THE BURST SUPPRESSION PARADOX IN ANESTHESIA

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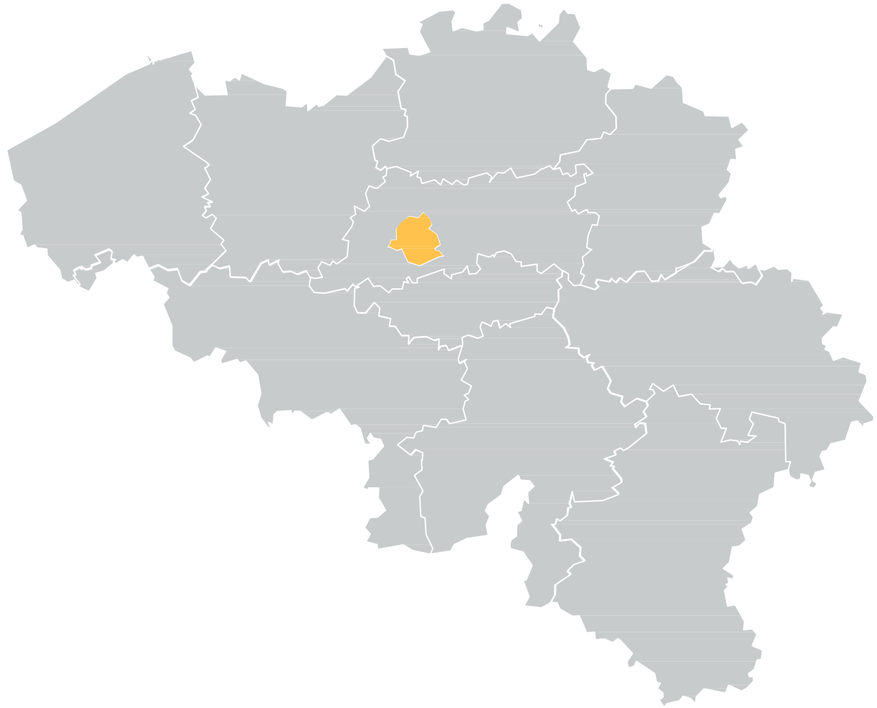
UNIVERSITÉ LAVAL, QC

JUNE 17TH 2018
CAS NEUROSECTION EVENT

BRUSSELS, BEL



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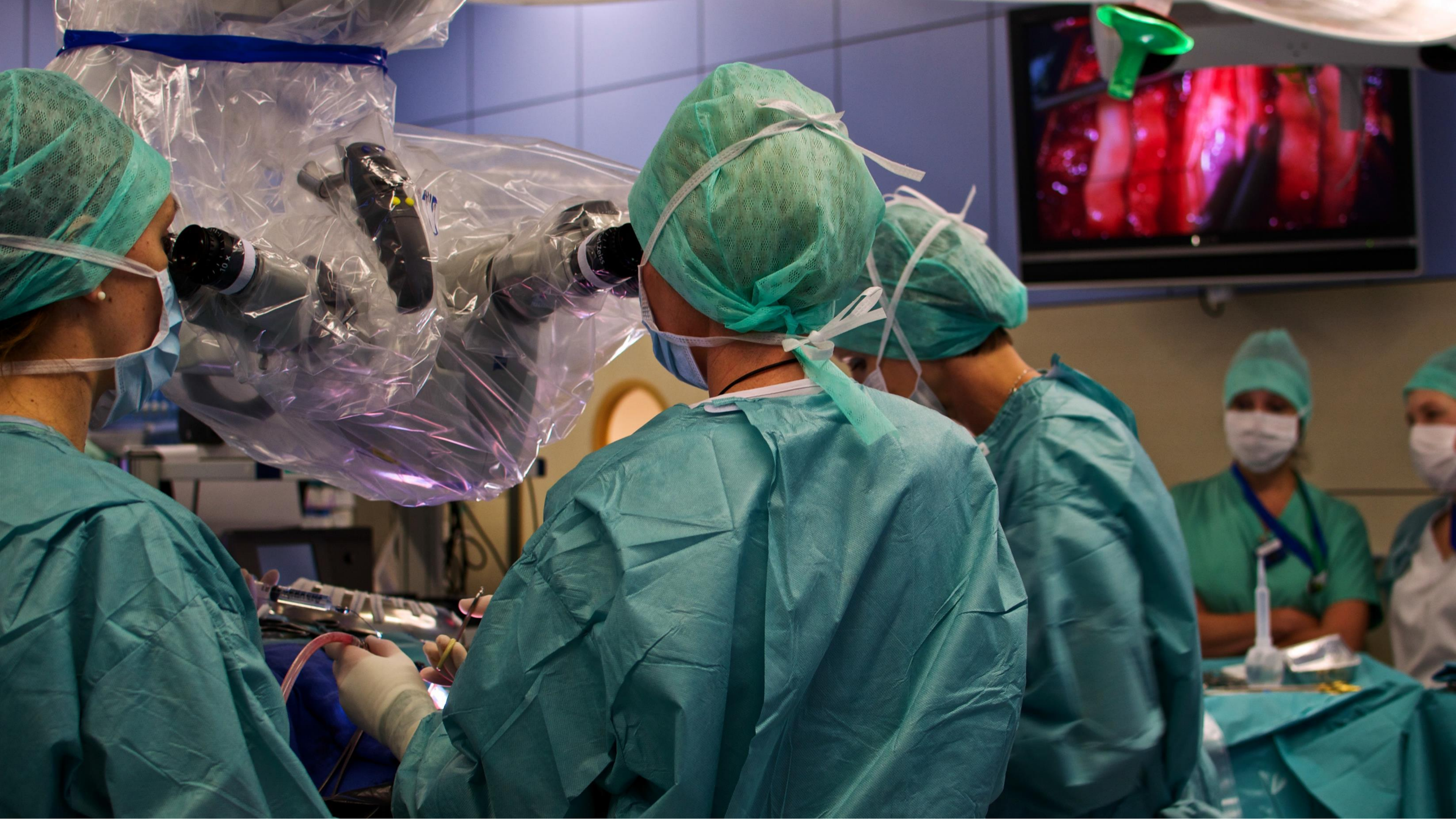
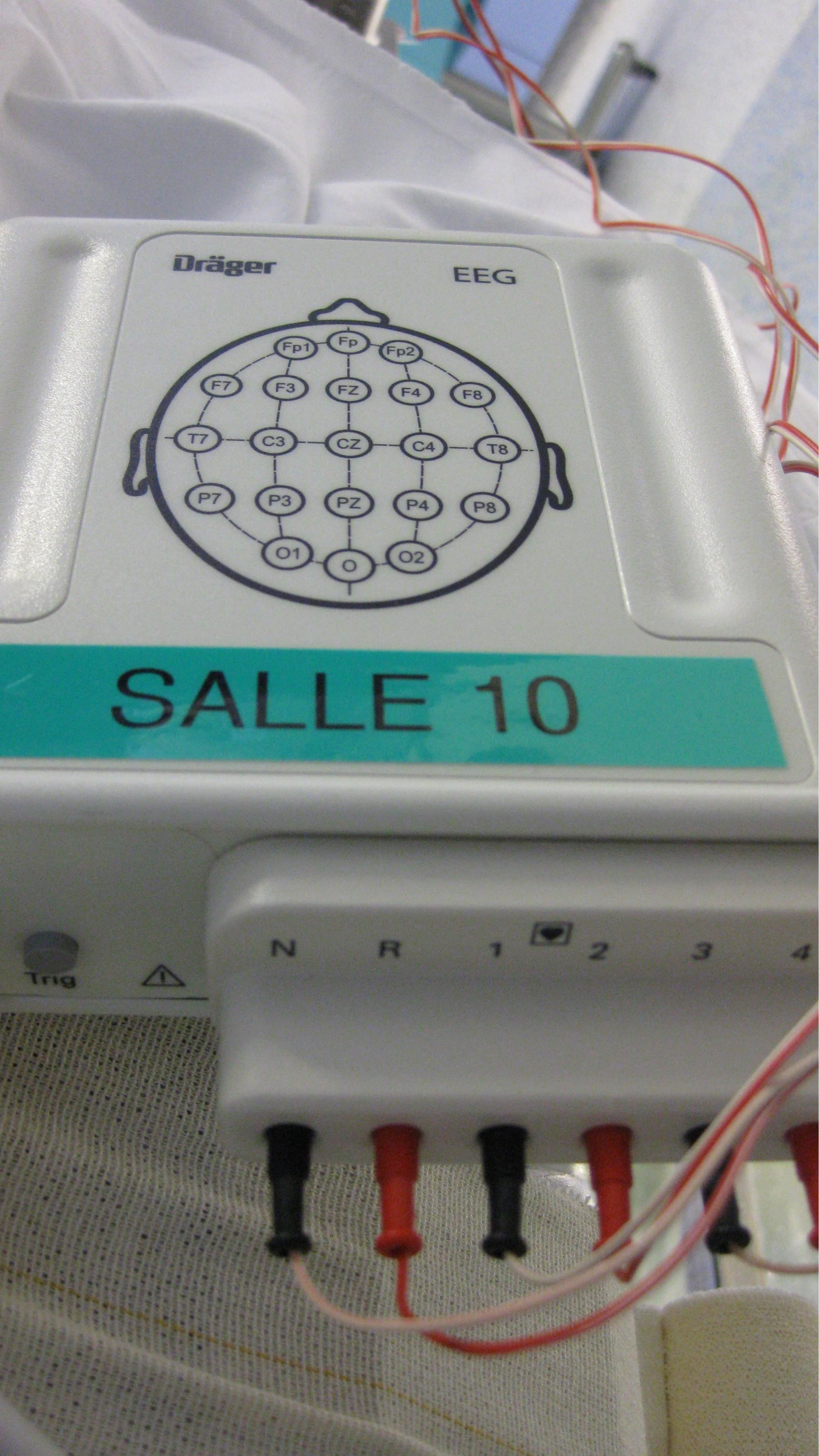
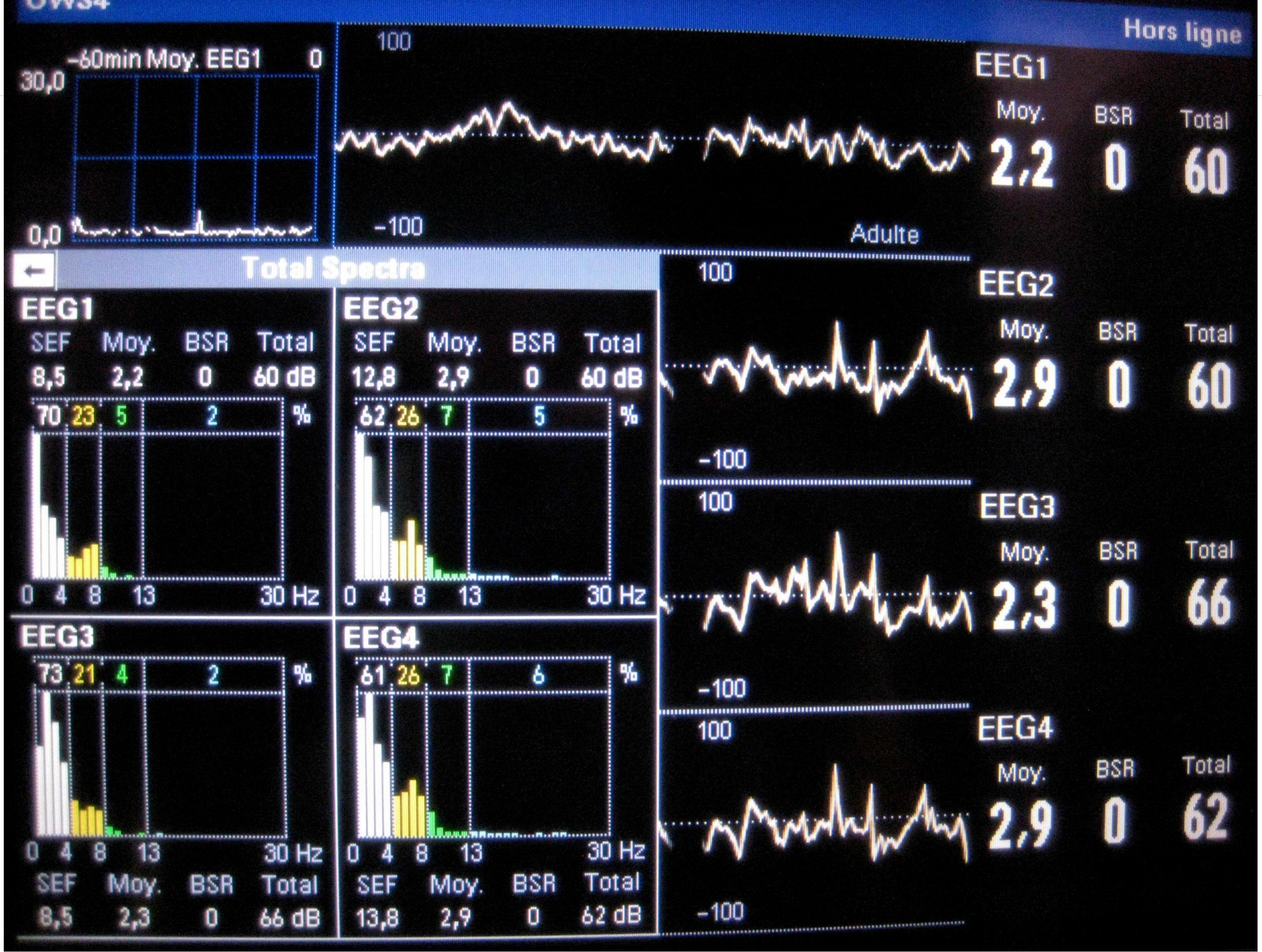
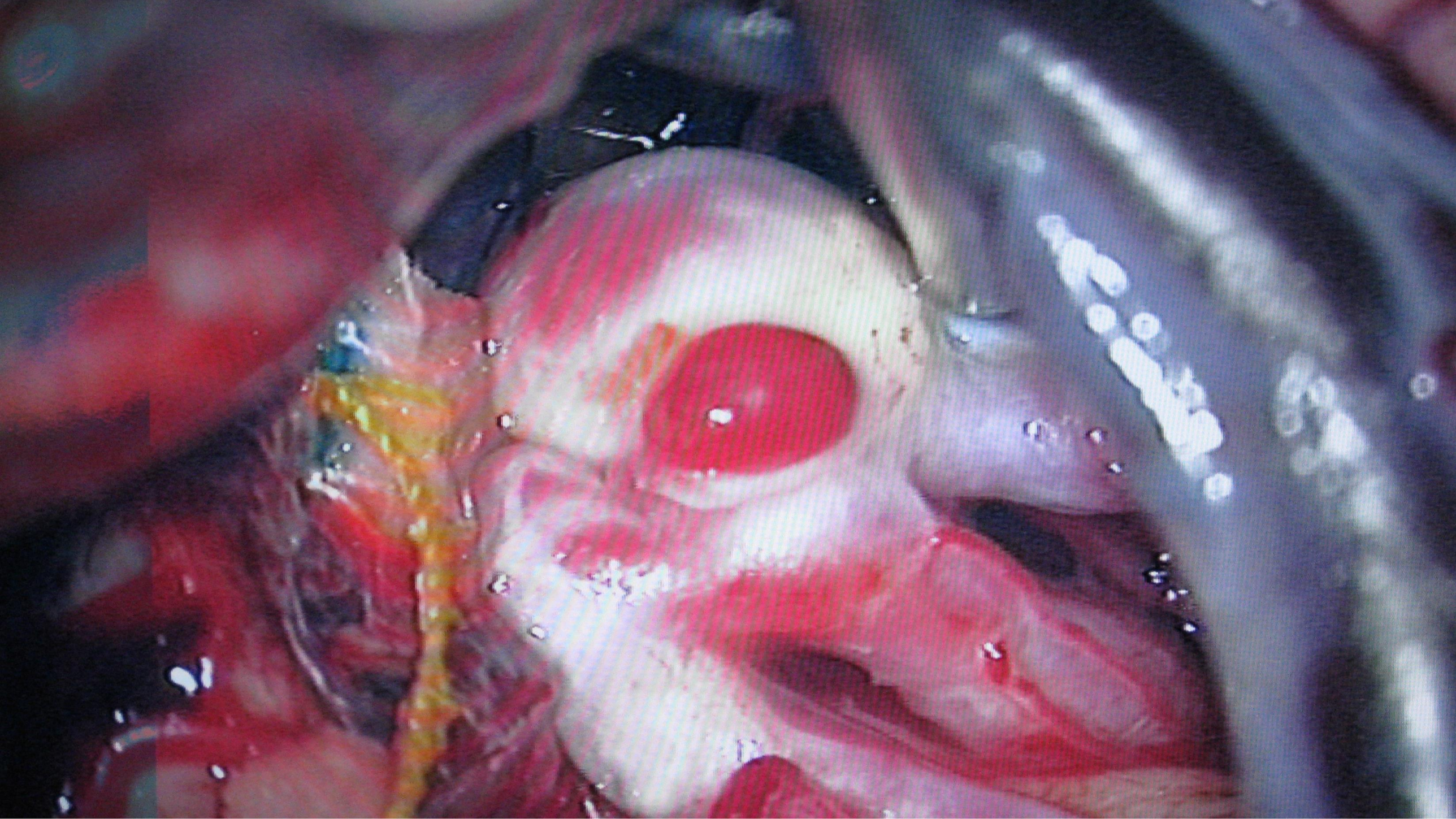



Dräger
EEG
Fp1
Fp
Fp2
F7
F3
FZ
F4
F8
T7
C3
CZ
C4
T8
P7
P3
PZ
P4
P8
O1
O
O2
SALLE 10
Trig
N
R
1
2
3
4


Hors ligne
-60min Moy. EEG1
30,0
0,0
0
100
-100
EEG1
Moy. BSR Total
2,2 0 60
Adulte
Total Spectra
EEG2
Moy. BSR Total
2,9 0 60
EEG3
Moy. BSR Total
2,3 0 66
EEG4
Moy. BSR Total
2,9 0 62
EEG1
SEF Moy. BSR Total
8,5 2,2 0 60 dB
70 23 5 2 %
EEG2
SEF Moy. BSR Total
12,8 2,9 0 60 dB
62 26 7 5 %
EEG3
73 21 4 2 %
SEF Moy. BSR Total
8,5 2,3 0 66 dB
EEG4
61 26 7 6 %
SEF Moy. BSR Total
13,8 2,9 0 62 dB
0 4 8 13 30 Hz




OWS4
Hors ligne
-60min Moy. EEG1
30,0
0,0
0
100
-100
EEG1
Moy. BSR Total
1,6 28 55
Adulte
Total Spectre
EEG2
Moy. BSR Total
1,5 20 56
EEG3
Moy. BSR Total
2,0 2 56
EEG4
Moy. BSR Total
1,8 15 56
EEG1
SEF Moy. BSR Total
8,1 1,6 28 55 dB
82 13 3 2 %
EEG2
SEF Moy. BSR Total
7,2 1,5 20 56 dB
85 10 3 2 %
EEG3
79 14 5 2 %
SEF Moy. BSR Total
8,3 2,0 2 56 dB
EEG4
85 10 3 2 %
SEF Moy. BSR Total
7,9 1,8 15 56 dB
0 4 8 13 30 Hz


NeuroExplorer Scenario: TIM2 Van Peteghem, Morgane
EMG
enreg. sc.
commentaire
électrodes
vidéo
démarr.tous
arrêt tous
imprimer
PEM
configuration
stimulateur
analyse
tendance
artéfact
démarr.PEM
réinitialiser
enregistrer
pause
BIO
CAS
AVG
tétière
05-27-2014-10-53-54.avi
10:54:51
Average: TES MEP
C1: 40.2 ms
C1: 30.5 ms
C2: 16.3 ms
dt: 14.3 ms
dv: 2.2 mV

THE EXISTENTIAL QUESTION

IS ANESTHESIA-INDUCED BURST SUPPRESSION NEUROPROTECTIVE OR NEUROTOXIC?

OUTLINE

1. WHAT IS THE PATHOPHYSIOLOGY OF BURST-SUPPRESSION?

2. HOW CAN WE MONITOR BURST-SUPPRESSION?

3. IS IATROGENIC BURST-SUPPRESSION PROTECTIVE OR TOXIC?

DEFINITION

“ PATTERN CHARACTERIZED BY THETA AND/OR DELTA WAVES,

AT TIMES INTERMIXED WITH FASTER WAVES,

AND INTERVENING PERIODS OF RELATIVE QUIESCENCE.”

INTERNATIONAL FEDERATION OF SOCIETIES FOR ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY (IF-SECN)


A2 - Fp2
0
Hz
30
V5
1 mV
ST
Art 180
90
0
Art
BIS 100 µV
EEG
BIS
-100 µV
100 µV
EEG2
-100 µV
CO2 40
CO2
mm
II 0.0
V5 0.5
aVL 0.6
aVL
0.6
mmHg Sys 100..180
124/69
(90)
28
IQS
EMG
RS 3
Mauvais contact électrode
Fm 2.0
BSR 0
Hz 15 30
mmHg ET 20..61
ET 33 FI 0
FR 12 /min
PNI
mmHg Sys Dia
101/64
Moy (73) 0 1 h
NMT
Mesure inopérante
Td4% ---
Total ---
SpO2 T1+T2
% 90..ARR °C T1:
99
T1 35.5
T2 ---
Gaz O2: FI 20..ARR
% O2 N2O Sev
ET 35 0 1.8
FI 40 0 2.2

1. WHAT IS THE PATHOPHYSIOLOGY OF BURST SUPPRESSION?

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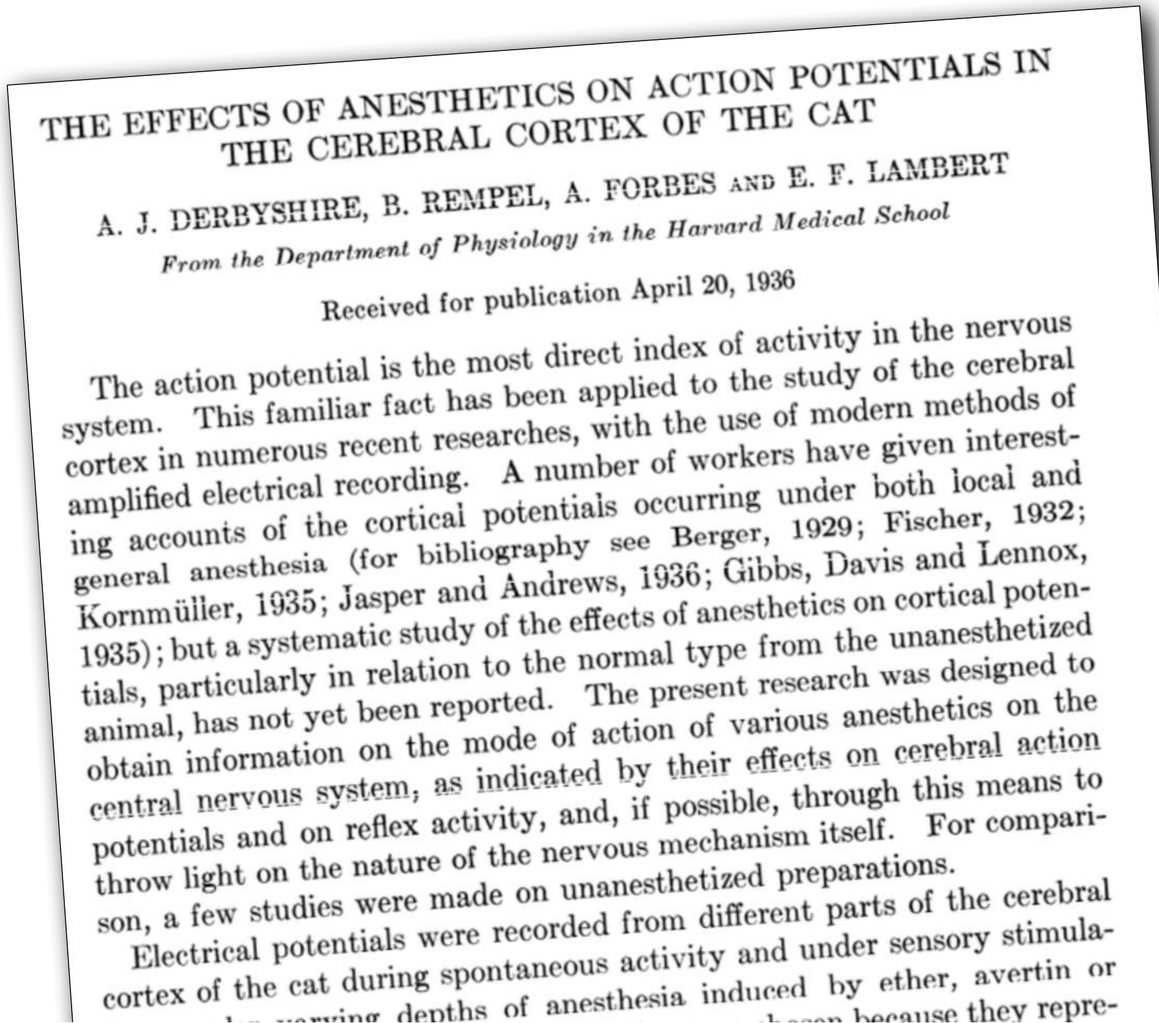
3. IS IATROGENIC BURST SUPPRESSION PROTECTIVE OR TOXIC?

DERBYSHIRE AJ, REMPEL B, FORBES A, LAMBERT EF. THE EFFECTS OF ANESTHETICS ON ACTION POTENTIALS IN THE CEREBRAL CORTEX OF THE CAT. AMERICAN JOURNAL OF PHYSIOLOGY–LEGACY CONTENT. 1936;116(3):577–596.

R. SWANK, C. WATSON
EFFECTS OF BARBITURATES AND ETHER ON SPONTANEOUS ELECTRICAL ACTIVITY OF DOG BRAIN
J NEUROPHYSIOL, 12 (1949), PP. 137-160



THE EFFECTS OF ANESTHETICS ON ACTION POTENTIALS IN THE CEREBRAL CORTEX OF THE CAT

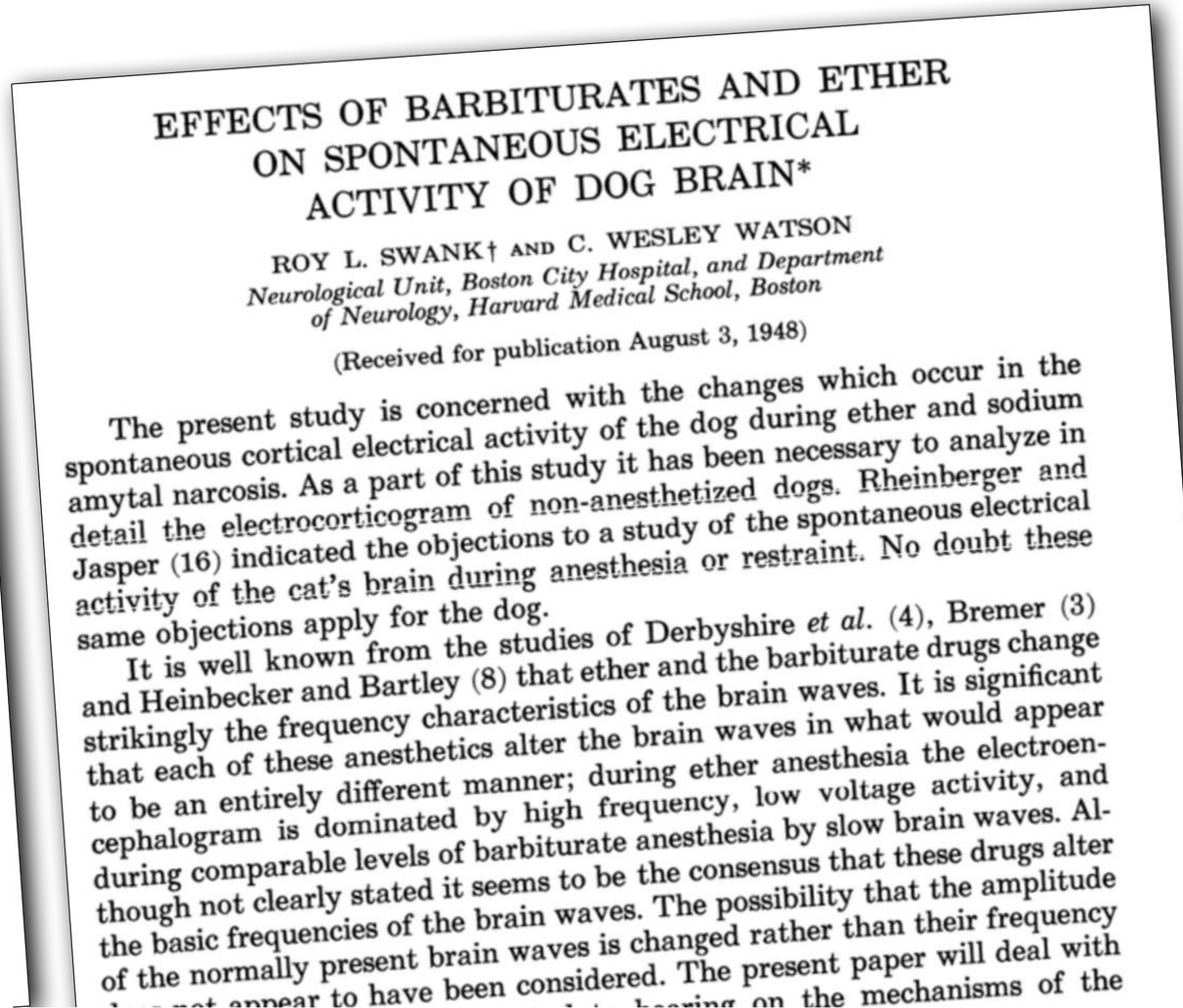
A. J. DERBYSHIRE, B. REMPEL, A. FORBES AND E. F. LAMBERT

From the Department of Physiology in the Harvard Medical School

Received for publication April 20, 1936

The action potential is the most direct index of activity in the nervous system. This familiar fact has been applied to the study of the cerebral cortex in numerous recent researches, with the use of modern methods of amplified electrical recording. A number of workers have given interesting accounts of the cortical potentials occurring under both local and general anesthesia (for bibliography see Berger, 1929; Fischer, 1932; Kornmüller, 1935; Jasper and Andrews, 1936; Gibbs, Davis and Lennox, 1935); but a systematic study of the effects of anesthetics on cortical potentials, particularly in relation to the normal type from the unanesthetized animal, has not yet been reported. The present research was designed to obtain information on the mode of action of various anesthetics on the central nervous system, as indicated by their effects on cerebral action potentials and on reflex activity, and, if possible, through this means to throw light on the nature of the nervous mechanism itself. For comparison, a few studies were made on unanesthetized preparations.

Electrical potentials were recorded from different parts of the cerebral cortex of the cat during spontaneous activity and under sensory stimula-



EFFECTS OF BARBITURATES AND ETHER ON SPONTANEOUS ELECTRICAL ACTIVITY OF DOG BRAIN*

ROY L. SWANK† AND C. WESLEY WATSON

Neurological Unit, Boston City Hospital, and Department of Neurology, Harvard Medical School, Boston

(Received for publication August 3, 1948)

The present study is concerned with the changes which occur in the spontaneous cortical electrical activity of the dog during ether and sodium amytal narcosis. As a part of this study it has been necessary to analyze in detail the electrocorticogram of non-anesthetized dogs. Rheinberger and Jasper (16) indicated the objections to a study of the spontaneous electrical activity of the cat's brain during anesthesia or restraint. No doubt these same objections apply for the dog.

It is well known from the studies of Derbyshire *et al.* (4), Bremer (3) and Heinbecker and Bartley (8) that ether and the barbiturate drugs change strikingly the frequency characteristics of the brain waves. It is significant that each of these anesthetics alter the brain waves in what would appear to be an entirely different manner; during ether anesthesia the electroencephalogram is dominated by high frequency, low voltage activity, and during comparable levels of barbiturate anesthesia by slow brain waves. Although not clearly stated it seems to be the consensus that these drugs alter the basic frequencies of the brain waves. The possibility that the amplitude of the normally present brain waves is changed rather than their frequency does not appear to have been considered. The present paper will deal with

FLORIAN AMZICA, PH.D.

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AMZICA’S LAB IN MTL

FLORIAN AMZICA, PH.D.

AMZICA'S HYPOTHESIS

Epilepsia, 50(Suppl. 12): 38–39, 2009
doi: 10.1111/j.1528-1167.2009.02345.x

PROCEEDINGS: THE INNSBRUCK COLLOQUIUM ON STATUS EPILEPTICUS

Basic physiology of burst-suppression

Florin Amzica

Department of Stomatology, School of Dentistry, Université de Montreal, succursale Centre-ville, Montreal, QC, Canada

Burst-suppression (BS) is an electroencephalography (EEG) pattern consisting of alternative periods of slow waves of high amplitude (the burst) and periods of so-called flat EEG (the suppression) (Swank & Watson, 1949). It is generally associated with comatose states of various etiologies (hypoxia, drug-related intoxication, hypothermia, and childhood encephalopathies, but also anesthesia). It has been studied extensively at the EEG level (see review by Brenner, 1985, also this issue), but only sparse information is available with respect to the cellular and ionic mechanisms underlying its patterns. Some of the most fascinating questions pertain to the genesis of bursts: Are they truly spontaneous, what triggers them, what mechanism dictates their quasi-periodicity? Moreover, in clinical practice bursting activities during BS are often associated with jerks resembling those present during epileptic fits. Is there any common link to known seizure mechanisms?

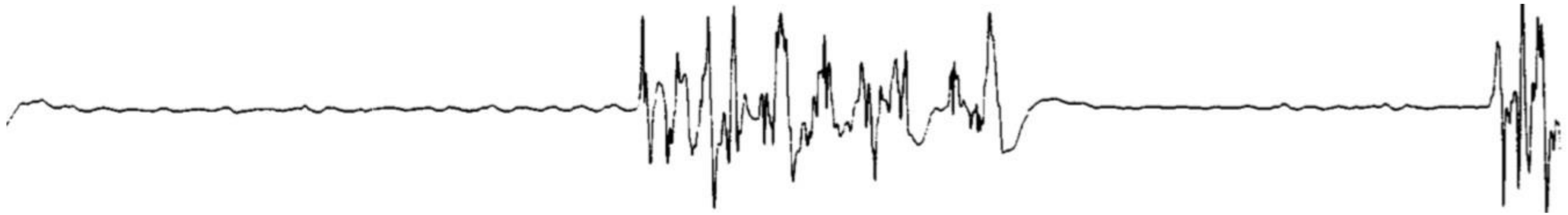
At the cortical level, EEG bursts are always associated with phasic synaptic depolarizing intracellular potentials, originally crowned by action potentials, in virtually all

glutamate uptake (isoflurane). In the latter case, hyperexcitability resulted from the reduction of cortical inhibition (Ferron et al., 2009), which was corroborated with an outburst of extracellular Cl^-, probably reflecting the lesser activity of γ-aminobutyric acid $(GABA)_A$ inhibitory synapses. It results that the excitatory–inhibitory balance leans toward excitation. The bursting process is limited in time because bursting activity is accompanied by a depletion of extracellular cortical Ca^{2+} at levels that are incompatible with synaptic transmission. This generates an overall disfacilitation in cortical networks (Kroeger & Amzica, 2007), which ultimately is responsible for the arrest of neocortical neuronal activities and the ensuing flat EEG. During suppression, the synaptic silence allows neuronal pumps to restore interstitial Ca^{2+} levels at control levels. At this moment, any external (or intrinsic) signal is able to trigger a new burst in the hyperexcitable cortex.

Therefore, the pseudo-rhythmicity of the BS pattern is dictated by the degree of extracellular Ca^{2+} depletion and the ability of neurons to restore this concentration. These phenomena are modulated by the general state of the nervous system and, therefore, the etiology and the serious-

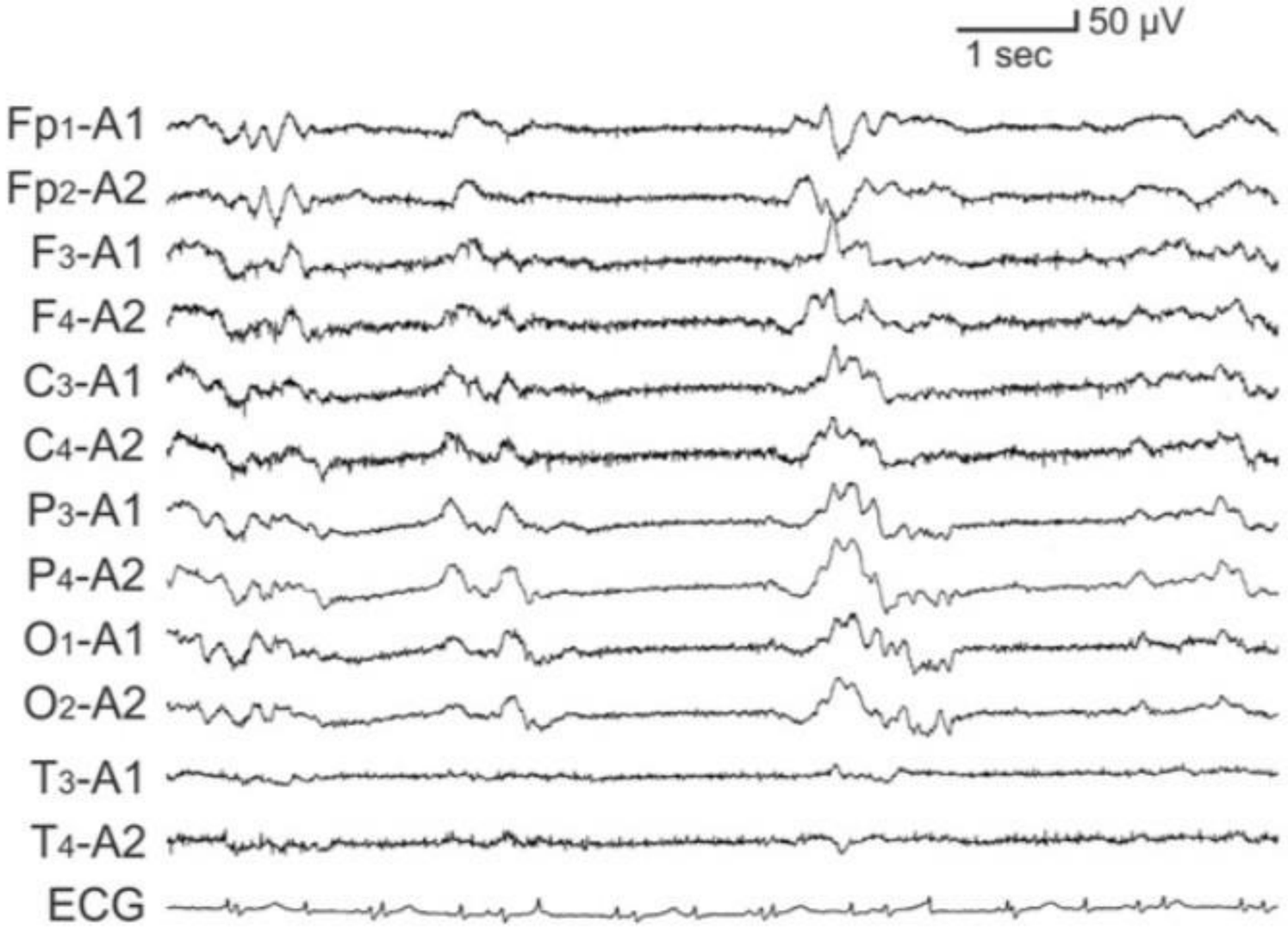
THE DISCONNECTION HYPOTHESIS

BURST SUPPRESSION IS NOT BRAIN REST



DISCONNECTION HYPOTHESIS

burst suppression is a state of cellular **hyperexcitability** caused by a disinhibition of cortical pyramidal neurons alternating with neuronal inactivity caused by depletion of extracellular calcium



CASE REPORT

unconscious 68 years old woman w/ GCS 4/15 on admission, with Cheyne-Stokes breathing

all labs normal, normal CTscan

was put un supportive treatment

EEG = burst suppression

woke up after 18 hours

OGAWA ET AL. EPILEPSY & BEHAVIOR CASE REPORTS 4 (2015) 82–83

AMANITA PANTHERINA

THE BURST SUPPRESSION MUSHROOM

widespread in Asia and North America

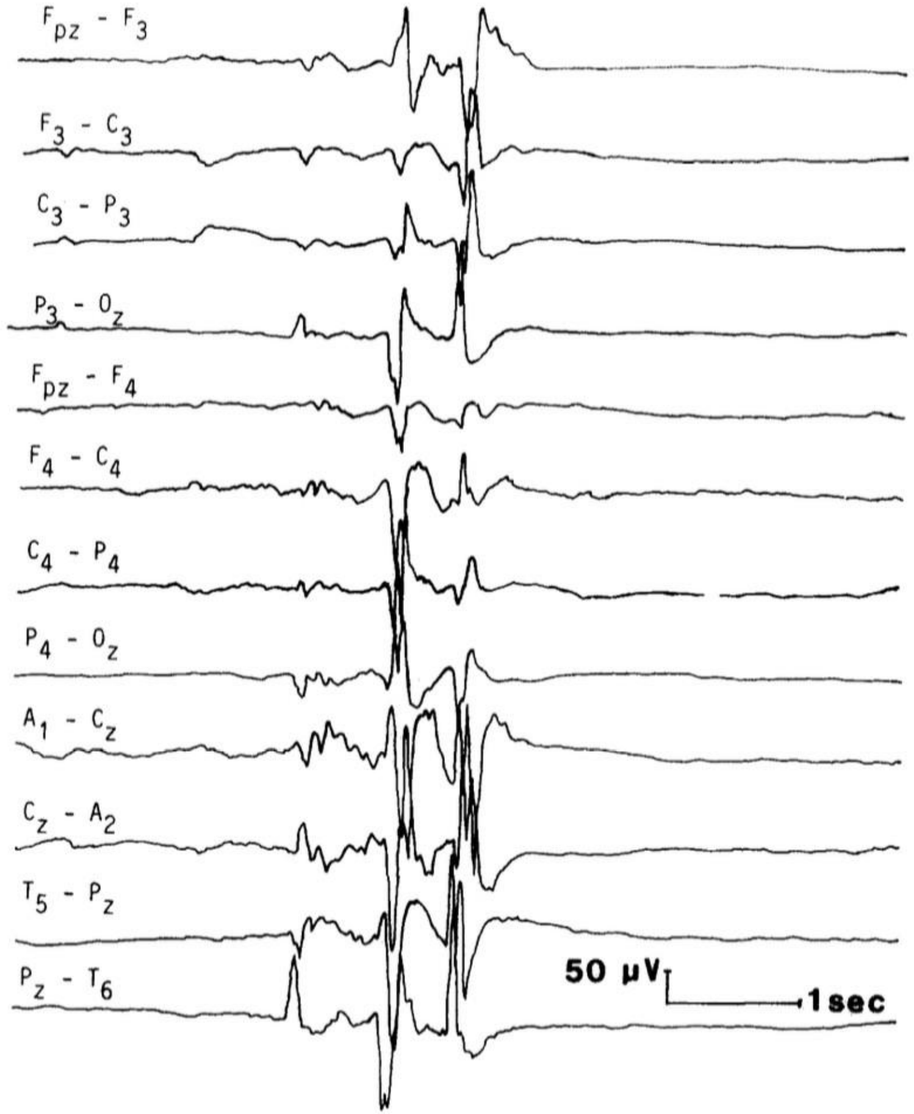
contains **muscimol** toxins that crosses the blood-brain barrier and acts as an agonist of GABA receptors

muscimol also known to produce burst-suppression EEG in rats cortical slices

PHOTO: H. KRISP, WIKIMEDIA COMMONS

CAPLINE HEADER ELEMENT

BURST SUPPRESSION IN BACLOFEN INTOXICATION



BURST SUPPRESSION OCCURS IN A WIDE RANGE OF PATHOLOGICAL STATES

HYPOXIC-ISCHEMIC ENCEPHALOPATHY

OHTAHARA SYNDROME

INFANTILE MYOCLONIC ENCEPHALOPATHY

DENGUE ENCEPHALOPATHY

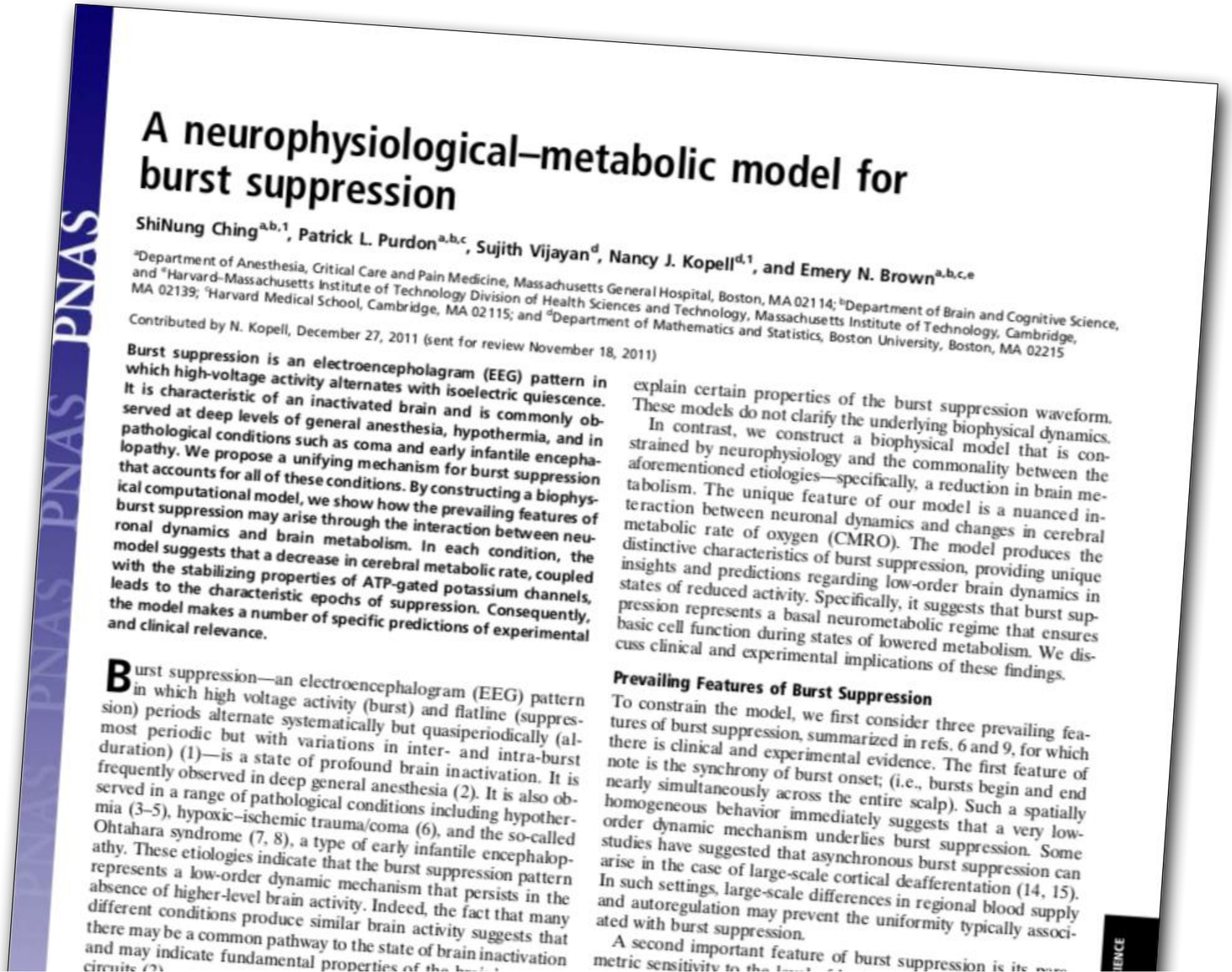
HYPOTHERMIA

VARIOUS INTRACORTICAL SPACE-OCCUPYING LESIONS

DEEP COMA

BURST-SUPPRESSION PATHOPHYSIOLOGY

BROWN & PURDON'S MODEL



A neurophysiological–metabolic model for burst suppression

ShiNung Ching[a,b,1], Patrick L. Purdon[a,b,c], Sujith Vijayan[d], Nancy J. Kopell[d,1], and Emery N. Brown[a,b,c,e]

[a]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, MA 02114; [b]Department of Brain and Cognitive Science, and [e]Harvard–Massachusetts Institute of Technology Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, MA 02139; [c]Harvard Medical School, Cambridge, MA 02115; and [d]Department of Mathematics and Statistics, Boston University, Boston, MA 02215

Contributed by N. Kopell, December 27, 2011 (sent for review November 18, 2011)

Burst suppression is an electroencepholagram (EEG) pattern in which high-voltage activity alternates with isoelectric quiescence. It is characteristic of an inactivated brain and is commonly observed at deep levels of general anesthesia, hypothermia, and in pathological conditions such as coma and early infantile encephalopathy. We propose a unifying mechanism for burst suppression that accounts for all of these conditions. By constructing a biophysical computational model, we show how the prevailing features of burst suppression may arise through the interaction between neuronal dynamics and brain metabolism. In each condition, the model suggests that a decrease in cerebral metabolic rate, coupled with the stabilizing properties of ATP-gated potassium channels, leads to the characteristic epochs of suppression. Consequently, the model makes a number of specific predictions of experimental and clinical relevance.

Burst suppression—an electroencephalogram (EEG) pattern in which high voltage activity (burst) and flatline (suppression) periods alternate systematically but quasiperiodically (almost periodic but with variations in inter- and intra-burst duration) (1)—is a state of profound brain inactivation. It is frequently observed in deep general anesthesia (2). It is also observed in a range of pathological conditions including hypothermia (3–5), hypoxic–ischemic trauma/coma (6), and the so-called Ohtahara syndrome (7, 8), a type of early infantile encephalopathy. These etiologies indicate that the burst suppression pattern represents a low-order dynamic mechanism that persists in the absence of higher-level brain activity. Indeed, the fact that many different conditions produce similar brain activity suggests that there may be a common pathway to the state of brain inactivation and may indicate fundamental properties of the brain circuits (2). explain certain properties of the burst suppression waveform. These models do not clarify the underlying biophysical dynamics.

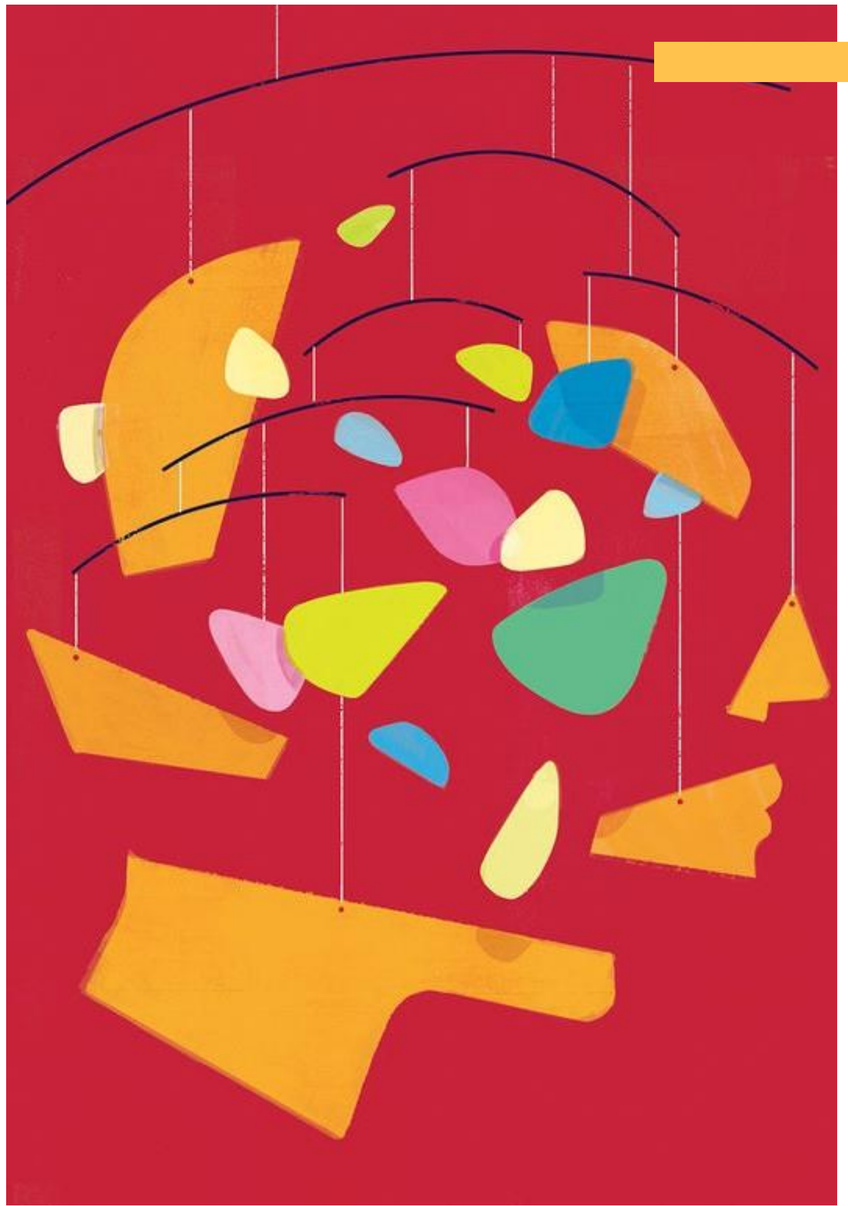
In contrast, we construct a biophysical model that is constrained by neurophysiology and the commonality between the aforementioned etiologies—specifically, a reduction in brain metabolism. The unique feature of our model is a nuanced interaction between neuronal dynamics and changes in cerebral metabolic rate of oxygen (CMRO). The model produces the distinctive characteristics of burst suppression, providing unique insights and predictions regarding low-order brain dynamics in states of reduced activity. Specifically, it suggests that burst suppression represents a basal neurometabolic regime that ensures basic cell function during states of lowered metabolism. We discuss clinical and experimental implications of these findings.

Prevailing Features of Burst Suppression

To constrain the model, we first consider three prevailing features of burst suppression, summarized in refs. 6 and 9, for which there is clinical and experimental evidence. The first feature of note is the synchrony of burst onset; (i.e., bursts begin and end nearly simultaneously across the entire scalp). Such a spatially homogeneous behavior immediately suggests that a very low-order dynamic mechanism underlies burst suppression. Some studies have suggested that asynchronous burst suppression can arise in the case of large-scale cortical deafferentation (14, 15). In such settings, large-scale differences in regional blood supply and autoregulation may prevent the uniformity typically associated with burst suppression.

A second important feature of burst suppression is its para-
metric sensitivity to the level-

Ching et al. PNAS, vol 109, 8, 3095-3100



BROWN & PURDON'S MODEL

SEARCHING FOR AN ALL-ENCOMPASSING EXPLANATION

the unifying feature of the different burst suppression etiologies is

aberrant neurometabolic dynamics

a biochemical candidate to explain the slow modulation AND link with brain metabolism is the

ATP-dependant potassium channel

BROWN & PURDON'S MODEL

BIOPHYSIOLOGICAL MODELING

rate of ATP consumption

sodium ATP pump
action potential
burst activity

AUTOREGULATION

$CMRO_2$

CBF

rate of ATP generation

ATP depletion

opens

K_{ATP} channel

hyperpolarization & cessation of spiking

suppression pattern

ATP regeneration

Ching et al. PNAS, vol 109, 8, 3095-3100

BROWN & PURDON'S MODEL

BIOPHYSIOLOGICAL MODELING

rate of ATP consumption

1

sodium ATP pump
action potential
burst activity

AUTOREGULATION

$CMRO_2$

CBF

rate of ATP generation

2

ATP regeneration

ATP depletion

opens

suppression pattern

hyperpolarisation & cessation of action potentials

K_{ATP} channel

Ching et al. PNAS, vol 109, 8, 3095-3100

1. WHAT IS THE PATHOPHYSIOLOGY OF BURST SUPPRESSION?

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WHAT IS THE PATHOPHYSIOLOGY OF BURST SUPPRESSION?

decreased cortical inhibition and cyclical depletion and recovery of **interstitial calcium**

Amzica et al. 2009

slow oscillations related to cyclical **ATP depletion** and regeneration

Ching et al. 2011

aberrant neurometabolic dynamics

1. WHAT IS THE PATHOPHYSIOLOGY OF BURST SUPPRESSION?

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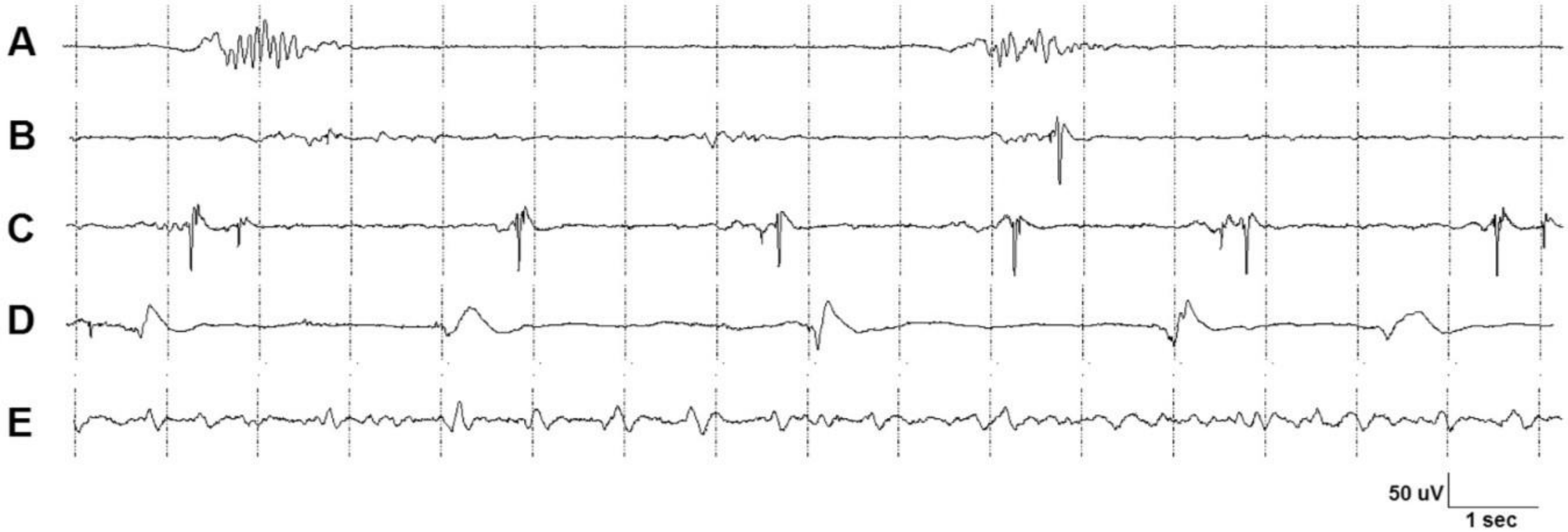
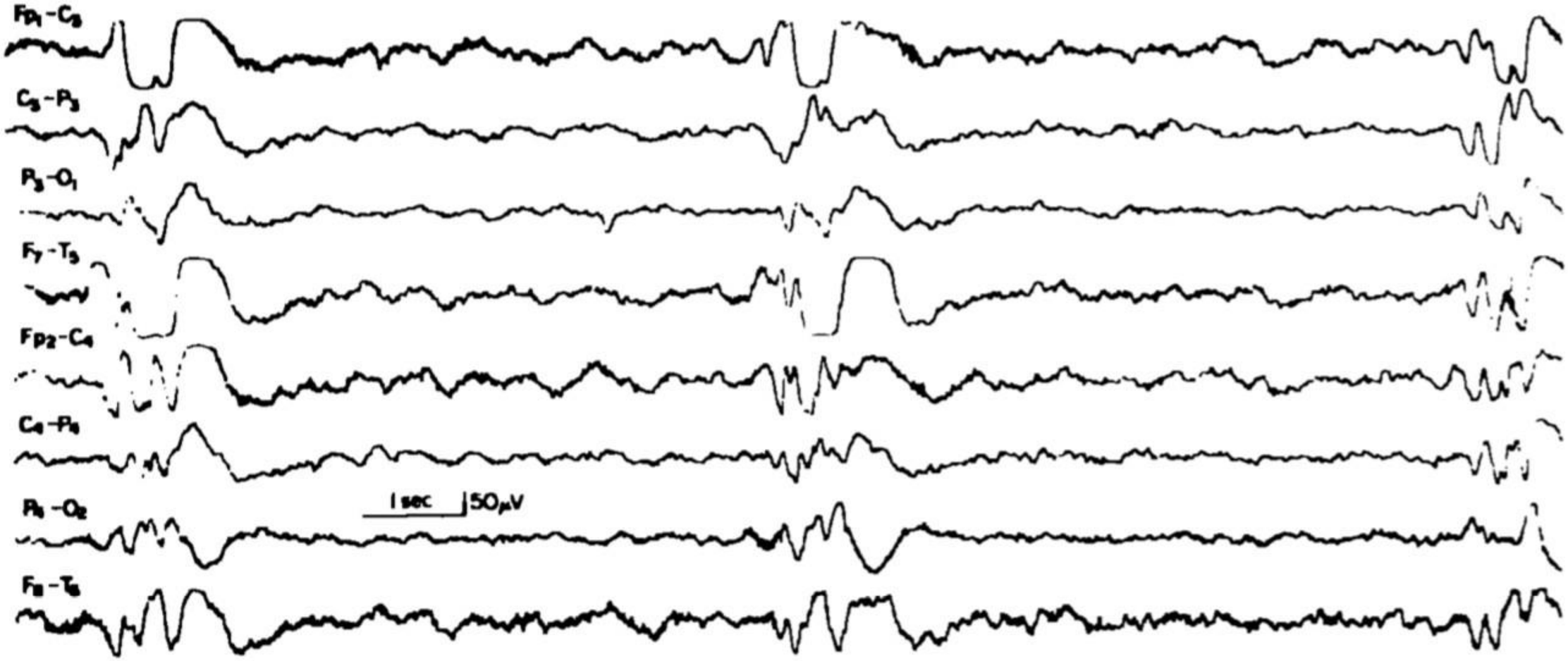
2. HOW CAN WE MONITOR BURST SUPPRESSION?

BURST SUPPRESSION MONITORING

RAW EEG TRACE

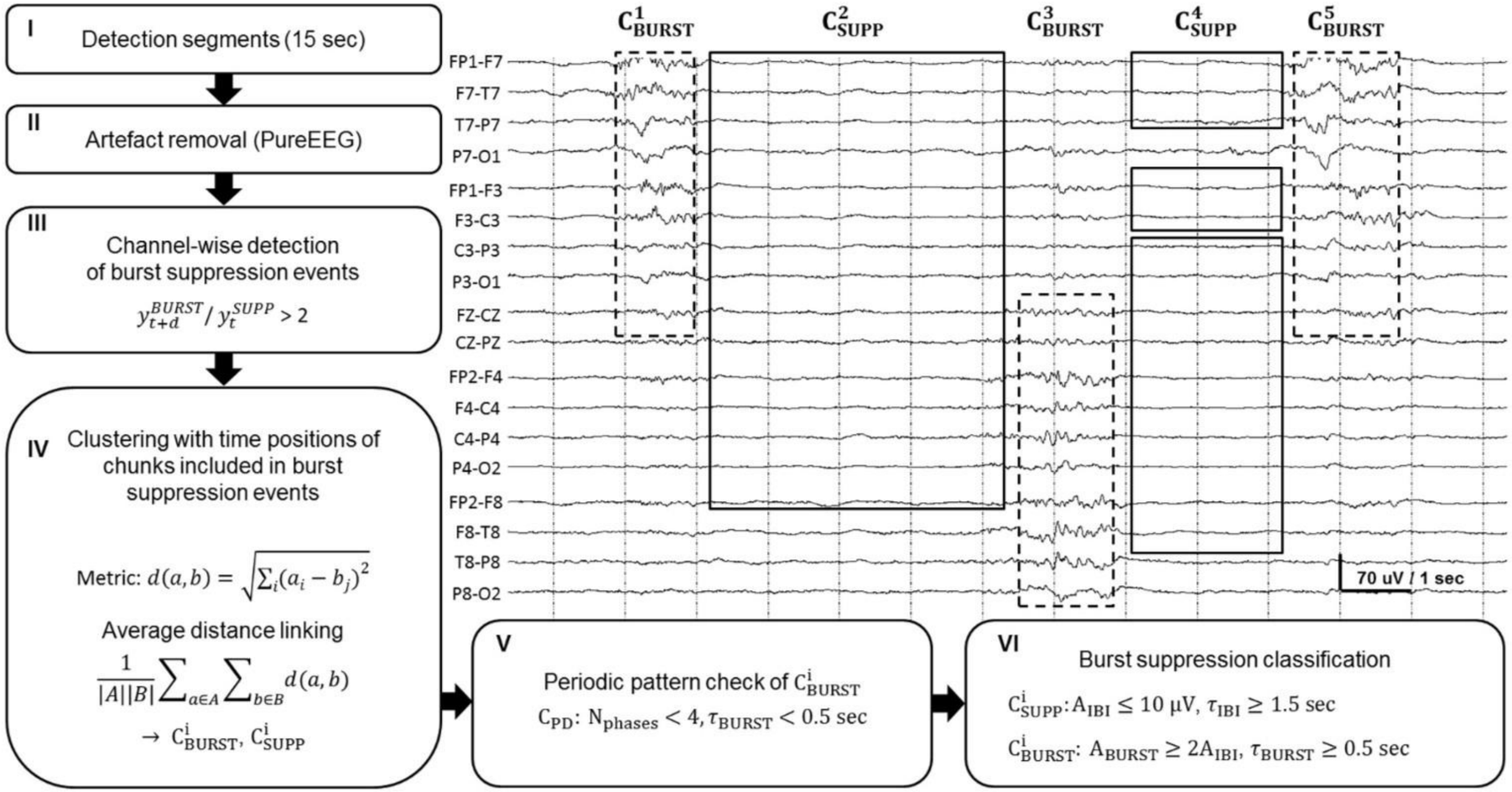


F. Fürbass et al. / Clinical Neurophysiology 127 (2016) 2038–2046 2041


Fp1-C3
C3-P3
P3-O1
F7-T3
Fp2-C4
C4-P4
P4-O2
F8-T4
1 sec
50μV

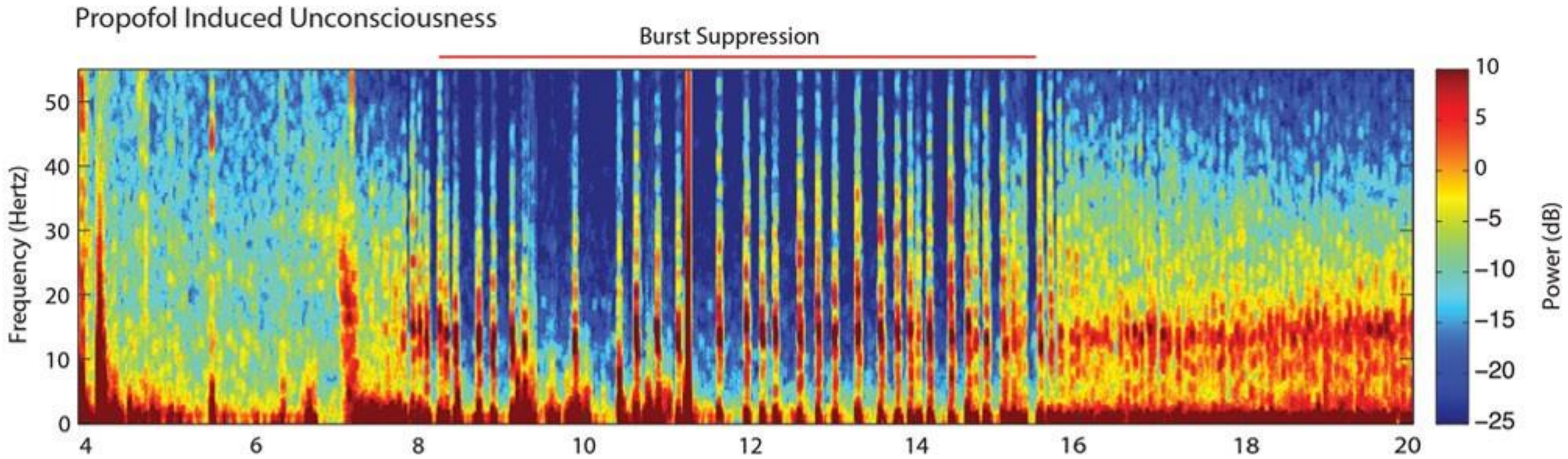
BURST SUPPRESSION

QUANTIFICATION & AUTOMATIC DETECTION



F. Fürbass et al. / Clinical Neurophysiology 127 (2016) 2038–2046 2041

DENSITY SPECTRAL ARRAY/ SPECTROGRAM



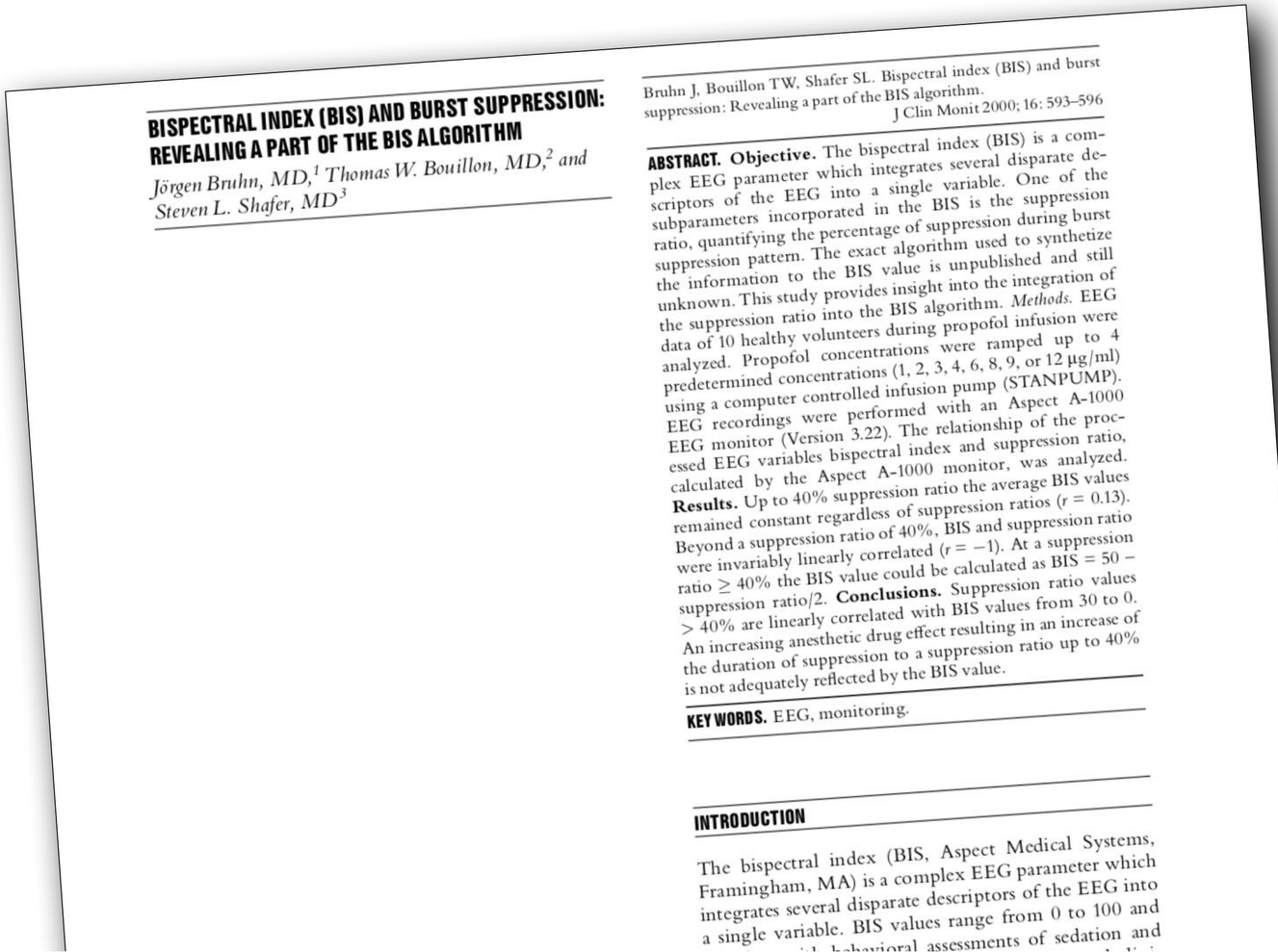
CAPLINE HEADER ELEMENT

BIS MONITORING OF BURST SUPPRESSION

Name	Involved Parameters	Range of Values	Classically Defined Thresholds
BIS	• Relative β activity • SFS activity • Quasi-flat activity • BS activity • Bispectrum	0-100	Wake state: >93 LOR: 80 RIV: 40-60

Marchant et al How Electroencephalography Serves the Anesthesiologist

REVERSE ENGINEERING THE BIS ALGORITHM



BISPECTRAL INDEX (BIS) AND BURST SUPPRESSION: REVEALING A PART OF THE BIS ALGORITHM

Jörgen Bruhn, MD,[1] Thomas W. Bouillon, MD,[2] and Steven L. Shafer, MD[3]

Bruhn J, Bouillon TW, Shafer SL. Bispectral index (BIS) and burst suppression: Revealing a part of the BIS algorithm.
J Clin Monit 2000; 16: 593–596

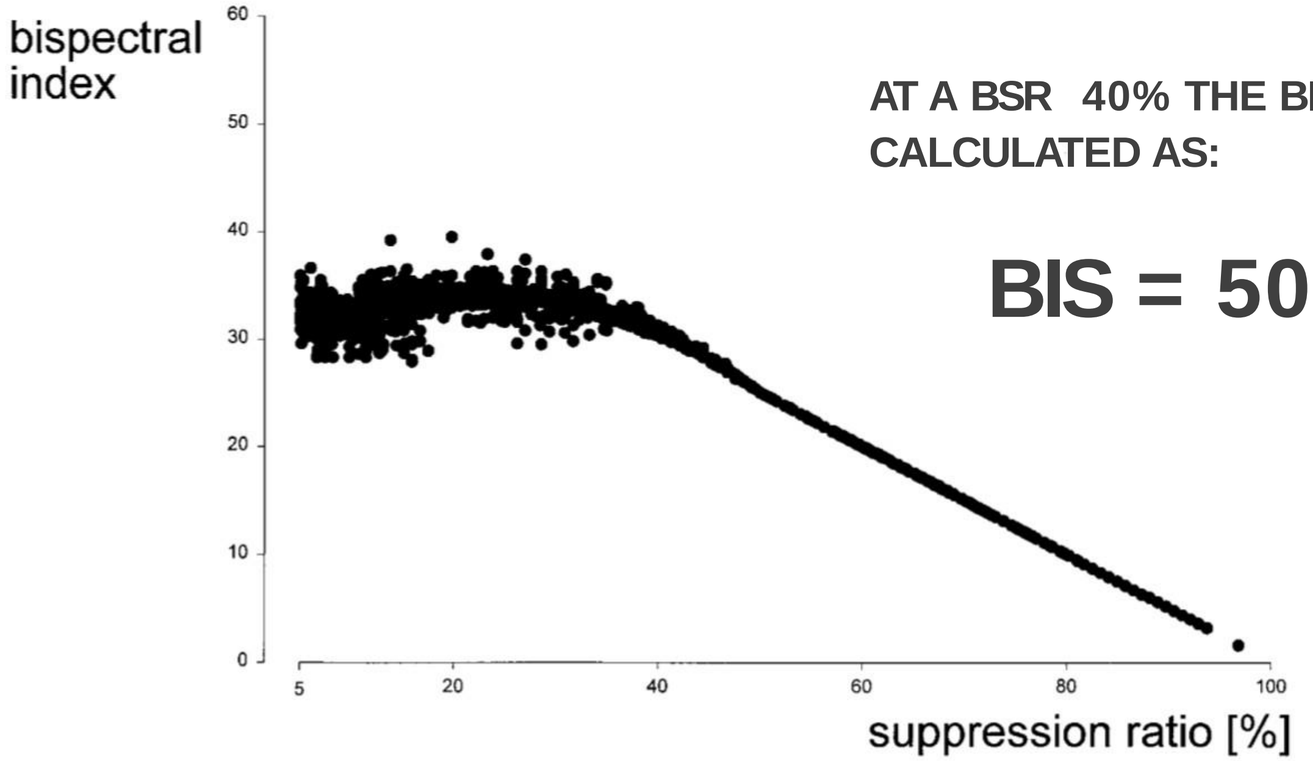
ABSTRACT. Objective. The bispectral index (BIS) is a complex EEG parameter which integrates several disparate descriptors of the EEG into a single variable. One of the subparameters incorporated in the BIS is the suppression ratio, quantifying the percentage of suppression during burst suppression pattern. The exact algorithm used to synthetize the information to the BIS value is unpublished and still unknown. This study provides insight into the integration of the suppression ratio into the BIS algorithm. *Methods.* EEG data of 10 healthy volunteers during propofol infusion were analyzed. Propofol concentrations were ramped up to 4 predetermined concentrations (1, 2, 3, 4, 6, 8, 9, or 12 μg/ml) using a computer controlled infusion pump (STANPUMP). EEG recordings were performed with an Aspect A-1000 EEG monitor (Version 3.22). The relationship of the processed EEG variables bispectral index and suppression ratio, calculated by the Aspect A-1000 monitor, was analyzed. **Results.** Up to 40% suppression ratio the average BIS values remained constant regardless of suppression ratios ($r = 0.13$). Beyond a suppression ratio of 40%, BIS and suppression ratio were invariably linearly correlated ($r = -1$). At a suppression ratio $\geq$ 40% the BIS value could be calculated as BIS = 50 − suppression ratio/2. **Conclusions.** Suppression ratio values > 40% are linearly correlated with BIS values from 30 to 0. An increasing anesthetic drug effect resulting in an increase of the duration of suppression to a suppression ratio up to 40% is not adequately reflected by the BIS value.

KEY WORDS. EEG, monitoring.

INTRODUCTION

The bispectral index (BIS, Aspect Medical Systems, Framingham, MA) is a complex EEG parameter which integrates several disparate descriptors of the EEG into a single variable. BIS values range from 0 to 100 and

BSR VALUES < 40% ARE LINEARLY CORRELATED WITH BIS VALUES FROM 30 TO 0



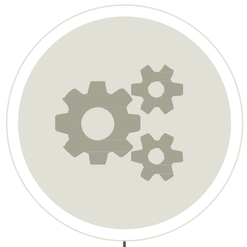
AT A BSR 40% THE BIS VALUE COULD BE CALCULATED AS:

$$BIS = 50 - BSR/2$$

1. WHAT IS THE PATHOPHYSIOLOGY OF BURST SUPPRESSION?

3. IS IATROGENIC BURST SUPPRESSION PROTECTIVE OR TOXIC?

2. HOW CAN WE MONITOR BURST SUPPRESSION?



1. WHAT IS THE PATHOPHYSIOLOGY OF BURST SUPPRESSION?

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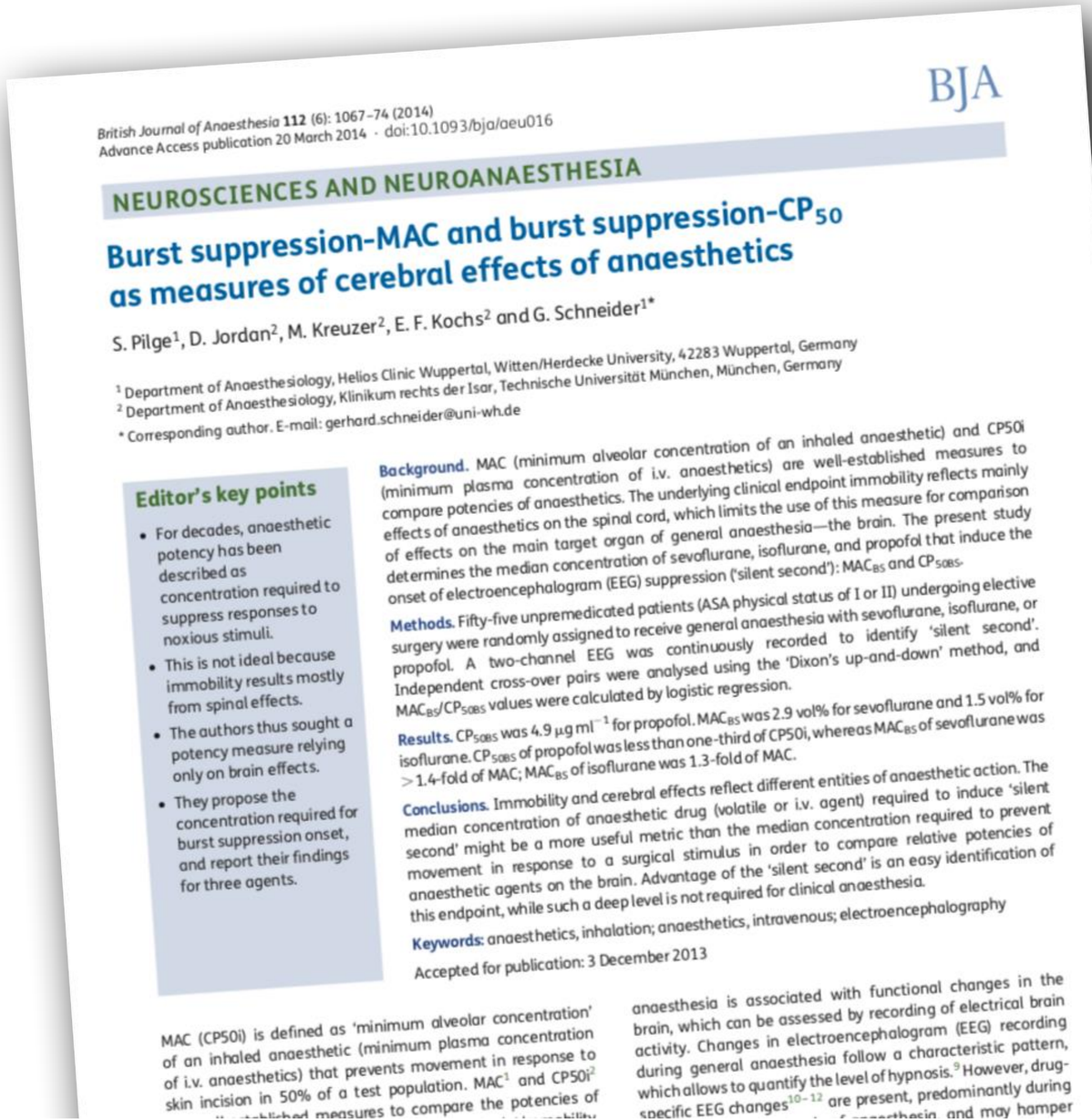
IATROGENIC BURST SUPPRESSION

ANESTHETIC AGENTS AND BURST SUPPRESSION



British Journal of Anaesthesia 112 (6): 1067–74 (2014)
Advance Access publication 20 March 2014 · doi:10.1093/bja/aeu016

BJA

NEUROSCIENCES AND NEUROANAESTHESIA

Burst suppression-MAC and burst suppression-CP_{50} as measures of cerebral effects of anaesthetics

S. Pilge[1], D. Jordan[2], M. Kreuzer[2], E. F. Kochs[2] and G. Schneider[1]*

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* Corresponding author. E-mail: gerhard.schneider@uni-wh.de

Editor's key points

- For decades, anaesthetic potency has been described as concentration required to suppress responses to noxious stimuli.
- This is not ideal because immobility results mostly from spinal effects.
- The authors thus sought a potency measure relying only on brain effects.
- They propose the concentration required for burst suppression onset, and report their findings for three agents.

Background. MAC (minimum alveolar concentration of an inhaled anaesthetic) and CP50i (minimum plasma concentration of i.v. anaesthetics) are well-established measures to compare potencies of anaesthetics. The underlying clinical endpoint immobility reflects mainly effects of anaesthetics on the spinal cord, which limits the use of this measure for comparison of effects on the main target organ of general anaesthesia—the brain. The present study determines the median concentration of sevoflurane, isoflurane, and propofol that induce the onset of electroencephalogram (EEG) suppression ('silent second'): MAC_{BS} and CP_{50BS}.

Methods. Fifty-five unpremedicated patients (ASA physical status of I or II) undergoing elective surgery were randomly assigned to receive general anaesthesia with sevoflurane, isoflurane, or propofol. A two-channel EEG was continuously recorded to identify 'silent second'. Independent cross-over pairs were analysed using the 'Dixon's up-and-down' method, and MAC_{BS}/CP_{50BS} values were calculated by logistic regression.

Results. CP_{50BS} was 4.9 $\mu g\,ml^{-1}$ for propofol. MAC_{BS} was 2.9 vol% for sevoflurane and 1.5 vol% for isoflurane. CP_{50BS} of propofol was less than one-third of CP50i, whereas MAC_{BS} of sevoflurane was >1.4-fold of MAC; MAC_{BS} of isoflurane was 1.3-fold of MAC.

Conclusions. Immobility and cerebral effects reflect different entities of anaesthetic action. The median concentration of anaesthetic drug (volatile or i.v. agent) required to induce 'silent second' might be a more useful metric than the median concentration required to prevent movement in response to a surgical stimulus in order to compare relative potencies of anaesthetic agents on the brain. Advantage of the 'silent second' is an easy identification of this endpoint, while such a deep level is not required for clinical anaesthesia.

Keywords: anaesthetics, inhalation; anaesthetics, intravenous; electroencephalography

Accepted for publication: 3 December 2013

MAC (CP50i) is defined as 'minimum alveolar concentration' of an inhaled anaesthetic (minimum plasma concentration of i.v. anaesthetics) that prevents movement in response to skin incision in 50% of a test population. MAC[1] and CP50i[2] established measures to compare the potencies of

anaesthesia is associated with functional changes in the brain, which can be assessed by recording of electrical brain activity. Changes in electroencephalogram (EEG) recording during general anaesthesia follow a characteristic pattern, which allows to quantify the level of hypnosis.[9] However, drug-specific EEG changes[10–12] are present, predominantly during

the propofol plasma concentration necessary to produce burst suppression in 50% of subjects ($CP50_{BS}$) was **4.85 mcg/ml (95% CI 4.25–5.40)**

whereas published concentration necessary to produce immobility ($CP50_i$) is more than three times greater ($CP50_i$ 15.2 mcg/ml)

Pilge et al. Br J Anaesth. 2014 Mar;112(6):1067-74.

PROPOFOL & BURST-SUPPRESSION

PREVIOUS STUDIES ON PROPOFOL BURST SUPPRESSION

5,5 mcg/mL

MEDIAN EFFECT-SITE CONCENTRATION TO ACHIEVE BURST SUPPRESSION

Newman et al.1995

5,5 mcg/mL

MINIMAL BRAIN CONCENTRATION REQUIRED TO OBSERVE BURST SUPPRESSION

Ludbrook et al. 2002

Ludbrook et al. Anesthesiology 2002; 97:1363–70
Newman et al. AnesthAnalg 1995;81:452

IATROGENIC BURST SUPPRESSION

BURST SUPPRESSION AND INHALED AGENTS

2,9 vol%

MAC_{BS} OF SEVOFLURANE

1.4-fold MAC

1,5 vol%

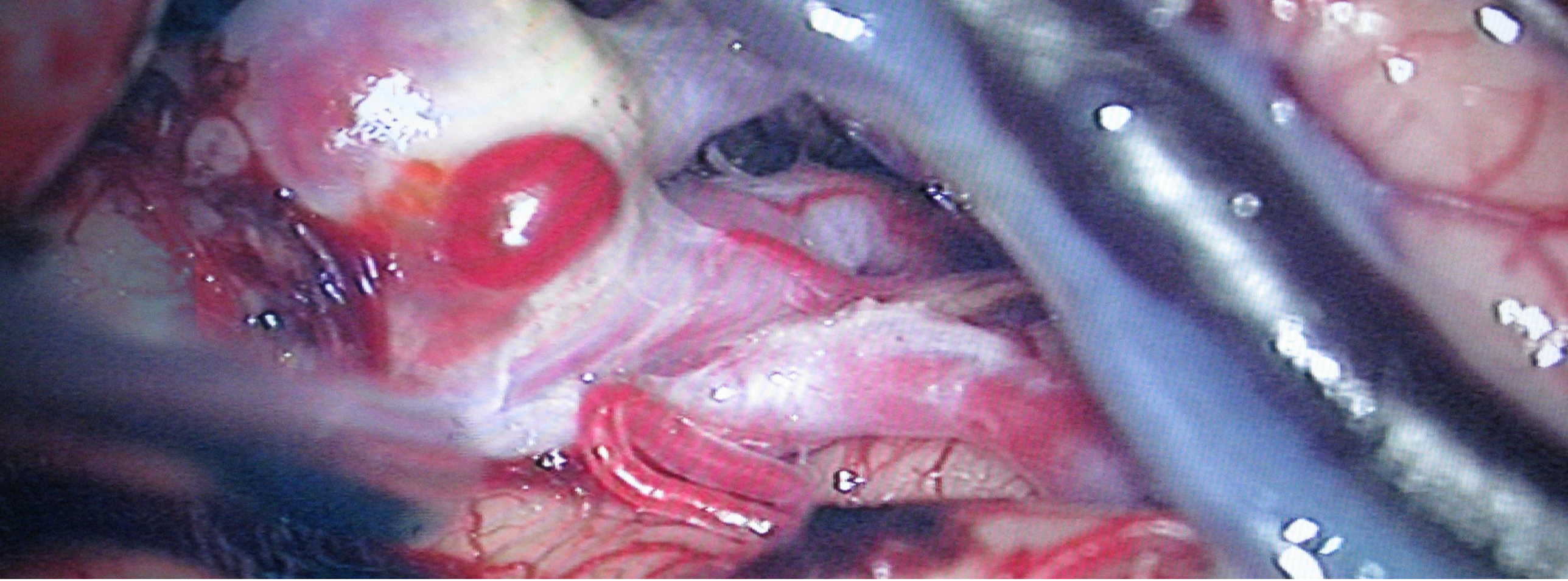
MAC_{BS} OF ISOFLURANE

1.3-fold MAC

Pilge et al. Br J Anaesth. 2014 Mar;112(6):1067-74.

IATROGENIC BURST SUPPRESSION

PART I : NEUROPROTECTION

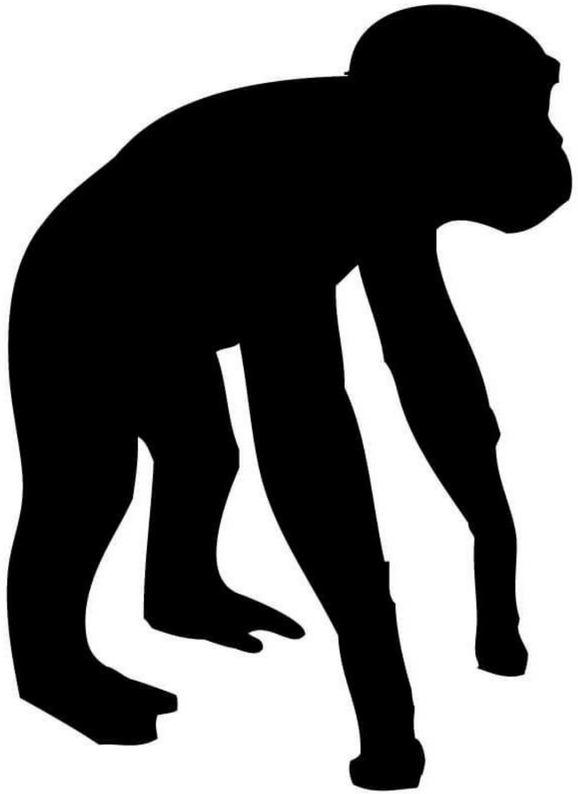


IATROGENIC BURST SUPPRESSION

BACK TO ANEURYSM SURGERY

IATROGENIC BURST SUPPRESSION

ANIMAL STUDIES



Kochs et al. Anesthesiology 76:245-252, 1992
Selman et al. J Neurosurg 55:220-226, 1981

in various animal models of middle cerebral artery occlusion, barbiturates given before or after occlusion reduce the size of cerebral infarction as compared to controls

Selman et al. 1981
Taylor et al. 1996

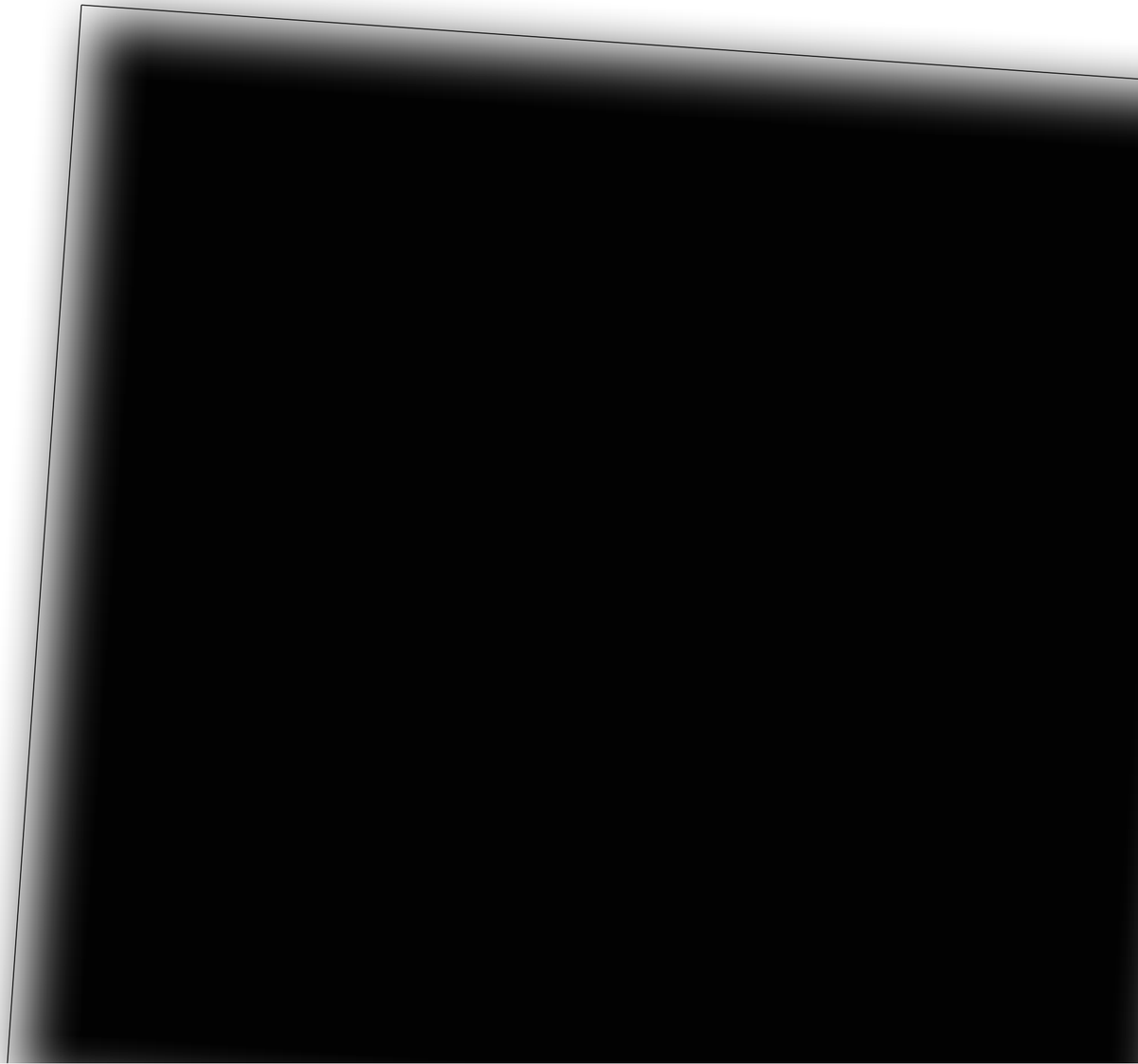
propofol has also been shown to improve neurologic outcome and neuronal death after ischemia in rat model

Kochs et al. 1992

IATROGENIC BURST-SUPPRESSION

> […] **significant advantage** when they are given **pentobarbital** as the primary neuroprotective agent or when they receive **propofol** or **etomidate** titrated to achieve **electroencephalographic burst suppression**

- LAVINE ET AL. 1997



Lavine et al. J Neurosurg 87:817–824, 1997

IATROGENIC BURST SUPPRESSION

A LANDMARK STUDY: **IHAST**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Mild Intraoperative Hypothermia during Surgery for Intracranial Aneurysm

Michael M. Todd, M.D., Bradley J. Hindman, M.D., William R. Clarke, Ph.D., and James C. Torner, Ph.D., for the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) Investigators*

ABSTRACT

BACKGROUND
Surgery for intracranial aneurysm often results in postoperative neurologic deficits. We conducted a randomized trial at 30 centers to determine whether intraoperative cooling during open craniotomy would improve the outcome among patients with acute aneurysmal subarachnoid hemorrhage.

METHODS
A total of 1001 patients with a preoperative World Federation of Neurological Surgeons score of I, II, or III ("good-grade patients"), who had had a subarachnoid hemorrhage no more than 14 days before planned surgical aneurysm clipping, were randomly assigned to intraoperative hypothermia (target temperature, 33°C, with the use of surface cooling techniques) or normothermia (target temperature, 36.5°C). Patients were followed closely postoperatively and examined approximately 90 days after surgery, at which time a Glasgow Outcome Score was assigned.

RESULTS
There were no significant differences between the group assigned to intraoperative hypothermia and the group assigned to normothermia in the duration of stay in the

From the Department of Anesthesia, Roy J. and Lucille A. Carver College of Medicine, University of Iowa (M.M.T., B.J.H.); and the Departments of Biostatistics (W.R.C.) and Epidemiology (J.C.T.) and the Data Management Center (W.R.C.), University of Iowa College of Public Health — both in Iowa City. Address reprint requests to Dr. Todd at the Department of Anesthesia, University of Iowa, 200 Hawkins Dr., 6546 JCP, Iowa City, IA 52242, or at michael-todd@uiowa.edu.

*Participating centers and investigators are listed in the Appendix.

N Engl J Med 2005;352:135-45.

the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST) was a randomized trial of mild systemic hypothermia (33°C) in patients undergoing surgery to treat an acutely ruptured intracranial aneurysm.

Todd at al. N Engl J Med 2005;352:135-45.

IATROGENIC BURST SUPPRESSION

NEUROSURGERY: IHAST

441 patients undergoing temporary clipping either had no additional protective intervention (n =263) or received supplemental protective drug during temporary clipping (thiopental, n=157; etomidate, n=20)

administration of supplemental pharmacologic agents during temporary clipping did not affect neurologic outcomes.

Hindman et al. Anesthesiology 2010; 112:86 –101

Anesthesiology 2010; 112:86–101

No Association between Intraoperative Hypothermia or Supplemental Protective Drug and Neurologic Outcomes in Patients Undergoing Temporary Clipping during Cerebral Aneurysm Surgery

Findings from the Intraoperative Hypothermia for Aneurysm Surgery Trial

Bradley J. Hindman, M.D.,* Emine O. Bayman, Ph.D.,† Wolfgang K. Pfisterer, M.D.,‡ James C. Torner, Ph.D.,§ Michael M. Todd, M.D.,‖; on behalf of the IHAST Investigators#

ABSTRACT

Background: Although hypothermia and barbiturates improve neurologic outcomes in animal temporary focal ischemia models, the clinical efficacy of these interventions during temporary occlusion of the cerebral vasculature during intracranial aneurysm surgery (temporary clipping) is not established.

Methods: A *post hoc* analysis of patients from the Intraoperative Hypothermia for Aneurysm Surgery Trial who underwent temporary clipping was performed. Univariate and multivariate logistic regression methods were used to test for associations between hypothermia, supplemental protective drug, and short- (24-h) and long-term (3-month) neurologic outcomes. An odds ratio more than 1 denotes better outcome.

Results: Patients undergoing temporary clipping (n = 441) were assigned to intraoperative hypothermia (33.3° ± 0.8°C, n = 208) or normothermia (36.7° ± 0.5°C, n = 233), with 178 patients also receiving supplemental protective drug (thiopental or etomidate) during temporary clipping. Three months after surgery, 278 patients (63%) had good outcome (Glasgow Outcome Score = 1). Neither hypothermia (P = 0.847; odds ratio = 1.043, 95% CI = 0.678–1.606) nor supplemental protective drug (P = 0.835; odds ratio = 1.048, 95% CI = 0.674–1.631) were associated with 3-month Glasgow Outcome Score. The effect of supplemental protective drug did not significantly vary with temperature. The effects of hypothermia and protective drug did not significantly vary with temporary clip duration. Similar findings were made for 24-h neurologic status and 3-month Neuropsychological Composite Score.

Conclusion: In the Intraoperative Hypothermia for Aneurysm Surgery Trial, neither systemic hypothermia nor supplemental protective drug affected short- or long-term neurologic outcomes of patients undergoing temporary clipping.

What We Already Know about This Topic

- Animal studies suggest that hypothermia and barbiturates protect the brain during transient focal ischemia, but the clinical relevance of this is unknown

What This Article Tells Us That Is New

- In a secondary analysis of 441 patients with temporary clipping during cerebral aneurysm surgery, neither hypothermia nor barbiturate treatment improved 24-h or 3-month neurologic outcome
- As opposed to results in animal studies, these interventions may not be protective in patients undergoing

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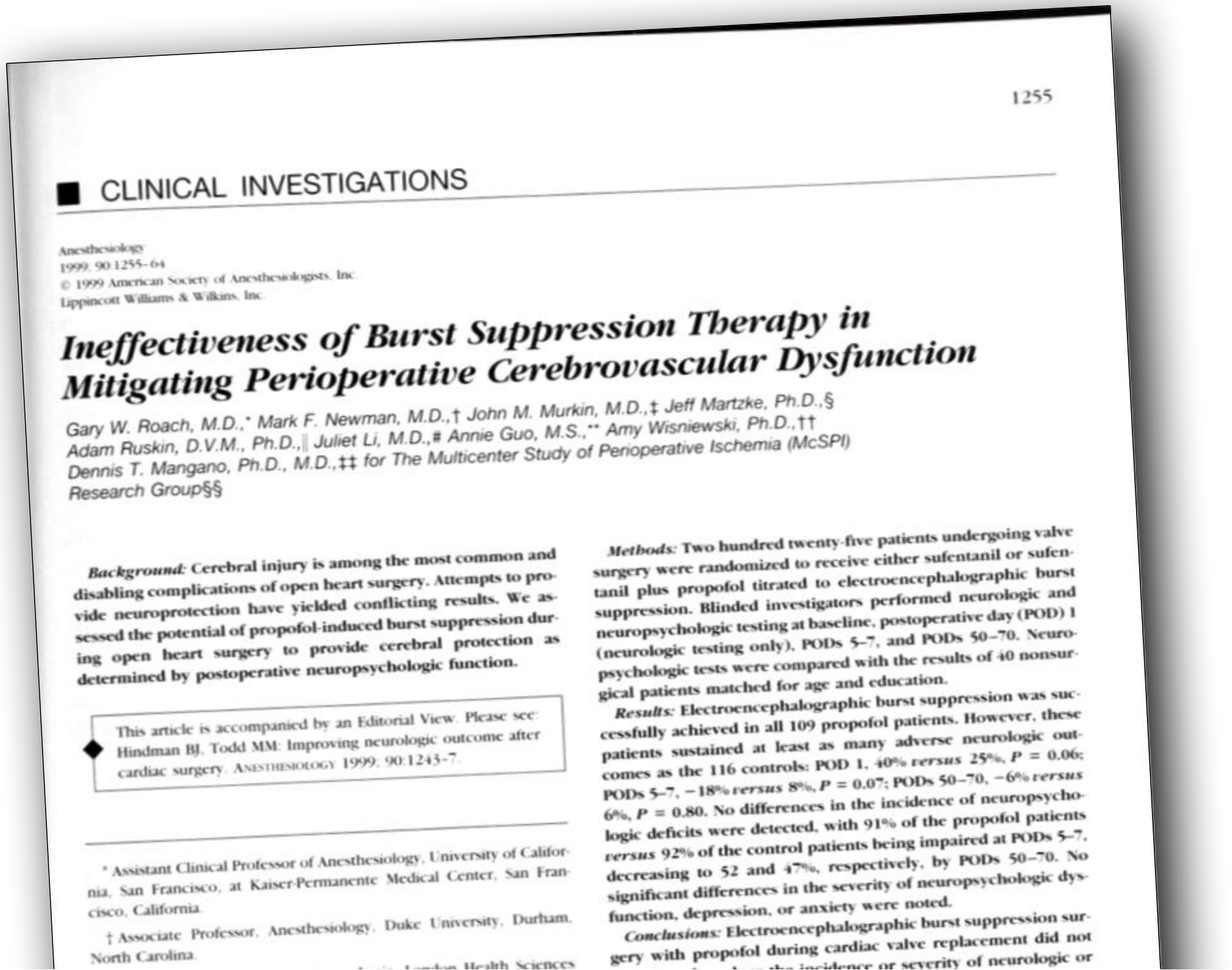
Received from Department of Anesthesia, Carver College

IATROGENIC BURST SUPPRESSION

A SIMILAR TALE: BURST SUPPRESSION IN CARDIAC SURGERY

IATROGENIC BURST SUPPRESSION

THE IHAST OF CARDIAC ANESTHESIA: MCSPI



1255

CLINICAL INVESTIGATIONS

Anesthesiology
1999; 90:1255–64

Ineffectiveness of Burst Suppression Therapy in Mitigating Perioperative Cerebrovascular Dysfunction

Gary W. Roach, M.D., Mark F. Newman, M.D.,† John M. Murkin, M.D.,‡ Jeff Martzke, Ph.D.,§ Adam Ruskin, D.V.M., Ph.D.,‖ Juliet Li, M.D.,# Annie Guo, M.S.,** Amy Wisniewski, Ph.D.,†† Dennis T. Mangano, Ph.D., M.D.,‡‡ for The Multicenter Study of Perioperative Ischemia (McSPI) Research Group§§*

Background: **Cerebral injury is among the most common and disabling complications of open heart surgery. Attempts to provide neuroprotection have yielded conflicting results. We assessed the potential of propofol-induced burst suppression during open heart surgery to provide cerebral protection as determined by postoperative neuropsychologic function.**

Methods: **Two hundred twenty-five patients undergoing valve surgery were randomized to receive either sufentanil or sufentanil plus propofol titrated to electroencephalographic burst suppression. Blinded investigators performed neurologic and neuropsychologic testing at baseline, postoperative day (POD) 1 (neurologic testing only), PODs 5–7, and PODs 50–70. Neuropsychologic tests were compared with the results of 40 nonsurgical patients matched for age and education.**

Results: **Electroencephalographic burst suppression was successfully achieved in all 109 propofol patients. However, these patients sustained at least as many adverse neurologic outcomes as the 116 controls: POD 1, 40% *versus* 25%, $P = 0.06$; PODs 5–7, −18% *versus* 8%, $P = 0.07$; PODs 50–70, −6% *versus* 6%, $P = 0.80$. No differences in the incidence of neuropsychologic deficits were detected, with 91% of the propofol patients *versus* 92% of the control patients being impaired at PODs 5–7, decreasing to 52 and 47%, respectively, by PODs 50–70. No significant differences in the severity of neuropsychologic dysfunction, depression, or anxiety were noted.**

Conclusions: **Electroencephalographic burst suppression surgery with propofol during cardiac valve replacement did not**

This article is accompanied by an Editorial View. Please see: Hindman BJ, Todd MM: Improving neurologic outcome after cardiac surgery. ANESTHESIOLOGY 1999; 90:1243–7.

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† Associate Professor, Anesthesiology, Duke University, Durham, North Carolina.

225 patients undergoing valve surgery randomized to sufentanil alone vs sufentanil + propofol titrated to burst suppression

neurologic and neuropsychologic testing post-operatively

Roach et al. Anesthesiology 1999; 90:1255-64.

Table 3. Incidence of Neurologic Outcome

	Group A Propofol + Sufenta Anesthesia (n = 109) (%)	Group B Sufenta Anesthesia (n = 116) (%)	*P* Value
POD 1			
Neurologic deficit	40/101 (40)	27/110 (25)	0.06
POD 6			
Neurologic deficit	18/98 (18)	8/103 (8)	0.07
POD 60			
Neurologic deficit	5/81 (6)	5/81 (6)	0.80

electroencephalographic burst suppression surgery with propofol did not significantly reduce incidence or severity of neurologic dysfunction

PHARMACOLOGICALLY INDUCED BURST SUPPRESSION DOES NOT YIELD BETTER NEUROLOGIC OUTCOMES IN CARDIAC SURGERY AND ANEURYSM SURGERY

BURST SUPPRESSION IS NOT BRAIN REST

remember Amzica!

(INVOLUNTARY) IATROGENIC BURST SUPPRESSION

PART II : NEUROTOXICITY

RISK FACTORS FOR BURST SUPPRESSION

Table 3 Independent risk factors of intraoperative SR. Adjusted on: ASA physical status (I–II *vs* III–IV), diabetes mellitus, hypertension, chronic renal failure, congestive heart failure, peroperative antihypertensive medication, peroperative vasopressive medication, trial of inclusion, and propofol and remifentanil dose (mg kg^{-1} h^{-1} and μg kg^{-1} min^{-1}, respectively). $P=0.67$ for the Hosmer–Lemeshow goodness of fit test. $T_{BIS\ 40-60}$, per cent of time spent in the BIS target range between 40 and 60

Risk factors	Odds ratio (95% CI)	*P*-value
Age		
<40 yr	1.00	
40–59 yr	2.16 (0.81–5.75)	0.068
60–80 yr	4.80 (1.85–12.43)	0.027
>80 yr	10.59 (3.76–29.81)	<0.0001
$T_{BIS\ 40-60}$	0.97 (0.96–0.98)	<0.0001
Coronary artery disease		
No	1.00	
Yes	2.53 (1.47–4.37)	0.001
Gender		
Female	1.00	
Male	1.57 (1.03–2.40)	0.03

AGE & BURST SUPPRESSION

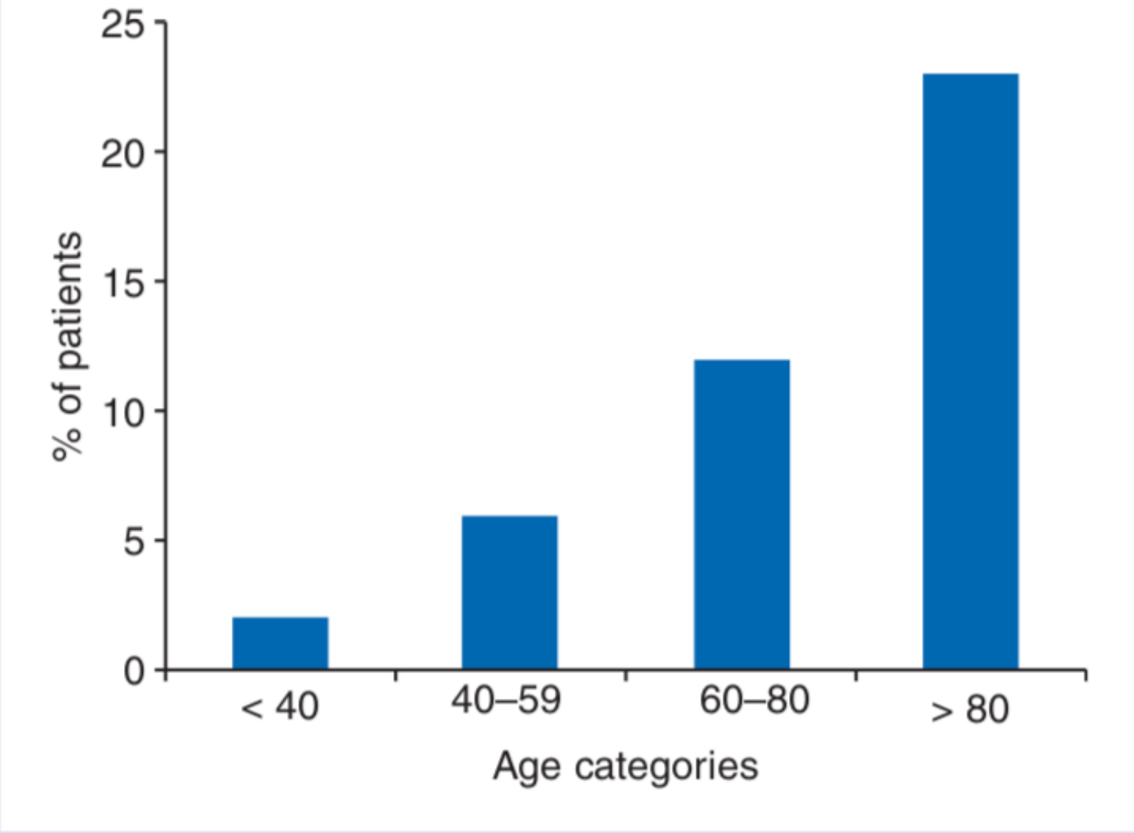

Fig 2 Proportion of patients from the SR group in each category of age.

THE AGEING BRAIN IS MORE LIKELY TO SHOW BURST SUPPRESSION

BURST SUPPRESSION DURING ANESTHESIA IS ASSOCIATED WITH POOR OUTCOME

British Journal of Anaesthesia 113 (6): 1001–8 (2014)
Advance Access publication 22 May 2014 · doi:10.1093/bja/aeu105

BJA

NEUROSCIENCES AND NEUROANAESTHESIA

Association between intraoperative electroencephalographic suppression and postoperative mortality‡

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[2] Department of Mathematics, Washington University in St Louis, Campus Box 1146, One Brookings Drive, St Louis, MO 63130, USA
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Editor's key points

- Previous studies have suggested a link between deep anaesthesia and mortality.
- The authors studied this association using data from two previous studies.
- A multivariate analysis did not show an association between >5 min of EEG suppression and mortality.
- EEG suppression and coincident hypotension were however strongly associated with mortality.

Background. Low bispectral index values frequently reflect EEG suppression and have been associated with postoperative mortality. This study investigated whether intraoperative EEG suppression was an independent predictor of 90 day postoperative mortality and explored risk factors for EEG suppression.

Methods. This observational study included 2662 adults enrolled in the B-Unaware or BAG-RECALL trials. A cohort was defined with >5 cumulative minutes of EEG suppression, and 1:2 propensity-matched to a non-suppressed cohort (≤5 min suppression). We evaluated the association between EEG suppression and mortality using multivariable logistic regression, and examined risk factors for EEG suppression using zero-inflated mixed effects analysis.

Results. Ninety day postoperative mortality was 3.9% overall, 6.3% in the suppressed cohort, and 3.0% in the non-suppressed cohort [odds ratio (OR) [95% confidence interval (CI)]=2.19 (1.48–3.26)]. After matching and multivariable adjustment, EEG suppression was not associated with mortality [OR (95% CI)=0.83 (0.55–1.25)]; however, the interaction between EEG suppression and mean arterial pressure (MAP) <55 mm Hg was [OR (95% CI)=2.96 (1.34–6.52)]. Risk factors for EEG suppression were older age, number of comorbidities, chronic obstructive pulmonary disease, and higher intraoperative doses of benzodiazepines, opioids, or volatile anaesthetics. EEG suppression was less likely in patients with cancer, preoperative alcohol, opioid or benzodiazepine consumption, and intraoperative nitrous oxide exposure.

Conclusions. Although EEG suppression was associated with increasing anaesthetic administration and comorbidities, the hypothesis that intraoperative EEG suppression is a predictor of postoperative mortality was only supported if it was coincident with low MAP.

Clinical trial registration. NCT00281489 and NCT00682825.

Keywords: anaesthesia, general; comorbidity; deep sedation; electroencephalography; risk assessment

Accepted for publication: 5 January 2014

(BIS) values and postoperative mortality.[2 5–8] The BIS is a pro-

secondary analysis BAG-RECALL and B-UNAWARE trials

unadjusted association between EEG suppression and postoperative mortality using a univariable logistic regression

Willingham et al. British Journal of Anaesthesia 113 (6): 1001–8 (2014)

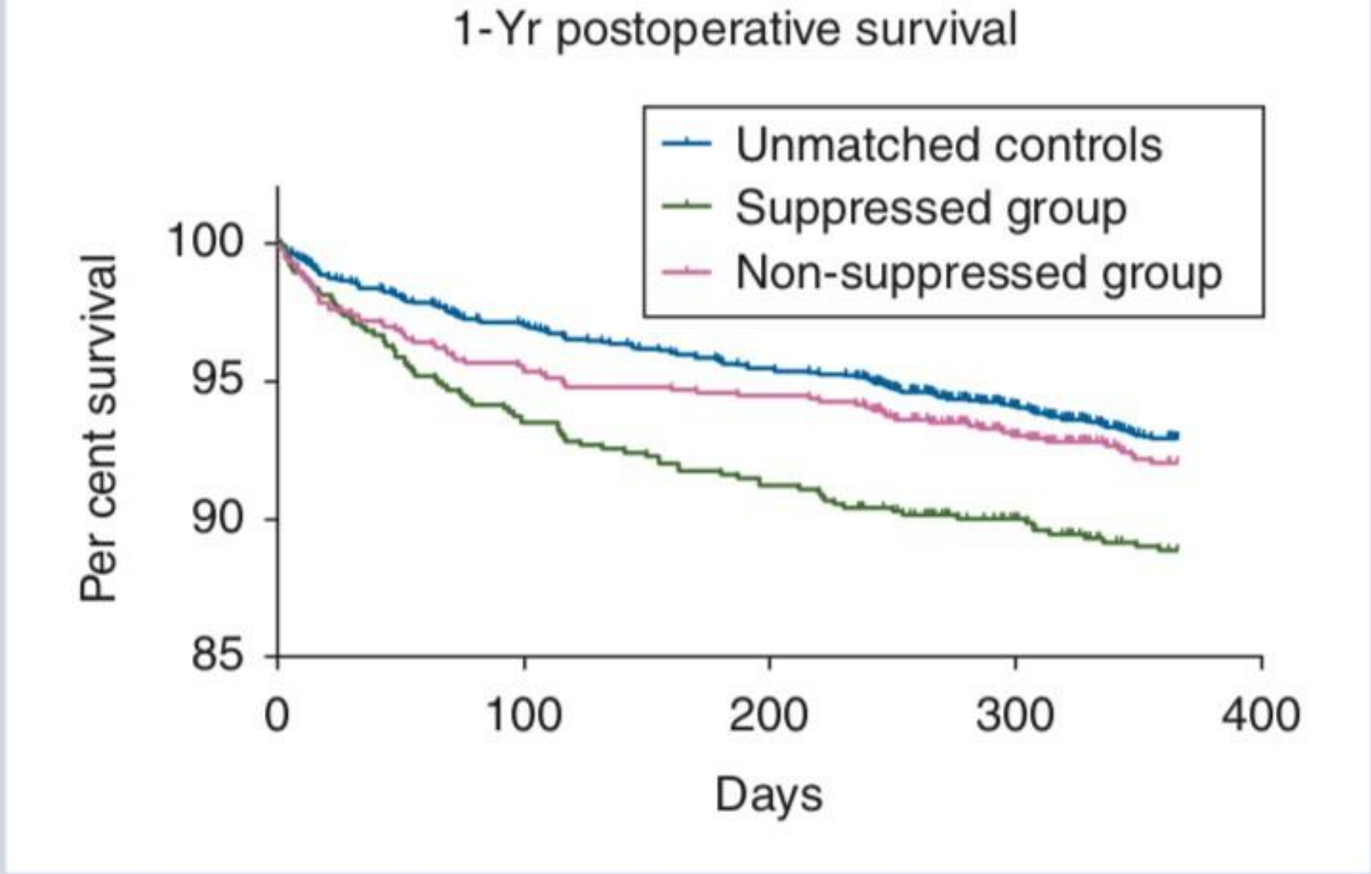

Fig 2 Per cent of the study population surviving after surgery.

after **propensity matching** each suppressed case with up to two non-suppressed controls based on their patient characteristics and comorbid covariates,

patients who experienced EEG suppression had **similar odds** of dying by 90 days as their non-suppressed counterparts

Willingham et al. British Journal of Anaesthesia 113 (6): 1001–8 (2014)

substudy of SATISFY SOS observational study

727 adult patients who received general anesthesia with planned intensive care unit admission

Intraoperative Electroencephalogram Suppression Predicts Postoperative Delirium

Bradley A. Fritz, MD,* Philip L. Kalarickal, MD,* Hannah R. Maybrier, BS,* Maxwell R. Muench, BS,* Doug Dearth, MD,* Yulong Chen, BA,* Krisztina E. Escallier, MD,* Arbi Ben Abdallah, PhD,* Nan Lin, PhD,† and Michael S. Avidan, MBBCh*

BACKGROUND: Postoperative delirium is a common complication associated with increased morbidity and mortality, longer hospital stays, and greater health care expenditures. Intraoperative electroencephalogram (EEG) slowing has been associated previously with postoperative delirium, but the relationship between intraoperative EEG suppression and postoperative delirium has not been investigated.

METHODS: In this observational cohort study, 727 adult patients who received general anesthesia with planned intensive care unit admission were included. Duration of intraoperative EEG suppression was recorded from a frontal EEG channel (FP1 to F7). Delirium was assessed twice daily on postoperative days 1 through 5 with the Confusion Assessment Method for the intensive care unit. Thirty days after surgery, quality of life, functional independence, and cognitive ability were measured using the Veterans RAND 12-item survey, the Barthel index, and the PROMIS Applied Cognition-Abilities-Short Form 4a survey.

RESULTS: Postoperative delirium was observed in 162 (26%) of 619 patients assessed. When we compared patients with no EEG suppression with those divided into quartiles based on duration of EEG suppression, patients with more suppression were more likely to experience delirium ($\chi^2(4) = 25$, $P < 0.0001$). This effect remained significant after we adjusted for potential confounders (odds ratio for log(EEG suppression) 1.22 [99% confidence interval, 1.06–1.40, $P = 0.0002$] per 1-minute increase in suppression). EEG suppression may have been associated with reduced functional independence (Spearman partial correlation coefficient −0.15, $P = 0.02$) but not with changes in quality of life or cognitive ability. Predictors of EEG suppression included greater end-tidal volatile anesthetic concentration and lower intraoperative opioid dose.

CONCLUSIONS: EEG suppression is an independent risk factor for postoperative delirium. Future studies should investigate whether anesthesia titration to minimize EEG suppression decreases the incidence of postoperative delirium. This is a substudy of the Systematic Assessment and Targeted Improvement of Services Following Yearlong Surgical Outcomes Surveys (SATISFY-SOS) surgical outcomes registry (NCT02032030). (Anesth Analg 2015;XXX:00–00)

Delirium is an acute cognitive disorder characterized by inattention, disorganized thinking, and a fluctuating course that develops over hours to days. Delirium is a common complication after surgery, with an incidence ranging from 10% to 70%, depending on the type of procedure.[1] Patients who experience postoperative delirium require longer stays in the intensive care unit (ICU), more days of mechanical ventilation, and increased hospital length of stay,[2] leading to a 31% increase in hospital costs during the index admission.[3] Even after hospital discharge, patients who experience postoperative delirium are at increased risk for institutionalization, death, and dementia.[4] These patients have an additional $60,000 in total health care costs over the first year after discharge[5] and also report decreased quality of life.[6] Preventing cases of postoperative delirium would be expected to shorten the postoperative hospital stay, reduce the risk of complications after discharge, and reduce health care costs for the patient and for society.

Certain features of the intraoperative electroencephalogram (EEG) have been associated previously with poor perioperative outcomes, such as postoperative delirium. During general anesthesia with ether-derived volatile agents, the EEG often shows a dominance of delta waves (0–4 Hz) coupled with theta waves (4–8 Hz) and/or alpha (8–12 Hz) and low beta (12–16 Hz) oscillations.[7] Patients

From the *Department of Anesthesiology, Washington University School of Medicine, St. Louis, Missouri; and †Department of Mathematics, Washington University, St. Louis, Missouri.

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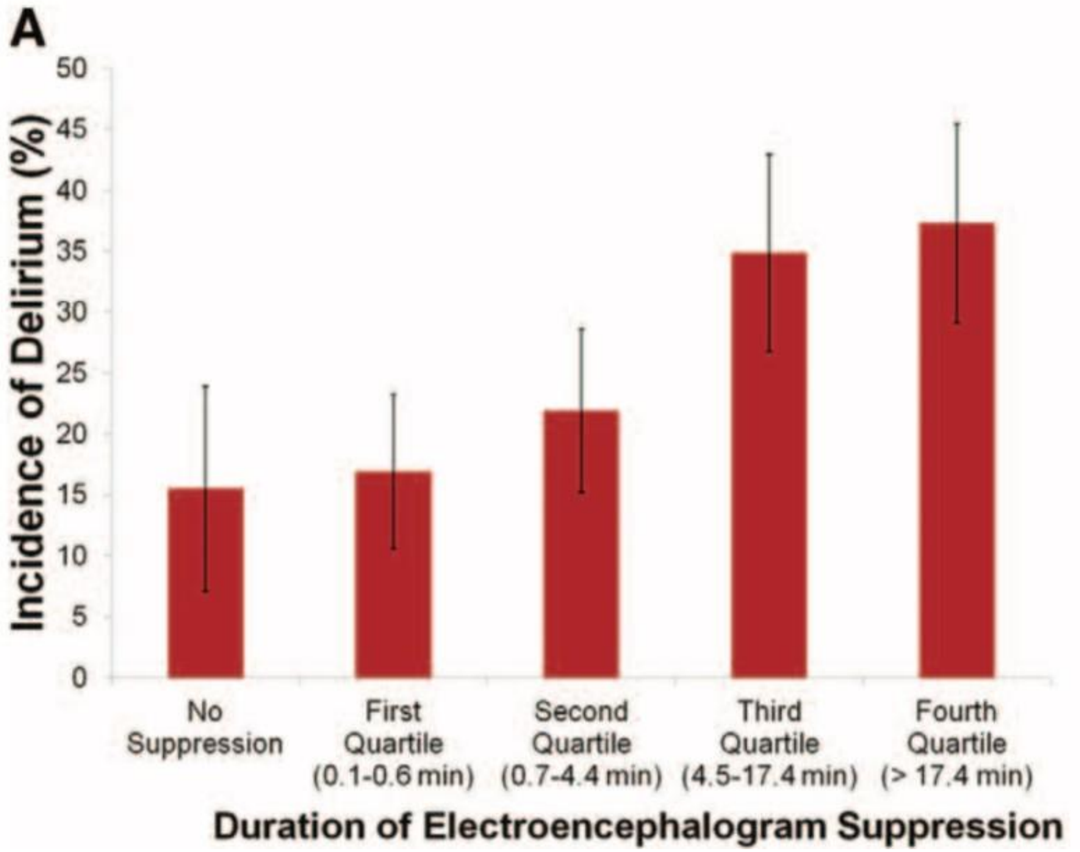

Fritz et al. Anesth Analg 2015

Table 2. Predictors of Postoperative Delirium in a Multiple Logistic Regression (*n* = 619)

	Non-transformed model		Transformed model[a]	
Variable	**Odds ratio (99% CI)**	***P***	**Odds ratio (99% CI)**	***P***
Age (per year)	1.01 (0.98–1.03)	0.37	1.00 (0.98–1.03)	0.69
Male sex	0.92 (0.69–1.23)	0.46	0.89 (0.67–1.19)	0.31
ASA physical status >3	0.81 (0.60–1.11)	0.08	0.80 (0.58–1.08)	0.06
Age-adjusted Charlson index (per unit)	1.10 (0.93–1.30)	0.15	1.09 (0.92–1.30)	0.18
Sensory impairment	1.04 (0.63–1.70)	0.83	1.03 (0.62–1.74)	0.85
Alcohol use >5 drinks per week	1.02 (0.62–1.66)	0.93	1.02 (0.62–1.68)	0.91
Surgery type				
Noncardiac	Reference		Reference	
Coronary artery bypass grafting	1.12 (0.62–1.66)	0.57	1.26 (0.76–2.11)	0.24
Open cardiac	0.95 (0.60–1.51)	0.77	1.03 (0.65–1.62)	0.89
Length of surgery (per minute)	1.00 (1.00–1.00)	0.65	1.00 (1.00–1.00)	0.61
Intraoperative ketamine use	0.70 (0.38–1.29)	0.13	0.71 (0.39–1.30)	0.15
Intraoperative opioid dose (per 1 morphine equivalent/kg increase)	1.08 (0.71–1.64)	0.65	1.05 (0.69–1.61)	0.76
Blood transfusion (dichotomous)[a]	—	—	1.82 (0.83–4.00)	0.05
Blood transfusion (per unit)[a]	1.29 (1.14–1.46)	<0.0001	1.77 (1.07–2.94)[a]	0.004
Mean end-tidal anesthetic concentration (per 0.1 MAC unit)	0.66 (0.50–0.87)	0.0001	0.66 (0.50–0.88)	0.0002
Duration of electroencephalogram suppression (in minutes)[a]	1.05 (1.003–1.103)[b]	0.0065	1.22 (1.06–1.40)	0.0002

Soehle et al. BMC Anesthesiology (2015) 15:61
DOI 10.1186/s12871-015-0051-7

BMC Anesthesiology

RESEARCH ARTICLE Open Access

Intraoperative burst suppression is associated with postoperative delirium following cardiac surgery: a prospective, observational study

Martin Soehle[1*†], Alexander Dittmann[2†], Richard K Ellerkmann[1], Georg Baumgarten[1], Christian Putensen[1] and Ulf Guenther[1]

Abstract

Background: Postoperative delirium (POD) occurs frequently after cardiac surgery and is associated with increased morbidity and mortality. We analysed whether perioperative bilateral BIS monitoring may detect abnormalities before the onset of POD in cardiac surgery patients.

Methods: In a prospective observational study, 81 patients undergoing cardiac surgery were included. Bilateral Bispectral Index (BIS)-monitoring was applied during the pre-, intra- and postoperative period, and BIS, EEG Asymmetry (ASYM), and Burst Suppression Ratio (BSR) were recorded. POD was diagnosed according to the Confusion Assessment Method for the Intensive Care Unit, and patients were divided into a delirium and non-delirium group.

Results: POD was detected in 26 patients (32%). A trend towards a lower ASYM was observed in the delirium group as compared to the non-delirium group on the preoperative day (ASYM = 48.2 ± 3.6% versus 50.0 ± 4.7%, mean ± sd, $p = 0.087$) as well as before induction of anaesthesia, with oral midazolam anxiolysis (median ASYM = 49.5%, IQR [47.4;51.5] versus 50.6%, IQR [49.1;54.2], $p = 0.081$). Delirious patients remained significantly ($p = 0.018$) longer in a burst suppression state intraoperatively (107 minutes, IQR [47;170] versus 44 minutes, IQR [11;120]) than non-delirious patients. Receiver operating analysis revealed burst suppression duration (area under the curve = 0.73, $p = 0.001$) and BSR (AUC = 0.68, $p = 0.009$) as predictors of POD.

Conclusions: Intraoperative assessment of BSR may identify patients at risk of POD and should be investigated in further studies. So far it remains unknown whether there is a causal relationship or rather an association between intraoperative burst suppression and the development of POD.

Trial registration: clinicaltrials.gov NCT01048775

Keywords: Cardiac surgery, Postoperative delirium, Outcome, Electroencephalogram, Burst suppression, Bispectral Index

Background

Delirium is defined as an acute disturbance of consciousness with a fluctuating course that affects attention, cognition, emotionality, and the sleep-wake cycle [1]. Following cardiac surgery using extracorporeal circulation, postoperative delirium (POD) occurs frequently with a reported incidence ranging between 14 and 51% [2-5]. It is associated with a prolonged stay in the intensive care unit, as well as an increased morbidity and mortality [5-7]. Hence, the success of cardiac surgery is seriously imperiled by the development of POD, and measures to predict and prevent POD are urgently sought.

The electroencephalogram (EEG) has been shown to be affected by POD in terms of an increased delta- and theta- as well as a decreased alpha- and beta-activity [8-10]. The main generators of this delirium-related theta increase have been reported to be localized in the anterior cingu-

prospective observational case control

hypothesis: patients with postoperative delirium will spend more time in burst suppression and exhibit a higher burst suppression rate than nondelirious patients.

81 patients undergoing cardiac surgery

BSR monitoring with BIS (pre, intra and postop)

main outcome: post-op delirium (CAM-ICU assessment every day)

Soehle et al. BMC Anesthesiology (2015) 15:61

Table 2 Comorbidity and plasma electrolyte concentrations in comparison between delirious and non-delirious patients

		Patients with delirium (n = 26)	Patients without delirium (n = 55)	p-value
Comorbidity				
Congestive heart failure		9	24	0.48
Myocardial infarction		6	18	0.44
Diabetes mellitus		7	15	1.00
COPD		5	8	0.75
Peripheral vascular disease		2	5	1.00
Cerebrovascular disease		3	4	0.20
Preoperative plasma electrolyte concentrations				
Sodium	[mmol/l]	140 [137.8;142.3]	140 [139;141]	0.83
Potassium	[mmol/l]	3.7 [3.6; 4.1]	3.8 [3.5;4.1]	0.96

The number of patients with certain comorbities is shown in the upper part. COPD = chronic obstructive pulmonary disease. Electrolyte concentrations are expressed as medians and interquartile range. Groups did not differ significantly with respect to the above shown parameters.

Table 6 Time spent in a state of burst suppression, i.e. a BSR > 0%

	Patients		
Group	**With delirium**	**Without delirium**	**p-value**
Duration of burst suppression as obtained during the entire period of surgery			
Left side	131 min [50;183]	48 min [13;127]	0.034
Right side	85 min [46;142]	35 min [7;89]	0.009
Duration of burst suppression from intubation to onset of cardiopulmonary bypass			
Left side	59 min [17;77]	20 min [3;58]	0.008
Right side	53 min [18;77]	13 min [2;37]	0.001

All data are shown as median and interquartile range.

BURST SUPPRESSION AND MORTALITY IN THE ICU

Presence of electroencephalogram burst suppression in sedated, critically ill patients is associated with increased mortality

Paula L. Watson, MD; Ayumi K. Shintani, MPH, PhD; Richard Tyson, MD;
Pratik P. Pandharipande, MD, MSCI; Brenda T. Pun, RN, MSN, ACNP; E. Wesley Ely, MD, MPH

Objectives: This study investigates the possibility of a relationship between oversedation and mortality in mechanically ventilated patients. The presence of burst suppression, a pattern of severely decreased brain wave activity on the electroencephalogram, may be unintentionally induced by heavy doses of sedatives. Burst suppression has never been studied as a potential risk factor for death in patients without a known neurologic disorder or injury.

Design: Post hoc analysis of a prospectively observational cohort study.

Setting: Medical intensive care units of a tertiary care, university-based medical center.

Patients: A total of 125 mechanically ventilated, adult, critically ill patients.

Measurements and Main Results: A validated arousal scale (Richmond Agitation-Sedation Scale) was used to measure sedation level, and the bispectral index monitor was used to capture electroencephalogram data. Burst suppression occurred in 49 of 125 patients (39%). For analysis, the patients were divided into those with burst suppression (49 of 125, 39%) and those without burst suppression (76 of 125, 61%). All baseline variables were similar between the two groups, with the overall cohort demonstrating a high severity of illness (Acute Physiology and Chronic Health Evaluation II scores of 27.4 ± 8.2) and 98% receiving sedation. Of those with burst suppression, 29 of 49 (59%) died within 6 months compared with 25 of 76 (33%) who did not demonstrate burst suppression. Using time-dependent Cox regression to adjust for clinically important covariates (age, Charlson comorbidity score, baseline dementia, Acute Physiology and Chronic Health Evaluation II, Sequential Organ Failure Assessment, coma, and delirium), patients who experienced burst suppression were found to have a statistically significant higher 6-month mortality [Hazard's ratio = 2.04, 95% confidence interval, 1.12–3.70, $p = 0.02$].

Conclusion: The presence of burst suppression, which was unexpectedly high in this medical intensive care unit population, was an independent predictor of increased risk of death at 6 months. This association should be studied prospectively on a larger scale in mechanically ventilated, critically ill patients. (Crit Care Med 2008; 36:3171–3177)

KEY WORDS: intensive care; mechanical ventilation; burst suppression; bispectral index; processed encephalogram; sedation; analgesia; delirium

Critically ill, mechanically ventilated patients nearly universally receive large doses of sedative and analgesic medications that frequently lead to deep sedation. Little is known regarding the mor-

controversial study, Monk et al. (2) reported that cumulative intraoperative deep hypnotic time was an independent risk factor for increased mortality during the first year after surgery. Sedation management has been shown to affect various clinical outcome variables such

as duration of mechanical ventilation, length of intensive care unit (ICU) and hospital stays, and healthcare cost (3, 4). Current sedation guidelines recommend titration of sedation to a goal level using a valid and reliable clinical assessment tool (5). However, once a patient is se-

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Burst Suppression on Processed Electroencephalography as a Predictor of Post-Coma Delirium in Mechanically Ventilated ICU Patients

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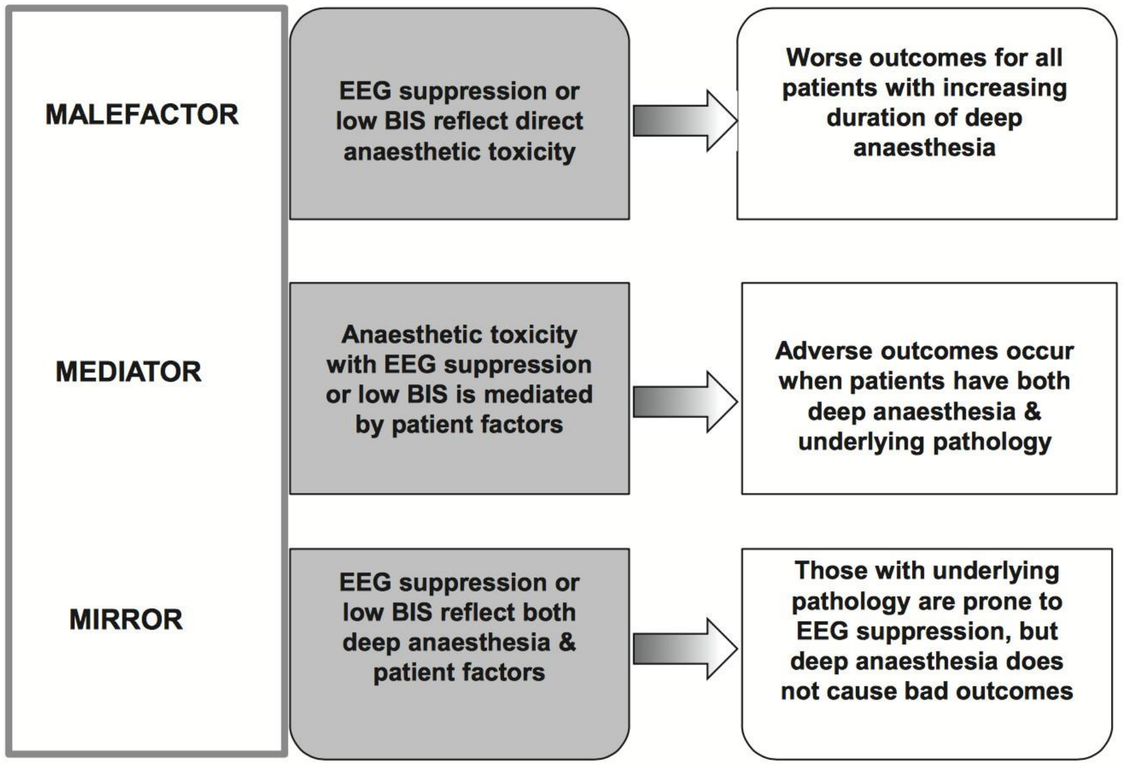
[7]Department of Biostatistics, Vanderbilt University Medical Center; Nashville, TN

Abstract

Objectives—Many patients, due to a combination of illness and sedatives, spend a considerable amount of time in a comatose state that can include time in burst suppression. We sought to determine if burst suppression measured by processed electroencephalography (pEEG) during coma in sedative-exposed patients is a predictor of post-coma delirium during critical illness.

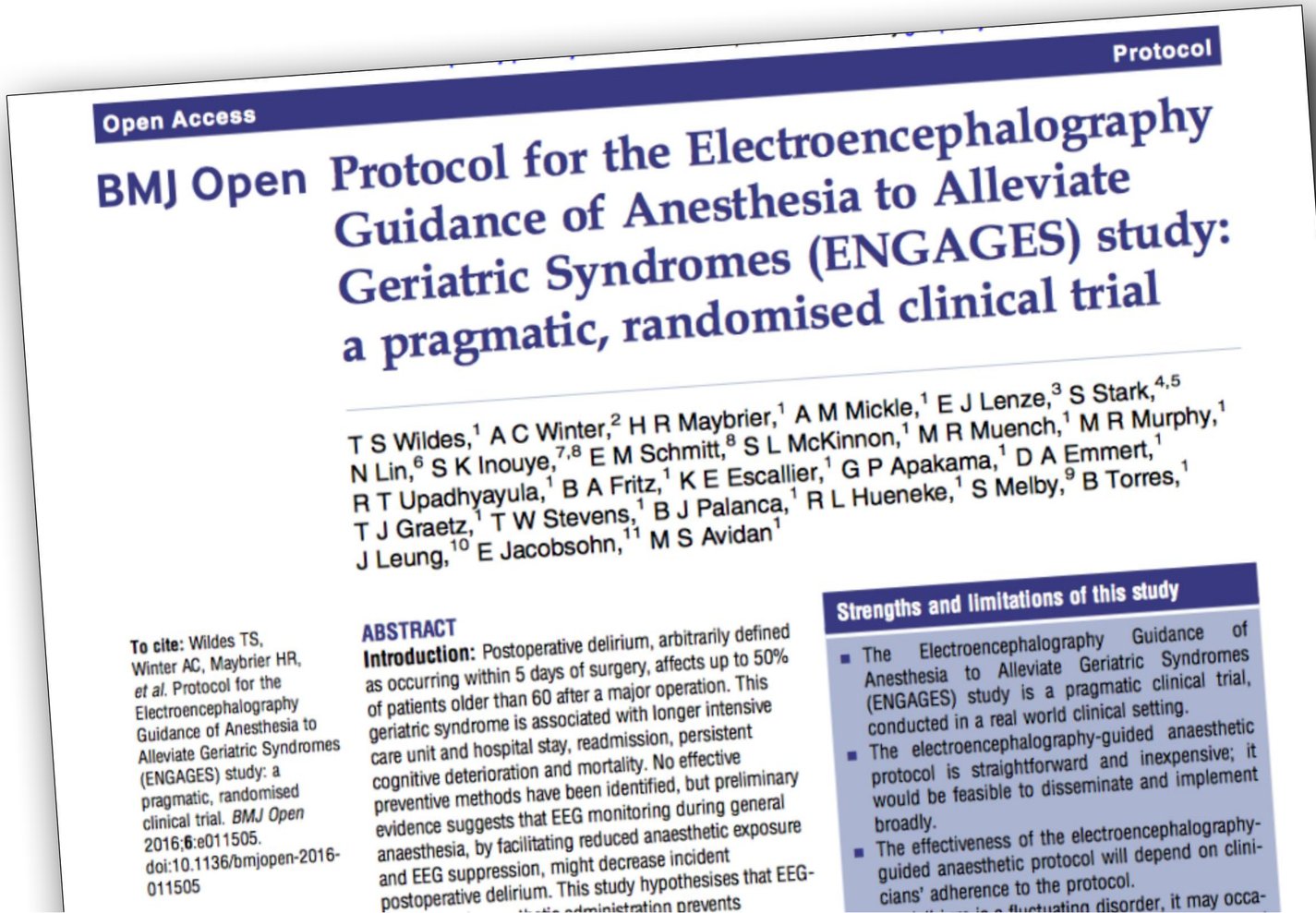
ASSOCIATIVITY VS CAUSALITY

MEDIATOR, MALEFACTOR OR MIRROR



Escallier et al., Brain monitoring and peri-operative outcomes. Anaesthesia 2015, 69, 899–910

ONGOING RCT: ENGAGES STUDY



Open Access Protocol

BMJ Open

Protocol for the Electroencephalography Guidance of Anesthesia to Alleviate Geriatric Syndromes (ENGAGES) study: a pragmatic, randomised clinical trial

T S Wildes,[1] A C Winter,[2] H R Maybrier,[1] A M Mickle,[1] E J Lenze,[3] S Stark,[4,5] N Lin,[6] S K Inouye,[7,8] E M Schmitt,[8] S L McKinnon,[1] M R Muench,[1] M R Murphy,[1] R T Upadhyayula,[1] B A Fritz,[1] K E Escallier,[1] G P Apakama,[1] D A Emmert,[1] T J Graetz,[1] T W Stevens,[1] B J Palanca,[1] R L Hueneke,[1] S Melby,[9] B Torres,[1] J Leung,[10] E Jacobsohn,[11] M S Avidan[1]

To cite: Wildes TS, Winter AC, Maybrier HR, *et al*. Protocol for the Electroencephalography Guidance of Anesthesia to Alleviate Geriatric Syndromes (ENGAGES) study: a pragmatic, randomised clinical trial. *BMJ Open* 2016;**6**:e011505. doi:10.1136/bmjopen-2016-011505

ABSTRACT

Introduction: Postoperative delirium, arbitrarily defined as occurring within 5 days of surgery, affects up to 50% of patients older than 60 after a major operation. This geriatric syndrome is associated with longer intensive care unit and hospital stay, readmission, persistent cognitive deterioration and mortality. No effective preventive methods have been identified, but preliminary evidence suggests that EEG monitoring during general anaesthesia, by facilitating reduced anaesthetic exposure and EEG suppression, might decrease incident postoperative delirium. This study hypothesises that EEG-

Strengths and limitations of this study

- The Electroencephalography Guidance of Anesthesia to Alleviate Geriatric Syndromes (ENGAGES) study is a pragmatic clinical trial, conducted in a real world clinical setting.
- The electroencephalography-guided anaesthetic protocol is straightforward and inexpensive; it would be feasible to disseminate and implement broadly.
- The effectiveness of the electroencephalography-guided anaesthetic protocol will depend on clini-

Wildes TS, et al. BMJ Open 2016;6:e011505. doi: 10.1136/bmjopen-2016-011505

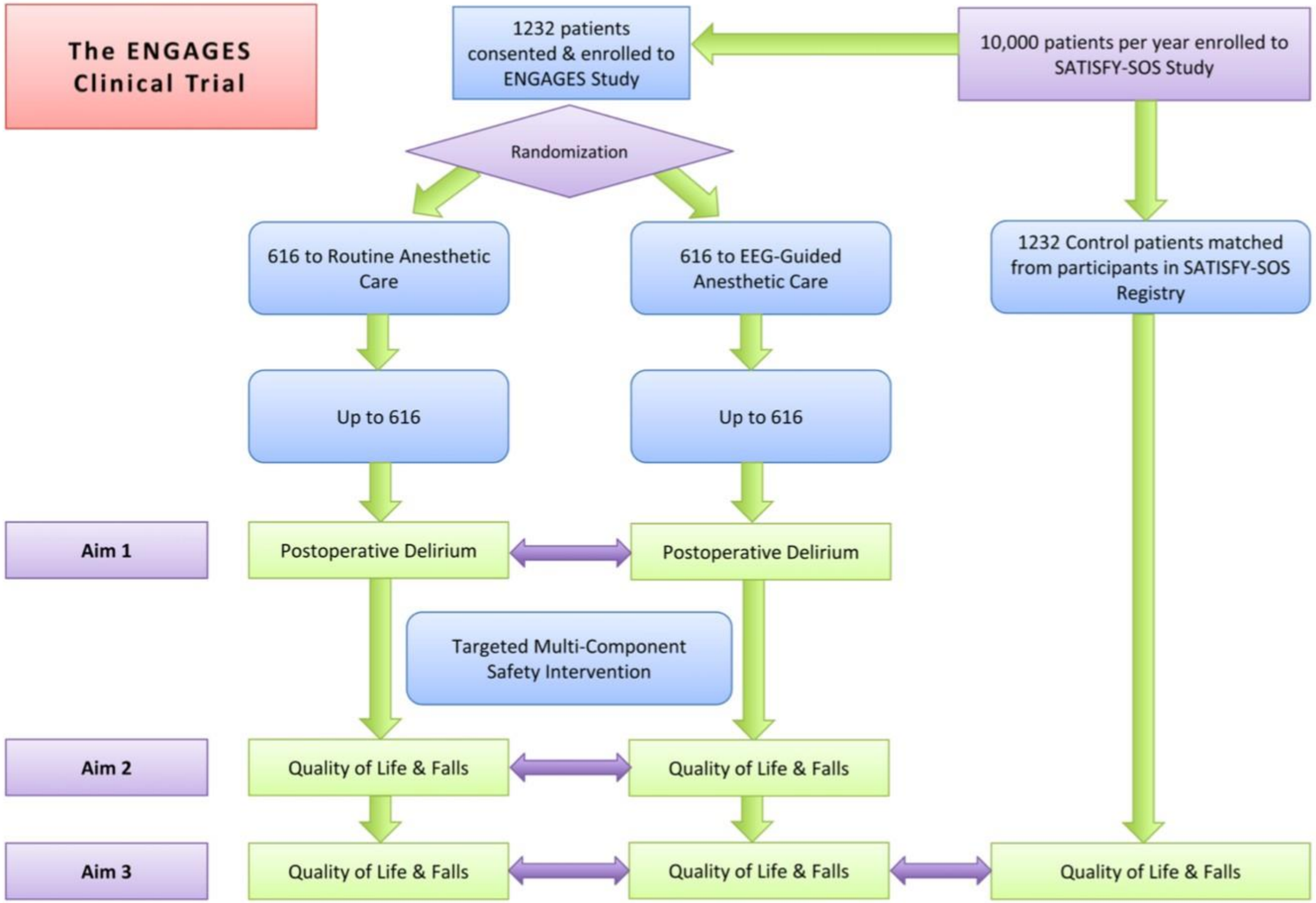


Figure 2 Flow diagram showing design overview for ENGAGES study.

PHILIPPE.DESJARDINS.1@ULAVAL.CA

AU PLAISIR!

OUTLINE

1. WHAT IS THE PATHOPHYSIOLOGY OF BURST-SUPPRESSION?

2. HOW CAN WE MONITOR BURST-SUPPRESSION?

3. IS IATROGENIC BURST-SUPPRESSION PROTECTIVE OR TOXIC?

NARRATIVE REVIEW OF LITERATURE

METHODOLOGY

NCBI Resources How To Sign in to NCBI

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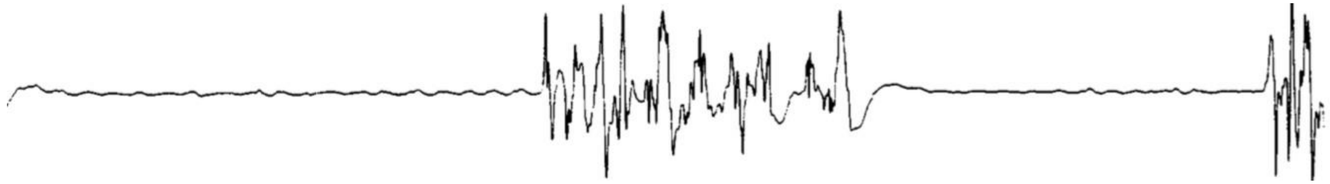
NEURONAL BASIS OF BURST SUPPRESSION



SUPPRESSION

absence of synaptic activity among cortical neurons

depletion of extracellular cortical calcium levels

arrest of synaptic transmission - flat EEG

synaptic silence allows neuronal pumps to restore interstitial calcium levels to trigger a new burst

refractoriness caused by disfacilitation

BURST

hyperexcitability caused by reduced cortical inhibition (lesser activity of GABA inhibitory synapses)

Ferron et al. 2009

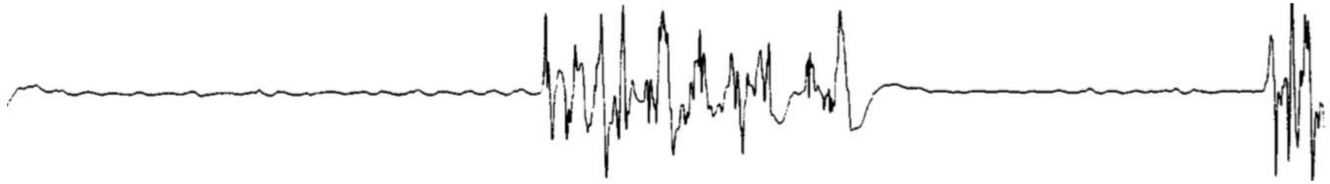
excitatory-inhibitory balance leans toward excitation

rythmicity of bursts is dictated by Ca2+ depletion and its restoration

bursts can be triggered by a variety of internal and external stimuli

Amzica et al., Epilepsia, 50 (Suppl. 12):38–39, 2009

NEURONAL BASIS OF BURST SUPPRESSION

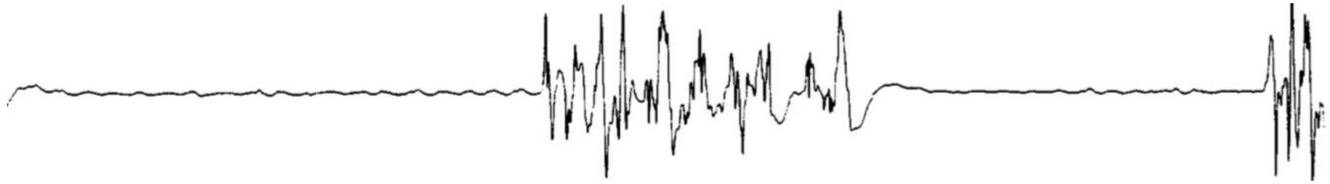


SUPPRESSION **BURST**

absence of synaptic activity among cortical neurons

Steriad et al. Electroencephalography and clinical Neurophysiology, 90 (1994) 1-16

NEURONAL BASIS OF BURST SUPPRESSION



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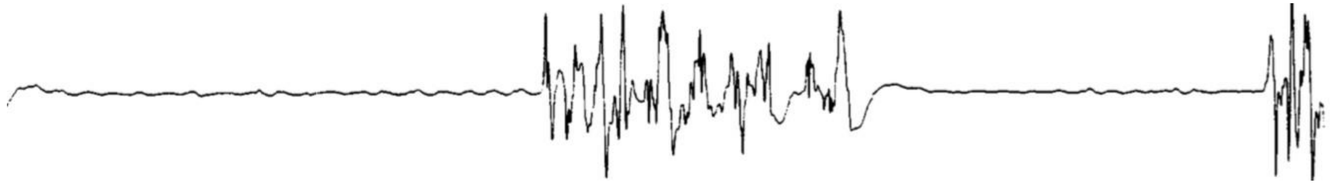

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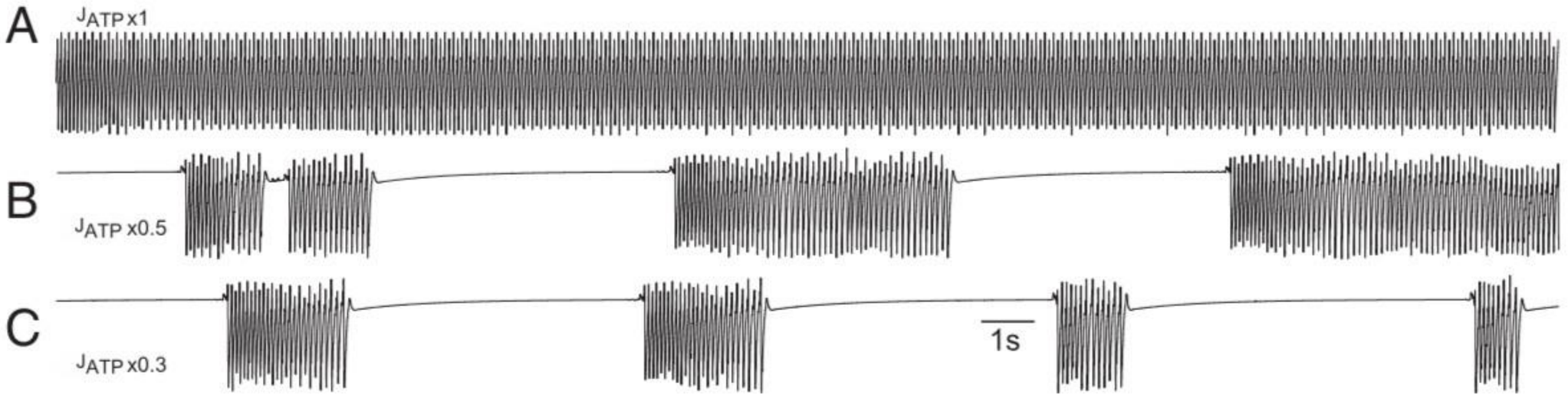
PREVAILING FEATURES OF BURST SUPPRESSION

spatial homogeneity of bursts

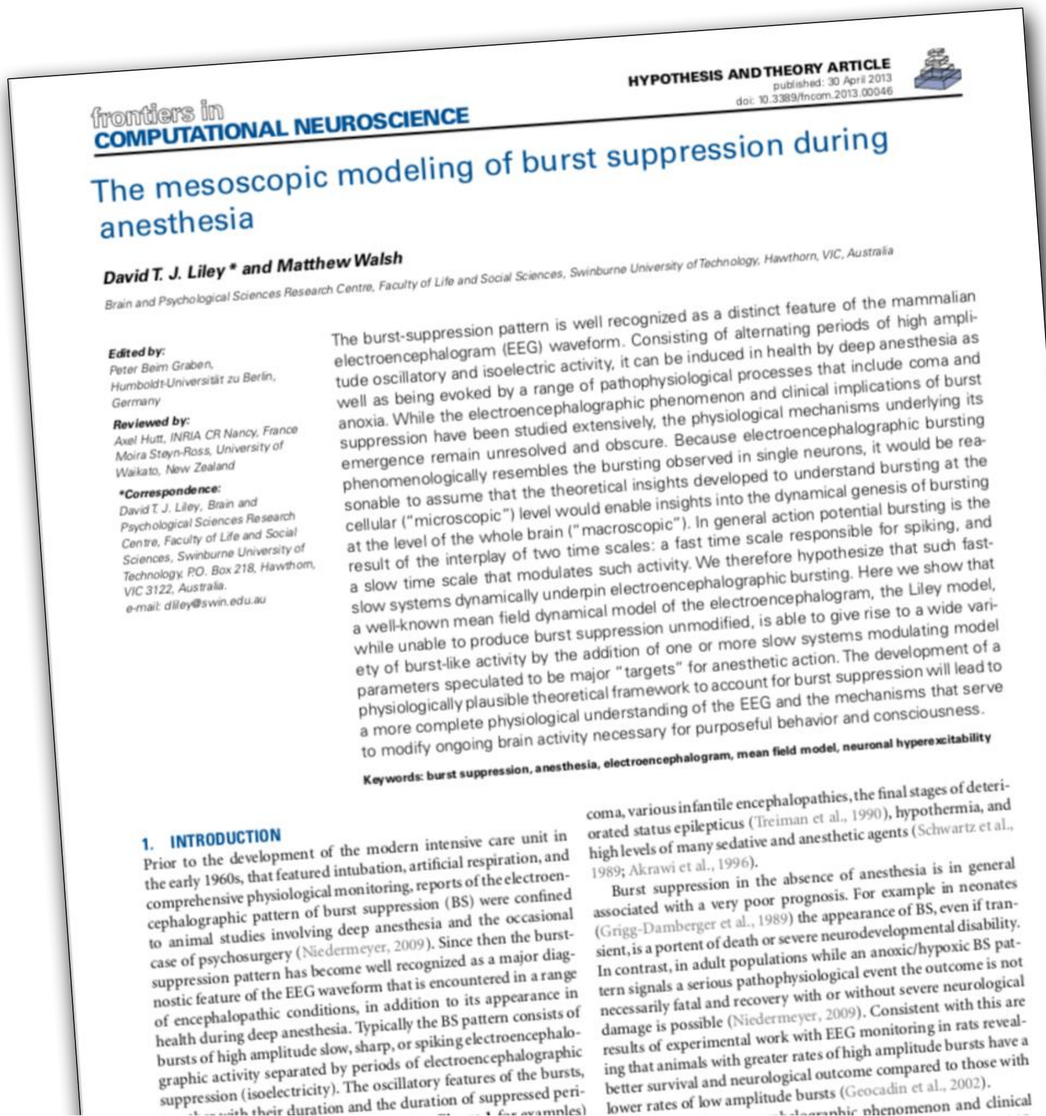
periodic nature of suppression

parametric sensitivity to level of brain depression

much **slower time scale** vs other brain patterns



Ching et al. PNAS, vol 109, 8, 3095-3100



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The mesoscopic modeling of burst suppression during anesthesia

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The burst-suppression pattern is well recognized as a distinct feature of the mammalian electroencephalogram (EEG) waveform. Consisting of alternating periods of high amplitude oscillatory and isoelectric activity, it can be induced in health by deep anesthesia as well as being evoked by a range of pathophysiological processes that include coma and anoxia. While the electroencephalographic phenomenon and clinical implications of burst suppression have been studied extensively, the physiological mechanisms underlying its emergence remain unresolved and obscure. Because electroencephalographic bursting phenomenologically resembles the bursting observed in single neurons, it would be reasonable to assume that the theoretical insights developed to understand bursting at the cellular ("microscopic") level would enable insights into the dynamical genesis of bursting at the level of the whole brain ("macroscopic"). In general action potential bursting is the result of the interplay of two time scales: a fast time scale responsible for spiking, and a slow time scale that modulates such activity. We therefore hypothesize that such fast-slow systems dynamically underpin electroencephalographic bursting. Here we show that a well-known mean field dynamical model of the electroencephalogram, the Liley model, while unable to produce burst suppression unmodified, is able to give rise to a wide variety of burst-like activity by the addition of one or more slow systems modulating model parameters speculated to be major "targets" for anesthetic action. The development of a physiologically plausible theoretical framework to account for burst suppression will lead to a more complete physiological understanding of the EEG and the mechanisms that serve to modify ongoing brain activity necessary for purposeful behavior and consciousness.

Keywords: burst suppression, anesthesia, electroencephalogram, mean field model, neuronal hyperexcitability

1. INTRODUCTION

Prior to the development of the modern intensive care unit in the early 1960s, that featured intubation, artificial respiration, and comprehensive physiological monitoring, reports of the electroencephalographic pattern of burst suppression (BS) were confined to animal studies involving deep anesthesia and the occasional case of psychosurgery (Niedermeyer, 2009). Since then the burst-suppression pattern has become well recognized as a major diagnostic feature of the EEG waveform that is encountered in a range of encephalopathic conditions, in addition to its appearance in health during deep anesthesia. Typically the BS pattern consists of bursts of high amplitude slow, sharp, or spiking electroencephalographic activity separated by periods of electroencephalographic suppression (isoelectricity). The oscillatory features of the bursts, both with their duration and the duration of suppressed periods (for examples) coma, various infantile encephalopathies, the final stages of deteriorated status epilepticus (Treiman et al., 1990), hypothermia, and high levels of many sedative and anesthetic agents (Schwartz et al., 1989; Akrawi et al., 1996).

Burst suppression in the absence of anesthesia is in general associated with a very poor prognosis. For example in neonates (Grigg-Damberger et al., 1989) the appearance of BS, even if transient, is a portent of death or severe neurodevelopmental disability. In contrast, in adult populations while an anoxic/hypoxic BS pattern signals a serious pathophysiological event the outcome is not necessarily fatal and recovery with or without severe neurological damage is possible (Niedermeyer, 2009). Consistent with this are results of experimental work with EEG monitoring in rats revealing that animals with greater rates of high amplitude bursts have a better survival and neurological outcome compared to those with lower rates of low amplitude bursts (Geocadin et al., 2002).

$$\left[\frac{\partial}{\partial t}+\gamma_{lk}(\varepsilon_{lk})\right]\left[\frac{\partial}{\partial t}+\tilde{\gamma}_{lk}(\varepsilon_{lk})\right]I_{lk}(r,t)$$
$$=\tilde{\gamma}_{lk}(\varepsilon_{lk})\exp[\gamma_{lk}(\varepsilon_{lk})/\gamma_{lk}^{0}]\Gamma_{lk}A_{lk}(r,t), \quad (7)$$

$$\gamma_{lk}(\varepsilon_{lk})=\varepsilon_{lk}\gamma_{lk}^{0}/(e^{\varepsilon_{lk}}-1), \quad \tilde{\gamma}_{lk}=\gamma_{lk}(\varepsilon)e^{\varepsilon_{lk}} \quad (8)$$

6th Annual International IEEE EMBS Conference on Neural Engineering
San Diego, California, 6 - 8 November, 2013

A Probabilistic Framework for Time-Frequency Detection of Burst Suppression *

Michael J. Prerau, Patrick L. Purdon, *Member, IEEE*

***Abstract*— General anesthesia is a drug-induced, reversible condition comprised of hypnosis, amnesia, analgesia, akinesia, and autonomic stability. During the deepest levels of anesthesia, *burst suppression* is observed in the EEG, which consists of alternating periods of bursting and isoelectric activity. By accurately tracking anesthesia-induced burst suppression, it may be possible to provide a higher level of care for patients receiving general anesthesia. We develop a probabilistic framework for detecting burst suppression events. The algorithm uses multinomial regression to estimate the probability of burst, suppression, and artifact states at each time given EEG frequency-domain data. We test the efficacy of this method on clinical EEG acquired during operating room surgery with GA under propofol.**

I. Introduction

General anesthesia (GA) is a drug-induced, reversible condition comprised of hypnosis (loss of consciousness), amnesia (loss of memory), analgesia (loss of pain sensation), akinesia (immobility), and autonomic stability. Every day, in United States alone, over 100,000 patients depend on general anesthesia for the ability to undergo vital clinical procedures. During GA, patients must be adequately anesthetized to prevent awareness or post-operative recall. However, patients should not be over-anesthetized, which can delay emergence and could contribute to post-operative delirium or cognitive dysfunction. It is therefore important to be able to characterize and monitor clinically observable biomarkers of depth of anesthesia so that complications from over- or under-anesthetizing patients may be mitigated.

One such biomarker is the phenomenon of *burst suppression*, which is a state occurring at the deepest levels of GA, consisting of alternating epochs of electrical bursting and isoelectric activity in the EEG. As the level of anesthetic drug is increased, the period between the burst epochs increases. Thus, tracking burst suppression provides an important tool in monitoring depth of anesthesia. Burst suppression is also observed in coma patients, and can be induced using anesthetic drugs or cooling as a neuroprotective therapy. Consequently, accurate characterization of burst suppression has broad applicability in neuro-critical care as well. The current clinical standard for evaluating burst suppression is through visual inspection of filtered EEG time-domain traces by a trained clinician or technician. There is currently no single, universally-accepted

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Research Article

Detection of Burst Suppression Patterns in EEG Using Recurrence Rate

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Burst suppression is a unique electroencephalogram (EEG) pattern commonly seen in cases of severely r such as overdose of general anesthesia. It is important to detect burst suppression reliably during the admini or sedative agents, especially for cerebral-protective treatments in various neurosurgical diseases. This study i plot (RP) analysis for the detection of the burst suppression pattern (BSP) in EEG. The RP analysis is applied to BSPs collected from 14 patients. Firstly we obtain the best selection of parameters for RP analysis. Then, the determinism (DET), and entropy (ENTR) are calculated. Then RR was selected as the best BSP index one-wa (ANOVA) and multiple comparison tests. Finally, the performance of RR analysis is compared with spectra analysis, approximate entropy, and the nonlinear energy operator (NLEO). ANOVA and multiple comparis the RR could detect BSP and that it was superior to other measures with the highest sensitivity of suppressio $P = 0.03$). Tracking BSP patterns is essential for clinical monitoring in critically ill and anesthetized patien may provide an effective burst suppression detector for developing new patient monitoring systems.

1. Introduction

diseases. It is commonly used as a monit of sedatives in order to achieve a maxi cerebral metabolic rate [5].

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Real-time segmentation of burst suppression patterns in critical care EEG monitoring

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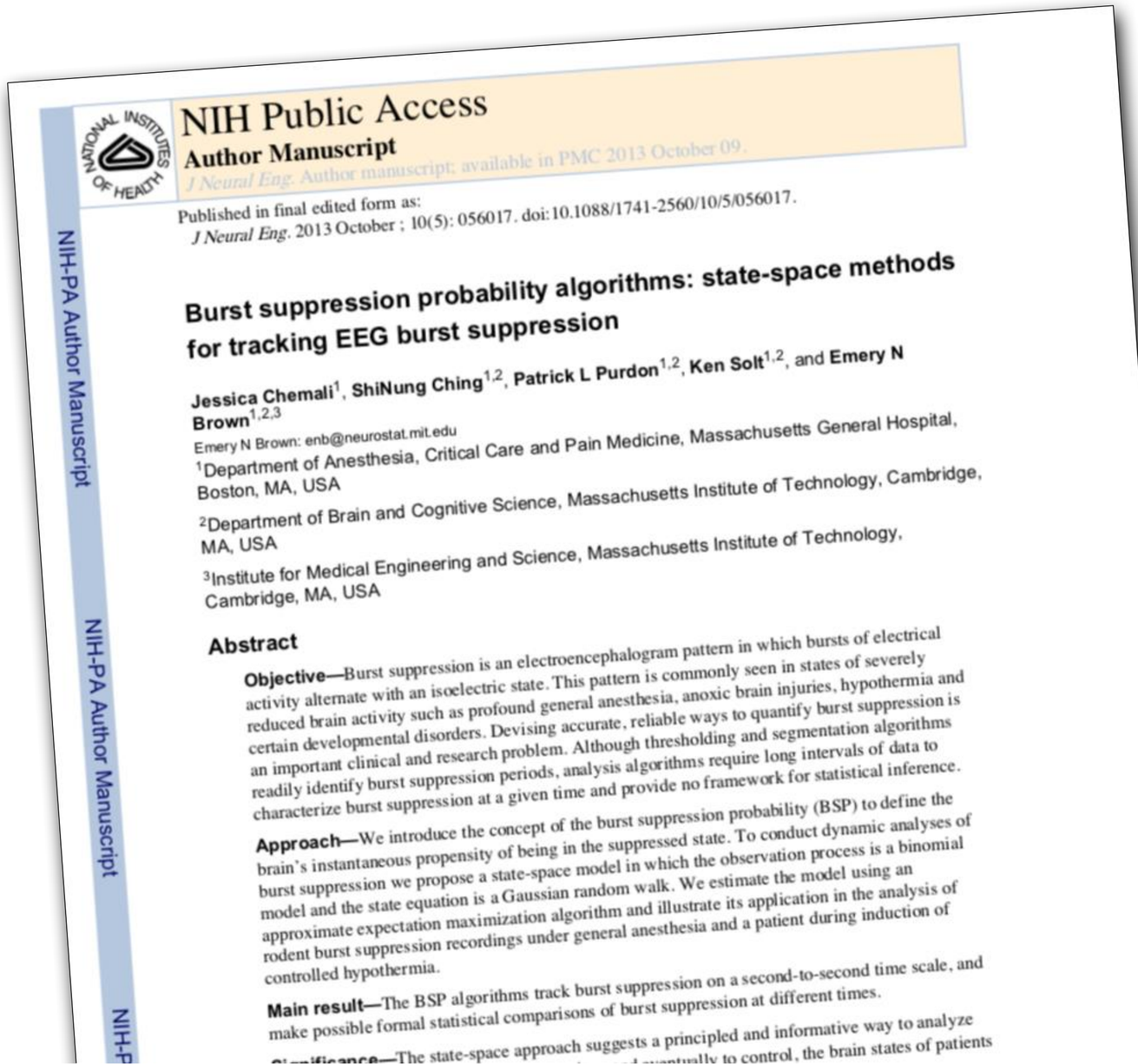
Abstract

Objective—Develop a real-time algorithm to automatically discriminate suppressions from non-suppressions (bursts) in electroencephalograms of critically ill adult patients.

Methods—A real-time method for segmenting adult ICU EEG data into bursts and suppressions is presented based on thresholding local voltage variance. Results are validated against manual segmentations by two experienced human electroencephalographers. We compare inter-rater agreement between manual EEG segmentations by experts with inter-rater agreement between human vs automatic segmentations, and investigate the robustness of segmentation quality to variations in algorithm parameter settings. We further compare the results of using these segmentations as input for calculating the burst suppression probability (BSP), a continuous measure of depth-of-suppression.

Results—Automated segmentation was comparable to manual segmentation, i.e. algorithm-vs-human agreement was comparable to human-vs-human agreement, as judged by comparing raw EEG segmentations or the derived BSP signals. Results were robust to modest variations in

BURST SUPPRESSION RATIO VS BURST SUPPRESSION PROBABILITY



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Burst suppression probability algorithms: state-space methods for tracking EEG burst suppression

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Abstract

Objective—Burst suppression is an electroencephalogram pattern in which bursts of electrical activity alternate with an isoelectric state. This pattern is commonly seen in states of severely reduced brain activity such as profound general anesthesia, anoxic brain injuries, hypothermia and certain developmental disorders. Devising accurate, reliable ways to quantify burst suppression is an important clinical and research problem. Although thresholding and segmentation algorithms readily identify burst suppression periods, analysis algorithms require long intervals of data to characterize burst suppression at a given time and provide no framework for statistical inference.

Approach—We introduce the concept of the burst suppression probability (BSP) to define the brain's instantaneous propensity of being in the suppressed state. To conduct dynamic analyses of burst suppression we propose a state-space model in which the observation process is a binomial model and the state equation is a Gaussian random walk. We estimate the model using an approximate expectation maximization algorithm and illustrate its application in the analysis of rodent burst suppression recordings under general anesthesia and a patient during induction of controlled hypothermia.

Main result—The BSP algorithms track burst suppression on a second-to-second time scale, and make possible formal statistical comparisons of burst suppression at different times.

Significance—The state-space approach suggests a principled and informative way to analyze [illegible] eventually to control, the brain states of patients

PROPOFOL BURST SUPPRESSION: MORE NUMBERS

15 mcg/mL

CONCENTRATION REQUIRED TO PRODUCE MAXIMAL SUPPRESSION

Ludbrook et al. 2002

6-8 mcg/mL

CONCENTRATION AT WHICH NEAR MAXIMAL DEPRESSION OF CBF IS OBTAINED

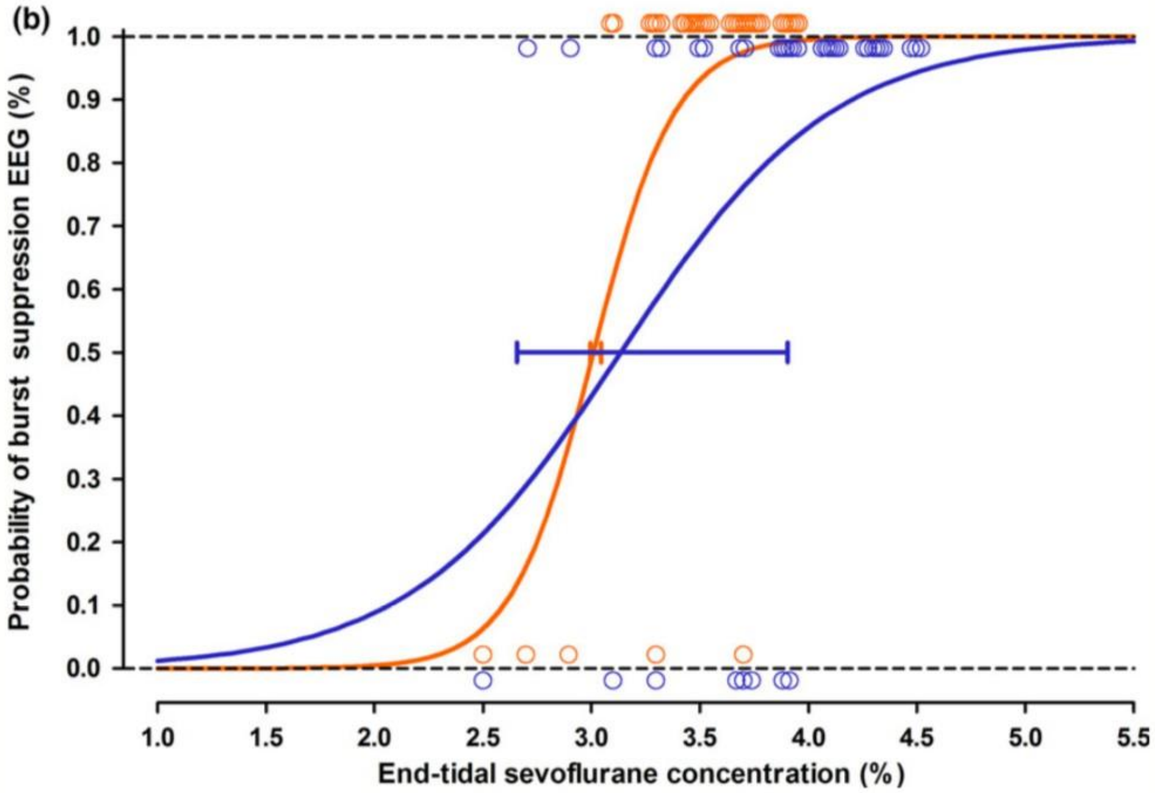
Ludbrook et al. 2002

Ludbrook et al. Anesthesiology 2002; 97:1363–70

IATROGENIC BURST SUPPRESSION

EFFECT OF NITROUS OXIDE ON BURST SUPPRESSION

N2O is neither additive nor antagonistic to the effect of sevoflurane on burst suppression



Niu et al. Anaesthesia 2017, 72, 570–579

IATROGENIC BURST SUPPRESSION

PHARMACOLOGIC CONSIDERATIONS: ETOMIDATE

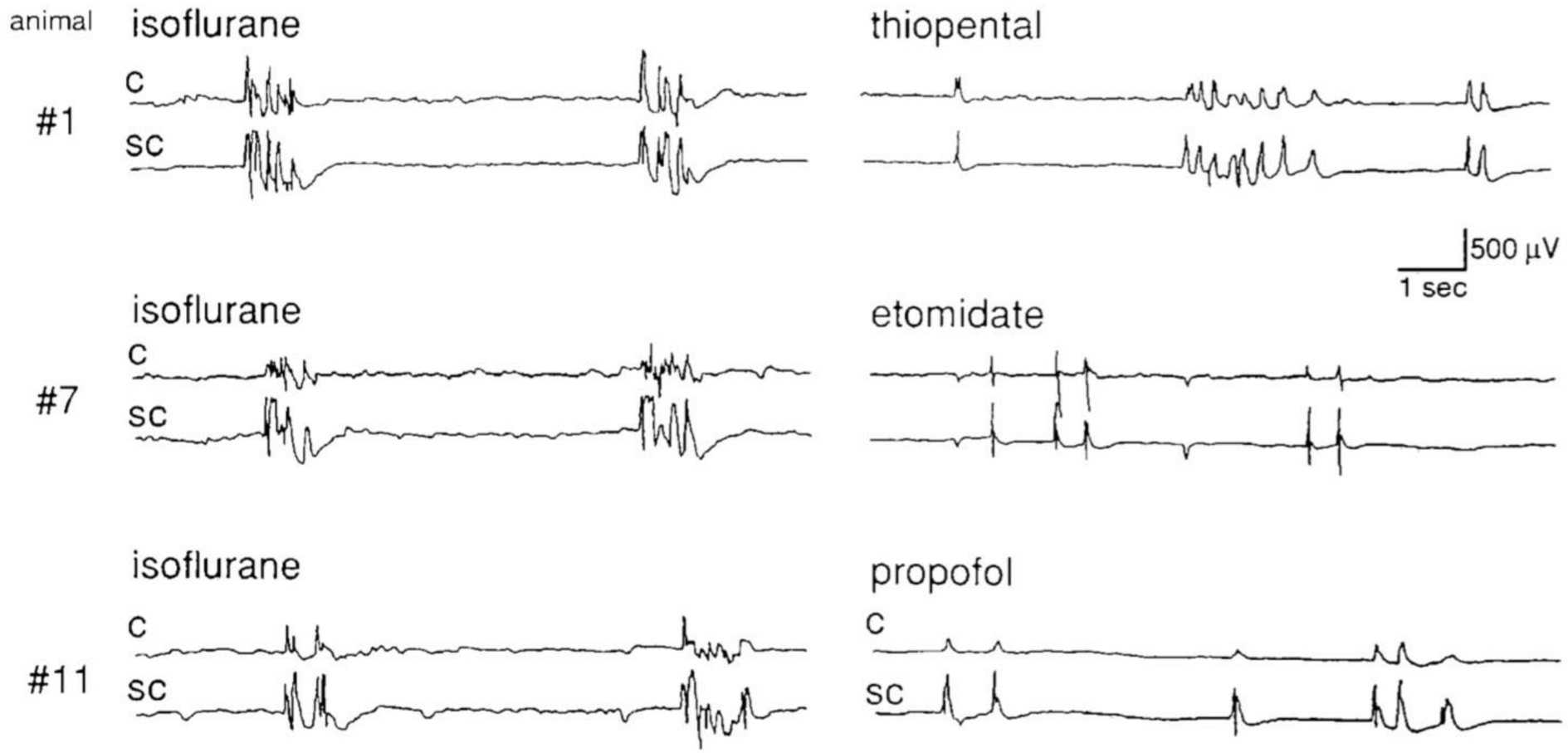
burst suppression pattern upon induction of anesthesia with etomidate prevented increase in ICP and maintained CPP during laryngoscopy

could be used as a target of deep anesthesia in raised ICP patients

TABLE III Time to dose requirement and duration of EEG burst suppression produced by etomidate

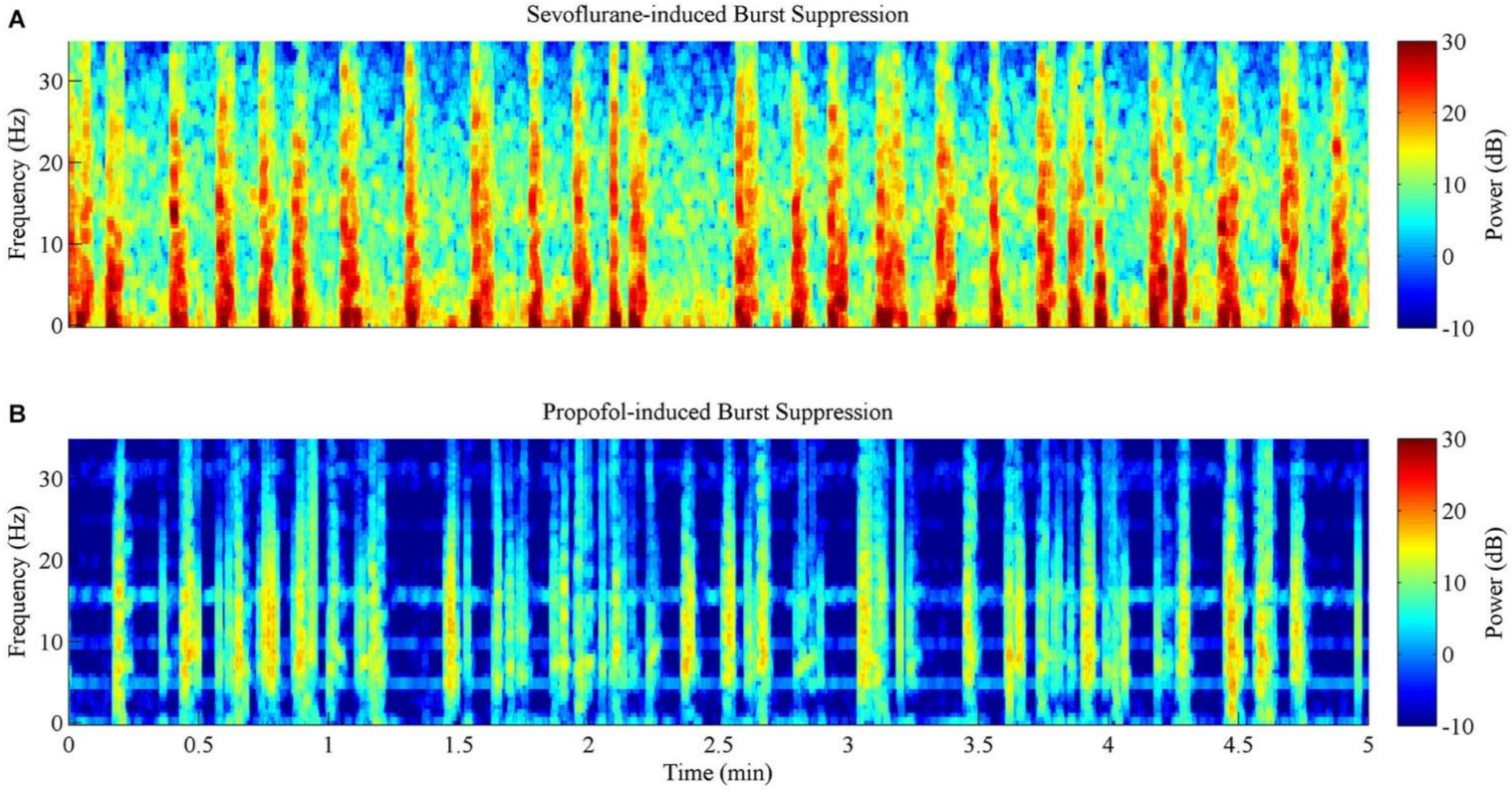
Time from etomidate bolus until EEG burst suppression:	240 ± 33 sec
Etomidate dose (bolus plus infusion) to reach burst suppression:	1.28 ± 0.11 mg · kg^{-1}
Total duration of burst suppression:	211 ± 25 sec

Modica et al. Can J Anesth 1992 / 39:3 / pp236-41

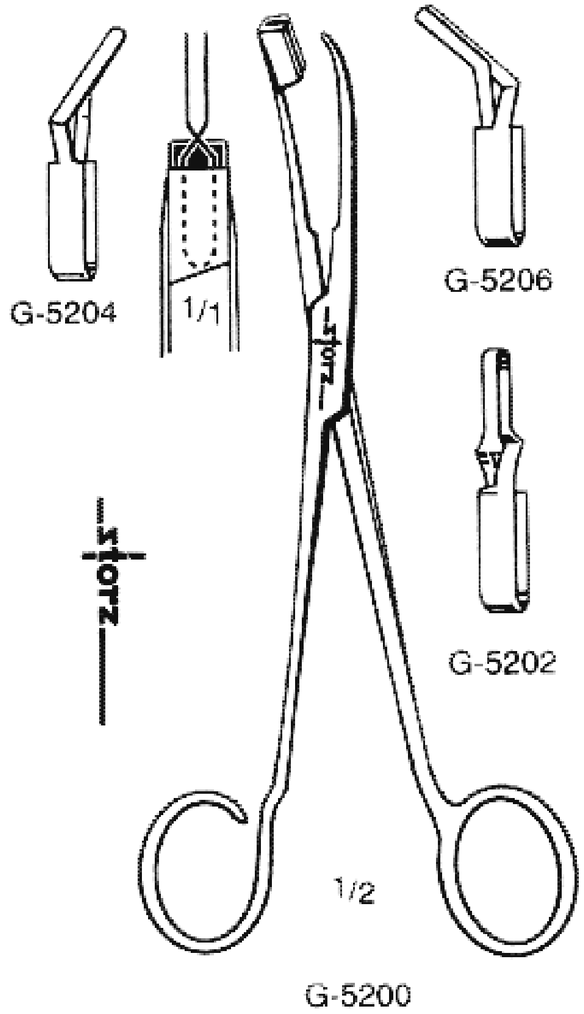

animal
isoflurane
thiopental
#1
c
sc
500 µV
1 sec
isoflurane
etomidate
#7
c
sc
isoflurane
propofol
#11
c
sc
c
sc

IATROGENIC BURST-SUPPRESSION

DIFFERENCES IN PROPOFOLAND SEVOFLURANE INDUCED BURST SUPPRESSION



DIFFERENT ANESTHETIC AGENTS INDUCE (SLIGHTLY) DIFFERENT BURST SUPPRESSION PATTERNS



Schwartz intracranial temporary arterial clamps and applying forceps from the Storz Surgical Instruments catalog, circa 1948.

Taylor et al. Neurosurgery, Volume 39, Issue 5, 1 November 1996, Pages 893–906,

rate of ATP consumption

sodium ATP pump

action potential
burst activity

AUTOREGULATION

$CMRO_2$

CBF

rate of ATP generation

ATP regeneration

burst activity

ATP lacking

suppression pattern

stops action potentials

K_{ATP} channel

if suppression of metabolic activity has a part in cerebral protection, complete EEG silence may give more protection than 50% burst suppression.

Doyle et al.British Journal of Anaesthesia **83 (4)**: 580–4 (1999)

IATROGENIC BURST SUPPRESSION

BARBITURATE PROTECTION

Taylor et al. Neurosurgery, Volume 39, Issue 5, 1 November 1996, Pages 893–906,

normoglycemia, mild hypothermia, elevated mean arterial pressure before temporary clip application

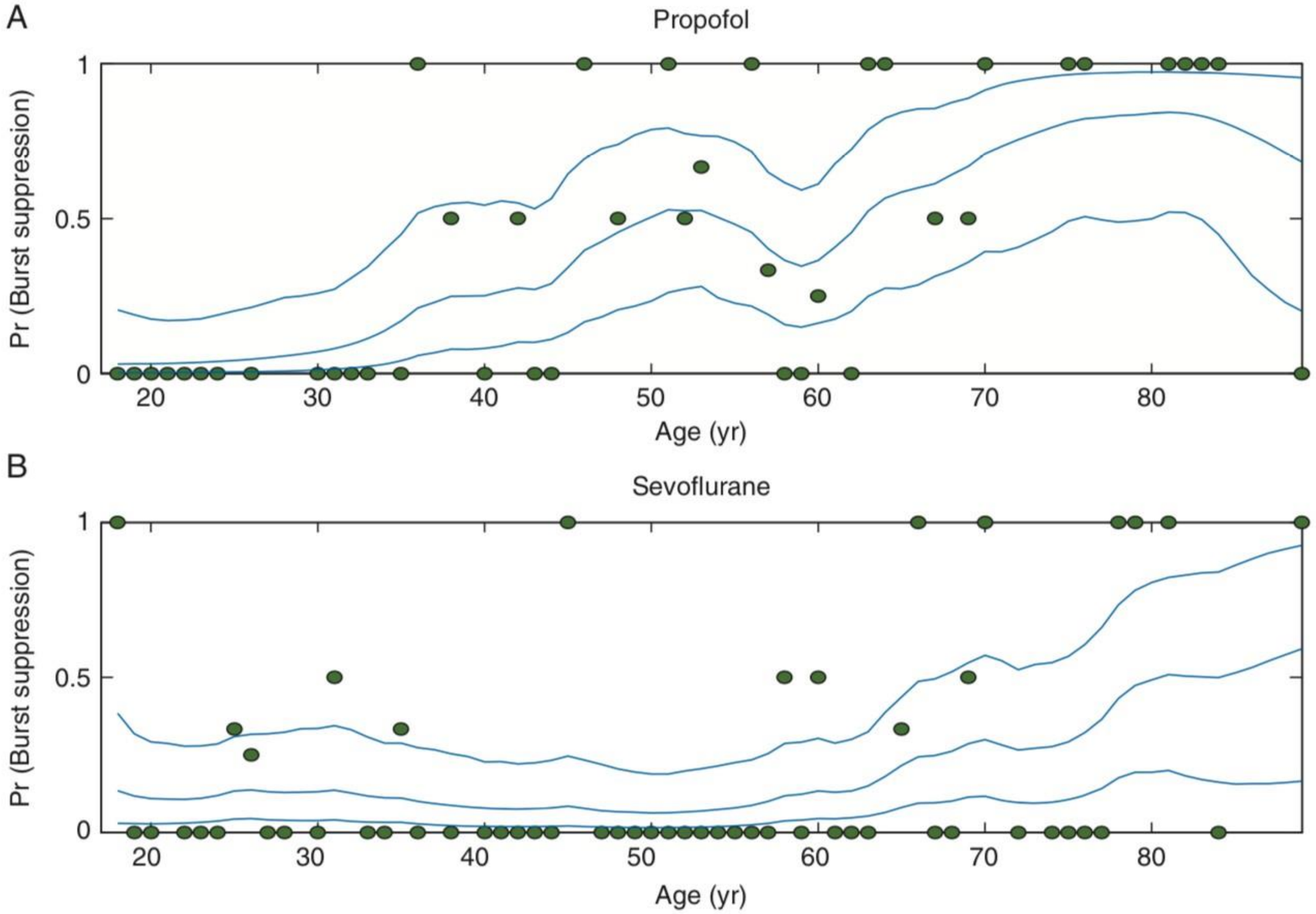
10 mg/kg loading dose
thiopental
followed by maintenance dose 5-10 mg/kg/h, titrated to EEG burst suppression

RAVUSSIN'S PROTOCOL

Ravussin et al. Neurosurgery, volume 32(2), February 1993, p 236–240.

propofol infusion increased to 500 mcg/kg/min prior to temporary clipping

titrated to burst suppression


A
Propofol
Pr (Burst suppression)
1
0.5
0
20
30
40
50
60
70
80
Age (yr)
B
Sevoflurane
Pr (Burst suppression)
1
0.5
0
20
30
40
50
60
70
80
Age (yr)

“ INTRAOPERATIVE ASSESSMENT OF BSR MAY IDENTIFY PATIENTS AT RISK OF POD AND SHOULD BE INVESTIGATED IN FURTHER STUDIES. SO FAR

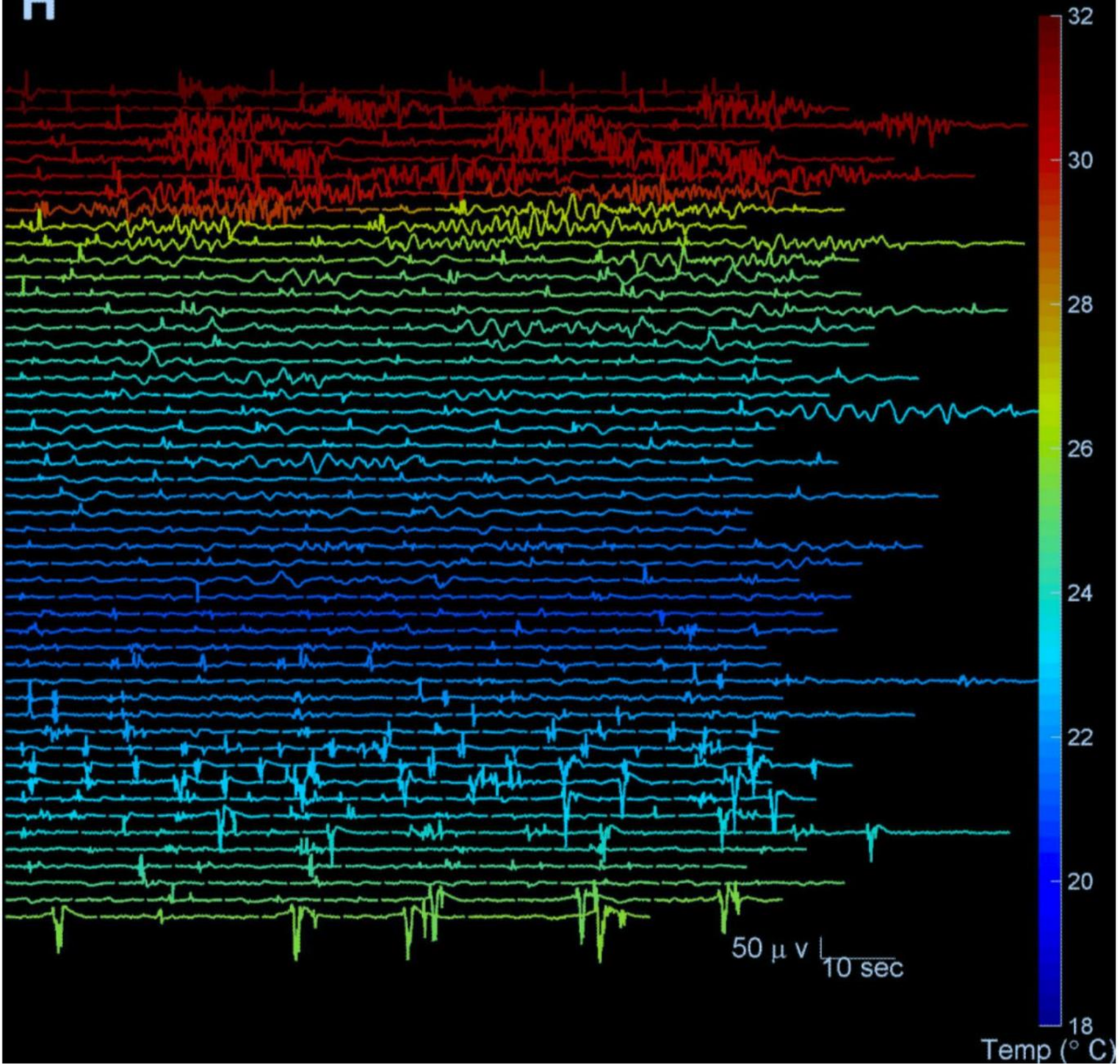
IT REMAINS UNKNOWN WHETHER THERE IS A CAUSAL RELATIONSHIP OR RATHER AN ASSOCIATION BETWEEN INTRAOPERATIVE BURST SUPPRESSION AND THE DEVELOPMENT OF POSTOPERATIVE DELIRIUM.

- SOELHE ET AL, BMC ANESTH 2015

Soehle et al. BMC Anesthesiology (2015) 15:61

CAPLINE HEADER ELEMENT

BURST-SUPPRESSION AND HYPOTHERMIA



Most importantly, under the same dose of isoflurane, ECI is attained at different temperatures in different patients, and fluctuations into and out of ECI once despite maintenance of relatively constant temperature and anesthetic conditions are relatively common. Consequently, it is not possible to reliably predict an individual patient's level of burst suppression or to ensure maintenance of ECI by simply targeting a predetermined temperature plus anesthetic combination. In turn, continuous EEG monitoring to allow continual fine-tuning of brain temperature and anesthetic levels is essential in cases for which maintaining a specific target level of BS or ECI are necessary to provide cerebral metabolic protection.

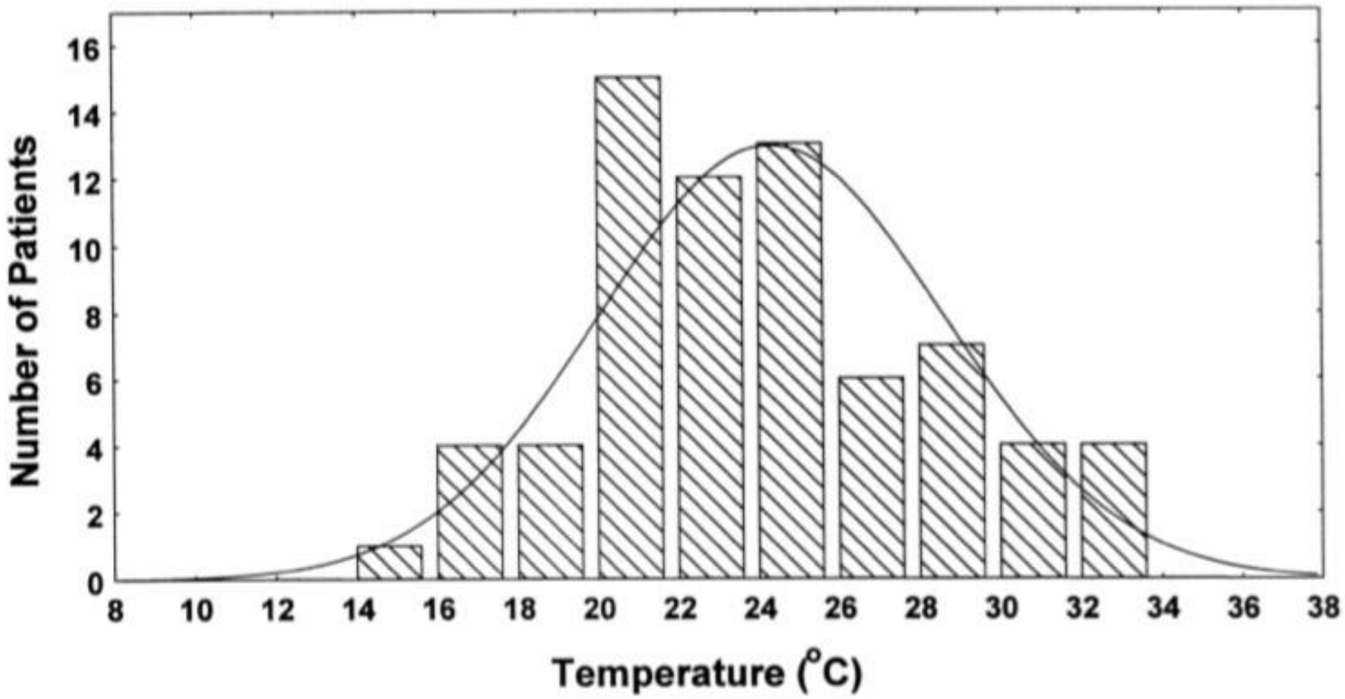
IATROGENIC BURST-SUPPRESSION

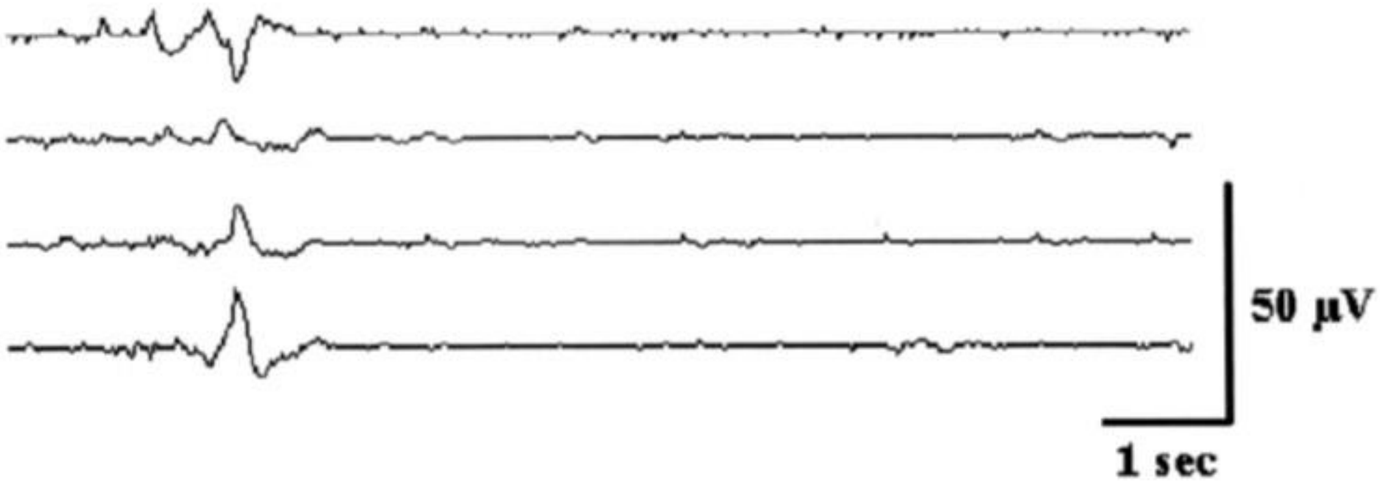
CIRCULATORY ARREST: RATIONALE

- The most important cerebral protective measure used during procedures requiring circulatory arrest is deep hypothermia [1]. Therefore, the selection of an optimal temperature for circulatory arrest is critical. A circulatory arrest temperature that is too high [2] may predispose to cerebral ischemia. A circulatory arrest temperature that is too low prolongs the periods of cooling and rewarming and hence the time on cardiopul- monary bypass (CPB) and its associated risks [3]. In addition, extremely low temperatures may produce brain injury [4 –7] as a result of the formation of intracellular ice crystals or denaturation of proteins [8].

Burst suppression appeared in all patients between 2 and 28 minutes (mean, 12.7 6 minutes) after the start of cooling, with nasopharyngeal temperatures ranging from 15.7°C to 33.0°C (mean, 24.4°C 4°C).

Ann Thorac Surg STECKER ET AL 15 2001;71:14–21


Number of Patients
0
2
4
6
8
10
12
14
16
8
10
12
14
16
18
20
22
24
26
28
30
32
34
36
38
Temperature (°C)


50 µV
1 sec

Trials from numerous centers from around the world have demonstrated the clinical efficacy of adult aortic arch repair with ACP and mild to moderate hypothermia in the range of 22 C to 30 C.