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在旋转式血栓弹力计与血栓弹力图中评估血小板对血凝块（血小板成分）强度影响的计算方法

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

研究血栓的粘弹性性质最常使用血栓弹力图（TEG®）和旋转式血栓弹力计（ROTEM®）。基于 ROTEM®的出血治疗算法推荐，一旦血栓的 ROTEM®纤维强度试验(FIBTEM) 得到修正，给予低运转血凝块强度的患者使用血小板（例如，凝块幅度在 10 分钟[A10] < 40 毫米）。基于 TEG®算法通常使用最大振幅的低值（例如，<50 毫米）作为给药的一个触发。然而，这个参数反映了各种血液成分的血凝块，包括血小板和纤维蛋白/纤维蛋白原的影响。相较全血血栓振幅 TEG®或 Rotem®法测定，血栓强度的血小板组分可对血小板缺乏提供更为敏感的指示。已形成血栓的血小板成分是来自 TEG®/ Rotem®试验和血小板有无抑制的结果。在本文中,我们审查了为什么这个计算应该基于血栓弹性（例如，TEG®的 E 参数和 ROTEM®的 CE 参数）相对于血栓振幅（例如，TEG®或 Rotem®的 A 参数）的依据。这是因为血栓的弹性，不同于血栓的振幅，反映了在设备内的血液凝块抵抗旋转的力量，且血栓振幅（变量 X）和血栓弹性（变量 Y）之间的关系是非线性的。根据不同的初始值，一个特定的增量 X（Δx）将与不同的 Y 增量（ΔY）相关。当正确时计算，使用血栓弹性数据，该血凝块的血小板成分可以对急性出血时的血小板缺乏给出有价值的提示。

（黄凫卿 译，李士通 审校）

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.

在健康志愿者中静脉输注镇静麻醉药物 azd3043 后一个对药代动力学和对脑电双频指数的影响的循环模型

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 是一种 γ-氨基丁酸 A 型受体阳性变构调节剂，具有镇静和麻醉作用。我们描述一个在健康志愿者中动静脉 azd3043 的浓度和药效学效应对脑电双频指数（BIS）的作用的群体药代动力学（PK）模型。

方法：在 2 个临床研究 125 名健康志愿者中测量动脉和静脉 AZD3043 血浆浓度

和 BIS 值，AZD3043 给予一个 1 分钟的单次剂量（1-6 毫克/公斤），一个 30 分钟的输注（1-81 毫克/公斤/小时），或 0.8 + 10，1 + 15，3 + 30，4 + 40（毫克/千克单次剂量+ 毫克/公斤/小时 30 分钟输注）。群体药代动力学 /药效学分析，使用 NONMEM。

结果：一个循环模型，包括一系列的 5 个室用于静脉和动脉血浆药物之间的运输，2 个周围分布室，和 1 个为从动脉到静脉血浆药物的非分配运输室，描述了 AZD3043 的药代动力学。全身清除率高（2.2 升/分钟；95%置信区间，2.12-2.25），表观分布容积低，导致一个短的消除半衰期。动脉和外周室分布的表观体积随剂量的增加而增加，总的表观体积为最低剂量后的 15 升和最大剂量后的 37 升。乙状结肠最大效应（Emax），15.6 克/毫升的 EC50 和 1.7 的 γ 描述了 AZD3043 效应部位浓度 EC50 和 BIS 之间的关系模型。个体间变异的 EC50 为 37%。效应室模型半衰期平衡速率常数 ke0 为 1.1 分钟，描述了有关的动脉血浆浓度效果的延迟。

结论：AZD3043 具有较高的清除和较低的分布容积，导致半衰期减短。而表观体积分布呈剂量依赖性（P<0.001），导致半衰期与剂量的增加。效应位置的分布快速且同步于短血浆半衰期导致的快速起效和失效作用。

（黄鸟卿 译，李士通 审校）

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.

对比术中胸骨上及食管多普勒，上腹部大手术改变心脏生物电抗输出读数，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：在麻醉过程中，建议使用微创连续心输出量测量来指导液体治疗，但这种测量必需可靠的趋势变化。NICOM（Cheetah 公司），一种生物电抗检测仪，正在被推荐用于术中使用。为了验证它的使用方法，多普勒，胸骨上 USCOM 及食管 CardiQ 串联使用，可提供可靠的估计心输出量的变化趋势。初步比较表明，上腹部手术引起的 NICOM 校准偏移。本研究的目的是确认和测量这些校准偏移。

方法：大手术的患者，年龄在 58 岁（32~78），12 个男性和 15 个女性，分为 4 组：（a 组）对照组下腹部或外周手术（9 例）；（b 组）气腹腹腔镜手术（6 例）；（C 组）放置大的多叶牵开器的开放上腹部手术（6 例）和（d 组）头颈机器人手术（6 例）。NICOM 和多普勒每 15 到 30 分钟同时读数。在个别时间绘制图表，对 NICOM-USCOM 和 CardioQ-USCOM 读数进行回归分析。同时进行 Bland-Altman 分析和趋势（一致性）分析。

结果：390 例 NICOM 对照被收集。手术时间为 4（1 至 11）小时，每例 7 至 22 组。平均（SD）USCOM 心脏指数为 3.5（1.0）L/min/m。个别时间图显示外科手术期间心脏指数在 NICOM 校准相对多普勒（USCOM）的变化为±0.9 (0.6-1.4) L/min/m 。18 例中 13 例（72%），变化呈下降趋势，但上升变化也有发现。在个体之间的相关性显示出良好的趋势 CardioQ-USCOM R = 0.87（范围，0.60-0.97）。在对照组中，NICOM-USCOM 也表现出良好的趋势 R = 0.89（0.69-0.97）。然而，趋势是在干预组不明显，R = 0.43（0.03-0.71；P＜0.0001）。Bland-Altman 分析的误差百分比在 NICOM-USCOM 之间（57 [54-60] %）大于 CardioQ-USCOM 之间（42 [40-44]%）（P＜0.0001）。一致率分别为 101 个数据对的 82（77-88）% 和 72 个数据对的 95 (90-99)% 。

结论：多普勒监测串联使用，提供了对心输出量的变化有效的趋势线与 NICOM 读数可以相比较。术中，可靠地跟踪的 NICOM 被证明在大多数情况下显示心输出量的变化。然而，上腹部外科手术引起的读数改变 >1 L/min/m，且方向的变化是不可预测的。每当术中应用 NICOM，麻醉医生需要知道这些校准变化并且预见其发生。

（黄凫卿 译，李士通 审校）

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.

一种改善麻醉后复苏室交接的多模式干预

A Multimodal Intervention Improves Postanesthesia Care Unit Handovers

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背景：沟通失败是围术期不良事件一个的主要因素。护理的转变可能特别容易。我们试图改善术后交接。

方法：我们介绍了一种成人及小儿麻醉后复苏室多模式干预以改善麻醉实施者（AP）与麻醉后复苏室注册护士(RN)间的术后交接。干预措施由一个标准化电子交接报表、教学性的网络研讨会、以集中提高跨专业交流的强制模拟训练及培训后绩效反馈组成。利用盲法，培训后的护士采用由 8 个分量表和一个整体的评分（1-5 级）组成的结构式工具对麻醉后复苏室交接进行评分。多因素 logistic 回归分析对交接时整体评分等级≥3 所占的比例来评价干预效果。

结果：观察和评估了受过模拟培训的 452 名临床医生及 981 次交接。在成人 PACU,估算 AP 与 RN 之间可接受的交接（整体评分≥3）的比例。AP-RN 均未接受模拟训练，该比例在 0 天为 3%（95%的可信区间 1%-11%），训练开始后 40 天为 10%（5%-19%），训练一年后（405 天）为 57%（33%-78%）；而在 AP-PN 其中至少有一个接受模拟训练者，该比例在 40 天及 405 天分别为 18%（11%-28%）及 68%（57%-76%）。在未经训练的 AP-PN 组与训练有素的 AP-PN 组，可接受的交接百分比在 405 天时均显著高于 40 天（P<0.001）。在儿童 PACU 观察到类似的情况。培训三年后，据不精确估计可接受的交接比例在成人 PACU 及儿童 PACU 分别约为 87%（72%-95%）及 56%（40%-72%）。

结论：这一多模式干预显著改善了包括未接受正规模拟训练的临床医生 PACU 的跨专业交接，3 年后显效。

（徐卉红 译，李士通 审校）

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.

兰尼定受体 1 型 p.Arg2508 位几个基因的突变是导致恶性高热的潜在来源

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

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背景：恶性高热（MH）是一种药物遗传性疾病，易感个体在使用吸入麻醉药和去极化肌松药后出现。兰尼定受体 1 型（RYR1）基因突变被认为是导致 MH 发生的原因，它们主要分布在 3 个被称为“热点”的区域。在 RYR1 同一位点时常可有多个突变。尽管 RYR1 的 p.Arg2508 位于“热点”外，但是一些突变或变体（包括已知的导致 MH 的 p.Arg2508Cys 突变）被确认存在于这一区域。我们假定在 RYR 1 的 p.Arg2508 任何突变或变体均能导致与 MH 相关的重要的病理性变化。在该项研究中，我们分析了 4 个包含 p.Arg2508RYR1 不同突变体的功能。

方法：我们制备和分析了 4 个 RYR1 突变基因的功能：p.Arg2508His 和 p.Arg2508Gly 是与 MH 相关的突变体，然而 p.Arg2508Ser 和 p.Arg2508Lys 尚未报道。由于赖氨酸的生化特性类似于精氨酸，因此我们认为 p.Arg2508Lys 可能具备极其类似野生型 RYR1 的特性。我们将 p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser, 和 p.Arg2508Lys 这 4 个 RYR1 基因的突变体引入兔 cDNA，将所得到的克隆体转染到人胚肾 293(HEK293)细胞。利用比例测量染料 Fura-2 AM,采用 340/380nm 两个荧光比值来分析细胞在给予咖啡因和 4-氯间甲酚（4CmC）后钙稳态的变化。我们计算了转染每种 RYR1 突变体细胞的半数最大激活浓度（EC50），同时与表达野生型 RYR1 细胞的 EC50 比较。利用未配对双尾 t 检验计算 EC50 值之间的统计学意义。我们使用了 300 个不同的细胞，野生型和每种突变型各 30 个。

结果：分别转染突变体 p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser 或 p.Arg2508Lys 的细胞较转染野生型细胞对咖啡因和 4CmC 更敏感（所有 4 组 P≤0.0004）。咖啡因 EC50 的均值±标准差在野生型、p.Arg2508His, p.Arg2508Gly, p.Arg2508Ser 及 p.Arg2508Lys 分别为 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 值分别为 125.92± 38.11, 70.42 ± 27.09, 79.30 ± 39.04, 73.03 ± 19.20 和 72.81 ± 28.44 mM。

结论：这 4 个 RYR1 的任何一个突变都可能导致与 MH 相关的重要改变。研究 RYR1 上 2508 位氨基酸的变化对 RYR1 这个大蛋白分子的影响可能会让我们更好地理解 MH 病理过程。

（徐卉红 译，李士通 审校）

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.

应激增加慢性疼痛对海马神经元发生的不利影响

Stress Increases the Negative Effects of Chronic Pain on Hippocampal Neurogenesis

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背景：慢性疼痛患者常常经受情感性精神障碍和认知功能减退，明显降低患者生活质量。此外，大多数这类患者存在与病情无关的应激进而加重他们的症状。海马接受伤害感受的传入，慢性疼痛时海马神经元可能发生适应不良性的可塑性改变。海马是参与情感、学习和记忆的大脑结构。慢性疼痛时，海马齿状回颗粒细胞层中的增殖细胞减慢其周转。但是，海马处新生神经元的成熟、存活及整合是否受慢性疼痛的影响还不清楚。此外，应激是否加重这一影响还不清楚。

方法：我们分别通过慢性压迫性神经损伤（CCI）和限制大鼠活动法建立大鼠神经病理性疼痛模型和应激模型，通过评估溴脱氧鸟苷掺入增殖细胞和免疫染色法来评估无应激或伴应激 CCI 模型大鼠新生海马神经的增殖、分化及存活。

结果：所得的数据表明：神经损伤后 8 天神经病理性疼痛的大鼠增殖细胞的数量减少且应激加重了这一效应。此外，神经损伤后 4 周，神经病理性疼痛与海马颗粒层中神经母细胞及存活的新生成熟神经元均减少相关，应激同样加重了这一现象。但是在此模型中海马神经元的分化率没有受到影响。

结论：神经病理性疼痛对海马神经元发生（增殖和存活）产生不利影响，应激加重这一效应。神经元这些类型的可塑性的变化可能解释慢性疼痛患者的情感和认知功能障碍。

（徐卉红 译，李士通 审校）

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.

术中注射镁剂不能减少心脏手术术后房颤的发生率

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

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背景：低镁血症与术后房颤（POAF）发生率增加相关。尽管已有研究提示镁剂治疗的有益效果，但是这些研究均受限于过小的样本量和过低的镁剂剂量。本研究假设大剂量镁剂能减少新发 POAF 的发生率，选取了一项评估镁剂对心脏手术患者的认知转归影响的前瞻性实验的数据来验证此假设。

方法：总数 389 名接受心脏手术的患者被纳入了这项双盲、安慰剂对照的实验。研究对象随机接受了 50mg/kg 镁剂作为负荷剂量，麻醉诱导后即刻给予总量为 50mg/kg，持续输注 3 小时的镁剂（总量 100mg/kg），而对照组则给予生理盐水。采用 logistic 回归法评估镁剂对 POAF 的治疗效果，并用多中心研究的心脏手术术后房颤的围术期缺血风险指数来校正房颤(AF)风险。

结果：排除术前发生急慢性房颤的病人后， 共 363 名对象纳入分析（安慰剂组 n=177，镁剂治疗组 n=186）。镁剂治疗组的 POAF 新发率为 42.5（95%可信区间[CI], 35%–50%），安慰剂组则为 37.9%(95% CI, 31%–45%)，两组无统计学差异（P=0.40）。4.6%的绝对风险差异的 95%CI 为 5.5%到 14.7%。两组 POAF 起始时间也是相同的，在校正 AF 风险后，用 logistic 回归法分析镁剂治疗未见显著效果。

结论：术中大剂量镁剂疗法未能降低心脏手术术后新发 POAF 的概率。

（宣伟　译　陈杰　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.

对健康志愿者单次静脉注射及静注后持续泵注一种研发中的静脉镇静/麻醉药 AZD3043 的安全性及药效学研究

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)是一个研发中的，可被血液和肝脏中的酯酶快速代谢的苯丙烷类镇静/麻醉药。在其首次人体研究中,使用 AZD3043 持续静脉输注 30min 行麻醉诱导并无重大安全性或耐受性问题，且具有快速复苏的特点。

方法: 这个临床 1 期、单中心、开放性研究（临床试验，编号 NCT00984880）的主要目标是评估单次静脉推注及单次静注后持续泵注 AZD3043 的安全性和耐受性。次要目标包括评估 AZD3043 的药效学特征和疗效。递增剂量队列研究中 8 名 18 岁到 65 岁的健康志愿者分别接受单次 1min 静脉推注 (A 队)或 1min 静注后持续泵注 30min(B 队)该药。评估项目包括不良反应、生命体征、血气、实验室检查、镇静/麻醉的临床体征和脑电双频指数。

结果: 72 名志愿者(8 名女性,64 名男性)接受 1min 静注 1、1.5、2、4、6 mg/kg（A 队）或 0.8、1、3、4 mg/kg 静注后分别泵注 10、15、30、40 mg/kg/h 的 AZD3043 持续 30min(B 队)。本研究中没有患者脱落。发生超过 1 例的不良反应包括头痛(n = 15；21%)、恶心(n = 7；10%)、呕吐(n = 3；4%)和倦怠(n = 2；3%)。21 名受试者出现至少 1 种不良反应。暂无证据表明药物与不良反应间存在量效关系。呼吸不受影响，但心率增快存在剂量相关性。没有注射痛报告。麻醉对象为 32 名受试者，包括 A 队中的最高剂量组和 B 队中 2 个高剂量组的所有对象。麻醉复苏较快,定位和本体感受迅速恢复。除 A 队的 2 mg/kg 组和 B 队的 4 mg/kg 静注+ 40 mg/kg/h 泵注 30min 组各 1 名受试者外，其他受试者在用药结束 30min 后的首次评估中均能在没有任何支撑下行走 10 米，另 2 名受试者停药 45min 后的再次评估中通过行走测试。在高剂量组中可观察到无意识体动伴随肌肉张力增加。

结论: 需要进一步的临床研究来证实 AZD3043 提供快速麻醉复苏并维持正常通气的能力。

（程鑫宇　译　陈杰　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.

快速代谢和超短效氯胺酮类似物的发展

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

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背景：氯胺酮是一种经典的，起效迅速的分离性麻醉药。由于可能出现精神病样症状，临床应用受限，且此药往往需与催眠药物合用。本研究假设，具有超短效消除时间的氯胺酮酯类似物可能显着地降低突发的烦躁现象，即增加一个氯胺酮样的催眠和镇痛效用。本研究寻求对 5 酯（（1-（2-氯苯基）-2-氧代环己基）氨基）戊酸甲酯盐酸盐，即第一个设计目的为超快代谢的氯胺酮类似物，进行药理学研究。

方法：比较 5 种去甲氯胺酮酯类似物（R1-R5）削弱大鼠翻正反射和产生痛觉钝化的能力。在大鼠中对 2 种类似物(R1,R5)进行毒性测试并评估 50%致命剂量(LD50)。通过高效液相色谱法对兔血浆和全血进行体外代谢稳定性测试。观察兔子的行为和血流动力学影响。最后估计这些类似物在兔子中的药代动力学特征。

结果：在研究的模型中，所有的 5 种去甲氯胺酮酯都能迅速地使翻正反射消失和踏板撤出减弱，且药物效应能超快速地消除（R1 与氯胺酮在大鼠翻正反射恢复时间方面的比较：87 秒[四分位距（IQR）78-131] vs 996 秒[IQR 840-1304]; P <0.01）。它们与氯胺酮在 LD50 方面具有可比性（R1 LD50: 50.2mg/kg [95％置信区间，30-63]）。所有的类似物在水解唯一羧酸衍生物方面从快至慢，依次为体内（R1 清除率：L/kg/min [IQR 0.40-2.42]）、全血和血浆。相对于其镇静作用，类似物 R5 表现出更强大的痛觉钝化效应（踏板撤回评分，与 R1 相比，P <0.001）。

结论：5 种去甲氯胺酮酯类似物保留母体药物的催眠特性，并由于超速代谢而消除更快。

（冯迪　译　陈杰　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.

在麻醉团队中运用麻醉诱导前清单来改进信息交流、关键信息获取、安全观念以及可能的团队协作观念

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：通过 5 项团队层面预后来介绍和评估麻醉诱导前清单(APIC)的实施，每项预后指标都是患者安全性的一项替代终点：信息交流 (总共十二个项目组成的清单：团队交流的完成百分比情况); 关键信息获取(总共五项例如过敏事件组成的关键信息：每个团队成员报告的百分比)； 安全观念 (团队成员用连续评定量表给出的中位数得分)；团队协作观念(团队成员用连续评定量表给出的中位数得分)；临床表现(14 项任务，例如呼吸机检查的完成百分比).

方法： 采用多方法设计进行此项前瞻性干预研究，比较使用 APIC 的实验组和不使用 APIC 的对照组之间的差异。训练有素的观察员评价信息交流和在麻醉诱导现场观察临床表现。观察后，每个团队成员阐述他们所知道的关键信息及对安全和团队协作的看法。

结果: 将 105 个使用 APIC 的团队使与 100 个不使用的团队相比较。实验组与对照组的团队层面预后评分中位数分别为：信息交流：100% vs 33% ($P < 0.001$), 关键信息获取：100% vs 90% ($P < 0.001$)， 安全观念: 91% vs 84% ($P < 0.001$), 团队协作观念: 90% vs 86% ($P = 0.028$), 和临床表现: 93% vs 93% ($P = 0.60$).

结论：本研究结果表明，麻醉诱导前清单的应用大大地提高了麻醉团队内信息交换, 关键信息获取和安全观念，所有参数都与患者安全相关。趋势表明团队协作观念改善。

（刘洋　译　陈杰　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.

血小板减少症产妇的椎管内麻醉：一项多位点回顾性队列研究

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评估对血小板减小症产妇进行椎管内麻醉操作，其相关的椎管内血肿的风险。

方法：设计此项多中心回顾性队列研究，用于评估血小板计数<100,000 /mm3 的产妇接受椎管内麻醉时发生脊髓硬膜外血肿的风险；并评估血小板减少症产妇接受全身麻醉时并发症风险。

结果：对 102 例接受硬膜外麻醉和 71 例接受脊麻的血小板减少症产妇进行观察，没有发现任何椎管内血肿。数据包括之前已发表的系列报道（共 n=499），脊髓-硬膜外血肿风险的二项置信区间为 0%至 0.6%。鉴于在每个特定的血小板计数上都存在一些患者人群，故研究也呈现了个体化的血小板计数分层所对应的理论风险。 全麻女性继发于血小板减少症的严重并发症发生率为 6.5%（95%可信区间为 2.1%-14.5%）。

结论：本研究的结论支持椎管内麻醉对有轻度血小板减少症产妇相对安全，且评估了未作椎管内麻醉的产妇相关母体并发症的发生率。而在很低的血小板计数时风险存在不确定性，故建立一项国家性“低血小板”症注册表对于更精确的评估患者发生硬膜外血肿的风险至关重要，并将有助于麻醉实践的标准化。

（袁亚伟　译　陈杰　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.

临床研究方法论 1：源于实验设计和方法学的错误

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

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临床研究可以通过数据收集的时间分为回顾性和前瞻性两种。临床研究同样可以按实验设计分类。在病例对照研究中，研究者在疾病后期状态不同（广义包括病情发展和对治疗的反应）的组别中比较早期暴露因素（包括遗传和其他个人因素、环境影响和药物治疗）。在队列研究中，实验者则对比一个或多个暴露因素不同的组别间的疾病发病率。比较性临床试验是一种前瞻性队列研究，研究者比较分配给病人的不同治疗方案。大部分临床研究结果的错误可以由约 5 类可分辨的方法学问题引起：选择性偏移、混杂、计量偏差、因果颠倒和过分的机会变差。

（孙佳昕　译　陈杰　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.

对侧爪的传出神经传导参与了单侧爪内注射内皮素-1 后引起对侧爪的痛觉过敏现象

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

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背景：单侧损伤后出现对侧痛觉过敏，常常被解释为脊髓和大脑的中枢敏化。先前研究报道了在大鼠后爪注射内皮素-I(ET-1)可延长对侧后爪机械和化学性的致敏作用。本文研究在这一过程中对侧传出神经活动所起的作用。

方法：将(2 nmol, 10 μL)ET-1 皮下注射入右后爪（同侧）的趾部皮肤，分别通过对同侧及对侧进行足底辐射加热和 von Frey 纤维丝测痛测定热反应潜伏期和疼痛反应缩足的机械阈。一部分大鼠在注射 ET-1 前 30min，后爪注射（0.25%, 40 μL）布比卡因麻醉 60min。

另一部分在注射 ET-1 前 30min，皮下注射比卡因释放微粒阻滞对侧坐骨神经 6 至 12h。通过在颈部正中线的皮下注射来模拟这些布比卡因制剂的全身作用。

结果:注射 ET-1 后，同侧和对侧后爪的机械阈第 2 h 开始下降，24 h 降到最低，第 48h 开始恢复直至第 72h 到达注射前的水平。注射 ET-1 前，同侧后爪注射布比卡因可以抑制此超敏反应。对侧后爪注射布比卡因在每个测试时段也都能抑制超敏反应；除了在超敏反应期间第 2h，同侧后爪注射布比卡因组敏感度增加，其余情况类似。当布比卡因释放微粒阻滞对侧坐骨神经时，这种类似变化的模式也会出现。布比卡因制剂的全身作用要相对微弱得多且只有在 ET-1 注射后第 24 小时才有显著性差异。同侧和对侧后爪在注射 ET-1 后都出现了热超敏，表明对两种对侧麻醉操作的反应模式是相同的。

结论:这些结果表明通过后爪对侧神经支配的传出神经传导对于对侧 ET-1 的敏感性是必要的，提出远端神经末梢释放的物质也涉及其中。释放到外周的物质对于对侧 ET-1 的敏感性非常重要，这可能也与手术或神经损伤后，出现在离原发损伤较远位点的继发性痛觉过敏有关。

（李悦　译　陈杰　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.

首例研究镇静麻醉药物 AZD3043 的人类临床试验：一项给健康男性志愿者输注 30 分钟 AZD3043 后评价药物安全性、药代动力学及药效学的临床剂量递增试验

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 是一种 γ-氨基丁酸 A 型受体的正向别构调节剂，可被血液和肝脏中的酯酶快速代谢为一种无活性产物。临床前期研究提示 AZD3043 作为超短效静脉用镇静/麻醉药物，具有快速可预知的复苏特性、优越的使用安全性及耐受性。

方法：我们第一阶段、单中心、开放性研究的主要目标是评估静脉输注 AZD3043 的安全性及耐受性，并预测其最大可耐受剂量。次要目标包括评估 AZD3043 的药代动力学、药效学及疗效。将一群年龄 18-45 岁的健康男性志愿者分为 5-6 人一组，按组别依次给予剂量递增的 AZD3043，给药方式为 30 分钟单次输注。评价指标包括药物不良反应，受试者的生命体征，实验室检查，临床表现和双频谱指数（BIS）。

结果：53 例受试者按组别接受 AZD3043 的输注速率分别为 1, 3, 6, 12, 18, 27, 36, 54 和 81 mg/kg/h。试验中无中途停药，但在达到预定义的暴露极限时终止增加剂量。药物不良反应发生大于 1 例的有头痛（n=4），红斑（n=3），胸部不适（n=2），恶心（n=2）及呼吸困难（n=2）。不良反应发生的频率及种类与药物剂量无关。受试者并无注射痛的主诉，且无临床相关的改变表现在呼吸频率及动脉血压上。然而，心率在输注速率＞18mg/kg/h 时有剂量依赖性增高。镇静/麻醉的情况与药物剂量相一致；在预定义的时间点产生镇静/麻醉临床表现的药物最低输注速率是 12 mg/kg/h（6 例受试者中有 1 例达到标准），3 组最高速率组的所有受试者都达到麻醉标准。最高输注速率组的麻醉平均起效时间为 4 分钟而 12 mg/kg/h 组为 29 分钟。12 mg/kg/h 组在停止药物输注后 3 分钟恢复对口头指令的反应，而 81 mg/kg/h 组平均耗时 25 分钟。随着肌张力的恢复，小到抽搐大到伸展运动等不自主活动也相继恢复。

结论：在首次人类临床试验中 AZD3043 证实可被较好耐受，加上其短暂的起效及恢复时间，预示 AZD3043 将会是一种应用良好的短效镇静和麻醉药物。

（殷悦 译 薛张纲 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.

一种新型羟-5α-孕烷二酮的水剂与丙泊酚在效能和安全性上的比较的临床 1c 期药物试验

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，密西根坎墩化学实验室）是一种 10 毫克/毫升的羟-5α-孕烷二酮和 13% 7-磺丁基醚 β-环糊精（β-环糊精复合物）的水溶液。在临床前期研究中，PHAX 是一种和异丙酚一样起效快-失效快的静脉麻醉药，但对心血管的抑制更少。本项是其第一次用于人体的药物试验，旨在找到 PHAX 的麻醉剂量以及与等效剂量的丙泊酚比较安全性、效能、麻醉恢复及苏醒质量。

方法：本研究坚持贯彻 GCP 的规定（临床试验注册号，actrn12611000343909）。本项研究随机、双盲，研究使用贝叶斯算法来确定 PHAX 和丙泊酚对脑电双频指数（BIS）的效应的等效剂量。受试者为男性志愿者，ASA 分级 I 级，知情同意（分为丙泊酚和 PHAX 两组，每组 12 人）。评价参量为药物注射（单次剂量）80 分钟后的注射痛、不自主运动、脑电双频指数、血压、是否需要气道支持以及作为苏醒恢复质量的评价指标的 Richmond 躁动镇静量表和数字符号替换测试。动脉血液的抽取用于生化，血液学和补体水平的测定。

结果：PHAX 组的受试者没有一例报告注射痛，而 12 例丙泊酚组的受试者中有 8 例报告了注射痛。达到等效的 BIS 值≤50 的受试者，PHAX 组有 9 例，丙泊酚组有 8 例，分别所需要的中位数剂量为 PHAX 组：0.5 (0.5-0.6)mg/kg；丙泊酚组：2.9 (2.4-3.0) mg/kg。两组中能达到的最低 BIS 中位数值都是 27-28，两组起效的时间和 BIS 值的恢复时间都没有显著的差异。伴随的收缩压和舒张压的中位数值变化，PHAX 组与丙泊酚组相比分别是收缩压-11% vs -19%，舒张压-25% vs -37%。丙泊酚组 12 例受试者中 9 例需要气道支持，PHAX 组受试者均无需要。达到等效的 BIS 值≤50 的受试者中：Richmond 躁动镇静量表和数字符号替换测试达到 0 时，丙泊酚受试者和 PHAX 的中位数起效时间分别为为 5（IQR，5-10）分钟和 15（IQR，10-20）分钟。丙泊酚组和 PHAX 组受试者的 BIS 值恢复到 90 所需要的时间分别是 21 分钟（SD，10.1）和 21 分钟（SD 9.2）丙泊酚组和 PHAX 组受试者的数字符号替换测试分数恢复到静脉用药前水平需要的时间的中位数分别为为 50（IQR，35-72.5）分钟和 42.5（IQR，35-76.3）分钟。两种药物在注射后 C3 和 C4 补体水平均没有增加。

结论：PHAX 能与丙泊酚提供类似的起效快-失效快和短时间麻醉的快速认知恢复，但心血管抑制更少，气道阻塞更少，且无注射痛。

（俞启蒙 译 薛张纲 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 调查中妇女接受脊髓镇痛的分娩体验：一项开放性回答的内容分析

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：大多数在美国医院进行生产的妇女在分娩时接受脊髓镇痛。在这项分析中，我们在一个全美母亲的样本中调查了脊髓镇痛的体验。

方法：我们的数据来自 Listening to Mothers II 调查，这个全国性的样本包括了 2005 年在美国医院中分娩了单胎的妇女（N=1573）。我们研究的对象是计划剖腹产却进行了自然

分娩并接受脊髓镇痛的妇女（n=914）。我们采用定性内容分析的方法，分析了妇女在分娩过程中与脊髓镇痛相关的最好和最糟糕方面的开放性的回答。

结果：30%的的妇女在他们的开放性回答中提到了脊髓镇痛（n=300）。我们发现能够有效地缓解疼痛是接受了脊髓镇痛的妇女最常提到的积极方面。然而一些妇女提到了在脊髓镇痛中与时效有关的问题，包括在等待进行脊髓镇痛时的疼痛，在分娩过程中太晚进行脊髓镇痛以及镇痛效果消退得太快。另一些接受脊髓镇痛的妇女提到的问题包括知情同意，副作用以及计划和预期的问题。

结论：这项调查结果显示妇女们对于脊髓镇痛在生产过程中缓解疼痛的作用很满意。尽管脊髓镇痛有效地控制了疼痛，但在接受脊髓镇痛的过程中还有另外的影响因素。麻醉师可以和产科医生、护士、分娩指导员以及孕妇和正在分娩的妇女一起合作来减少在时机、交流、脊髓镇痛的实施和效果预期方面的问题来改善妇女的生产体验。

（施芸岑 译 薛张纲 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.

脊柱侧弯矫正手术史妇女在分娩镇痛时椎管内置管时间和药物剂量需求：一项病例对照研究

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：椎管内镇痛技术是分娩镇痛的最有效的形式。10 到 20 年前的小样本量的研究（9-21 人）指出，脊柱侧凸矫正手术史的患者椎管内分娩镇痛的成功率仅 50~66%。较新的矫

正手术方法使得硬膜外腔置管更容易，但术后的变化仍可能影响椎管内分娩镇痛的效果。本前瞻性病例对照研究旨在比较矫正手术史产妇与无背部手术史产妇椎管内置管时间和每小时布比卡因需求剂量。

方法：期间研究纳入了所有普伦蒂斯女子医院内既往有脊柱内手术治疗脊柱侧弯矫形史并要求行椎管内分娩镇痛的妇女。对照组选择以麻醉师水平经验作为匹配内容。主要观察指标是椎管内成功置管时间和每小时布比卡因需求剂量。次要观察结果包括补充镇痛要求和椎管内镇痛失败率和并发症。

结果：研究统计并分析了 41 位脊柱侧凸矫正手术史女性和 41 位对照组女性的椎管内分娩镇痛数据。两组间产科及人口学特征并无统计学差异。脊柱手术史组中位数每小时布比卡因消费量为 15.2 毫克(12.5-18.7)，对照组为 14.2 毫克（11.8-16.0），中位数的差异为 1 毫克（95％置信区间：-1.3～3.0，P = 0.38）。两组间总体布比卡因消耗量、病人自控镇痛次数以及需要高浓度布比卡因的个体数量没有差异。脊柱手术史组镇痛失败 5 例（12％），较对照组（0 例）发生率提高 12%（95％置信区间： 0.3％至 25％，P = 0.06）。脊柱手术史组完成置管所需的平均时间为 41％（95％置信区间：7％-108％，P = 0.01）较对照组显著延长。此外，脊柱手术史组还需要更多穿刺针重定向、间隙尝试次数，或更换更有经验的麻醉医生。

结论：本研究的结果表明，既往脊柱侧凸矫正手术不影响椎管内分娩镇痛药物需求量，但椎管内操作难度明显提升。我们认为既往有脊柱侧凸矫正手术史的产妇可以接受椎管内分娩镇痛，但知情同意书中应注明技术困难及镇痛失败的可能。

（俞颖 译 薛张纲 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.

让父母参与到自己孩子的麻醉诱导中:一组随机对照试验

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

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让父母参与到自己孩子的麻醉诱导中:一组随机对照试验支持父母的行为以及双亲生产性能可以减少他们孩子的术前焦虑

背景：这项研究的目的是为了将有父母陪伴的具有准备干预的麻醉诱导与标准麻醉诱导产生的效果做比较。

方法：在儿童医院即将行择期手术的年龄为 2-10 岁之间的 93 个孩子与他们的父母一起参与了这项研究。父母在他们的孩子麻醉诱导前将会被随机分配到麻醉诱导准备组或者标准麻醉诱导组。被分配到这两组的父母的孩子将会在以下四方面做比较：术前焦虑程度，诱导中的配合度，有无谵妄，术后疼痛。父母将会被比较他们在手术室中的焦虑程度以及自我角色重要程度。

结果：在稳定阶段，父母陪伴这个干预因素对于减少孩子术前焦虑的效果并不明显。（P=0.15，Wilcoxon Mann Whitney 校验，[WMWodds; 95%置信区间{CI}]= 1.41 [0.75–3.10]），家庭离开等候区的时间点(P = 0.39, WMWodds [95% CI] = 1.18 [0.60–2.45]), 他们进入手术室的时间点(P =0.28, WMWodds [95% CI] = 1.23 [0.65–2.67]), 或者孩子扣上加压面罩的时间点(P = 1.3, WMWodds [95% CI] = 1.23 [0.64–2.63]). 然而，麻醉诱导准备组的父母相对于麻醉诱导标准组的父母，他们更趋向于认为自己在手术室中的自我效能高(P = 0.03, WMWodds [95% CI] = 1.69 [1.07–2.87])。

结论：一项利用父母在孩子麻醉诱导时的陪伴来减少其术前焦虑的基于视频的简要干预研究并不成功。但是，在此研究中的父母是否按照干预中的指示去表现自己以减少孩子的焦虑这件事还有待商榷。将来的研究应监督父母的行为以及双亲生产性能来减少他们孩子的术前焦虑。

（王洁 译 薛张纲 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.

临床研究方法 3：随机对照试验

Clinical Research Methodology 3: Randomized Controlled Trials

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随机分配可以排除反向因果关系和选择偏倚，并且研究足够大时可以有效地防止混杂偏倚。实施盲法可以防止测量偏倚。包括以上保护措施的研究被称为随机盲法临床试验。当有足够数量的患者，该方法可以提供最有效的结果。虽然以上概念简单明确，但在设计临床试验时需要在各个相互矛盾的方案中仔细权衡。所选择的方案会影响招募患者的数量、招募时间、内部和外部有效性、评估治疗之间的相互作用和成本。

（邬其玮 译 薛张纲 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.

传统标志引导正中入路与术前超声引导旁正中入路方式在蛛网膜下腔阻滞的比较

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

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背景：多次脊髓重复穿刺麻醉会增加腰麻后头痛、感觉异常、脊髓血肿的发生率。我们假设常规使用超声引导蛛网膜下腔阻滞旁正中方法，相比传统的标志引导的正中入路，可以降低重复穿刺的次数。

方法：100 名签署知情同意计划进行全关节（髋关节或膝关节）置换的患者被随机分成 C 组（传统组）和 P 组（操作前超声引导旁正中方法组），每组 50 人。患者不知道自己被分到哪个研究组。所有的蛛网膜下腔阻滞都是由高年资麻醉医生实施。在 C 组，蛛网膜

下腔阻滞通过临床可触及标志确定正中入路。在 P 组，操作前超声引导用于标记旁正中入路位点，蛛网膜下腔阻滞通过旁正中入路。

结果：平均穿刺次数（定义为穿刺针进入椎间隙所用的次数，比如，不离开皮肤的退针和重新进针）在 P 组大约为 C 组的 0.34 倍，具有统计学意义（P=0.01）。相似的，平均尝试（定义为穿刺针退出并重新插入的次数）在 P 组是 C 组的 0.25 倍（P=0.0021）。在 P 组，平均比 C 组寻找可触及标志所用时间长 81.5 秒（99%置性区间：68.4-97 秒）（P=0.0002）。所有其它参数，包括可触及标志分级，蛛网膜下腔阻滞注射用时，操作期间疼痛评分，操作期间患者不适感直观类比标度评分，改全麻率，感觉异常率，进针时神经根痛的发生率，在两组之间是相似的。

结论：对矫形外科接受关节置换手术的患者常规进行旁正中蛛网膜下腔阻滞，通过术前超声检查引导，可以显著降低进针和穿刺针尝试进入蛛网膜下隙的次数。

（袁伟 译 薛张纲 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.