Integration of Neuromonitoring Technologies into Practice: Opportunities Ahead

Andrew Davidson

No disclosures

Outline

- What are we measuring
- EEG depth monitoring
- Paediatric anaesthesia
- Nocicpeption monitors
- Future

What are we trying to do?

Measure something → **Titrate your drugs** → **Better outcomes**

Measure something	Titrate your drugs	Better outcomes
Depth of anaesthesia	Sevoflurane	Faster awakening
Nociception	Propofol	Less delirium
Brain concentration	Opioids	Less awareness
	? Remimazolam	Less toxicity
	? Dexmedetomidine	

Questions

- What are we measuring, and can we measure it?
- Will measuring and titrating improve outcomes?

- How are children different?

What are we trying to do?

Measure something → Titrate your drugs → Better outcomes

Measure something	Titrate your drugs	Better outcomes
Depth of anaesthesia	Sevoflurane	Faster awakening
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Brain concentration	Opioids	Less awareness
	? Remimazolam	Less toxicity
	? Dexmedetomidine	

What is anaesthesia depth?

Anaesthesia

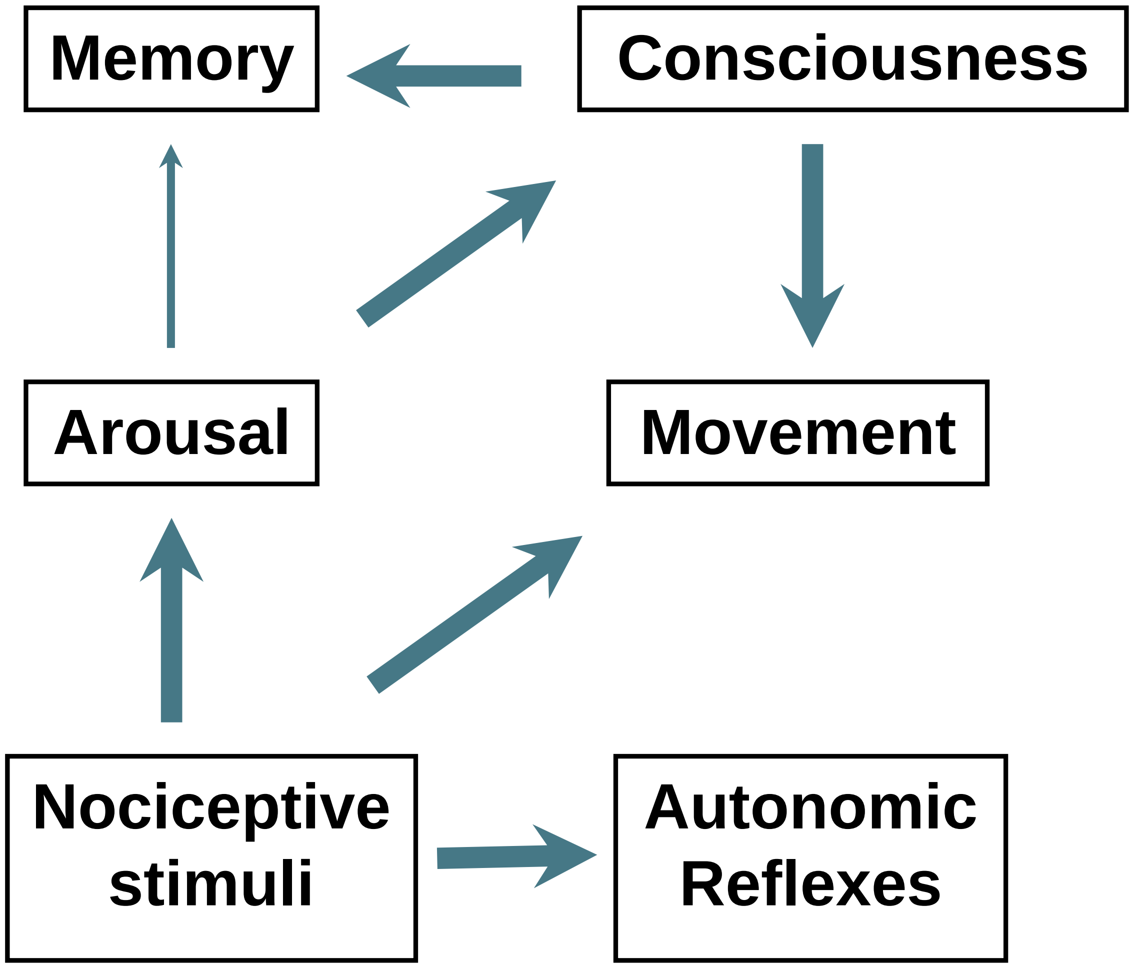
Memory

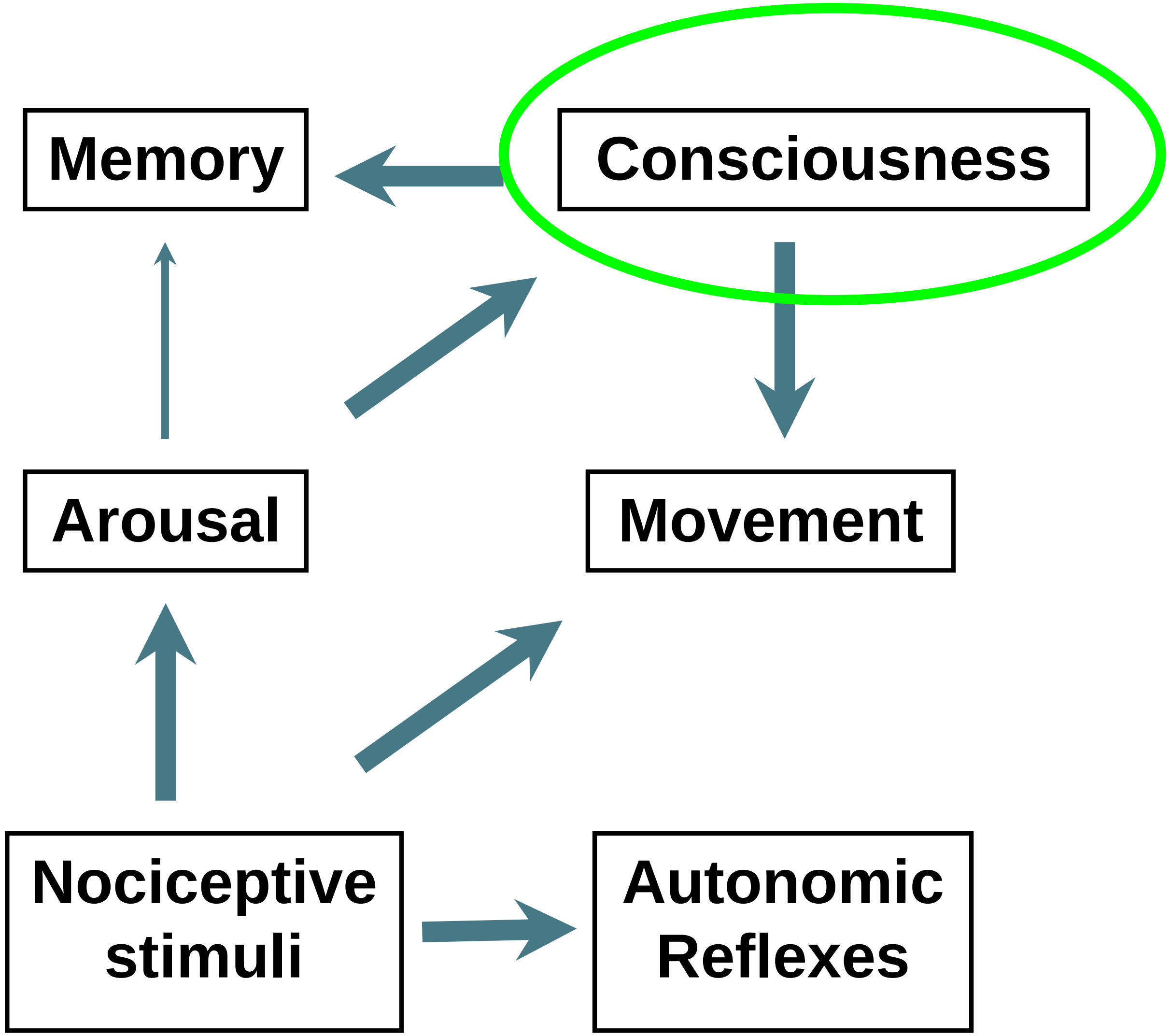
Consciousness

Movement

Autonomic Reflexes

The anaesthesia construct




Memory
Consciousness
Arousal
Movement
Nociceptive stimuli
Autonomic Reflexes

Measuring consciousness

- EEG is *not* a *direct* measure of consciousness
- No EEG “ signature” which indicates consciousness
- Some patterns which preclude it
  - Alpha band
  - Burst suppression
  - High relative delta activity

“Dysaesthesia”

- Using isolated forearm technique, many subjects respond to command under anaesthesia
- Do not move spontaneously
- Do not remember anything

- Not “thinking”
- Responsive but not conscious

Editorial

Monitoring (un)consciousness: the implications of a new definition of ‘anaesthesia’

What should we properly monitor, when we monitor the brain for ‘anaesthesia’? Any answer is likely to depend on what we mean by ‘anaesthesia’. The article by Escallier et al. in this issue of *Anaesthesia* is an important review of the status of processed EEG (pEEG) monitoring in anaesthesia [1]. Central to the role of pEEG (or any other type) of ‘depth of anaesthesia’ monitors is their putative ability to detect when a paralysed patient is suitably anaesthetised or not; apparently a simple binary decision-making process. Yet, this article contains a profound sentence whose implications, if widely accepted, are likely to change our entire view of ‘anaesthesia’, for reasons I will explain in this editorial. The apparently innocuous sentence is: “*There is a growing consensus that intra-operative awareness is a spectrum of brain states*” [my emphasis]. The following questions immediately come to mind: what is the basis for this new consensus? What does this consensus imply for mechanisms of anaesthesia? And what does it imply for monitoring of the anaesthetic state?

The emerging consensus that intra-operative awareness is a spectrum of brain states

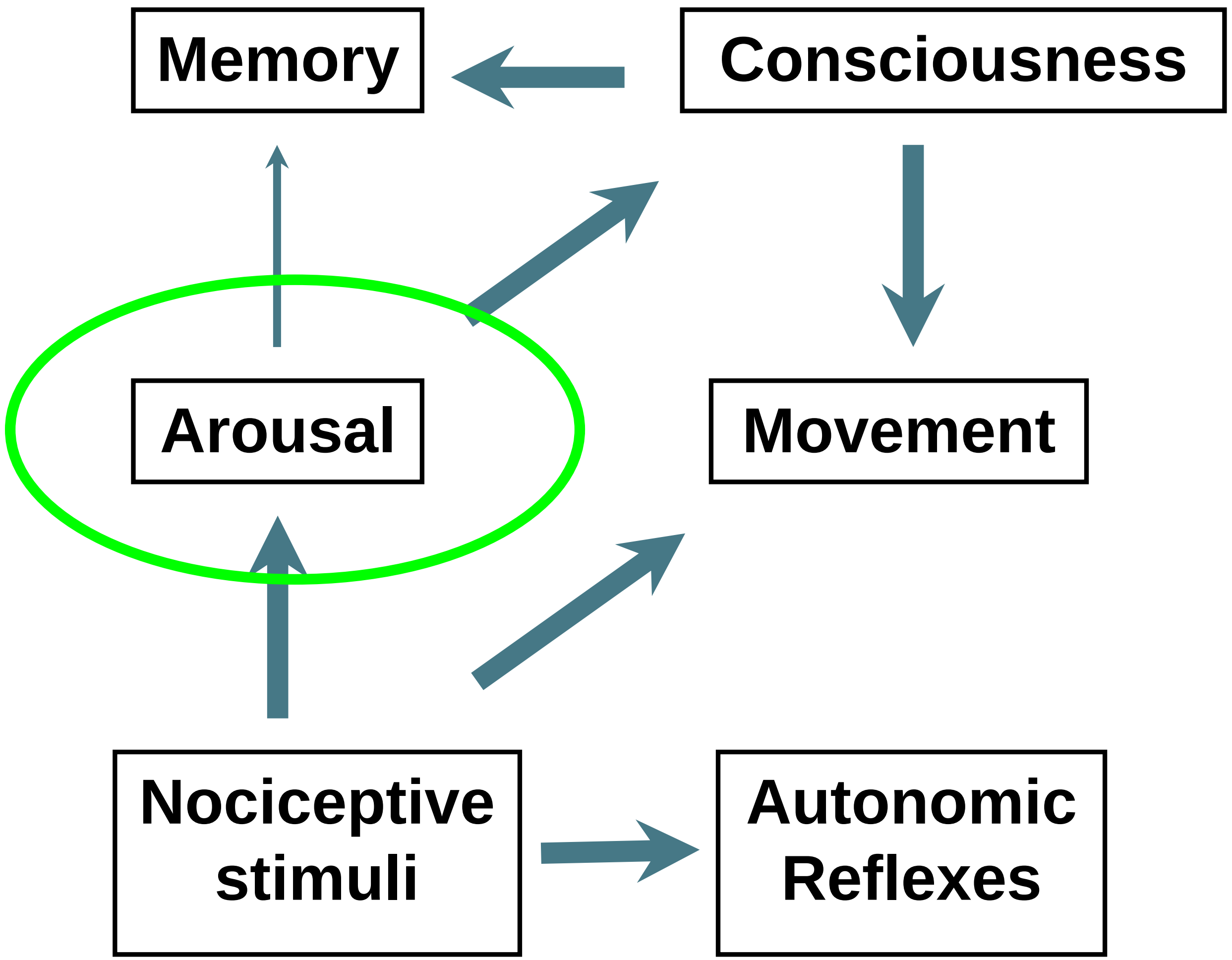
Traditionally, anaesthesia has been regarded as an all-or-nothing, binary phenomenon. This view was most clearly proposed by Prys-Roberts when he wrote: “*There cannot be degrees of anaesthesia nor for that matter can there be variable depths of anaesthesia*” [2], a statement that was unsupported by other references but a sentiment that became nevertheless widely repeated in standard texts [3]. Superficially, this makes sense: either you are anaesthetised or you are not. Once you are anaesthetised, it is difficult to conceive then how you can be ‘more’ anaesthetised. It is not (to borrow Sleigh’s phrase [4]) as if ‘the patient is a submarine’!

Yet, things are never really so simple and this traditional view is now challenged in several ways. Assuming that anaesthetic drugs act at protein channel receptor targets, we know that dose-response pharmacology is not binary or all-or-nothing. Rather, the drug-dose-response relationship is characteristically continuous, described by relatively simple models in which the drug effect is non-linearly proportional to drug concentration, up to some maximum receptor effect. At some concentration of drug lower than this maximum, the active drug-receptor combination reaches a threshold that triggers the intended response (in this case, ‘anaesthesia’). If there were no variability in individual organism sensitivity or receptor state, then all animals of a species would become anaesthetised at exactly the same anaesthetic concentration. We know that this is not true: at a given clinically relevant concentration, there will always be some proportion of animals not anaesthetised (this proportion dependent upon the steepness of the population ‘dose-response’ relationship for the drug) [5]. In this way, Dilger has elegantly summarised how continuous dose-response relationships at molecular level can translate into near (but not quite) binary relationships at population level [6] (Fig. 1).

Figure 1 also raises another question. Even if anaesthesia is

Consciousness

- Hard to define
- Cannot measure directly with EEG

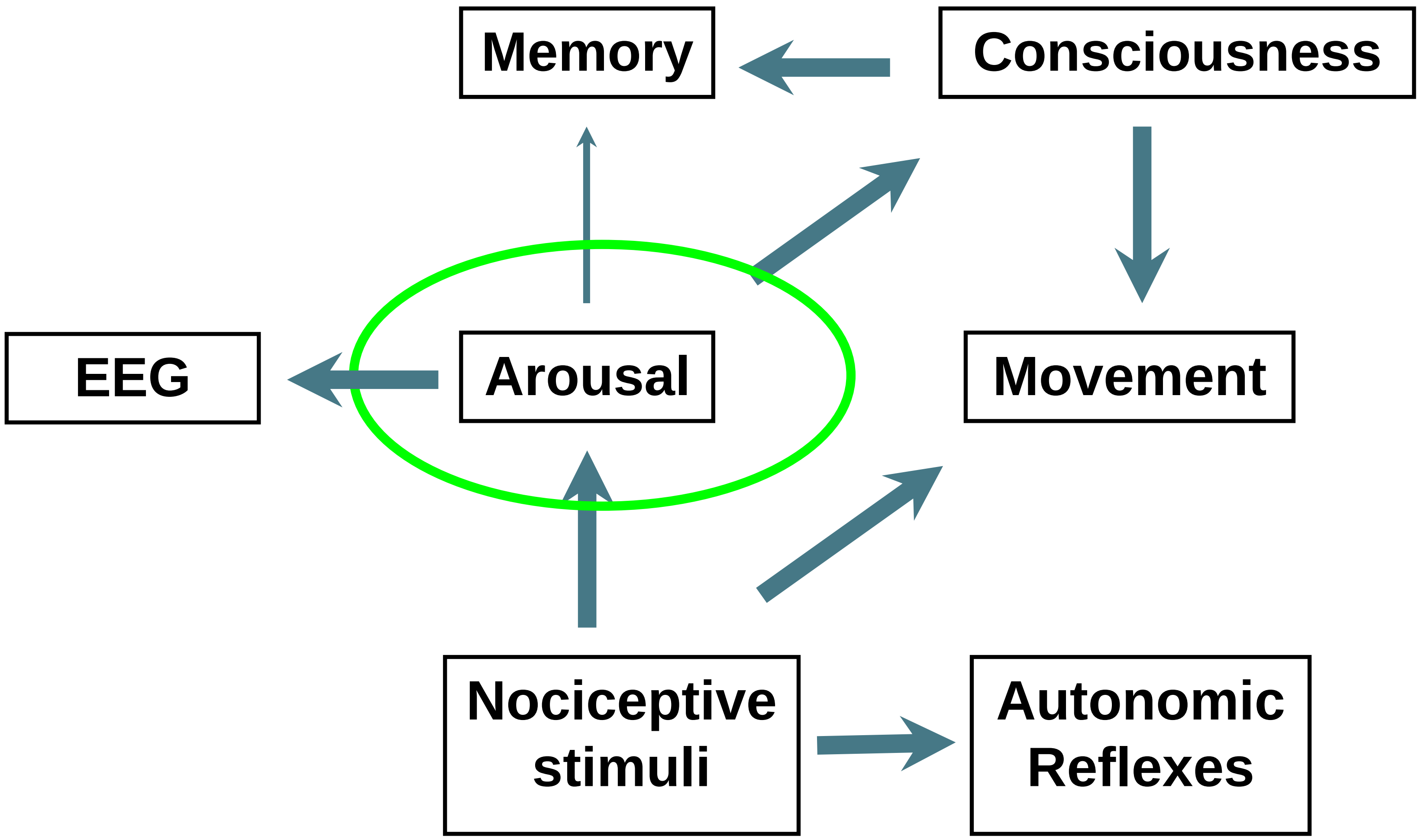

Memory
Consciousness
Arousal
Movement
Nociceptive stimuli
Autonomic Reflexes

Is there a "Depth" of arousal

- If you have a low concentration of an anaesthetic and you provide a stimulus the patient may wake up, but not at a higher concentration, implying different levels of "rousability"

- Similarly, if you provide a surgical stimulus to an unconscious patient then you may see EEG changes

- Increasing concentration of anaesthetic changes the EEG
  - Does this reflect changing the underlying arousal?
  - Or, is it just a direct drug effect?


Memory
Consciousness
EEG
Arousal
Movement
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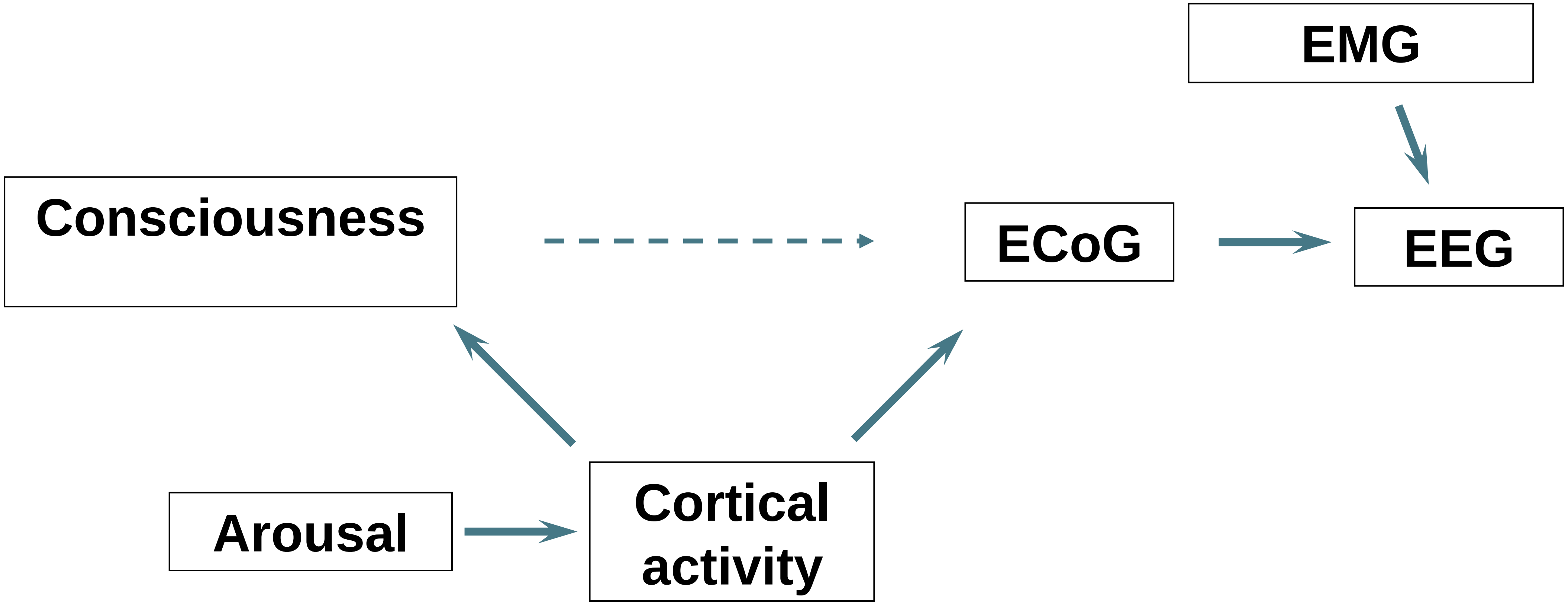
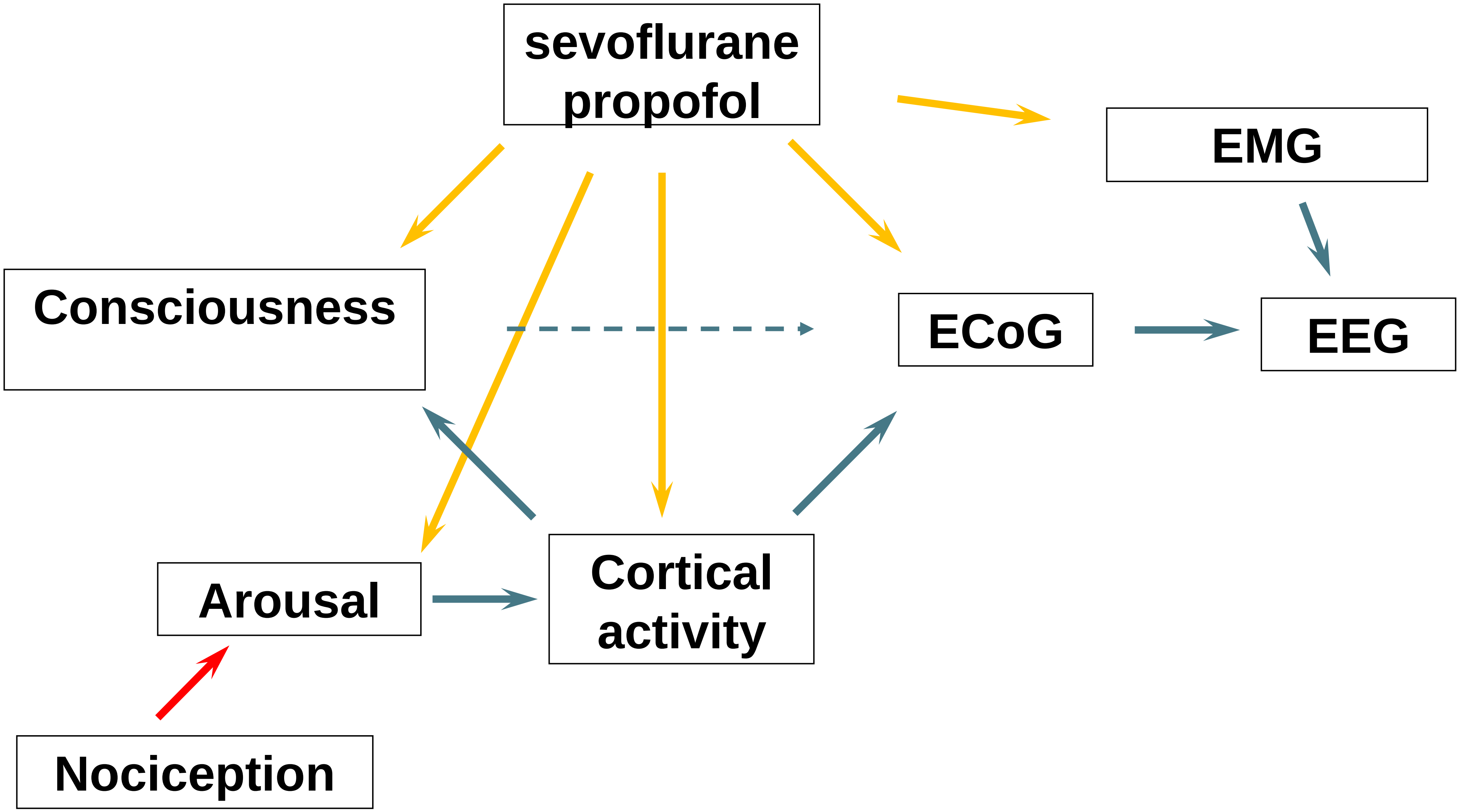
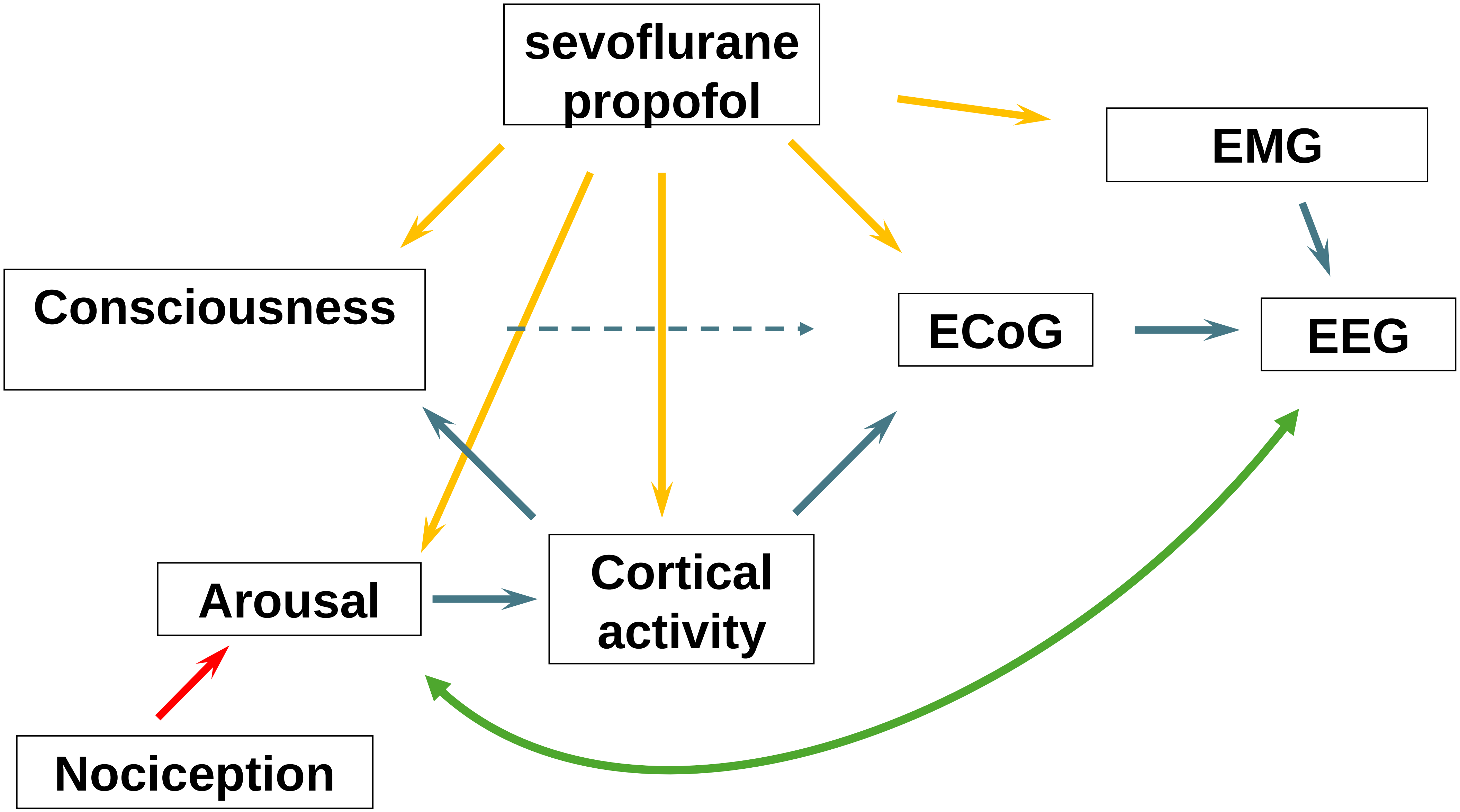
stimuli
Autonomic
Reflexes

Putting it all together




sevoflurane
propofol
EMG
Consciousness
ECoG
EEG
Arousal
Cortical activity
Nociception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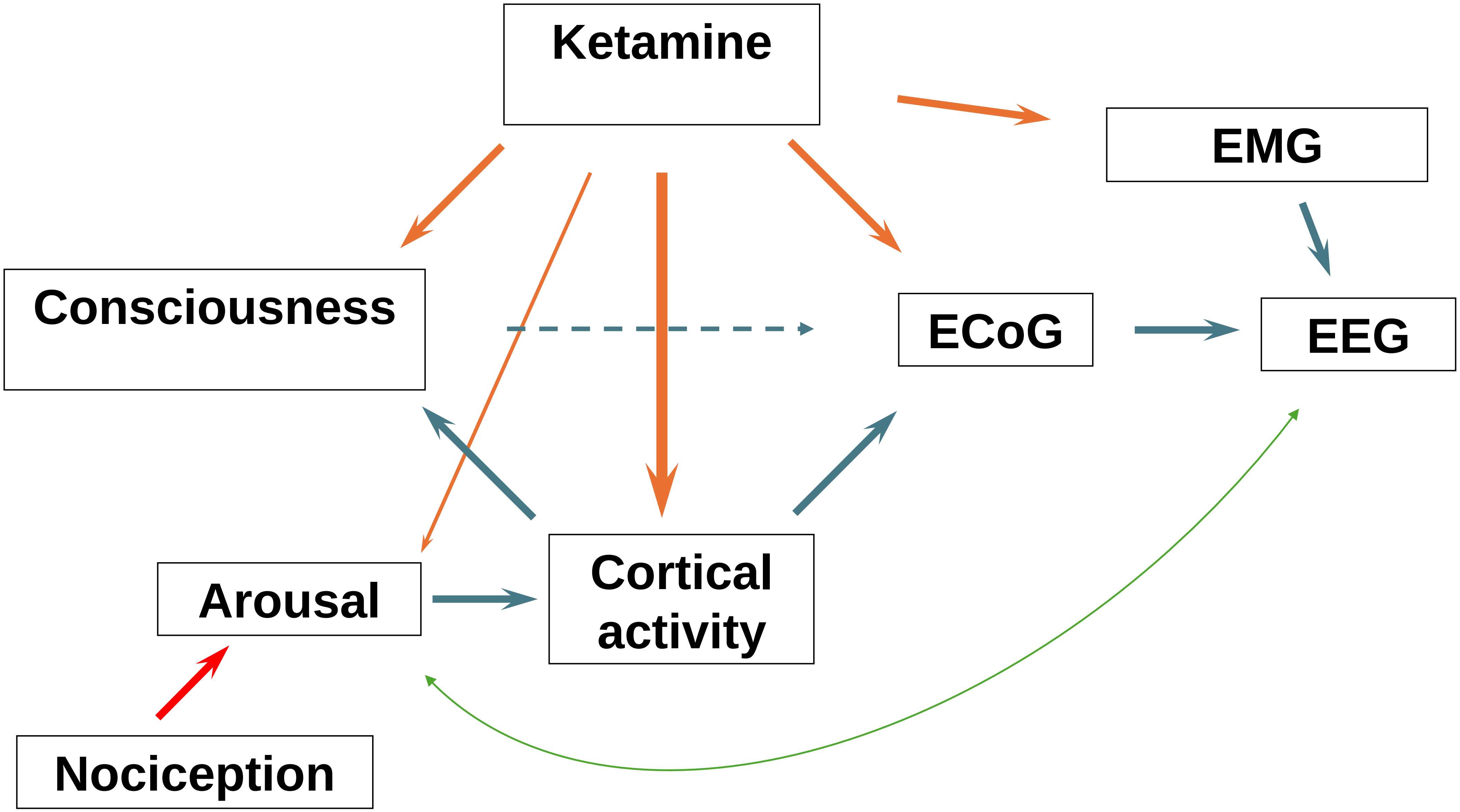


Ketamine
EMG
Consciousness
ECoG
EEG
Cortical activity
Arousal
Nociception

Anaesthesia depth

- A useful but abstract construct
- EEG can measure anaesthesia depth

- Probably measuring underlying arousal
- Indirectly give you an indication of the likelihood of being conscious
- Agent dependent

Processed EEG monitors

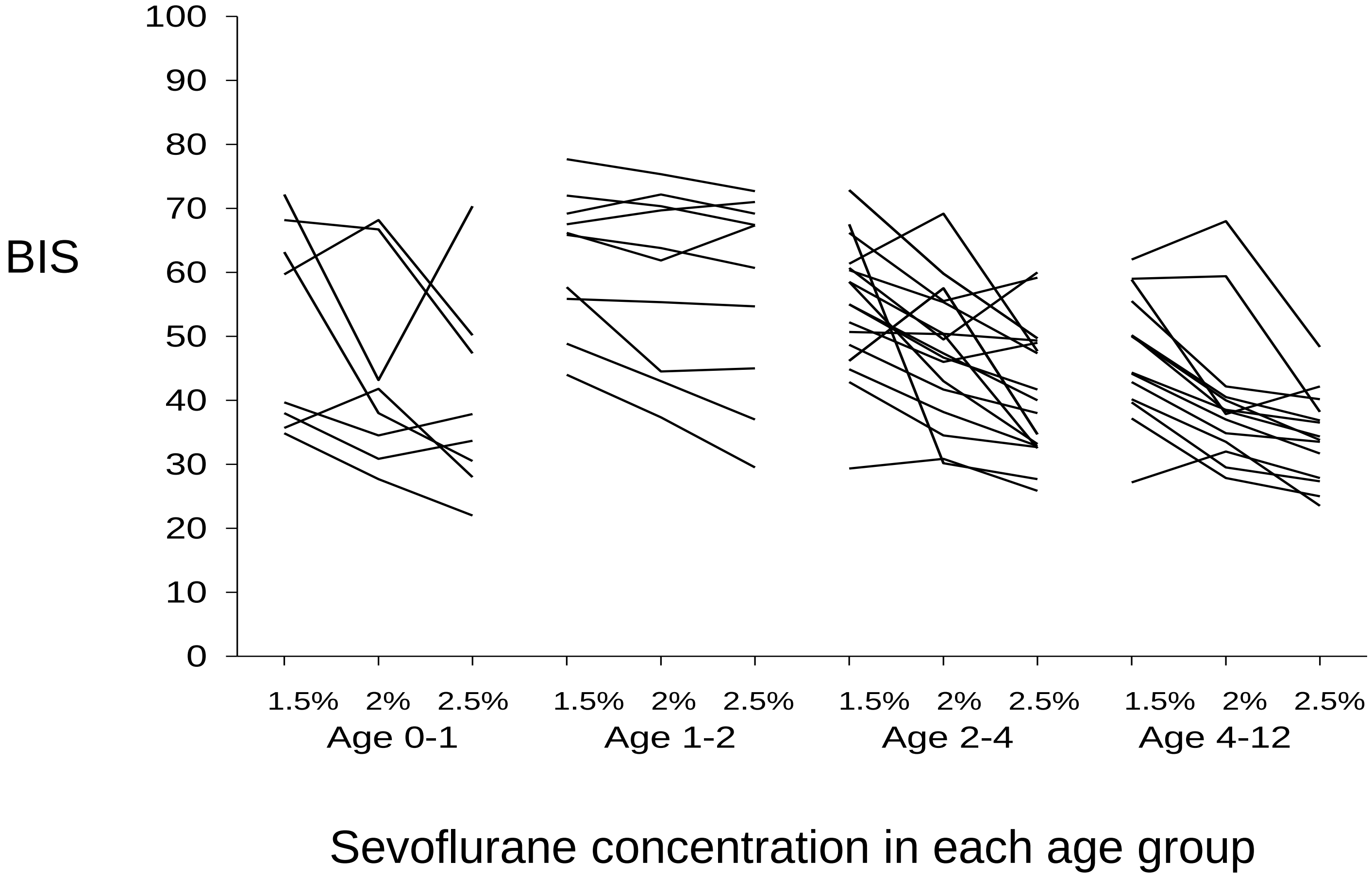
- BIS
- Narcotrend
- Patient State Index (Sedline)
- Entropy

- Power frequency relationships
- Burst suppression
- Chaos (entropy)

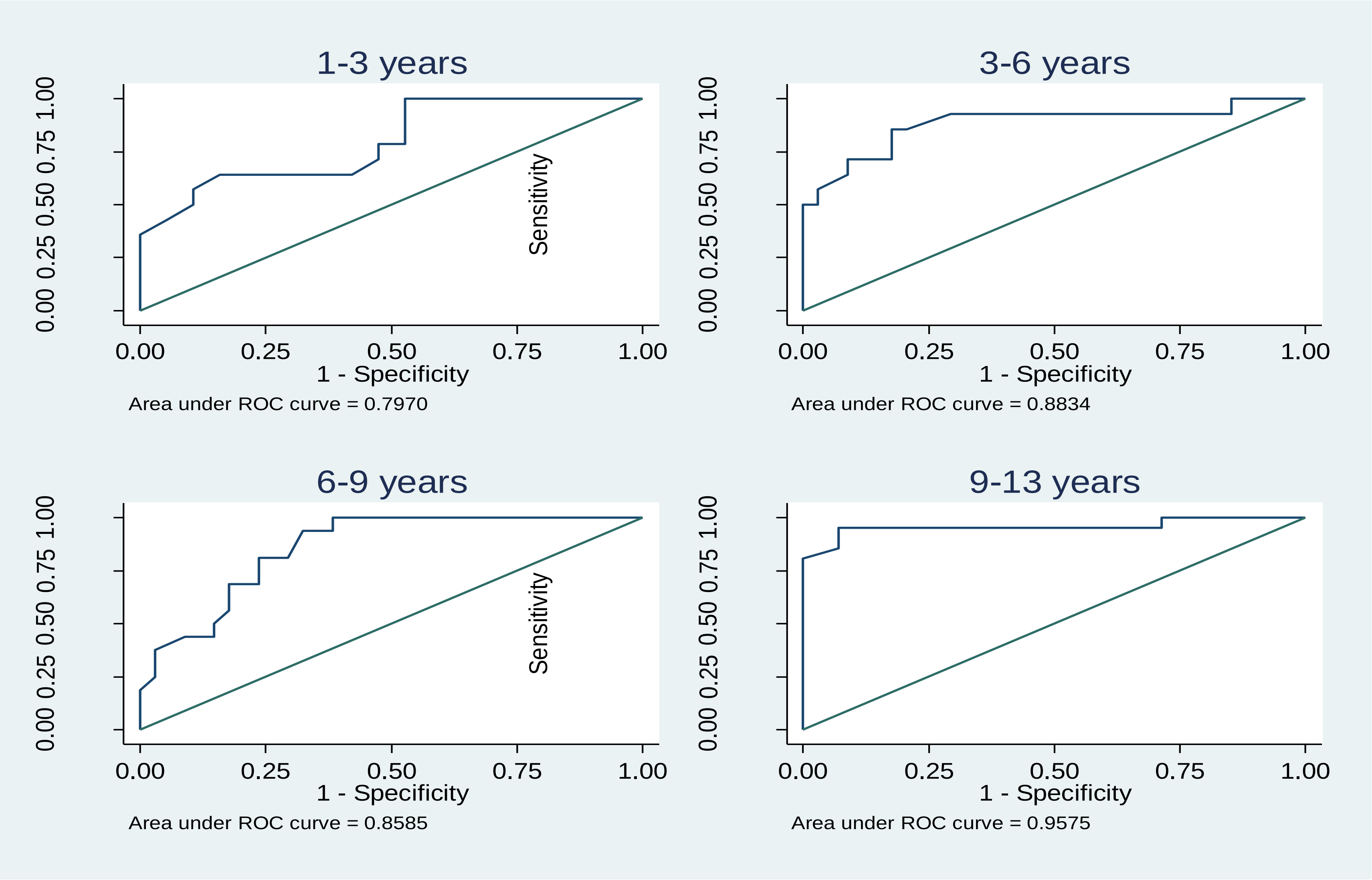
- Dimensionless number

Do they work in children?

BIS “works” in older children



BIS and consciousness



Davidson et al Anaesth Int Care 2008

Older children: > 1-2 years

- EEG changes during anaesthesia in a way similar to adults

- All “work” in older children
- Indices decrease with increasing dose of hypnotic
- Differentiate between conscious and unconscious

EEG during anaesthesia in children up to 3yrs

- 90 children aged 0-3yrs
- Multichannel EEG during sevoflurane anaesthesia

- Delta oscillations in all ages
- Theta and alpha appear at about 4 months
- Alpha oscillations increase up to 10 months
- Alpha frontal oscillations become coherent at about 10 months


BJA

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Neuroscience and Neuroanaesthesia

Electroencephalographic markers of brain development during sevoflurane anaesthesia in children up to 3 years old

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Abstract

Background: General anaesthetics generate spatially defined brain oscillations in the EEG that relate fundamentally to neural-circuit architecture. Few studies detailing the neural-circuit activity of general anaesthesia in children have been described. The study aim was to identify age-related changes in EEG characteristics that mirror different stages of early human brain development during sevoflurane anaesthesia.

Methods: Multichannel EEG recordings were performed in 91 children aged 0–3 yr undergoing elective surgery. We mapped spatial power and coherence over the frontal, parietal, temporal, and occipital cortices during maintenance anaesthesia.

Results: During sevoflurane exposure: (i) slow–delta (0.1–4 Hz) oscillations were present in all ages, (ii) theta (4–8 Hz) and alpha (8–12 Hz) oscillations emerge by ~4 months, (iii) alpha oscillations increased in power from 4 to 10 months, (iv) frontal alpha-oscillation predominance emerged at ~6 months, (v) frontal slow oscillations were coherent from birth until 6 months, and (vi) frontal alpha oscillations became coherent ~10 months and persisted in older ages.

Conclusions: Key developmental milestones in the maturation of the thalamo-cortical circuitry likely generate changes in EEG patterns in infants undergoing sevoflurane general anaesthesia. Characterisation of anaesthesia-induced EEG oscillations in children demonstrates the importance of developing age-dependent strategies to monitor properly the brain states of children receiving general anaesthesia. These data have the potential to guide future studies investigating neurodevelopmental pathologies involving altered excitatory–inhibitory balance, such as epilepsy or Rett syndrome.

Keywords: anaesthesia; general; child; development

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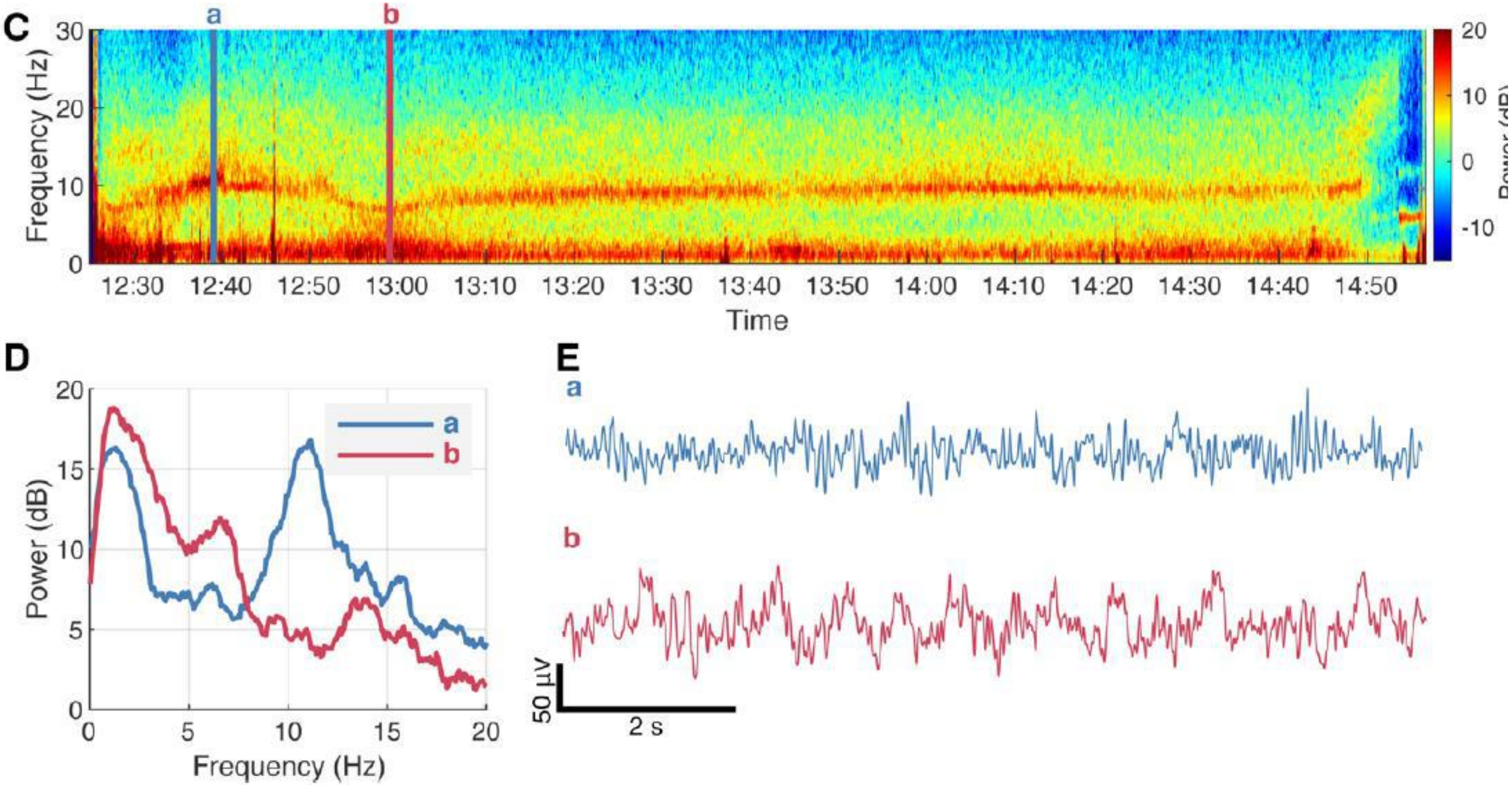
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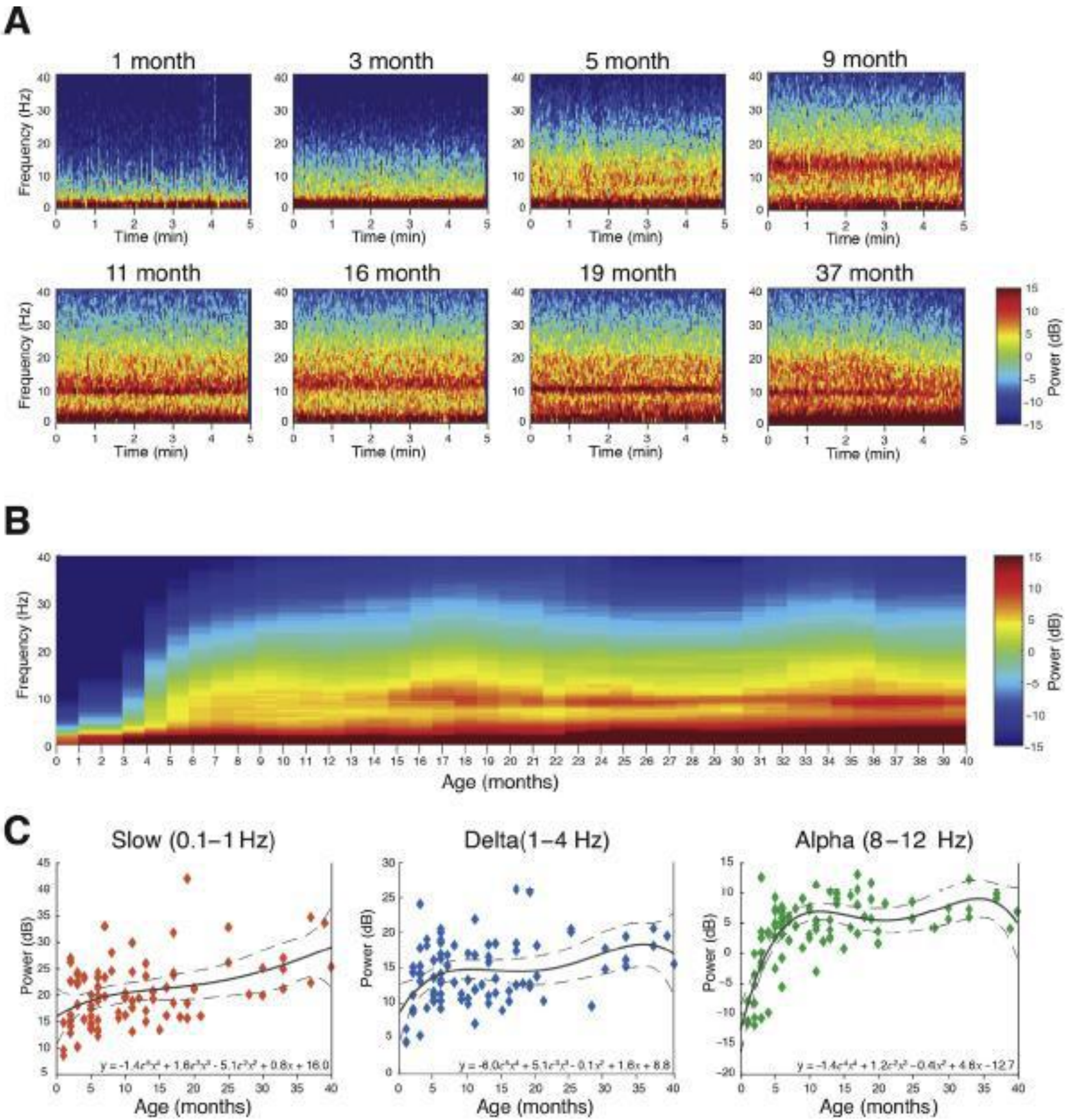
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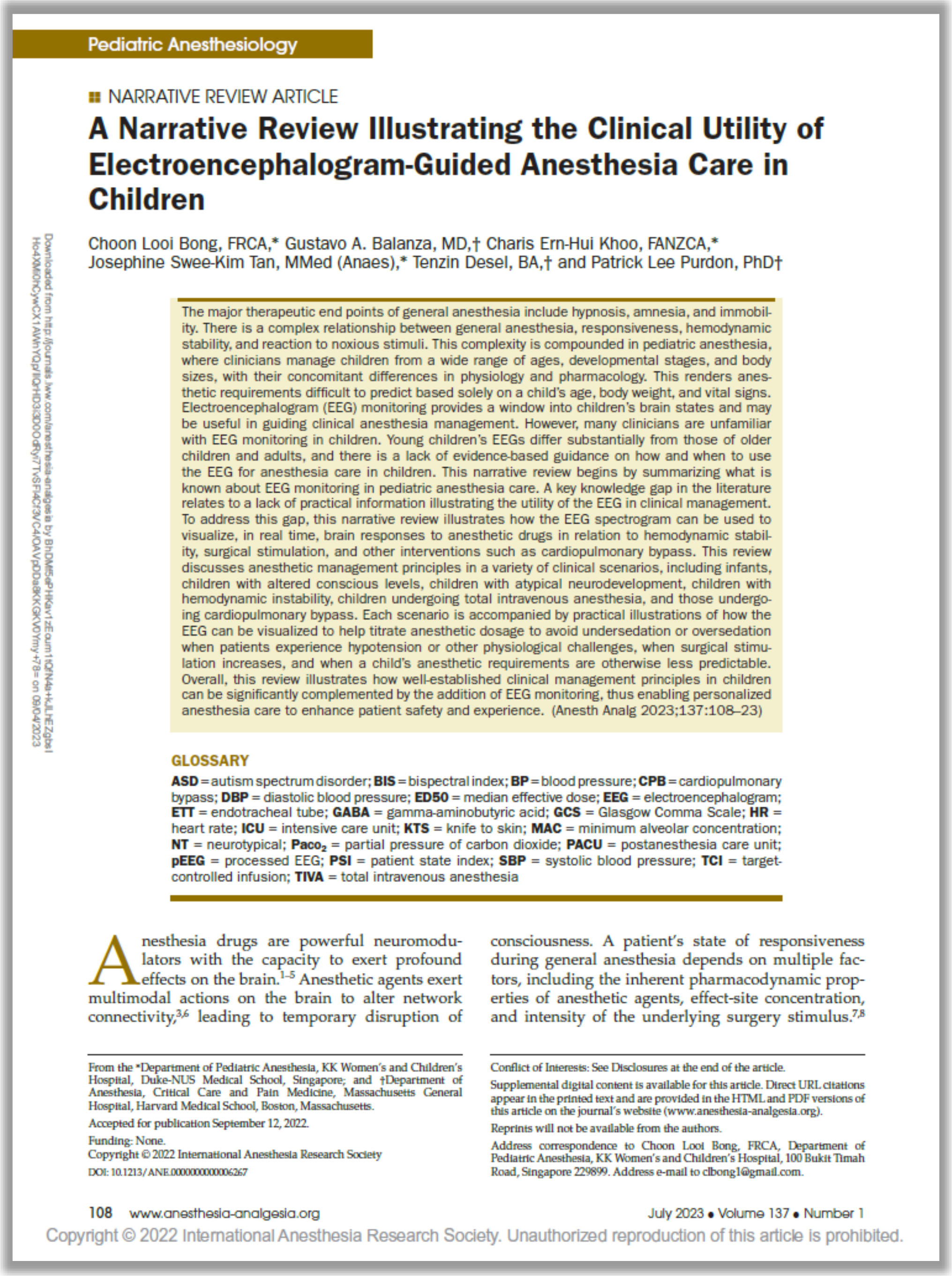
3 month
5 month
9 month
11 month
16 month
19 month
37 month
Frequency (Hz)
Time (min)
Power (dB)
B
Frequency (Hz)
Age (months)
Power (dB)
C
Slow (0.1–1 Hz)
Delta(1–4 Hz)
Alpha (8–12 Hz)
Power (dB)
Age (months)

Children

- EEG *is* different
- Is it more useful to look at the raw EEG and the spectrogram?



NARRATIVE REVIEW ARTICLE

A Narrative Review Illustrating the Clinical Utility of Electroencephalogram-Guided Anesthesia Care in Children

Choon Looi Bong, FRCA,* Gustavo A. Balanza, MD,† Charis Ern-Hui Khoo, FANZCA,* Josephine Swee-Kim Tan, MMed (Anaes),* Tenzin Desel, BA,† and Patrick Lee Purdon, PhD†

The major therapeutic end points of general anesthesia include hypnosis, amnesia, and immobility. There is a complex relationship between general anesthesia, responsiveness, hemodynamic stability, and reaction to noxious stimuli. This complexity is compounded in pediatric anesthesia, where clinicians manage children from a wide range of ages, developmental stages, and body sizes, with their concomitant differences in physiology and pharmacology. This renders anesthetic requirements difficult to predict based solely on a child's age, body weight, and vital signs. Electroencephalogram (EEG) monitoring provides a window into children's brain states and may be useful in guiding clinical anesthesia management. However, many clinicians are unfamiliar with EEG monitoring in children. Young children's EEGs differ substantially from those of older children and adults, and there is a lack of evidence-based guidance on how and when to use the EEG for anesthesia care in children. This narrative review begins by summarizing what is known about EEG monitoring in pediatric anesthesia care. A key knowledge gap in the literature relates to a lack of practical information illustrating the utility of the EEG in clinical management. To address this gap, this narrative review illustrates how the EEG spectrogram can be used to visualize, in real time, brain responses to anesthetic drugs in relation to hemodynamic stability, surgical stimulation, and other interventions such as cardiopulmonary bypass. This review discusses anesthetic management principles in a variety of clinical scenarios, including infants, children with altered conscious levels, children with atypical neurodevelopment, children with hemodynamic instability, children undergoing total intravenous anesthesia, and those undergoing cardiopulmonary bypass. Each scenario is accompanied by practical illustrations of how the EEG can be visualized to help titrate anesthetic dosage to avoid undersedation or oversedation when patients experience hypotension or other physiological challenges, when surgical stimulation increases, and when a child's anesthetic requirements are otherwise less predictable. Overall, this review illustrates how well-established clinical management principles in children can be significantly complemented by the addition of EEG monitoring, thus enabling personalized anesthesia care to enhance patient safety and experience. (Anesth Analg 2023;137:108–23)

GLOSSARY

ASD = autism spectrum disorder; **BIS** = bispectral index; **BP** = blood pressure; **CPB** = cardiopulmonary bypass; **DBP** = diastolic blood pressure; **ED50** = median effective dose; **EEG** = electroencephalogram; **ETT** = endotracheal tube; **GABA** = gamma-aminobutyric acid; **GCS** = Glasgow Comma Scale; **HR** = heart rate; **ICU** = intensive care unit; **KTS** = knife to skin; **MAC** = minimum alveolar concentration; **NT** = neurotypical; **$Paco_2$** = partial pressure of carbon dioxide; **PACU** = postanesthesia care unit; **pEEG** = processed EEG; **PSI** = patient state index; **SBP** = systolic blood pressure; **TCI** = target-controlled infusion; **TIVA** = total intravenous anesthesia

Anesthesia drugs are powerful neuromodulators with the capacity to exert profound effects on the brain.[1–5] Anesthetic agents exert multimodal actions on the brain to alter network connectivity,[3,6] leading to temporary disruption of consciousness. A patient's state of responsiveness during general anesthesia depends on multiple factors, including the inherent pharmacodynamic properties of anesthetic agents, effect-site concentration, and intensity of the underlying surgery stimulus.[7,8]

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Reprints will not be available from the authors.

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Do they change outcomes in children?

What are we trying to do?

Measure something → Titrate your drugs → Better outcomes

Depth of anaesthesia
Nociception
Brain concentration

Sevoflurane
Propofol
Opioids
? Remimazolam
? Dexmedetomidine

Faster awakening
Less delirium
Less awareness
Less toxicity

- 200 children aged 1-6
- RCT, DSA guided sevoflurane anaesthesia

- Less sevoflurane, less burst suppression
- No difference in delirium
- No difference in PACU times

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ELSEVIER

Original Contribution

Sevoflurane requirements during electroencephalogram (EEG)-guided vs standard anesthesia Care in Children: A randomized controlled trial

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ARTICLE INFO

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EEG-guided anesthesia
Pediatric anesthesia
Sevoflurane anesthesia depth
Depth of anesthesia monitoring
Emergence delirium

ABSTRACT

Study Objectives: Intra-operative electroencephalographic (EEG) monitoring utilizing the spectrogram allows visualization of children's brain response during anesthesia and may complement routine cardiorespiratory monitoring to facilitate titration of anesthetic doses. We aimed to determine if EEG-guided anesthesia will result in lower sevoflurane requirements, lower incidence of burst suppression and improved emergence characteristics in children undergoing routine general anesthesia, compared to standard care.
Design: Randomized controlled trial.
Setting: Tertiary pediatric hospital.
Patients: 200 children aged 1 to 6 years, ASA 1 or 2, undergoing routine sevoflurane anesthesia for minor surgery lasting 30 to 240 min.
Interventions: Children were randomized to either EEG-guided anesthesia (EEG-G) or standard care (SC). EEG-G group had sevoflurane titrated to maintain continuous slow/delta oscillations on the raw EEG and spectrogram, aiming to avoid burst suppression and, as far as possible, maintain a patient state index (PSI) between 25 and50. SC group received standard anesthesia care and the anesthesia teams were blinded to EEG waveforms.
Measurements: The primary outcomes were the average end-tidal sevoflurane concentration during induction and maintenance of anesthesia. Secondary outcomes include incidence and duration of intra-operative burst suppression and Pediatric Anesthesia Emergence Delirium (PAED) scores.
Results: The EEG-G group received lower end-tidal sevoflurane concentrations during induction [4.80% vs 5.67%, −0.88% (−1.45, −0.31) $p = 0.003$] and maintenance of anesthesia [2.23% vs 2.38%, −0.15% (−0.25, −0.05) $p = 0.005$], and had a lower incidence of burst suppression [3.1% vs 10.9%, $p = 0.044$] compared to the SC group. PAED scores were similar between groups. Children <2 years old required higher average end-tidal sevoflurane concentrations, regardless of group.
Conclusions: EEG-guided anesthesia care reduces sevoflurane requirements in children undergoing general anesthesia, possibly lowering the incidence of burst suppression, without altering emergence characteristics. EEG monitoring allows direct visualization of brain responses in real time and allows clearer appreciation of varying sevoflurane requirements in children of different ages.

1. Introduction

General anesthesia is a state of drug-induced unconsciousness resulting from disruption of normal cortical and thalamic communication by anesthetic agents [1]. Intra-operative EEG monitoring has yet to be routinely employed for anesthesia care in children. Current practice relies on delivering inhalational anesthetic doses based on population pharmacology models to estimate the patient's anesthetic requirements, [2,3] with the concept of minimum alveolar concentration (MAC) [4] being the key guidance principle. Anesthetic doses are typically titrated

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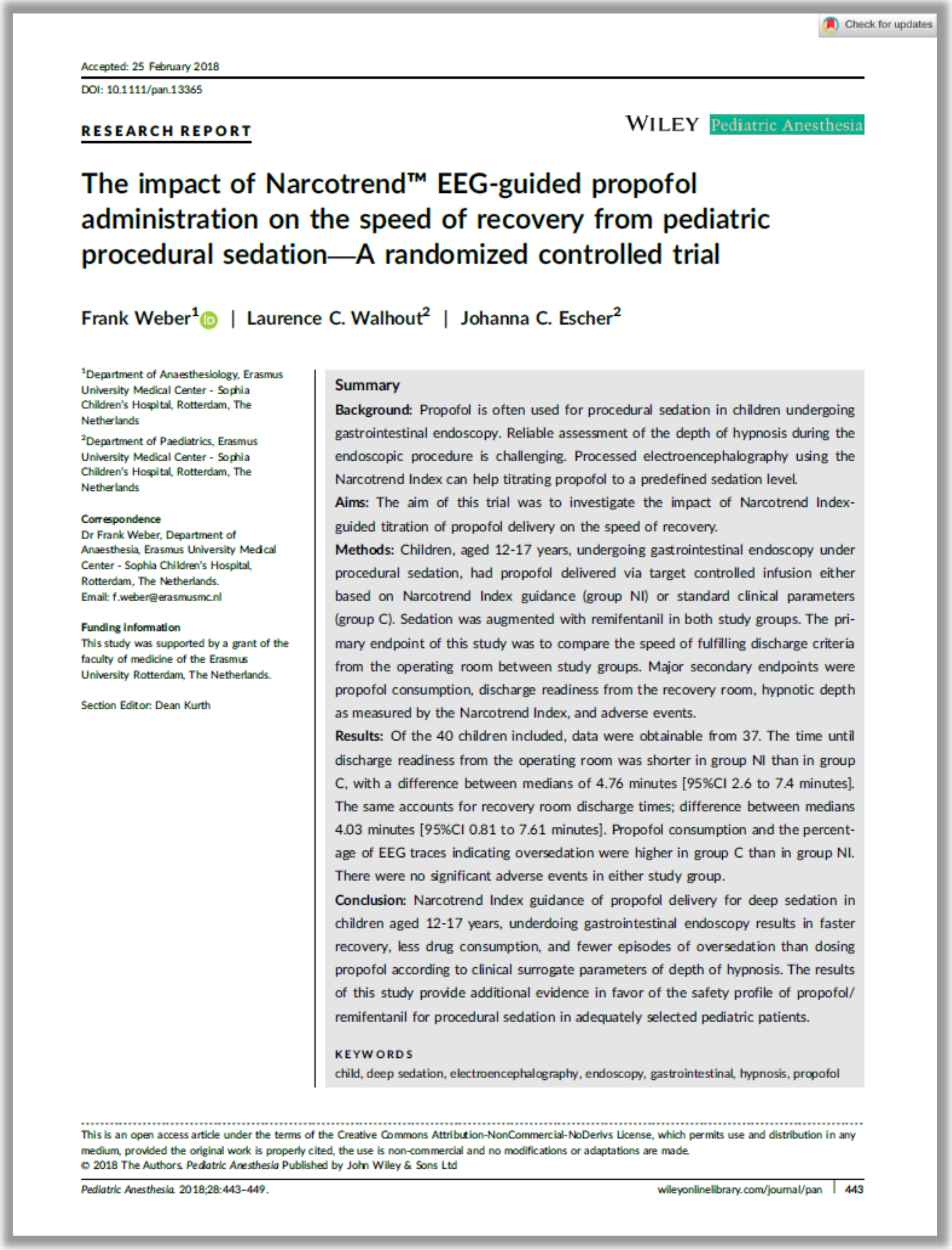
- 40 children, 12-17 years
- RCT Narcotrend guided propofol sedation

- Less propofol
- Faster recovery times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Accepted: 25 February 2018
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RESEARCH REPORT

WILEY Pediatric Anesthesia

The impact of Narcotrend™ EEG-guided propofol administration on the speed of recovery from pediatric procedural sedation—A randomized controlled trial

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Section Editor: Dean Kurth

Summary

Background: Propofol is often used for procedural sedation in children undergoing gastrointestinal endoscopy. Reliable assessment of the depth of hypnosis during the endoscopic procedure is challenging. Processed electroencephalography using the Narcotrend Index can help titrating propofol to a predefined sedation level.

Aims: The aim of this trial was to investigate the impact of Narcotrend Index-guided titration of propofol delivery on the speed of recovery.

Methods: Children, aged 12-17 years, undergoing gastrointestinal endoscopy under procedural sedation, had propofol delivered via target controlled infusion either based on Narcotrend Index guidance (group NI) or standard clinical parameters (group C). Sedation was augmented with remifentanil in both study groups. The primary endpoint of this study was to compare the speed of fulfilling discharge criteria from the operating room between study groups. Major secondary endpoints were propofol consumption, discharge readiness from the recovery room, hypnotic depth as measured by the Narcotrend Index, and adverse events.

Results: Of the 40 children included, data were obtainable from 37. The time until discharge readiness from the operating room was shorter in group NI than in group C, with a difference between medians of 4.76 minutes [95%CI 2.6 to 7.4 minutes]. The same accounts for recovery room discharge times; difference between medians 4.03 minutes [95%CI 0.81 to 7.61 minutes]. Propofol consumption and the percentage of EEG traces indicating oversedation were higher in group C than in group NI. There were no significant adverse events in either study group.

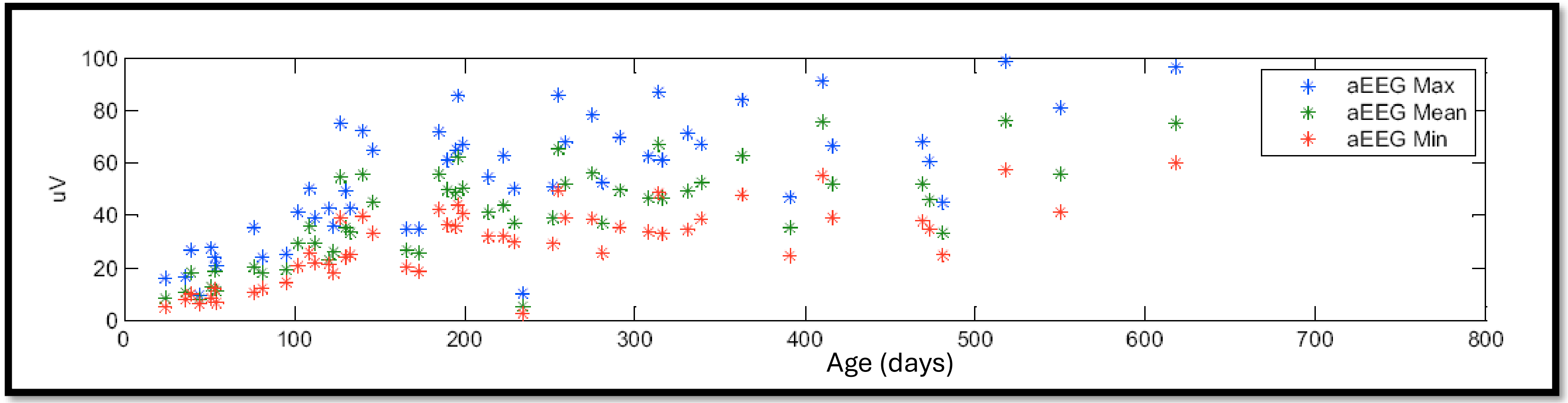
Conclusion: Narcotrend Index guidance of propofol delivery for deep sedation in children aged 12-17 years, underdoing gastrointestinal endoscopy results in faster recovery, less drug consumption, and fewer episodes of oversedation than dosing propofol according to clinical surrogate parameters of depth of hypnosis. The results of this study provide additional evidence in favor of the safety profile of propofol/remifentanil for procedural sedation in adequately selected pediatric patients.

KEYWORDS
child, deep sedation, electroencephalography, endoscopy, gastrointestinal, hypnosis, propofol

Neonates

EEG during anaesthesia: Power and age

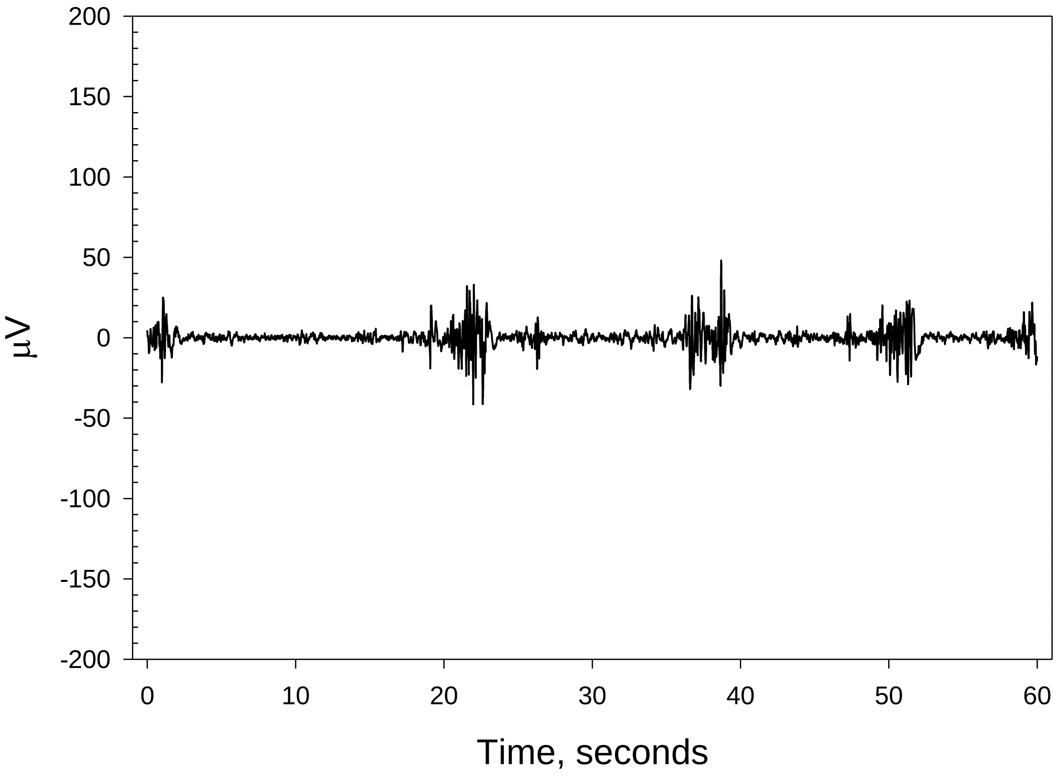
- Power very low in infants, increases with age (peak mid childhood)



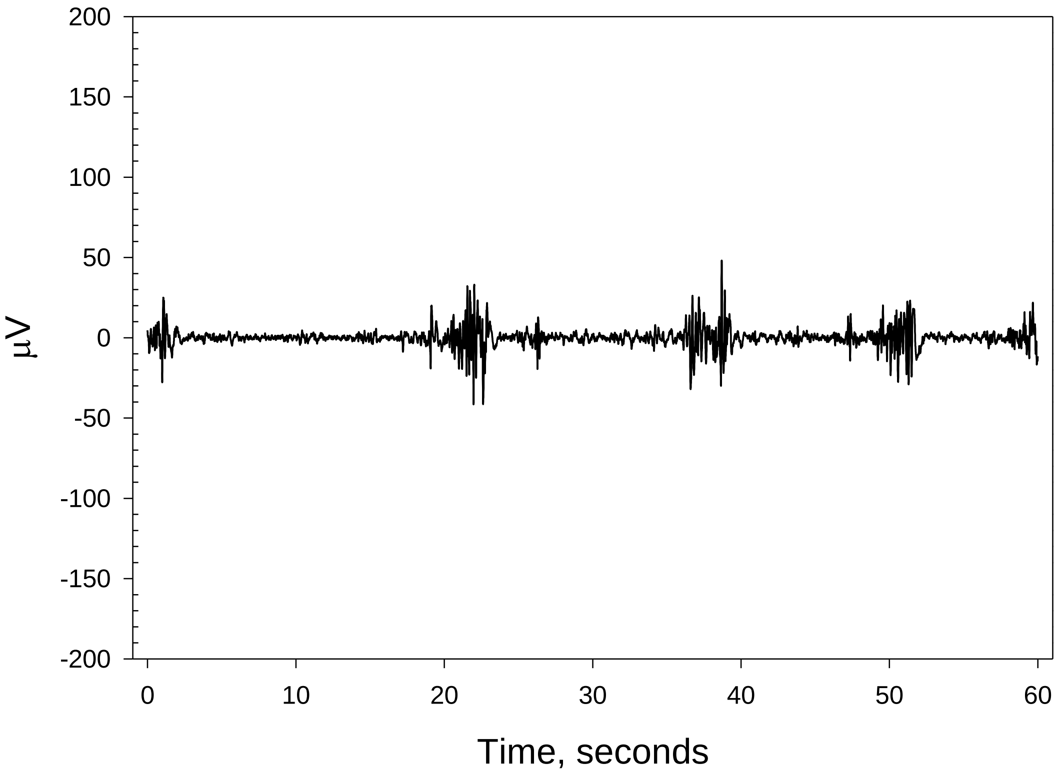
EEG in neonates and infants

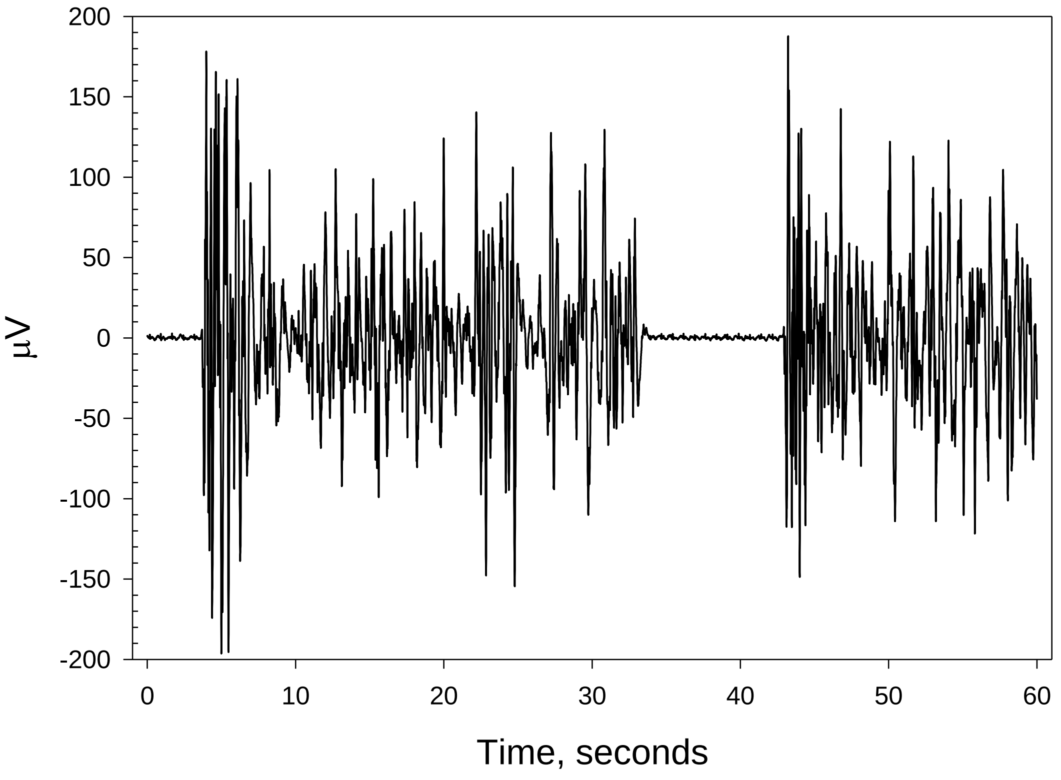
- Some activity form 12 weeks gestation
- 24-27 weeks: discontinuous EEG

- Discontinuous EEG pathological in the awake term baby
- But, common during anaesthesia

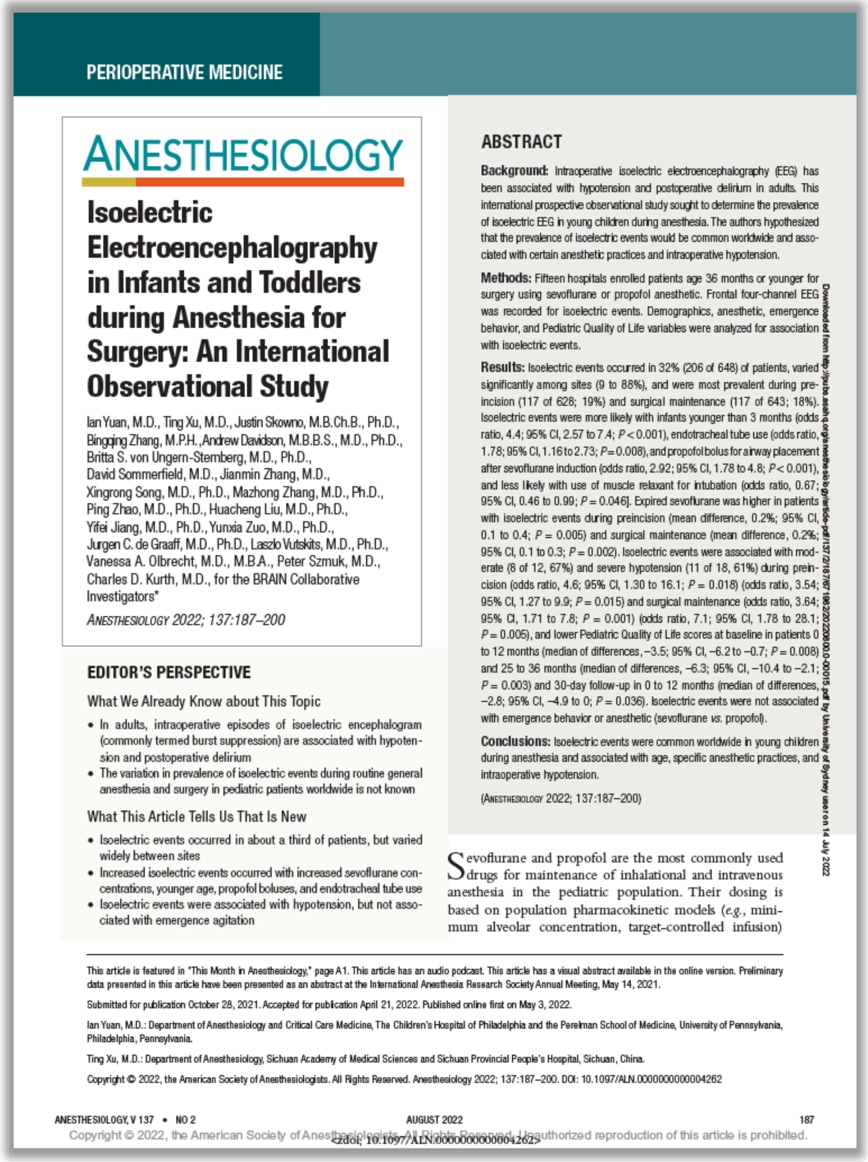


EEG after bolus of propofol in a child





“burst suppression” in infants



ANESTHESIOLOGY

Isoelectric Electroencephalography in Infants and Toddlers during Anesthesia for Surgery: An International Observational Study

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ABSTRACT

Background: Intraoperative isoelectric electroencephalography (EEG) has been associated with hypotension and postoperative delirium in adults. This international prospective observational study sought to determine the prevalence of isoelectric EEG in young children during anesthesia. The authors hypothesized that the prevalence of isoelectric events would be common worldwide and associated with certain anesthetic practices and intraoperative hypotension.

Methods: Fifteen hospitals enrolled patients age 36 months or younger for surgery using sevoflurane or propofol anesthetic. Frontal four-channel EEG was recorded for isoelectric events. Demographics, anesthetic, emergence behavior, and Pediatric Quality of Life variables were analyzed for association with isoelectric events.

Results: Isoelectric events occurred in 32% (206 of 648) of patients, varied significantly among sites (9 to 88%), and were most prevalent during preincision (117 of 628; 19%) and surgical maintenance (117 of 643; 18%). Isoelectric events were more likely with infants younger than 3 months (odds ratio, 4.4; 95% CI, 2.57 to 7.4; $P < 0.001$), endotracheal tube use (odds ratio, 1.78; 95% CI, 1.16 to 2.73; $P = 0.008$), and propofol bolus for airway placement after sevoflurane induction (odds ratio, 2.92; 95% CI, 1.78 to 4.8; $P < 0.001$), and less likely with use of muscle relaxant for intubation (odds ratio, 0.67; 95% CI, 0.46 to 0.99; $P = 0.046$]. Expired sevoflurane was higher in patients with isoelectric events during preincision (mean difference, 0.2%; 95% CI, 0.1 to 0.4; $P = 0.005$) and surgical maintenance (mean difference, 0.2%; 95% CI, 0.1 to 0.3; $P = 0.002$). Isoelectric events were associated with moderate (8 of 12, 67%) and severe hypotension (11 of 18, 61%) during preincision (odds ratio, 4.6; 95% CI, 1.30 to 16.1; $P = 0.018$) (odds ratio, 3.54; 95% CI, 1.27 to 9.9; $P = 0.015$) and surgical maintenance (odds ratio, 3.64; 95% CI, 1.71 to 7.8; $P = 0.001$) (odds ratio, 7.1; 95% CI, 1.78 to 28.1; $P = 0.005$), and lower Pediatric Quality of Life scores at baseline in patients 0 to 12 months (median of differences, –3.5; 95% CI, –6.2 to –0.7; $P = 0.008$) and 25 to 36 months (median of differences, –6.3; 95% CI, –10.4 to –2.1; $P = 0.003$) and 30-day follow-up in 0 to 12 months (median of differences, –2.8; 95% CI, –4.9 to 0; $P = 0.036$). Isoelectric events were not associated with emergence behavior or anesthetic (sevoflurane *vs.* propofol).

Conclusions: Isoelectric events were common worldwide in young children during anesthesia and associated with age, specific anesthetic practices, and intraoperative hypotension.

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EDITOR’S PERSPECTIVE

What We Already Know about This Topic

- In adults, intraoperative episodes of isoelectric encephalogram (commonly termed burst suppression) are associated with hypotension and postoperative delirium
- The variation in prevalence of isoelectric events during routine general anesthesia and surgery in pediatric patients worldwide is not known

What This Article Tells Us That Is New

- Isoelectric events occurred in about a third of patients, but varied widely between sites
- Increased isoelectric events occurred with increased sevoflurane concentrations, younger age, propofol boluses, and endotracheal tube use
- Isoelectric events were associated with hypotension, but not associated with emergence agitation

Sevoflurane and propofol are the most commonly used drugs for maintenance of inhalational and intravenous anesthesia in the pediatric population. Their dosing is based on population pharmacokinetic models (*e.g.*, minimum alveolar concentration, target-controlled infusion)

This article is featured in “This Month in Anesthesiology,” page A1. This article has an audio podcast. This article has a visual abstract available in the online version. Preliminary data presented in this article have been presented as an abstract at the International Anesthesia Research Society Annual Meeting, May 14, 2021.

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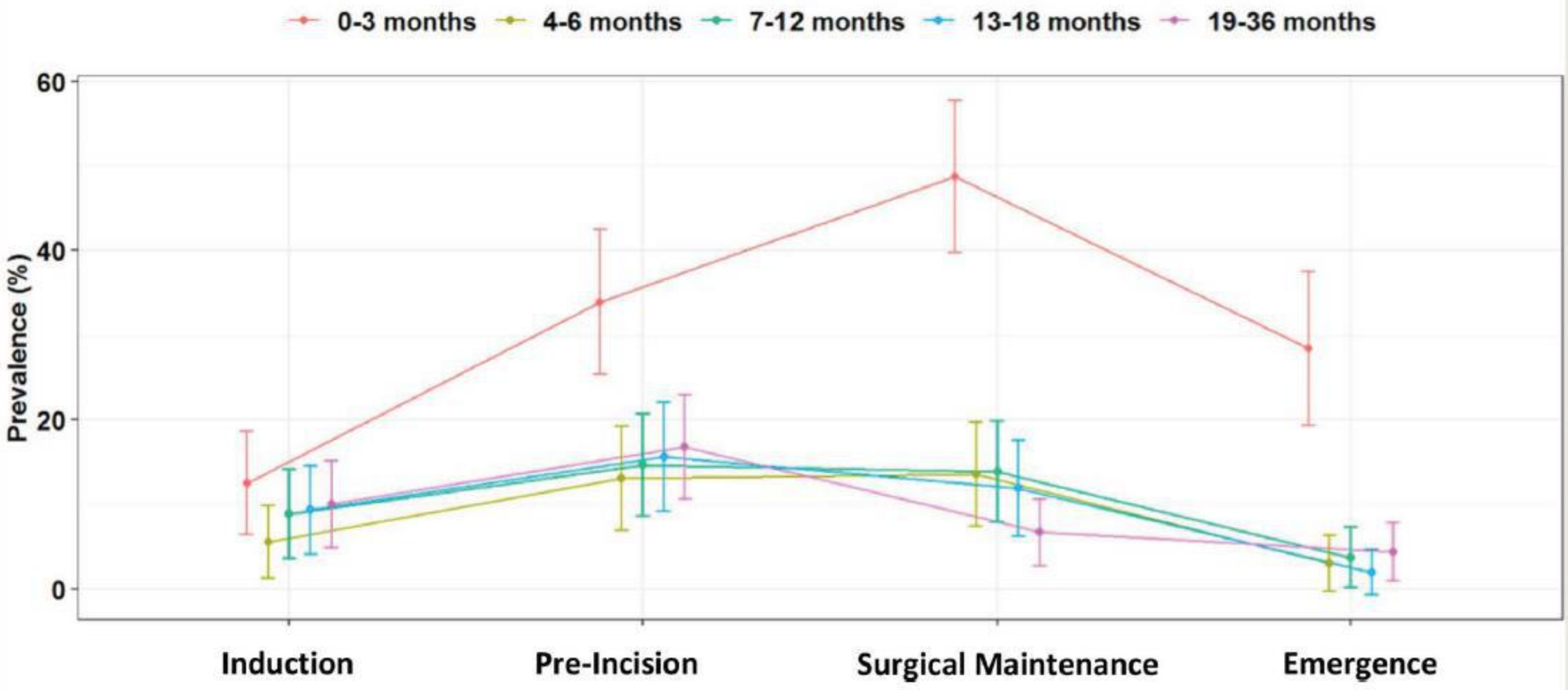

Fig. 3. Prevalence of isoelectric electroencephalography stratified by age groups. Median (*dot*) and 95% CI (*vertical lines*) displayed.

“burst suppression” in infants

- No evidence that it is harmful or reflects excessive anaesthesia

Differential Suppression of Spontaneous and Noxious-evoked Somatosensory Cortical Activity by Isoflurane in the Neonatal Rat

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ABSTRACT

Background: The effect of neonatal anesthesia and pain on the developing brain is of considerable clinical importance, but few studies have evaluated noxious surgical input to the infant brain under anesthesia. Herein, the authors tested the effect of increasing isoflurane concentration on spontaneous and evoked nociceptive activity in the somatosensory cortex of rats at different postnatal ages.

Methods: Intracortical extracellular field potentials evoked by hind paw C-fiber electrical stimulation were recorded in the rat somatosensory cortex at postnatal day (P) 7, P14, P21, and P30 during isoflurane anesthesia (n = 7 per group). The amplitudes of evoked potentials and the energies of evoked oscillations (1 to 100 Hz over 3s) were measured after equilibration at 1.5% isoflurane and during step increases in inspired isoflurane. Responses during and after plantar hind paw incision were compared at P7 and P30 (n = 6 per group).

Results: At P7, cortical activity was silent at 1.5% isoflurane but noxious-evoked potentials decreased only gradually in amplitude and energy with step increases in isoflurane. The resistance of noxious-evoked potentials to isoflurane at P7 was significantly enhanced after surgical hind paw incision (69 ± 16% *vs.* 6 ± 1% in nonincised animals at maximum inspired isoflurane). This resistance was age dependent; at P14 to P30, noxious-evoked responses decreased sharply with increasing isoflurane (step 3 [4%] P7: 50 ± 9%, P30: 4 ± 1% of baseline). Hind paw incision at P30 sensitized noxious-evoked potentials, but this was suppressed by higher isoflurane concentrations.

Conclusions: Despite suppression of spontaneous activity, cortical-evoked potentials are more resistant to isoflurane in young rats and are further sensitized by surgical injury. (Anesthesiology 2016; 124:885-98)

AN optimal level of neonatal anesthesia achieves both hypnosis and antinociception while maintaining physiologic stability and minimizing potential neurotoxicity.[1,2] As both anesthesia and uncontrolled pain may alter cortical activity and impair neurodevelopmental outcomes,[3–5] the impact of anesthetic agents on both spontaneous and noxious-evoked neural activity in the developing brain requires further evaluation. An important aspect of neonatal anesthesia research is the effect of nociceptive sensory input on activity within cortical sensory circuits and the degree to which central nociceptive activity is modulated by anesthesia and analgesia. Both animal and clinical evidence point to long-term consequences of early life procedural and surgical tissue injury on somatosensory and nociceptive systems,[6,7] highlighting the need to consider the impact of postnatal age on changes in both spontaneous and noxious-evoked cortical activity during surgery and anesthesia.

Extracellular field recording, including electroencephalogram, electrocorticogram, and local field potentials (intracortical activity) are commonly used to monitor ongoing spontaneous brain activity and levels of anesthesia in human and rodent neonates but are also used to record specific potentials evoked by a sensory stimulus. Somatosensory potentials evoked by experimental noxious cutaneous stimulation[8–11] are commonly used to measure pain activity in the adult human and rodent brain.[12] Specific nociceptive potentials are

What We Already Know about This Topic

- Considerable evidence indicates that neonatal anesthesia and tissue injury have long-term consequences on somatosensory and nociceptive systems
- The anesthetic sensitivity of noxious cutaneous-evoked activity in the neonatal somatosensory cortex, with or without surgical trauma, is unknown

What This Article Tells Us That Is New

- Extracellular somatosensory cortex field potentials evoked by hind paw C-fiber electrical stimulation were resistant to isoflurane compared with spontaneous activity in neonatal rat
- Surgical hind paw incision enhanced the resistance of noxious-evoked responses to isoflurane, an effect that declined with age, indicating critical age-dependent differences in anesthetic suppression of cortical nociceptive activity

Corresponding article on page 758.

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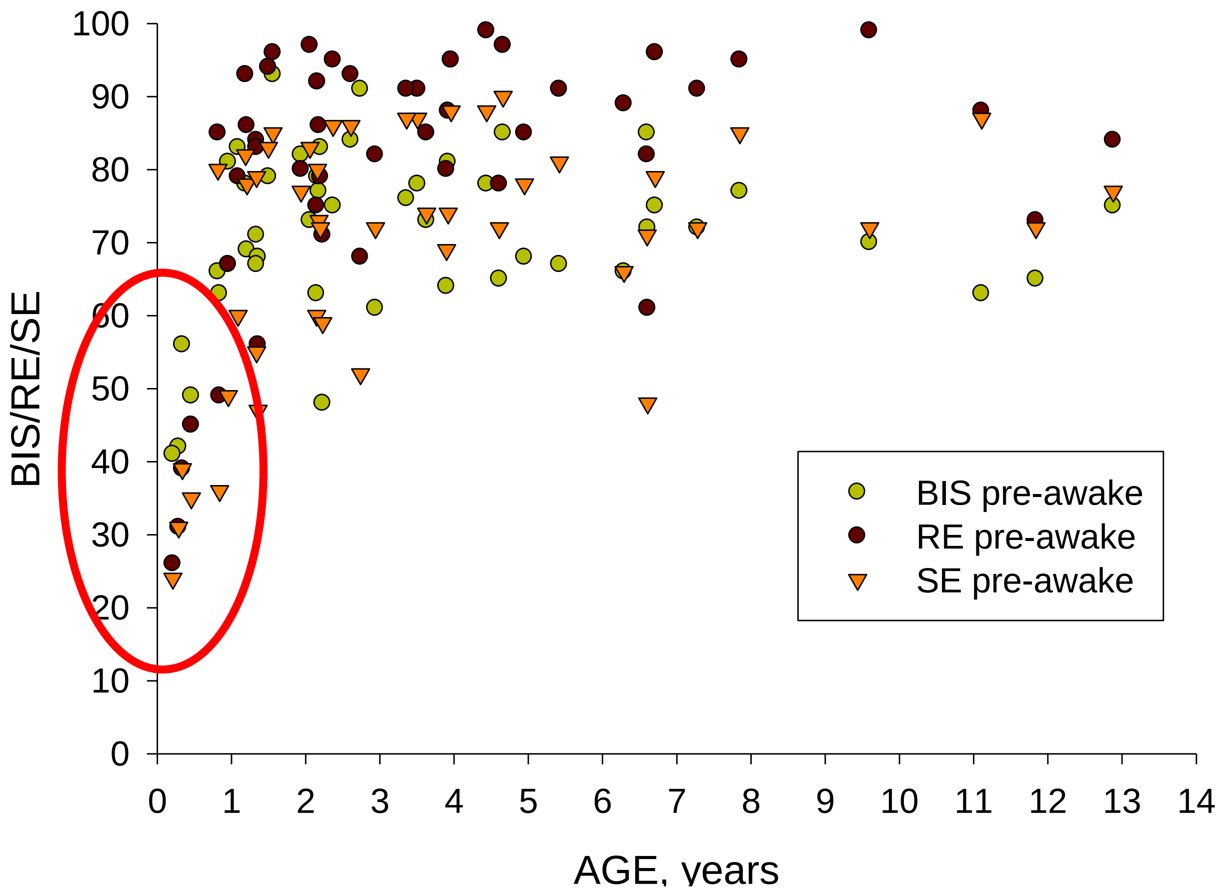
- Neonatal rats
- 1.5% isoflurane – flat line EEG
- Noxious stimuli generate cortical activity – persisted with increasing doses of isoflurane

- Older rats
- Increasing burst suppression with isoflurane >1.5%
- Noxious stimuli were readily ablated with increasing doses of isoflurane

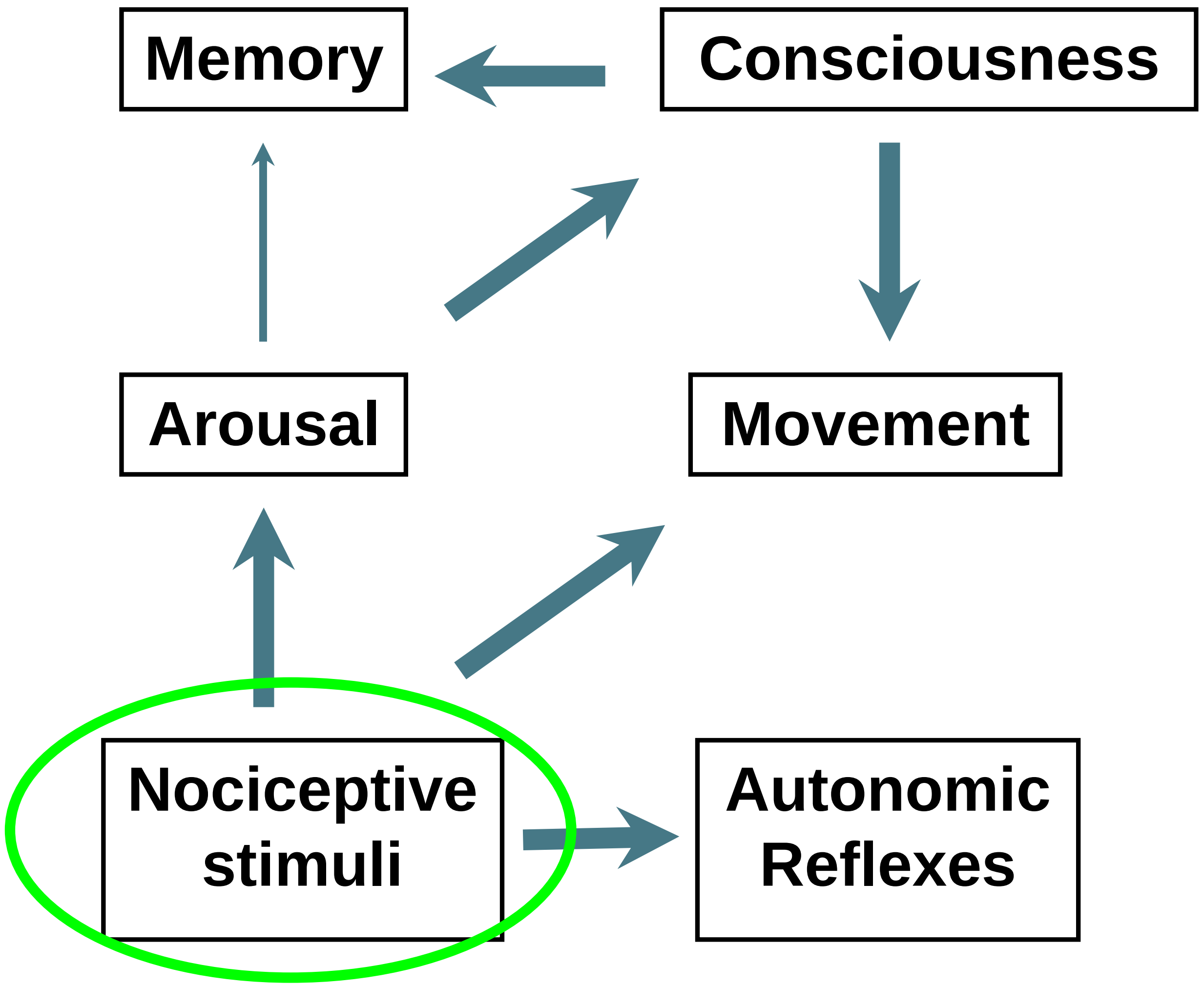
- Volatile agents profoundly suppress the neonatal brain when no surgical stimulus
- In neonates, volatile agents very poor at suppressing activity with noxious stimulus

- Burst suppression may be “just enough” rather than “excessive”

BIS prior to awakening



Measuring Nociception


Memory
Consciousness
Arousal
Movement
Nociceptive stimuli
Autonomic Reflexes

Nociception monitors

- Motor reflexes
- CNS
- Autonomic

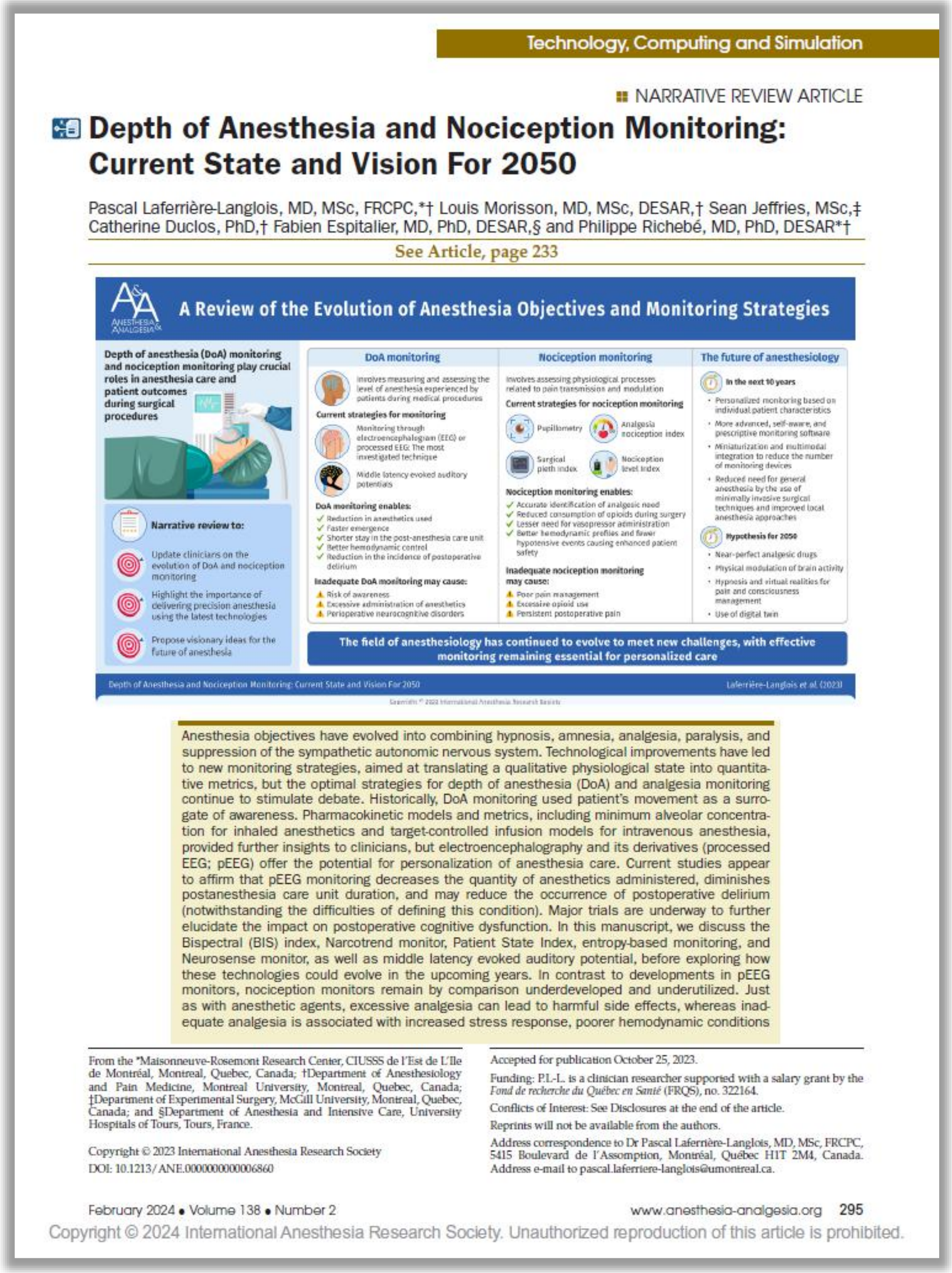
Nociception monitors

- In adults – can be used to titrate opioids and predict post op needs

- Very little, if any, use in children

The future

- Personalised monitors
- Closed loop with agent delivery
- Combined tech



NARRATIVE REVIEW ARTICLE

Depth of Anesthesia and Nociception Monitoring: Current State and Vision For 2050

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See Article, page 233

Anesthesia objectives have evolved into combining hypnosis, amnesia, analgesia, paralysis, and suppression of the sympathetic autonomic nervous system. Technological improvements have led to new monitoring strategies, aimed at translating a qualitative physiological state into quantitative metrics, but the optimal strategies for depth of anesthesia (DoA) and analgesia monitoring continue to stimulate debate. Historically, DoA monitoring used patient's movement as a surrogate of awareness. Pharmacokinetic models and metrics, including minimum alveolar concentration for inhaled anesthetics and target-controlled infusion models for intravenous anesthesia, provided further insights to clinicians, but electroencephalography and its derivatives (processed EEG; pEEG) offer the potential for personalization of anesthesia care. Current studies appear to affirm that pEEG monitoring decreases the quantity of anesthetics administered, diminishes postanesthesia care unit duration, and may reduce the occurrence of postoperative delirium (notwithstanding the difficulties of defining this condition). Major trials are underway to further elucidate the impact on postoperative cognitive dysfunction. In this manuscript, we discuss the Bispectral (BIS) index, Narcotrend monitor, Patient State Index, entropy-based monitoring, and Neurosense monitor, as well as middle latency evoked auditory potential, before exploring how these technologies could evolve in the upcoming years. In contrast to developments in pEEG monitors, nociception monitors remain by comparison underdeveloped and underutilized. Just as with anesthetic agents, excessive analgesia can lead to harmful side effects, whereas inadequate analgesia is associated with increased stress response, poorer hemodynamic conditions

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The future in paediatrics

- Better processed EEG for older children – probably not
- Finding their place to improve care – maybe

- Neonates…

Thank you

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