EKT Narkose

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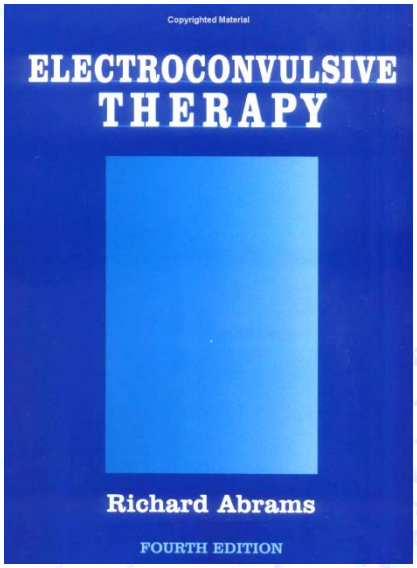
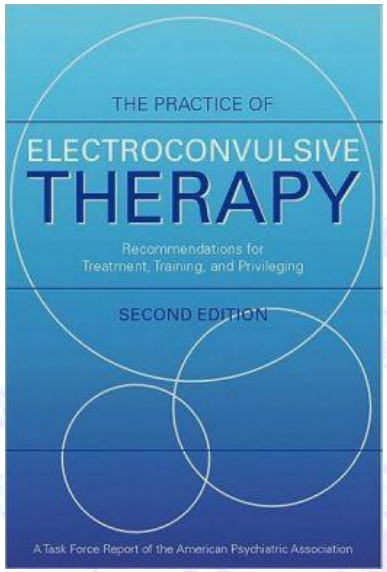
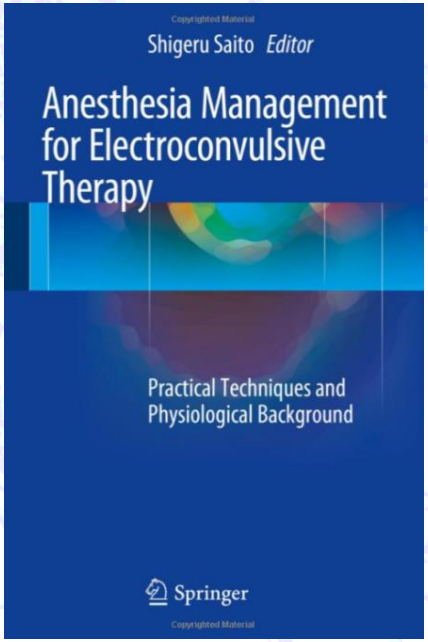
Münsingen, 5.10.2019





3 pages on anesthesia – together!



ECT – anesthesia:

1. Typical anesthetic drugs (p, e, m ,t)

a. Ketofol – two stones to catch one bird ?

2. Some typical problems / solutions …

a. ASTI
b. Oxygen
c. PAS / PIA
d. Cardiac

substance	typical dose range (mg/kg)	anticonvulsive effect (relative)	remarks
methohexital	0,75-1.0	1-2	former gold standard, cardiovascular depression
thiopental	2-5	2	cardiovascular depression
propofol	1-2	3	shorter seizures, higher seizure threshold
etomidate	0.2-0.3	0	myocloni
S-ketamine	0.5-1.5	0	low doses pro-psychotic, higher blood pressure
alfentanil	0.01-0.015	0	longer time of apnoe, cardiovascular depression
remifentanil	0.001-0.008	1	similar to alfentanil ?

Black Box Warning *

Rote-Hand-Briefe **

***

* Hikma Pharmaceuticals stopped the production of methohexital 2019

** Good Manufacturing Practice (GMP) problems at Lampugnani Pharmaceutici SPA

*** In Germany: more or less obsolete for critically ill patients and for non-single induction use

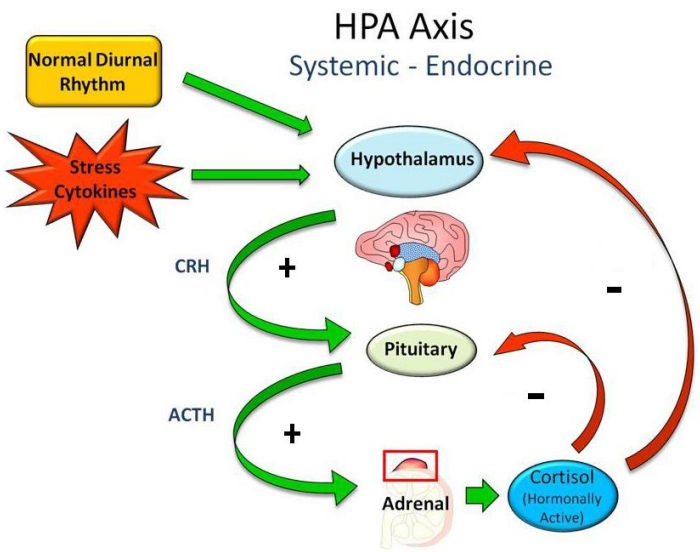
Adapted from:

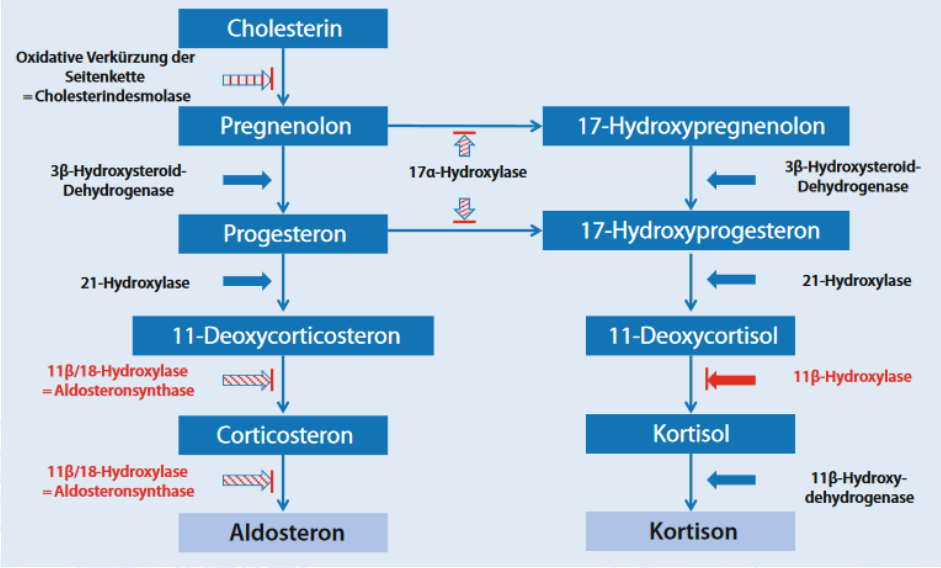
Folkerts HW.
Electroconvulsive therapy. Indications, procedure and treatment results
Nervenarzt. 2011 Jan;82(1):93-102

Swartz CM
Electroconvulsive and neuromodulation therapies.
2009 Cambridge Univ, Cambridge New York Melbourne

ECT – anesthesia:

- thiopental	3-5 mg/kg
- methohexital	50-120 mg
- etomidate	0.15-0.3 mg/kg
- propofol	1-2 mg/kg





Etomidate: to use or not to use for endotracheal intubation in the critically ill?
Smischney NJ, Kashyap R, Gajic O.
J Thorac Dis. 2015 Sep;7(9):E347-9.

Etomidate for intravenous induction of anaesthesia
Dumps C, Bolkenius D, Halbeck E.
Anaesthesist. 2017 Dec;66(12):969-980.

Optimistic viewpoint:
Raeder J., Curr Opin Anaesthesiol. 2019 Sep 9. [Epub ahead of print]
Procedural sedation in ambulatory anaesthesia: what's new?

This debate is ongoing …
… and of course there are no long term studies in ECT patients…

The theoretical problem of a cumulative risk remains, because of a „chronic“ HPA suppression with repeated use of etomidate.

At least in Germany anesthesiologists become more and more „careful“ with the use of etomidate in ECT.

ECT – anesthesia:

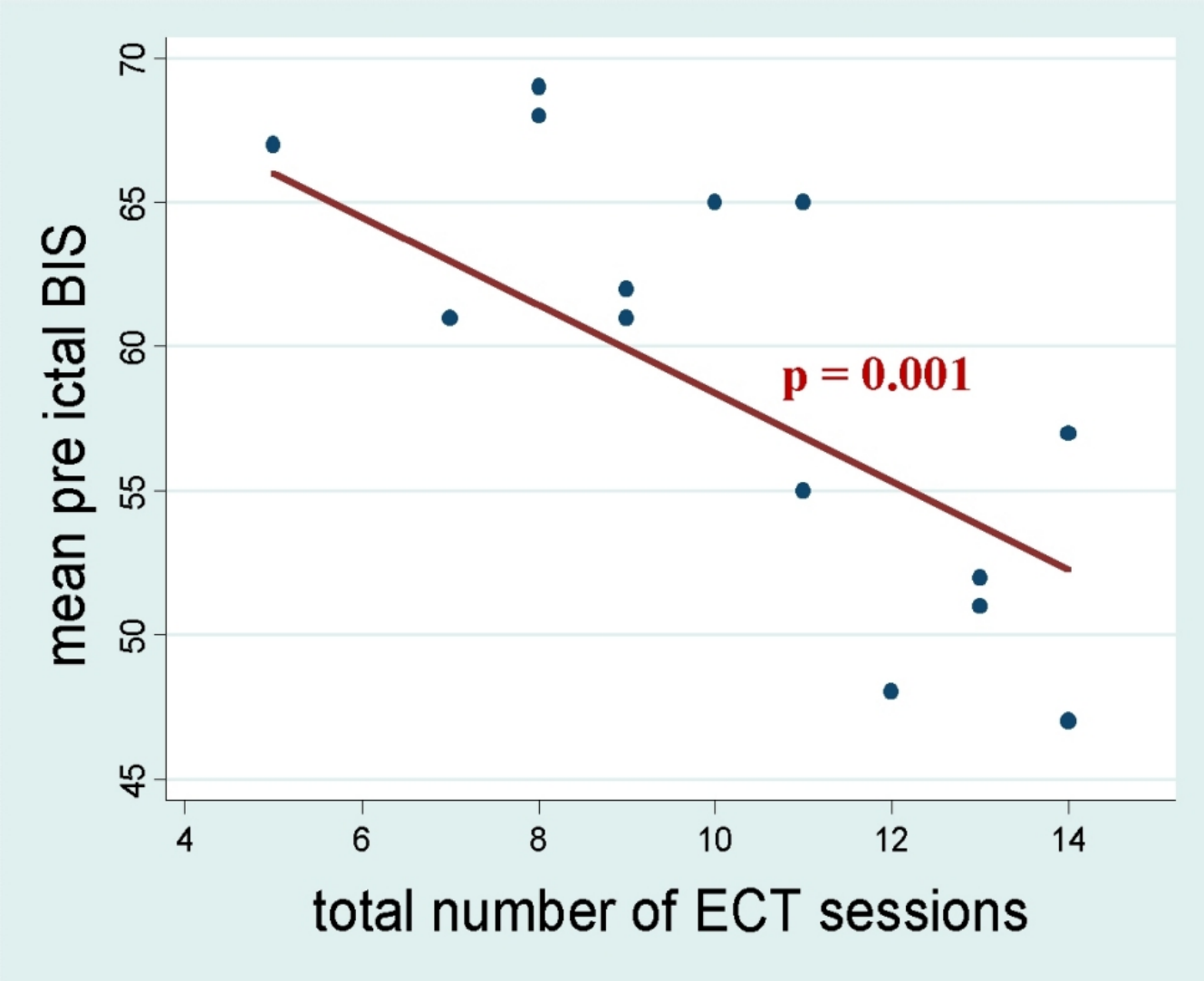
- thiopental	3-5 mg/kg
- methohexital	50-120 mg
- etomidate	0.15-0.3 mg/kg
- propofol	1-2 mg/kg

German guidelines for tx of status epilepticus *

1	=>	lorazepam	up to 10mg i.v.
2	=>	phenytoin	up to 20 mg/kg i.v.
or	=>	phenobarbital	20 mg/kg i.v.
3	**=>**	**thiopental**	**5 mg/kg i.v.**
		vs. propofol	**2 mg/kg i.v.**
		vs. midazolam or valproate or levetiracetam	

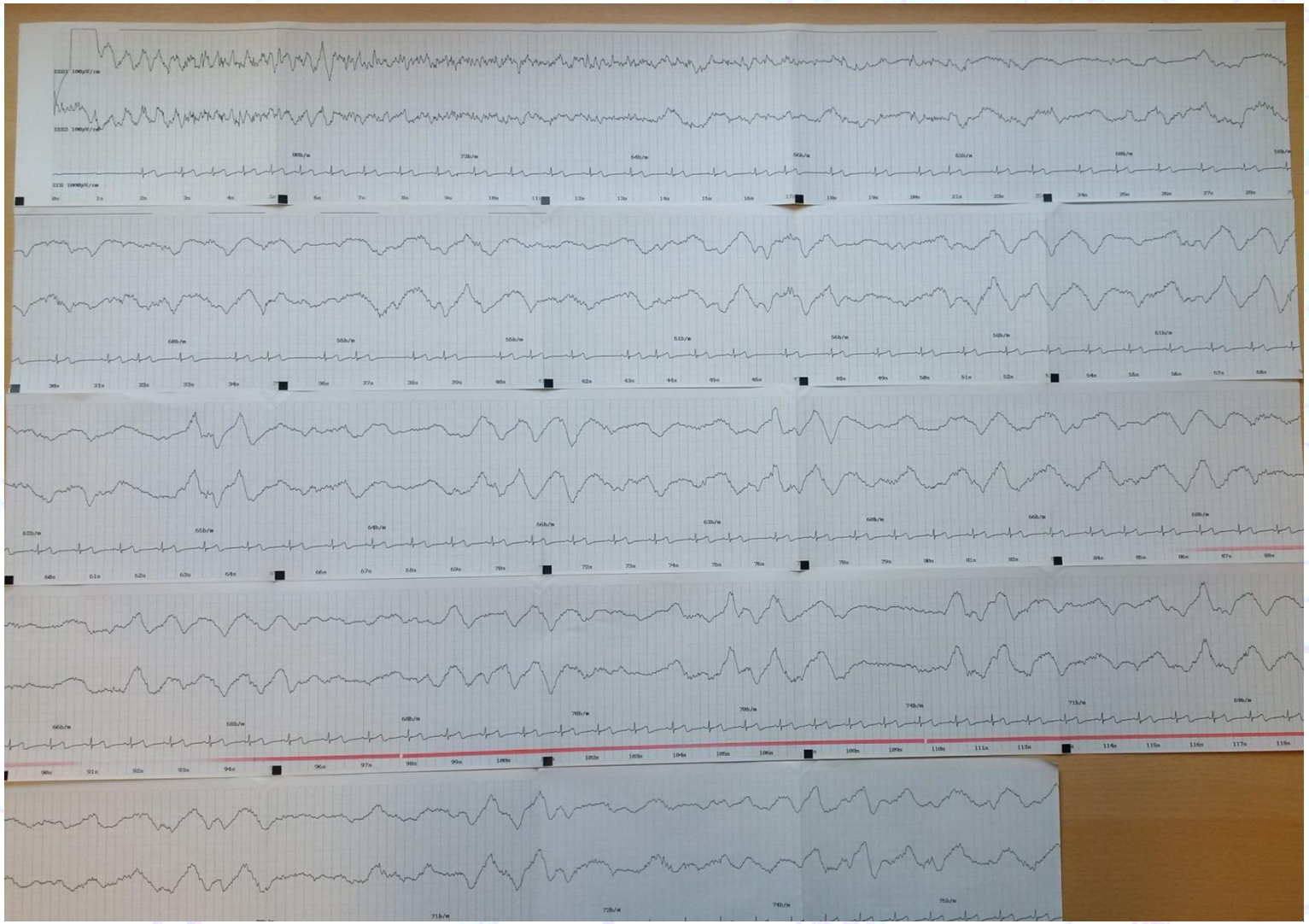
* German Association for Neurology

ECT – anesthesia: Thiopental



A. Sartorius et al., ECT anesthesia: the lighter the better? Pharmacopsychiatry. 2006 Nov;39(6):201-4.

Courtesy of Michael Guhra, Bielefeld



32 years, “always had good seizures”, now 250 mg propofol

ECT – anesthesia: All four gone ?

- thiopental	3-5 mg/kg
- methohexital	50-120 mg
- etomidate	0.15-0.3 mg/kg
- propofol	1-2 mg/kg

ECT – anesthesia: All four gone ?

- thiopental	3-5 mg/kg
- methohexital	50-120 mg
- etomidate	0.15-0.3 mg/kg
- propofol	1-2 mg/kg

Of course not, but all have major drawbacks.

What about ketamine ?

ketamine in general anesthesia:

- is listed as an essential drug by the WHO

- often used in emergeny medicine

- treatment of status asthmaticus

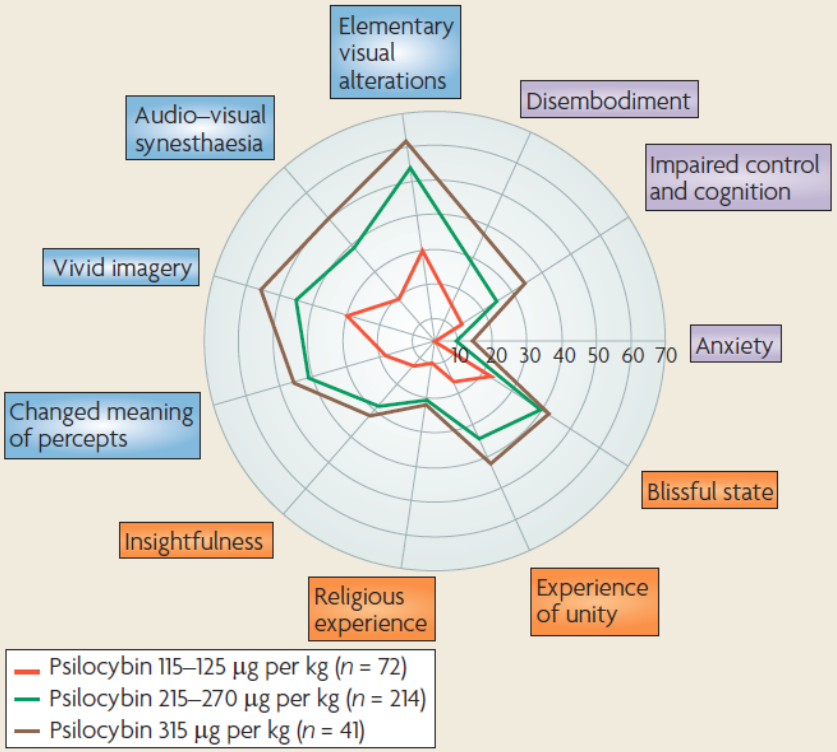
- analgesia of intubated patients

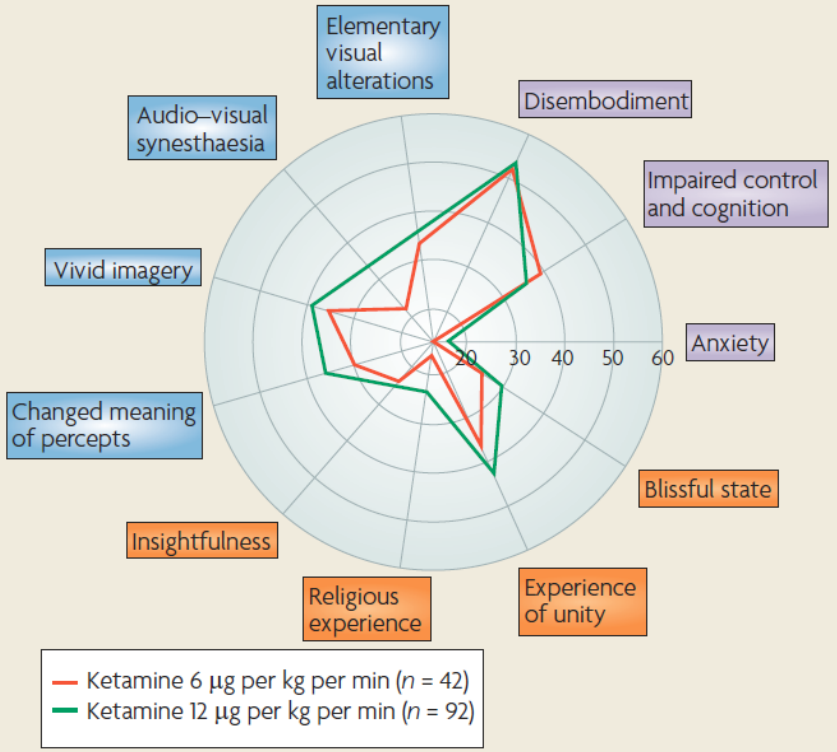
- preferred for childs and ado‘s

- still in use for general and regional anesthesia
  - alone and in combination with hypnotics

- off-label for chronic pain patients

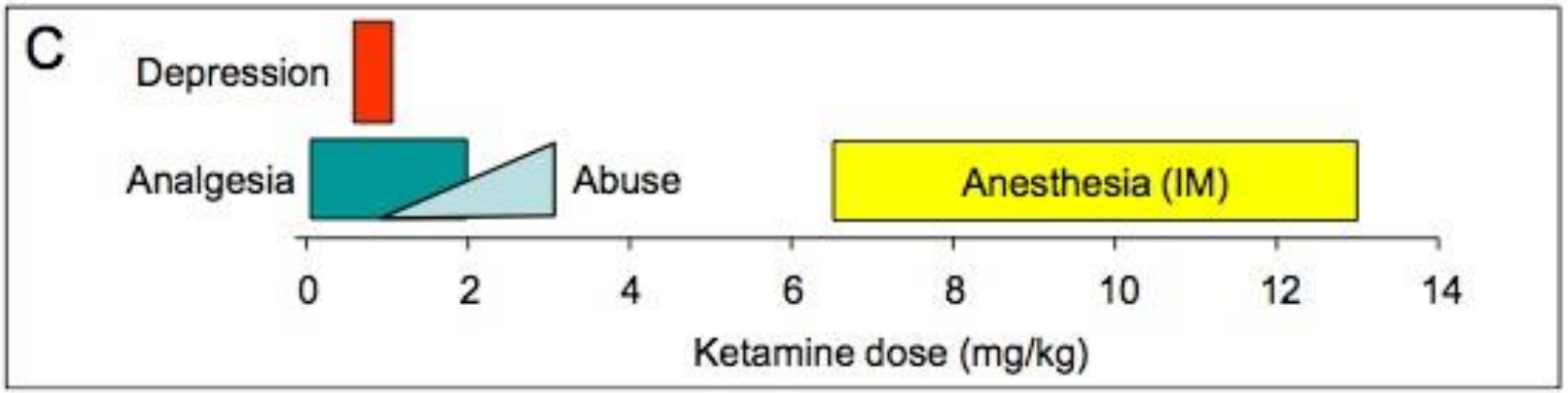
Box 1 | **Assessing altered states of consciousness**





The neurobiology of psychedelic drugs: implications for the treatment of mood disorders.
Vollenweider FX, Kometer M.
Nat Rev Neurosci. 2010 Sep;11(9):642-51.

dose-effect relation



Glue et al., Biol Psychiatry, 2011

ketamine racemate in mg/kg bw i.m. as bolus

ECT and ketamine

pros:

1. **Ketamine probably posseses a unique intrinsic antidepressive potential**

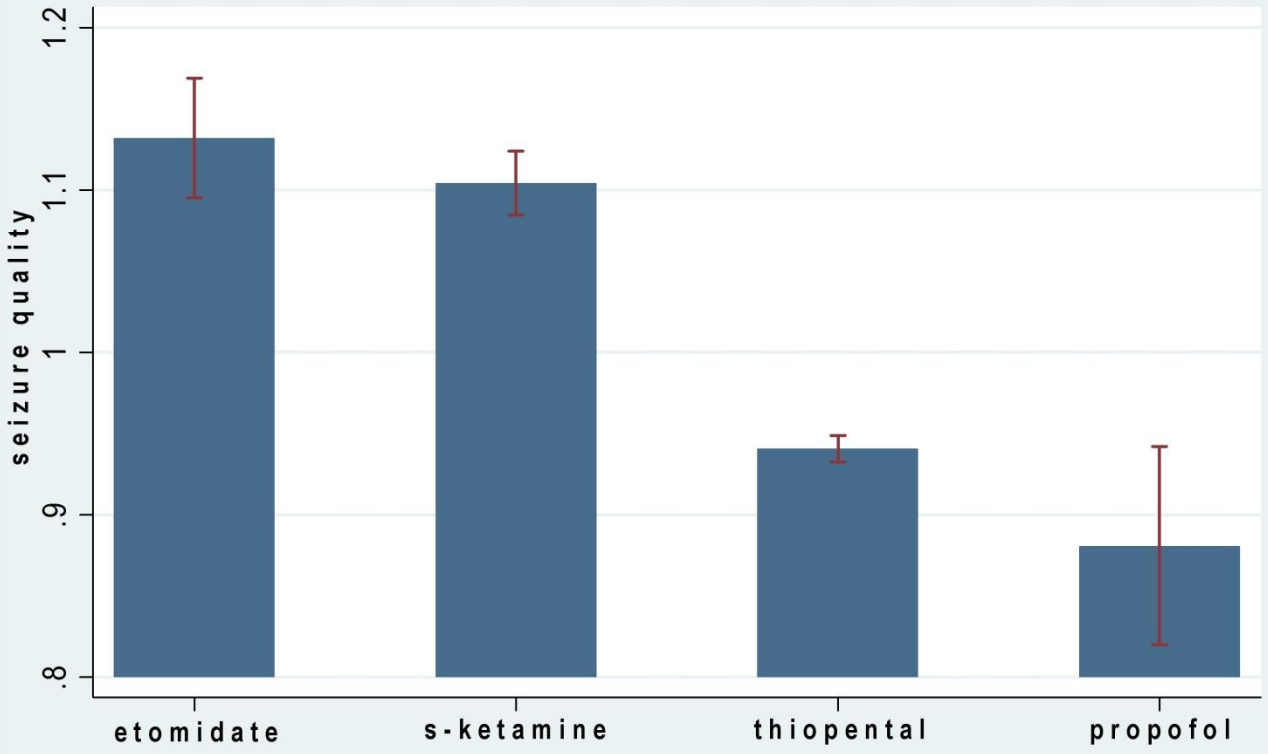
2. **Ketamine has no anticonvulsive action**

3. **Ketamine may posses neuroprotective properties as an NMDA-antagonist**

cons:

1. **Ketamine acts non-depressively on the cardio-vascular systeme (like e.g. barbiturates)**

2. **Ketamine dose-dependently induces psychiatric side-effects**
   (basically derealisation and depersonalisation, which can lead to anxiety)



in a multiple logistic regression model, higher adequacy was significantly related with anesthesia ($p<0.001$) - favoring etomidate and ketamine over thiopental and propofol

Impact of ketamine, etomidate, thiopental and propofol as anesthetic on seizure parameters and seizure quality in electroconvulsive therapy: A retrospective study
Carolin Hoyer, Laura Kranaster, Christoph Janke, Alexander Sartorius
Eur Arch Psychiatry Clin Neurosci 2014 Apr;264(3):255-61.

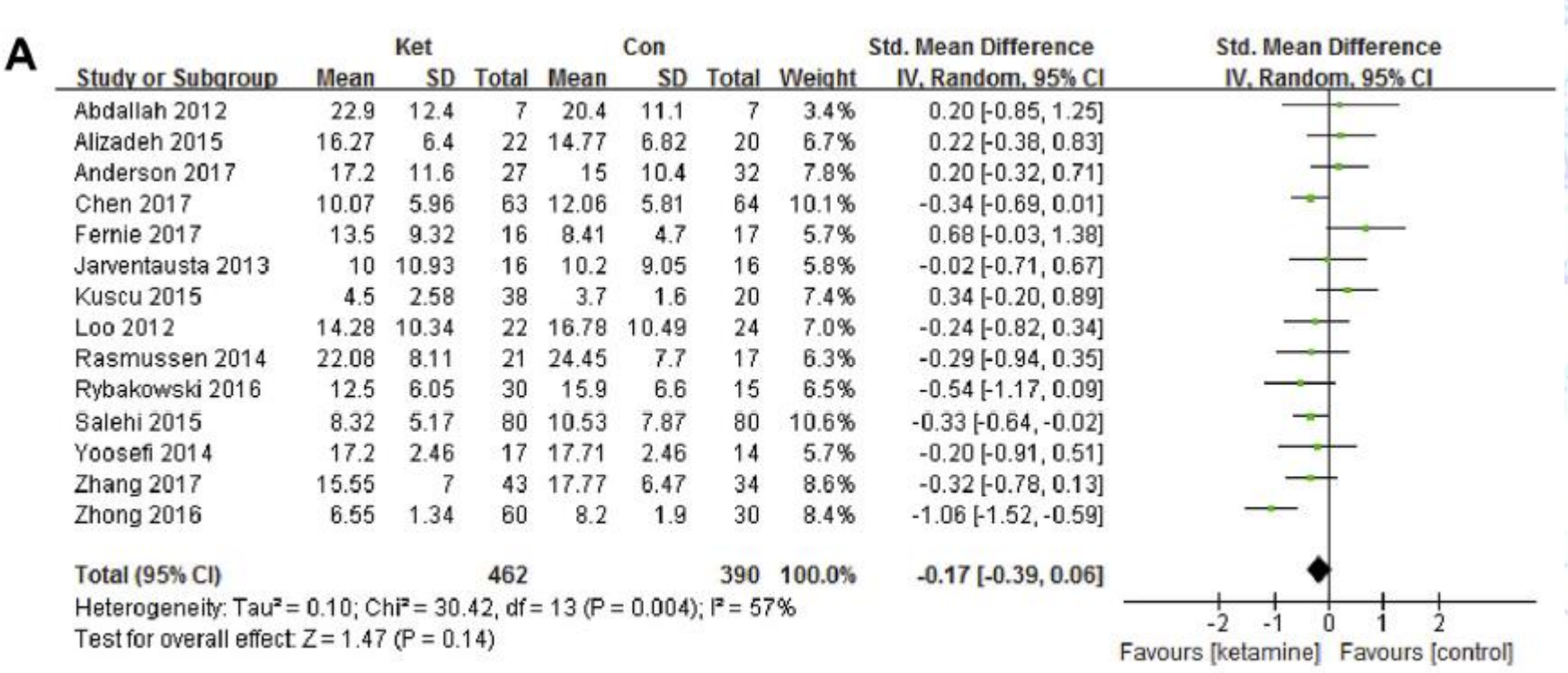


Fig. 2. (A): Meta-analysis of depressive symptoms with ketamine at the end of ECT course.

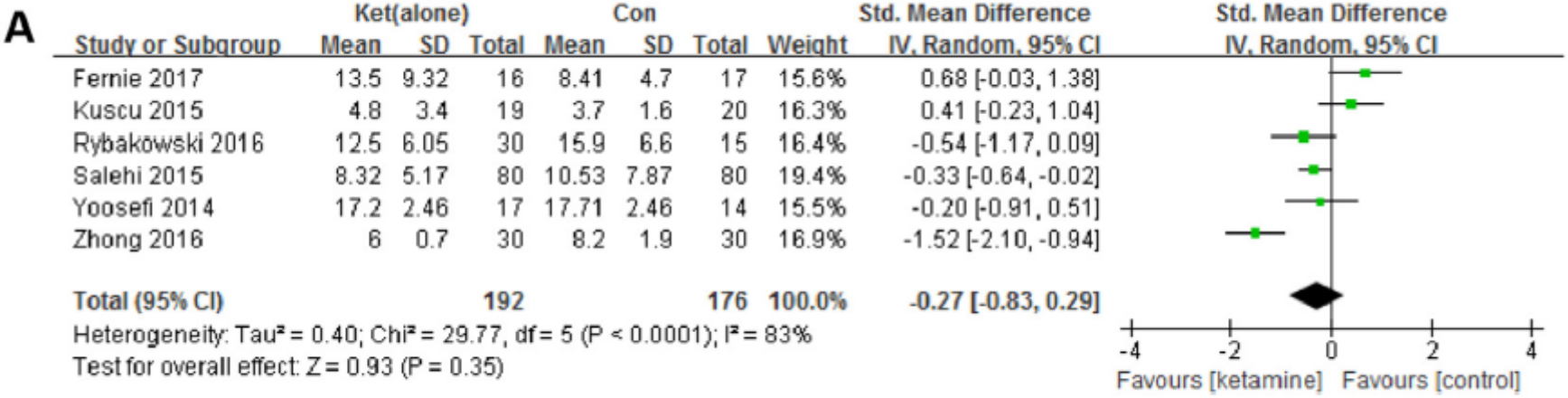


Fig. 4. (A): Meta-analysis of depressive symptoms with ketamine alone at the end of ECT course.

But:

Cognitive function outcomes.

Study	Cognitive evaluation	Findings
Shams et al., 2015	"Cognitive Performance Recovery Time" after each ECT	Ketamine group had a shorter cognitive performance recovery time compared to propofol group.
Anderson et al., 2017	Hopkins Verbal Learning Test-Revised (HVLT-R-DR); originally Controlled Oral Word Association Test (COWAT); Autobio- graphical Memory Interview-Short Form (AMI-SF); Medical College of Georgia Complex Figure Test (MCGCFT), linical digit span forwards and backward; Self-reported Global Self Evaluation of Memory (GSE-My)	No significant differences between ketamine + propofol or thiopental and propofol or thiopental groups
Chen et al., 2017	MMSE; Wechsler Memory Scale-Chinese Revision (WMS-RC)	MMSE score was significantly lower in the ketamine group compared to the propofol group; WMS-RC score was significantly lower in propofol group compared to ketamine + propofol group
Loo et al., 2012	Medical College of Georgia Complex Figure (CFT); Hopkins Verbal Learning Test (HVLT); Controlled Oral Word Association Test (COWAT); Symbol Digit Modalities Test (SDMT); Woodcock Johnson Cross-Out Test; Autobiographical Memory Interview—short form (AMI-SF).	No significant differences between ketamine + thiopental and thiopental groups
Zhong et al., 2016	The Word Fluency Test; the Digit Symbol Test; the Digit Span test; the Wisconsin Card Sorting test (WCST); the Tower of Hanoi; the Trail Making Test (TMT); the Visual Regeneration Test.	Ketamine group showed a lower degree of executive cognitive impairment compared to the ketamine + propofol and propofol groups
Zhang et al., 2017	Speed of Processing (SoP), Attention/Vigilance (AV); Working Memory (WM); Verbal Learning (Vrbl Lrng); Visual Learning (Vis Lrng) Reasoning and Problem Solving (RPS) Social Cognition (SC)	No significant difference was found on the MCCB between the propofol group and the ketamine plus propofol group
Fernie et al., 2017	Cambridge Automated Neuropsychological Test Battery Spatial Recognition Memory Task (CANTAB SRM)	No significant difference was found on the CANTAB SRM between the propofol group and the ketamine group
Yoosefi et al., 2014	Mini-Metal State Examination (MMSE)	A significantly better cognitive performance was evident in ketamine-receiving group
Rasmussen et al., 2014	Mini-Metal State Examination (MMSE)	No significant difference was found in MMSE
Ray-Griffith et al., 2017	Mini-Metal State Examination (MMSE)	No significant difference was found in MMSE
Rybakowski et al., 2016	Tests assessing visual-spatial function Tests assessing verbal auditory function Tests assessing working memory and executive function	No difference was found in the test of visual-spatial function. Impairment of verbal memory and verbal fluency were greater with ketamine.

Adjunctive ketamine and electroconvulsive therapy for major depressive disorder: A meta-analysis of randomized controlled trials.
Zheng W, Li XH, Zhu XM, Cai DB, Yang XH, Ungvari GS, Ng CH, Ning YP, Hu YD, He SH, Wang G, Xiang YT.
J Affect Disord. 2019 May 1;250:123-131.

To conclude so far, ketamine is

- Probably not as side effectively as it was feared

- Probably not more, but definitely not less effective as the grand old four (metho, thio, propo and eto)

- Our experience is that we need less charge for ketamine which explains no difference in response rates, but still could lead into less cognitive side effects (still has to be verified)

- no study has controlled for mean charge so far

ECT – anesthesia :

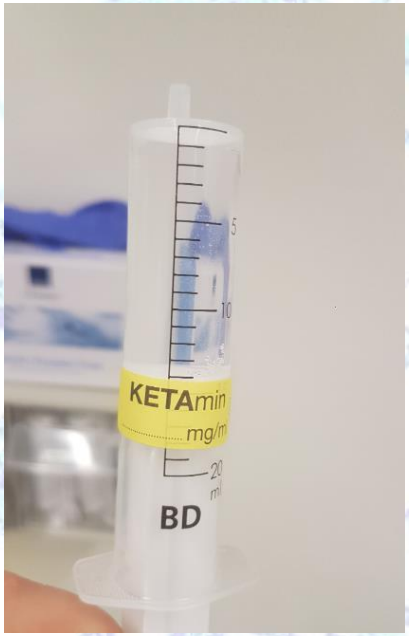
- thiopental 3-5 mg/kg
- methohexital 50-120 mg

- etomidate 0.15-0.3 mg/kg
- propofol 1-2 mg/kg

- ketamine (instead-of OR also an add-on?)


Propofol 20 mg
Rossaint
Werner
Zwißler
Odenwald
Quelle
Naturelle

+


KETAmin
BD

=

ketofol !

propofol plus ketamine = ketofol:

Mind the order :

ketofol: first propofol – followed by ketamine !

Own experiences with ketofol:

- anesthesiologists are excited
- less time in recovery room
- propofol is still critical regarding seizure threshold/induction

- But how to mix propofol and ketamine ???

ECT – anesthesia: propofol+ketamine 1 : 1 ?

Acta Neuropsychiatr. 2018 Apr;30(2):61-69.

Anaesthesia for electroconvulsive therapy - new tricks for old drugs: a systematic review.

Stripp TK, Jorgensen MB, Olsen NV.

OBJECTIVE:
The objective of this review is to investigate existing literature in order to delineate whether the use of anaesthesia and timing of seizure induction in a new and optimised way may improve the efficacy of electroconvulsive therapy (ECT).
METHODS:
PubMed/MEDLINE was searched for existing literature, last search on 24 June 2015. Relevant clinical studies on human subjects involving choice of anaesthetic, ventilation and bispectral index (BIS) monitoring in the ECT setting were considered. The references of relevant studies were likewise considered.
RESULTS:
Propofol yields the shortest seizures, etomidate and ketamine the longest. Etomidate and ketamine+propofol 1 : 1 seems to yield the seizures with best quality. Seizure quality is improved when induction of ECT is delayed until the effect of the anaesthetic has waned - possibly monitored with BIS values. Manual hyperventilation with 100% O2 may increase the pO2/pCO2-ratio, which may be correlated with better seizure quality.
CONCLUSION:
Etomidate or a 1 : 1 ketamine and propofol combination may be the best method to achieve general anaesthesia in the ECT setting. **There is a need for large randomised prospective studies comparing the effect of methohexital, thiopental, propofol, ketamine, propofol+ketamine 1 : 1 and etomidate in the ECT treatment of major depressed patients. These studies should investigate safety and side effects, and most importantly have antidepressant efficacy and cognitive side effects as outcome measures instead of seizure quality.**

ECT: a new look at an old friend

Pavan Kumar Kadiyala[a] and Lakshmi Deepthi Kadiyala[b]

KEY POINTS

- ECT is improving into a new form that may be perceived with a lower degree of social stigma.
- Anesthesia and augmentation strategies have a significant influence on clinical efficacy and tolerability of ECT. Etomidate, or a ketamine-propofol combination, may be the first choice. Dexmedetomidine or remifentanil may be added in selected patients.
- Hyperventilation protocols and ASTI influence the clinical outcome of ECT.
- Refinements in stimulus parameters and electrode placements leading to increased focality have led to a reduction of cognitive adverse effects. RUL brief pulse ECT represents an acceptable first-line form of ECT.
- EEG ictal indices (specifically mid-ictal amplitude, postictal suppression) during ECT procedure should be monitored for therapeutic adequacy of seizure.

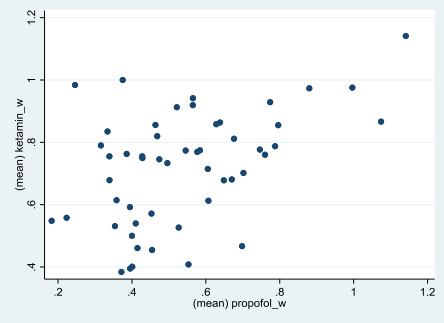
← **propofol+ketamine 1 : 1 ?**

Curr Opin Anaesthesiol. 2018 Aug;31(4):453-458.

Own experiences with ketofol (unpublished):

- 52 patients treated with ketofol, 912 ECT sessions included:

	mean	min	max
- propofol	0.54 mg/kg	10 mg	100 mg
- **S-**ketamine	0.72 mg/kg	30 mg	90 mg



- mean ratio of propofol + S-ketamine = 1 : 1.5
- this corresponds to a ratio of **propofol+ketamine = 1:3 !**
- **less seizure quality** was predicted by age and **dose of propofol**

Take home for ketofol:

- reduce both, dose of k and dose of p
- apply p and then k
- use p : k = 1: 3 (OR p : S-k = 1: 1.5)

ECT – anesthesia:

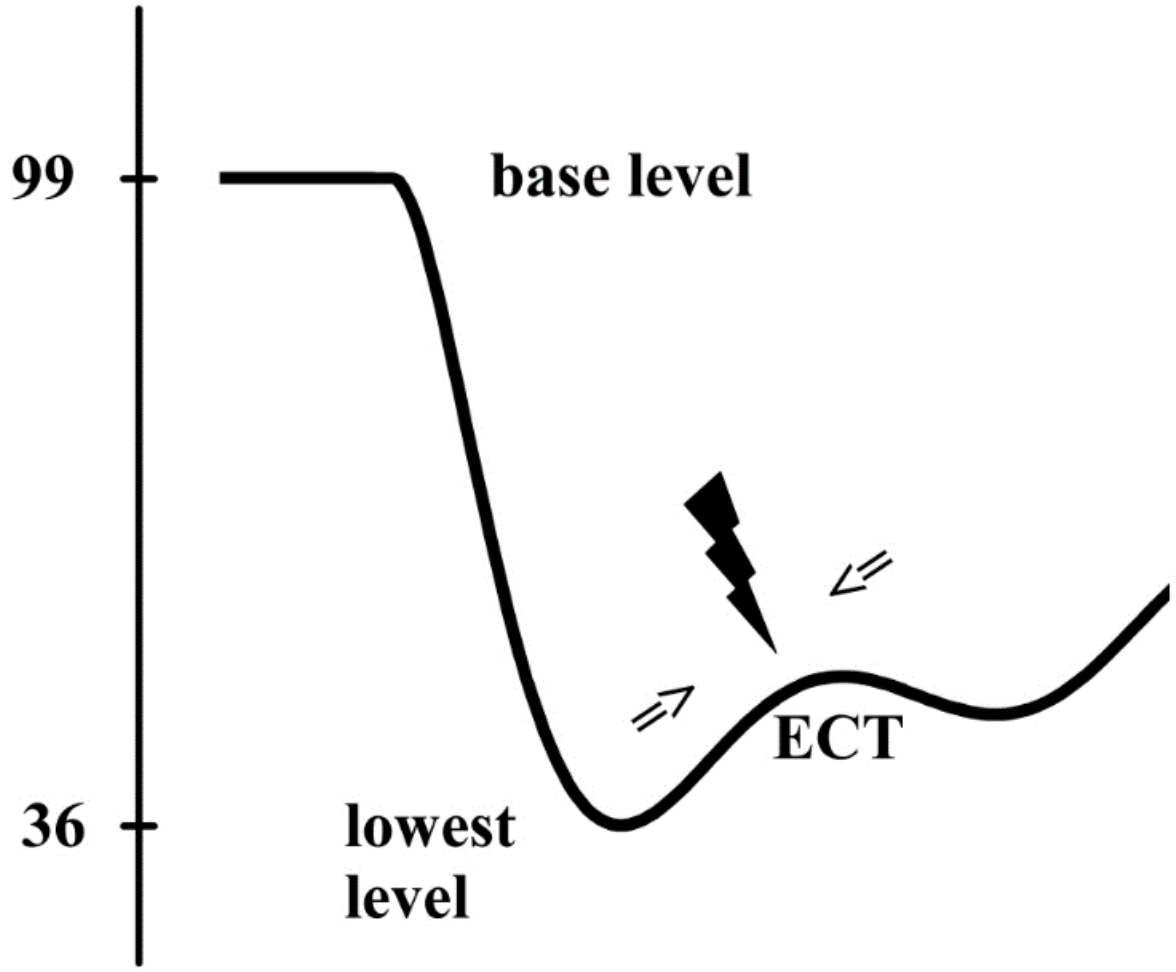
1. Typical anesthetic drugs (p, e, m ,t)

    a. Ketofol – two stones to catch one bird ?

2. Some typical problems / solutions …

    a. **ASTI** (**a**nesthesia-to-**s**timulation **t**ime **i**nterval)
    b. Oxygen
    c. PAS / PIA
    d. Cardiac

ECT – anesthesia: Dosing or Timing ?



bispectrum (BIS) as a surrogate of the depth of the induced anesthesia

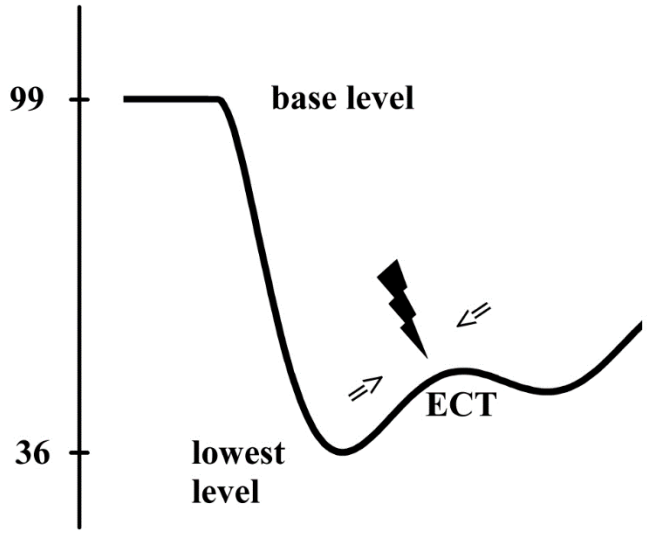
ECT – anesthesia: Dosing

- dose = 0 (at unmodified ECT) results in post ictal agitation (PIA) rates of 10-50%

(Andrade, Shah, Tharyan et al., Indian J Psychiatry. 2012)

- PIA is in an individual patient perfectly predicted by BIS

(Kranaster, Janke, Hoyer, Sartorius, J ECT. 2012)
(Janke, Hambsch, Bumb, Kranaster, Thiel, Sartorius, Aksay, ANIN 2017)



$\Rightarrow$ lower doses of anesthetic are not a good solution

ECT – anesthesia: Timing !!!

- ECT anesthesia: the lighter the better?
Sartorius A, Muñoz-Canales EM, Krumm B, Krier A, Andres FJ, Bender HJ, Henn FA.
Pharmacopsychiatry. 2006 Nov;39(6):201-4.

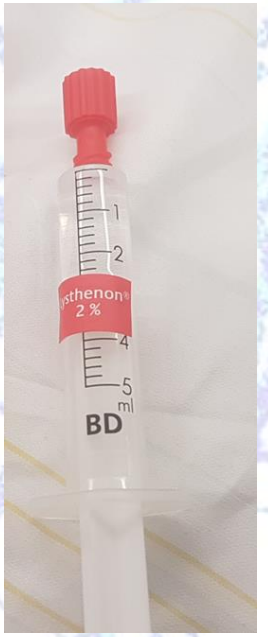
- The Anaesthetic-ECT Time Interval in Electroconvulsive Therapy Practice--Is It Time to Time?
Gálvez V, Hadzi-Pavlovic D, Wark H, Harper S, Leyden J, Loo CK.
Brain Stimul. 2016 Jan-Feb;9(1):72-7.

- The influence of the anesthesia-to-stimulation time interval (ASTI) on seizure quality parameters in electroconvulsive therapy.
Jorgensen A, Christensen SJ, Jensen AEK, Olsen NV, Jorgensen MB.
J Affect Disord. 2018 Apr 15;231:41-43.

ECT – anesthesia: ASTI

propofol / thiopental / methohexital

succinyl-choline



1-2 mins

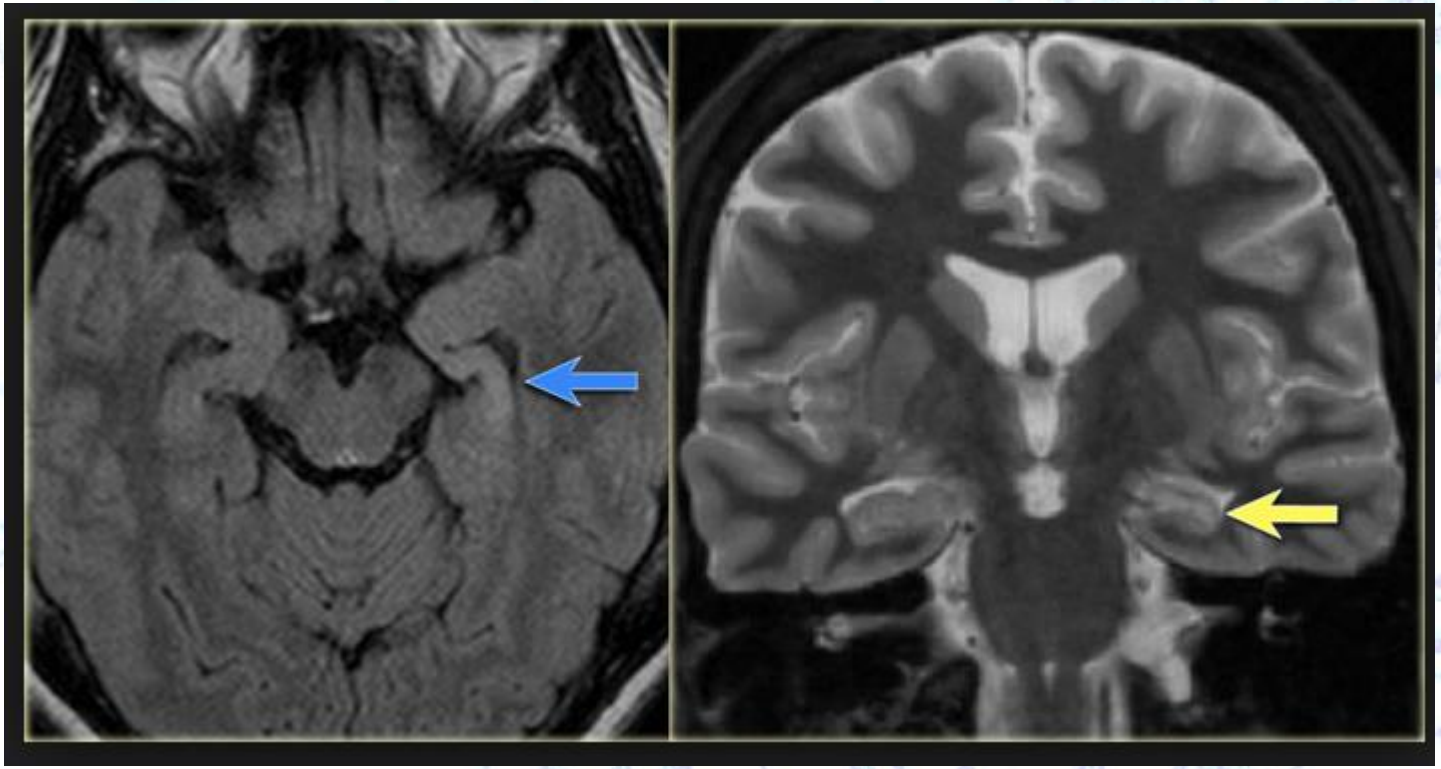
2 - 3 mins

> 4 mins

ECT – anesthesia: Oxygen

What's the difference between grand mal seizures and ECT ?

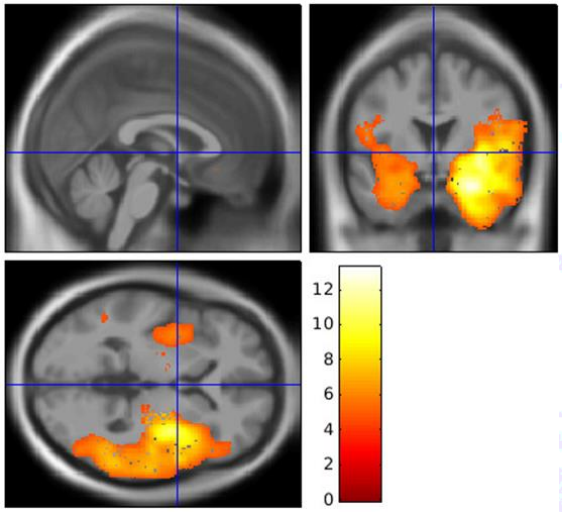
ECT – anesthesia: Oxygen



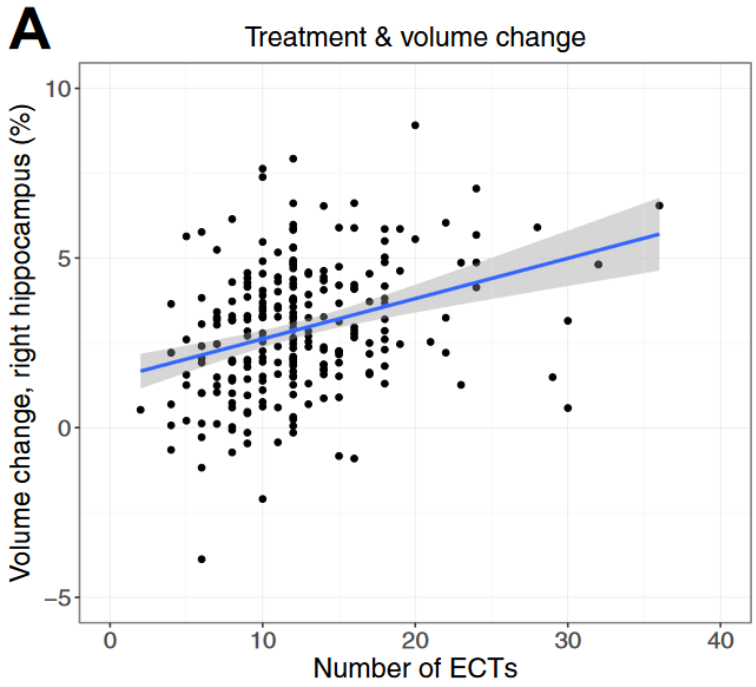
35-year-old patient with refractory temporal lobe epilepsy.

MR shows subtle hyperintensity of the left hippocampus on the axial FLAIR (blue arrow) and atrophy of the left hippocampus on coronal images (yellow arrow).

ECT induced grey matter volume increase

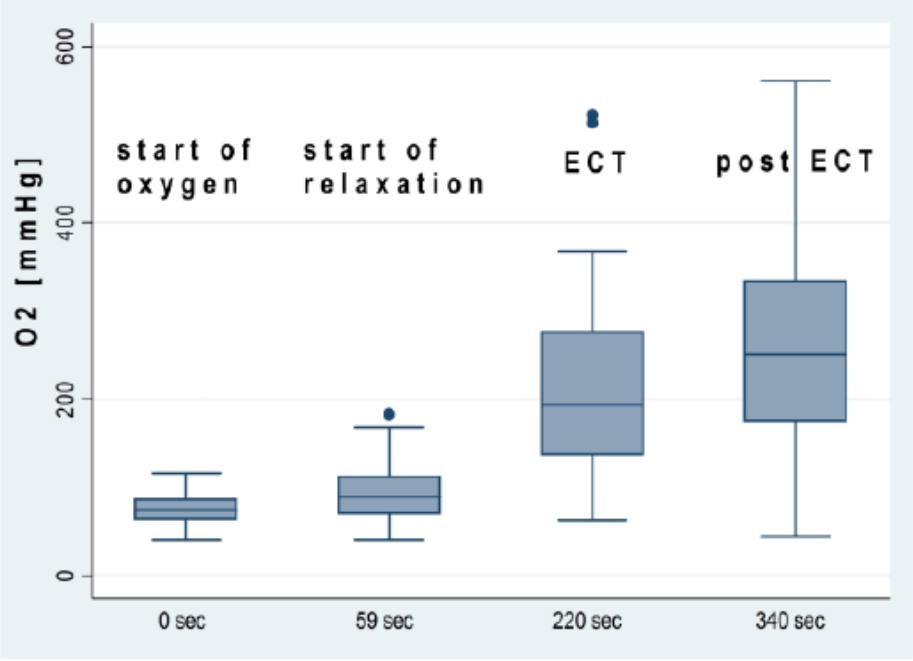


Electroconvulsive therapy induced gray matter increase is not necessarily correlated with clinical data in depressed patients.
Sartorius A, Demirakca T, Böhringer A, Clemm von Hohenberg C, Aksay SS, Bumb JM, Kranaster L, Nickl-Jockschat T, Grözinger M, Thomann PA, Wolf RC, Zwanzger P, Dannlowski U, Redlich R, Zavorotnyy M, Zöllner R, Methfessel I, Besse M, Zilles D, Ende G.
Brain Stimul. 2019 Mar - Apr;12(2):335-343.



Volume of the Human Hippocampus and Clinical Response Following Electroconvulsive Therapy.
Oltedal L, Narr KL, Abbott C, Anand A, Argyelan M, Bartsch H, Dannlowski U, Dols A, van Eijndhoven P, Emsell L, Erchinger VJ, Espinoza R, Hahn T, Hanson LG, Hellemann G, Jorgensen MB, Kessler U, Oudega ML, Paulson OB, Redlich R, Sienaert P, Stek ML, Tendolkar I, Vandenbulcke M, Oedegaard KJ, Dale AM
Biol Psychiatry. 2018 May 29.

Capnometria:



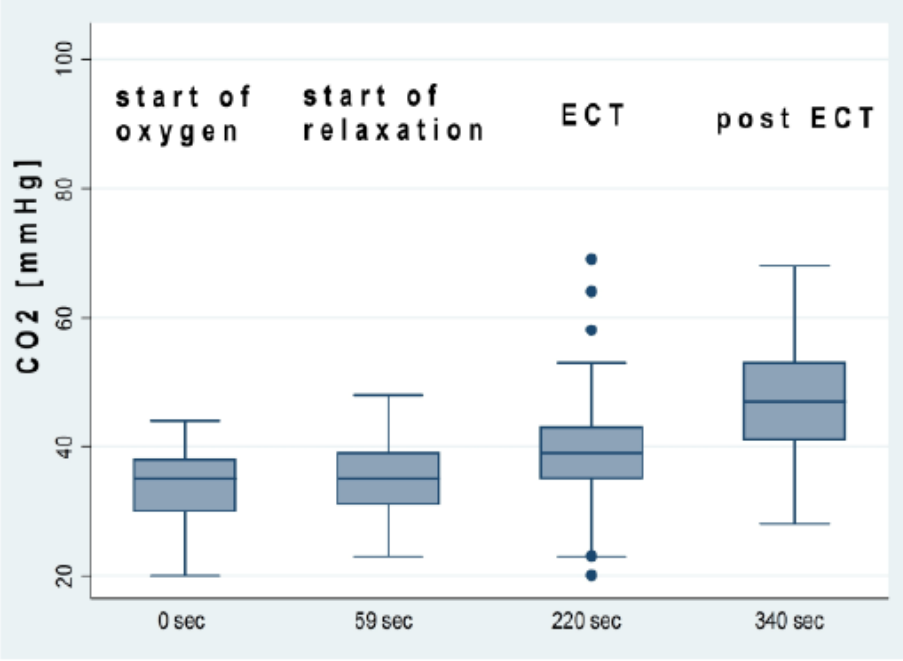
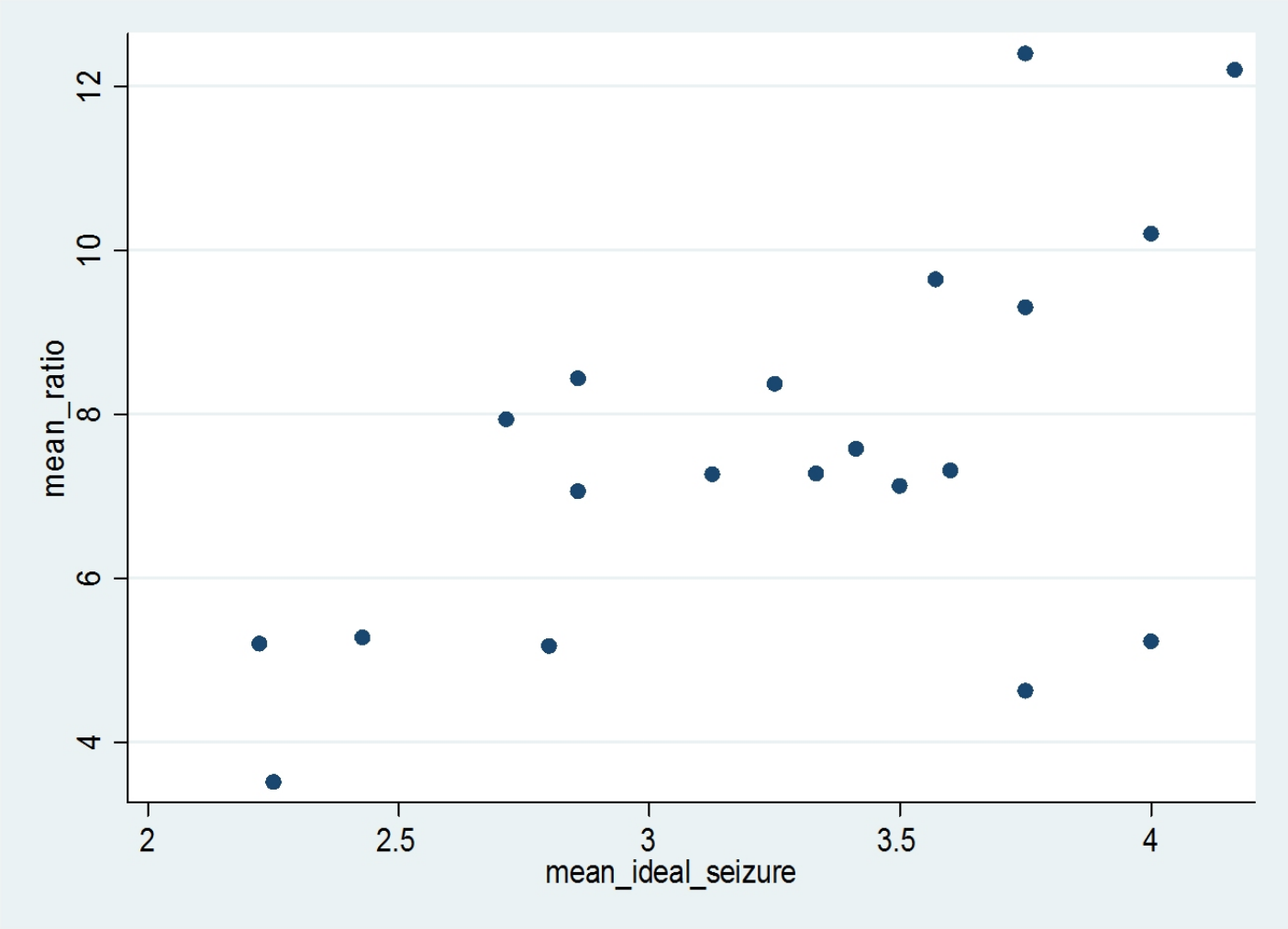


Figure 2: Mean time course of transcutaneously measured pCO_2 and pO_2 level. The mean onset of (pre-)oxygenation, muscle relaxation, start of ECT and 2 minutes post ECT are labeled.

New Evidence for Seizure Quality Improvement by Hyperoxia and Mild Hypocapnia.
Aksay SS, Bumb JM, Janke C, Hoyer C, Kranaster L, Sartorius A.
J ECT. 2014 Mar 12.

Capnometria:

O_2/CO_2



New Evidence for Seizure Quality Improvement by Hyperoxia and Mild Hypocapnia.
Aksay SS, Bumb JM, Janke C, Hoyer C, Kranaster L, Sartorius A.
J ECT. 2014 Mar 12.

ECT – anesthesia: Oxygen

win –win:

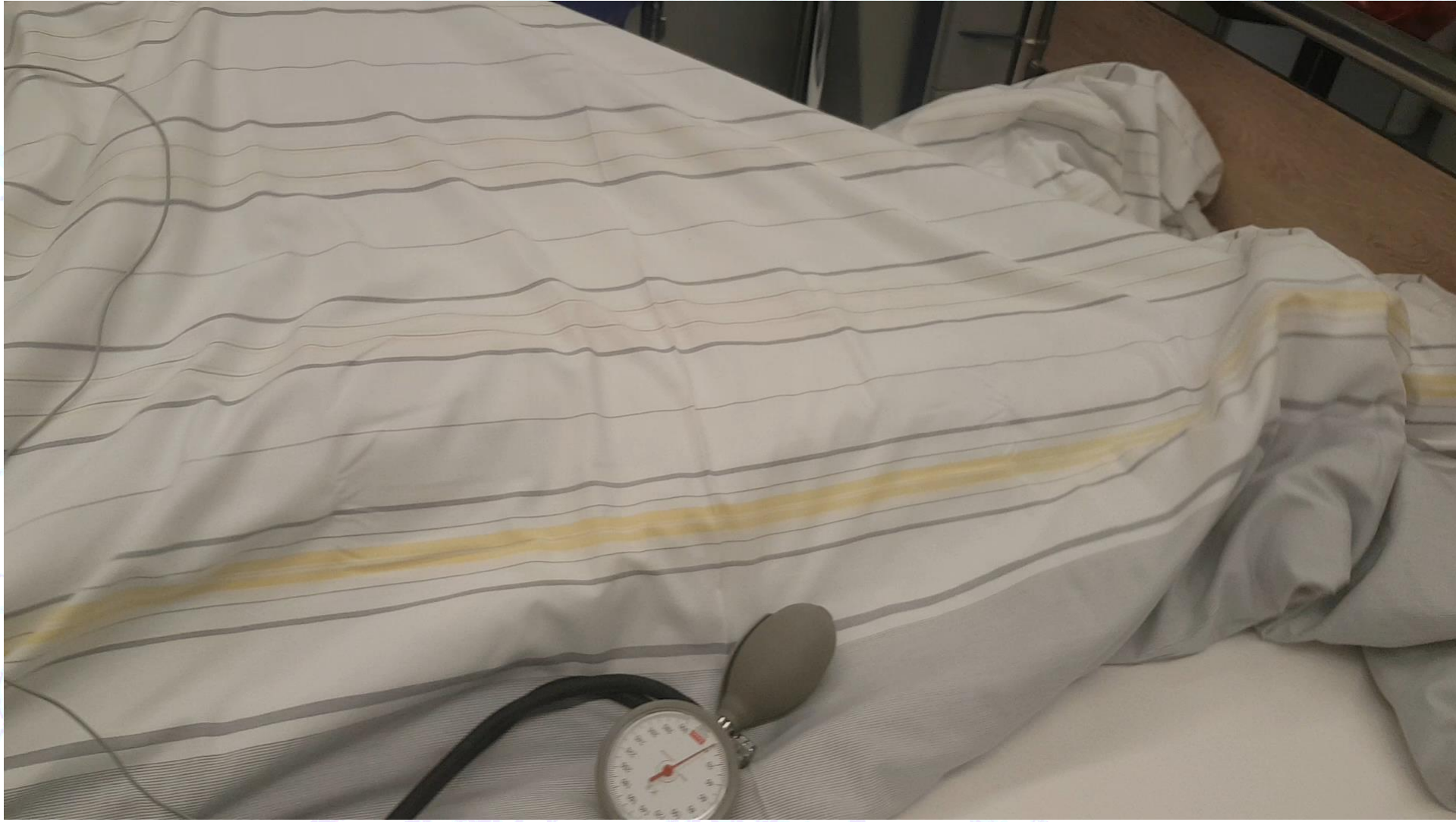
- O_2 makes the procedure safe

- O_2 lowers seizure threshold

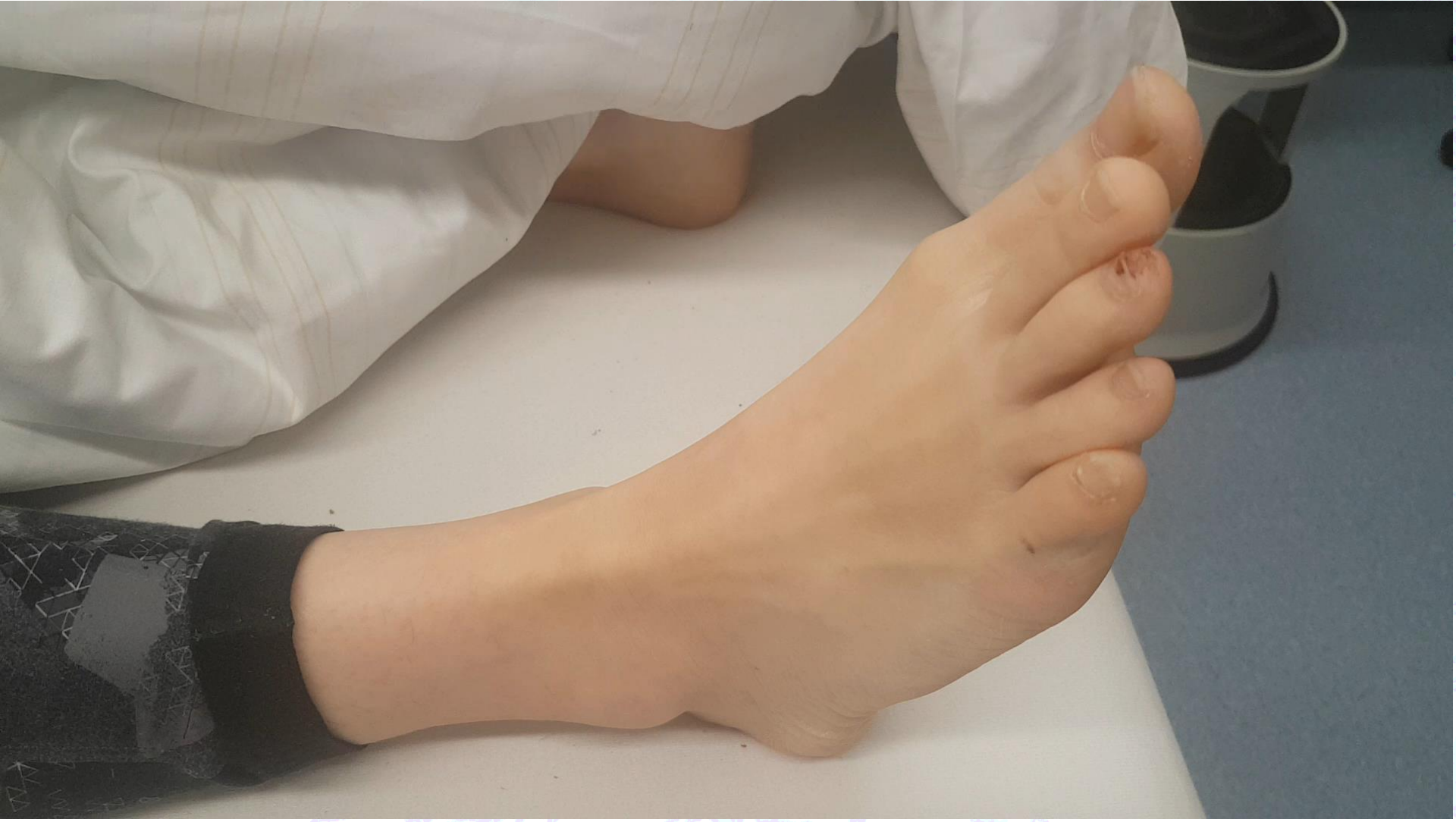
Charles Kellner: “The green gas is the good one !”

ECT – anesthesia: PAS and PIA

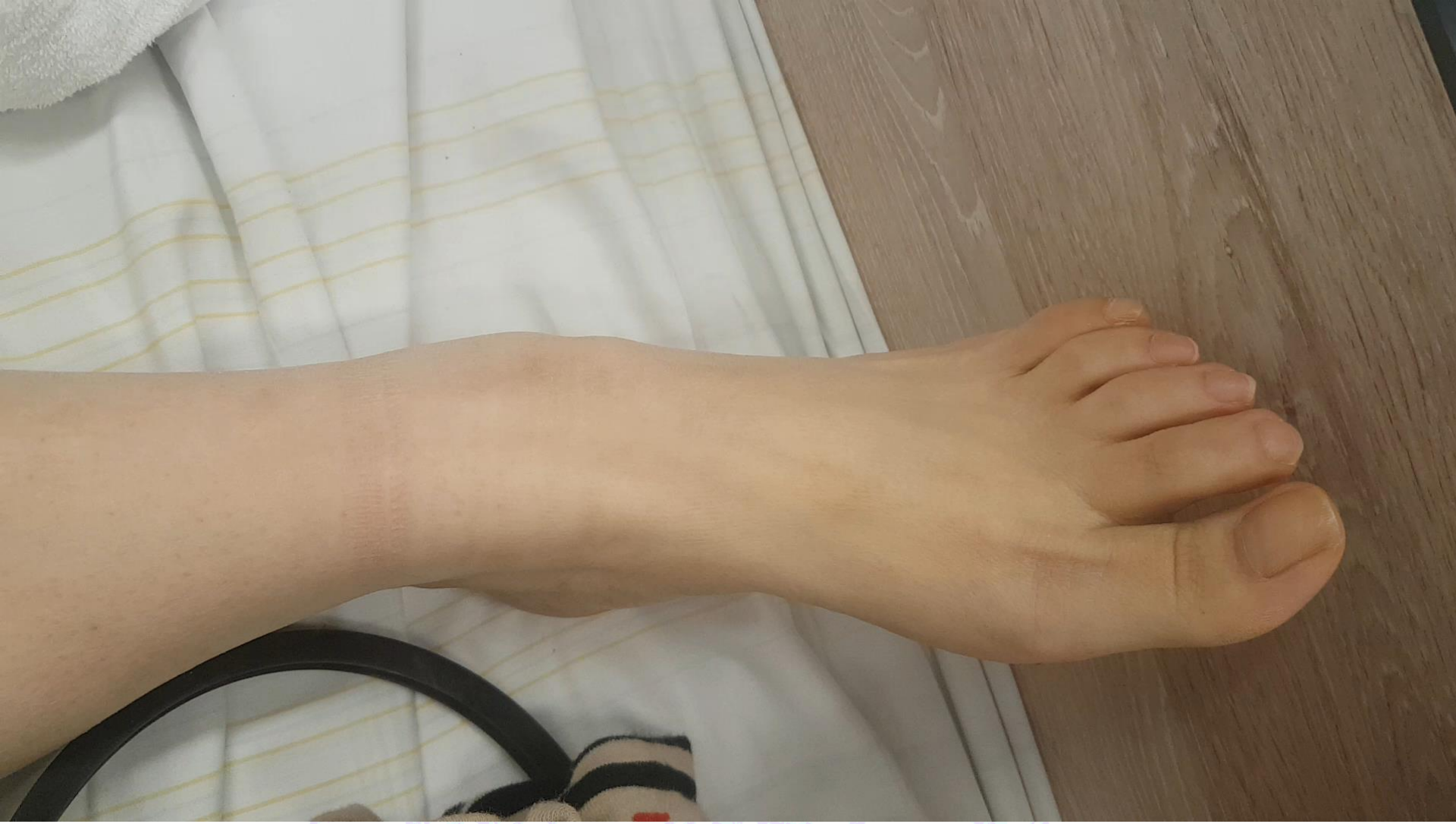
Or problems with “movements” peri-ECT …



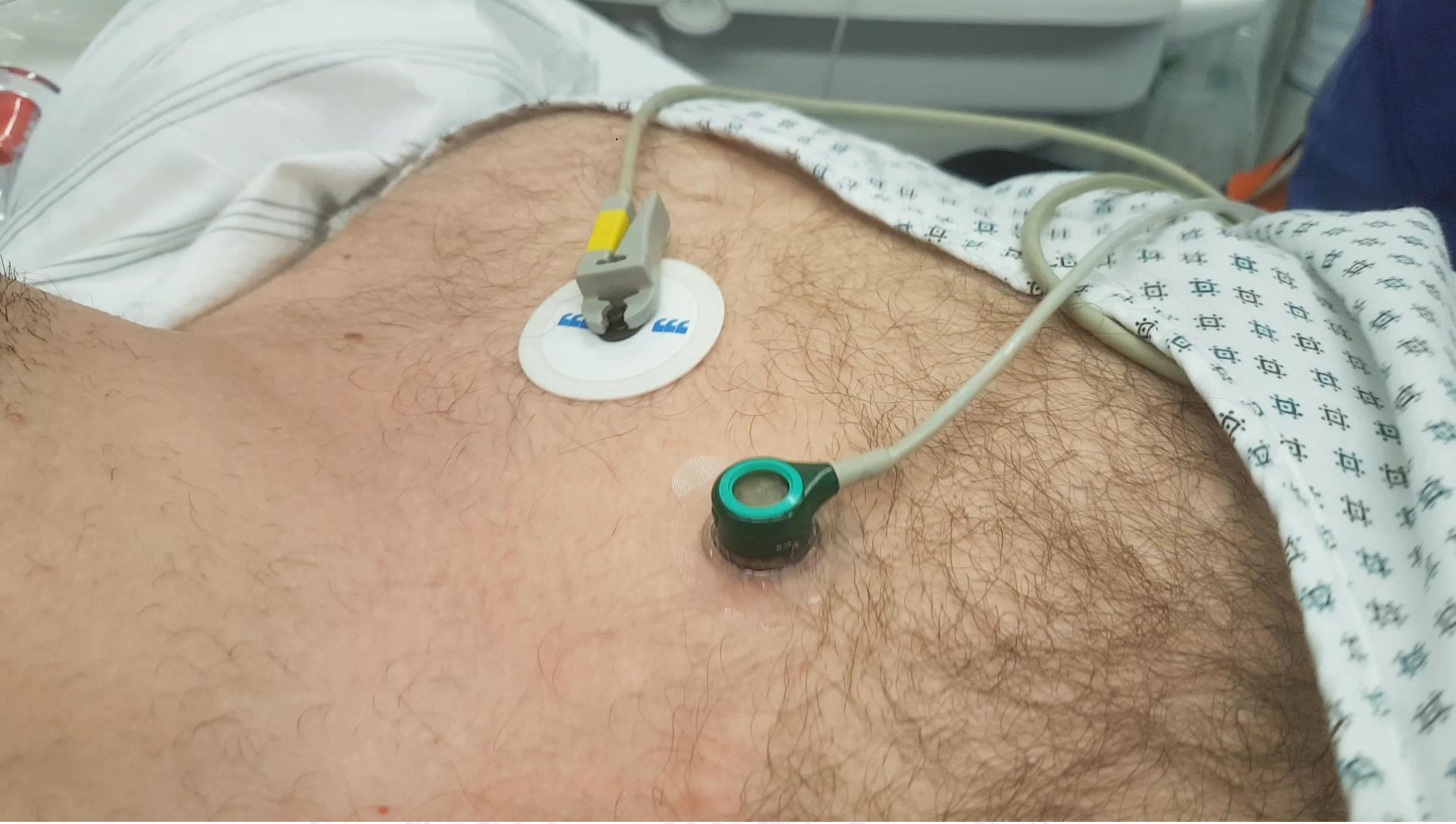
A rare side effect of propofol: acute restless legs syndrome pre ECT
Also possible after flumazenine in the recovery room post ECT



Myocloni frequently seen with etomidate and sometimes even with S-ketamine (not a seizure – as formerly suspected!)

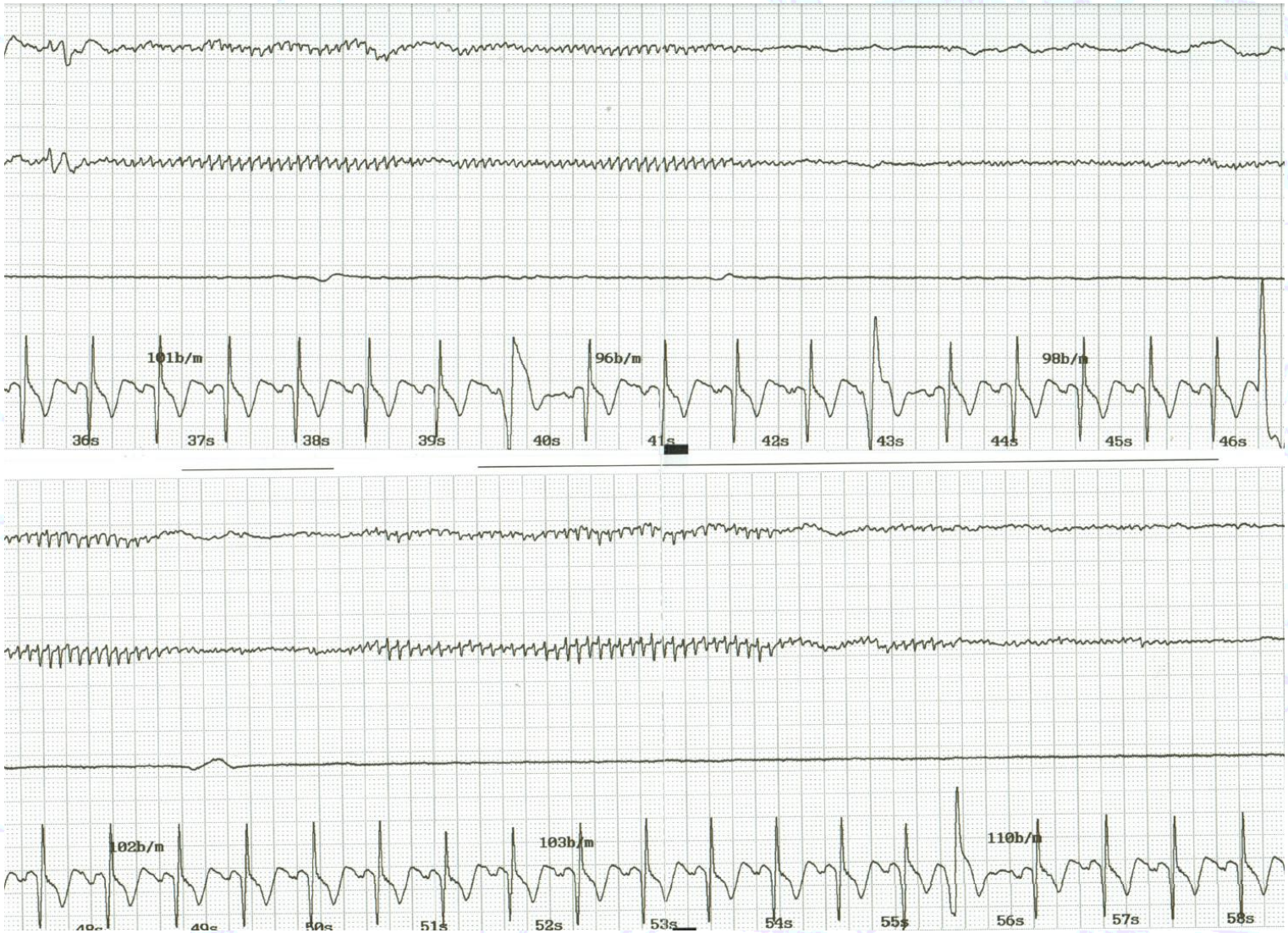


Typical fasciculations due to succinylcholine

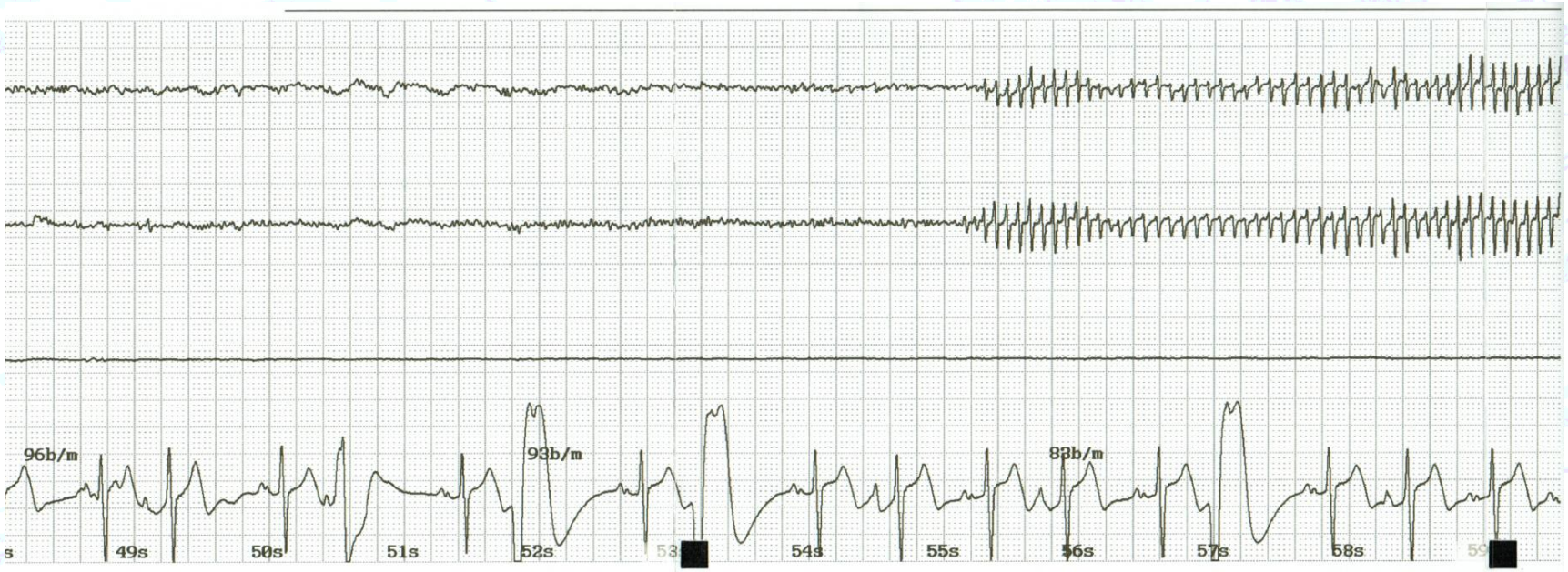


post anesthetic shivering (PAS)

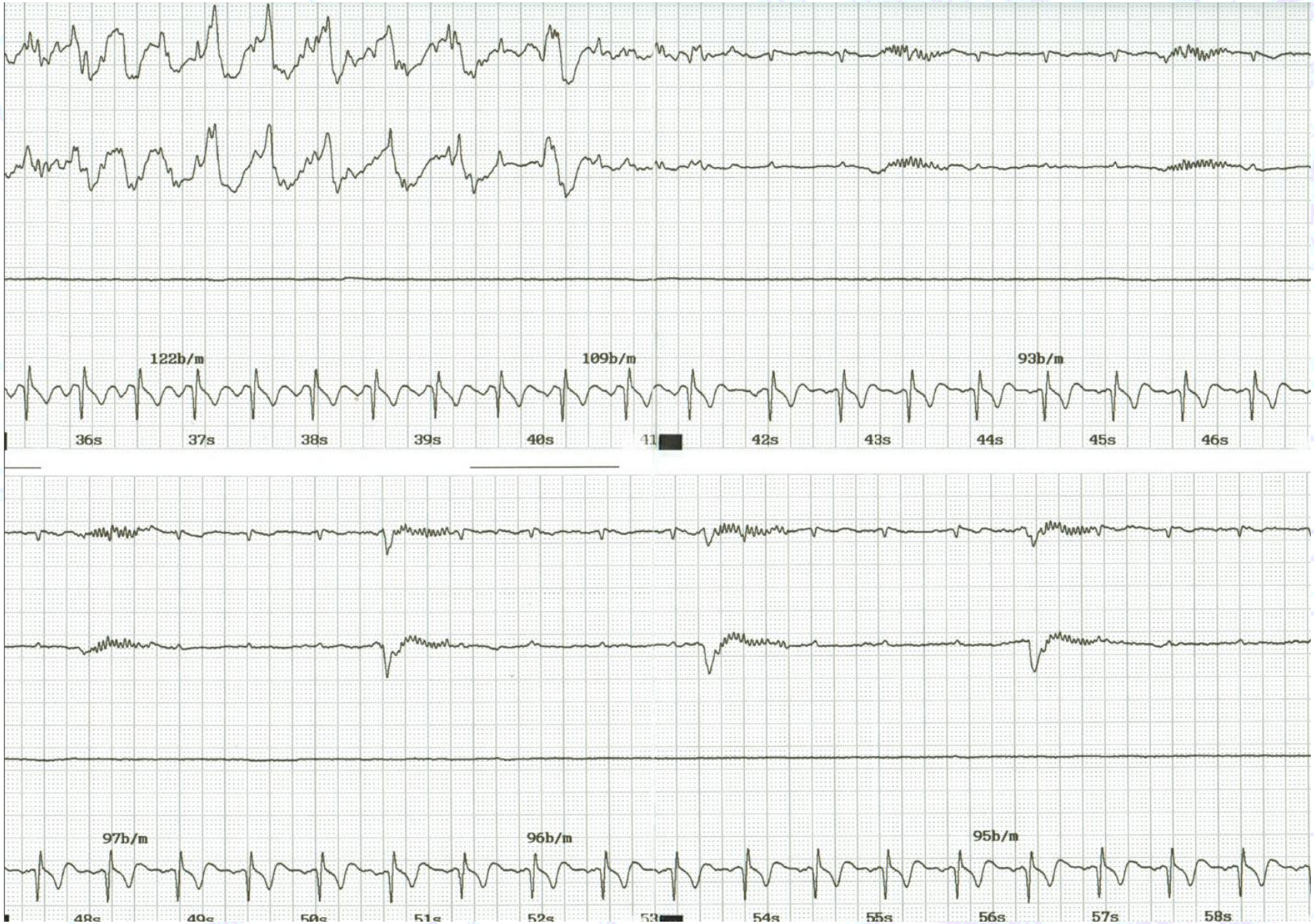
Shivering


101b/m
96b/m
98b/m
36s
37s
38s
39s
40s
41s
42s
43s
44s
45s
46s
102b/m
103b/m
110b/m
49s
50s
51s
52s
53s
54s
55s
56s
57s
58s

Another shivering



snooring


122b/m
109b/m
93b/m
36s
37s
38s
39s
40s
42s
43s
44s
45s
46s
97b/m
96b/m
95b/m
56s
57s
58s

Postanesthetic shivering (PAS) is shivering after anesthesia

is not fasciculating, is not myocloni, is not restless legs !

The intensity of PAS may be graded using the scale described by Crossley and Mahajan:

Table 1. The shivering classification.

Grade	Description
0	No shivering.
1	No visible muscle activity, but one or more of piloerection, peripheral vasoconstriction or peripheral cyanosis (other causes excluded).
2	Muscular activity in only one muscle group.
3	Moderate muscular activity in more than one muscle group, but not generalised shaking.
4	Violent muscular activity that involves the entire body.

The intensity of postoperative shivering is unrelated to axillary temperature.
Crossley AW, Mahajan RP.
Anaesthesia. 1994 Mar;49(3):205-7

Treatment of PAS

1. **clonidine**
2. dexmedetomidine
3. mivacurium instead of succinylcholine
4. probably more often with barbiturates / propofol and less with ketamine

What is the place of clonidine in anesthesia? Systematic review and meta-analyses of randomized controlled trials.
Sanchez Munoz MC, De Kock M, Forget P.
J Clin Anesth. 2017 May;38:140-153. Review.

Systematic Quality Assessment of Published Antishivering Protocols.
Choi KE, Park B, Moheet AM, Rosen A, Lahiri S, Rosengart A.
Anesth Analg. 2017 May;124(5):1539-1546. Review.

Efficiency and safety of ondansetron in preventing postanaesthesia shivering.
He K, Zhao H, Zhou HC.
Ann R Coll Surg Engl. 2016 Jul;98(6):358-66. Review.

Effectiveness of dexmedetomidine use in general anesthesia to prevent postoperative shivering: a systematic review.
Hoffman J, Hamner C.
JBI Database System Rev Implement Rep. 2016 Jan 15;13(12):287-313. Review.

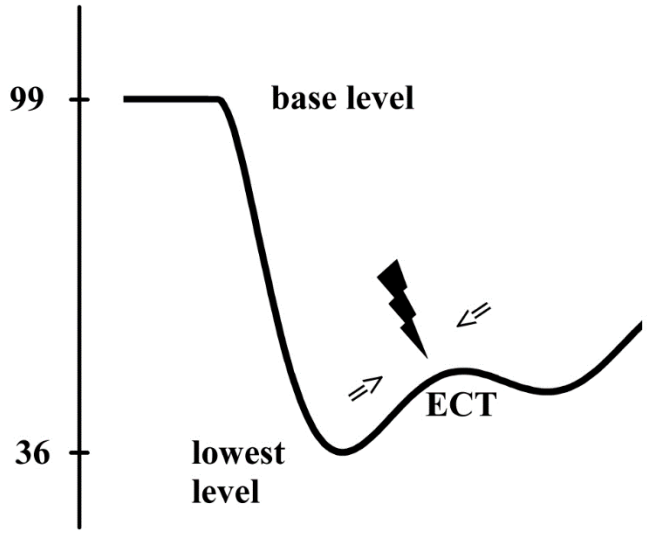
ECT – anesthesia: post ictal agitation (PIA)

- dose = 0 (unmodified ECT) results in post ictal agitation (PIA) rates of 10-50%

(Andrade, Shah, Tharyan et al., Indian J Psychiatry. 2012)

- PIA is in an individual patient perfectly predicted by BIS

(Kranaster, Janke, Hoyer, Sartorius, J ECT. 2012)
(Janke, Hambsch, Bumb, Kranaster, Thiel, Sartorius, Aksay, ANIN 2017)



$\Rightarrow$ lower doses of anesthetic are not a good solution

ECT – anesthesia: post ictal agitation (PIA)

- Do not restrain !!! (=> otherwise increase of PIA)

- Keep everything calm and use as less physical limitation as possible

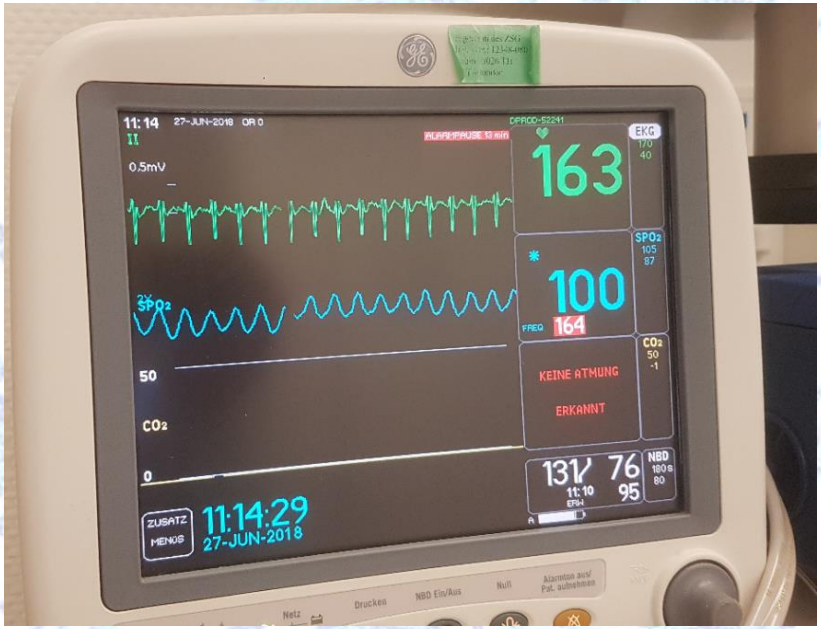
- Self limitating in most cases within 20 mins

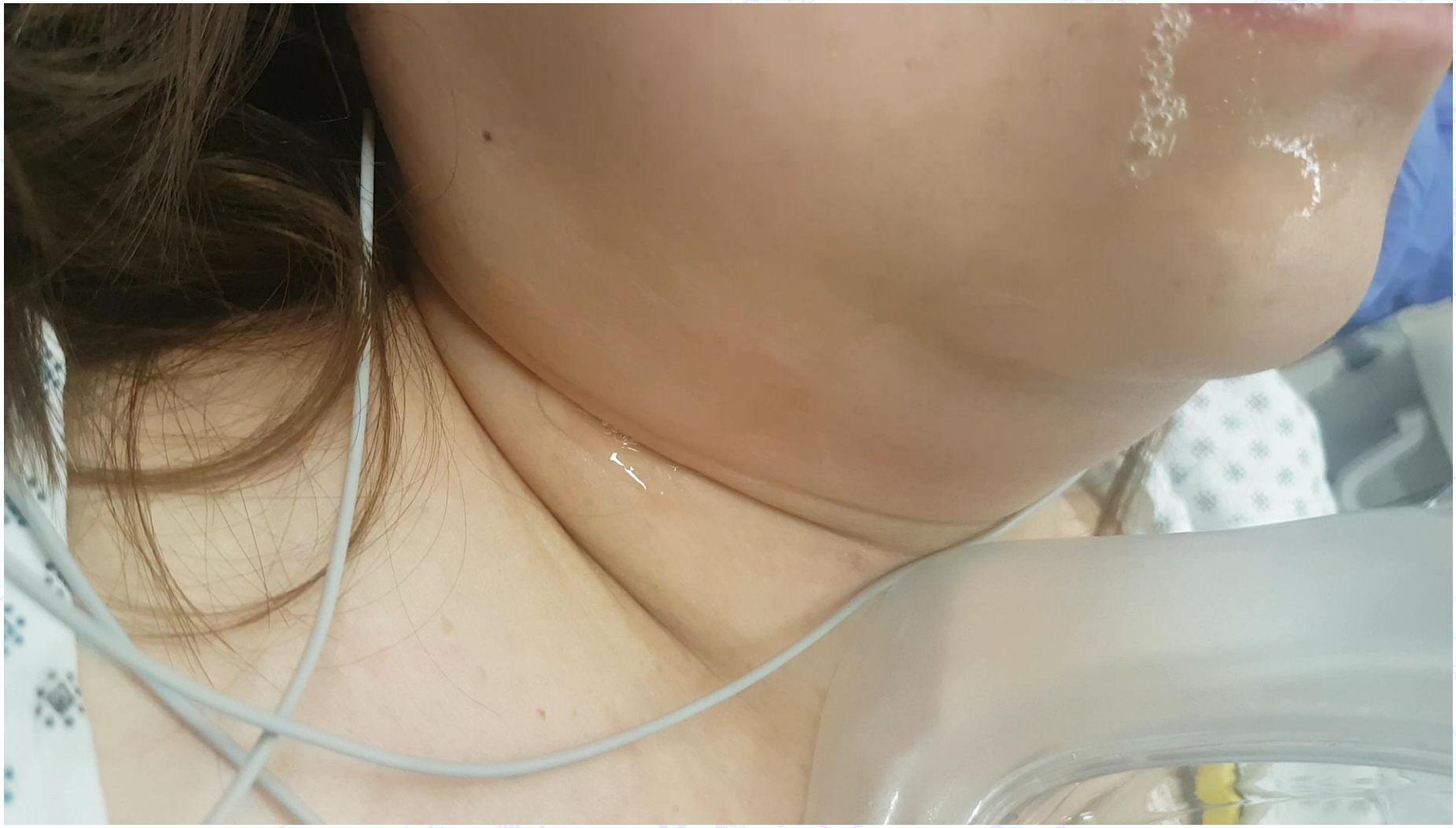
- Severe forms: Escalate staff

- Severe forms: Use i.v. diazepam e.g. 10mg

- Increase dose of anesthetic next ECT

ECT – anesthesia: cardiac

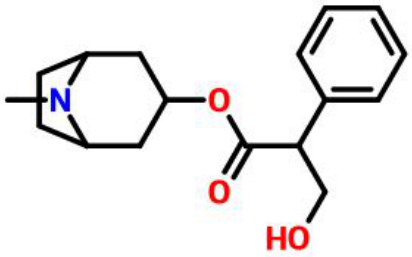




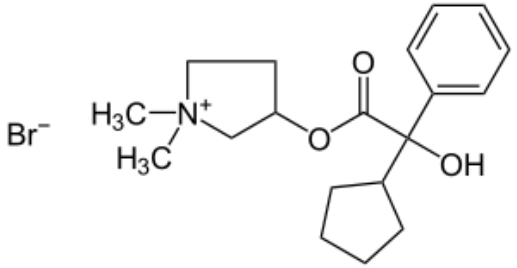
hypersalivation / sialorrhoe

- Former times: atropine, which is basically obsolete. Why ?
- Today: glycopyrrolate as muscarinic receptor antagonist

- Both reduce hypersalivation (parasympatholytic)
- atropine reduces initial bradycardia, but increases ictal hypertension *

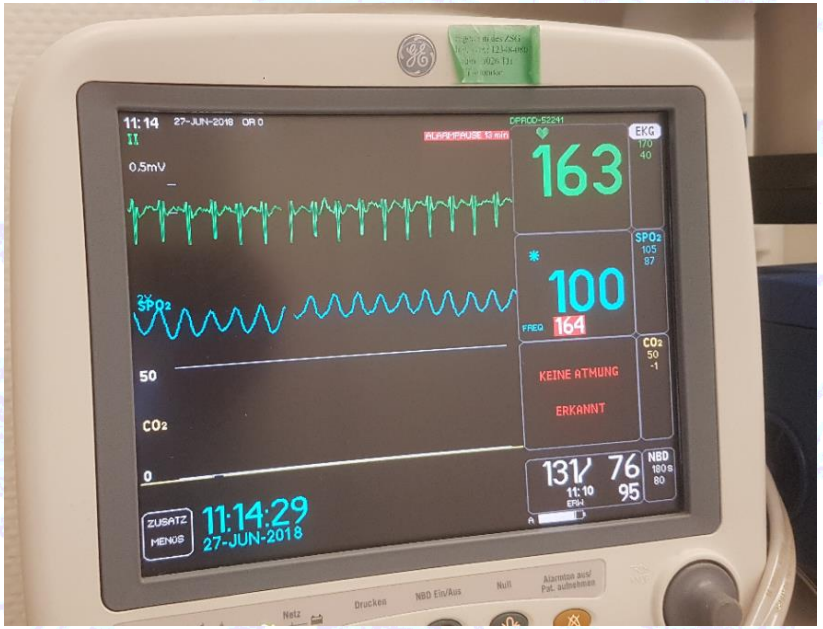


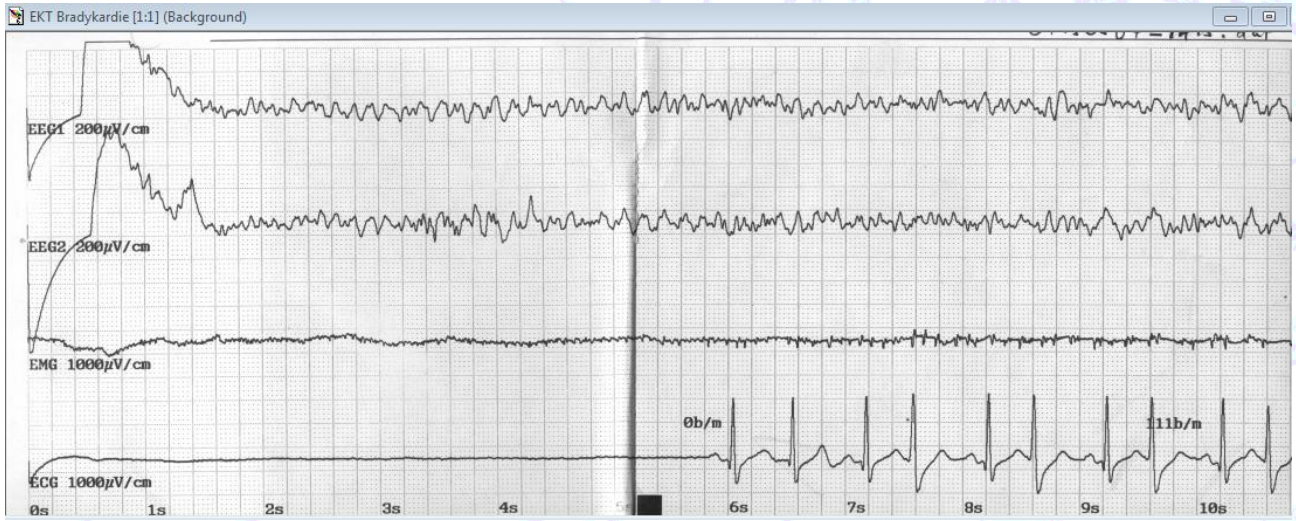
=>



* Psychiatry Res. 2019 Jan;271:239-246
Electro convulsive therapy: Modification of its effect on the autonomic nervous system using anti-cholinergic drugs.
Christensen STJ, Staalsø JM, Jørgensen A, Weikop P, Olsen NV, Jørgensen MB.

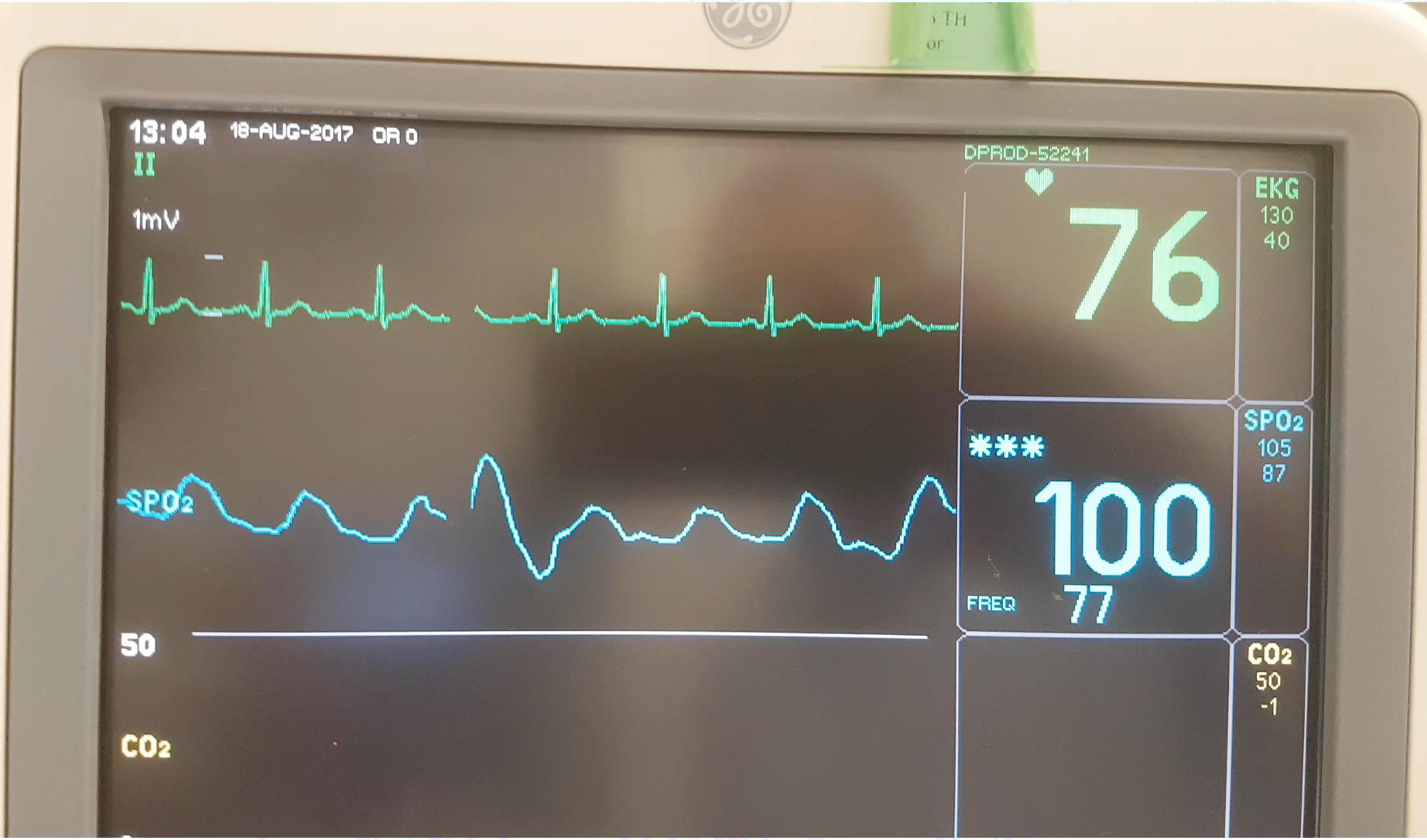
ECT – anesthesia: cardiac





J ECT. 2019 May 14.
The Brady Bunch:
A Montage of Typical Sinus Pauses in Electroconvulsive Therapy.

Kellner CH, Paparone P



Asystolia appears shorter in our printout
(printout starts at the end of charge delivery!)

Die Position der Stimulationselektroden und die Herzfrequenz bei Elektrokrampftherapie

Placement of Stimulus Electrodes and Heart Rate during Electroconvulsive Therapy

Autor J. Nagler

Institut Klinikum Schloß Winnenden (Ärztlicher Direktor Dr. G. Hetzel)

Incidence of post-stimulus asystole

- > 50% !!!

- conclusion:
  1. frequent ! (probably very physiologic, low risk)
  2. BIL > RUL > BF
  3. age

International Journal of Neuropsychopharmacology (2011), **14**, 585–594. © CINP 2010
doi:10.1017/S1461145710001458

ARTICLE

CINP

The effect of electrode placement and pulsewidth on asystole and bradycardia during the electroconvulsive therapy stimulus

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[2] *The Northside Clinic & Wesley Hospital, Sydney, Australia*
[3] *St George Hospital, Sydney, Australia*
[4] *Black Dog Institute, Sydney, Australia*
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Table 3. Asystole during ECT stimulus

	Pulsewidth				Electrode placement			
Covariate	*B*	S.E.	*p*	OR	*B*	S.E.	*p*	OR
Electrode placement								
RUL *vs.* BF					**5.334**	1.333	0.000[b]	207.239
RUL *vs.* BT					**2.158**	0.774	0.005[b]	8.654
BT *vs.* BF					**3.176**	1.348	0.018[c]	23.947
Pulsewidth								
1.0 *vs.* 0.3	**3.818**	1.161	0.001	45.527				

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E. Burgunder

Dr. Aksay

Dr. Kranaster

Dr. Bumb