# Clinical and biological effects of different stimulation techniques


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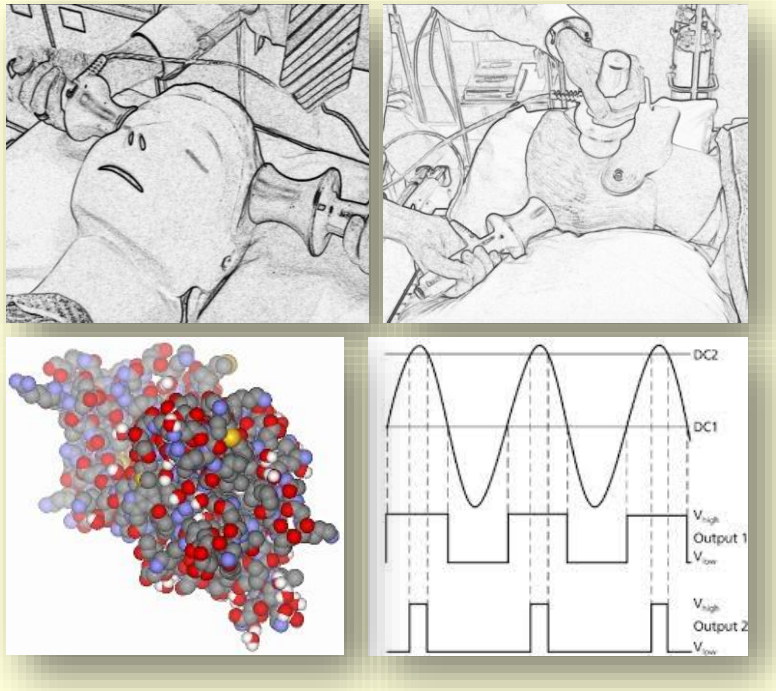



**May 23, 2014**
**NACT: ECT – optimizing treatment and preventing relapse**


**Disclosures: funded by the Health Research Board, Ireland**


St Patrick's Mental Health Services
Empowering recovery

TRINITY COLLEGE
Institute of Neuroscience
from molecules to mind

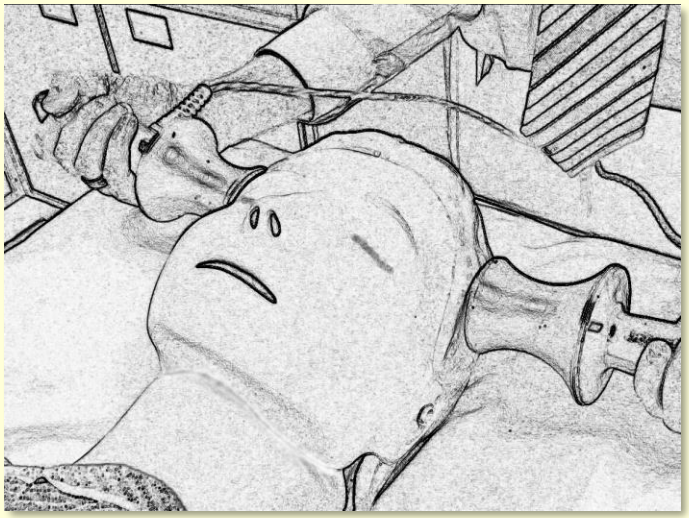
HRB
Health Research Board

1. Electrode placement
2. Pulse width
3. Preventing relapse
4. The EFFECT-Dep Trial

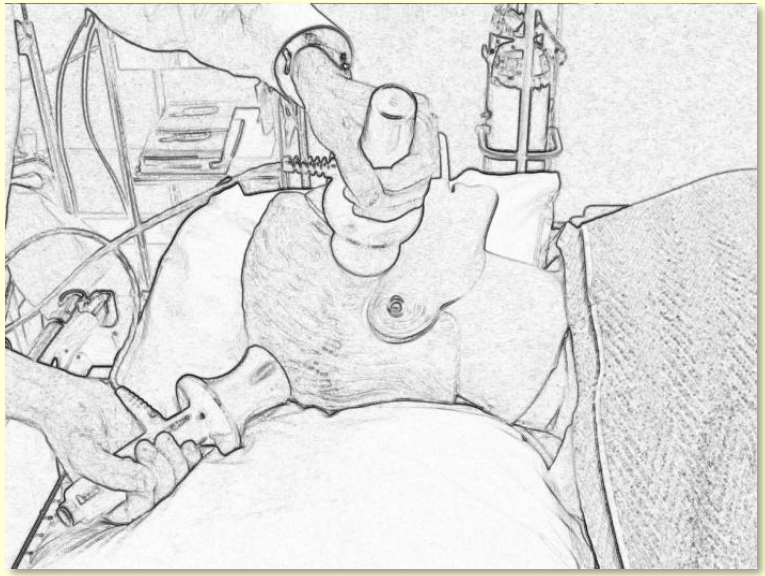
(Electrode placement revisited)

# 1. Electrode placement

- Laterality
- Waveform
- Pulse width
- Stimulus intensity



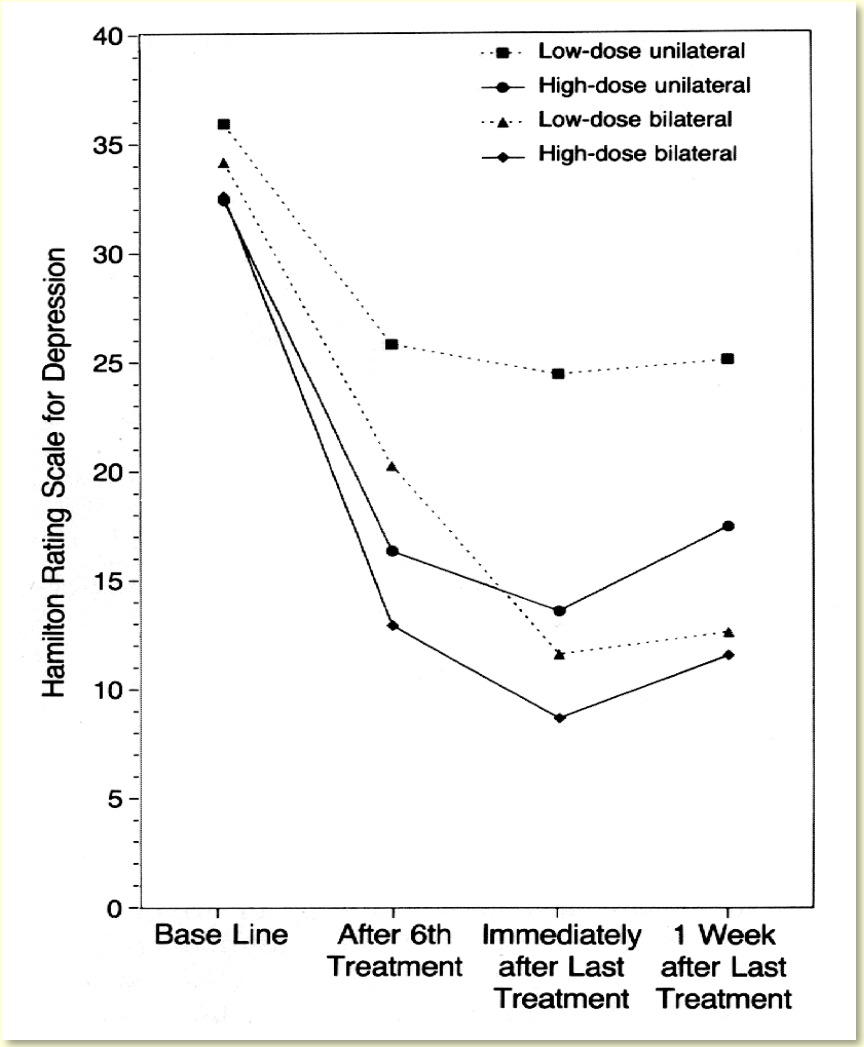
Bitemporal



Right unilateral

Bifrontal

# Not all forms of ECT are equal!!




Sackeim HA et al, *NEJM* 1993

**Effects of Stimulus Intensity and Electrode Placement on the Efficacy and Cognitive Effects of Electroconvulsive Therapy**

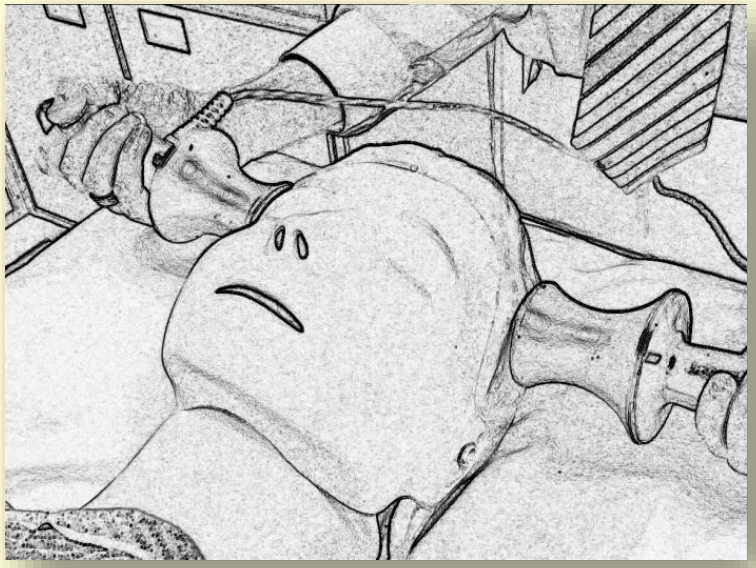
***Conclusions***

**Increasing the electrical dosage increases the efficacy of right unilateral electroconvulsive therapy, although not to the level of bilateral therapy.**

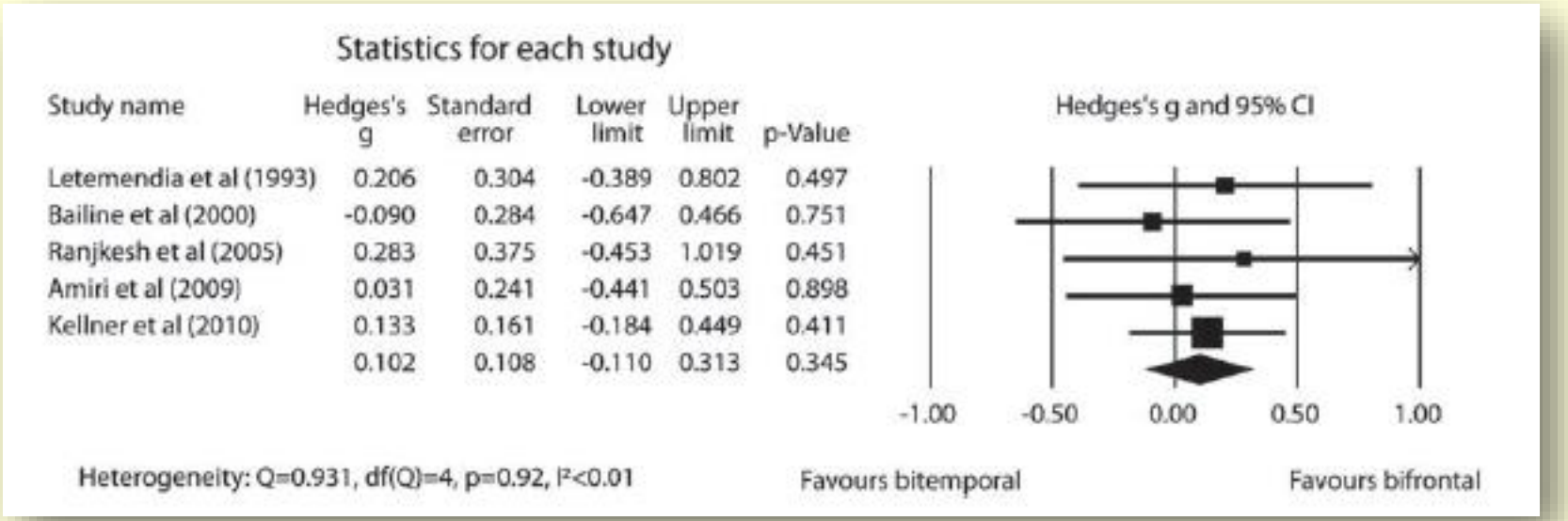
**High electrical dosage is associated with a more rapid response, and unilateral treatment is associated with less severe cognitive side effects after treatment.**

# Systematic review and meta-analysis of bifrontal ECT versus bitemporal and unilateral ECT for depression

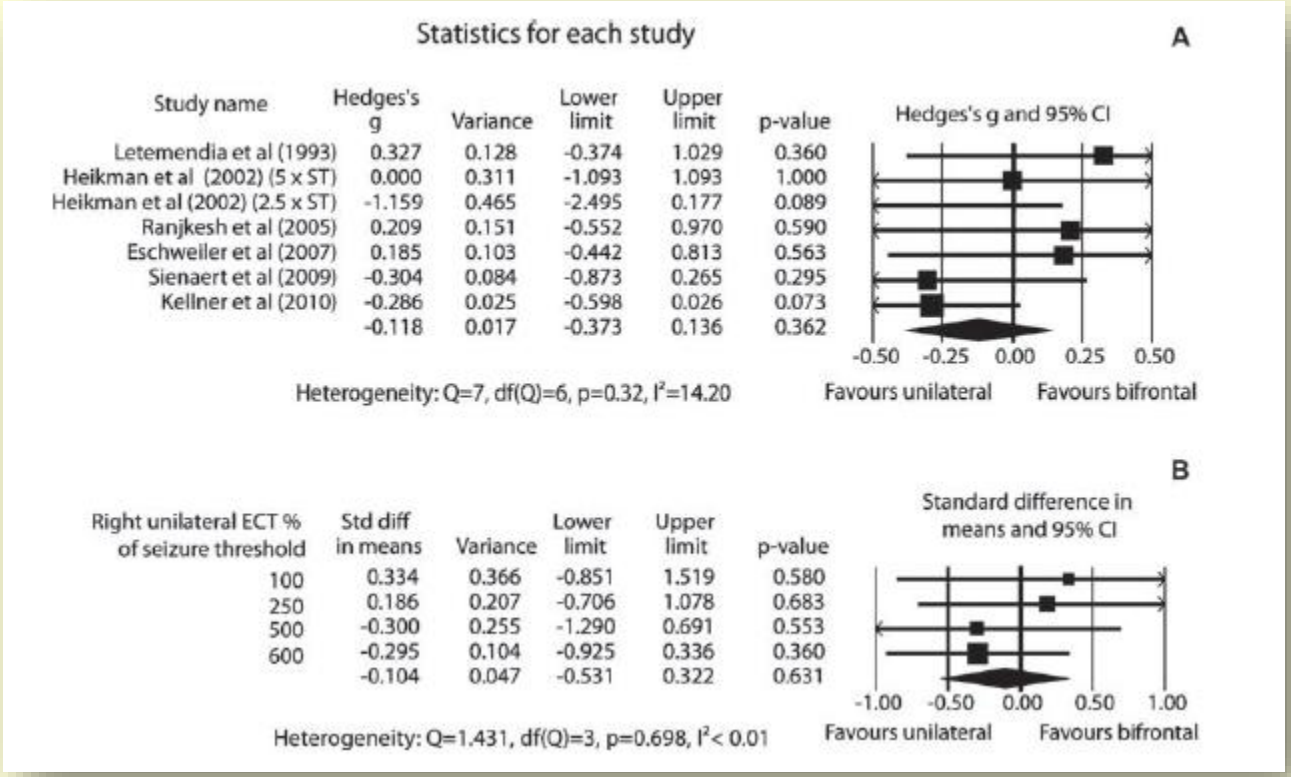
**vs**



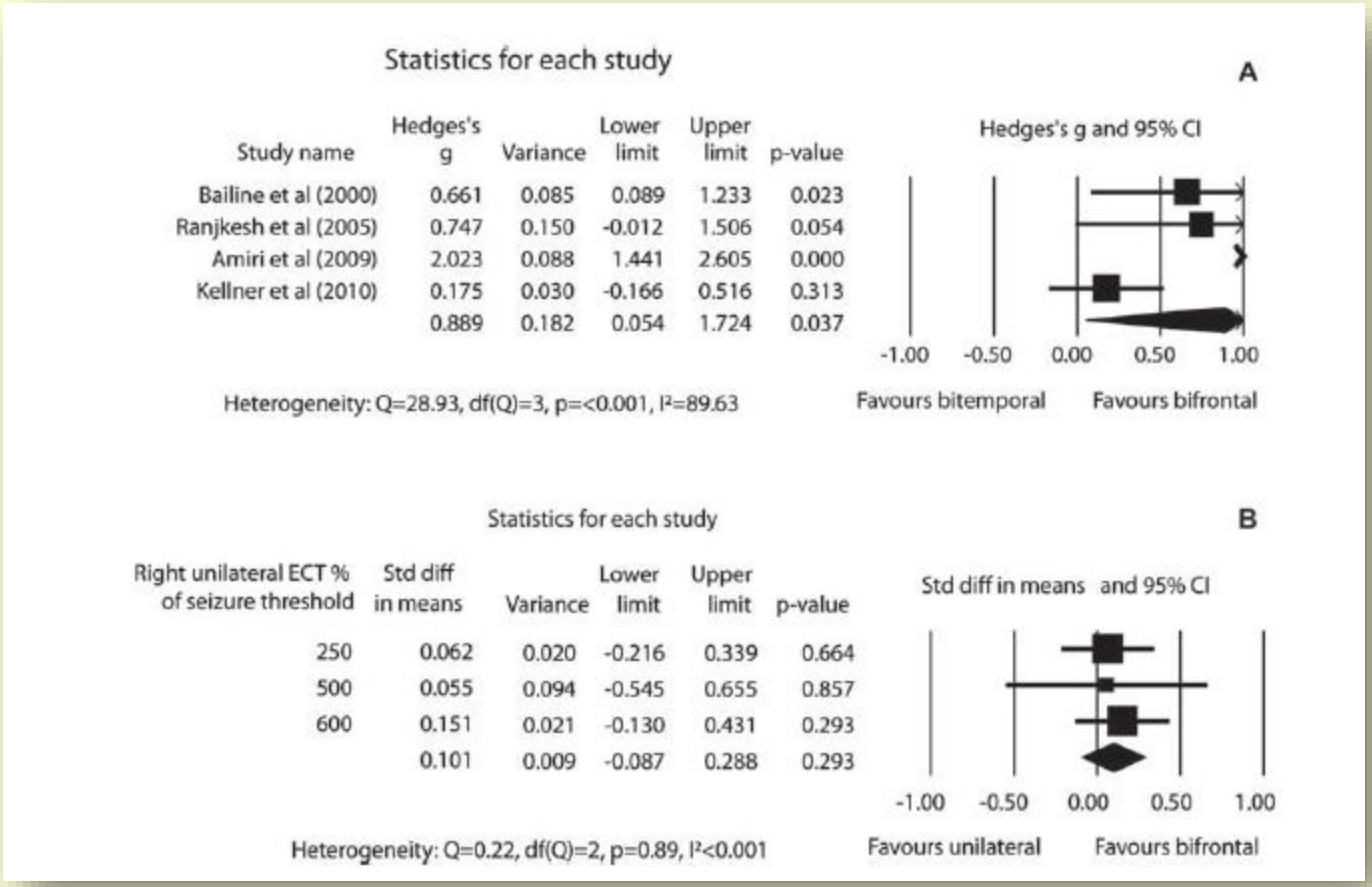
**Dunne & McLoughlin (2012)** ***World J Biol Psychiatry***




# BT vs BF ECT: no significant difference in depression rating (HDRS)




# RUL vs BF ECT: no significant difference in depression rating (HDRS)




**Global cognition (MMSE): slight advantage for BF over BT ECT but not over RUL ECT.**

Table II. Results of synthesis of cognitive testing.

| | Study | Hedges' *g* | SE | *P* value | $I^2$ (*P* value) |
|---|---|---|---|---|---|
| RAVLT 1–5 | Kellner et al. (2010) | –0.94 | 0.19 | <0.01 | |
| | Sienaert et al. (2010) | 0.16 | 0.25 | 0.52 | |
| | Pooled | –0.405 | 0.553 | 0.464 | 92 (*P*<0.001) |
| RAVLT 7 | Kellner et al. (2010) | –0.807 | 0.189 | <0.01 | |
| | Sienaert et al. (2010) | –2.14 | 0.31 | <0.01 | |
| | Pooled | –1.45 | 0.665 | 0.029 | 93.1 (*P*<0.001) |
| TMT–A | Kellner et al. (2010) | 1.77 | 0.21 | <0.01 | |
| | Sienaert et al. (2010) | –12.28 | 1.11 | <0.01 | |
| | Pooled | –5.5 | 6.74 | 0.46 | 99.35 (*P*<0.001) |
| TMT–B | Kellner et al. (2010) | –0.477 | 0.184 | 0.01 | |
| | Sienaert et al. (2010) | 123.7 | 10.94 | <0.01 | |
| | Pooled | 61.13 | 62.1 | 0.325 | 99.2 (*P*<0.001) |
| Complex figure (delayed) | Echweiler et al. (2007) | 0.82 | 0.22 | <0.01 | |
| | Kellner et al. (2010) | 0.72 | 0.18 | <0.01 | |
| | Pooled | 0.76 | 0.177 | 0.01 | <0.01 (*P*=0.124) |
| Verbal fluency (letters) | Echweiler et al. (2007) | 0.246 | 0.208 | 0.235 | |
| | Kellner et al. (2010) | –0.007 | 0.176 | 0.966 | |
| | Pooled | 0.099 | 0.135 | 0.462 | <0.01 (*P*=0.35) |

Positive values of Hedges's *g* demonstrate better cognition after bifrontal than unilateral ECT compared to pre-ECT assessment; a negative value demonstrates a worse performance for bifrontal relative to unilateral ECT. RAVLT, Rey auditory verbal learning test (first part: 1–5; second part: 7); TMT, Trail-making tests A or B; SE, standard error of Hedges's *g*.

**Delayed verbal recall; advantage to RUL**

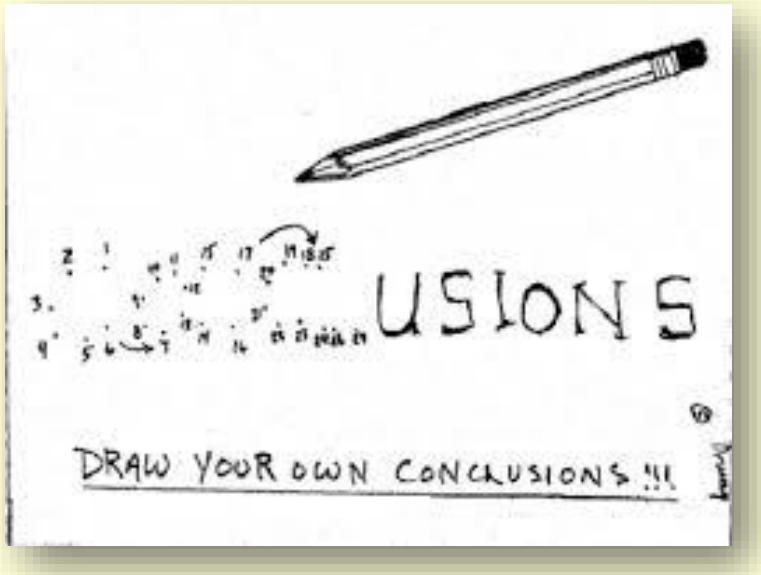
**Delayed visual recall; advantage to BT**

# Cognition: insufficient data to recommend BT ECT.

# Conclusion #1

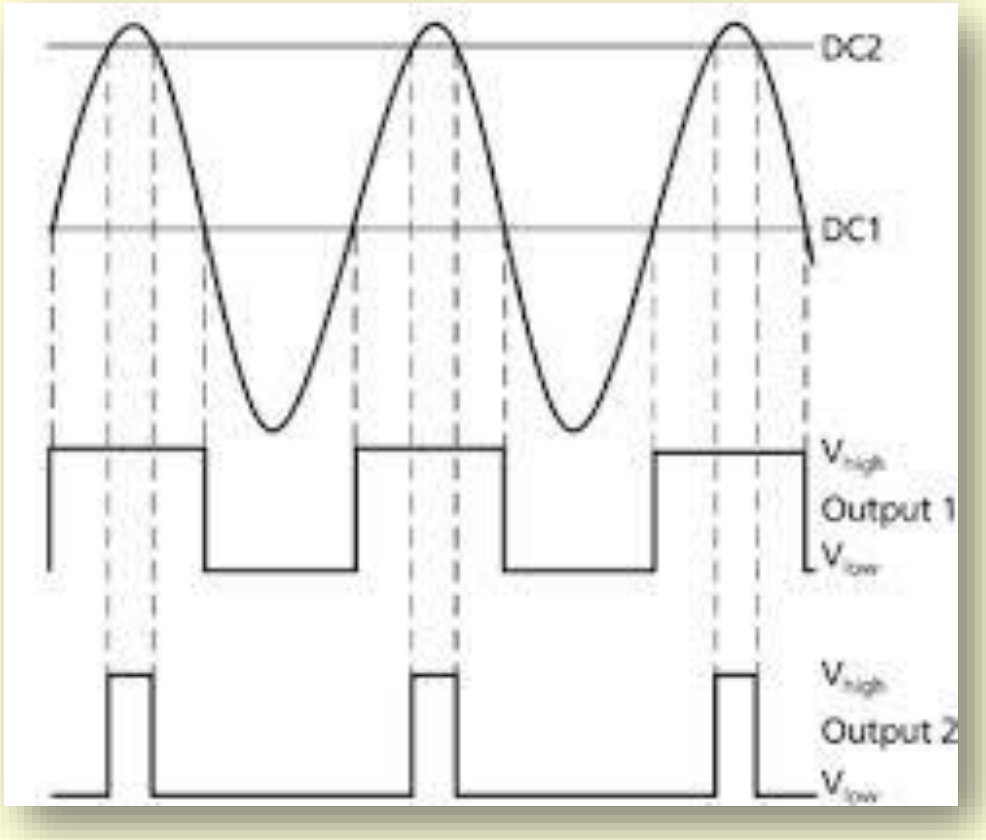
**There appears to be no particular major advantage to Bifrontal ECT compared to Bitemporal or high-dose RUL ECT.**

**Maybe less cardiac effects?**



# 2. Ultrabrief pulse ECT

- Shortening pulse widths
- Ultrabrief : <0.5ms
- Increasingly used
  - 26% of Dutch clinics in 2009
- Efficacy unclear



Contents lists available at ScienceDirect

Journal of Affective Disorders

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

Review

# Efficacy of ultrabrief pulse electroconvulsive therapy for depression: A systematic review

Harm-Pieter Spaans [a,*], King H. Kho [a], Esmée Verwijk [a], Rob M. Kok [a], Max L. Stek [b]

[a] Parnassia Psychiatric Institute, The Hague, The Netherlands
[b] GGZinGeest/VUmc, Amsterdam, The Netherlands

*Conclusion:* The literature shows no clear advantage for the efficacy of ultrabrief pulse over brief pulse ECT using unilateral as well as bilateral electrode placement. The increasing use of unilateral brief pulse ECT as first line method for depression is not supported by the current evidence.

**Few RCTs**
**Heterogeneity ++**
**Very variable outcomes; 6-77% remission rates in RCTs!**

J Clin Psychiatry. 2013 Nov;74(11):e1029-36. doi: 10.4088/JCP.13m08538.

**Efficacy and cognitive side effects after brief pulse and ultrabrief pulse right unilateral electroconvulsive therapy for major depression: a randomized, double-blind, controlled study.**

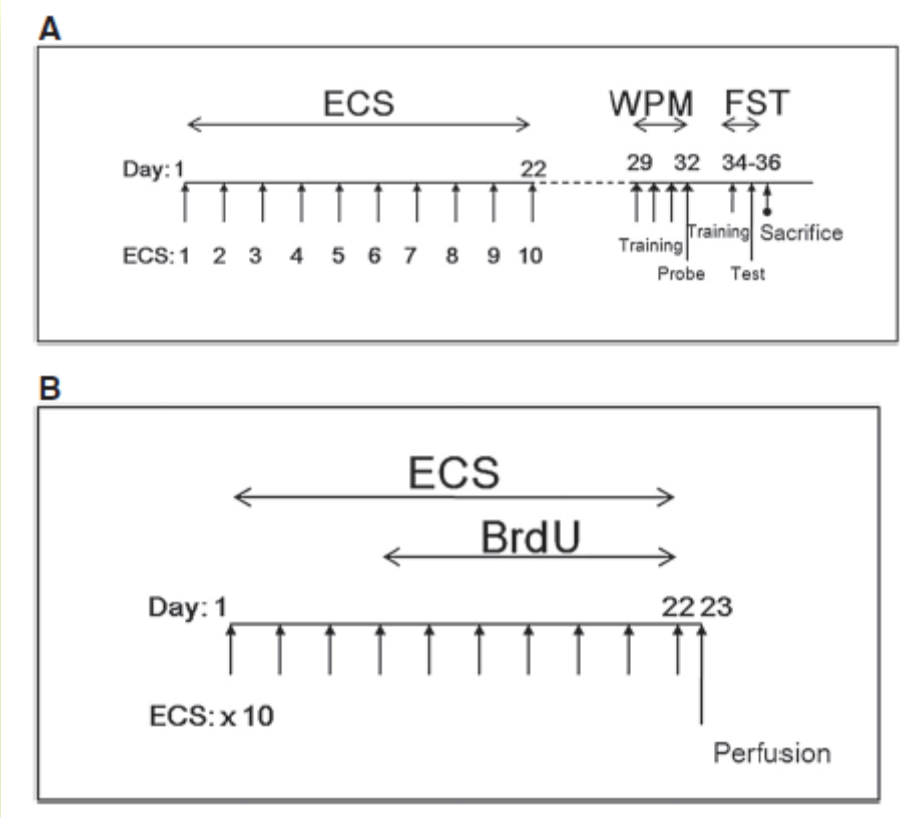
Spaans HP[1], Verwijk E, Comijs HC, Kok RM, Sienaert P, Bouckaert F, Fannes K, Vandepoel K, Scherder EJ, Stek ML, Kho KH.

# 8 x ST in both groups; high drop-out in BP group

**RESULTS:**

- ITT remission rates: BP 50% (29/58) vs UBP 41.4% (24/58) (P = .039)
- Completer remission rates: BP 68.4% (26/38) vs UBP 49.0% (24/49) (P = .019)
- Fewer treatment sessions to achieve remission: 7.1 (2.6) vs 9.2 (2.3) (P = .008).
- No significant group differences for cognitive assessments (retrograde amnesia, semantic memory, and lexical memory)

# ECS Study #1: Sham vs Brief-pulse vs Ultrabrief-pulse

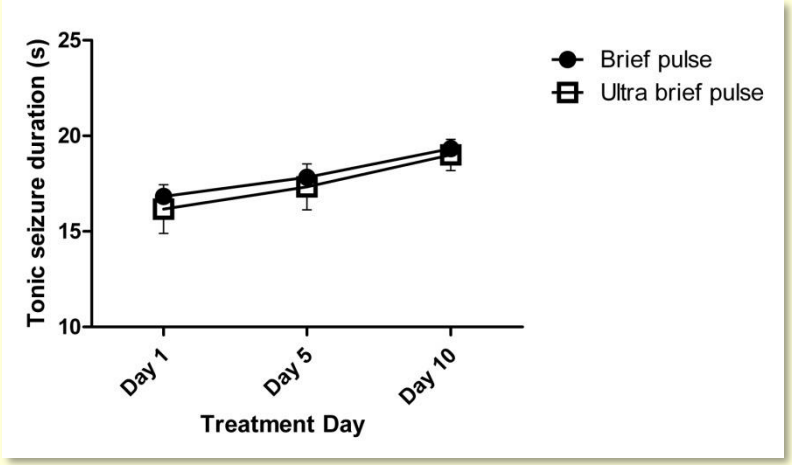


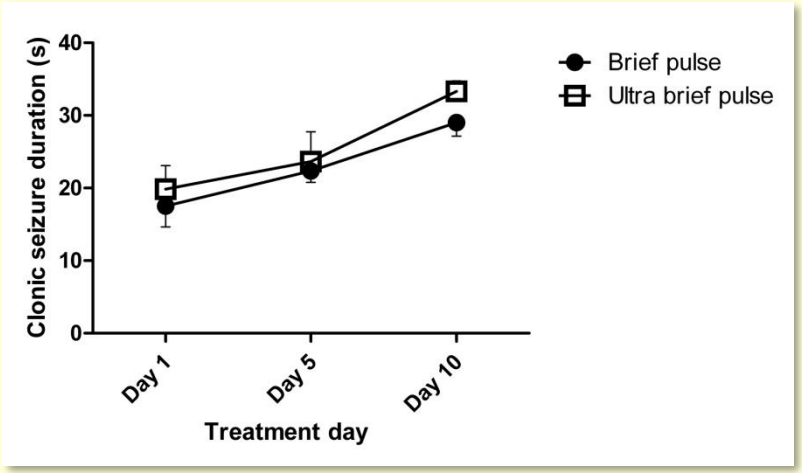

A comparison of brief pulse and ultrabrief pulse electroconvulsive stimulation on rodent brain and behaviour

Sinead O'Donovan [a,b], Mark Kennedy [a], Blaithin Guinan [a], Shane O'Mara [a], Declan M. McLoughlin [a,b,*]

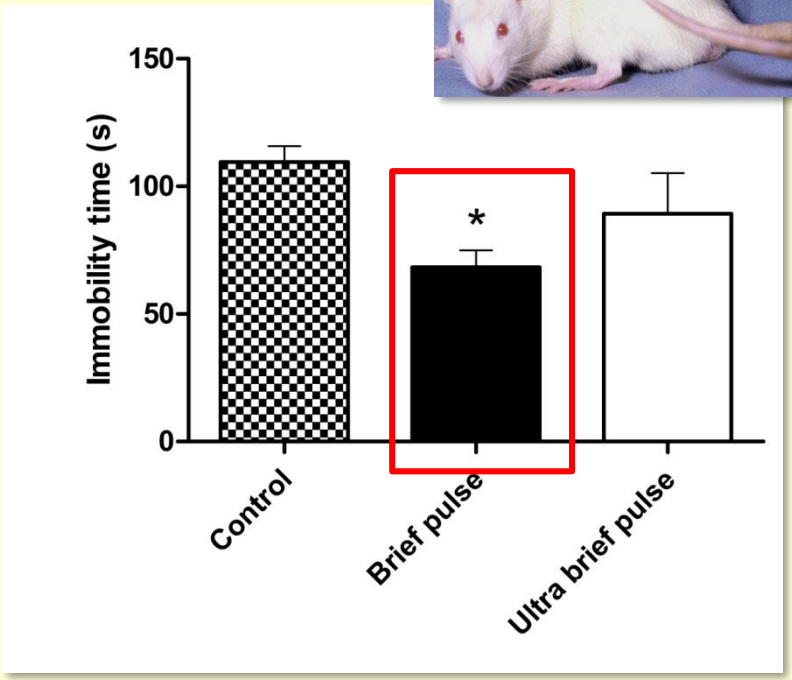
Progress in Neuro-Psychopharmacology & Biological Psychiatry 37 (2012) 147–152

# ECS: Sham vs Brief-pulse vs Ultrabrief-pulse



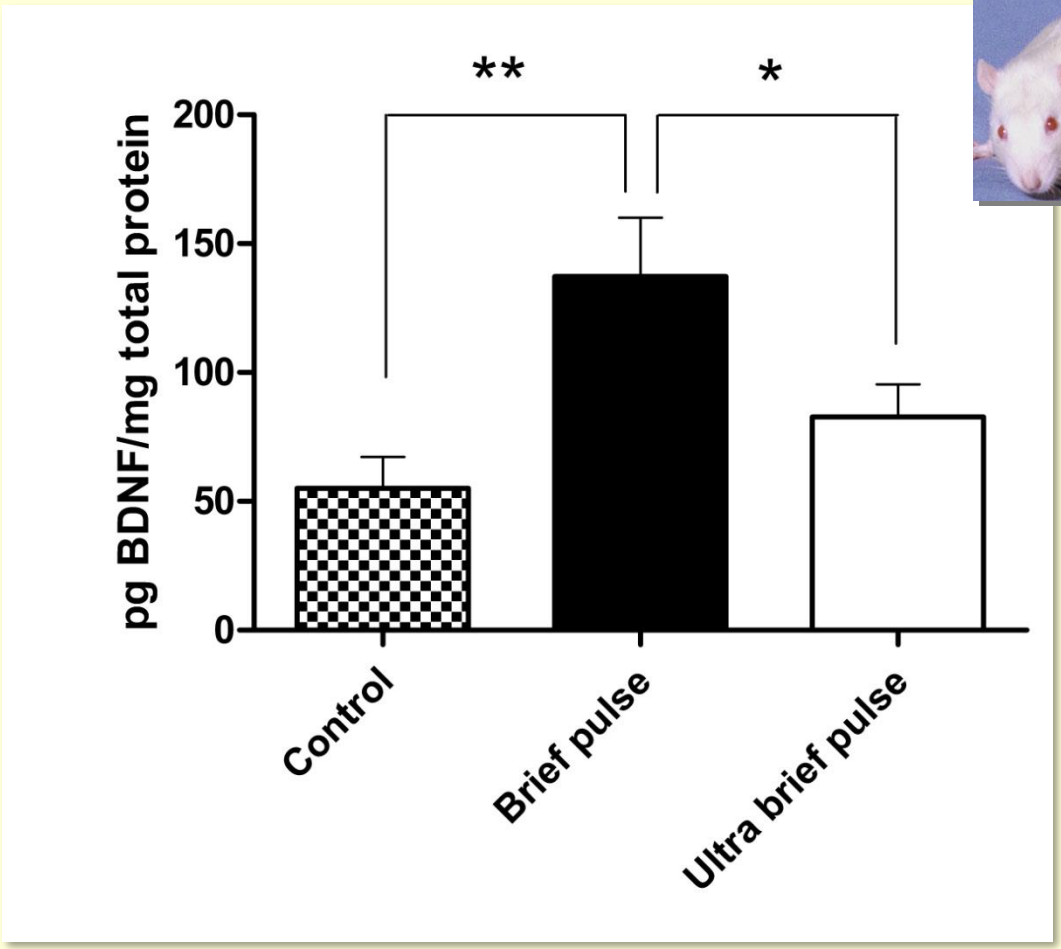

Seizure durations: no differences




**Behavioural antidepressant effect – Forced swim test**

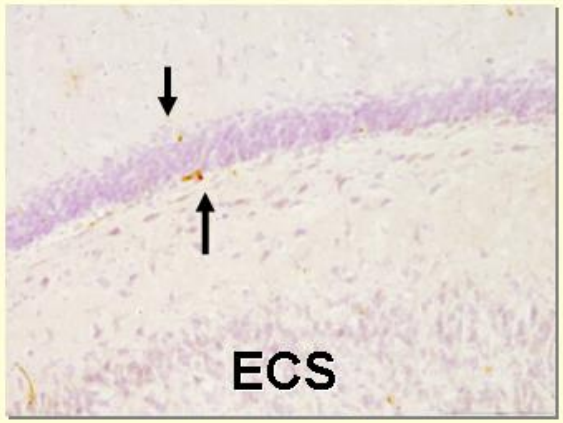
n=6 per group, *p<0.05 compared to control group.

O'Donovan et al (2012)

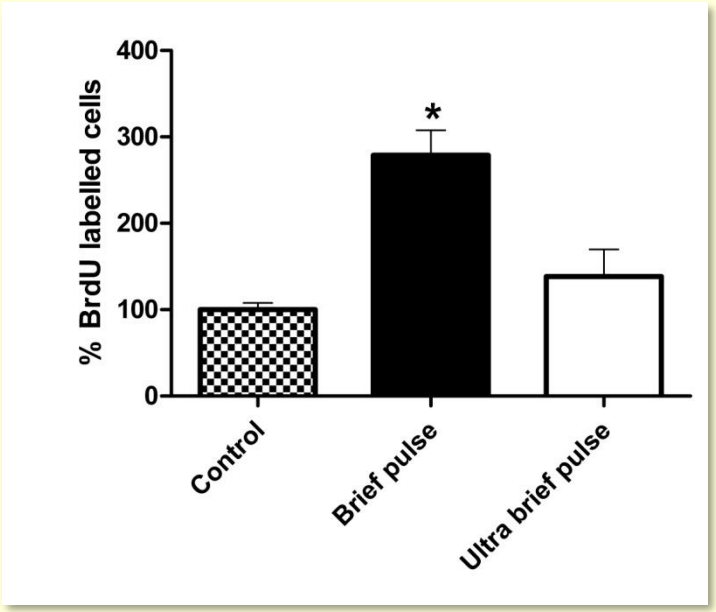



# BDNF protein levels in the hippocampus following ECS

n=6 per group, *p<0.05, **p<0.01 compared to control and UBP groups.



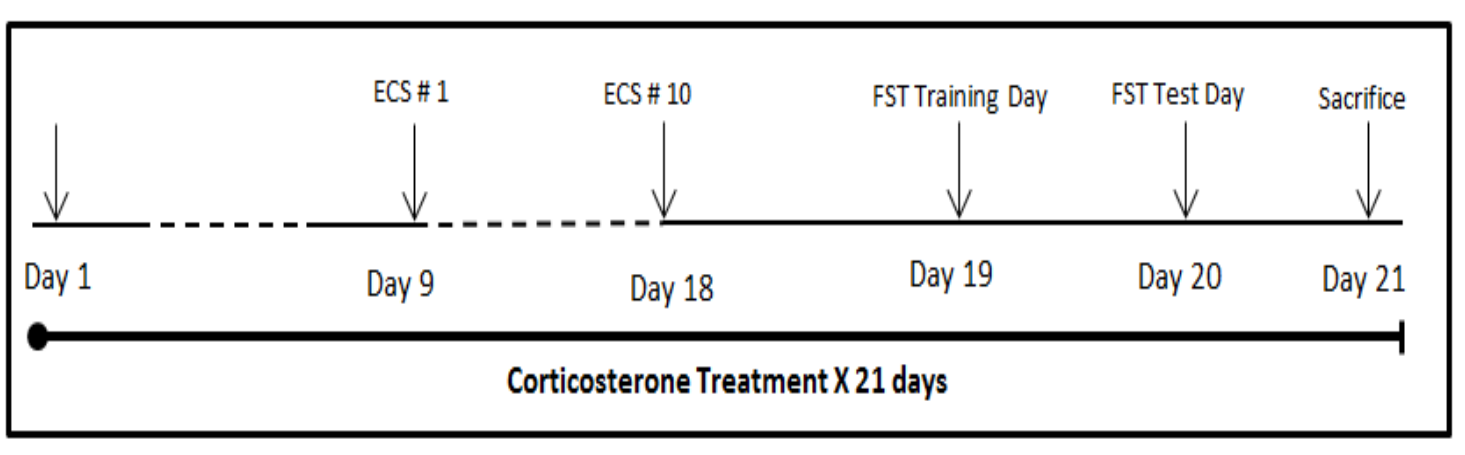


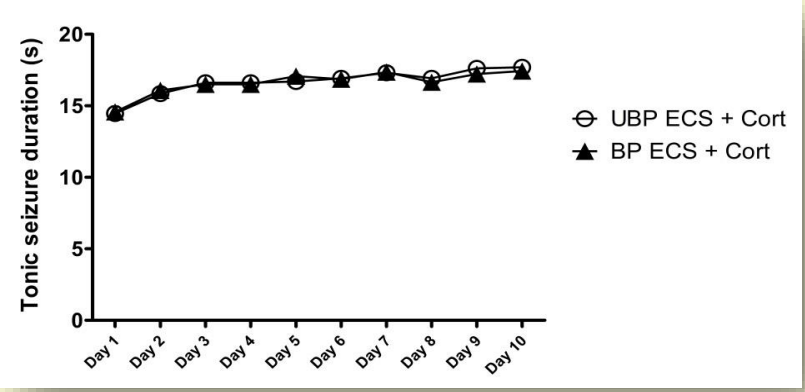


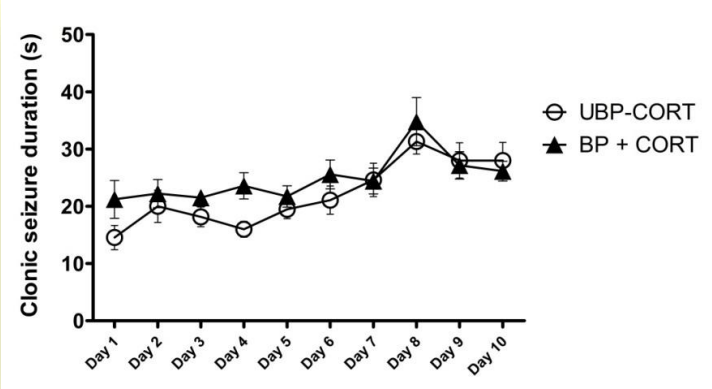

Cell proliferation following ECS. BP treatment significantly increased the relative number of BrdU-labelled cells in the dentate gyrus compared to sham-treated control animals ($p<0.05$)

# Hippocampal “neurogenesis”

# ECS study #2: Sham vs Brief-pulse vs Ultrabrief-pulse in the cortisol model of depression

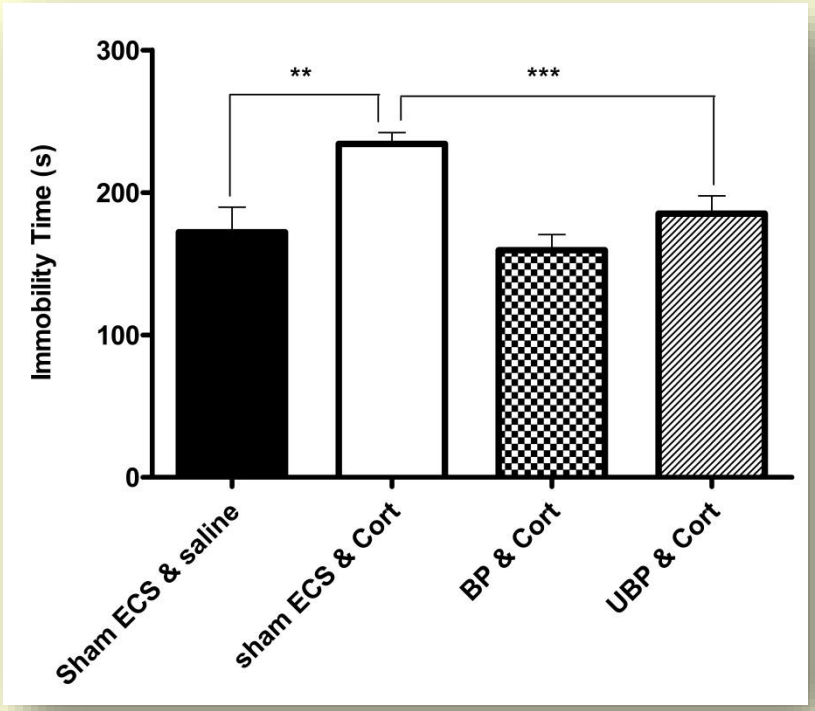


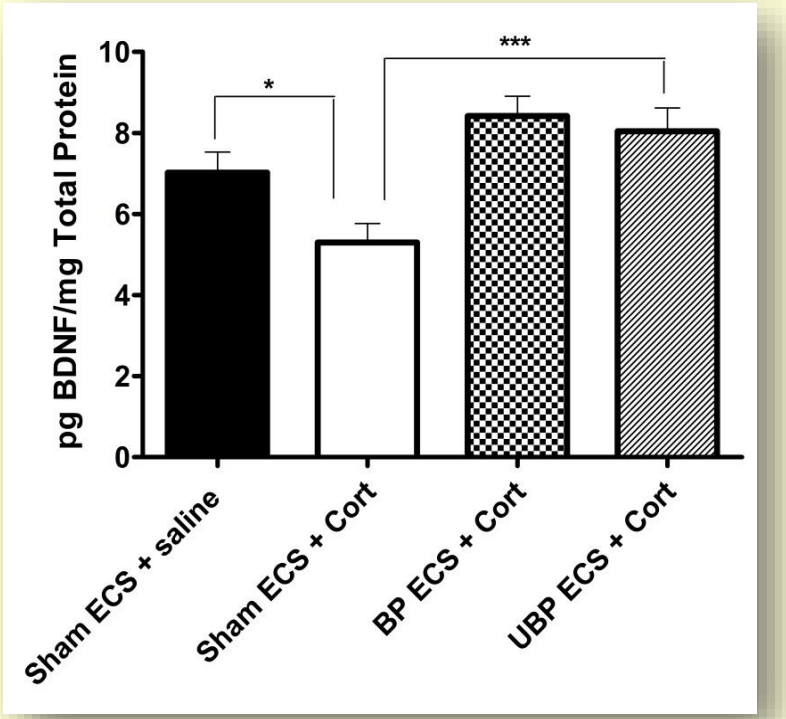




Sinead O'Donovan[1]*, Victoria Dalton[1]*, Andrew Harkin[2] and Declan M. McLoughlin[3]

*International Journal of Neuropsychopharmacology*, Page 1 of 10. © CINP 2014
doi:10.1017/S1461145714000200




**Behaviour: Forced Swim Test**
**N=11-14/group**

**Molecular: BDNF**
**N=11-14/group**

# Conclusion #2

## Ultrabrief pulse ECT: confusion reigns!

- **Optimal parameters not yet identified**
- **Probably requires high stimulus dose but then may not be able to maintain 0.3 msec pulse width**
- **Not for routine use**
- **Experimental for now**

# 3. Relapse rates

## 6 months

(a) **34.0%** (95% CI=27.2-41.5%, $I^2$=76%) of patients (N=844) treated with continuation pharmacotherapy relapsed.

NB: historical trend effects

(b) post DSM-III era (N=710): **37.7%** (95% CI=30.7-45.2%, $I^2$=70%)

- No effect of tx resistance (p=0.43)
- Lower relapse with:
  - Psychosis (p=0.004)
  - Age (p=0.04)

**Figure 2a**

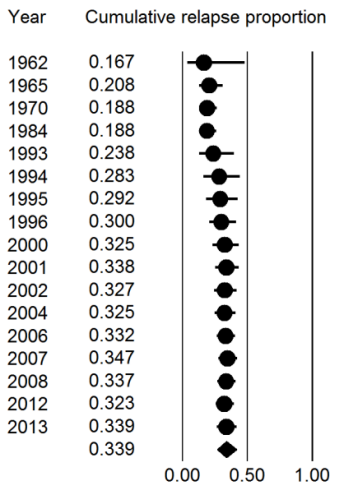
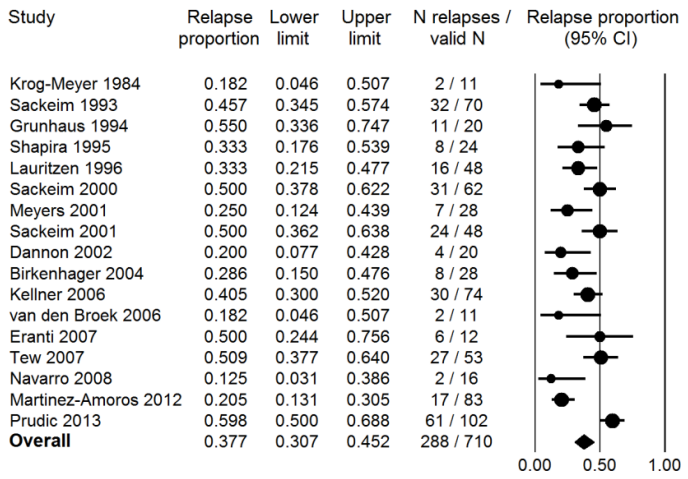



**Figure 2b**




Jelovac et al (2013) *Neuropsychopharmacology*

# Relapse rates: (a) 3, (b) 12 and (c) 24 months

## 3 months

**27.1%** of patients (N=350) on continuation pharmacotherapy had relapsed (95% CI=20.5-34.8%, $I^2$=48%)

## 12 months

**51.1%** (95% CI=44.7-57.4%, $I^2$=27%) (N=348)

## 24 months

**50.4%** (95% CI=41.2-59.6%, $I^2$=0) (N=111)

**Figure 3a**

| Study | Relapse proportion | Lower limit | Upper limit | N relapses / valid N |
|---|---|---|---|---|
| Cosgriff 1990 | 0.308 | 0.120 | 0.591 | 4 / 13 |
| Sackeim 1993 | 0.257 | 0.168 | 0.372 | 18 / 70 |
| Grunhaus 1994 | 0.500 | 0.294 | 0.706 | 10 / 20 |
| Shapira 1995 | 0.308 | 0.162 | 0.505 | 8 / 26 |
| Lauritzen 1996 | 0.196 | 0.109 | 0.327 | 10 / 51 |
| Grunhaus 2001 | 0.286 | 0.161 | 0.454 | 10 / 35 |
| Meyers 2001 | 0.143 | 0.055 | 0.324 | 4 / 28 |
| Sackeim 2001 | 0.417 | 0.287 | 0.559 | 20 / 48 |
| Dannon 2002 | 0.100 | 0.025 | 0.324 | 2 / 20 |
| Navarro 2008 | 0.029 | 0.002 | 0.336 | 0 / 16 |
| Yildiz 2010 | 0.261 | 0.122 | 0.472 | 6 / 23 |
| **Overall** | 0.271 | 0.205 | 0.348 | 92 / 350 |

Relapse proportion (95% CI)

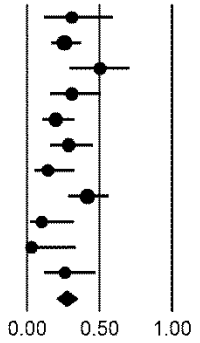



**Figure 3b**

| Study | Relapse proportion | Lower limit | Upper limit | N relapses / valid N |
|---|---|---|---|---|
| Spiker 1985 | 0.500 | 0.333 | 0.667 | 16 / 32 |
| Sackeim 1993 | 0.586 | 0.468 | 0.695 | 41 / 70 |
| Sackeim 2000 | 0.532 | 0.409 | 0.652 | 33 / 62 |
| Birkenhager 2004 | 0.357 | 0.204 | 0.546 | 10 / 28 |
| Birkenhager 2005 | 0.418 | 0.296 | 0.551 | 23 / 55 |
| Navarro 2008 | 0.375 | 0.179 | 0.623 | 6 / 16 |
| Sackeim 2008 | 0.567 | 0.440 | 0.685 | 34 / 60 |
| Nordenskjold 2013 | 0.640 | 0.440 | 0.801 | 16 / 25 |
| **Overall** | 0.511 | 0.447 | 0.574 | 179 / 348 |

Relapse proportion (95% CI)

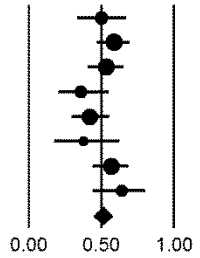
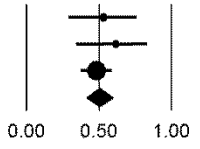



**Figure 3c**

| Study | Relapse proportion | Lower limit | Upper limit | N relapses / valid N |
|---|---|---|---|---|
| Flint 1998 | 0.533 | 0.293 | 0.759 | 8 / 15 |
| Navarro 2008 | 0.615 | 0.344 | 0.830 | 8 / 13 |
| Martinez-Amoros 2012 | 0.482 | 0.377 | 0.589 | 40 / 83 |
| **Overall** | 0.504 | 0.412 | 0.596 | 56 / 111 |

Relapse proportion (95% CI)



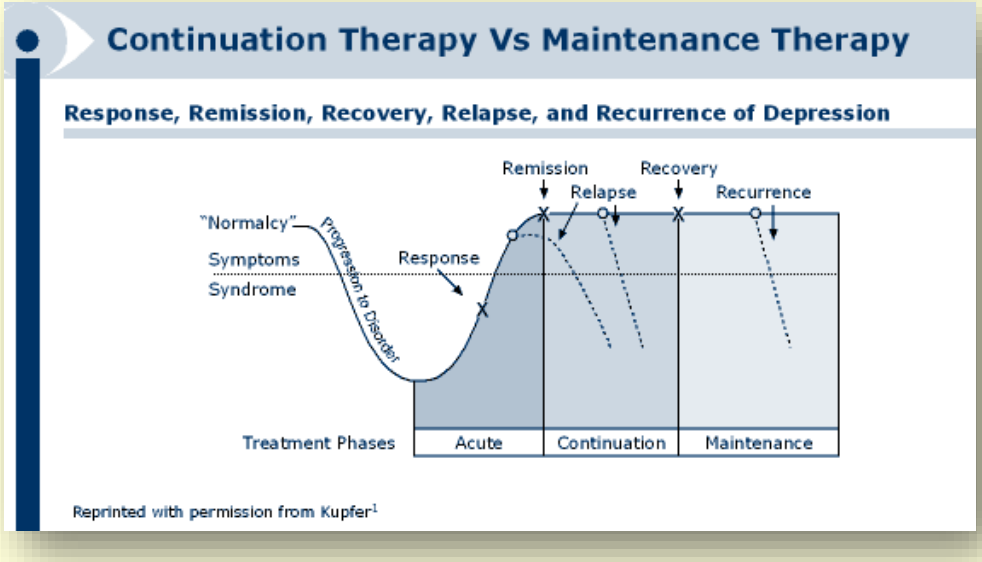
# Relapse rates with continuation ECT

## 6-months

**37.2%** (95% CI=23.4-53.5%, $I^2$=57%), four eligible C-ECT samples (N=146), i.e. same as modern-era AD-treated patients (37.7%).

**39.5%** (95% CI=31.9-47.7%, $I^2$=81%) for <u>any form</u> of recognised continuation therapy across 19 eligible studies (N=1001).

**45.4%** (95% CI=35.2-55.9%, $I^2$=0), two studies of C-ECT <u>only</u> (N=86).



# Relapse rates in untreated samples

## Unmedicated patients

- **3 months**
  - **47.9%** (95% CI=38.1-57.9%, $I^2$=0); two studies (1973).


## Placebo-treated samples

- **3 months**
  - **62.7%** (95% CI=47.6-75.8%, $I^2$=0); three RCTs (1996-2010)

- **6 months**
  - **65.5%** (95% CI=49.7-78.5%, $I^2$=72%); seven RCTs (1965-2006)

  - **78.0%** (95% CI=66.1-86.5%, $I^2$=0); four RCTs (N=65) (1984-2006)

# Relative risk of relapse on continuation antidepressants vs. placebo

## 3 months

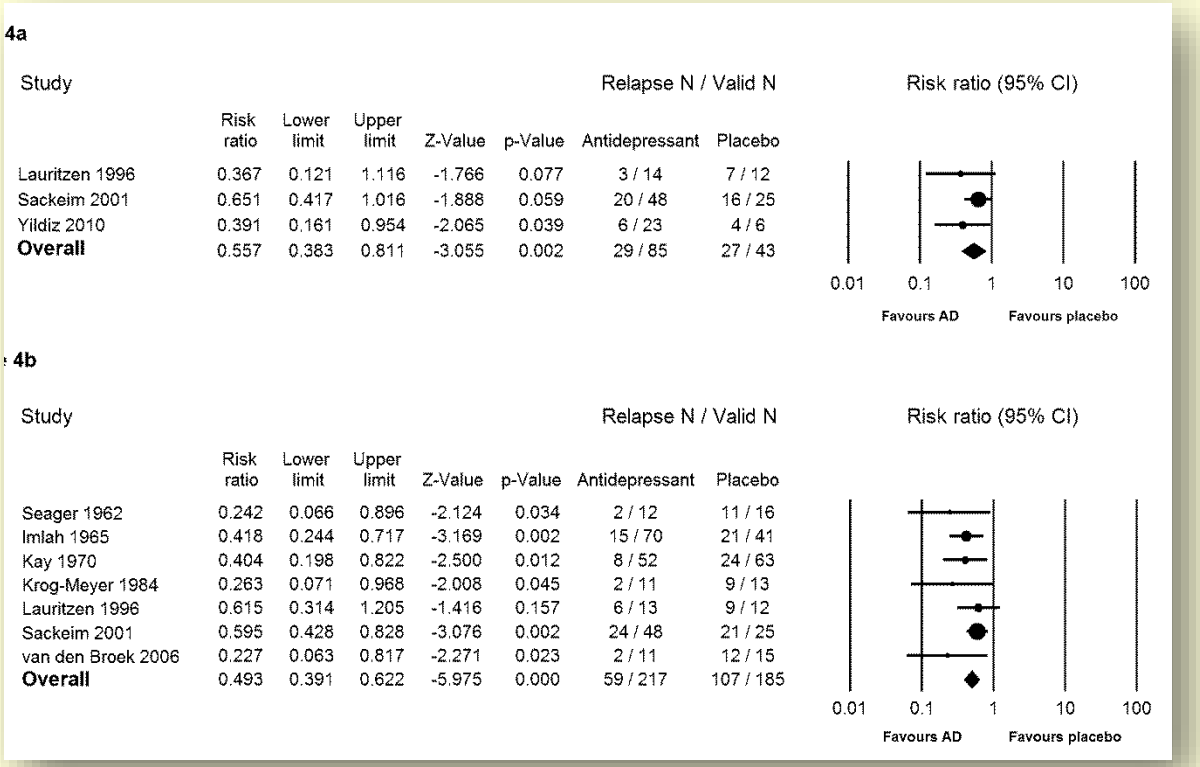
Any AD vs placebo; 3 studies

**RR=0.56** (95% CI=0.38-0.81, p=0.002, NNT=3.5, $I^2$=0)

## 6 months

Any AD vs placebo; 7 studies (n=402)

**RR=0.49** (95% CI=0.39-0.62, p<0.0001, NNT=3.3, $I^2$=0)



**4a**

| Study | Risk ratio | Lower limit | Upper limit | Z-Value | p-Value | Relapse N / Valid N: Antidepressant | Relapse N / Valid N: Placebo |
|---|---|---|---|---|---|---|---|
| Lauritzen 1996 | 0.367 | 0.121 | 1.116 | -1.766 | 0.077 | 3 / 14 | 7 / 12 |
| Sackeim 2001 | 0.651 | 0.417 | 1.016 | -1.888 | 0.059 | 20 / 48 | 16 / 25 |
| Yildiz 2010 | 0.391 | 0.161 | 0.954 | -2.065 | 0.039 | 6 / 23 | 4 / 6 |
| **Overall** | 0.557 | 0.383 | 0.811 | -3.055 | 0.002 | 29 / 85 | 27 / 43 |

Risk ratio (95% CI)

0.01 0.1 1 10 100

Favours AD Favours placebo

**4b**

| Study | Risk ratio | Lower limit | Upper limit | Z-Value | p-Value | Relapse N / Valid N: Antidepressant | Relapse N / Valid N: Placebo |
|---|---|---|---|---|---|---|---|
| Seager 1962 | 0.242 | 0.066 | 0.896 | -2.124 | 0.034 | 2 / 12 | 11 / 16 |
| Imlah 1965 | 0.418 | 0.244 | 0.717 | -3.169 | 0.002 | 15 / 70 | 21 / 41 |
| Kay 1970 | 0.404 | 0.198 | 0.822 | -2.500 | 0.012 | 8 / 52 | 24 / 63 |
| Krog-Meyer 1984 | 0.263 | 0.071 | 0.968 | -2.008 | 0.045 | 2 / 11 | 9 / 13 |
| Lauritzen 1996 | 0.615 | 0.314 | 1.205 | -1.416 | 0.157 | 6 / 13 | 9 / 12 |
| Sackeim 2001 | 0.595 | 0.428 | 0.828 | -3.076 | 0.002 | 24 / 48 | 21 / 25 |
| van den Broek 2006 | 0.227 | 0.063 | 0.817 | -2.271 | 0.023 | 2 / 11 | 12 / 15 |
| **Overall** | 0.493 | 0.391 | 0.622 | -5.975 | 0.000 | 59 / 217 | 107 / 185 |

Risk ratio (95% CI)

0.01 0.1 1 10 100

Favours AD Favours placebo

# Conclusion #3

**Relapse rates following ECT are high: 30% at 3 mths, 40% at 6 mths and 50% at 12 mths**

- similar to STAR*D Study which had lower remission rates
- but don't forget superior remission rates with ECT

- **relapse rates have increased over time**

- **vigorous maintenance therapy required post ECT**
  - not yet clear what is best
  - most studies on older TCAs
  - C-ECT to be optimised

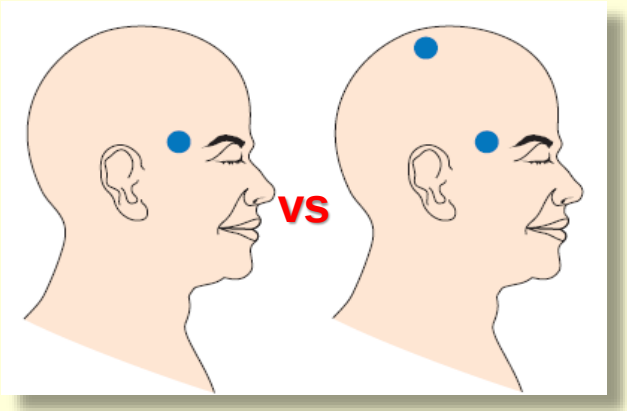
# 4. The EFFECT-Dep Trial

## EFFECT-Dep Trial

Enhancing the Effectiveness of ECT in Severe Depression

ISRCTN23577151

**OBJECTIVE:** **to perform a pragmatic, randomised, non-inferiority trial comparing standard bitemporal ECT (1.5 x ST) and high-dose unilateral ECT (6 x ST) in severe depression in routine practice**



# Background

- **Global treated person (<65) rate: 2.34/10,000 population**

  **→1.4 million per year**

- **Global average no. of treatments: 8 per course**

- **Western countries: older, female, depression**

  **Asian countries: younger, males, schizophrenia**

- **Wide variation but bilateral ECT is the most common form**

**Contemporary use and practice of electroconvulsive therapy worldwide**

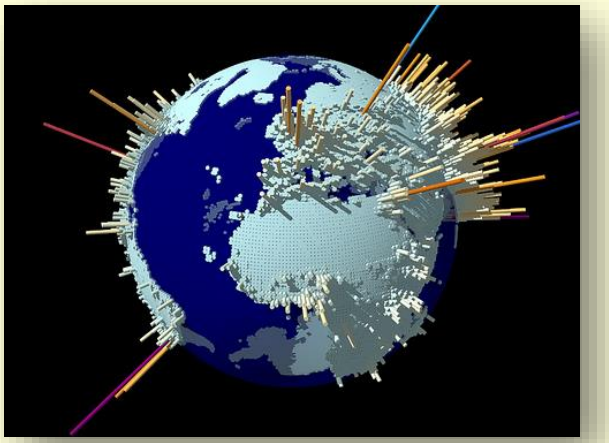
Kari Ann Leiknes[1,2], Lindy Jarosh-von Schweder[3,4] & Bjørg Høie[5]

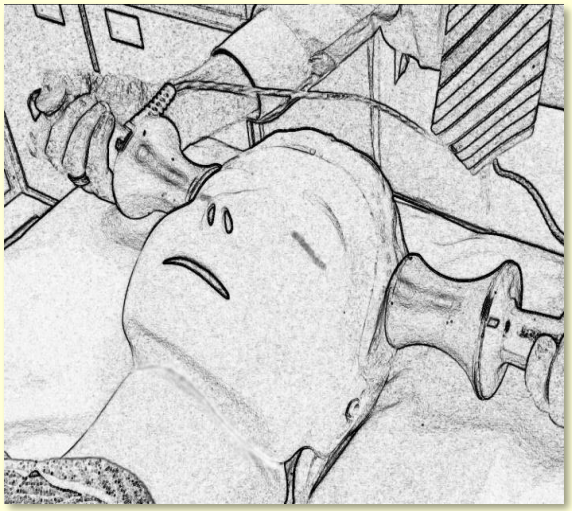
*Brain and Behavior* 2012; 2(3): 283–345

Comparison of Electroconvulsive Therapy Practice Between London and Bengaluru

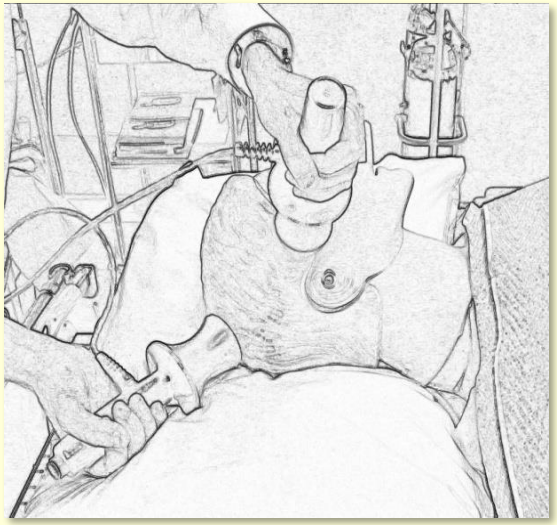
*Savithasri V. Eranti, MRCPsych, MD, PhD,*† Jagadisha Thirthalli, MD,‡ Vivek Pattan, MRCPsych,§ Andrew Mogg, PhD, MRCPsych,† Graham Pluck, PhD,|| Latha Velayudhan, DPM, DNB,¶ Jenifer Chan, MRCPsych,† Bangalore N. Gangadhar, MD,‡ and Declan M. McLoughlin, PhD, MRCPI, MRCPsych, FTCD#*

***J ECT*** **2011: 27(4):275-80**





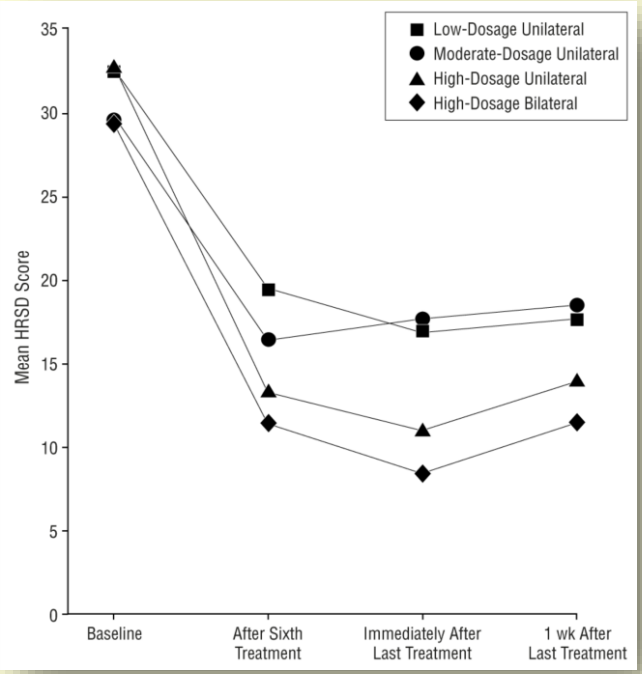
vs



## Goal: Decrease side-effects but maintain effectiveness

## RCTs of bitemporal vs high-dose RUL ECT

1. Sackeim et al (2000) *Arch Gen Psychiatry* (n=20/group)
2. McCall et al (2002) *J ECT* (n~40/group)
3. Ranjkesh et al (2005) *J ECT* (n~13/group)
4. Sackeim et al (2008) *Brain Stimulation* (n~22/group)
5. Sackeim et al (2009) *Arch Gen Psychiatry* (+pharmacotx; n~45-70/group)
6. Kellner et al (2010) *Br J Psychiatry* (n~72/group)




From: **A Prospective, Randomized, Double-blind Comparison of Bilateral and Right Unilateral Electroconvulsive Therapy at Different Stimulus Intensities**

Sackeim HA , et al. *Arch Gen Psychiatry* (2000)

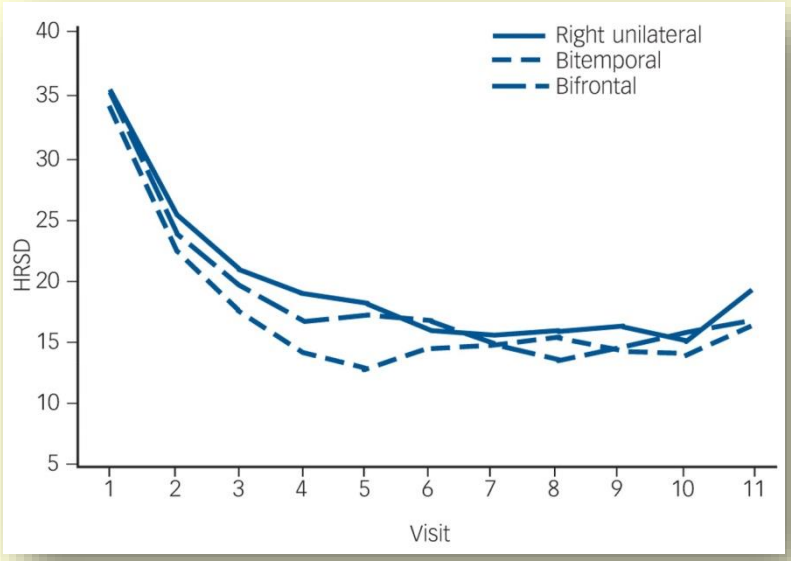
- underpowered
- thrice weekly ECT
- 2.5 x ST for BT ECT → ↑ side-effects
- meds stopped x ≥5 days; lorazepam rescue

Bifrontal, bitemporal and right unilateral electrode placement in ECT: randomised trial†

Charles H. Kellner, Rebecca Knapp, Mustafa M. Husain, Keith Rasmussen, Shirlene Sampson, Munro Cullum, Shawn M. McClintock, Kristen G. Tobias, Celena Martino, Martina Mueller, Samuel H. Bailine, Max Fink and Georgios Petrides

BJPsych The British Journal of Psychiatry (2010) 196, 226–234. doi: 10.1192/bjp.bp.109.066183

- 30% drop-out during tx phase
- thrice weekly ECT
- meds stopped



# *St Patrick's University Hospital*

'He gave what little wealth he had
To build a house for fools and mad;
And show'd by one satiric touch,
No nation wanted it so much.

*Dean Jonathan Swift*
*(1667-1745)*
*A Tale of a Tub*
*A Modest Proposal*
*Gulliver's Travels*

# EFFECT-Dep Trial

**Design:** two-group parallel-design randomised non-inferiority trial; continued on usual care. Treated at St Patrick's University Hospital, Dublin (ECTAS-accredited).

**Randomisation:** minimisation stratification (source of referral; previous ECT; age, ≥65) with variable block sizes; just before 1st ECT session; independent & computerised - Clinical Trials Unit, IOP, KCL

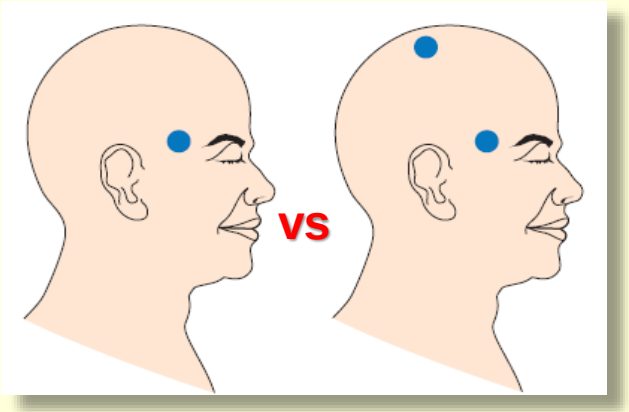
**Blinding:** patients, clinicians, raters

**Inclusion**: major depressive episode (DSM-IV; SCID) referred for ECT; HDRS-24 ≥21; ≥ 18 years

**Exclusion:** unfit for general anaesthesia; ECT in previous six months; dementia or other Axis 1 diagnosis; alcohol/other substance abuse in previous six months; inability/refusal to consent.

**Ethical approval:** St Patrick's University Hospital Research Ethics Committee

# EFFECT-Dep Trial




## ECT

- twice weekly
- Mecta 5000M device (Mecta Corporation, USA)
- methohexitone (0.75-1.0 mg/kg) and suxamethonium (0.5-1.0 mg/kg)
- EEG monitoring
- seizure threshold (ST) was established by a method of limits at the first session and subsequent treatments given at 1.5 x ST for BT ECT and 6.0 x ST for RUL ECT
- Stimulus charge is titrated upward as required during treatment courses following a standard stimulus dosing protocol.
- number of ECTs determined by referring physicians, up to 12 sessions (as per Mental Health Commission)

# EFFECT-Dep Trial

## Clinical outcomes

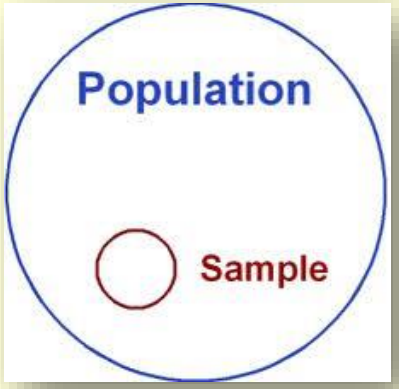
**Primary: 24-item Hamilton Rating Scale for Depression (HDRS)**

- baseline; after every 2 ECTs; during 12 mth follow-up
- Response: ≥60% decrease in HDRS from baseline and score ≤16

- Remission: ≥60% decrease in HDRS from baseline and score ≤10 on two occasions separated by one week

- Relapse: ≥10 point increase in HDRS compared to end-of-treatment score plus HDRS ≥16; increase in the HDRS should be maintained two weeks later. Hospital admission, further ECT, and deliberate self-harm/suicide also constitute relapse.

# EFFECT-Dep Trial




## Sample size estimation & clinical significance

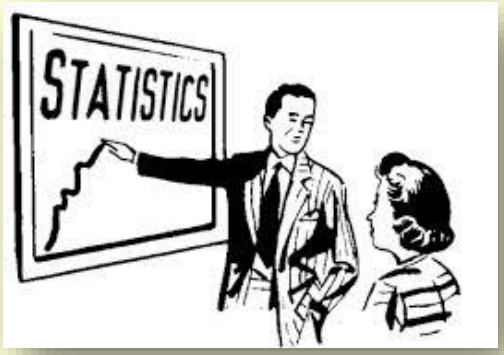
In a large series (*n* = 253) of depressed patients, Petrides *et al*. (2001) found a mean (SD) reduction in 24-item HDRS of 25.6 (9.4) after treatment with BT ECT (1.5 x ST).

We estimated that:

- **69 patients** required per treatment group
- to have **80% power**
- to demonstrate, using a one-sided equivalence *t*-test at **5% level**
- that mean reduction in 24-item HDRS achieved using high-dose RUL ECT is **no more than 4 points** (i.e. equivalent to 3 points on 17-item HDRS) less than that achieved using standard BT ECT, assuming a common within-group SD of change scores of 9.4 and equal expected group mean change scores.

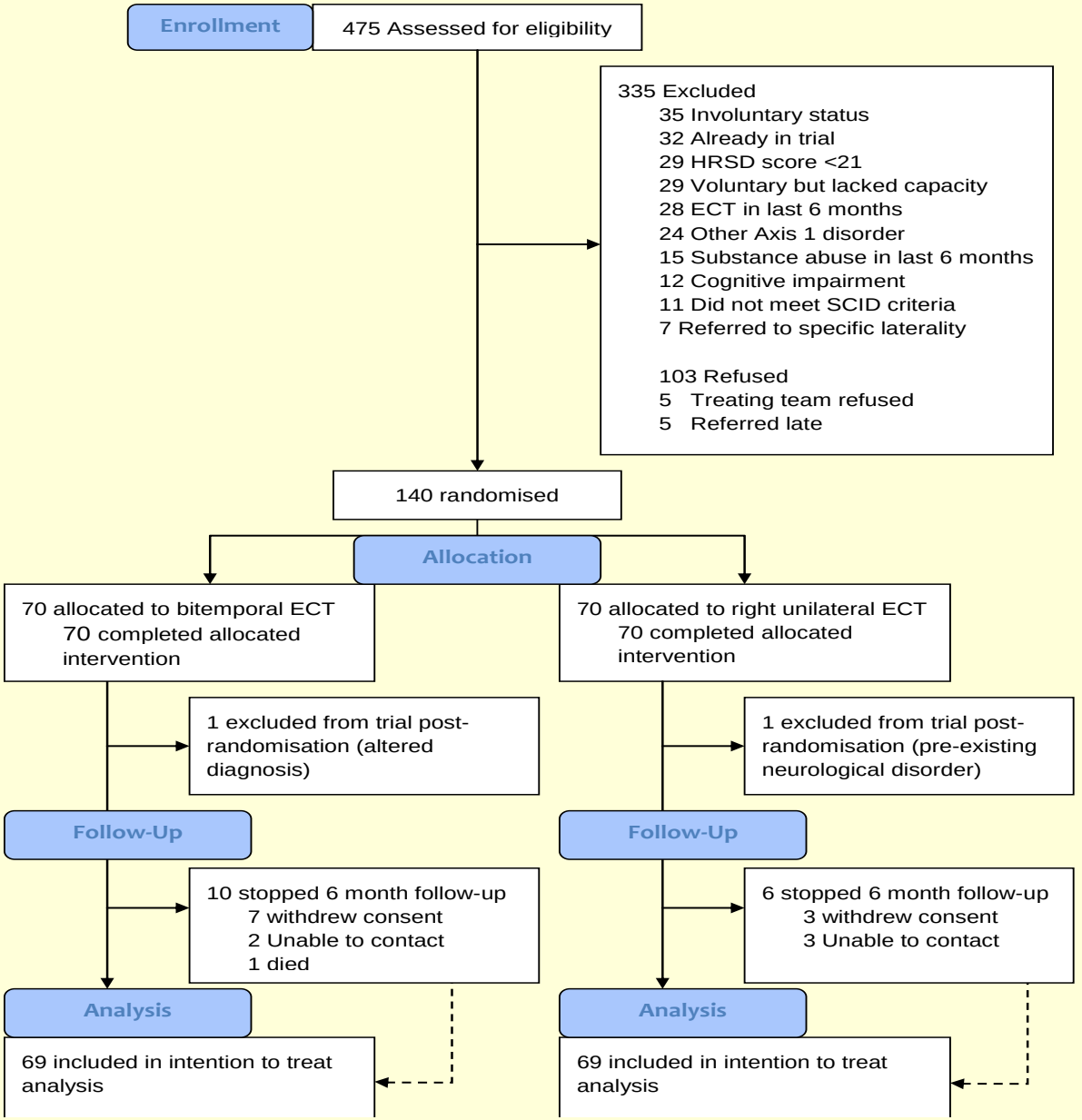
# Statistical inferential analyses

- Intention to treat
- Single primary experimental hypothesis
- No planned subgroup analyses
- No planned interim analysis
- Statistician blinded
- Linear mixed models for HDRS
- Multiple imputation for missing data



# Results

## Effect-Dep Flow Diagram May 2008- Oct 2012

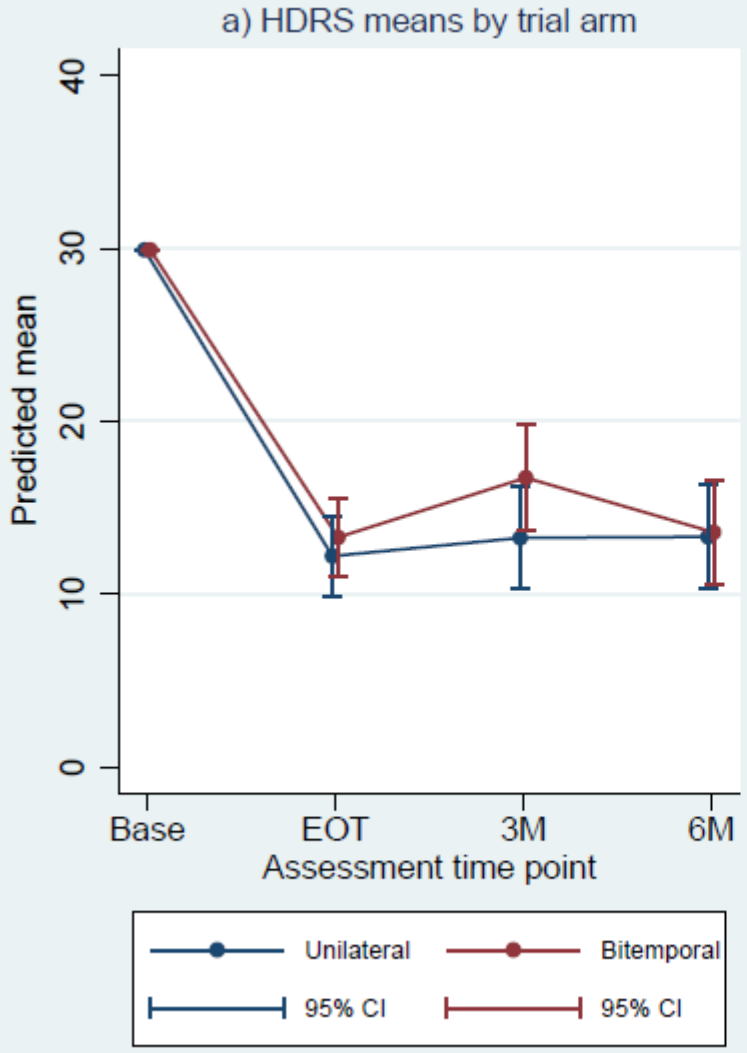


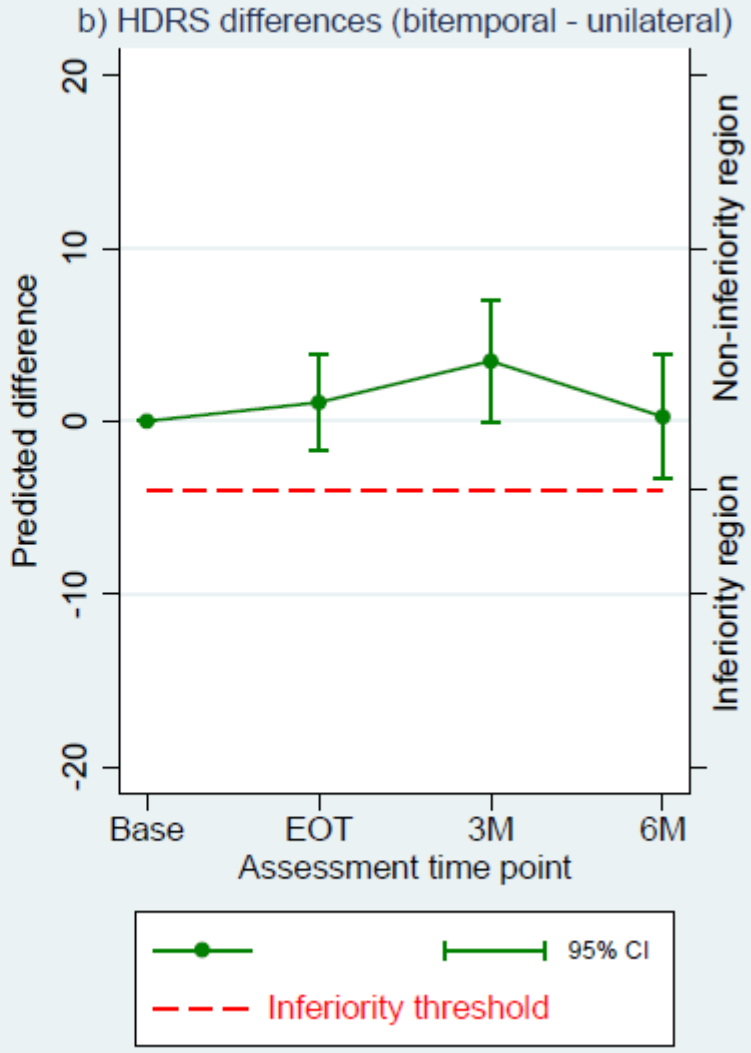
| | Total sample (n=138) | Right Unilateral (n=69) | Bitemporal (n=69) |
|---|---|---|---|
| **Demographics** | | | |
| Age, years | 56.7(14.8) | 56.6(15.3) | 56.8(14.4) |
| Gender, female (%) | 87(63.0%) | 40(58.0%) | 47(68.1%) |
| Education: years | 13.1(3.4) | 13.7(3.0) | 12.6(3.8) |
| Socio-economic group (1-5) | 3.1(1.4) | 2.9(1.3) | 3.3(1.5) |
| Marital status | | | |
| Married | 76(55.9%) | 38(56.7%) | 38(55.1%) |
| Single | 35(25.7%) | 17(25.4%) | 18(26.1%) |
| Widowed/divorced | 25(18.1%) | 12(17.9%) | 13(18.8%) |
| **Clinical characteristics** | | | |
| Bipolar depression | 32(23.2%) | 16(23.2%) | 16(23.2%) |
| Presence of psychosis | 29(21.0%) | 16(23.2%) | 13(18.8%) |
| Treatment resistance | 98(71.0%) | 45(65.2%) | 53(76.8%) |
| History of previous ECT | 53(38.4%) | 26(37.7%) | 27(39.1%) |
| Episode duration: weeks | 31.6(52.0) | 26.7(31.0) | 36.7(66.9) |
| Number of previous episodes | 5.3(4.5) | 5.7(4.8) | 5.1(4.4) |
| HRSD-24 baseline | 29.9(6.2) | 30.4(6.1) | 29.5(6.3) |
| MMSE baseline | 27.7(2.1) | 28(1.8) | 27.4(2.4) |
| NART | 108.3(6.8) | 109.2(5.6) | 107.4(7.8) |
| CGI-S baseline | 5.3(0.7) | 5.4(0.7) | 5.3(0.7) |
| Psychotropic medications | | | |
| Number of psychotropics | 4.2(1.4) | 4.3(1.3) | 4.2(1.5) |
| SSRIs | 29 | 15 | 14 |
| SNRIs | 67 | 32 | 35 |
| Tricyclic antidepressants | 39 | 20 | 19 |
| Tetracyclic antidepressants | 6 | 6 | 0 |
| Mirtazapine | 46 | 24 | 22 |
| Agomelatine | 2 | 1 | 1 |
| Lithium | 56 | 28 | 28 |
| Anticonvulsants* | 39 | 18 | 21 |
| Benzodiazepines | 81 | 35 | 46 |
| Antipsychotics | 97 | 48 | 49 |
| Z-hypnotic | 69 | 34 | 35 |
| Tryptophan | 2 | 1 | 1 |
| Buproprion | 4 | 2 | 2 |
| MAO-I | 1 | 0 | 1 |
| Buspirone | 1 | 0 | 1 |

Data are mean (SD) or n (%), unless otherwise indicated. Treatment resistance was based on the Antidepressant Treatment History Form. HRSD-24: 24-item Hamilton Rating Scale for Depression. MMSE: Mini-Mental State Examination. NART: National Adult Reading Test. CGI-S: Clinical Global Assessment of Severity Scale. SSRIs: Selective serotonin reuptake inhibitor. SNRIs: Serotonin and Noradrenaline Reuptake Inhibitor. *Anticonvulsants include Lamotrigine, Sodium Valproate and Pregabalin prescribed as mood stabilisers or anxiolytic.

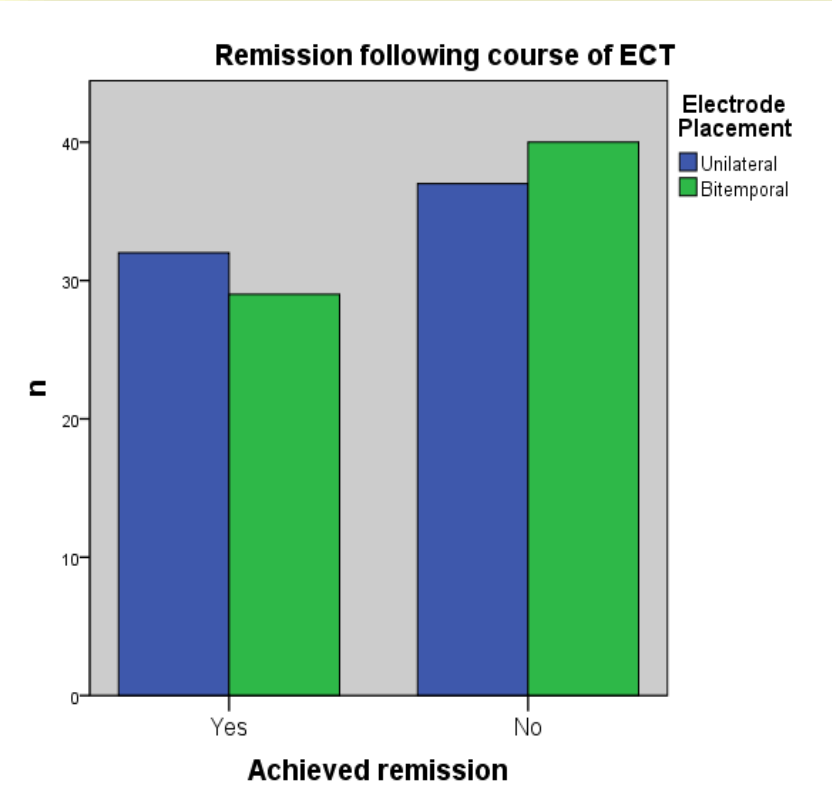
*Table 1*: Baseline characteristics

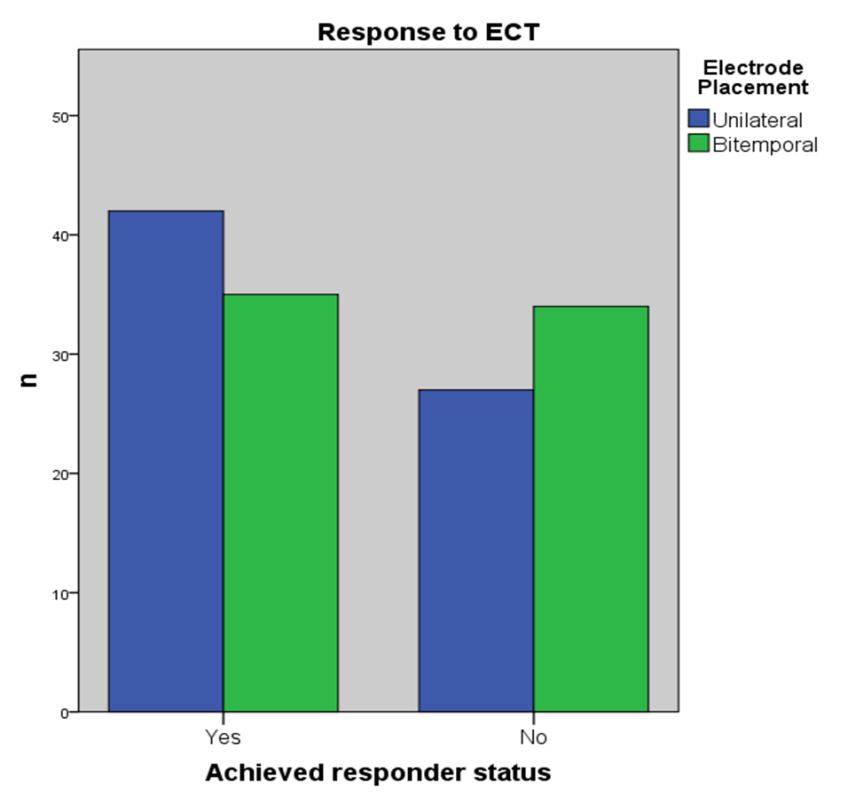
# Baseline characteristics



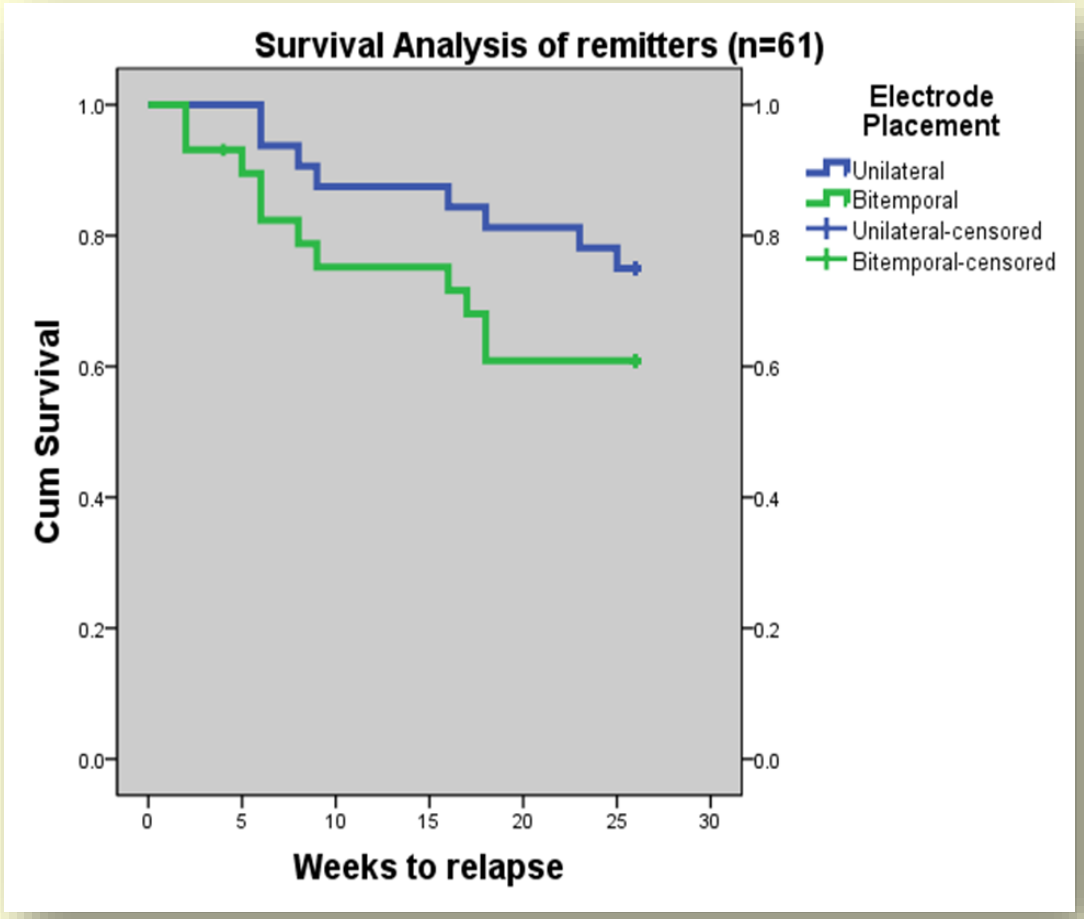




**Mean HDRS estimated to be 1.2 points higher in the Bitemporal group; 95% CI, -1.510 to 3.995, i.e. within the non-inferiority threshold.**




| | Whole group | RUL ECT | BT ECT | Fisher's exact test |
|---|---|---|---|---|
| Remission | 61/138 (44.2%) | 32/69 (46.4%) | 29/69 (42.0%) | P=0.30 |
| Response | 77/138 (55.8%) | 42/69 (60.9%) | 35/69 (50.7%) | P=0.70 |




**Overall 6 month relapse rate for remitters was 31%**

**25% (RUL) vs 38% (BT)**

**Case Processing Summary**

| Electrode Placement | Remitters | Relapses | Censored(did not relapse) | |
|---|---|---|---|---|
| | | | N | Percent |
| Unilateral | 32 | 8 | 24 | 75.0% |
| Bitemporal | 29 | 11 | 18 | 62.1% |
| Overall | 61 | 19 | 42 | 68.9% |

**Overall Comparisons**

| | Chi-Square | df | Sig. |
|---|---|---|---|
| Log Rank (Mantel-Cox) | 1.723 | 1 | .189 |

Test of equality of survival distributions for the different levels of Electrode Placement.

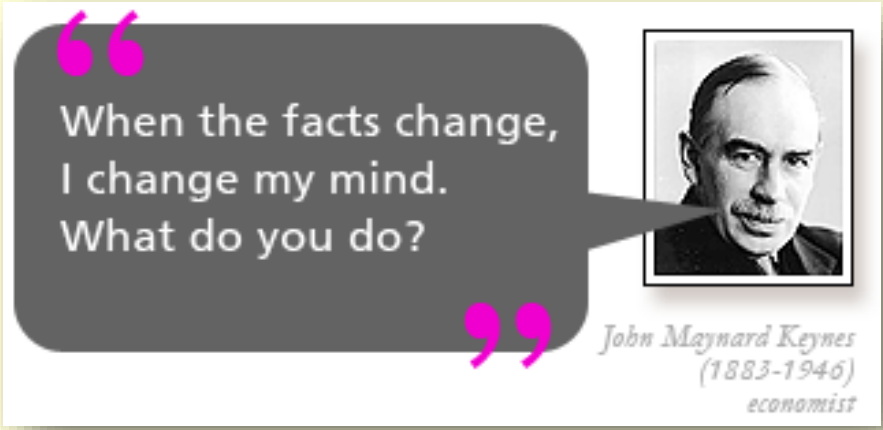
| | Predicted mean* RUL (*n*=69) | Predicted mean* Bitemporal (*n*=69) | Comparison of randomisation groups** | |
|---|---|---|---|---|
| | | | Estimated difference in means (95% CI) BT - RUL | Statistical significance test (p-value) |
| **Total side effects: CSSES total score*** ** | | | | |
| Baseline (sample average) | 22.42 (*n*=50) | 22.42 (*n*=48) | | |
| EOT | 14.15 (*n*=63) | 17.25 (*n*=62) | 1.22 (0.93 to 1.60) | *z*=1.44 (*p*=0.15) |
| 3 Months | 12.45 (*n*=47) | 13.40 (*n*=32) | 1.08 (0.73 to 1.58) | *z*=0.38 (*p*=0.71) |
| 6 Months | 8.72 (*n*=39) | 12.09 (*n*=38) | 1.39 (0.90 to 2.13) | *z*=1.49 (*p*=0.14) |
| **Cognitive side effects: CSSES cognitive score*** ** | | | | |
| Baseline (sample average) | 5.0 (*n*=52) | 5.0 (*n*=48) | | |
| EOT | **3.80** (*n*=63) | **5.48** (*n*=62) | **1.44 (1.06 to 1.96)** | ***z*=2.32 (*p*=0.02)** |
| 3 Months | 4.21 (*n*=47) | 4.86 (*n*=32) | 1.15 (0.82 to 1.61) | *z*=0.83 (*p*=0.41) |
| 6 Months | **3.28** (*n*=39) | **4.91** (*n*=38) | **1.50 (1.05 to 2.13)** | ***z*=2.24 (*p*=0.025)** |

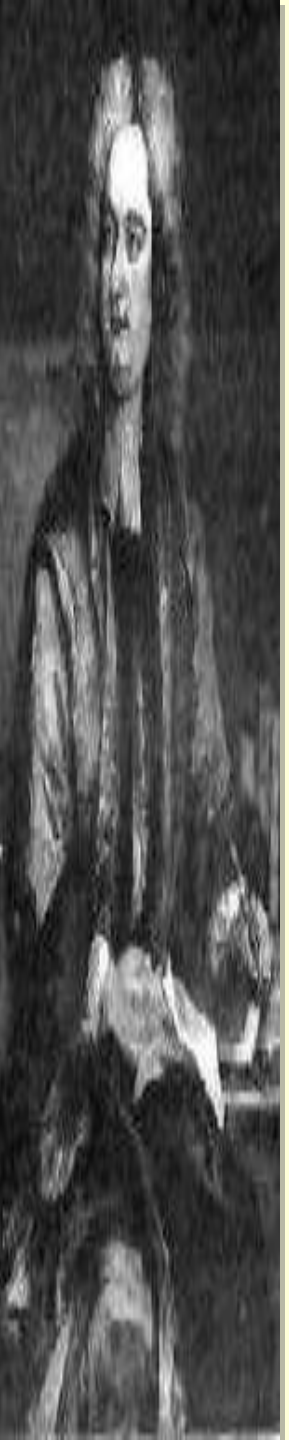
* Means are predicted for patients with average baseline outcome value, who are of younger age (≤65 years), referred from St. Patrick's and have no previous experience of ECT **All analyses were carried out using multiple imputation with 200 imputations (see Statistical Analysis). *** Analysis carried out on the log-scale, means backtransformed and effect estimates representing factor changes, MMSE: Mini-Mental State Examination TMT: Trail Making Test (versions A and B); FCSRT: Free and Cued Selective Reminding Test; CFT: Complex Figure Test.

# Subjective cognitive complaints: less with RUL ECT

# Conclusion #4

- RUL ECT (6xST) is **not** inferior to standard BT ECT (1.5xST)
- RUL ECT (6xST) has cognitive advantages
- RUL ECT (6xST) should be the first-line form of ECT for depression





# Aitäh!

## EFFECT-Dep Trial

Maria Semkovska
Martha Noone
Ana Jelovac
- Ross Dunne
- Adam Kavanagh
- Eric Kolshus
- Sabine Landau (IOP, KCL)
  - Mary Carton
  - Diarmaid O'Lonergan
  - Sinead Lambe
  - Caroline McHugh

## ECT Relapse meta-analysis

Ana Jelovac, Erik Kolshus

## Bifrontal meta-analysis

Ross Dunne

## Biomarker & pre-clinical studies

Karen Ryan
Sinead O'Donovan
Victoria Dalton
Nino Glaviano

St Patrick's Mental Health Services
Empowering recovery

Trinity College Institute of Neuroscience
from molecules to mind

HRB Health Research Board