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DELIRIUM Y DISFUNCIÓN COGNITIVA POSTOPERATORIA

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Hospital Clínico Universitario

Valencia

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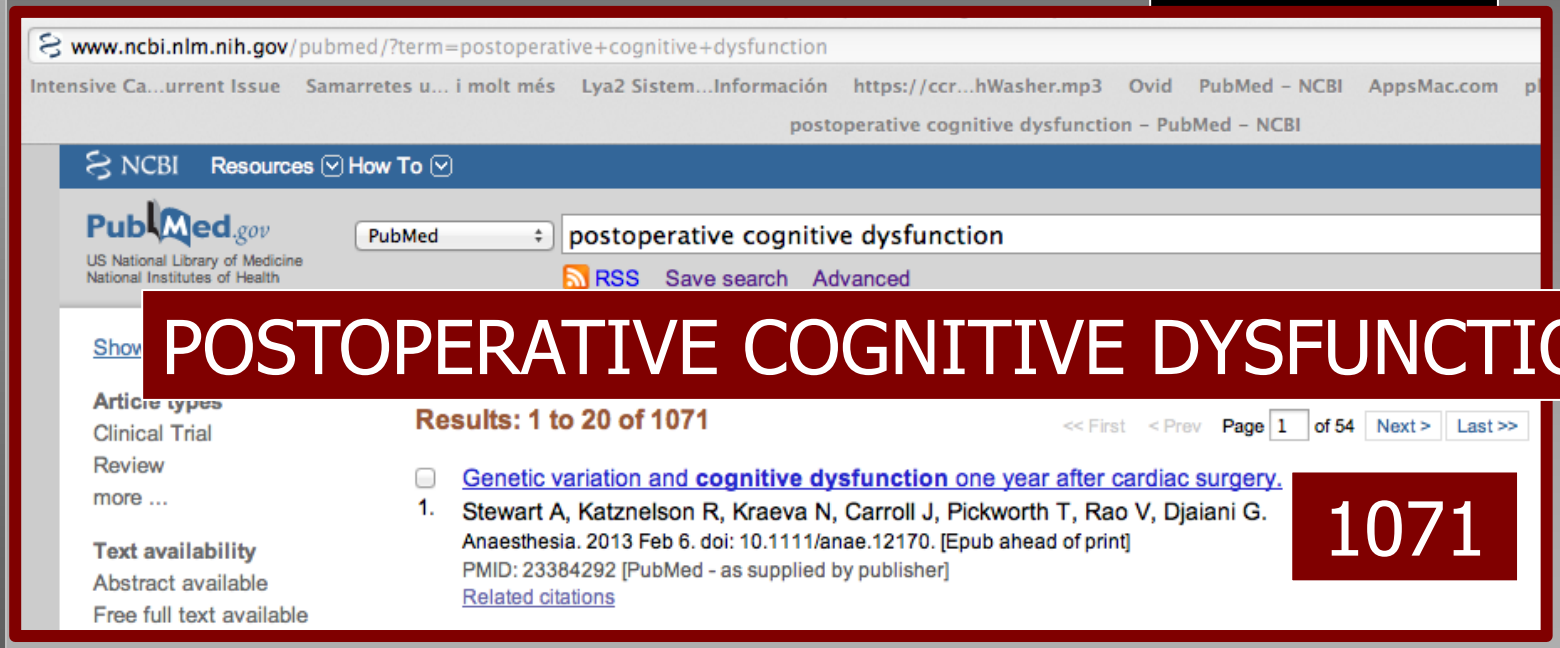
POSTOPERATIVE DELIRIUM

1395



POSTOPERATIVE COGNITIVE DYSFUNCTION

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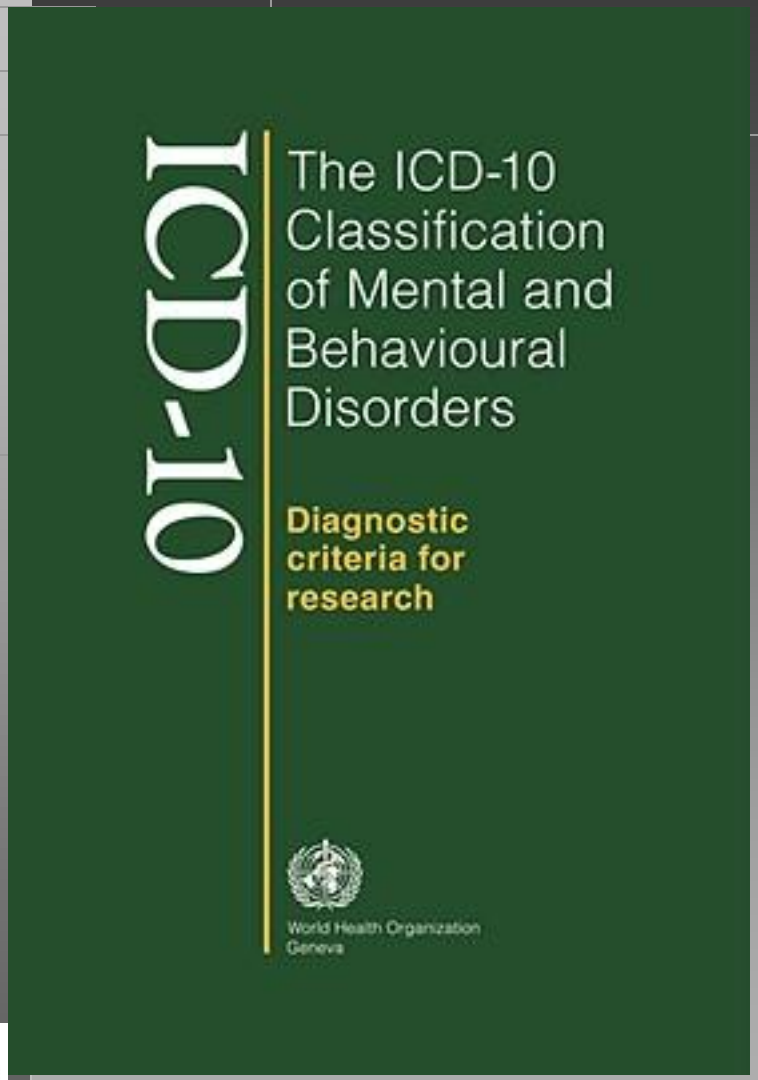

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Delirium is defined, accordingly to the World Health Organizaition´s classification of Mental and Behavioural Disorders (ICD-10), (9) as a clinical condition characterised by:

A. Altered level of **consciousness**, (with reduced clarity of awareness and inattention.)

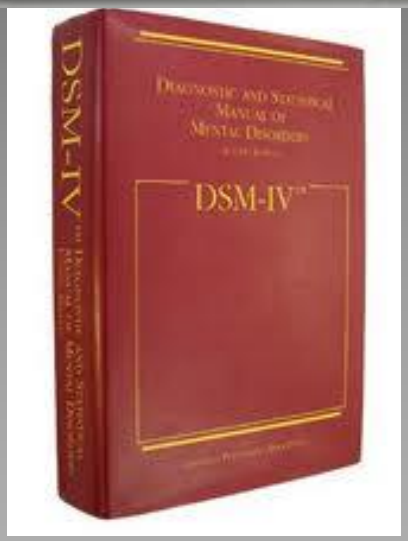
B. Disturbance of **cognition**, with impairment of recent **memory** and **disorientation** (in time, place or person).

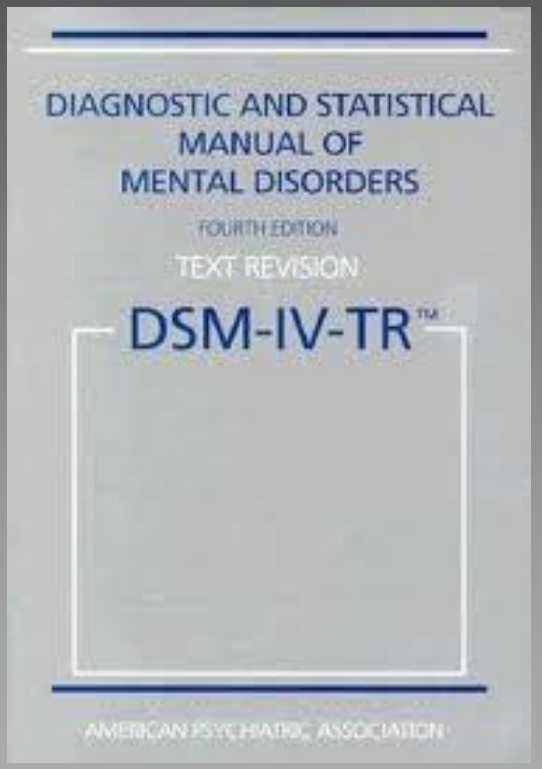
C. **Psychomotor disturbances** such as: rapid, unpredictable shifts from hypo-activity to hyper-activity; increased reaction time; increased or decreased flow of speech and enhanced startle reaction.

D. Disturbance of sleep or the **sleep-wake cycle**, manifest by: insomnia, nocturnal worsening of symptoms and/or disturbing dreams and nightmares.

E. **Rapid onset and fluctuations** of the symptoms over the course of the day.

F. Evidence that the disturbance is caused by the direct physiological consequences of a **general medical condition**.





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Postoperative cognitive dysfunction

POCD is a subtle impairment of memory, concentration, and information processing that is distinct from delirium and dementia. Despite the fact that POCD is not a formal psychiatric diagnosis, the term is commonly used in the literature and is considered to be a mild neurocognitive disorder. The DSM-IV [3] states that a mild neurocognitive disorder can only be diagnosed if the cognitive disturbance does not meet the criteria for three other conditions (delirium, dementia, or amnestic disorder). It further specifies that the diagnosis of mild neurocognitive disorder must be corroborated by the results of neuropsychological testing showing that an individual has a new onset of deficits in at least two areas of cognitive functioning lasting for a period of at least 2 weeks. These diagnostic criteria make it impossible to accurately identify POCD during the hospital stay. Due to the

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REVIEW

Postoperative delirium and cognitive dysfunction

Rafael Badenes*, Maria Jesús Montero, Marina Soro, Francisco Javier Belda

Comparative table between PD and POCD. CAM: Confusion assessment method. Nu-DESC: Nursing delirium screening scale. DDS: Delirium detection scale. ICDSC: Intensive care delirium screening checklist. CAM-ICU: modified CAM for ICU patients.

	PD	POCD
Start	Acute, 1–3 days after surgery.	Subtle, 2 weeks to 2 months after surgery.
Length	Commonly self-limited, days or weeks.	Weeks or months.
Symptoms	Inattention, change in cognition, fluctuation over time.	Impairment of memory, concentration and information processing.
Diagnosis	DSM-IV criteria and Scales (CAM, Nu-Desc, DDS, ICDSC, CAM-ICU)	Failure on >2 tests on a neuropsychological test battery.
Reversibility	Usually.	Normally, but long-range.

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Postoperative delirium and postoperative cognitive dysfunction in the elderly – what are the differences?

(Minerva Anestesiol 2011;77:742-9)

L. KRENK [1, 2, 3], L. S. RASMUSSEN [1]

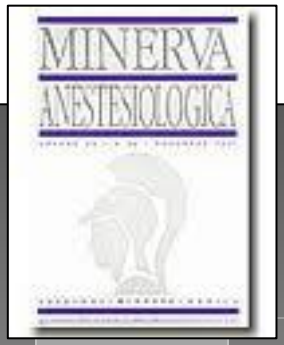

TABLE I.—*Timeline for postoperative cognitive deterioration.*

Features	Delirium	POCD
Debut	Hours to days	Weeks to months
Onset	Acute	Subtle
Duration	Days to weeks	Weeks to months
Attention	Impaired	Impaired
Consciousness	Altered	Normal
Reversibility	Usually	Usually, but can be long lasting

POCD: Post Operative Cognitive Dysfunction.

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Delirium is associated with early postoperative cognitive dysfunction

J. L. Rudolph,[1] E. R. Marcantonio,[2] D. J. Culley,[3] J. H. Silverstein,[4] L. S. Rasmussen,[5] G. J. Crosby[6] and S. K. Inouye[7]

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland
Anaesthesia, 2008, **63**, pages 941–947

Table 2 The association of delirium and postoperative cognitive dysfunction.

7-days after surgery (n = 1018)				3-months after surgery (n = 946)			
POCD when:				POCD when:			
Delirium present (n = 75)	Delirium absent (n = 943)	Crude RR	Adjusted RR†	Delirium present (n = 61)	Delirium absent (n = 883)	Crude RR	Adjusted RR†
33 (44%)	232 (25%)	1.8 [1.4–2.4]*	1.6 [1.1–2.1]*	9 (15%)	85 (10%)	1.5 [0.8–2.9]	1.3 [0.6–2.4]

The relative risks (RR) presented compare the risk of POCD in those with and without delirium at any time within the postoperative period. Values are number (%), or RR (95% CI).
*$p < 0.05$.
†Relative risk adjusted for age, education, and duration of surgery with logistic regression using the method of Zhang and Yu [22].

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Duration of delirium	Risk of postoperative cognitive dysfunction					
	7-day postoperative assessment			3-month postoperative assessment		
	n	Crude RR	Adjusted RR†	*n*	Crude RR	Adjusted RR†
≥ 3 days	18	2.5 [1.7–3.6]*	2.2 [1.2–3.1]*	12	1.7 [0.5–6.3]	1.6 [0.4–4.8]
< 3 days	57	1.6 [1.1–2.2]*	1.4 [0.9–2.0]	49	1.5 [0.7–3.0]	1.2 [0.6–2.5]

Values are numbers, or relative risk (95% CI).
*$p < 0.05$.
†Adjusted for age, education, and duration of surgery with logistic regression using the method of Zhang and Yu [22].

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Crit Care Clin 24 (2008) 789–856

CRITICAL
CARE
CLINICS

Pathoetiological Model of Delirium: a Comprehensive Understanding of the Neurobiology of Delirium and an Evidence-Based Approach to Prevention and Treatment

José R. Maldonado, MD, FAPM, FACFE

Departments of Psychiatry and Medicine, Stanford University School of Medicine, 401 Quarry Road, Suite 2317, Stanford, CA 94305, USA

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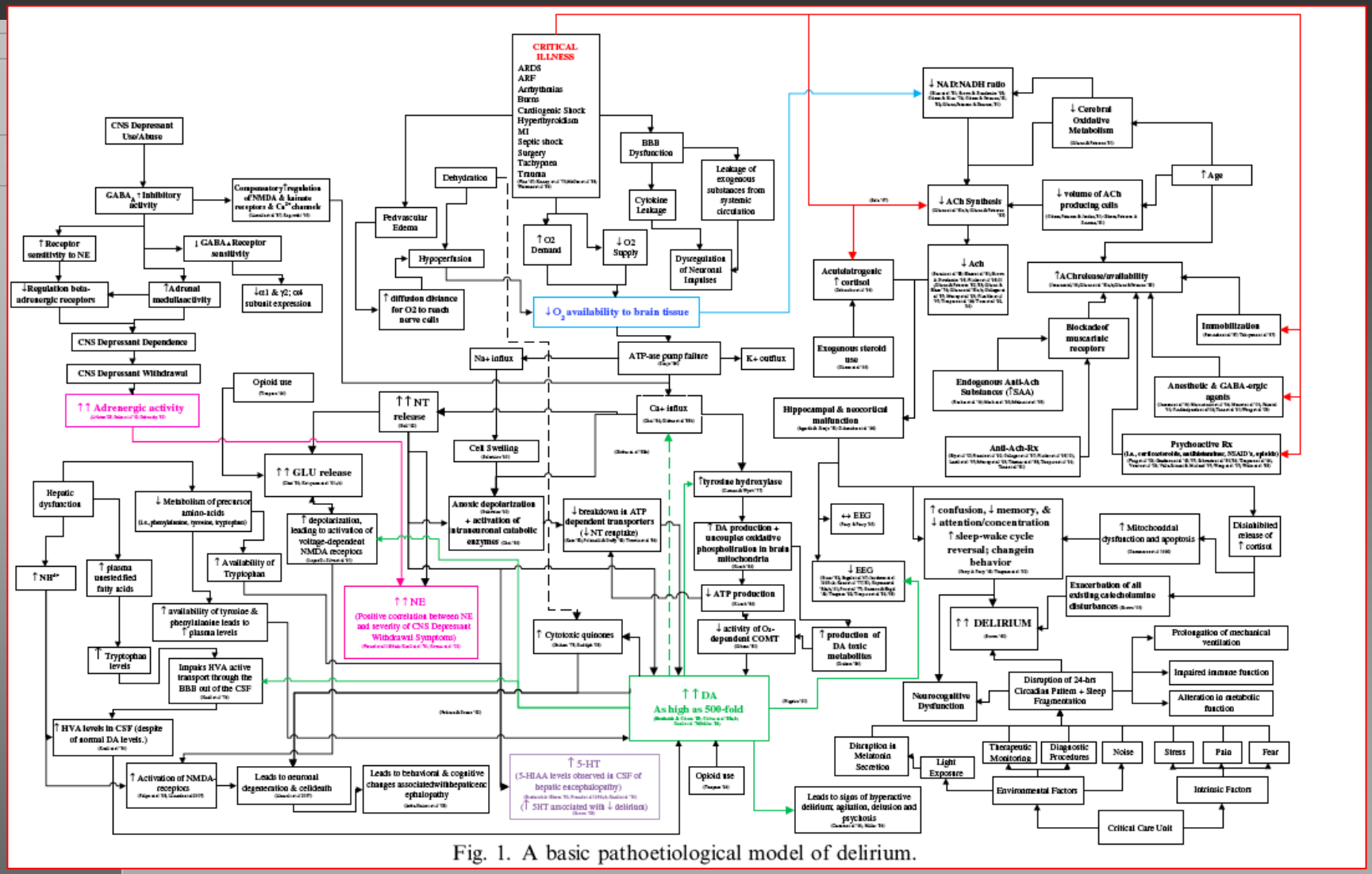

Fig. 1. A basic pathoetiological model of delirium.

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Evidence for the diagnostic criteria of delirium: an update

Dan G. Blazer[a] *and Adrienne O. van Nieuwenhuizen*[b]

Curr Opin Psychiatry 2012, 25:239–243

KEY POINTS

- The core diagnostic symptom of delirium is a problem with attention/awareness.
- Subsyndromal delirium predicts a poorer outcome than the absence of delirium, yet the fluctuating course of delirium makes subsyndromal delirium difficult to diagnose.
- Delirium can be categorized into one of three motoric subtypes: hyperactive, hypoactive, and normal/mild.

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Schoen *et al. Critical Care* 2011, **15**:R218
http://ccforum.com/content/15/5/R218

CRITICAL CARE

RESEARCH Open Access

Preoperative regional cerebral oxygen saturation is a predictor of postoperative delirium in on-pump cardiac surgery patients: a prospective observational trial

Julika Schoen, Joscha Meyerrose, Hauke Paarmann, Matthias Heringlake*, Michael Hueppe and Klaus-Ulrich Berger

Incidence of delirium

Sixty-two patients (26.8%) developed postoperative delirium. In 45 (72.6%) cases, delirium developed on day 1, in 16 (25.8%) on day 2, and in 1 case (1.6%) on day 3 after surgery. The hypoactive form of delirium was present in 69.4% of cases.

CME

Postoperative Delirium: Acute Change with Long-Term Implications

(Anesth Analg 2011;112:1202–11)

James L. Rudolph, MD, SM,*†§ and Edward R. Marcantonio, MD, SM†§

Table 1. Incidence of Postoperative Delirium

Surgery	Incidence of delirium (%)	References
Abdominal aortic aneurysm (infrarenal)	33–54	92–95
Abdominal	5–51	67, 92, 96, 97
Cataract	4	98
Coronary artery bypass graft surgery	37–52	14, 99
Elective orthopedic	9–15	92, 100
Head and neck (major)	17	101
Hip fracture	35–65	102
Peripheral vascular	30–48	93, 94
Urologic	4–7	99

JAMA®
The Journal of the American Medical Association

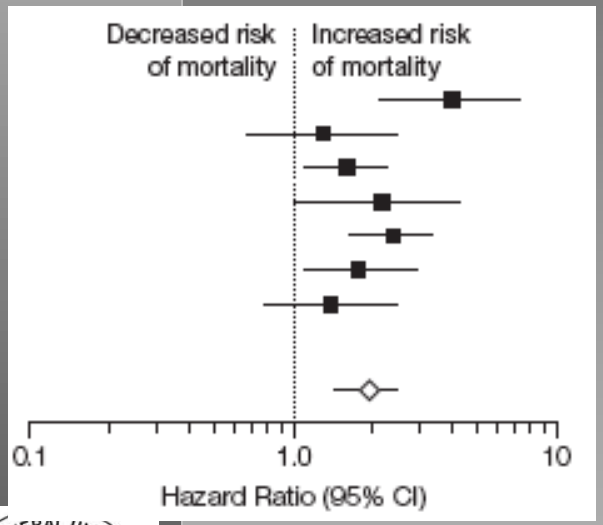
Delirium in Elderly Patients and the Risk of Postdischarge Mortality, Institutionalization, and Dementia

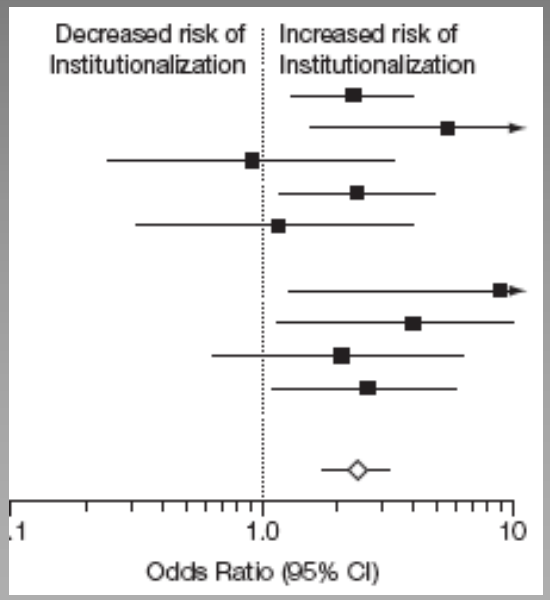
A Meta-analysis

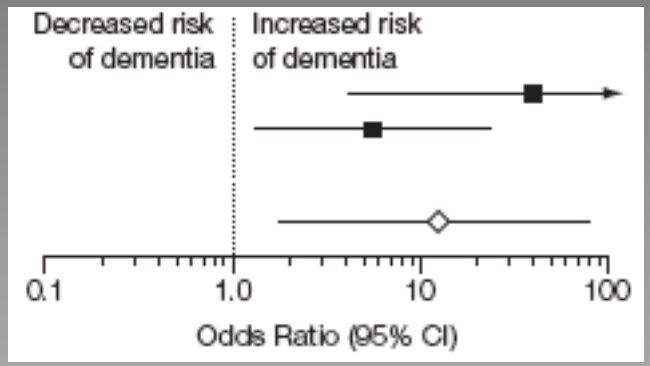
JAMA, July 28, 2010—Vol 304, No. 4

Joost Witlox, MSc

The results of this meta-analysis provide evidence that delirium in elderly patients is associated with an increased risk of death, institutionalization, and dementia, independent of age, sex, comorbid illness or illness severity, and presence of dementia at base-







J Am Geriatr Soc. 2010 April ; 58(4): 643–649. doi:10.1111/j.1532-5415.2010.02762.x.

Delirium: An Independent Predictor of Functional Decline After Cardiac Surgery

Delirium and Risk of Functional Decline

	Rate of Functional Decline*		Risk of Functional Decline†	
	With delirium n/N (%)	Without delirium n/N (%)	Unadjusted Risk Ratio (95% CI)	Adjusted Risk Ratio‡ (95% CI)
1-month				
1-month functional decline*	37/74 (50%)	28/105 (27%)	1.9 (1.3, 2.8)	1.8 (1.2, 2.6)
12-month				
1-month functional decline*	16/78 (21%)	11/100 (11%)	1.9 (0.9, 3.8)	1.5 (0.6, 3.3)

CI – Confidence Interval

* Functional decline is defined as a decline of ≥2 Instrumental Activities of Daily Living (IADL) points at the follow up assessment relative to the preoperative assessment

† Risk of functional decline in those with delirium relative to those without delirium

‡ Adjusted analyses use Poisson regression to adjust for age, Charlson Comorbidity Index, Mini Mental State Examination, and baseline IADL scores

Best Practice & Research Clinical Anaesthesiology
Vol. 20, No. 2, pp. 315–330, 2006
doi:10.1016/j.bpa.2005.10.011
available online at http://www.sciencedirect.com

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7

Postoperative cognitive dysfunction: Incidence and prevention

Lars S. Rasmussen* MD, PhD
Department of Anaesthesia, Centre of Head and Orthopaedics, Section 4231, Copenhagen University Hospital, Rigshospitalet, DK-2100 Copenhagen, Denmark

For more than 30 years, it has been well known that brain complications are common after cardiac surgery, and one of these complications is POCD. The reported incidence of POCD, however, varies enormously depending on the definition, composition of the test battery, and time of postoperative assessment. Accordingly, the incidence is reported to be 30–80% a few weeks after cardiac surgery and 10–60% after 3–6 months.[1–6] The primary focus of this chapter is POCD after non-cardiac surgery; POCD after cardiac procedures has been well covered in a recent review.[7]

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Postoperative cognitive dysfunction: Incidence and prevention

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Department of Anaesthesia, Centre of Head and Orthopaedics, Section 4231, Copenhagen University Hospital, Rigshospitalet, DK-2100 Copenhagen, Denmark

In the International Study of Postoperative Cognitive Dysfunction (ISPOCD1) study 1218 elderly patients undergoing major non-cardiac surgery were included, and an incidence of POCD of 25.8% was found after 1 week and 9.9% after 3 months.[14] This was significantly higher than in a control group of 176 healthy

3.4 and 2.8%, respectively.[15] In another study, it was reported that POCD occurred in 45% of 29 patients with a mean age of 60 years at 6–12 weeks after thoracic or vascular surgery.[16] The definition was based on detection of a 20% deterioration in

Table 4. Predisposing and Precipitating Factors for Delirium After Surgery

Predisposing factors, preoperative	Precipitating factors: Intraoperative	Precipitating factors: Postoperative
Demographics	Type of operation	Early complications of operation
Increasing age	Hip fracture	Low hematocrit
Male gender	Cardiac surgery	Cardiogenic shock
Comorbidities	Vascular surgery	Hypoxemia
Impaired cognition	Complexity of operation	Prolonged intubation
Dementia	Operation time	Sedation management
Mild cognitive impairment	Shock/hypotension	Pain
Preoperative memory complaint	Arrhythmia	Later complications of operation
Atherosclerosis	Decreased cardiac output	Low albumin
Intracranial stenosis	Emergency surgery	Abnormal electrolytes
Carotid stenosis	Operative factors	Iatrogenic complications
Peripheral vascular disease	Intraoperative temperature	Pain
Prior stroke/transient ischemic attack	Benzodiazepine administration	Infection
Diabetes	Propofol administration	Liver failure
Hypertension	Blood transfusion	Renal failure
Atrial fibrillation	Anesthesia factors	Sleep-wake disturbance
Low albumin	Type of anesthesia	Alcohol withdrawal
Electrolyte abnormalities	Duration of anesthesia	
Psychiatric disease	Cognitively active medications	
Anxiety		
Depression		
Benzodiazepine use		
Function		
Impaired functional status		
Sensory impairment		
Lifestyle factors		
Alcohol use		
Sleep deprivation		
Smoking		

Postoperative delirium

(Minerva Anestesiol 2011;77:448-56)

E. L. WHITLOCK [1, 2], A. VANNUCCI [2], M. S. AVIDAN [1, 2]

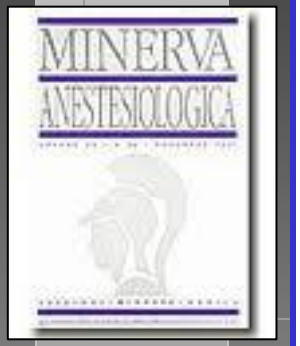

TABLE I.—*Risk factors for delirium.*

Predisposing [19]	Precipitating [19, 21]	
Reduced cognitive reserve:	Medications or medication withdrawal:	
Dementia	Anticholinergics	Psychotropic medications:
Depression	Muscle relaxants	Antidepressants
Advanced age	Antihistamines	Antiepileptics
Reduced physical reserve:	Gastrointestinal antispasmodics	Antipsychotics
Atherosclerotic disease	Opioid analgesics [29]	Benzodiazepines
Renal impairment	Antiarrhythmics	
Pulmonary disease	Corticosteroids	
Advanced age	>6 total medications	
Preoperative beta blockade [30]	>3 new inpatient medications	
Sensory impairment (vision, hearing)	Pain31	
Alcohol abuse	Hypoxemia	
Malnutrition	Electrolyte abnormalities	
Dehydration [29]	Malnutrition	
Apolipoprotein E4 genotype [32]	Dehydration [29]	
	Environmental change (e.g. ICU admission)	
	Sleep-wake cycle disturbances [33]	
	Urinary catheter use	
	Restraint use	
	Infection	

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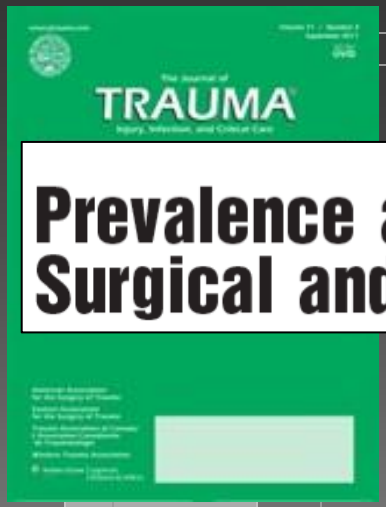
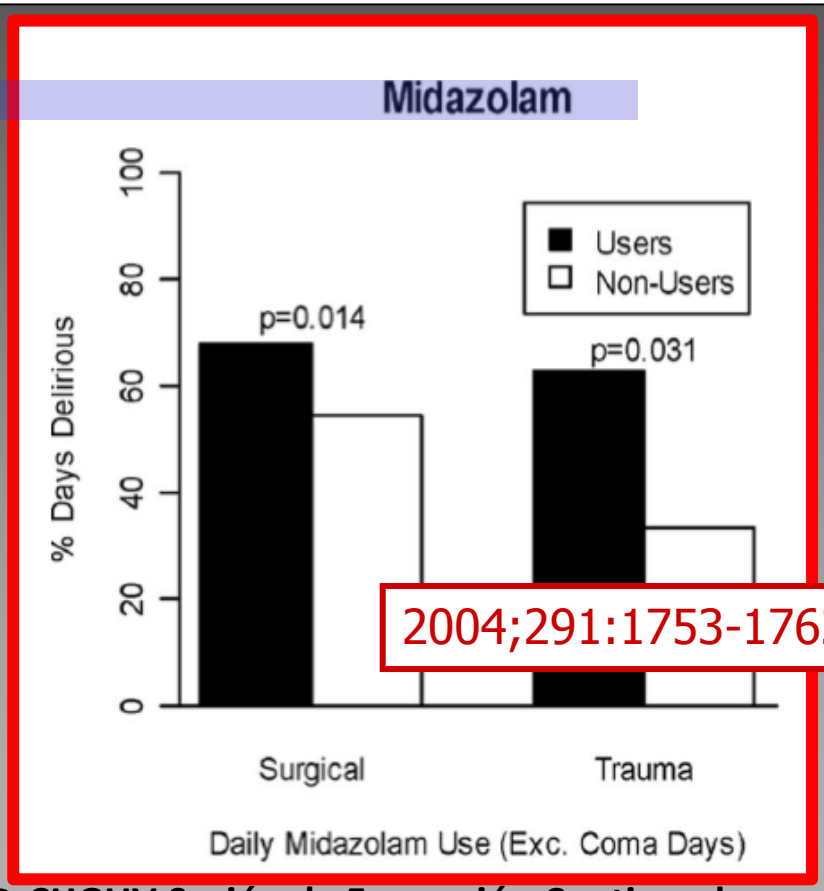


J Trauma 2008;65:34-41

Prevalence and Risk Factors for Development of Delirium in Surgical and Trauma Intensive Care Unit Patients



2004;291:1753-1762

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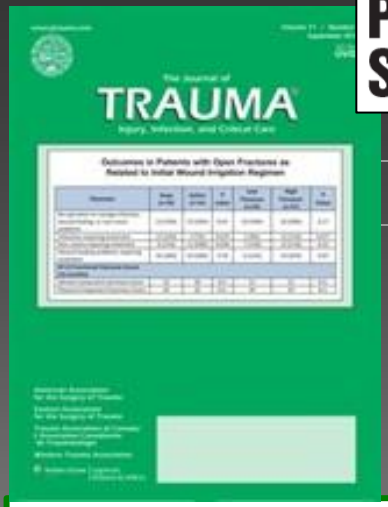
Prevalence and Risk Factors for Development of Delirium in Surgical and Trauma Intensive Care Unit Patients



J Trauma 2008;65:34-41

Table 2 Multivariable Analysis of Sedative and Analgesic Medications as Risk Factors for Transitioning to Delirium

Medication	Odds Ratio (95% CI)*	p†
Surgical and trauma patients (n = 97)		
Anesthetics	0.52 (0.23–1.16)	0.108
H2 blockers	1.45 (0.80–2.62)	0.217
Lorazepam	0.45 (0.16–1.27)	0.131
Midazolam	2.75 (1.44–5.26)	0.002
Fentanyl	1.88 (0.99–3.55)	0.053
Morphine	0.36 (0.16–0.82)	0.015
Surgical patients (n = 45)		
Anesthetics	1.23 (0.37–4.04)	0.735
H2 blockers	1.71 (0.74–3.95)	0.212
Lorazepam	0.46 (0.10–2.05)	0.307
Midazolam	3.22 (1.27–8.20)	0.014
Fentanyl	3.99 (1.47–10.85)	0.007
Morphine	0.37 (0.13–1.08)	0.069
Trauma patients (n = 52)		
Anesthetics	0.18 (0.04–0.77)	0.020
H2 blockers	1.25 (0.52–3.04)	0.618
Lorazepam	0.51 (0.12–2.17)	0.360
Midazolam	2.45 (1.09–5.52)	0.031
Fentanyl	1.03 (0.47–2.25)	0.936
Morphine	0.22 (0.06–0.82)	0.024

* Odds ratios in this table can be interpreted as indicating the odds of transitioning to delirium for patients who received any dose of the given medication in the previous 24 hours, adjusted for the following baseline variables: age, body mass index, Charlson Comorbidity Index, APACHE II severity of illness score, and diagnosis of sepsis, septic shock, or ARDS.

† $p \leq 0.05$ considered statistically significant.

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Delirium as a Predictor of Mortality in Mechanically Ventilated Patients in the Intensive Care Unit

JAMA

2004;291:1753-1762

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Reducing delirium in elderly patients with hip fracture: a multi-factorial intervention study

K. B. Björkelund[1,2], A. Hommel[2,3], K.-G. Thorngren[3], L. Gustafson[4], S. Larsson[5] and D. Lundberg[1]

Acta Anaesthesiologica Scandinavica

Acta Anaesthesiol Scand 2010; **54**: 678–688
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The multi-factorial program for patients in the intervention group ($n = 131$) undergoing surgery for hip fracture, starting pre-hospitally.

1. *Supplemental oxygen 3–4 l/min*: in the ambulance and continually (including transfers between wards/departments) until day 2 post-operatively, the patient is mobilized, or the patient's oxygen saturation is $\geq$ 95% without oxygen in order to increase oxygen delivery into the tissues[6,13,40]

2. *Intravenous (i.v.) fluid supplementation and extra nutrition*: fructose/glucose 1.0 l in the ambulance or immediately after admittance to the A&E for improvement of fluid balance and tissue perfusion. Additional i.v. supplementation in case of increased fasting. Extra oral multi-nutrient drinks daily post-operatively for improvement of nutritional balance[30,41–43]

3. *Increased monitoring of vital physiological parameters*: especially oxygen saturation (a pulse-oximeter should be kept adherent to every patient) starting at the place of injury until post-operatively, day 5. Systolic blood pressure should be maintained $\geq$ 90–100 mmHg. Red blood cell transfusion should be considered if hemoglobin $<$100 g/l. Body temperature should be kept normal; avoid hypo-/hyperthermia[13,30,31,44]

4. *Adequate pain relief*: immediately after admittance at the A&E with a combination of opioids i.v. and paracetamol. Pain should be measured several times on a daily basis $\geq$ day 5 as pain: yes/no, and as intensity of pain: 1–10. Patient should be kept continually pain-relieved[27,28]

5. *Avoid delay in transfer logistics*: nurse assessment (RN) of patient immediately ($\leq$ 5 min) after admittance to the A&E. Assessment by the orthopedic surgeon ($\leq$ 30 min) before referral to the X-ray department. After X-ray directly to the orthopedic ward without a second visit to the A&E (routine before the intervention) with the purpose of decreasing the waiting time and an overload of staff–patient interactions[13,33,34]

6. *Screen for delirium through daily testing with the OBS scale*: one researcher is always available day and night. All staff is educated and instructed to pay increased attention to symptoms of delirium[6,22]

7. *Avoid polypharmacia*: sedatives/hypnotics and drugs with anticholinergic properties should be administered with restriction[6,29]

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Table 5

Clinical and post-operative outcome of patients of the control group ($n = 132$) and the intervention group ($n = 131$) undergoing surgery for hip fracture

Group	Control ($n = 132$)	Intervention ($n = 131$)	*P*-value
Delirium during hospitalization	45 (34.1)	29 (22.1)	0.031
Post-operative delirium	44 (33.3)	28 (21.4)	0.030
Delirium ≤ 1 / ≥ 2 days	23 (17.4)/22 (16.7)	14 (10.7)/15 (11.5)	0.09
OBS max score ≤ 6 / ≥ 7	97 (73.5)/35 (26.5)	105 (80.2)/26 (19.8)	0.20

Conclusion: The use of a multi-factorial intervention program in elderly hip fracture patients, lucid at admission, reduced the incidence of delirium during hospitalization by 35%.

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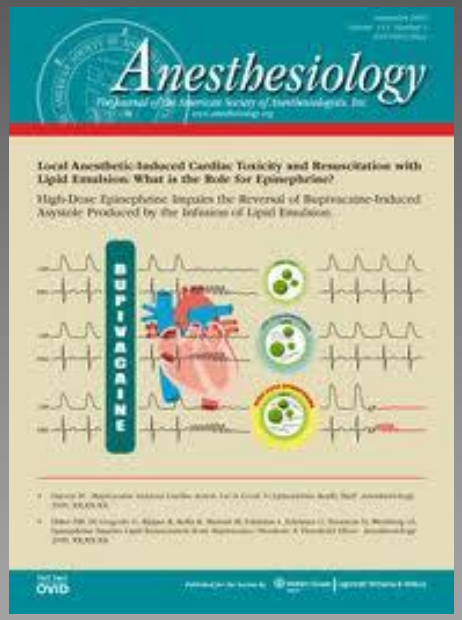
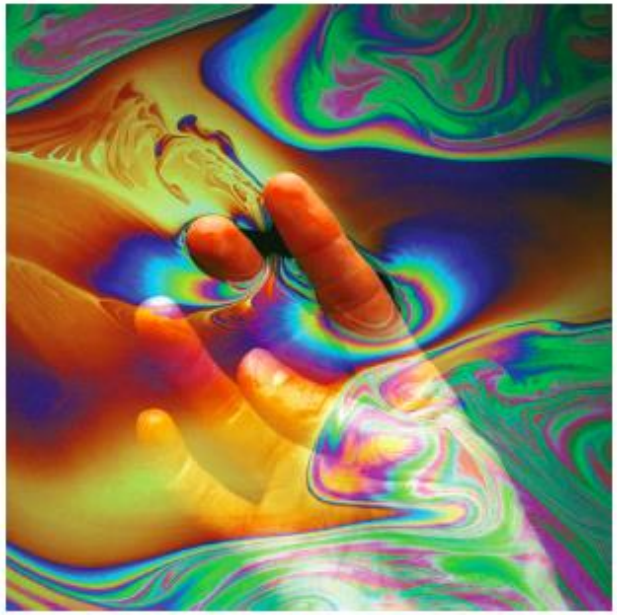
Targeted Prophylaxis of Postoperative Delirium

Anesthesiology 2012; 116:975-6





"… targeted prophylaxis [for delirium] substantially reduces the number of patients requiring drug administration."

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Early Treatment with Risperidone for Subsyndromal Delirium after On-pump Cardiac Surgery in the Elderly

A Randomized Trial

Sameh M. Hakim, M.D.,* Ahmed I. Othman, M.D.,† Dina O. Naoum, M.Sc.‡

Table 3. Outcome Measures in Both Study Groups

Variable	Risperidone Group (n = 51)	Placebo Group (n = 50)	*P* Value
Score >3 on the ICDSC	8 (15.7%)	19 (38%)	0.011
Clinical delirium by DSM criteria	7 (13.7%)	17 (34%)	0.031
Length of ICU stay, days	2 (2 to 3)	3 (2 to 3)	0.517
Length of hospital stay, days	6 (5 to 7)	6 (5 to 8)	0.056
Extrapyramidal side effects	2 (3.9%)	1 (2%)	1.0

Early Treatment with Risperidone for Subsyndromal Delirium after On-pump Cardiac Surgery in the Elderly

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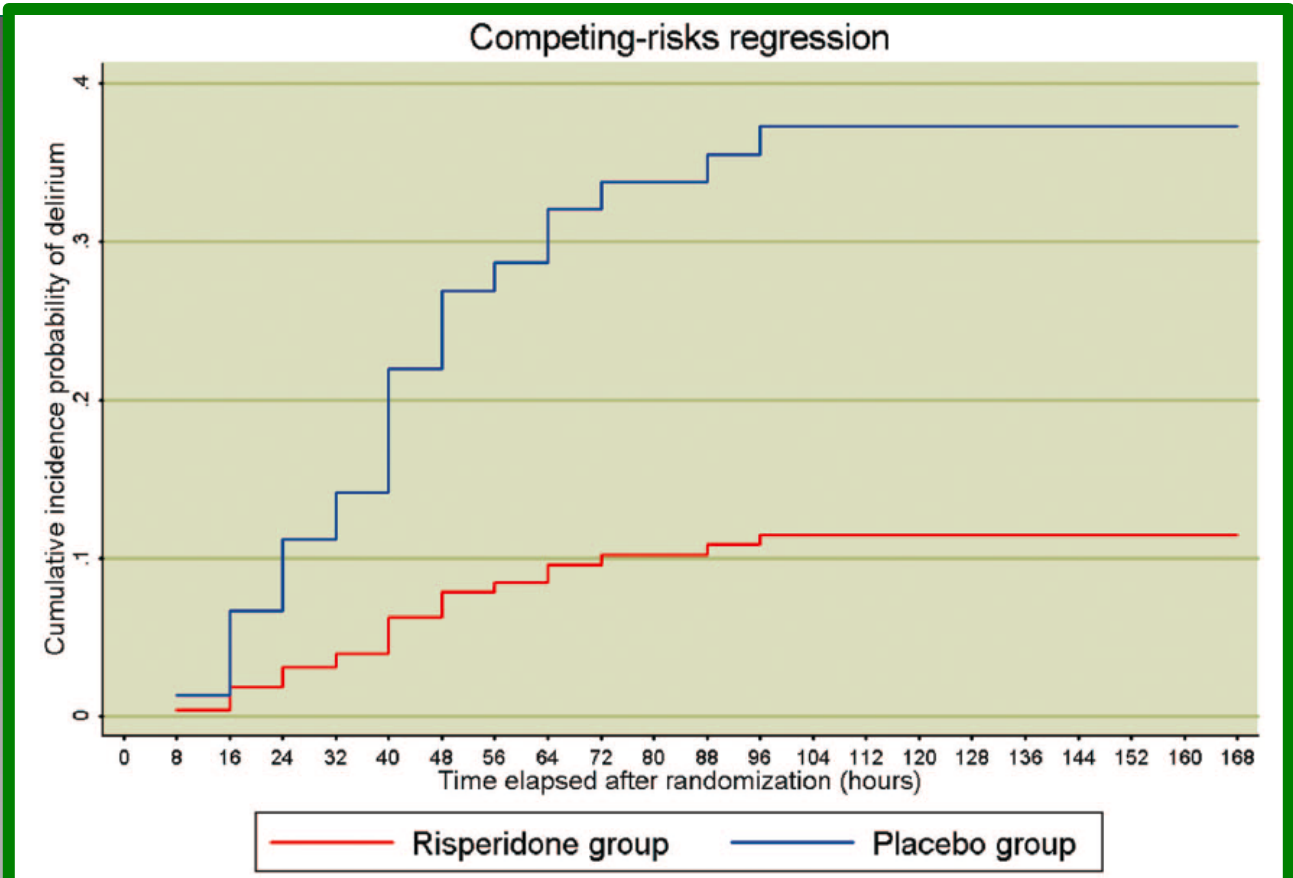

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Acta Anaesthesiol Scand 2010; **54**: 951–956
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ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2010.02268.x

Review Article

New insights into the pathophysiology of postoperative cognitive dysfunction

L. KRENK[1,2,3], L. S. RASMUSSEN[1] and H. KEHLET[2,3]

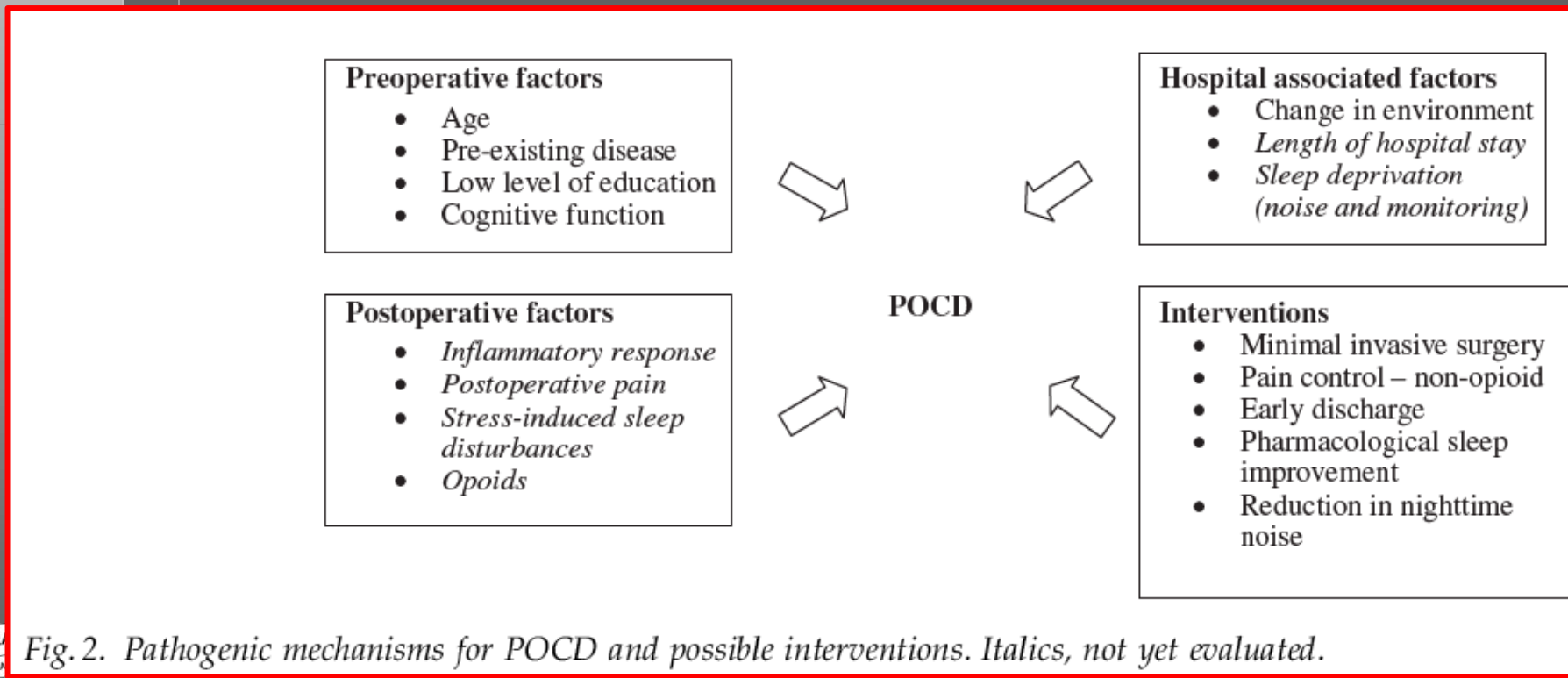

Fig. 2. Pathogenic mechanisms for POCD and possible interventions. Italics, not yet evaluated.

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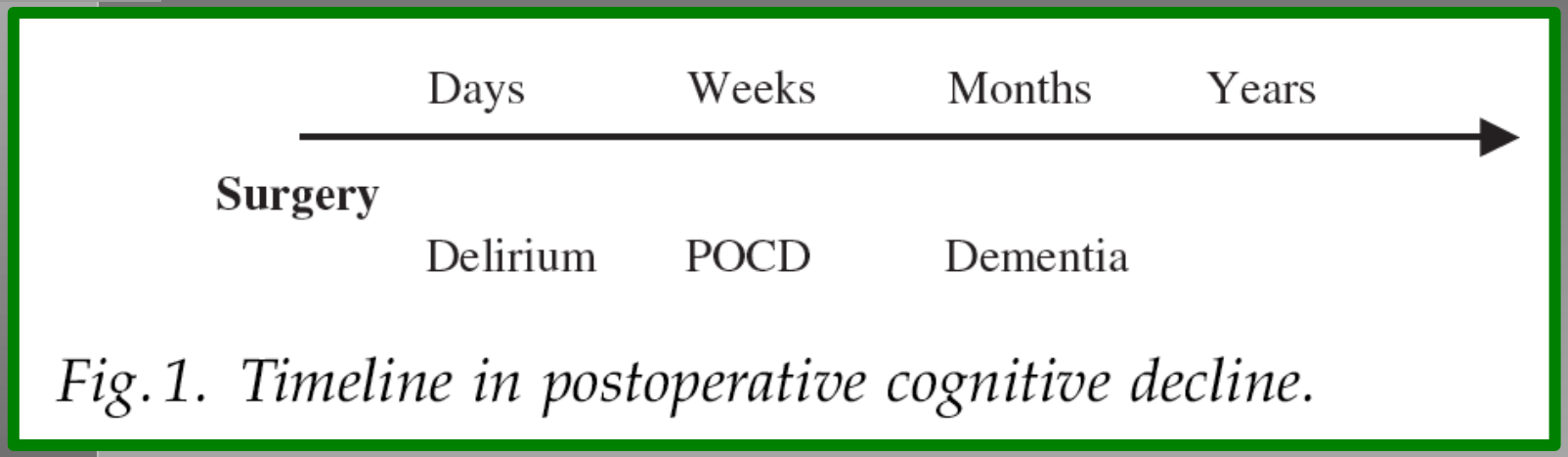

Fig. 1. Timeline in postoperative cognitive decline.

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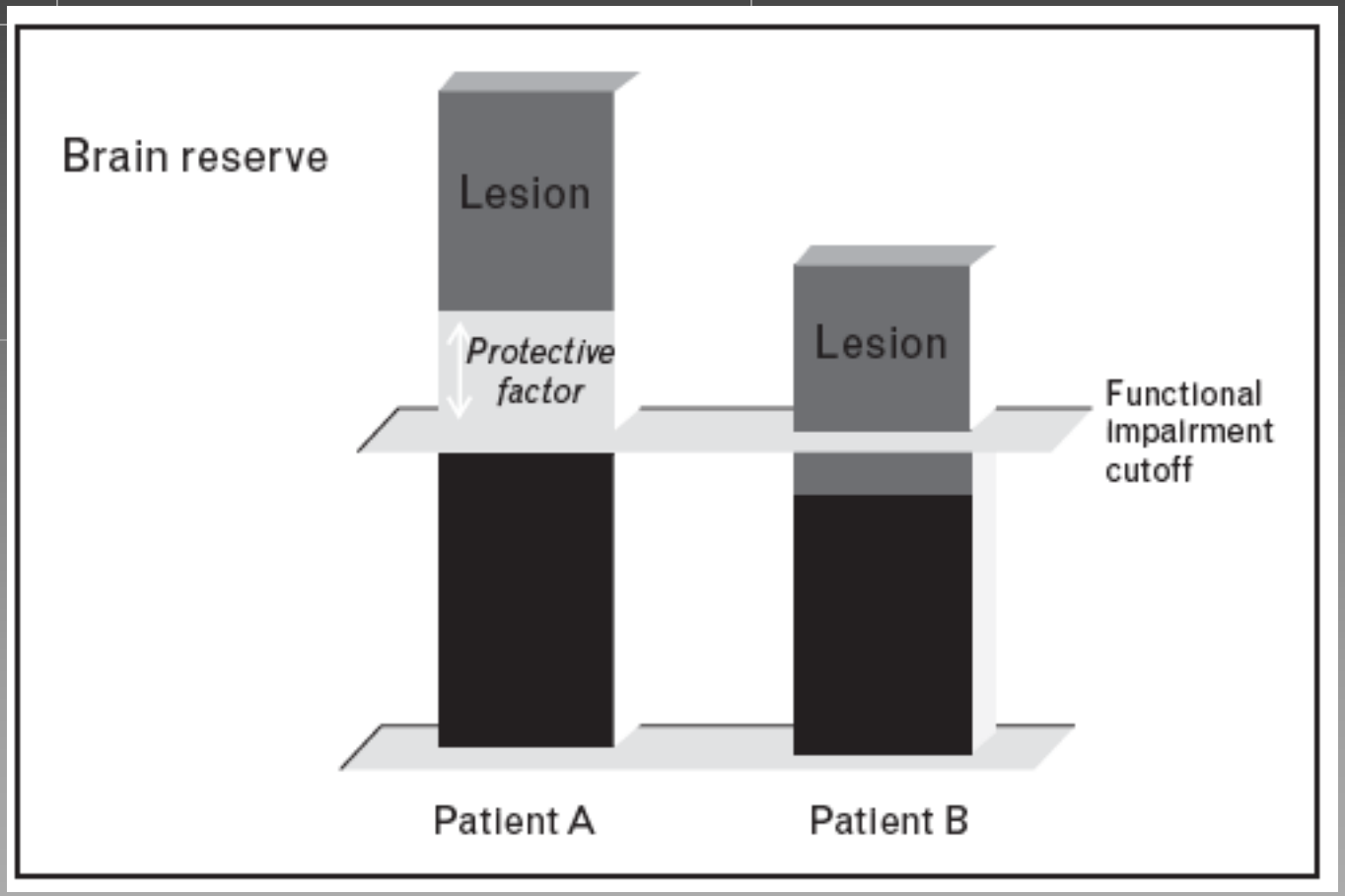

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MOUNT SINAI JOURNAL OF MEDICINE 79:75–94, 2012

Developmental Disability in the Young and Postoperative Cognitive Dysfunction in the Elderly After Anesthesia and Surgery: Do Data Justify Changing Clinical Practice?

James E. Cottrell, MD, and John Hartung, PhD

State Univ

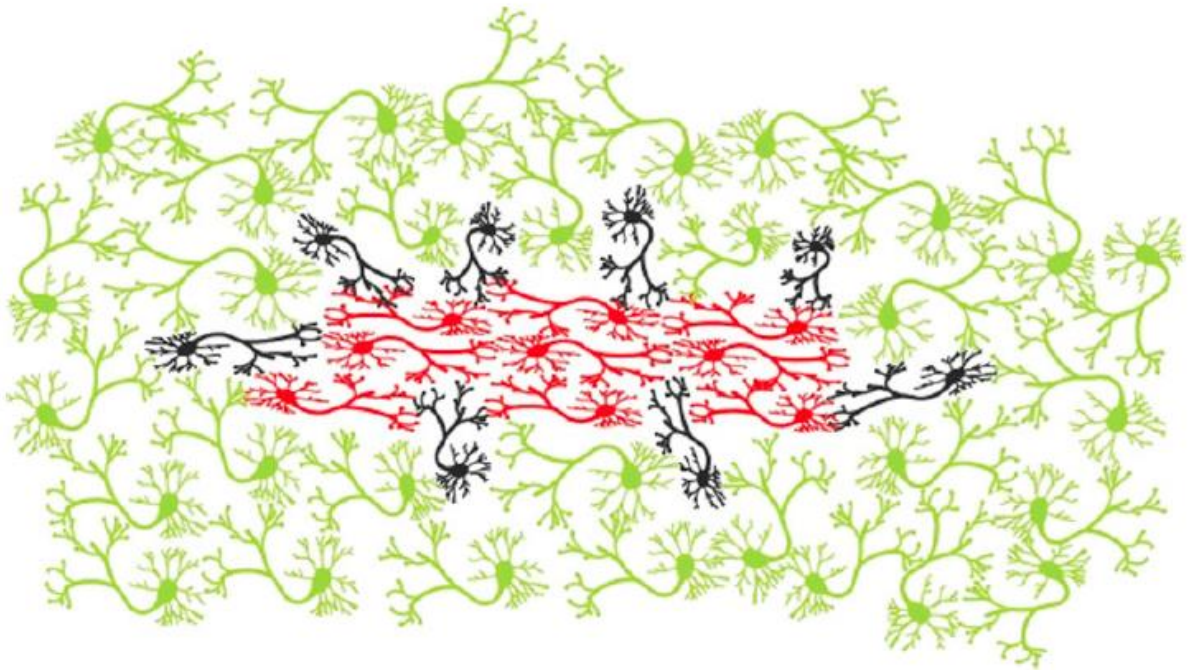

Fig 2. Neurons in nonanesthetized cortical subregions (red and black) may be in a sort of reverse penumbra–a penumbra where the cluster in the center

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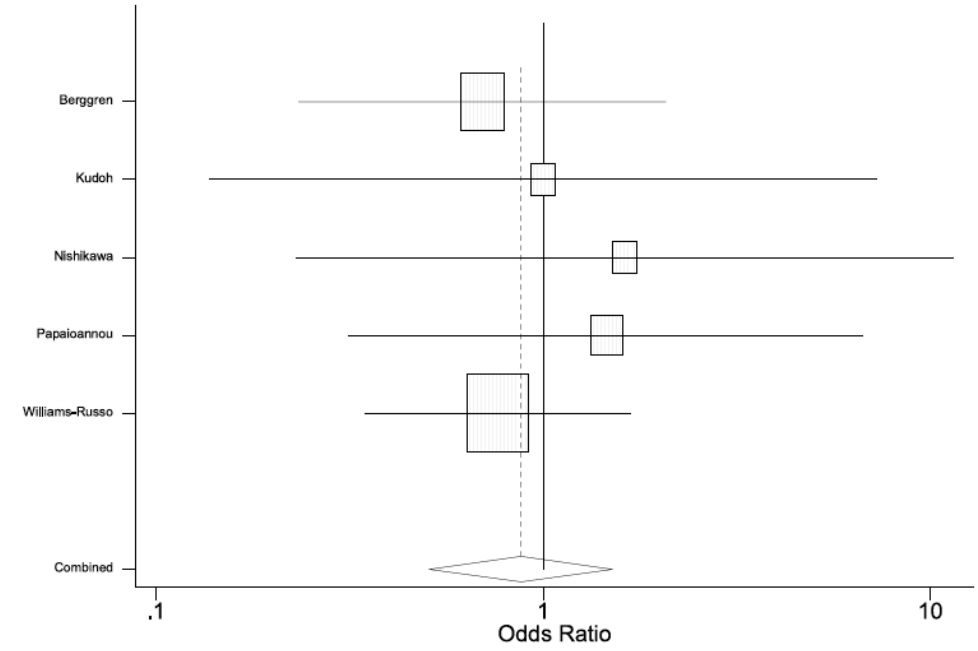
Journal of Alzheimer's Disease 22 (2010) S67–S79
DOI 10.3233/JAD-2010-101086
IOS Press

The Impact of General and Regional Anesthesia on the Incidence of Post-Operative Cognitive Dysfunction and Post-Operative Delirium: A Systematic Review with Meta-Analysis



Test for heterogeneity: Q= 1.11; *df*=4 (p= 0.89)

Fig. 1. Forest plot of the five studies which compare GA with RA in the development of POD. GA – General Anesthesia; RA – Regional Anesthesia.

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The influence of propofol or desflurane on postoperative cognitive dysfunction in patients undergoing coronary artery bypass surgery*

Anaesthesia
Journal of the Association of Anaesthetists of Great Britain and Ireland
Anaesthesia, 2011, 66, pages 455–464

C. F. Royse,[1] D. T. Andrews,[2] S. N. Newman,[3] J. Stygall,[4] Z. Williams,[5] J. Pang[6] and

Table 3 Independent predictors of outcome variables in patients undergoing coronary artery bypass surgery, from multiple logistic regression analysis.

Outcome variable	Independent predictors	p value	Odds ratio (95% CI)
Cognitive deficit at discharge	Group (propofol)	0.011	2.31 (1.21–4.43)
	Maximal intra-operative temperature	0.012	2.72 (1.24–5.95) (per 1 °C)
Cognitive deficit at 3 months	Age	0.009	1.08 (1.02–1.15) (per year)
	Ventilation time	0.035	1.001 (1.00–1.002) (per min)
CAM defined delirium	Body mass index > 30 $kg.m^{-2}$	0.043	2.80 (1.30–7.56) (per $kg.m^{-2}$)
Peri-operative morbidity	Group (propofol)	0.022	2.60 (1.15–5.92)
	EuroSCORE	0.023	1.25 (1.03–1.52) (per 1 unit in EuroSCORE)
	Ventilation time	0.013	1.003 (1.001–1.005) (per min)
Hospital LOS > 5 days	Age	0.002	1.06 (1.02–1.1) (per year)
	Female sex	0.032	5.34 (1.16–24.7)
	Ventilation time	0.008	1.002 (1.001–1.004) (per min)

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Anaesthesia, 2011, 66, pages 455–464

C. F. Royse,[1] D. T. Andrews,[2] S. N. Newman,[3] J. Stygall,[4] Z. Williams,[5] J. Pang[6] and

This study has shown that the choice of primary anaesthetic agent (desflurane or propofol) did not significantly affect the incidence of POCD at 3 months following coronary artery bypass surgery. There was, however, a significantly higher incidence in POCD before hospital discharge with propofol. The only difference in postoperative morbidity outcomes was a higher incidence of superficial wound infection with propofol.

Acta Anaesthesiol Scand 2004; 48: 162–168
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ACTA ANAESTHESIOLOGICA SCANDINAVICA

Recovery characteristics and post-operative delirium after long-duration laparoscope-assisted surgery in elderly patients: propofol-based vs. sevoflurane-based anesthesia

K. Nishikawa[1], M. Nakayama[2], K. Omote[2] and A. Namiki[2]

Table 5

Emergence times and complications.

	Propofol	Sevoflurane	*P*-value
Eye opening (min)	11.1 ± 1.9	9.1 ± 1.9	0.016
Extubation (min)	12.3 ± 2.4	10.4 ± 2.3	0.045
Following simple commands (min)	13.8 ± 2.5	12.5 ± 2.5	NS
Orientation (min)	15.2 ± 2.4	14.0 ± 2.7	NS
Emergence complications			
breath holding (*n*,%)	1 (4%)	3 (12%)	NS
coughing (*n*,%)	5 (20%)	4 (16%)	NS
excitement (*n*,%)	1 (4%)	3 (12%)	NS
excess salivation (*n*,%)	3 (12%)	1 (4%)	NS
nausea (*n*,%)	0 (0%)	1 (4%)	NS

Values are mean ± SD or number (%). NS: not statistically significant.

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ACTA ANAESTHESIOLOGICA SCANDINAVICA

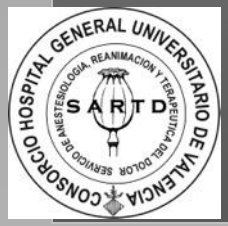
Recovery characteristics and post-operative delirium after long-duration laparoscope-assisted surgery in elderly patients: propofol-based vs. sevoflurane-based anesthesia

K. Nishikawa[1], M. Nakayama[2], K. Omote[2] and A. Namiki[2]

Incidences of post-operative delirium (POD) and the Delirium Rating Scale (DRS) score.

	Propofol	Sevoflurane	*P*-value
Incidence of POD			
1st PO day (*n*, %)	0 (0%)	0 (0%)	NS
2nd PO day (*n*, %)	1 (4%)	0 (0%)	NS
3rd PO day (*n*, %)	3 (12%)	0 (0%)	NS
Total (*n*, %)	4 (16%)	0 (0%)	NS
DRS score			
Pre-operative day	0 (0–3)	0 (0–2)	NS
Ist PO day	1 (0–6)†	1 (0–1)†	NS
2nd PO day	5 (1–13)*†	2 (0–5)†	0.007
3rd PO day	6 (1–15)*†	2 (0–5)†	0.002

Values are number (%) or median (range). NS: not statistically significant. 1st, 2nd, and 3rd PO day = the first, second, and third post-operative day. *$P < 0.05$ compared with 1st PO day. †$P < 0.05$ compared with pre-operative day.



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Cognitive function after sevoflurane- *vs* propofol-based anaesthesia for on-pump cardiac surgery: a randomized controlled trial

British Journal of Anaesthesia **106** (6): 840–50 (2011)

J. Schoen*, L. Husemann, C. Tiemeyer, A. Lueloh, B. Sedemund-Adib, K.-U. Berger, M. Hueppe and M. Heringlake

Cognitive dysfunction is a frequent complication after cardiac surgery and has been found to be associated with decreases in cerebral oxygen saturation (Sc_{O_2}) measured with near-infrared spectroscopy. Sevoflurane has neuroprotective properties *in vitro* and in animal models. This study was designed to determine cognitive and clinical outcomes after sevoflurane- compared with propofol-based anaesthesia for on-pump cardiac surgery and the impact of decreases in Sc_{O_2} under different anaesthesia regimens.

Cognitive function after sevoflurane- *vs* propofol-based anaesthesia for on-pump cardiac surgery: a randomized controlled trial

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Table 1 Anaesthesia protocol in the study groups. CPB, cardiopulmonary bypass; MAC, mean alveolar concentration; BIS, bispectral index

	I.V. group (PROP)	Volatile group (SEVO)
Induction of anaesthesia	Etomidate 0.2–0.3 mg kg^{-1}, sufentanil 1 μg kg^{-1}, pancuronium 0.07–0.1 mg kg^{-1}	
Maintenance of anaesthesia before and after CPB	Remifentanil 0.2–0.25 μg kg^{-1} min^{-1}, propofol 3–5 mg kg^{-1} h^{-1} achieving a BIS of 40–50	Remifentanil 0.2–0.25 μg kg^{-1} min^{-1}, sevoflurane 0.6–1 MAC (age-adapted) achieving a BIS of 40–50
During CPB	Propofol 3–5 mg kg^{-1} h^{-1} according to BIS (aim 40–50)	

Cognitive function after sevoflurane- *vs* propofol-based anaesthesia for on-pump cardiac surgery: a randomized controlled trial

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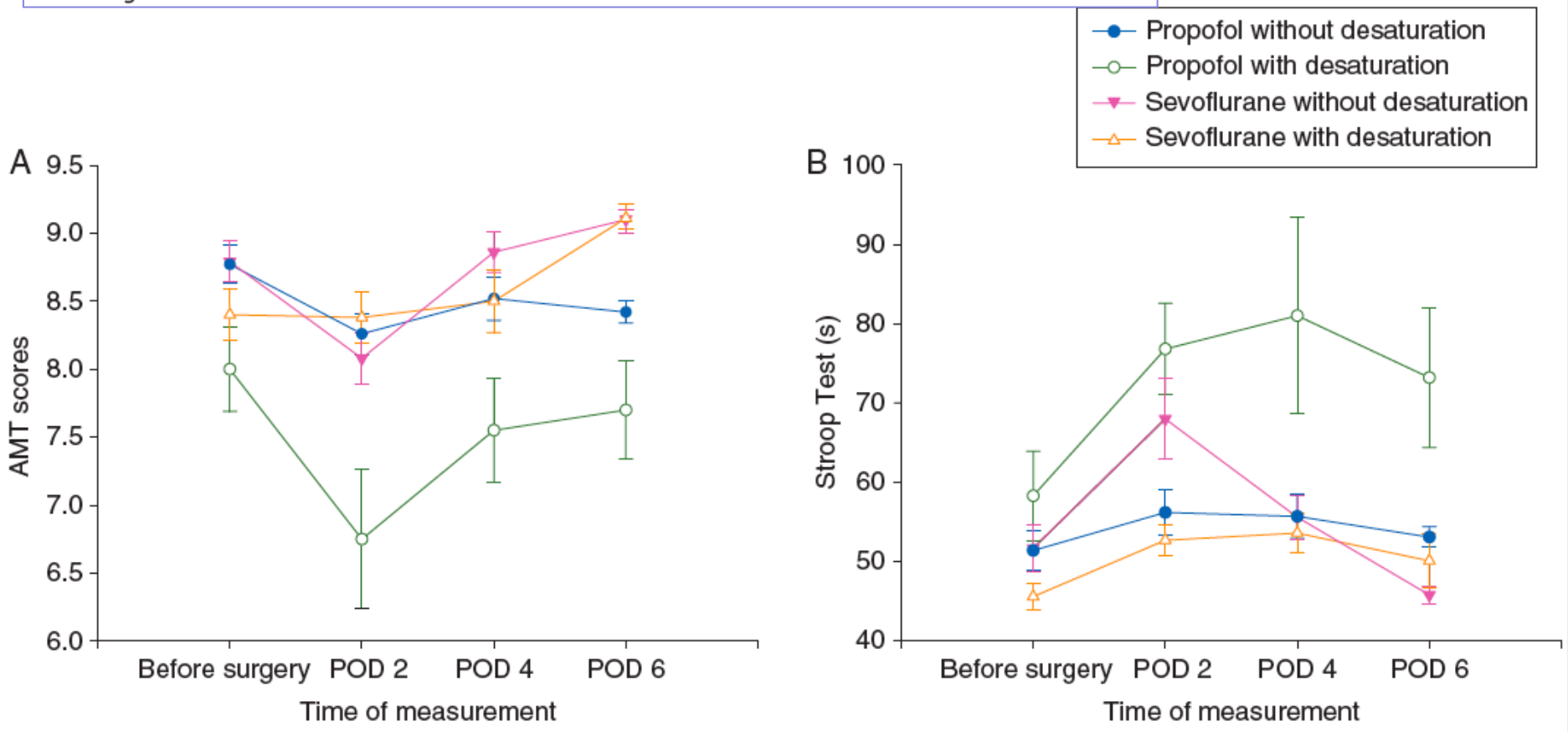

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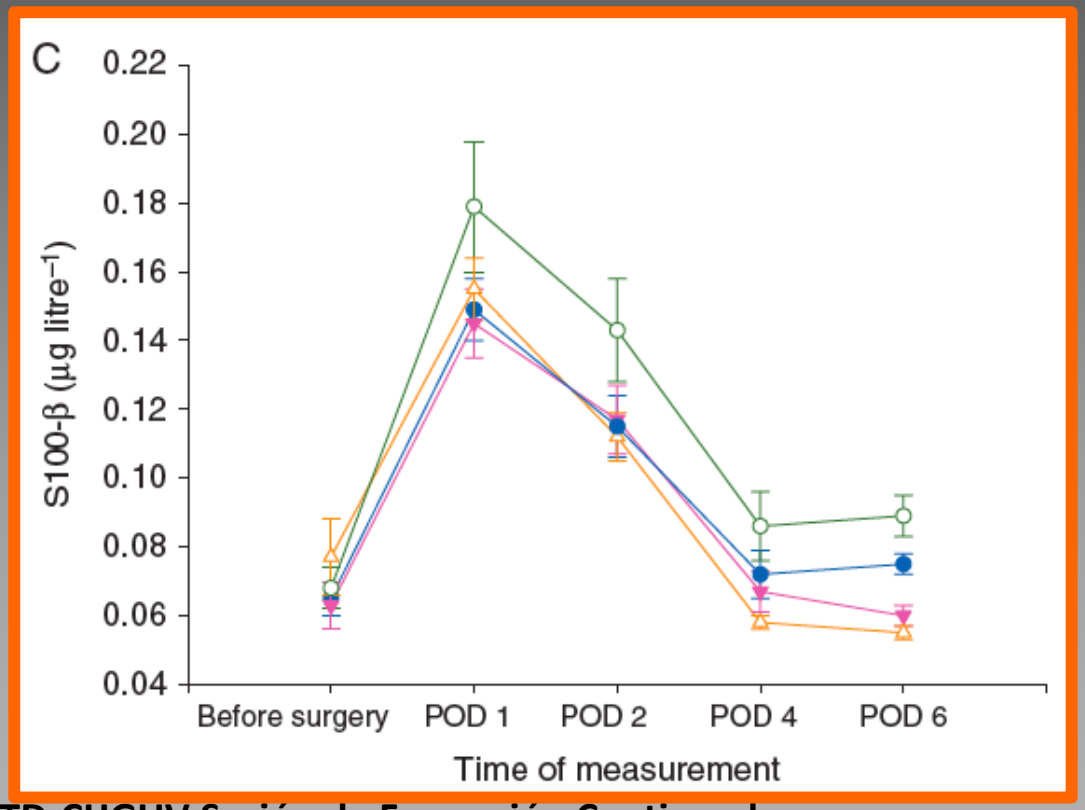
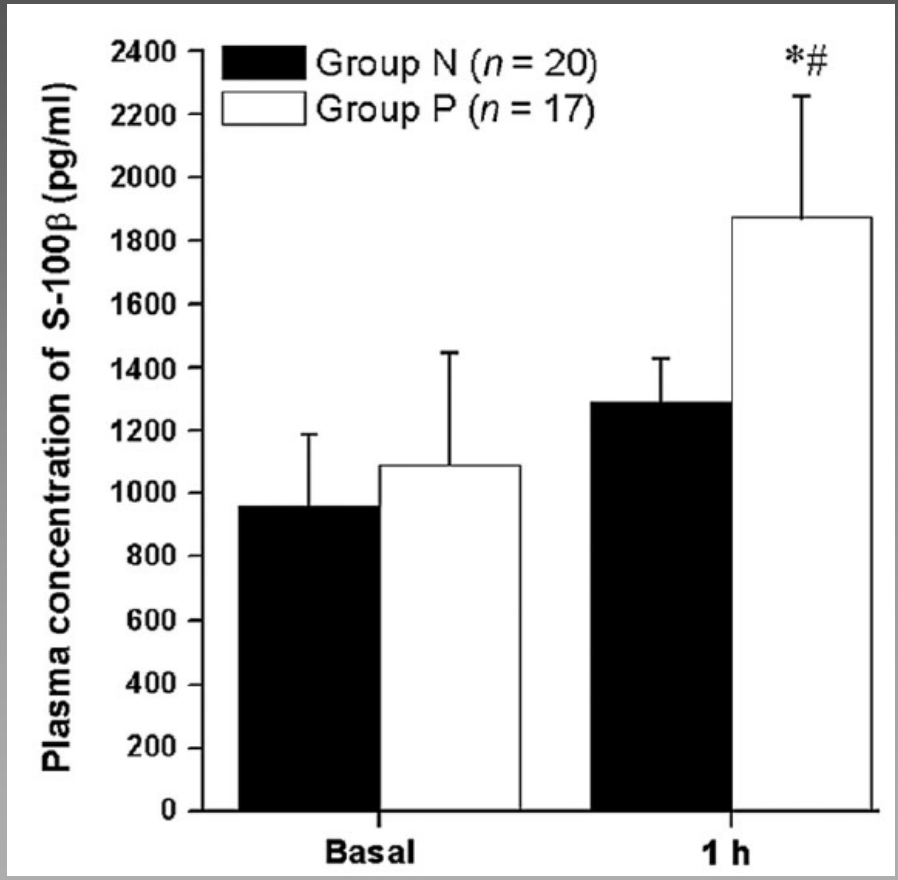
particular risk for intraoperative cerebral insult. A sevoflurane-based anaesthesia was associated with better short-term postoperative cognitive performance than propofol.



Perioperative inflammatory response and protein S-100β concentrations – relationship with post-operative cognitive dysfunction in elderly patients

Acta Anaesthesiologica Scandinavica

Acta Anaesthesiol Scand 2012; **56:** 595–600



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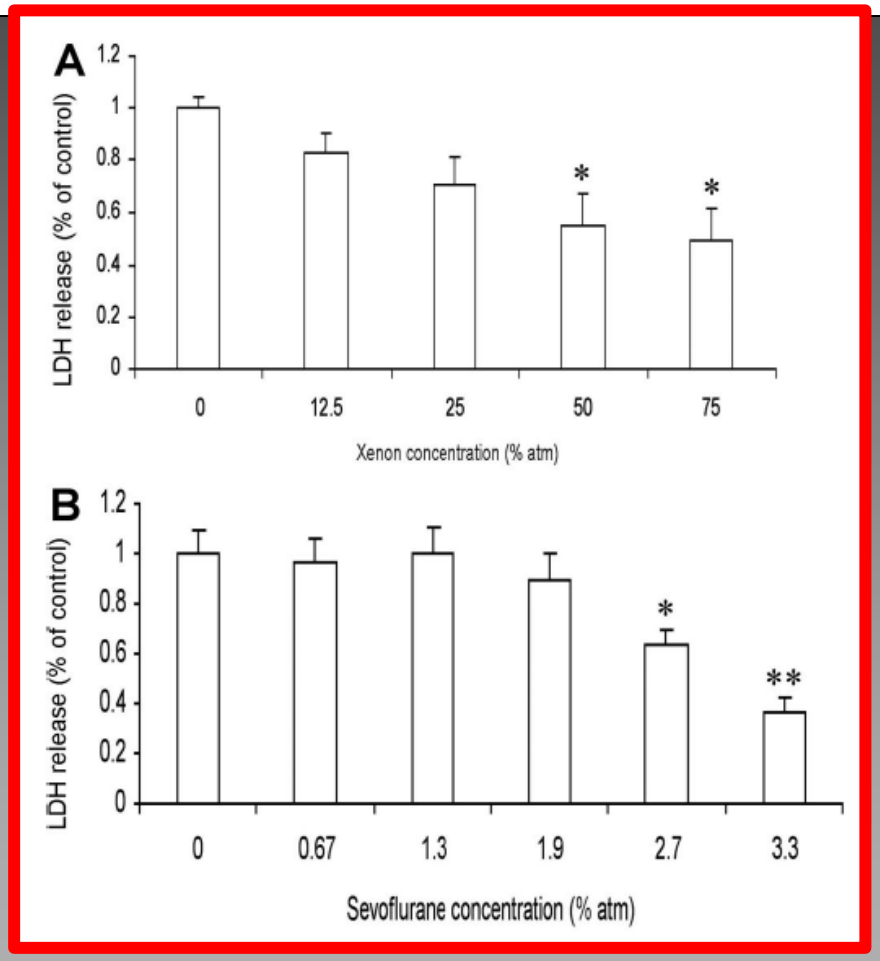
Anesthesiology 2008; 109:782–9

Xenon and Sevoflurane Protect against Brain Injury in a Neonatal Asphyxia Model

Yan Luo, M.D., Daqing Ma, M.D., Ph.D.,† Edmund Ieong, M.B., B.S.,‡ Robert D. Sanders, M.B., B.S.,§ Buwei Yu, M.D.,‖ Mahmuda Hossain, Ph.D.,# Mervyn Maze, M.B., Ch.B., F.R.C.A., F.Med.Sci.***



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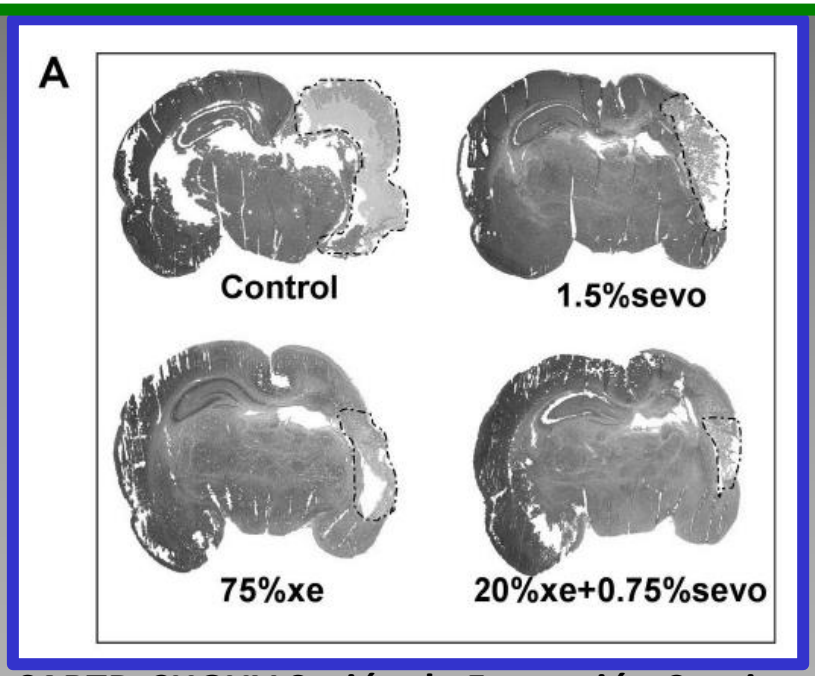
In summary, we have shown that the combination of xenon and sevoflurane can precondition against ischemic injury *in vitro* and *in vivo* and these effects are mediated by PI3K and pCREB signaling. If translatable to



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Trends in Anaesthesia and Critical Care xxx (2013) 1–6

Contents lists available at SciVerse ScienceDirect

Trends in Anaesthesia and Critical Care

journal homepage: www.elsevier.com/locate/tacc

REVIEW

Postoperative delirium and cognitive dysfunction

Regarding the role of anaesthesia, there are some measures that decrease the development of delirium. Some studies have suggested a lower incidence of delirium when inhalational agents are used compared to intravenous ones.[52,57,58] While studies like that carried out by Royse et al.[36] found no difference in delirium rates between patients anaesthetised with propofol and those with sevoflurane. But there is a difference in early postoperative cognitive dysfunction that was significantly higher with propofol than with desflurane (67.5% vs. 49.4%). Another aspect to note about anaesthesia is its depth. In the latest research, the

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Sedation Depth During Spinal Anesthesia and the Development of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Repair

Mayo Clin Proc. 2010;85(1):18-26

FREDERICK E. SIEBER, MD; KHWAJI J. ZAKRIYA, MBBS; ALLAN GOTTSCHALK, MD, PHD;

TABLE 4. **Univariate Predictors of Postoperative Delirium**[a]

Variable	OR (95% CI)	χ^2 test	*P* value[b]
Deep sedation vs light sedation	2.83 (1.20-6.62)	6.13	.01
Average BIS	0.97 (0.954-0.995)	6.64	.01
Duration of surgery	1.007 (0.996-1.019)	1.73	.19
Duration BIS <50	1.011 (1.000-1.023)	3.70	.05
Age	1.045 (0.984-1.108)	2.19	.14
Preoperative dementia[c]	3.56 (1.52-8.32)	8.97	.003
Preoperative Mini-Mental State Examination score	0.86 (0.78-0.95)	10.76	.001
Education	0.84 (0.55-1.26)	0.80	.37
Preoperative ADL	0.72 (0.54-0.98)	5.09	.02
Preoperative IADL	0.88 (0.75-1.02)	2.96	.09
Living independently	0.70 (0.28-1.79)	0.55	.46
Inouye risk	0.66 (0.25-1.76)	0.73	.25
No. of systemic illnesses[d]	1.29 (0.94-1.75)	2.63	.11
Propofol dose	1.01 (0.95-1.09)	0.14	.71
Midazolam dose	0.97 (1.02-1.07)	0.92	.34
Duration of surgery	0.99 (0.98-1.00)	1.73	.19
Conversion to general anesthesia	0.61 (0.16-2.3)	0.52	.47
Use of bone cement	1.10 (0.45-2.69)	0.04	.84
Duration of intraoperative hypotension	0.99 (0.97-1.01)	0.49	.50
Erythrocyte transfusion	1.99 (0.85-4.66)	2.65	.10
Units of packed erythrocytes transfused	1.58 (1.12-2.22)	7.29	.007
≥1 Postoperative complications[e]	2.48 (1.07-5.75)	4.76	.03
No. of postoperative complications[f]	1.50 (1.08-2.09)	6.09	.02
Admission to intensive care unit without prior delirium[f]	8.19 (1.44-46.4)	5.86	.02
Length of intensive care unit stay	1.28 (1.02-1.59)	5.48	.02

Sedation Depth During Spinal Anesthesia and the Development of Postoperative Delirium in Elderly Patients Undergoing Hip Fracture Repair

Mayo Clin Proc. 2010;85(1):18-26

FREDERICK E. SIEBER, MD; KHWAJI J. ZAKRIYA, MBBS; ALLAN GOTTSCHALK, MD, PHD;

CONCLUSION: **The use of light propofol sedation decreased the prevalence of postoperative delirium by 50% compared with deep sedation. Limiting depth of sedation during spinal anesthesia is a simple, safe, and cost-effective intervention for preventing post-operative delirium in elderly patients that could be widely and readily adopted.**

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Valencia 15 de Octubre de 2013

(*J Neurosurg Anesthesiol* 2013;25:33–42)

BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

Matthew T.V. Chan, MBBS, FANZCA, Benny C.P. Cheng, MBBS, FHKCA,† Tatia M.C. Lee, PhD,‡ Tony Gin, MD, FRCA, FANZCA,* and the CODA Trial Group*

TABLE 1. Patient Characteristics at Entry of the Trial

	BIS Group	Routine Care Group	*P*
No. patients	450	452	
Age (y)*	68.1 ± 8.2	67.6 ± 8.3	0.42
Male sex, no. (%)	280 (62.2)	273 (60.4)	
Weight (kg)*	62.0 ± 11.5	61.4 ± 10.7	0.47
ASA status, no. (%)			0.58
1-2	373 (82.8)	382 (84.5)	
3-4	76 (16.9)	70 (15.5)	
Preexisting medical conditions, no. (%)‡			
Cardiovascular	374 (83.1)	330 (73.0)	0.54
Respiratory	75 (16.7)	67 (14.8)	0.70
Endocrine	109 (24.2)	101 (22.3)	0.53
Others	80 (17.8)	87 (19.2)	0.63
Surgery for cancer, no. (%)	338 (75.1)	352 (77.9)	0.39
Duration of anesthesia (h)*	2.1 ± 1.0	2.0 ± 1.1	0.67
Years of education received†	6 (0-22)	6 (0-18)	0.84
Chinese Geriatric Depression Scale†	2 (0-13)	2 (0-14)	0.18
Mini-mental state examination score†	28 (24-30)	28 (24-30)	0.64

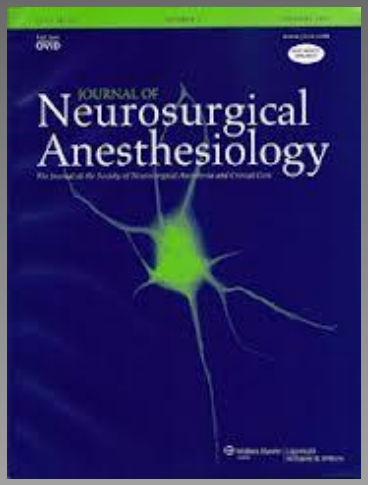

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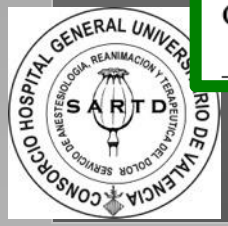
TABLE 2. Comparison of Anesthetic Techniques

	BIS Group	Routine Care Group	*P*
No. patients	450	452	
Propofol dose (mg)	136 ± 30	148 ± 33	0.64
Opioid dose			
Fentanyl (μg/kg)‡	1.6 ± 0.4	1.6 ± 0.3	0.75
No. (%)	400 (88.8)	411 (90.9)	
Morphine (mg)‡	0.12 ± 0.07	0.12 ± 0.06	0.20
No. (%)	373 (83.0)	381 (84.4)	
Midazolam dose (mg)‡	2.5 ± 1.1	2.9 ± 1.4	0.76
No. (%)	33 (7.3)	27 (5.9%)	
Estimated effect site propofol concentration (μg/mL)	2.7 ± 0.9	3.3 ± 1.1	<0.001
No. (%)	45 (10.0%)	54 (11.9%)	0.06
End-tidal volatile concentration (MAC equivalents)‡§	0.57 ± 0.29	0.93 ± 0.34	<0.001
No. (%)	405 (90.0%)	398 (88.1%)	0.06
Nitrous oxide use			
No. (%)	241 (53.5)	259 (57.4)	
End-tidal concentration (%)‡	63 ± 10	65 ± 10	0.70
Time average BIS values‡	53.2 ± 8.9	38.6 ± 6.5	<0.001
Median (interquartile range)	53 (48-57)	36 (31-49)	
Time when BIS < 40 (min)‡	7.2 ± 7.8	22.8 ± 7.3	<0.001
Median (interquartile range)	6.9 (4.4-9.8)	25.7 (7.7-55.8)	
Clinically significant hypotension*			
No. (%)	53 (11.7)	61 (14.0)	0.50
Clinically significant bradycardia†			
No. (%)	17 (3.7%)	20 (4.4%)	0.11



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BIS-guided Anesthesia Decreases Postoperative Delirium and Cognitive Decline

Matthew T.V. Chan, MBBS, FANZCA, Benny C.P. Cheng, MBBS, FHKCA,† Tatia M.C. Lee, PhD,‡ Tony Gin, MD, FRCA, FANZCA,* and the CODA Trial Group*

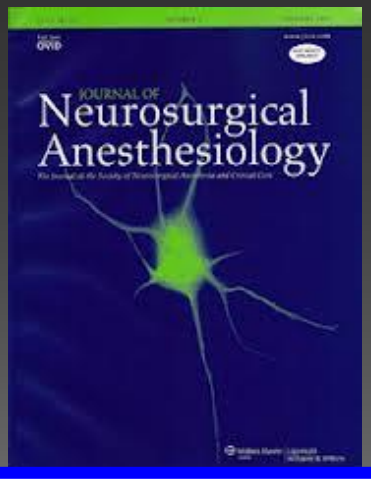

TABLE 4. Postoperative Cognitive Outcomes

	BIS Group	Routine Care Group	Odds Ratio (95% CI)	*P*
Cognitive failure questionnaire at 3 mo after surgery				
No./total no. (%)	29/412 (7.0%)	31/423 (7.3%)	0.95 (0.41-1.98)	0.14
Delirium				
No/total no. (%)	70/450 (15.6%)	109/452 (24.1%)	0.58 (0.41-0.80)	0.01
Postoperative cognitive dysfunction				
1 wk after surgery				
No./total no. (%)	83/382 (21.7%)	93/401 (23.1%)	0.92 (0.66-1.29)	0.06
3 mo after surgery				
No./total no. (%)	42/412 (10.2%)	62/423 (14.7%)	0.62 (0.39-0.97)	0.02

BIS indicates bispectral index.

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Delirium in the postanaesthesia period

Ulf Guenther[a] and Finn M. Radtke[b]

Current Opinion in Anesthesiology 2011, 24:670–675

Key points

- Delirium can be devastating on outcomes such as activity of daily living, cognitive performance and survival.
- Delirogenic factors such as preoperative fasting, deep sedation, disturbed sleep-wake cycle and delirogenic medication, including sedatives, may be avoided.
- Delirium must prompt clinical investigation to uncover medical causes of acute brain dysfunction, such as infection or ischemia.
- Routinely structured delirium screening is the precondition for early detection and treatment.
- Treatment options include cognitive training programmes and possibly anti-inflammatory and anti-psychotic drugs.

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British Journal of Anaesthesia **101** (3): 338–43 (2008)
doi:10.1093/bja/aen193 Advance Access publication July 3, 2008

BJA

Comparison of three scores to screen for delirium in the recovery room

F. M. Radtke[1], M. Franck[1], M. Schneider[1], A. Luetz[1], M. Seeling[1], A. Heinz[2], K. D. Wernecke[3] and C. D. Spies[1]*

for discharge'. Delirium monitoring was performed with the Confusion Assessment Method (CAM), the Delirium Detection Score (DDS), and the Nursing Delirium Screening Scale (Nu-DESC). The *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-IV criteria were used as the gold standard.

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Table 2 Sensitivity and specificity of the CAM, the DDS, and the Nu-DESC compared with the DSM-IV criteria, *n*=21/154 (14%)

	Delirium, *n* (%)	Sensitivity	Specificity
CAM	11 (7%)	0.43	0.98
DDS	4 (3%)	0.14	0.99
Nu-DESC	37 (24%)	0.95	0.87

Table 3 The AUC for the used scores compared with DSM-IV criteria calculated with the published cut-off points. AUC values; *95% confidence interval (CI)

	AUC	CI (95%)	*P*-value
CAM	0.71	0.57–0.85*	0.002
DDS	0.85	0.76–0.94*	<0.001
Nu-DESC	0.93	0.87–1.0*	<0.001

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STUDY PROTOCOL Open Access

Early postoperative cognitive dysfunction and postoperative delirium after anaesthesia with various hypnotics: study protocol for a randomised controlled trial - The PINOCCHIO trial

Bilotta *et al. Trials* 2011, **12**:170

Postoperative delirium (PD), defined as altered perception with hallucinations, acute decline in cognition and attention and inappropriate behaviour, is a severe and relatively common clinical problem. It develops in up to 56% of the patients (higher risk in elderly patients and after orthopaedic surgery) and is related to an increase in hospital morbidity neuro-functional decline, nursing time per patient, per-day hospital costs, length of hospital stay, rates of nursing home placement and mortality rates

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The PINOCCHIO study is a multicentre, double-blind, phase II, prospective, randomized, controlled clinical trial, designed to evaluate postoperative delirium rate after general anaesthesia with various hypnotics in patients undergoing surgical procedures other than cardiac or brain surgery. A secondary end point is to detect whether delayed postoperative cognitive recovery is related to an increased risk of PD.

STUDY PROTOCOL Bilotta *et al. Trials* 2011, **12**:170 Open Access

Early postoperative cognitive dysfunction and postoperative delirium after anaesthesia with various hypnotics: study protocol for a randomised controlled trial - The PINOCCHIO trial

Table 2 The Rancho Los Amigos Scale (RLAS)

Level I	No response to pain, touch, sound or sight
Level II	Generalized reflex response to pain
Level III	Localized response. Blinks to strong light, turns toward/ away from sound, responds to physical discomfort, inconsistent response to commands
Level IV	Confused/Agitated. Alert, performs motor activities but behavior is non purposeful, extremely short attention span
Level V	Confused/Non agitated. Gross attention to environment, highly distractible, inappropriate verbalization
Level VI	Confused/Appropriated. Inconsistent orientation to time and place, consistently follows simple directions
Level VII	Automatic/Appropriated. Skills noticeably deteriorated
Level VIII	Purposeful/Appropriate

STUDY PROTOCOL Bilotta *et al. Trials* 2011, **12**:170 Open Access

Early postoperative cognitive dysfunction and postoperative delirium after anaesthesia with various hypnotics: study protocol for a randomised controlled trial - The PINOCCHIO trial

Table 1 The Short Orientation Memory Concentration Test

What is the current year?	Correct answer scores: 4 Incorrect answer score: 0
What is the current month?	Correct answer scores: 3 Incorrect answer score: 0
What time is it?	Correct answer scores: 3 Incorrect answer score: 0
Count backwards from 20 to 1	Max score 4
Say the months of the year backwards	Max score 4
Repeat the information given in the preceding sentence	Max score 10

STUDY PROTOCOL Bilotta *et al. Trials* 2011, **12**:170 Open Access

Early postoperative cognitive dysfunction and postoperative delirium after anaesthesia with various hypnotics: study protocol for a randomised controlled trial - The PINOCCHIO trial

Table 3 The Nursing Delirium Screening Scale (Nu-DESC)

	Symptoms	Symptoms Rating 0 = no symptoms 1 = mild symptoms 2 = pronounced symptoms
1	**Disorientation** Verbal or behavioural manifestation of not being oriented to time or place or misperceiving persons in the environment.	
2	**Inappropriate behaviour** Behaviour inappropriate to place or for the person; e.g., pulling at tubes or dressings, attempting to get out of bed when that is contraindicated, and the like.	
3	**Inappropriate communication** Communication inappropriate to place or for the person; e.g., incoherence, noncommunicativeness, nonsensical or unintelligible speech.	
4	**Illusions/Hallucinations** Seeing or hearing things that are not there; distortions of visual objects.	
5	**Psychomotor retardation** Delayed responsiveness, few or no spontaneous actions/words; e.g., when the patient is prodded, reaction is deferred or the patient is unarousable	
	Total Score	
	Delirium	≥ 2

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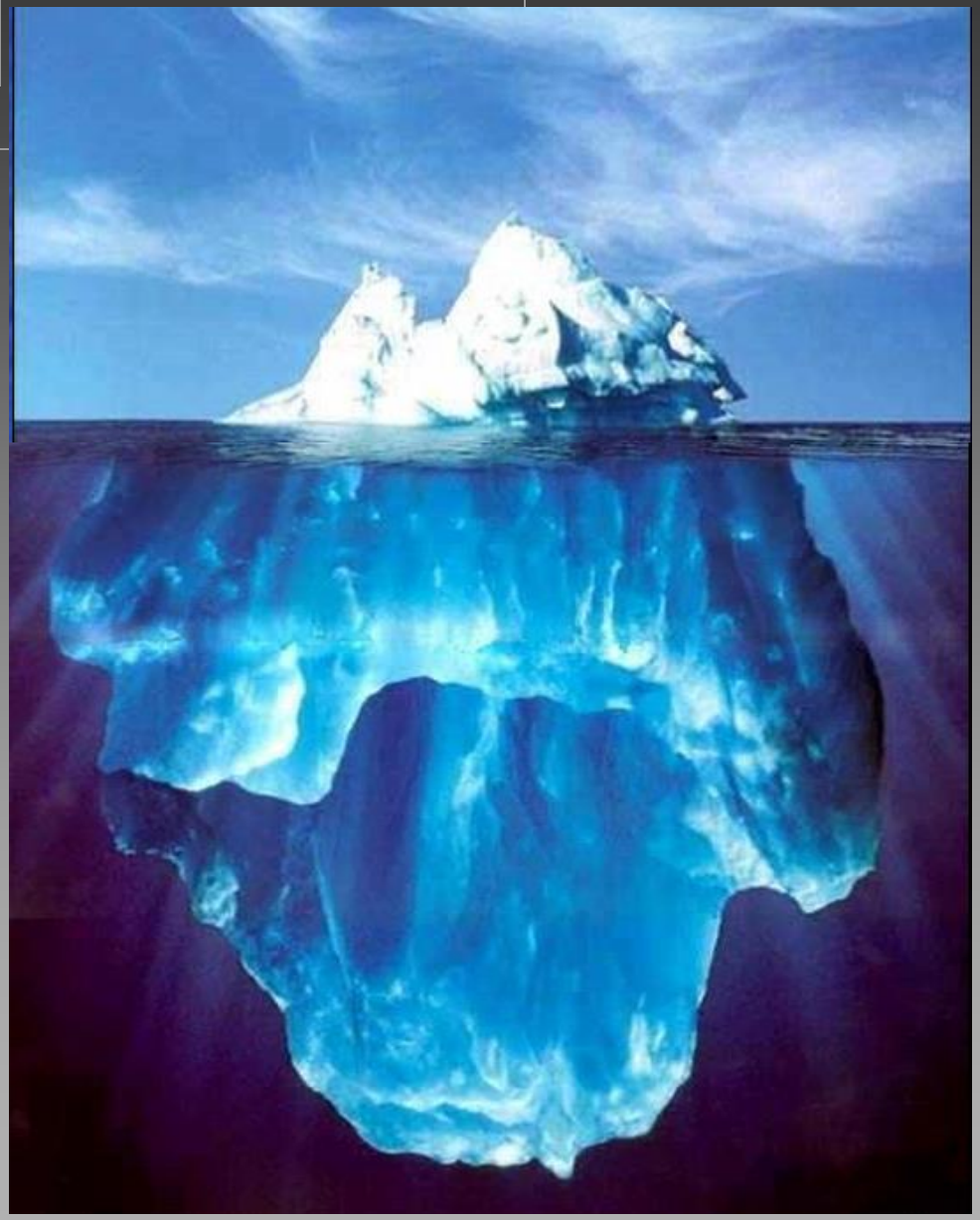
Early postoperative cognitive dysfunction and postoperative delirium after anaesthesia with various hypnotics: study protocol for a randomised controlled trial - The PINOCCHIO trial

In conclusion, the results of this comparative anaesthesiological trial should allow us to detect whether the use of each of the three hypnotics tested is related to a significant difference in PD rate. This information could ultimately help in selecting the most appropriate hypnotic to maintain anaesthesia in a specific subgroup of patients and especially those at high risk for PD.



MOUNT SINAI JOURNAL OF MEDICINE 79:75–94, 2012

Developmental Disability in the Young and Postoperative Cognitive Dysfunction in the Elderly After Anesthesia and Surgery: Do Data Justify Changing Clinical Practice?

James E. Cottrell, MD, and John Hartung, PhD

State University of New York at Downstate Medical Center, Brooklyn, NY

Most of us have heard friends or relatives say something like "since he had open-heart surgery, he's not the same . . . he can't think as well, he's not as happy."

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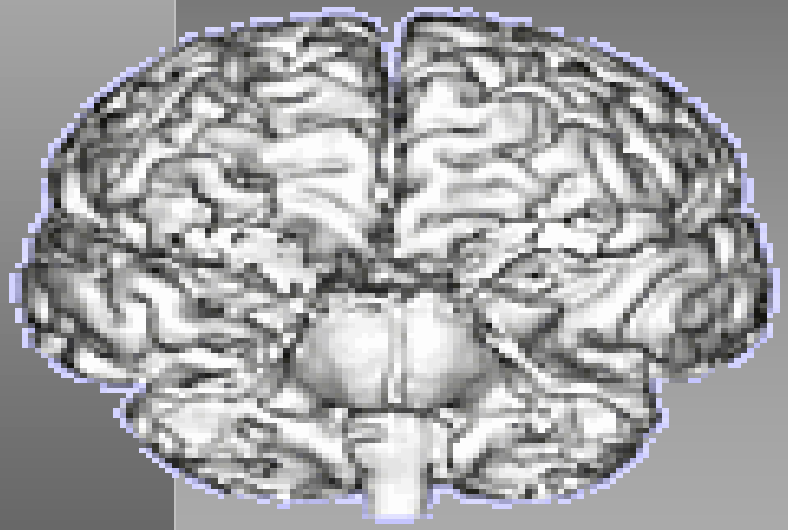

Muchas Gracias

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