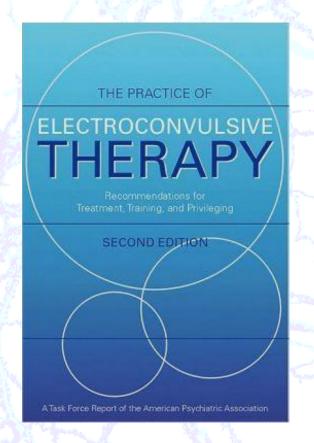




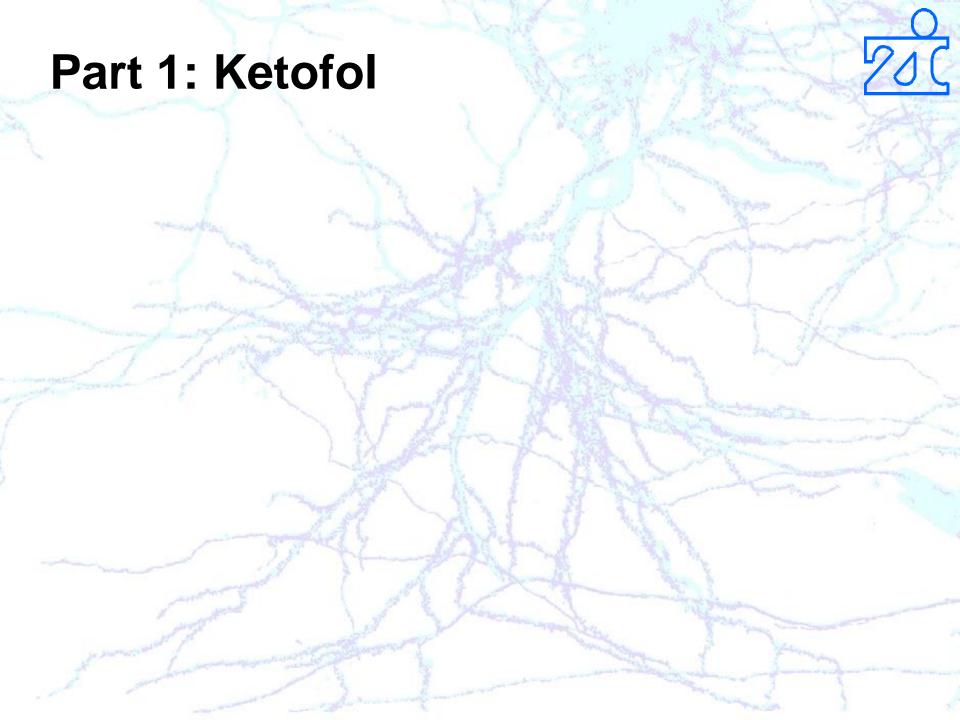
Copyrighted Material ELECTROCONVULSIVE THERAPY **Richard Abrams** FOURTH EDITION



### ECT – anesthesia:



- 1. Ketofol two stones to catch one bird?
- 2. Oxygen the good gas!
- 3. What's that on the printout / monitor?



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

0



low doses pro-psychotic,

cardiovascular depression

higher blood pressure

longer time of apnoe,

similar to alfentanil?

#### Adapted from:

remifentanil

S-ketamine

alfentanil

Folkerts HW.

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

0.5-1.5

0.01-0.015

0.001-0.008

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

#### ACTA ANAESTHESIOLOGICA SCANDINAVICA doi: 10.1111/aas.12289



#### Review Article

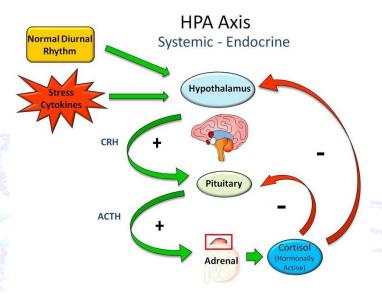
# Etomidate – a review of robust evidence for its use in various clinical scenarios

G. Erdoes, R. M. Basciani and B. Eberle

Department of Anaesthesiology and PainTherapy, University Hospital Bern, Bern, Switzerland

Etomidate is an intravenous hypnotic with a favourable clinical profile in haemodynamic high-risk scenarios. Currently, there is an active debate about the clinical significance of the drug's side effects and its overall risk-benefit ratio.

Etomidate-induced transient adrenocortical suppression is well documented and has been associated with increased mortality in sepsis. In surgical patients at risk of hypotensive complications, however, a review of current literature provides no robust evidence to contraindicate a single-bolus etomidate induction. Large randomised controlled trials as well as additional observational data are required to compare safety of etomidate and its alternatives.



# **ECT – anesthesia:** 3-5 mg/kg - thiopental - methohexital 50-120 mg - propofol 1-2 mg/kg

# German guidelines for tx of status epilepticus



- 1 => lorazepam up to 10mg i.v.
- 2 => phenytoin up to 30 mg/kg KG i.v.
- 3 => phenobarbital 20 mg/kg KG i.v.
- 4 => thiopental 4-7 mg/kg KG i.v.
  - vs. propofol 1-2 mg/kg KG i.v.

vs. midazolam or valproate

# **Dosing of ECT anesthetics**



- experience of the anesthesiologist
- experience from previous ECT sessions
  - time needed for full recovery
  - patient remembers muscle relaxation
  - systematic / non-systematic movements of the "cuffed" limb
- objective criteria for

"dosing" and "timing"

do not exist ...

Br J Psychiatry. 1995 Jan;166(1):118-9. Anaesthetic technique in the practice of ECT. Collins IP, Scott IF.

# **Bispectral Index Monitoring (BIS)**



- has been developed to prevent intraoperative awareness
- uses combined EEG/EMG to derive a measure for "cortical integrity" inter alia by analyzing coherences between different frequency bands
- More precisely: bispectrum is a 3<sup>rd</sup> order Fourier transformation that includes amplitude, phase AND coherence information. BIS is a normalized index function of the bispectrum.
  - 0 electrically silent brain00 fully vigilant patient

# **Bispectral Index Monitoring (BIS)**



- BIS more **valid** regarding "hypnosis" compared with other algorithms like spectral edge frequency (SEF), median frequency (MF), or delta, theta, alpha, beta power

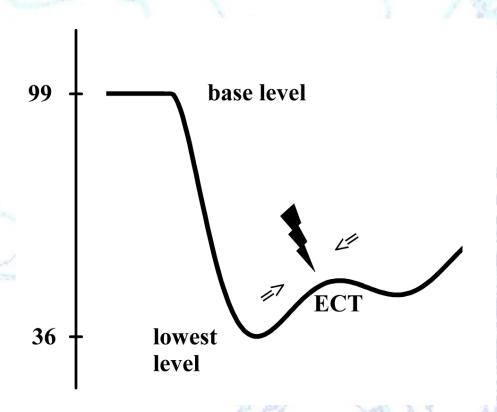




Liu J, Singh H, White PF (1996) Anesthesiology 84:64-69 Schmidt GN, Bischoff P, et al. (2005) Anaesthesia 60:228-234

# How does a typical BIS time course looks like?



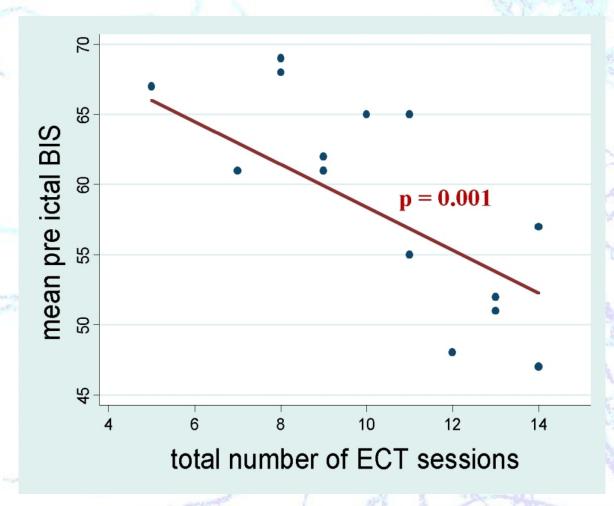


A. Sartorius et al., Br J Anaesth. 2006.

A. Sartorius et al., Pharmacopsychiatry. 2006.

# Our 1. study on depth of anesthesia: thiopental





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

#### **Depth of anesthesia:**



If BIS - or "light" anesthesia

- or better: less anticonvulsive action resulting from anesthetics is important

Why we don't use an anesthetic without anticonvulsive properties?

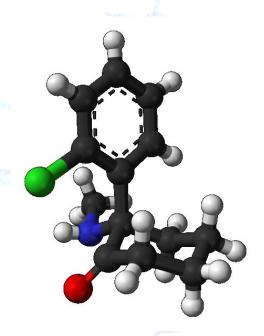


A. Sartorius<sup>1</sup> E. M. Muñoz-Canales<sup>1</sup> B. Krumm<sup>2</sup> A. Krier <sup>3,4</sup>

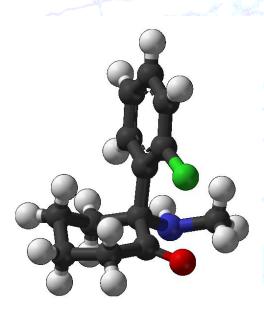
F. J. Andres<sup>4</sup>

H.-J. Bender<sup>4</sup>
F. A. Henn<sup>1</sup>

ECT Anesthesia: The Lighter the Better?







#### **ECT** and ketamine



#### pros:

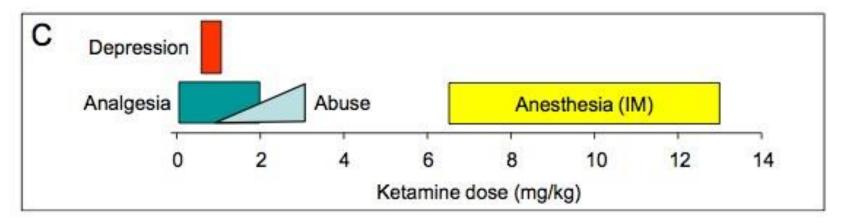
- 1. Ketamine probably posseses a unique intrinsic antidepressive potential
- 2. Ketamine has no anticonvulsive action
- 3. Ketamine may posses neuroprotective properties as an NMDA-antagonist
- 4. Ketamine is comparable with amantadine and memantine, which are used as 2nd / 3rd line therapy in catatonia.

#### cons:

- 1. Ketamine acts non-depressively on the cardio-vascular systemie (like e.g. barbiturates)
- 2. Ketamine dose-dependently induces psychiatric side-effects (basically derealisation and depersonalisation, which can lead to anxiety)

#### dose-effect relation





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

Glue et al., Biol Psychiatry, 2011

#### problem:

too much ketamine: longer recovery-room time

- too less ketamine: post ictal agitation, psychomimetic side effects

Other problems:

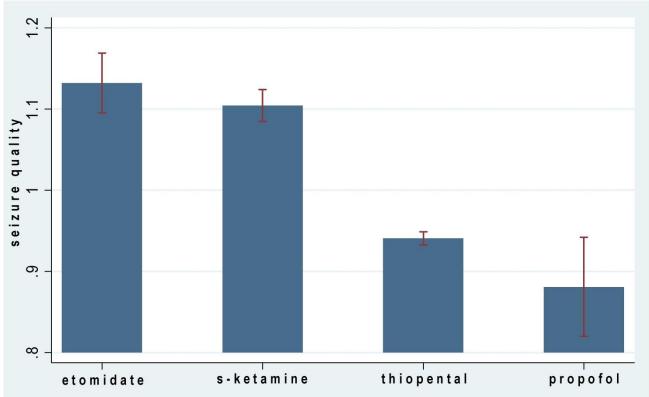
The use of ketamine in ECT anaesthesia:

A systematic review and critical commentary on efficacy, cognitive, safety and seizure outcomes.

Gálvez V, McGuirk L, Loo CK.

World J Biol Psychiatry. 2016 Nov 28:1-21.





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 2013

#### Propofol:



# Anesthetic of choice for short anesthesia! But it is an extremely potent anticonvulsant:

A Bayesian framework systematic review and meta-analysis of anesthetic agents effectiveness/tolerability profile in electroconvulsive therapy for major depression. Fond et al., Sci Rep. 2016

The aim of this study was to assess the efficacy and tolerability/acceptability of 6 anesthetic agents in ECT for depressive disorders. We systematically reviewed 14 double-blind randomized controlled trials (610 participants). Efficacy was measured by the mean scores on validated depression scales at 6 ECT (or the nearest score if not available), number of responders at the end of treatment and seizure duration. The acceptability was measured by the proportion of patients who dropped out of the allocated treatment, and the tolerability by the number of serious adverse events and post-treatment cognition assessment.

After excluding the trials responsible for heterogeneity, depression scores of patients who were administered methohexital were found to be significantly more improved than those who received propofol (p = 0.001). On the contrary, those who were administered propofol had lower depression scores than those with thiopental at the end of treatment (p = 0.002). Compared to propofol, methohexital was found to be significantly associated with higher seizure duration (p = 0.018). No difference was found for the acceptability profile (all p > 0.05). In summary, ketamine and methohexital may be preferred to propofol or thiopental in regard of effectiveness in depression scores and increased seizure duration. Further studies are warranted to compare ketamine and methohexital.

But: low number of included studies, problems with hetereogeneity, overall no impressive differences

#### combined anesthesia:

200

- S- ketamine plus remifentanil
- S- ketamine plus dexmedetomidine

opioid, syringe pump syringe pump

# **Dexmedetomidine studies:**



comparator	results	study type	published
propofol versus propofol + dexmedetomidine	seizure length and recovery time better for	retrospective	J ECT 2013
propofol + dexmedetomidine versus midazolam	less PIA and less propofol	RCT	J Anesth 2009
propofol + dexmedetomidine versus saline	less acute hyperdynamic response RCT A		Acta An Scand 2008
	prevents PIA	3 case reports	J ECT 2x 2013, 2010

#### Dexmedetomidine + S-Ketamine, own data...:



#### n=178 ECTs

Table 3: Multivariate repeated measurement logistic regression analysis for prediction of PIA-occurrence

	OR	Standard error	z	p>  z	[95% CI]
Dexmedetomidine use	0.059	0.049	-3.38	0.001	0.011-0.303
Unilateral	0.587	0.648	-0.48	0.630	0.067-5.114
S-ketamine dose	0.070	0.093	-2.01	0.045	0.005-0.937
Stimulation dose	1.010	0.008	1.21	0.226	0.993-1.027

PIA: postictal agitation syndrome, Unilateral: right unilateral electrode placement, OR: odds ratio, CI: confidence interval Number of observations: 176, number of groups: 7.

Dexmedetomidine for the management of postictal agitation after electroconvulsive therapy with S-ketamine anesthesia.

Aksay SS, Bumb JM, Remennik D, Thiel M, Kranaster L, Sartorius A, Janke C.

Neuropsychiatr Dis Treat. 2017 May 23;13:1389-1394.

#### combined anesthesia:

200

- S- ketamine plus remifentanil
- S- ketamine plus dexmedetomidine

opioid, syringe pump syringe pump

- S- ketamine plus propofol

#### combined anesthesia:



- ketamine plus propofol = ketofol:

But keep in mind:

- Ketofol is not i.v. ketamine and then add i.v. propofol !!!



You can apply either a mixture OR propofol and then ketamine

Create RSS Create alert Advanced

Format: Summary - Sort by: Most Recent - Per page: 20 -

Send to \*

#### Search results

Items: 6

The safety and efficacy of adjunctive ketamine in **electroconvulsive** therapy: Response to Drs.

Fond and Boyer.

McGirr A.

J Psychiatr Res. 2015 Sep;68:283-4. doi: 10.1016/j.jpsychires.2015.06.022. Epub 2015 Jul 3. No abstract available. PMID: 26163193

Similar articles

A systematic review and meta-analysis of randomized controlled trials of adjunctive ketamine in

2. electroconvulsive therapy: efficacy and tolerability.

McGirr A, Berlim MT, Bond DJ, Neufeld NH, Chan PY, Yatham LN, Lam RW. J Psychiatr Res. 2015 Mar;62:23-30. doi: 10.1016/j.jpsychires.2015.01.003. Epub 2015 Jan 26. Review. Erratum in: J Psychiatr Res. 2015 Sep;68:74-5.

PMID: 25684151 Similar articles

Ketofol-Dexmedetomidine combination in ECT: A punch for depression and agitation.

Shams T, El-Masry R.

Indian J Anaesth. 2014 May;58(3):275-80. doi: 10.4103/0019-5049.135037.

PMID: 25024469 Free PMC Article

Similar articles

Is ketamine-propofol mixture (ketofol) an appropriate alternative induction agent for

electroconvulsive therapy?

Firouzian A, Tabassomi F.

Saudi J Anaesth. 2013 Oct;7(4):476-7. doi: 10.4103/1658-354X.121053. No abstract available.

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Similar articles

Ketofol in electroconvulsive therapy anesthesia: two stones for one bird.

 Yalcin S, Aydoğan H, Selek S, Kucuk A, Yuce HH, Karababa F, Bilgiç T. J Anesth. 2012 Aug;26(4):562-7. doi: 10.1007/s00540-012-1378-6. Epub 2012 May 24.

PMID: 22623080

Similar articles

Ketofol (mixture of ketamine and propofol) administration in electroconvulsive therapy.

 Erdogan Kayhan G, Yucel A, Colak YZ, Ozgul U, Yologlu S, Karlidag R, Ersoy MO. Anaesth Intensive Care. 2012 Mar;40(2):305-10.

PMID: 22417026 Free Article

Similar articles



# Anesthesia beyond the usual suspects:



#### - Ketofol

Ketofol in electroconvulsive therapy anesthesia: two stones for one bird. Yalcin S, Aydoğan H, Selek S, Kucuk A, Yuce HH, Karababa F, Bilgiç T. J Anesth. 2012 Aug;26(4):562-7. doi: 10.1007/s00540-012-1378-6. Epub 2012 May 24.

Table 1 Seizure duration and recovery times of patients

Incident	Propofol group $(n = 30)$	Ketamine group $(n = 30)$	Ketofol group $(n = 30)$	p (ANOVA)
Motor seizure (s)	$29.3 \pm 5.1$	$37.2 \pm 3.2*$	$34 \pm 5.8*$	< 0.001
Spontaneous breathing (s)	$252 \pm 13.1$	$266.6 \pm 11.5*$	$260.7 \pm 8.3$	0.001
Open eyes (s)	$413.1 \pm 19.8$	$538.8 \pm 43.2^{*,+}$	$436.2 \pm 32.1$	< 0.001, < 0.001
Obey commands (s)	$514.3 \pm 38.7$	$576.5 \pm 37.6^{*,+}$	$519.9 \pm 31.1$	<0.001, <0.001

<sup>\*</sup> p < 0.001 (post hoc Bonferroni) compared with group propofol

 $<sup>^{+}</sup>$  p < 0.001 (post hoc Bonferroni) compared with group ketofol

Acta Neuropsychiatr. 2017 May 2:1-9.

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:**

<u>Etomidate or a 1:1 ketamine and propofol combination may be the best method to achieve</u> <u>general anaesthesia in the ECT setting.</u> 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

#### Own experiences with ketofol:



- anesthesiologists are excited
- less time in recovery room
- less side effects regarding post ictal agitation and psychomimetic problems
- propofol is still critical regarding seizure threshold/induction

#### Own experiences with ketofol:



Data\* on mixture (propofol/S-ketamine):

	mean	min max
- propofol	53 mg	20 mg 130 mg
- S-ketamine	62 mg	20 mg 100 mg
- Ratio of propofol/S-ketamine	0.87	0.4 2.5

Thus a ratio of ~1:1 propofol/S-ketamine was clinically sufficient,

Which corresponds to 1:2 propofol/ketamine

<sup>\*</sup> Retrospective data from the first 30 patients and ca. 500 ECT sessions

1. Lighter anesthesia is more effective (not so with ketamine and etomidate)



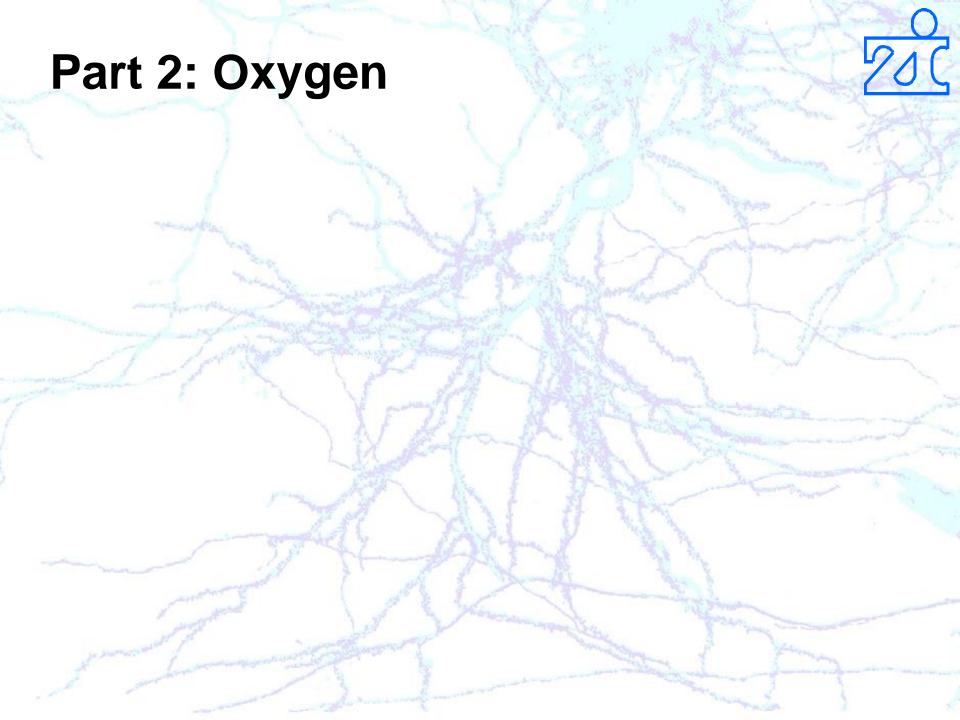
2. PIA risk increases with lighter anesthesia!

(up to 50% with unmodified ECT (Andrade et al., Indian J Psychiatry. 2012))

=> Not less anesthetic, but more time!

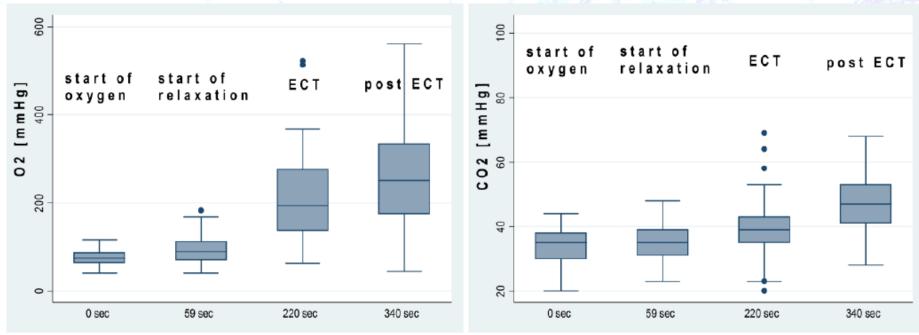
The Anaesthetic-ECT Time Interval in Electroconvulsive Therapy Practice--Is It Time to Time? Gálvez V, Hadzi-Pavlovic D, Wark H, Harper S, Leyden J, Loo CK. Brain Stimul. 2016 Jan-Feb;9(1):72-7.

- 3. PIA risk decreases with post ECT dexmedetomidine treatment
- 4. Ketofol decreases PIA risk and it might be anyway a good choice



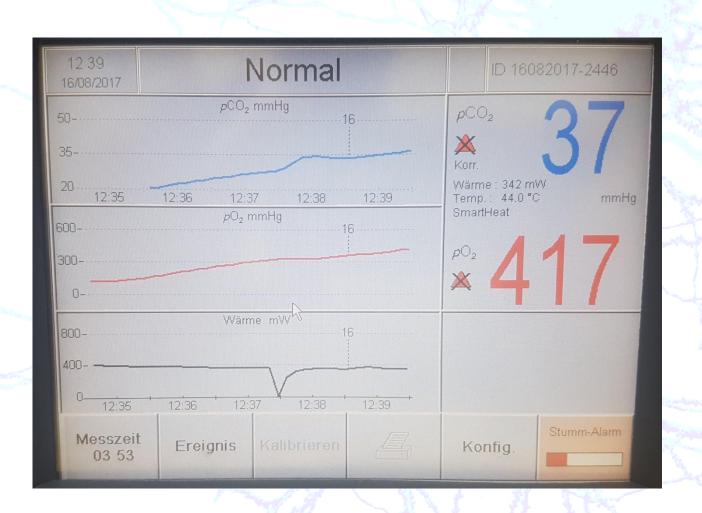
#### Capnometria:





**Figure 2:** Mean time course of transcutaneously measured pCO<sub>2</sub> and pO<sub>2</sub> 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.







**TABLE 4.** Stimulation "Energy" (%; 100% = 504 mC Charge) and Ideal Seizure Sum Score (Range 0–5) Depending on the Utmost and Lowest Quartile of Partial Pressures of Oxygen and Carbon Dioxide

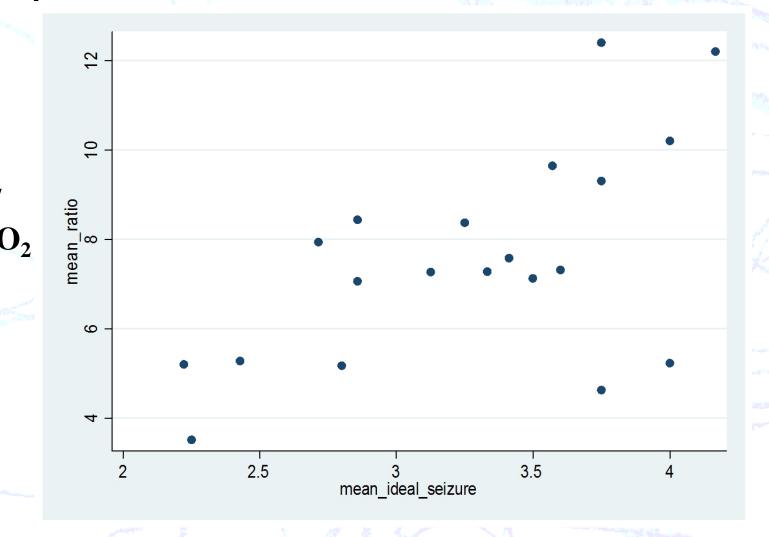
	Lowest Quartile of tcpO <sub>2</sub> (<199 mm Hg)		Utmost Quartile of tcpO2 (>357 mm Hg)	
	Energy	Seizure Quality	Energy	Seizure Quality
Lowest quartile of tcpCO <sub>2</sub> (<36 mm Hg)	63 ± 5	$3.41 \pm 0.17$	52 ± 11	$3.60 \pm 0.24$
Utmost quartile of tcpCO <sub>2</sub> (>45 mm Hg)	$72 \pm 4$	$3.16\pm0.28$	59 ± 9	$3.39 \pm 0.12$

Errors indicated are standard error of the mean.

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.

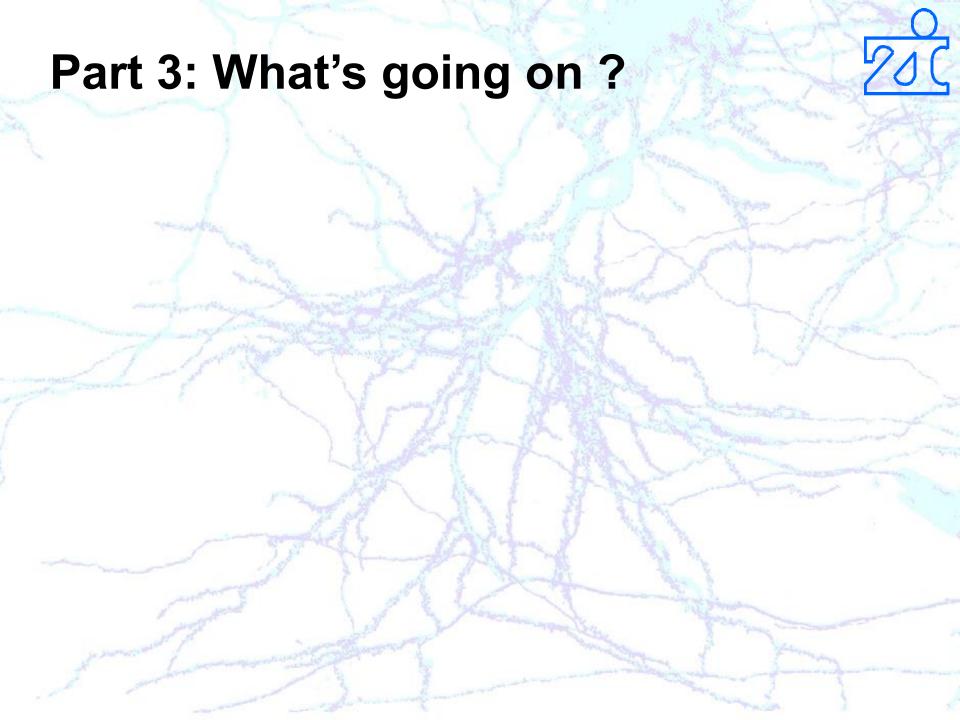
# Capnometria:





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

Sartorius A. J ECT. 2014 Mar 12.









# **Shivering**





## **Another shivering**





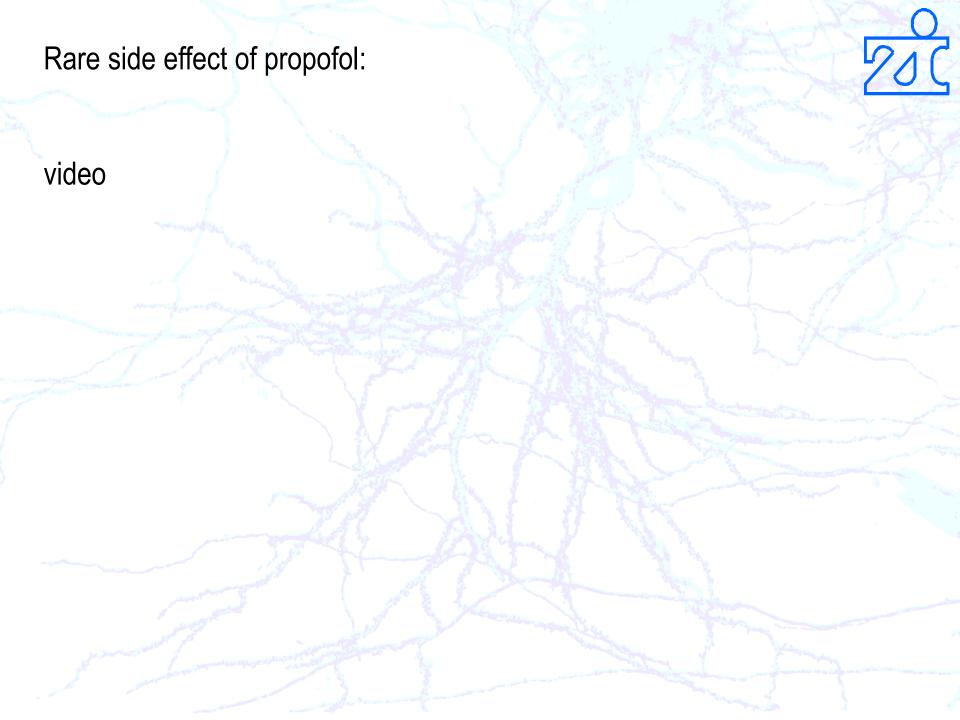
# Postanesthetic shivering (PAS) is shivering after anesthesia



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:

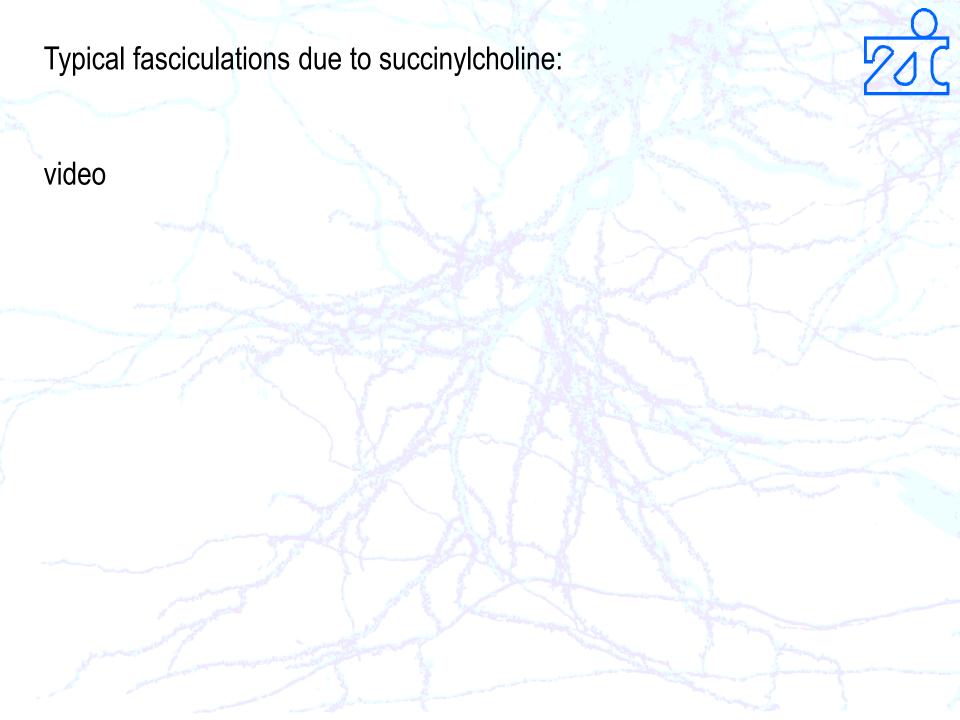
- 0 = no shivering;
- 1 = no visible muscle activity but piloerection, peripheral vasoconstriction, or both;
- 2 = muscular activity in only one muscle group;
- 3 = moderate muscular activity in more than one muscle group but no generalized shaking;
- 4 = violent muscular activity that involves the whole body.

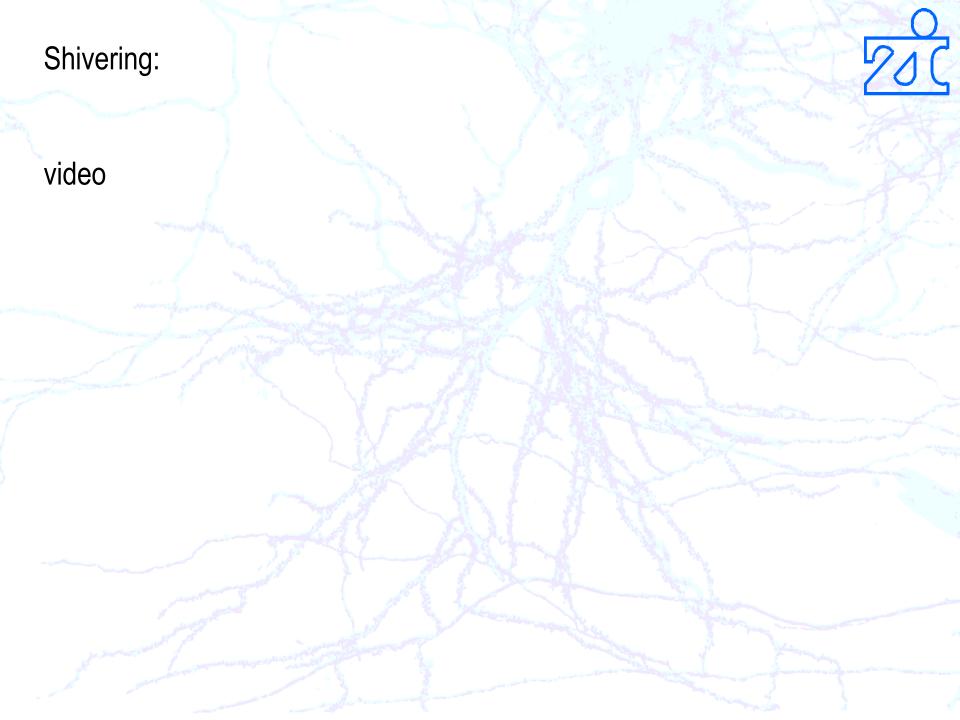


Very different from myocloni frequently seen with etomidate and sometimes even with S-ketamine:



video





### **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.

Snooring









Geriatric ECT at 160% RUL. Concordance 0.72. PSI 47% (artifact). Coherence 71%, max. heart rate 90 bpm. Midictal amplitude 63uV.

## Post stimulus asystole





Geriatric ECT at 160% RUL. Concordance 0.72. PSI 47% (artifact). Coherence 71%, max. heart rate 90 bpm. Midictal amplitude 63uV.



video

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



#### REVIEW ARTICLE

#### **CURRENT CONCEPTS**

# Medical Evaluation of Patients Undergoing Electroconvulsive Therapy

Anjala V. Tess, M.D., and Gerald W. Smetana, M.D.

## Risk factors for post-stimulus asystole

- 1. age
- 2. BIL
- 3. subconvulsive stimuli (especially together with beta-antagonists)

## Die Position der Stimulationselektroden und die Herzfrequenz bei Elektrokrampftherapie



Placement of Stimulus Electrodes and Heart Rate during Electroconvulsive Therapy

Autor

J. Nagler

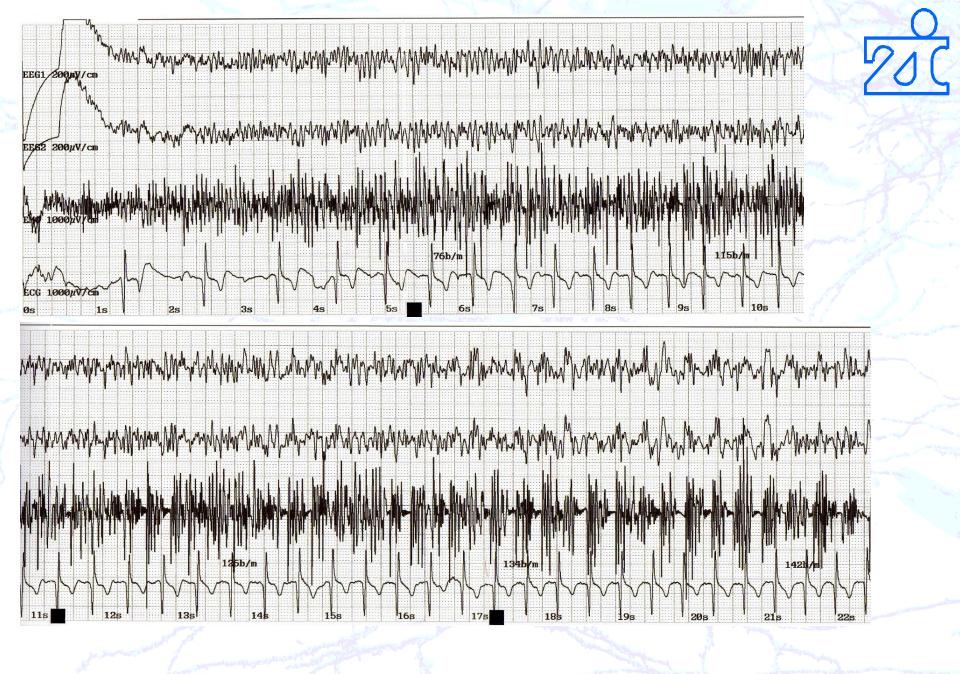
Institut

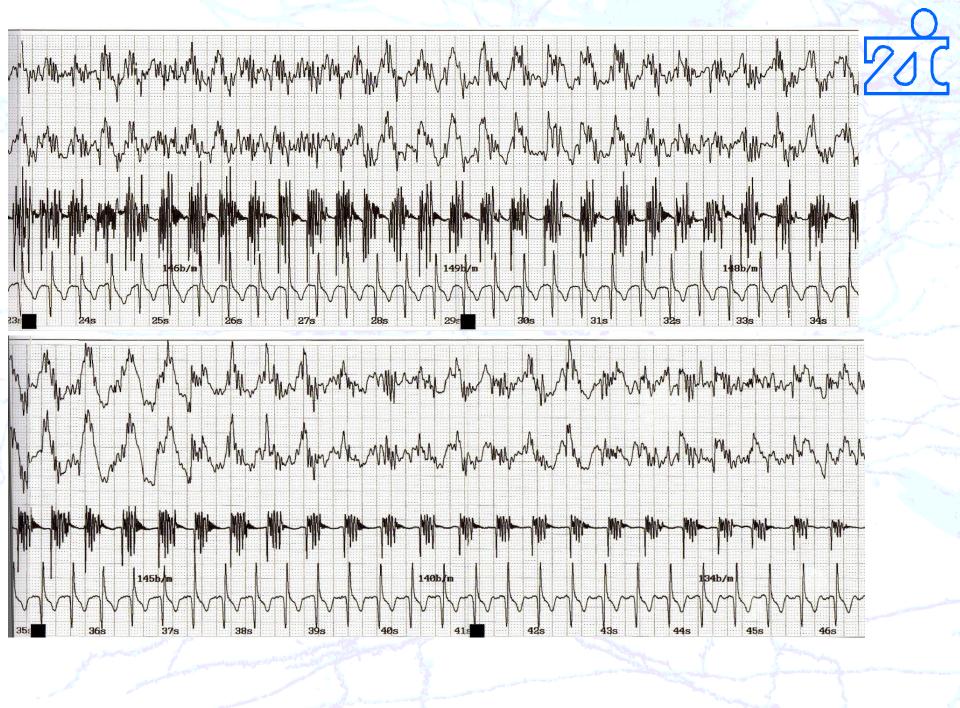
Klinikum Schloß Winnenden (Ärztlicher Direktor Dr. G. Hetzel)

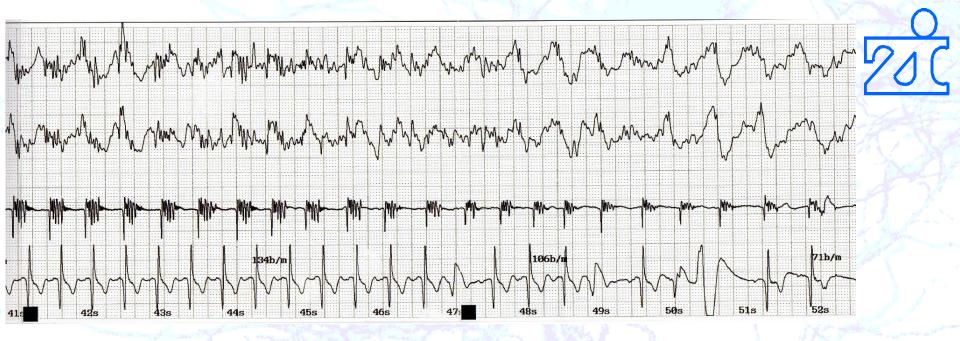
# Incidence of post-stimulus asystole

- **> 50%** !!!
- conclusion:

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







quetiapine 0-0-0-300 mg venlafaxin 75-0-0-0 mg

donepezil 0-0-0-5 mg

torasemid 5-0-0-0 mg

L-thyroxin 25-0-0-0 µg

aspirin 0-0-100 mg

pantoprazol 0-0-40-0 mg



Kranaster L, Janke C, Hausner L, Frölich L, Sartorius A. Venlafaxin-associated post-ictal asystole during electroconvulsive therapy. Pharmacopsychiatry. 2012 May;45(3):122-4.

### **Conclusion:**

20

Caution!

Noradrenergic drugs can massively increase blood pressure and are proarrhythmogenic!

Arch Gen Psychiatry. 2009 Jul;66(7):729-37

Effect of concomitant pharmacotherapy on electroconvulsive therapy outcomes: short-term efficacy and adverse effects. Sackeim HA, et al.



#### **Abstract**

**CONTEXT:** Medication resistance is the leading indication for use of electroconvulsive therapy (ECT) in major depression. The practice of stopping antidepressant medications prior to ECT derived from studies in the 1960s and 1970s in nonresistant samples. There is also continuing controversy regarding the relative efficacy and adverse effects of right unilateral and bilateral ECT.

**OBJECTIVE:** To test the hypotheses that, compared with placebo, concomitant treatment with nortriptline or venlafaxine during the ECT course enhances short-term efficacy without a meaningful effect on adverse effects and reduces the rate of post-ECT relapse, and to test the hypotheses that high-dose, right-sided, unilateral ECT is equivalent in efficacy to moderate-dosage bilateral ECT and retains advantages with respect to cognitive adverse effects.

**DESIGN:** Prospective, randomized, triple-masked, placebo-controlled study conducted from 2001 through 2005.

**SETTING:** Three university-based hospitals.

**PATIENTS:** Of approximately 750 consecutive patients referred for ECT, 319 with a major depressive episode consented, were randomized to pharmacological or ECT treatment conditions, and received at least 1 ECT treatment.

**MAIN OUTCOME MEASURES:** Scores on the Hamilton Rating Scale for Depression, remission rate following completion of ECT, and selective measures of cognitive adverse effects.

**RESULTS:** Treatment with nortriptyline enhanced the efficacy and reduced the cognitive adverse effects of ECT relative to placebo. Venlafaxine resulted in a weaker degree of improvement and tended to worsen cognitive adverse effects. High-dosage right unilateral ECT did not differ or was superior to bilateral ECT in efficacy and resulted in less severe amnesia.

**CONCLUSIONS:** The efficacy of ECT is substantially increased by the addition of an antidepressant medication, but such medications may differ in whether they reduce or increase cognitive adverse effects. High-dose, right-sided, unilateral ECT is at least equivalent to moderate-dosage bilateral ECT in efficacy, but retains advantages with respect to cognitive adverse effects.

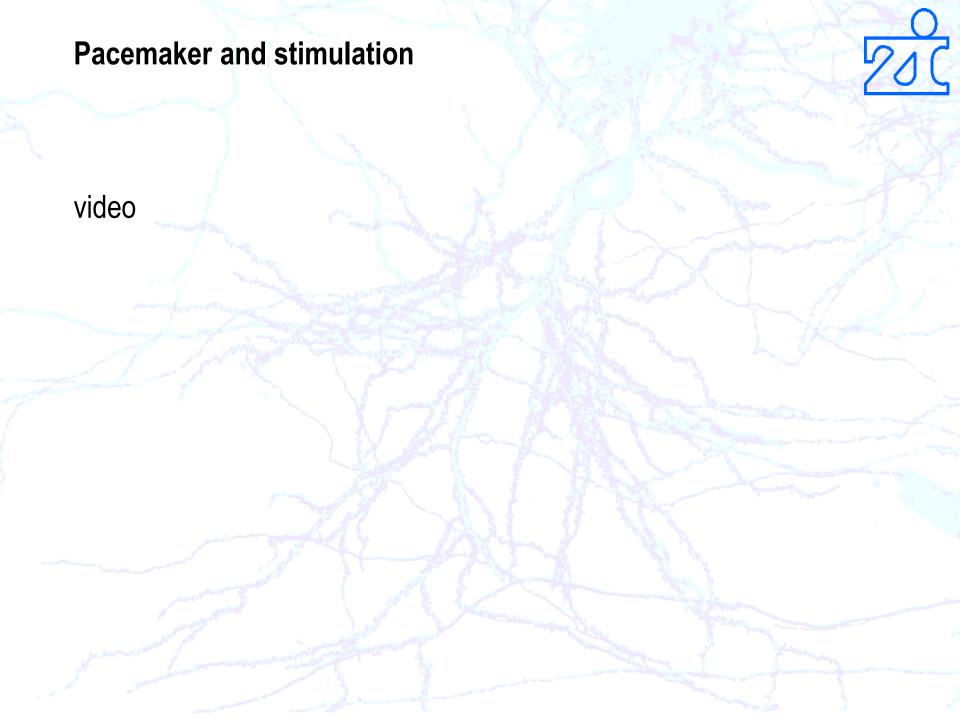


### **Pacemaker**



- ECT is per se proarrythmogenic (thus pacemaker is good)
- ICDs might be problematic due to theoretical dysfunction (i.e. stimulation) during the seizure





### to conclude:



- shivering / myocloni / fasciculations / restless legs can happen

- ECT proarrhythmogenic
- post stimulus asystolia is frequent and physiologic
- post ictal asystolia is rare and potentially problematic
- pacemaker / ICDs are non-problematic



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