-lower abdominal or peripheral surgery (n = 9); (b) laparoscopy with abdominal insufflation (n = 6); (c) open upper abdominal surgery with large multiblade retractor placement (n = 6) and (d) head-down robotic surgery (n = 6). Simultaneous NICOM and Doppler readings were taken every 15 to 30 minutes. Within-individual time plots were drawn, and regression analysis between NICOM-USCOM and CardioQ-USCOM readings was performed. Bland-Altman and trend (concordance) analyses were also performed.

RESULTS: Three hundred ninety NICOM comparisons were collected. Duration of surgeries was 4 (1 to 11) hours, with 7 to 22 sets of readings per case. Mean (SD) cardiac index from

USCOM readings was 3.5(1.0) L/min/m. Individual time plots showed shifts in NICOM calibration relative to Doppler (USCOM) in cardiac index of ±0.9 (0.6-1.4) L/min/m during the surgical interventions. In 13 of 18 patients (72%), the shift was downward, but upward shifts did occur. Within-individual correlations between CardioQ-USCOM showed good trending R = 0.87 (range, 0.60-0.97). In the control group, NICOM-USCOM also showed good trending R = 0.89 (0.69-0.97). However, trending was poor in the intervention groups, R = 0.43 (0.03-0.71; P < 0.0001). The Bland-Altman percentage error between NICOM-USCOM (57 [54-60]%) was greater than that between CardioQ-USCOM (42 [40-44]%) (P < 0.0001). Concordance rates were 82 (77-88)% from 101 data pairs and 95 (90-99)% from 72 data pairs, respectively.

CONCLUSIONS: Doppler monitoring used in tandem provided valid trend lines of cardiac output changes against which NICOM readings could be compared. Intraoperatively, the NICOM was shown to track changes in cardiac output reliably in most circumstances. However, surgical interventions to the upper abdomen caused shifts in readings by >1 L/min/m, and the direction of the shifts was unpredictable. Anesthesiologists need to be aware of these calibration shifts and anticipate their occurrence, whenever the NICOM is used intraoperatively.

一種改善麻醉後復蘇室交接的多模式干預

A Multimodal Intervention Improves Postanesthesia Care Unit Handovers

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背景：溝通失敗是圍術期不良事件一個的主要因素。護理的轉變可能特別容易。我們試圖改善術後交接。

方法：我們介紹了一種成人及小兒麻醉後復蘇室多模式干預以改善麻醉實施者（AP）與麻醉後復蘇室註冊護士(RN)間的術後交接。干預措施由一個標準化電子交接報表、教學性的網路研討會、以集中提高跨專業交流的強制模擬訓練及培訓後績效回饋組成。利用盲法，培訓後的護士採用由 8 個分量表和一個整體的評分（1-5 級）組成的結構式工具對麻醉後復蘇室交接進行評分。多因素 logistic 回歸分析對交接時整體評分等級≥3 所占的比例來評價干預效果。

結果：觀察和評估了受過模擬培訓的 452 名臨床醫生及 981 次交接。在成人 PACU,估算 AP 與 RN 之間可接受的交接（整體評分≥3）的比例。AP-RN 均未接受模擬訓練，該比例在 0 天爲 3%（95%的可信區間 1%-11%），訓練開始後 40 天爲 10%（5%-19%），訓練一年後（405 天）爲 57%（33%-78%）；而在 AP-PN 其中至少有一個接受模擬訓練者，該比例在 40 天及 405 天分別爲 18%（11%-28%）及 68%（57%-76%）。在未經訓練的 AP-PN 組與訓練有素的 AP-PN 組，可接受的交接百分比在 405 天時均顯著高於 40 天（P<0.001）。在兒童 PACU 觀察到類似的情況。培訓三年後，據不精確估計可接受的交接比例在成人 PACU 及兒童 PACU 分別約爲 87%（72%-95%）及 56%（40%-72%）。

結論：這一多模式干預顯著改善了包括未接受正規模擬訓練的臨床醫生 PACU 的跨專業交接，3 年後顯效。

（徐卉紅 譯，李士通 審校）

BACKGROUND: Failures of communication are a major contributor to perioperative adverse events.Transitions of care may be particularly vulnerable. We sought to improve postoperative handovers.

METHODS: We introduced a multimodal intervention in an adult and a pediatric postanesthesia care unit (PACU) to improve postoperative handovers between anesthesia providers (APs) and PACU registered nurses (RNs). The intervention included a standardized electronic handover report form, a didactic webinar, mandatory simulation training focused on improving interprofessional communication, and post-training performance feedback. Trained, blinded nurse observers scored PACU handovers during 17 months using a structured tool consisting of 8 subscales and a global score (1–5 scale). Multivariate logistic regression assessed the effect of the intervention on the proportion of observed handovers receiving a global effectiveness rating of ≥ 3.
RESULTS: Four hundred fifty-two clinicians received the simulation-based training, and 981 handovers were observed and rated. In the adult PACU, the estimated percentages of acceptable handovers (global ratings ≥3) among AP-RN pairs, where neither received simulation-based training (untrained dyads), was 3% (95% confidence interval, 1% – 11%) at day 0, 10% (5% – 19%) at training initiation (day 40), and 57% (33% – 78%) at 1-year post-training initiation (day 405). For AP-RN pairs where at least one received the simulation-based training (trained dyads), these percentages were estimated to be 18% (11%–28%) and 68% (57%–76%) on days 40 and 405, respectively. The percentage of acceptable handovers was significantly greater on day 405 than it was on day 40 for both untrained ($P < 0.001$) and trained dyads ($P < 0.001$). Similar patterns were observed in the pediatric PACU. Three years later, the unadjusted estimate of the probability of an acceptable handover was 87% (72%–95%) in the adult PACU and 56% (40%–72%) in the pediatric PACU.
CONCLUSIONS:A multimodal intervention substantially improved interprofessional PACU handovers, including those by clinicians who had not undergone formal simulation training. An effect appeared to be present >3 years later.

蘭尼定受體 1 型 p.Arg2508 位幾個基因的突變是導致惡性高熱的潛在來源

Several Ryanodine Receptor Type 1 Gene Mutations of p.Arg2508 Are Potential Sources of Malignant Hyperthermia

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背景：惡性高熱（MH）是一種藥物遺傳性疾病，易感個體在使用吸入麻醉藥和去極化肌松藥後出現。蘭尼定受體 1 型（RYR1）基因突變被認爲是導致 MH 發生的原因，它們主要分佈在 3 個被稱爲“熱點”的區域。在 RYR1 同一位點時常可有多個突變。儘管 RYR1 的 p.Arg2508 位於“熱點”外，但是一些突變或變體（包括已知的導致 MH 的 p.Arg2508Cys 突變）被確認存在於這一區域。我們假定在 RYR 1 的 p.Arg2508 任何突變或變體均能導致與 MH 相關的重要的病理性變化。在該項研究中，我們分析了 4 個包含 p.Arg2508RYR1 不同突變體的功能。

方法：我們製備和分析了 4 個 RYR1 突變基因的功能：p.Arg2508His 和 p.Arg2508Gly 是與 MH 相關的突變體，然而 p.Arg2508Ser 和 p.Arg2508Lys 尚未報導。由於賴氨酸的生化特性類似於精氨酸，因此我們認爲 p.Arg2508Lys 可能具備極其類似野生型 RYR1 的特性。我們將 p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser, 和 p.Arg2508Lys 這 4 個 RYR1 基因的突變體引入兔 cDNA，將所得到的克隆體轉染到人胚腎 293(HEK293)細胞。利用比例測量染料 Fura-2 AM,採用 340/380nm 兩個螢光比值來分析細胞在給予咖啡因和 4-氯間甲酚（4CmC）後鈣穩態的變化。我們計算了轉染每種 RYR1 突變體細胞的半數最大啓動濃度（EC50），同時與表達野生型 RYR1 細胞的 EC50 比較。利用未配對雙尾 t 檢驗計算 EC50 值之間的統計學意義。我們使用了 300 個不同的細胞，野生型和每種突變型各 30 個。

結果：分別轉染突變體 p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser 或 p.Arg2508Lys 的細胞較轉染野生型細胞對咖啡因和 4CmC 更敏感（所有 4 組 P≤0.0004）。咖啡因 EC50 的均值±標準差在野生型、p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser 及 p.Arg2508Lys 分別爲 2.53 ± 0.89, 1.72 ± 0.72, 1.73 ± 0.79, 1.69 ± 0.80 和 1.61 ± 0.74 mM，4CmC 的 EC50 值分別爲 125.92± 38.11, 70.42 ± 27.09, 79.30 ± 39.04, 73.03 ± 19.20 和 72.81 ± 28.44 mM。

結論：這 4 個 RYR1 的任何一個突變都可能導致與 MH 相關的重要改變。研究 RYR1 上 2508 位氨基酸的變化對 RYR1 這個大蛋白分子的影響可能會讓我們更好地理解 MH 病理過程。

（徐卉紅 譯，李士通 審校）

BACKGROUND: Malignant hyperthermia (MH) is a pharmacogenetic disorder that occurs in predisposed individuals after exposure to volatile anesthetics or depolarizing muscle relaxants. Genetic mutations of ryanodine receptor 1 (RYR1), which are considered to cause MH, are found mainly in 3 regions called "hotspots." There are sometimes multiple mutations at the same site of RYR1. Although p.Arg2508 of RYR1 is located outside hotspots, several mutations or variants (including the known MH causative mutation p.Arg2508Cys) have been identified in this region. We hypothesized that any mutations or variants in RYR1 p.Arg2508 cause important changes in pathological conditions related to MH. In this study, we analyzed the functions of 4 different *RYR1* variants containing mutations at p.Arg2508.
METHODS: We prepared and analyzed the functions of 4 mutated *RYR1* genes: p.Arg2508His and p.Arg2508Gly are MH-related variants, whereas p.Arg2508Ser and p.Arg2508Lys have not been previously reported. Because the biochemical characteristics of lysine are similar to arginine, we assumed that p.Arg2508Lys RYR1 would have characteristics most similar to those of the wild-type RYR1. We introduced these 4 mutated *RYR1* genes, p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser, and p.Arg2508Lys into rabbit *RYR1* cDNA and transfected the resultant clones into human embryonic kidney 293 cells. Using the ratiometric dye Fura-2 AM, we used the 340/380 nm ratio to analyze alterations in calcium homeostasis after stimulation with caffeine and 4-chloro-*m*-cresol (4CmC). We calculated the half-maximal activation concentrations (EC50) of cells transfected with each mutant and compared the EC50 value of cells expressing each mutant with that of cells expressing wild-type RYR1. Statistical significance between EC50 values were calculated using an unpaired 2-tailed *t* test. We used 300 different cells, by 30 cells in each of the wild type or mutant.
RESULTS: Cells transfected with each of the 4 mutants, p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser, or p.Arg2508Lys, were more sensitive to caffeine and 4CmC than cells transfected with the wild type (all 4 $P \leq 0.0004$). Mean ± SD of EC50 values for caffeine of wild type, p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser, and p.Arg2508Lys were 2.53 ± 0.89, 1.72 ± 0.72, 1.73 ± 0.79, 1.69 ± 0.80, and 1.61 ± 0.74 mM, respectively, and those for 4CmC were 125.92± 38.11, 70.42 ± 27.09, 79.30 ± 39.04, 73.03 ± 19.20, and 72.81 ± 28.44 mM, respectively.
CONCLUSIONS: Any of these 4 mutations in RYR1 p.Arg2508 may cause important changes related to MH. Studying the effects of changes in amino acids at 2508 in RYR1 on the movement of this large protein may lead to a better understanding of the pathology of MH events.

應激增加慢性疼痛對海馬神經元發生的不利影響

Stress Increases the Negative Effects of Chronic Pain on Hippocampal Neurogenesis

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背景：慢性疼痛患者常常經受情感性精神障礙和認知功能減退，明顯降低患者生活品質。此外，大多數這類患者存在與病情無關的應激進而加重他們的症狀。海馬接受傷害感受的傳入，慢性疼痛時海馬神經元可能發生適應不良性的可塑性改變。海馬是參與情感、學習和記憶的大腦結構。慢性疼痛時，海馬齒狀回顆粒細胞層中的增殖細胞減慢其周轉。但是，海馬處新生神經元的成熟、存活及整合是否受慢性疼痛的影響還不清楚。此外，應激是否加重這一影響還不清楚。

方法：我們分別通過慢性壓迫性神經損傷（CCI）和限制大鼠活動法建立大鼠神經病理性疼痛模型和應激模型，通過評估溴去氧鳥苷摻入增殖細胞和免疫染色法來評估無應激或伴應激 CCI 模型大鼠新生海馬神經的增殖、分化及存活。

結果：所得的資料表明：神經損傷後 8 天神經病理性疼痛的大鼠增殖細胞的數量減少且應激加重了這一效應。此外，神經損傷後 4 周，神經病理性疼痛與海馬顆粒層中神經母細胞及存活的新生成熟神經元均減少相關，應激同樣加重了這一現象。但是在此模型中海馬神經元的分化率沒有受到影響。

結論：神經病理性疼痛對海馬神經元發生（增殖和存活）產生不利影響，應激加重這一效應。神經元這些類型的可塑性的變化可能解釋慢性疼痛患者的情感和認知功能障礙。

（徐卉紅 譯，李士通 審校）

BACKGROUND: Patients with chronic pain often suffer from affective disorders and cognitive decline, which significantly impairs their quality of life. In addition, many of these patients also experience stress unrelated to their illness, which can aggravate their symptoms. These nociceptive inputs are received by the hippocampus, in which maladaptive neuroplastic changes may occur in the conditions of chronic pain. The hippocampus is a structure involved in emotionality, learning, and memory, and the proliferating cells in the granular layer of the hippocampal dentate gyrus respond to chronic pain by slowing their turnover. However, whether the maturation, survival, and integration of newborn cells in the hippocampus are affected by chronic pain remains unclear. In addition, it is unknown whether an added stress may increase this effect.
METHODS: We have evaluated the proliferation, differentiation, and survival of newborn hippocampal cells in a rat model of neuropathic pain (chronic constriction injury), with or without stress (chronic immobilization), by assessing the incorporation of bromodeoxyuridine into proliferating cells and immunostaining.
RESULTS: The data obtained indicated that there was a decrease in the number of proliferating cells 8 days after nerve injury in animals subjected to neuropathic pain, an effect that was exacerbated by stress. Moreover, 4 weeks after nerve injury, neuropathic pain was associated with a loss of neuroblasts and the reduced survival of new mature neurons in the hippocampal granular layer, phenomena that also were increased by stress. By contrast, the rate of differentiation was not affected in this paradigm.
CONCLUSIONS: Neuropathic pain negatively influences hippocampal neurogenesis (proliferation and survival), and this effect is exacerbated by stress. These neuroplastic changes may account for the affective and cognitive impairment seen in patients with chronic pain.

術中注射鎂劑不能減少心臟手術術後房顫的發生率

Intraoperative Magnesium Administration Does Not Reduce Postoperative Atrial Fibrillation After Cardiac Surgery

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背景：低鎂血症與術後房顫（POAF）發生率增加相關。儘管已有研究提示鎂劑治療的有益效果，但是這些研究均受限於過小的樣本量和過低的鎂劑劑量。本研究假設大劑量鎂劑能減少新發 POAF 的發生率，選取了一項評估鎂劑對心臟手術患者的認知轉歸影響的前瞻性實驗的資料來驗證此假設。

方法：總數 389 名接受心臟手術的患者被納入了這項雙盲、安慰劑對照的實驗。研究物件隨機接受了 50mg/kg 鎂劑作爲負荷劑量，麻醉誘導後即刻給予總量爲 50mg/kg，持續輸注 3 小時的鎂劑（總量 100mg/kg），而對照組則給予生理鹽水。採用 logistic 回歸法評估鎂劑對 POAF 的治療效果，並用多中心研究的心臟手術術後房顫的圍術期缺血風險指數來校正房顫(AF)風險。

結果：排除術前發生急慢性房顫的病人後， 共 363 名物件納入分析（安慰劑組 n=177，鎂劑治療組 n=186）。鎂劑治療組的 POAF 新發率爲 42.5（95%可信區間[CI], 35%–50%），安慰劑組則爲 37.9%(95% CI, 31%–45%)，兩組無統計學差異（P=0.40）。4.6%的絕對風險差異的 95%CI 爲 5.5%到 14.7%。兩組 POAF 起始時間也是相同的，在校正 AF 風險後，用 logistic 回歸法分析鎂劑治療未見顯著效果。

結論：術中大劑量鎂劑療法未能降低心臟手術術後新發 POAF 的概率。

（宣偉　譯　陳傑　校）

BACKGROUND: Hypomagnesemia has been associated with an increased risk of postoperative atrial fibrillation (POAF). Although previous studies have suggested a beneficial effect of magnesium (Mg) therapy, almost all of these are limited by small sample size and relatively low Mg dose. We hypothesized that high-dose Mg decreases the occurrence of new-onset POAF, and we tested this hypothesis by using data from a prospective trial that assessed the effect of Mg on cognitive outcomes in patients undergoing cardiac surgery.

METHODS: A total of 389 patients undergoing cardiac surgery were enrolled in this double-blind, placebo-controlled trial. Subjects were randomized to receive Mg as a 50-mg/kg bolus immediately after induction of anesthesia followed by another 50 mg/kg as an infusion given over 3 hours (total dose, 100 mg/kg) or placebo. We tested the effect of Mg therapy on POAF with logistic regression, adjusting for the risk of atrial fibrillation (AF) by using the Multicenter Study of Perioperative Ischemia risk index for Atrial Fibrillation after Cardiac Surgery.

RESULTS: Among the 363 patients analyzed, after we excluded patients with chronic or acute preoperative AF (placebo: n = 177; Mg: n = 186), the incidence of new-onset POAF was 42.5% (95% confidence interval [CI], 35%–50%) in the Mg group compared with 37.9% (95% CI, 31%–45%) in the placebo group (P = 0.40). The 95% CI for this absolute risk difference of 4.6% is −5.5% to 14.7%. The time to onset of POAF also was identical between the groups, and no significant effect of Mg was found in logistic regression analysis after we adjusted for AF risk (odds ratio, 1.09; 95% CI, 0.69–1.72; P = 0.73).

CONCLUSIONS: High-dose intraoperative Mg therapy did not decrease the incidence of new-onset POAF after cardiac surgery.

對健康志願者單次靜脈注射及靜注後持續泵注一種研發中的靜脈鎮靜/麻醉藥 AZD3043 的安全性及藥效學研究

A Bolus and Bolus Followed by Infusion Study of AZD3043, an Investigational Intravenous Drug for Sedation and Anesthesia: Safety and Pharmacodynamics in Healthy Male and Female Volunteers

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背景: AZD3043(THRX-918661)是一個研發中的，可被血液和肝臟中的酯酶快速代謝的苯丙烷類鎮靜/麻醉藥。在其首次人體研究中,使用 AZD3043 持續靜脈輸注 30min 行麻醉誘導並無重大安全性或耐受性問題，且具有快速復蘇的特點。

方法: 這個臨床 1 期、單中心、開放性研究（臨床試驗，編號 NCT00984880）的主要目標是評估單次靜脈推注及單次靜注後持續泵注 AZD3043 的安全性和耐受性。次要目標包括評估 AZD3043 的藥效學特徵和療效。遞增劑量佇列研究中 8 名 18 歲到 65 歲的健康志願者分別接受單次 1min 靜脈推注 (A 隊)或 1min 靜注後持續泵注 30min(B 隊)該藥。評估項目包括不良反應、生命體征、血氣、實驗室檢查、鎮靜/麻醉的臨床體征和腦電雙頻指數。

結果: 72 名志願者(8 名女性,64 名男性)接受 1min 靜注 1、1.5、2、4、6 mg/kg（A 隊）或 0.8、1、3、4 mg/kg 靜注後分別泵注 10、15、30、40 mg/kg/h 的 AZD3043 持續 30min(B 隊)。本研究中沒有患者脫落。發生超過 1 例的不良反應包括頭痛(n = 15；21%)、噁心(n = 7；10%)、嘔吐(n = 3；4%)和倦怠(n = 2；3%)。21 名受試者出現至少 1 種不良反應。暫無證據表明藥物與不良反應間存在量效關係。呼吸不受影響，但心率增快存在劑量相關性。沒有注射痛報告。麻醉物件爲 32 名受試者，包括 A 隊中的最高劑量組和 B 隊中 2 個高劑量組的所有物件。麻醉復蘇較快,定位和本體感受迅速恢復。除 A 隊的 2 mg/kg 組和 B 隊的 4 mg/kg 靜注+ 40 mg/kg/h 泵注 30min 組各 1 名受試者外，其他受試者在用藥結束 30min 後的首次評估中均能在沒有任何支撐下行走 10 米，另 2 名受試者停藥 45min 後的再次評估中通過行走測試。在高劑量組中可觀察到無意識體動伴隨肌肉張力增加。

結論: 需要進一步的臨床研究來證實 AZD3043 提供快速麻醉復蘇並維持正常通氣的能力。

（程鑫宇　譯　陳傑　校）

BACKGROUND: AZD3043 (THRX-918661) is an investigational phenylpropanoid sedative/anesthetic that is rapidly metabolized by esterases in blood and liver. In the first-in-man study, a 30-minute constant IV infusion of AZD3043 induced anesthesia without major safety or tolerability concerns and with rapid recovery characteristics.

METHODS: The primary objective of this phase 1, single-center, open-label study (clinicaltrials.gov NCT00984880) was to evaluate the safety and tolerability of AZD3043 administered as a single IV bolus and as a bolus followed by infusion. Secondary objectives included evaluation of AZD3043 pharmacodynamics and efficacy. Sequential ascending dose cohorts of 8 healthy volunteers aged 18 to 65 years received either a single 1-minute bolus IV infusion (part A) or a 1-minute bolus followed by a 30-minute infusion (part B). Assessments included adverse events, vital signs, blood gases, laboratory values, clinical signs of sedation/anesthesia, and bispectral index score.

RESULTS: Seventy-two subjects (8 females, 64 males) received AZD3043 doses of 1, 1.5, 2, 4, and 6 mg/kg bolus over 1 minute (part A) or 0.8 + 10, 1 + 15, 3 + 30, and 4 + 40 mg/kg bolus + mg/kg/h infusion for 30 minutes (part B). There were no discontinuations. Adverse events occurring in >1 subject were headache (n = 15; 21%), nausea (n = 7; 10%), vomiting (n = 3; 4%), and fatigue (n = 2; 3%). Twenty-one subjects experienced at least 1 adverse event. There seemed to be no dose relationship associated with any adverse event. Ventilation was maintained, but there was a dose-dependent increase in heart rate. There were no spontaneous reports of pain on injection. Thirty-two subjects were anesthetized, including all subjects in the highest dose group in part A and all subjects in the 2 highest dose groups in part B. Recovery from anesthesia was rapid, with swift return of orientation and proprioception. All subjects were able to walk 10 m without support at their first assessment, 30 minutes after end of dosing, except for 1 subject in each of the 2 mg/kg bolus (part A) and 4 mg/kg bolus + 40 mg/kg/h 30-minute infusion (part B) dose groups, who passed this test at the subsequent assessment, 45 minutes after the end of

dosing. Involuntary movements were observed at higher doses, accompanied by increased muscle tone.

CONCLUSIONS: AZD3043 provided rapid recovery from anesthesia with maintained ventilation. Further studies are warranted in a clinical setting.

快速代謝和超短效氯胺酮類似物的發展

Development of Rapidly Metabolized and Ultra-Short-Acting Ketamine Analogs

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背景：氯胺酮是一種經典的，起效迅速的分離性麻醉藥。由於可能出現精神病樣症狀，臨床應用受限，且此藥往往需與催眠藥物合用。本研究假設，具有超短效消除時間的氯胺酮酯類似物可能顯著地降低突發的煩躁現象，即增加一個氯胺酮樣的催眠和鎮痛效用。本研究尋求對 5 酯（（1-（2-氯苯基）-2-氧代環己基）氨基）戊酸甲酯鹽酸鹽，即第一個設計目的爲超快代謝的氯胺酮類似物，進行藥理學研究。

方法：比較 5 種去甲氯胺酮酯類似物（R1-R5）削弱大鼠翻正反射和產生痛覺鈍化的能力。在大鼠中對 2 種類似物(R1,R5)進行毒性測試並評估 50%致命劑量(LD50)。通過高效液相色譜法對兔血漿和全血進行體外代謝穩定性測試。觀察兔子的行爲和血流動力學影響。最後估計這些類似物在兔子中的藥代動力學特徵。

結果：在研究的模型中，所有的 5 種去甲氯胺酮酯都能迅速地使翻正反射消失和踏板撤出減弱，且藥物效應能超快速地消除（R1 與氯胺酮在大鼠翻正反射恢復時間方面的比較：87 秒[四分位距（IQR）78-131] vs 996 秒[IQR 840-1304]; P <0.01）。它們與氯胺酮在 LD50 方面具有可比性（R1 LD50: 50.2mg/kg [95％置信區間，30-63]）。所有的類似物在水解唯一羧酸衍生物方面從快至慢，依次爲體內（R1 清除率：L/kg/min [IQR 0.40-2.42]）、全血和血漿。相對于其鎮靜作用，類似物 R5 表現出更強大的痛覺鈍化效應（踏板撤回評分，與 R1 相比，P <0.001）。

結論：5 種去甲氯胺酮酯類似物保留母體藥物的催眠特性，並由於超速代謝而消除更快。

（馮迪　譯　陳傑　校）

BACKGROUND: Ketamine is a well-established, rapidly acting dissociative anesthetic. Clinical use is limited by prolonged psychotomimetic phenomena on emergence, often requiring the coadministration of additional hypnotic drugs. We hypothesized that the development of ketamine ester analogs with ultrashort offset times might markedly reduce the dysphoric emergence phenomena and, hence, increase the utility of a ketamine-like hypnotic and analgesic. Here, we describe the results of studies that seek to define the pharmacology of 5 esters of ((1-(2-chlorophenyl)-2-oxocyclohexyl)amino)pentanoate hydrochloride, the first ketamine analogs designed to be susceptible to ultrarapid metabolism.

METHODS: Five norketamine ester analogs (R1–R5) were compared by ability to produce loss of righting and nociceptive blunting in rats. Toxicity testing was performed for 2 analogs (R1, R5) with 50% lethal dose (LD50) estimation in rats. In vitro metabolic stability was tested in rabbit plasma and whole blood by high-performance liquid chromatography. Behavioral and hemodynamic effects were observed in rabbits. We estimated the pharmacokinetics of these analogs in rabbits.

RESULTS: All 5 norketamine esters produced rapid loss of righting reflex and diminished pedal withdrawal with ultrarapid offset in the models studied (return of righting reflex 87 seconds [interquartile range (IQR) 78–131] R1 vs 996 seconds [IQR 840–1304] ketamine in rats; P <

0.01). The LD50 was comparable to that of ketamine (LD50 R1 50.2 mg/kg [95% confidence interval, 30–63]). For all analogs, hydrolysis to sole carboxylic acid derivatives was most rapid in vivo (clearance 1.61 L/kg/min R1 [IQR 0.40–2.42]), followed by whole blood and then plasma. Analog R5 demonstrated relatively greater nociceptive blunting than hypnotic effect ($P < 0.001$; pedal withdrawal score comparison with R1).

CONCLUSIONS: The 5 norketamine ester analogs retain the hypnotic characteristics of the parent compound, yet display rapid offset due to ultrarapid metabolism.

在麻醉團隊中運用麻醉誘導前清單來改進資訊交流、關鍵資訊獲取、安全觀念以及可能的團隊協作觀念

An Anesthesia Preinduction Checklist to Improve Information Exchange, Knowledge of Critical Information, Perception of Safety, and Possibly Perception of Teamwork in Anesthesia Teams

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背景：通過 5 項團隊層面預後來介紹和評估麻醉誘導前清單(APIC)的實施，每項預後指標都是患者安全性的一項替代終點：資訊交流 (總共十二個專案組成的清單：團隊交流的完成百分比情況); 關鍵資訊獲取(總共五項例如過敏事件組成的關鍵資訊：每個團隊成員報告的百分比)； 安全觀念 (團隊成員用連續評定量表給出的中位數得分)；團隊協作觀念(團隊成員用連續評定量表給出的中位數得分)；臨床表現(14 項任務，例如呼吸機檢查的完成百分比).

方法： 採用多方法設計進行此項前瞻性干預研究，比較使用 APIC 的實驗組和不使用 APIC 的對照組之間的差異。訓練有素的觀察員評價資訊交流和在麻醉誘導現場觀察臨床表現。觀察後，每個團隊成員闡述他們所知道的關鍵資訊及對安全和團隊協作的看法。

結果: 將 105 個使用 APIC 的團隊使與 100 個不使用的團隊相比較。實驗組與對照組的團隊層面預後評分中位數分別爲：資訊交流：100% vs 33% ($P < 0.001$), 關鍵資訊獲取：100% vs 90% ($P < 0.001$)， 安全觀念: 91% vs 84% ($P < 0.001$), 團隊協作觀念: 90% vs 86% ($P = 0.028$), 和臨床表現: 93% vs 93% ($P = 0.60$).

結論：本研究結果表明，麻醉誘導前清單的應用大大地提高了麻醉團隊內資訊交換, 關鍵資訊獲取和安全觀念，所有參數都與患者安全相關。趨勢表明團隊協作觀念改善。

（劉洋　譯　陳傑　校）

BACKGROUND: An anesthesia preinduction checklist (APIC) to be performed before anesthesia induction was introduced and evaluated with respect to 5 team-level outcomes, each being a surrogate end point for patient safety: information exchange (the percentage of checklist items exchanged by a team, out of 12 total items); knowledge of critical information (the percentage of critical information items out of 5 total items such as allergies, reported as known by the members of a team); team members' perceptions of safety (the median scores given by the members of a team on a continuous rating scale); their perception of teamwork (the median scores given by the members of a team on a continuous rating scale); and clinical performance (the percentage of completed items out of 14 required tasks, e.g., suction device checked).

METHODS: A prospective interventional study comparing anesthesia teams using the APIC with a control group not using the APIC was performed using a multimethod design. Trained observers rated information exchange and clinical performance during on-site observations of

anesthesia inductions. After the observations, each team member indicated the critical information items they knew and their perceptions of safety and teamwork.

RESULTS: One hundred five teams using the APIC were compared with 100 teams not doing so. The medians of the team-level outcome scores in the APIC group versus the control group were as follows: information exchange: 100% vs 33% (P < 0.001), knowledge of critical information: 100% vs 90% (P < 0.001), perception of safety: 91% vs 84% (P < 0.001), perception of teamwork: 90% vs 86% (P = 0.028), and clinical performance: 93% vs 93% (P = 0.60).

CONCLUSIONS: This study provides empirical evidence that the use of a preinduction checklist significantly improves information exchange, knowledge of critical information, and perception of safety in anesthesia teams—all parameters contributing to patient safety. There was a trend indicating improved perception of teamwork.

血小板減少症產婦的椎管內麻醉：一項多位元點回顧性佇列研究

Neuraxial Anesthesia in Parturients with Thrombocytopenia: A Multisite Retrospective Cohort Study

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背景：本研究的主要目的是評估對血小板減小症產婦進行椎管內麻醉操作，其相關的椎管內血腫的風險。

方法：設計此項多中心回顧性佇列研究，用於評估血小板計數<100,000 /mm3 的產婦接受椎管內麻醉時發生脊髓硬膜外血腫的風險；並評估血小板減少症產婦接受全身麻醉時併發症風險。

結果：對 102 例接受硬膜外麻醉和 71 例接受脊麻的血小板減少症產婦進行觀察，沒有發現任何椎管內血腫。資料包括之前已發表的系列報導（共 n=499），脊髓-硬膜外血腫風險的二項置信區間爲 0%至 0.6%。鑒於在每個特定的血小板計數上都存在一些患者人群，故研究也呈現了個體化的血小板計數分層所對應的理論風險。 全麻女性繼發於血小板減少症的嚴重併發症發生率爲 6.5%（95%可信區間爲 2.1%-14.5%）。

結論：本研究的結論支持椎管內麻醉對有輕度血小板減少症產婦相對安全，且評估了未作椎管內麻醉的產婦相關母體併發症的發生率。而在很低的血小板計數時風險存在不確定性，故建立一項國家性“低血小板”症註冊表對於更精確的評估患者發生硬膜外血腫的風險至關重要，並將有助於麻醉實踐的標準化。

（袁亞偉　譯　陳傑　校）

BACKGROUND: The primary aim of this study was to estimate the risk of neuraxial hematoma associated with neuraxial anesthetic procedures in thrombocytopenic parturients.

METHODS: A multicenter retrospective cohort study design was used to estimate the risk for spinal-epidural hematoma in parturients with a platelet count of <100,000/mm3 receiving neuraxial anesthesia and the risk of complications in thrombocytopenic parturients who receive general anesthesia.

RESULTS: No cases of spinal hematoma were observed in 102 thrombocytopenic parturients receiving epidural analgesia or 71 receiving spinal anesthesia. Including data from the previous published series (total n = 499), the exact binomial 95% confidence interval for the risk of spinal-epidural hematoma was 0% to 0.6%. Given the small number of patients at each specific platelet count, the theoretical risks at individual platelet count strata are presented. Overall

aggregate serious morbidity rate in women who received general anesthesia secondary to thrombocytopenia was 6.5% (95% confidence interval, 2.1%–14.5%).

CONCLUSIONS: Our work supports the relative maternal safety of neuraxial anesthesia in parturients with mild thrombocytopenia and estimates the maternal complication rate associated with the avoidance of neuraxial anesthesia. Remaining uncertainties at lower platelet counts make a national "low platelet" registry critical to a more accurate assessment of the risk of epidural hematoma and would aid in standardization of anesthesia practice.

臨床研究方法論 1：源于實驗設計和方法學的錯誤

Clinical Research Methodology 1: Study Designs and Methodologic Sources of Error

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臨床研究可以通過資料收集的時間分爲回顧性和前瞻性兩種。臨床研究同樣可以按實驗設計分類。在病例對照研究中，研究者在疾病後期狀態不同（廣義包括病情發展和對治療的反應）的組別中比較早期暴露因素（包括遺傳和其他個人因素、環境影響和藥物治療）。在佇列研究中，實驗者則對比一個或多個暴露因素不同的組別間的疾病發病率。比較性臨床試驗是一種前瞻性佇列研究，研究者比較分配給病人的不同治療方案。大部分臨床研究結果的錯誤可以由約 5 類可分辨的方法學問題引起：選擇性偏移、混雜、計量偏差、因果顛倒和過分的機會變差。

（孫佳昕　譯　陳傑　校）

Clinical research can be categorized by the timing of data collection: retrospective or prospective. Clinical research also can be categorized by study design. In case-control studies, investigators compare previous exposures (including genetic and other personal factors, environmental influences, and medical treatments) among groups distinguished by later disease status (broadly defined to include the development of disease or response to treatment). In cohort studies, investigators compare subsequent incidences of disease among groups distinguished by one or more exposures. Comparative clinical trials are prospective cohort studies that compare treatments assigned to patients by the researchers. Most errors in clinical research findings arise from 5 largely distinguishable classes of methodologic problems: selection bias, confounding, measurement bias, reverse causation, and excessive chance variation.

對側爪的傳出神經傳導參與了單側爪內注射內皮素-1 後引起對側爪的痛覺過敏現象

Contralateral Hyperalgesia from Injection of Endothelin-1 into the Ipsilateral Paw Requires Efferent Conduction into the Contralateral Paw

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背景：單側損傷後出現對側痛覺過敏，常常被解釋爲脊髓和大腦的中樞敏化。先前研究報導了在大鼠後爪注射內皮素-I(ET-1)可延長對側後爪機械和化學性的致敏作用。本文研究在這一過程中對側傳出神經活動所起的作用。

方法：將(2 nmol, 10 μL)ET-1 皮下注射入右後爪（同側）的趾部皮膚，分別通過對同側及對側進行足底輻射加熱和 von Frey 纖維絲測痛測定熱反應潛伏期和疼痛反應縮足的機械閾。一部分大鼠在注射 ET-1 前 30min，後爪注射（0.25%, 40 μL）布比卡因麻醉 60min。

另一部分在注射 ET-1 前 30min，皮下注射比卡因釋放微粒阻滯對側坐骨神經 6 至 12h。通過在頸部正中線的皮下注射來模擬這些布比卡因製劑的全身作用。

結果:注射 ET-1 後，同側和對側後爪的機械閾第 2 h 開始下降，24 h 降到最低，第 48h 開始恢復直至第 72h 到達注射前的水準。注射 ET-1 前，同側後爪注射布比卡因可以抑制此超敏反應。對側後爪注射布比卡因在每個測試時段也都能抑制超敏反應；除了在超敏反應期間第 2h，同側後爪注射布比卡因組敏感度增加，其餘情況類似。當布比卡因釋放微粒阻滯對側坐骨神經時，這種類似變化的模式也會出現。布比卡因製劑的全身作用要相對微弱得多且只有在 ET-1 注射後第 24 小時才有顯著性差異。同側和對側後爪在注射 ET-1 後都出現了熱超敏，表明對兩種對側麻醉操作的反應模式是相同的。

結論:這些結果表明通過後爪對側神經支配的傳出神經傳導對於對側 ET-1 的敏感性是必要的，提出遠端神經末梢釋放的物質也涉及其中。釋放到外周的物質對於對側 ET-1 的敏感性非常重要，這可能也與手術或神經損傷後，出現在離原發損傷較遠位點的繼發性痛覺過敏有關。

（李悅　譯　陳傑　校）

BACKGROUND: Contralateral hyperalgesia, occurring after unilateral injury, is usually explained by central sensitization in spinal cord and brain. We previously reported that injection of endothelin-1 (ET-1) into one rat hindpaw induces prolonged mechanical and chemical sensitization of the contralateral hindpaw. Here, we examined the role of contralateral efferent activity in this process.

METHODS: ET-1 (2 nmol, 10 μL) was injected subcutaneously into the plantar surface of right (ipsilateral) hindpaw (ILP), and the thermal response latency and mechanical threshold for nocifensive withdrawal were determined by the use of, respectively, plantar radiant heating and von Frey filaments, for both ILP and contralateral hindpaws (CLP). Either paw was anesthetized for 60 minutes by direct injection of bupivacaine (0.25%, 40 μL), 30 minutes before ET-1. Alternatively, the contralateral sciatic nerve was blocked for 6 to 12 hours by percutaneous injection of bupivacaine-releasing microspheres 30 minutes before injection of ET-1. Systemic actions of these bupivacaine formulations were simulated by subcutaneous injection at the nuchal midline.

RESULTS: After the injection of ET-1, the mechanical threshold of both ILP and CLP decreased by 2 hours, appeared to be lowest around 24 hours, and recovered through 48 hours to preinjection baseline at 72 hours. These hypersensitive responses were suppressed by bupivacaine injected into the ipsilateral paw before ET-1. Injection of the CLP by bupivacaine also suppressed the hypersensitivity of the CLP at all test times, and that of the ILP, except at 2 hours when it increased the sensitivity. This same pattern of change occurred when the contralateral sciatic nerve was blocked by bupivacaine-releasing microspheres. The systemic actions of these bupivacaine formulations were much smaller and only reached significance at 24 hours post−ET-1. Thermal hypersensitivity after ET-1 injection also occurred in both ILP and CLP and showed the same pattern in response to the 2 contralateral anesthetic procedures.

CONCLUSIONS: These results show that efferent transmission through the contralateral innervation into the paw is necessary for contralateral sensitization by ET-1, suggesting that the release of substances by distal nerve endings is involved. The release of substances in the periphery is essential for contralateral sensitization by ET-1 and may also contribute to secondary hyperalgesia, occurring at loci distant from the primary injury, that occurs after surgery or nerve damage.

首例研究鎮靜麻醉藥物 AZD3043 的人類臨床試驗：一項給健康男性志願者輸注 30 分鐘 AZD3043 後評價藥物安全性、藥代動力學及藥效學的臨床劑量遞增試驗

First Human Study of the Investigational Sedative and Anesthetic Drug AZD3043: A Dose-Escalation Trial to Assess the Safety, Pharmacokinetics, and Efficacy of a 30-Minute Infusion in Healthy Male Volunteers

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背景：AZD3043 是一種 γ-氨基丁酸 A 型受體的正向別構調節劑，可被血液和肝臟中的酯酶快速代謝爲一種無活性產物。臨床前期研究提示 AZD3043 作爲超短效靜脈用鎮靜/麻醉藥物，具有快速可預知的復蘇特性、優越的使用安全性及耐受性。

方法：我們第一階段、單中心、開放性研究的主要目標是評估靜脈輸注 AZD3043 的安全性及耐受性，並預測其最大可耐受劑量。次要目標包括評估 AZD3043 的藥代動力學、藥效學及療效。將一群年齡 18-45 歲的健康男性志願者分爲 5-6 人一組，按組別依次給予劑量遞增的 AZD3043，給藥方式爲 30 分鐘單次輸注。評價指標包括藥物不良反應，受試者的生命體征，實驗室檢查，臨床表現和雙頻譜指數（BIS）。

結果：53 例受試者按組別接受 AZD3043 的輸注速率分別爲 1, 3, 6, 12, 18, 27, 36, 54 和 81 mg/kg/h。試驗中無中途停藥，但在達到預定義的暴露極限時終止增加劑量。藥物不良反應發生大於 1 例的有頭痛（n=4），紅斑（n=3），胸部不適（n=2），噁心（n=2）及呼吸困難（n=2）。不良反應發生的頻率及種類與藥物劑量無關。受試者並無注射痛的主訴，且無臨床相關的改變表現在呼吸頻率及動脈血壓上。然而，心率在輸注速率＞18mg/kg/h 時有劑量依賴性增高。鎮靜/麻醉的情況與藥物劑量相一致；在預定義的時間點產生鎮靜/麻醉臨床表現的藥物最低輸注速率是 12 mg/kg/h（6 例受試者中有 1 例達到標準），3 組最高速率組的所有受試者都達到麻醉標準。最高輸注速率組的麻醉平均起效時間爲 4 分鐘而 12 mg/kg/h 組爲 29 分鐘。12 mg/kg/h 組在停止藥物輸注後 3 分鐘恢復對口頭指令的反應，而 81 mg/kg/h 組平均耗時 25 分鐘。隨著肌張力的恢復，小到抽搐大到伸展運動等不自主活動也相繼恢復。

結論：在首次人類臨床試驗中 AZD3043 證實可被較好耐受，加上其短暫的起效及恢復時間，預示 AZD3043 將會是一種應用良好的短效鎮靜和麻醉藥物。

（殷悅 譯 薛張綱 校）

BACKGROUND: AZD3043 is a positive allosteric modulator of the gamma-aminobutyric acid type A receptor that is rapidly metabolized to an inactive metabolite by esterases present in blood and liver. Preclinical results suggest that AZD3043 has the potential as a short-acting IV sedative/anesthetic drug with rapid and predictable recovery characteristics and a favorable safety and tolerability profile.

METHODS: Our primary objective in this phase 1, single-center, open-label study was to evaluate the safety and tolerability of AZD3043 after IV infusion and to estimate the maximal tolerated dose. Secondary objectives included the evaluation of AZD3043 pharmacokinetics, pharmacodynamics, and efficacy. Sequential ascending-dose cohorts of 5 or 6 healthy male volunteers aged 18 to 45 years received a single 30-minute IV infusion of AZD3043. Assessments included adverse events, vital signs, blood gases, laboratory values, clinical signs of sedation/anesthesia, and bispectral index.

RESULTS: Fifty-three subjects received AZD3043 in infusion rate cohorts of 1, 3, 6, 12, 18, 27, 36, 54, and 81 mg/kg/h. There were no discontinuations, and dose escalation was stopped on reaching the predefined exposure limit. Adverse events occurring in >1 subject were headache (n = 4), erythema (n=3), chest discomfort (n=2), nausea (n=2), and dyspnea (n=2). The frequency and character of adverse events appeared unrelated to dose. There were no spontaneous reports of pain on injection and no clinically relevant changes in respiratory rate or arterial blood

pressure. However, heart rate increased dose-dependently at infusion rates >18 mg/kg/h. Occurrence of sedation/anesthesia corresponded with dose; the lowest applied infusion rate to induce anesthesia according to clinical signs of sedation/anesthesia at predefined time points was 12 mg/kg/h (1 of 6 subjects anesthetized), and all subjects in the 3 highest dose groups were anesthetized. The onset of anesthesia ranged from 4 minutes in the highest infusion rate group to 29 minutes in the 12-mg/kg/h infusion rate group. Return of response to oral command occurred at 3 minutes after the end of infusion in the single subject who was anesthetized in the 12-mg/kg/h group and median 25 minutes in the 81-mg/kg/h group. Involuntary movements ranging from minor twitches to extensive movements were accompanied by increased muscle tone.

CONCLUSIONS: AZD3043 was well tolerated in this first human study and seems to exhibit rapid onset and recovery, indicating potential use as a short-acting drug for anesthesia and sedation.

一種新型羥-5α-孕烷二酮的水劑與丙泊酚在效能和安全性上的比較的臨床 1c 期藥物試驗

A Phase 1c Trial Comparing the Efficacy and Safety of a New Aqueous Formulation of Alphaxalone with Propofol

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背景：Phaxan™（即 PHAX，密西根坎墩化學實驗室）是一種 10 毫克/毫升的羥-5α-孕烷二酮和 13% 7-磺丁基醚 β-環糊精（β-環糊精複合物）的水溶液。在臨床前期研究中，PHAX 是一種和異丙酚一樣起效快-失效快的靜脈麻醉藥，但對心血管的抑制更少。本項是其第一次用於人體的藥物試驗，旨在找到 PHAX 的麻醉劑量以及與等效劑量的丙泊酚比較安全性、效能、麻醉恢復及蘇醒品質。

方法：本研究堅持貫徹 GCP 的規定（臨床試驗註冊號，actrn12611000343909）。本項研究隨機、雙盲，研究使用貝葉斯演算法來確定 PHAX 和丙泊酚對腦電雙頻指數（BIS）的效應的等效劑量。受試者爲男性志願者，ASA 分級 I 級，知情同意（分爲丙泊酚和 PHAX 兩組，每組 12 人）。評價參量爲藥物注射（單次劑量）80 分鐘後的注射痛、不自主運動、腦電雙頻指數、血壓、是否需要氣道支援以及作爲蘇醒恢復品質的評價指標的 Richmond 躁動鎮靜量表和數位記號替換測試。動脈血液的抽取用於生化，血液學和補體水準的測定。

結果：PHAX 組的受試者沒有一例報告注射痛，而 12 例丙泊酚組的受試者中有 8 例報告了注射痛。達到等效的 BIS 值≤50 的受試者，PHAX 組有 9 例，丙泊酚組有 8 例，分別所需要的中位數劑量爲 PHAX 組：0.5 (0.5-0.6)mg/kg；丙泊酚組：2.9 (2.4-3.0) mg/kg。兩組中能達到的最低 BIS 中位數值都是 27-28，兩組起效的時間和 BIS 值的恢復時間都沒有顯著的差異。伴隨的收縮壓和舒張壓的中位數值變化，PHAX 組與丙泊酚組相比分別是收縮壓-11% vs -19%，舒張壓-25% vs -37%。丙泊酚組 12 例受試者中 9 例需要氣道支援，PHAX 組受試者均無需要。達到等效的 BIS 值≤50 的受試者中：Richmond 躁動鎮靜量表和數位記號替換測試達到 0 時，丙泊酚受試者和 PHAX 的中位數起效時間分別爲爲 5（IQR，5-10）分鐘和 15（IQR，10-20）分鐘。丙泊酚組和 PHAX 組受試者的 BIS 值恢復到 90 所需要的時間分別是 21 分鐘（SD，10.1）和 21 分鐘（SD 9.2）丙泊酚組和 PHAX 組受試者的數位記號替換測試分數恢復到靜脈用藥前水準需要的時間的中位數分別爲爲 50（IQR，35-72.5）分鐘和 42.5（IQR，35-76.3）分鐘。兩種藥物在注射後 C3 和 C4 補體水平均沒有增加。

結論：PHAX 能與丙泊酚提供類似的起效快-失效快和短時間麻醉的快速認知恢復，但心血管抑制更少，氣道阻塞更少，且無注射痛。

（俞啓蒙 譯 薛張綱 校）

BACKGROUND: Phaxan™ (PHAX, Chemic Labs, Canton, MA) is an aqueous solution of 10 mg/mL alphaxalone and 13% 7-sulfobutylether β-cyclodextrin (betadex). In preclinical studies, PHAX is a fast onset-offset IV anesthetic like propofol, but causes less cardiovascular depression. This first-in-man study was designed to find the anesthetic dose of PHAX and to compare it with an equivalent dose of propofol for safety, efficacy, and quality of recovery from anesthesia and sedation.

METHODS: The study adhered to compliance with Good Clinical Practices regulations (clinical trials registry number, ACTRN12611000343909). This randomized, double-blind study compared PHAX and propofol using a Bayesian algorithm to determine dose equivalence for effects on the bispectral index (BIS). Male volunteers, ASA physical status I, gave written informed consent (n = 12 per group; PHAX or propofol). Parameters assessed for 80 minutes after drug injection (single bolus dose) were pain on injection, involuntary movement, BIS, blood pressure, need for airway support, and, as measures of recovery from sedation, the Richmond Agitation and Sedation Scale and the Digit Symbol Substitution Test. Arterial blood was withdrawn for biochemistry, hematology, and complement levels.

RESULTS: No subject complained of pain on injection with PHAX, whereas 8 of the 12 subjects given propofol did. Nine PHAX and 8 propofol subjects reached BIS values of ≤50: median (interquartile range [IQR]) mg/kg dose = 0.5 (0.5-0.6) for PHAX and 2.9 (2.4-3.0) for propofol. The lowest median BIS reached was 27 to 28 for both agents with no significant differences between them for timing of onset and recovery of BIS. The concomitant median changes in systolic and diastolic blood pressures were -11% vs -19% for systolic and -25% vs -37% for diastolic in PHAX- and propofol-treated subjects, respectively. Nine of the 12 propofol-treated subjects and none of 12 PHAX-treated subjects required airway support. For subjects reaching an equivalent BIS of ≤50: a Richmond Agitation and Sedation Scale score of 0 was reached at a median of 5 (IQR, 5-10) and 15 (IQR, 10-20) minutes after PHAX and propofol, respectively; BIS returned to 90 at a mean of 21 (SD, 10.1) and 21 (SD, 9.2) minutes after PHAX and propofol, respectively; and Digit Symbol Substitution Test scores returned to predrug injection values at median of 50 (IQR, 35-72.5) and 42.5 (IQR, 35-76.3) minutes after PHAX and propofol, respectively. There was no increase in C3 and C4 complement fractions after either drug.

CONCLUSIONS:PHAX causes fast-onset, short-duration anesthesia with fast cognitive recovery similar to propofol, but with less cardiovascular depression, or airway obstruction and no pain on injection.

在 Listening to Mothers II 調查中婦女接受脊髓鎮痛的分娩體驗：一項開放性回答的內容分析

Women's Experiences with Neuraxial Labor Analgesia in the Listening to Mothers II Survey: A Content Analysis of Open-Ended Responses

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背景：大多數在美國醫院進行生產的婦女在分娩時接受脊髓鎮痛。在這項分析中，我們在一個全美母親的樣本中調查了脊髓鎮痛的體驗。

方法：我們的資料來自 Listening to Mothers II 調查，這個全國性的樣本包括了 2005 年在美國醫院中分娩了單胎的婦女（N=1573）。我們研究的物件是計畫剖腹產卻進行了自然

分娩並接受脊髓鎮痛的婦女（n=914）。我們採用定性內容分析的方法，分析了婦女在分娩過程中與脊髓鎮痛相關的最好和最糟糕方面的開放性的回答。

結果：30%的的婦女在他們的開放性回答中提到了脊髓鎮痛（n=300）。我們發現能夠有效地緩解疼痛是接受了脊髓鎮痛的婦女最常提到的積極方面。然而一些婦女提到了在脊髓鎮痛中與時效有關的問題，包括在等待進行脊髓鎮痛時的疼痛，在分娩過程中太晚進行脊髓鎮痛以及鎮痛效果消退得太快。另一些接受脊髓鎮痛的婦女提到的問題包括知情同意，副作用以及計畫和預期的問題。

結論：這項調查結果顯示婦女們對於脊髓鎮痛在生產過程中緩解疼痛的作用很滿意。儘管脊髓鎮痛有效地控制了疼痛，但在接受脊髓鎮痛的過程中還有另外的影響因素。麻醉師可以和產科醫生、護士、分娩指導員以及孕婦和正在分娩的婦女一起合作來減少在時機、交流、脊髓鎮痛的實施和效果預期方面的問題來改善婦女的生產體驗。

（施芸岑 譯 薛張綱 校）

BACKGROUND: Most women who give birth in United States hospitals receive neuraxial analgesia to manage pain during labor. In this analysis, we examined themes of the patient experience of neuraxial analgesia among a national sample of U.S. mothers.

METHODS: Data are from the Listening to Mothers II survey, conducted among a national sample of women who delivered a singleton baby in a U.S. hospital in 2005 (N = 1,573). Our study population consisted of women who experienced labor, did not deliver by planned cesarean, and who reported neuraxial analgesia use (n = 914). We analyzed open-ended responses about the best and worst parts of women's birth experiences for themes related to neuraxial analgesia using qualitative content analysis.

RESULTS: Thirty-three percent of women (n = 300) mentioned neuraxial analgesia in their open-ended responses. We found that effective pain relief was frequently spontaneously mentioned as a key positive theme in women's experiences with neuraxial analgesia. However, some women perceived timing-related challenges with neuraxial analgesia, including waiting in pain for neuraxial analgesia, receiving neuraxial analgesia too late in labor, or feeling that the pain relief from neuraxial analgesia wore off too soon, as negative aspects. Other themes in women's experiences with neuraxial analgesia were information and consent, adverse effects of neuraxial analgesia, and plans and expectations.

CONCLUSIONS: The findings from this analysis underscored the fact that women appreciate the effective pain relief that neuraxial analgesia provides during childbirth. Although pain control was 1 important facet of women's experiences with neuraxial analgesia, their experiences were also influenced by other factors. Anesthesiologists can work with obstetric clinicians, nurses, childbirth educators, and pregnant and laboring patients to help mitigate some of the challenges with timing, communication, neuraxial analgesia administration, or expectations that may have contributed to negative aspects of women's birth experiences.

脊柱側彎矯正手術史婦女在分娩鎮痛時椎管內置管時間和藥物劑量需求：一項病例對照研究

Labor Analgesia Consumption and Time to Neuraxial Catheter Placement in Women with a History of Surgical Correction for Scoliosis: A Case-Matched Study

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背景：椎管內鎮痛技術是分娩鎮痛的最有效的形式。10 到 20 年前的小樣本量的研究（9-21 人）指出，脊柱側凸矯正手術史的患者椎管內分娩鎮痛的成功率僅 50~66％。較新的矯

正手術方法使得硬膜外腔置管更容易，但術後的變化仍可能影響椎管內分娩鎮痛的效果。本前瞻性病例對照研究旨在比較矯正手術史產婦與無背部手術史產婦椎管內置管時間和每小時布比卡因需求劑量。

方法：期間研究納入了所有普倫蒂斯女子醫院內既往有脊柱內手術治療脊柱側彎矯形史並要求行椎管內分娩鎮痛的婦女。對照組選擇以麻醉師水準經驗作爲匹配內容。主要觀察指標是椎管內成功置管時間和每小時布比卡因需求劑量。次要觀察結果包括補充鎮痛要求和椎管內鎮痛失敗率和併發症。

結果：研究統計並分析了 41 位脊柱側凸矯正手術史女性和 41 位對照組女性的椎管內分娩鎮痛數據。兩組間產科及人口學特徵並無統計學差異。脊柱手術史組中位數每小時布比卡因消費量爲 15.2 毫克(12.5-18.7)，對照組爲 14.2 毫克（11.8-16.0），中位數的差異爲 1 毫克（95％置信區間：-1.3～3.0，P = 0.38）。兩組間總體布比卡因消耗量、病人自控鎮痛次數以及需要高濃度布比卡因的個體數量沒有差異。脊柱手術史組鎮痛失敗 5 例（12％），較對照組（0 例）發生率提高 12%（95％置信區間： 0.3％至 25％，P = 0.06）。脊柱手術史組完成置管所需的平均時間爲 41％（95％置信區間：7％-108％，P = 0.01）較對照組顯著延長。此外，脊柱手術史組還需要更多穿刺針重定向、間隙嘗試次數，或更換更有經驗的麻醉醫生。

結論：本研究的結果表明，既往脊柱側凸矯正手術不影響椎管內分娩鎮痛藥物需求量，但椎管內操作難度明顯提升。我們認爲既往有脊柱側凸矯正手術史的產婦可以接受椎管內分娩鎮痛，但知情同意書中應注明技術困難及鎮痛失敗的可能。

（俞穎 譯 薛張綱 校）

BACKGROUND: Neuraxial analgesic techniques are the most effective form of labor analgesia. Small studies (9-21 patients), conducted 10 to 20 years ago, demonstrated successful neuraxial labor analgesia in only 50% to 66% of patients with surgical correction for scoliosis. Newer surgical techniques for scoliosis correction make the epidural space more accessible, but postsurgical changes may still alter the efficacy of neuraxial labor analgesia. The purpose of this prospective case-matched study was to compare hourly bupivacaine consumption and time to placement of neuraxial technique in laboring women with spinal instrumentation compared with women without previous back surgery.

METHODS: All women with previous spinal instrumentation surgery for scoliosis correction who requested neuraxial labor analgesia at Prentice Women's Hospital during the study period were approached. Control subjects were matched for anesthesiologist level of experience. The primary outcomes were bupivacaine consumption per hour of labor analgesia and time to placement of the neuraxial technique. Secondary outcomes included supplemental analgesia requirements and neuraxial analgesia failures and complications.

RESULTS: Data from 41 women with surgical correction for scoliosis and 41 control subjects requesting neuraxial labor analgesia were analyzed. Obstetric and demographic characteristics of study participants were not different between groups. Median (interquartile range) hourly bupivacaine consumption was 15.2 mg/h (12.5-18.7) in the spinal instrumentation group and 14.2 mg/h (11.8-16.0) in the control group; the difference in medians was 1 mg/h (95% confidence interval [CI], -1.3 to 3.0; P = 0.38). The total bupivacaine consumption, number of manual reboluses, and number of subjects requiring greater bupivacaine concentrations did not differ between groups. Neuraxial analgesia failure occurred in 5 (12%) of women in the spinal instrumentation group but in none of the control patients (difference [95% CI], 12% [-0.3% to 25%]; P = 0.06). The mean time required to complete the neuraxial technique was 41% (95% CI, 7%-108%; P = 0.01) longer in the spinal instrumentation group than in the control group. The spinal instrumentation group also required a greater number of needle redirections, attempted interspaces, and need to switch to a more experienced provider than matched controls.

CONCLUSIONS: The findings of this investigation suggest that previous surgery for scoliosis repair does not affect neuraxial labor analgesia consumption, but performance of the neuraxial technique is more difficult. Our findings suggest that neuraxial labor analgesia should be offered

to parturients with previous surgery for scoliosis repair although informed consent should include a discussion of the possibility of technical difficulties and surgical anesthesia failure.

讓父母參與到自己孩子的麻醉誘導中:一組隨機對照試驗

Preparing Parents to Be Present for Their Child's Anesthesia Induction: A Randomized Controlled Trial

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讓父母參與到自己孩子的麻醉誘導中:一組隨機對照試驗支持父母的行爲以及雙親生產性能可以減少他們孩子的術前焦慮

背景：這項研究的目的是爲了將有父母陪伴的具有準備干預的麻醉誘導與標準麻醉誘導產生的效果做比較。

方法：在兒童醫院即將行擇期手術的年齡爲 2-10 歲之間的 93 個孩子與他們的父母一起參與了這項研究。父母在他們的孩子麻醉誘導前將會被隨機分配到麻醉誘導準備組或者標準麻醉誘導組。被分配到這兩組的父母的孩子將會在以下四方面做比較：術前焦慮程度，誘導中的配合度，有無譫妄，術後疼痛。父母將會被比較他們在手術室中的焦慮程度以及自我角色重要程度。

結果：在穩定階段，父母陪伴這個干預因素對於減少孩子術前焦慮的效果並不明顯。（P=0.15，Wilcoxon Mann Whitney 校驗，[WMWodds; 95%置信區間{CI}]= 1.41 [0.75–3.10]），家庭離開等候區的時間點(P = 0.39, WMWodds [95% CI] = 1.18 [0.60–2.45]), 他們進入手術室的時間點(P =0.28, WMWodds [95% CI] = 1.23 [0.65–2.67]), 或者孩子扣上加壓面罩的時間點(P = 1.3, WMWodds [95% CI] = 1.23 [0.64–2.63]). 然而，麻醉誘導準備組的父母相對于麻醉誘導標準組的父母，他們更趨向於認爲自己在手術室中的自我效能高(P = 0.03, WMWodds [95% CI] = 1.69 [1.07–2.87])。

結論：一項利用父母在孩子麻醉誘導時的陪伴來減少其術前焦慮的基於視頻的簡要干預研究並不成功。但是，在此研究中的父母是否按照干預中的指示去表現自己以減少孩子的焦慮這件事還有待商榷。將來的研究應監督父母的行爲以及雙親生產性能來減少他們孩子的術前焦慮。

（王潔 譯 薛張綱 校）

Preparing Parents to Be Present for Their Child's Anesthesia Induction: A Randomized Controlled Trial parent behavior and support parental performance to reduce their children's preoperative anxiety.。

BACKGROUND: The purpose of this study is to compare the effectiveness of a brief preparation intervention for parental presence during induction of anesthesia (PPIA preparation) with a PPIA with standard preparation (PPIA standard).

METHODS: Ninety-three children, aged 2 to 10 years, undergoing elective surgery at a children's hospital participated together with their parents. Parents were randomly assigned to receive either PPIA preparation or PPIA standard before their children's induction of anesthesia. Children of parents assigned to each group were compared on measures of preoperative anxiety, cooperation at induction, emergence delirium, and postoperative pain. Parents were compared on measures of state anxiety and self-efficacy about their role in the operating room (OR).

RESULTS: The effectiveness of parental presence in reducing children's preoperative anxiety was not improved by the intervention at the holding stage (P =0.15, Wilcoxon Mann-Whitney odds [WMWodds; 95% confidence interval {CI}] = 1.41 [0.75–3.10]), the point at which the

family left the holding area (P = 0.39, WMWodds [95% CI] = 1.18 [0.60–2.45]), the point that they entered the OR (P =0.28, WMWodds [95% CI] = 1.23 [0.65–2.67]), or the point at which the anesthesia mask was introduced (P = 1.3, WMWodds [95% CI] = 1.23 [0.64–2.63]). However, parents who received PPIA preparation trended toward greater self-efficacy about their role in the OR than those who received PPIA standard (P = 0.03, WMWodds [95% CI] = 1.69 [1.07–2.87]).

CONCLUSIONS: A brief, video-based intervention aimed at preparing parents to be present for their child's anesthesia induction was not successful in reducing the children's preoperative anxiety. However, it is unclear whether parents included in this study actually performed as instructed in the intervention to reduce their children's anxiety. Future research should monitor parent behavior and support parental performance to reduce their children's preoperative anxiety.

臨床研究方法 3：隨機對照試驗

Clinical Research Methodology 3: Randomized Controlled Trials

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隨機分配可以排除反向因果關係和選擇偏倚，並且研究足夠大時可以有效地防止混雜偏倚。實施盲法可以防止測量偏倚。包括以上保護措施的研究被稱爲隨機盲法臨床試驗。當有足夠數量的患者，該方法可以提供最有效的結果。雖然以上概念簡單明確，但在設計臨床試驗時需要在各個相互矛盾的方案中仔細權衡。所選擇的方案會影響招募患者的數量、招募時間、內部和外部有效性、評估治療之間的相互作用和成本。

（鄔其瑋 譯 薛張綱 校）

Randomized assignment of treatment excludes reverse causation and selection bias and, in sufficiently large studies, effectively prevents confounding. Well-implemented blinding prevents measurement bias. Studies that include these protections are called randomized, blinded clinical trials and, when conducted with sufficient numbers of patients, provide the most valid results. Although conceptually straightforward, design of clinical trials requires thoughtful trade-offs among competing approaches-all of which influence the number of patients required, enrollment time, internal and external validity, ability to evaluate interactions among treatments, and cost.

傳統標誌引導正中入路與術前超聲引導旁正中入路方式在蛛網膜下腔阻滯的比較

Conventional Landmark-Guided Midline Versus Preprocedure Ultrasound-Guided Paramedian Techniques in Spinal Anesthesia

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背景：多次脊髓重複穿刺麻醉會增加腰麻後頭痛、感覺異常、脊髓血腫的發生率。我們假設常規使用超聲引導蛛網膜下腔阻滯旁正中方法，相比傳統的標誌引導的正中入路，可以降低重複穿刺的次數。

方法：100 名簽署知情同意計畫進行全關節（髖關節或膝關節）置換的患者被隨機分成 C 組（傳統組）和 P 組（操作前超聲引導旁正中方法組），每組 50 人。患者不知道自己被分到哪個研究組。所有的蛛網膜下腔阻滯都是由高年資麻醉醫生實施。在 C 組，蛛網膜

下腔阻滯通過臨床可觸及標誌確定正中入路。在 P 組，操作前超聲引導用於標記旁正中入路位元點，蛛網膜下腔阻滯通過旁正中入路。

結果：平均穿刺次數（定義爲穿刺針進入椎間隙所用的次數，比如，不離開皮膚的退針和重新進針）在 P 組大約爲 C 組的 0.34 倍，具有統計學意義（P=0.01）。相似的，平均嘗試（定義爲穿刺針退出並重新插入的次數）在 P 組是 C 組的 0.25 倍（P=0.0021）。在 P 組，平均比 C 組尋找可觸及標誌所用時間長 81.5 秒（99%置性區間：68.4-97 秒）（P=0.0002）。所有其它參數，包括可觸及標誌分級，蛛網膜下腔阻滯注射用時，操作期間疼痛評分，操作期間患者不適感直觀類比標度評分，改全麻率，感覺異常率，進針時神經根痛的發生率，在兩組之間是相似的。

結論：對矯形外科接受關節置換手術的患者常規進行旁正中蛛網膜下腔阻滯，通過術前超聲檢查引導，可以顯著降低進針和穿刺針嘗試進入蛛網膜下隙的次數。

（袁偉 譯 薛張綱 校）

BACKGROUND: Multiple passes and attempts while administering spinal anesthesia are associated with a greater incidence of postdural puncture headache, paraesthesia, and spinal hematoma. We hypothesized that the routine use of a preprocedural ultrasound-guided paramedian technique for spinal anesthesia would reduce the number of passes required to achieve entry into the subarachnoid space when compared with the conventional landmark-guided midline approach.

METHODS: One hundred consenting patients scheduled for elective total joint replacements (hip and knee) were randomized into group C (conventional) and group P (preprocedural ultrasound-guided paramedian technique) with 50 in each group. The patients were blinded to the study group. All spinal anesthetics were administered by a consultant anesthesiologist. In group C, spinal anesthetic was done via the midline approach using clinically palpated landmarks. In group P, a preprocedural ultrasound scan was used to mark the paramedian insertion site, and spinal anesthetic was performed via the paramedian approach.

RESULTS: The average number of passes (defined as the number of forward advancements of the spinal needle in a given interspinous space, i.e., withdrawal and redirection of spinal needle without exiting the skin) in group P was approximately 0.34 times that in group C, a difference that was statistically significant (P = 0.01). Similarly, the average number of attempts (defined as the number of times the spinal needle was withdrawn from the skin and reinserted) in group P was approximately 0.25 times that of group C (P = 0.0021). In group P, on an average, it took 81.5 (99% confidence interval, 68.4–97 seconds) seconds longer to identify the landmarks than in group C (P = 0.0002). All other parameters, including grading of palpated landmarks, time taken for spinal anesthetic injection, periprocedural pain scores, periprocedural patient discomfort visual analog scale score, conversion to general anesthetic, paresthesia, and radicular pain during needle insertion, were similar between the 2 groups.

CONCLUSIONS: Routine use of paramedian spinal anesthesia in the orthopedic patient population undergoing joint replacement surgery, guided by preprocedure ultrasound examination, significantly decreases the number of passes and attempts needed to enter the subarachnoid space.