ELICITING AND ENSURING AN OPTIMIZED SEIZURE

Per Bergsholm, MD/PhD - Førde, Norway
NACT, Gjøvik - May 24, 2019
The first ECT - April 1938
Rome university psychiatric clinic
Lucio Bini’s notebook for Enrico X

Titration with alternating current

April 11
11.15 h  80 volt ¼ s – no seizure
11.25 h  80 volt ½ s – no seizure
11.40 h  80 volt ¾ s – no seizure

April 20
92 volt ½ s – tonic-clonic seizure
no breath 105 s

Total 10-11 sessions

March 1940 Readmitted to Mombello psychiatric hospital, Milano

Edward Shorter, David Healy
DOSING/CHARGE

1. Tonic phase liminal stimulation
2. High-dose 75% to 100%
3. Age-dependant: Age and half-age
4. Placement-dependant percentage
5. Threshold multiplied dose
Pulse-width and pulse-train duration

«The therapeutic efficiency with the Elther was somewhat lower ... may be due to subtotal, but grand mal-like, seizure patterns sometimes induced with ultrabrief stimulus. The influence on memory functions did not differ»

Börje Cronholm (1913-83), Jan-Otto Ottosson (1925-), Stockholm

*Ultrabrief stimulus technique in electroconvulsive therapy*

J Nerv Ment Dis 1963;137

I. Influence on retrograde amnesia ... 117-23

II. Comparative studies of therapeutic effects ... 268-76
The Scandinavian liminal titration method

**STIMULATION**
1. **Unilateral** nondominant with long electrode distance
2. Stimulus duration **not prefixed**
3. Current **interrupted** as soon as the clonic contractions shift to the **tonic** phase, most readily observed in the plantar extension of the **great toes**

**Observation**
1. The optimal convulsion usually **ends by degrees**, and is succeeded by a **comatose** stage from which consciousness is **gradually regained**
2. The **dissociative** convulsion is followed by **early awakening**
3. The **clonic** form has no tonic phase, ends **abruptly** and simultaneously in the whole body, last only **10 to 20 s**
   Both have **lower** antidepressant efficacy

**Giacomo d’Elia** (1934-), **Jan-Otto Ottosson** (1925-), Gothenburg, **Lizzie Sand Strömgren** (1928-2007), Aarhus

Present Practice of Electroconvulsive Therapy in Scandinavia. *Arch Gen Psychiatry* 1983;40:577-81
Electrode placement

Comparisons of antidepressant efficiency according to interelectrode distance
24 studies 1962-1988

<table>
<thead>
<tr>
<th>Electrode position</th>
<th>Interelectrode distance</th>
<th>Number of studies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bilateral better than unilateral</td>
<td>Bilateral equal to unilateral</td>
</tr>
<tr>
<td>Lancaster et al</td>
<td>6 – 8 cm</td>
<td>9</td>
</tr>
<tr>
<td>Other unilateral</td>
<td>12-15 cm</td>
<td>2</td>
</tr>
</tbody>
</table>

Jan-Otto Ottosson
Is unilateral nondominant ECT as efficient as bilateral ECT? A new look at the evidence
Convulsive Therapy 1991;7:190-200
The Scandinavian liminal titration method - «The Last Waltz»

**TABLE 2. Treatment variables**

<table>
<thead>
<tr>
<th></th>
<th>U-ECT (n = 22)</th>
<th>B-ECT (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. treatments in each ECT series</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>7.7</td>
<td>8.0</td>
</tr>
<tr>
<td>Range</td>
<td>4–11</td>
<td>6–11</td>
</tr>
<tr>
<td>Duration of stimulus pulse train(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>6.3</td>
<td>6.0</td>
</tr>
<tr>
<td>Range</td>
<td>4.1–10</td>
<td>4.6–9.5</td>
</tr>
<tr>
<td>Stimulus charge (mC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>403</td>
<td>384</td>
</tr>
<tr>
<td>Range</td>
<td>262–640</td>
<td>294–608</td>
</tr>
<tr>
<td>Mean seizure duration(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>37.7</td>
<td>36.6</td>
</tr>
<tr>
<td>Range</td>
<td>34–91</td>
<td>30–86</td>
</tr>
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</table>

= 1.5 ms pulse width close to brief-pulse

Current push button on one of the electrode handles

Flexible stimulus duration with a long maximum of 10 s

Low frequency 25 or 50 pps. Short pulses \( \sim 1.5 \text{ ms} \)
European v US devices

Some traditional European devices allows the duration of the stimulus to be determined by the therapist watching for motor signs and ending the energy stream when an «adequate seizure» has been elicited.

United State devices, however, require delivery of a preset amount of energy

Georgios Petrides and Max Fink, New York
The «half-age» stimulation strategy for ECT dosing
Convulsive Therapy 1996;12:138-46
Fixed high dose and Full age dosing

1. **Fixed** dosage at 75% of energy
2. **Full-age dosing**, $5 \text{ mC} \times \text{age}$, averaging about 2.5 times threshold in bitemporal ECT

Richard Abrams and Conrad M Swartz, Illinois

- Abrams R, Swartz CM, Vedak C. Antidepressant effect of right versus left unilateral electroconvulsive therapy. *Arch Gen Psychiatry* 1991;48:746-8
Half age method for bitemporal ECT

- We examined an energy estimate for bilateral ECT at half the patient’s age
- Required only one stimulation
- Increments of 10% when motor seizure duration was less than 30 sec
- All patients recovered (in their first group, n=35)

The unilateral-bilateral controversy

- The relative efficacy of unilateral right ECT and bilateral ECT continues to be a source of controversy
- At least 35 clinical trials. The majority failed to observe significant differences
- Traditionally, the dose has been kept the same for all patients, regardless of modality

Harold A. Sackeim, P. Decina, M. Kanzler, B. Kerr, S. Malitz. New York

*Effects of electrode placement on the efficacy of titrated, low-dose ECT*

*Am J Psychiatry 1987;144:1449-66*
Dose titration method

- Low titrated threshold dose
- Bilateral markedly superior
- Dose in excess of seizure threshold may contribute, particularly with unilateral
- The generalized seizure may be necessary, but not sufficient

Harold A Sackeim et al. New York
"Effects of electrode placement on the efficacy of titrated, low-dose ECT"
Am J Psychiatry 1987;144:1449-66
Stimulus dose and electrode placement

800 mA
1.5 ms
20-140 Hz
Max 2 s

RUL threshold (86 mC)

BT threshold

(212 mC)

RUL 2.5 × (175 mC)

BT 2.5 × (321 mC)

800 mA
1.5 ms
20-140 Hz
Max 4 s

RUL 1.5 × (132 mC)

RUL 2.5 × (173 mC)

RUL 6 × (349 mC)

BT 2.5 × (244 mC)
**TITRATED MODERATELY SUPRATHRESHOLD VS FIXED HIGH-DOSE RIGHT UNILATERAL ELECTROCONVULSIVE THERAPY**

William Vaughn McCall (NC), DM Reboussin, RD Weiner, HA Sackeim

*Arch Gen Psychiatry 2000;57:438-44*

![Graph showing % Responders for 2.25x threshold vs fixed dose 403 mC.](image)

- **Electrical dose (MECTA brief-pulse)**
- **2.25x threshold**
- **fixed dose 403 mC**

% Responders
TITRATED MODERATELY SUPRATHRESHOLD VS FIXED HIGH-DOSE RIGHT UNILATERAL ELECTROCONVULSIVE THERAPY

Willian Vaughn McCall (NC), DM Reboussin, RD Weiner, HA Sackeim

Arch Gen Psychiatry 2000;57:438-44

Electrical dose as a multiple of the seizure threshold (MECTA brief-pulse)

- 2.25x
- 3-5x
- 8-12x

Antidepressant odds ratio
TITRATED MODERATELY SUPRATHRESHOLD VS FIXED HIGH-DOSE RIGHT UNILATERAL ELECTROCONVULSIVE THERAPY

Willian Vaughn McCall (NC), DM Reboussin, RD Weiner, HA Sackeim

Arch Gen Psychiatry 2000;57:438-44

Electrical dose as a multiple of the seizure threshold (MECTA brief-pulse)

[Graph showing bar chart with data points for 2.25x, 3-5x, and 8-12x electrical dose, with corresponding global cognitive disturbance odds ratio]
Towards the **Modal** ECT Treatment

For most patients dose titration is unnecessary

- Right unilateral ECT $\approx 75\%$ of the device's maximal output
- Bilateral ECT in the middle third
- Bifrontal ECT probably about 50%

Charles H. Kellner, SC/NY

*Editorial: Towards the modal ECT treatment*

*J ECT 2001; 17:1-2*
Right unilateral vs Bifrontal vs Bitemporal

Far better to *take the bull by the horns* and give every patient a treatment that has the best chance of success:

- Maximum-dose unilateral ECT
- Age-based bifrontal ECT
- Half-age-based bitemporal ECT

and with no demonstrated long-term or persistent side effects.

*Richard Abrams, IL*

*Stimulus titration and ECT dosing:*

*Response to commentaries on stimulus titration and ECT dosing*

*J ECT 2002;18:14-5*
ELECTRODE PLACEMENTS
Bitemporal (BT)

Bifrontal (BF)

Left anterior right temporal (LART)

Right unilateral (RUL)

**RUL**: A common variation relocates the upper electrode backwards midway between the vertex and the occiput, over the parietal lobe. Probably most unilateral ECT in the United States is given with this variation. With its spacing wider it should be at least as effective.

*Conrad M Swarts 2009*

It stands to reason that side effect aggregation should be diminished by decreasing the repetition of any particular placement. **Why not rotate** among the four modern placements until the ECT course is concluded?

*Conrad M. Swartz*

High-dose unilateral ECT does not differ from moderate-dose bitemporal ECT in antidepressant efficacy but has a cognitive advantages on retrograde autobiographical memory.

The only study that favoured bitemporal ECT (although not statistically significant) in terms of autobiographical memory used right unilateral ECT at 8 × seizure threshold (McCall et al 2002). This indicates that there is no cognitive advantage in going beyond 6 × seizure threshold for right unilateral ECT.

Erik Kolshus, Ana Jelovac, Declan McLoughlin (Dublin)
Bitemporal v. high-dose right unilateral electroconvulsive therapy for depression:
a systematic review and meta-analysis of randomized controlled trials
Psychological Medicine 2017;47:518-30
Bifrontal vs Bitemporal and Right unilateral
Review and meta-analysis of 8 studies (n=617) 1993-2010

• Efficacy was equal between BF and BT ECT, and BF and RUL ECT
• Post-treatment MMSE score decline was less for BF than for BT ECT, but not less than for RUL ECT
• RUL ECT impaired Complex figure recall more than BF ECT
• BF ECT impaired word recall more than RUL ECT
• BF ECT has potential advantages, but requires better characterization

Ross A Dunne, Declan M McLoughlin
Systematic review and meta-analysis of bifrontal electroconvulsive therapy versus bilateral and unilateral electroconvulsive therapy in depression
Design for switch studies in non-responders

Unilateral non-response
- High-dose unilateral
- Bilateral

Bilateral non-response
- The same bilateral position
- High-dose RUL

Bilateral non-response
- The same bilateral position
- A different bilateral position
When the first 6-10 right unilateral ECT sessions have produced no improvement

Retrospective comparison

<table>
<thead>
<tr>
<th></th>
<th>Continued RUL (n = 34)</th>
<th>Switched to BT (n = 27)</th>
<th>$\chi^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Considerable improvement</td>
<td>19 (59%)</td>
<td>11 (41%)</td>
<td>0.84</td>
</tr>
<tr>
<td>No considerable improvement</td>
<td>15</td>
<td>16</td>
<td>NS</td>
</tr>
</tbody>
</table>

Since bilateral ECT may severely impair memory for weeks or months the patients should not be stressed by a change to this technique

Lizzy Sand Strømgren. Aarhus, Denmark

When the first 5-8 right unilateral ECT sessions have produced no response in older depressed patients

Randomized prospective comparison

<table>
<thead>
<tr>
<th></th>
<th>RUL ECT 5.5 × (n=13)</th>
<th>BT ECT 2.5 × (n=11)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in HAM-D, %</td>
<td>68</td>
<td>60</td>
<td>0.707</td>
</tr>
<tr>
<td>Remission, %</td>
<td>46 (6/13)</td>
<td>18 (2/11)</td>
<td>0.211</td>
</tr>
<tr>
<td>Response, %</td>
<td>62 (8/13)</td>
<td>64 (7/11)</td>
<td>0.999</td>
</tr>
<tr>
<td>MMSE change</td>
<td>1.5</td>
<td>-3.6</td>
<td>0.048</td>
</tr>
</tbody>
</table>

Older patients who fail to respond to moderate-charge [2.5 × threshold] RUL ECT may benefit from a switch to high-charge RUL ECT rather than BL ECT

Tew JD Jr, Mulsant BH, Haskett RF, Dolata D, Hixson L, Mann JJ. Pittsburg, USA
A randomized comparison of high-charge right unilateral electroconvulsive therapy and bilateral electroconvulsive therapy in older depressed patients who failed to respond to 5 to 8 moderate-charge right unilateral treatments

_J Clin Psychiatry 2002;63:1102-5_
INTERACTIONS BETWEEN PULSE WIDTH, PULSE FREQUENCY, STUMULUS DURATION, CHARGE, CURRENT and ELECTRODE PLACEMENT
Surprise!
Bitemporal ultrabrief (0.30 ms) inferior
Randomized controlled

Sackeim HA et al (NY)
Effects of pulse width and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy
Brain Stimulation 2008;1:71-83

MECTA
800 mA
Pulse frequency and train duration: ?
**Bitemporal ultrabrief** (0.1 ms) not quite so good as **brief** (1.5 ms) Prospective randomized

<table>
<thead>
<tr>
<th>Outcome (n=41)</th>
<th>Pulse Width 0.1 ms</th>
<th>Pulse Width ~1.5 ms</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in depression score</td>
<td>−8.1</td>
<td>−9.9</td>
<td>0.10</td>
</tr>
<tr>
<td>Pronounced improvement</td>
<td>13/21 (62%)</td>
<td>18/20 (90%)</td>
<td>0.10 &gt;p &gt; 0.05</td>
</tr>
<tr>
<td>Recovered</td>
<td>8/21 (42%)</td>
<td>13/20 (65%)</td>
<td></td>
</tr>
<tr>
<td>Number of treatments</td>
<td>7.3</td>
<td>6.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Konvulsator III, 700 mA. Elther ES, 2100 mA**

Cronholm B, Ottosson J-O
Stockholm, Sweden

*Ultrabrief stimulus technique in electroconvulsive therapy. II. Comparative studies of therapeutic effects and memory disturbances in treatment of endogenous depression with the Elther ES electroshock apparatus and Siemens Konvulsator III.*

*J Nerv Ment Dis* 1963;137:268-76
Bitemporal ultrabrief (0.25 ms) as good as brief (0.5 ms) Retrospective

Thymatron IV, 900 mA

<table>
<thead>
<tr>
<th>Outcome (n=65)</th>
<th>Pulse Width 0.25 ms</th>
<th>Pulse Width 0.5 ms</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in HAM-D</td>
<td>−20.1 (8.9)</td>
<td>−19.3 (9.7)</td>
<td>0.947</td>
</tr>
<tr>
<td>Response</td>
<td>14/19 (73.6%)</td>
<td>34/46 (75.6%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Remission</td>
<td>8/19 (42.1%)</td>
<td>21/46 (46.6%)</td>
<td>0.794</td>
</tr>
</tbody>
</table>

Niemantsverdriet L, Birkenhäuser TK, van den Broek WW
Rotterdam, The Netherlands
The efficacy of ultrabrief-pulse (0.25 millisecond) versus brief-pulse (0.50 millisecond) bilateral electroconvulsive therapy in major depression
J ECT 2011;27:55-8
<table>
<thead>
<tr>
<th>Author, year</th>
<th>El plac</th>
<th>Efficiency by threshold↓ &amp; clinical response</th>
<th>&gt; = better than</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swartz &amp; Larson 1989, USA</td>
<td>BT</td>
<td>Duration↑ 2 s &gt; 1 s (2 s with 0.75 ms/60 Hz or 1.5/30 &gt; 1 s with 1.5 /60)</td>
<td></td>
</tr>
<tr>
<td>Isenberg et al 1996, USA</td>
<td>BT, RUL</td>
<td>Duration↑ and Width↓ until 8 s/0.5 ms &gt; 2 sec/1 ms</td>
<td></td>
</tr>
<tr>
<td>Devanand et al 1998, USA</td>
<td>BT</td>
<td>Duration↑ &gt; Frequency↑ (1→3.5 s/30 Hz &gt; 40→140 Hz/0.75 s)</td>
<td></td>
</tr>
<tr>
<td>Swartz CM &amp; Manly 2000, USA</td>
<td>LART</td>
<td>Width↓ 0.5 ms &gt; 1 ms (0.5 ms/30 or 60 Hz &gt; 1 ms/30 or 60 Hz)</td>
<td></td>
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<tr>
<td>Chanpattana et al 2000, Thai</td>
<td>BT</td>
<td>Width↓ Duration↑ lower threshold in 79%</td>
<td></td>
</tr>
<tr>
<td>Andrade et al 2002, India</td>
<td>rats</td>
<td>Duration↑ &gt; Amplitude↑ or Frequency↑</td>
<td></td>
</tr>
<tr>
<td>Sudha et al 2003, India</td>
<td>rats</td>
<td>Width↓ 0.6 ms &gt; 2.0 ms. Frequency↑ 100 Hz &gt; 30 Hz</td>
<td></td>
</tr>
<tr>
<td>Girish et al 2003, India</td>
<td>BT</td>
<td>Frequency↓ &gt; ↑ (50 pps/0.5→4.5 s &gt; 200 pps/0.125→1.125 s) (charge↓)</td>
<td></td>
</tr>
<tr>
<td>Kotresh et al 2004, India</td>
<td>RUL</td>
<td>Frequency↓ &gt; ↑ Response ↔ (RCT n=40) (charge↓)</td>
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<tr>
<td>Sackeim et al 2008, USA</td>
<td>BT, RUL</td>
<td>Width↓ 0.3 ms &gt; 1.5 ms. Response BT 0.3 ms↓ RUL 0.3 = RUL 1.5 = BT 1.5</td>
<td></td>
</tr>
<tr>
<td>Roepke et al 2011, Germany</td>
<td>RUL</td>
<td>Frequency↓ 40 Hz &gt; 100 Hz → Response↑ (RCT n=40)</td>
<td></td>
</tr>
<tr>
<td>Andrade on Roepke et al 2011</td>
<td>BT</td>
<td>Frequency↓ + Duration↑ ± charge↑</td>
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<tr>
<td>Ravishankar et al 2013, Ind</td>
<td>BT</td>
<td>Frequency↓/Duration↑ 50 pps/9 s &gt; 125 pps/3.6 s Response↑ (n=1) (540 mC)</td>
<td></td>
</tr>
<tr>
<td>Thirthalli et al 2017, India</td>
<td>BT, BF,RUL</td>
<td>Frequency↓/Duration? 50 pps &gt; 125 pps Response↑ (n=10) (charge?)</td>
<td></td>
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<tr>
<td>Andrade on Thirtalli 2018, India</td>
<td>BT, BF</td>
<td>Lower pulse frequency or longer stimulus duration?</td>
<td></td>
</tr>
<tr>
<td>Thanki et al 2018, India</td>
<td>BT, BF</td>
<td>Lower pulse frequency, not longer stimulus duration (however, somewhat)</td>
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</table>
### Unsuccessful seizure with 125 pps (BT)

<table>
<thead>
<tr>
<th>Session</th>
<th>Charge (mC)</th>
<th>Train duration (s)</th>
<th>Motor seizure (s)</th>
<th>Charge (mC)</th>
<th>Train duration (s)</th>
<th>Motor seizure (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>180</td>
<td>1.2</td>
<td>0</td>
<td>540</td>
<td>9.0 (+150%)</td>
<td>47</td>
</tr>
<tr>
<td>2</td>
<td>360</td>
<td>2.4</td>
<td>0</td>
<td>540</td>
<td>9.0 (+150%)</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>480</td>
<td>3.2</td>
<td>0</td>
<td>540</td>
<td>9.0 (+150%)</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>540</td>
<td>3.6</td>
<td>15-17-0</td>
<td>540</td>
<td>9.0 (+150%)</td>
<td>26</td>
</tr>
</tbody>
</table>

### Successful seizure with 50 pps (BT) (-60%)

<table>
<thead>
<tr>
<th>Session</th>
<th>Charge (mC)</th>
<th>Train duration (s)</th>
<th>Motor seizure (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>540</td>
<td>9.0 (+150%)</td>
<td>47</td>
</tr>
</tbody>
</table>

### Patient Details

<table>
<thead>
<tr>
<th>Pat. No</th>
<th>Age</th>
<th>Sex</th>
<th>Electrode placement</th>
<th>Number of sessions with 125 pps</th>
<th>Electrode placement</th>
<th>Number of sessions with 50 pps (-60%)</th>
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<tbody>
<tr>
<td>1</td>
<td>45, M</td>
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<td>BF</td>
<td>4</td>
<td>BF</td>
<td>9</td>
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<tr>
<td>2</td>
<td>59, M</td>
<td></td>
<td>BT</td>
<td>4</td>
<td>RUL</td>
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<tr>
<td>3</td>
<td>59, F</td>
<td></td>
<td>BF</td>
<td>6</td>
<td>BF</td>
<td>8</td>
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<td>4</td>
<td>44, F</td>
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<td>BT</td>
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<td>5</td>
<td>49, F</td>
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<td>BT</td>
<td>8</td>
<td>BT</td>
<td>10</td>
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<tr>
<td>6</td>
<td>71, M</td>
<td></td>
<td>RUL,BF,BT</td>
<td>4</td>
<td>BF</td>
<td>7</td>
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<tr>
<td>7</td>
<td>52, M</td>
<td></td>
<td>BF</td>
<td>11</td>
<td>BF</td>
<td>4</td>
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<td>8</td>
<td>62, M</td>
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<td>BF</td>
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<td>9</td>
<td>71, M</td>
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<td>BF</td>
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<td>10</td>
<td>54, F</td>
<td></td>
<td>BT</td>
<td>2</td>
<td>BT</td>
<td>4</td>
</tr>
</tbody>
</table>
Facilitating electroconvulsive therapy seizure induction: Lower pulse frequency or longer stimulus duration?
Chittaranjan Andrade. *Brain Stimulation* 2018;11/1:244

If stimulus duration was unchanged, implying total charge was reduced, lowering pulse frequency reduced the threshold.
If stimulus duration was increased to compensate for the reduced pulse frequency, then it is a moot point [a matter of opinion] whether eliciting an adequate seizure resulted from reduced pulse frequency or increased stimulus duration.

Lower pulse frequency, and not longer stimulus duration, helps reduce seizure threshold in ECT

Thanki MV ... Gangadhar BN. *Brain Stimulation* 2018;11/3:656-7

<table>
<thead>
<tr>
<th>Pat. No</th>
<th>Age, Sex</th>
<th>Electrode placement</th>
<th>Last unsuccessful seizure with 125 pps and charge rate 150 mC/s</th>
<th>First successful seizure with 50 pps and charge rate 60 mC/s (-60%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Charge (mC)</td>
<td>Train duration (s)</td>
</tr>
<tr>
<td>11</td>
<td>37, M</td>
<td>BT</td>
<td>540</td>
<td>3.6</td>
</tr>
<tr>
<td>12</td>
<td>46, F</td>
<td>BF</td>
<td>480</td>
<td>3.2</td>
</tr>
<tr>
<td>13</td>
<td>39, F</td>
<td>BF</td>
<td>540</td>
<td>3.6</td>
</tr>
<tr>
<td>14</td>
<td>53, F</td>
<td>BF</td>
<td>480</td>
<td>3.2</td>
</tr>
</tbody>
</table>
Reducing **frequency** and/or increasing stimulus **duration**

Towards Scandinavian Konvulsator-long pulse-train, or longer? 😊

Below 0.5 msec, within 8 seconds, particularly high frequency is necessary. This may degrade efficiency by 'stimulus crowding'

**Swartz & Manly 2000**

**Increasing current**

Stimulus dose in ‘volume of seizure foci’ is proportional to charge \( \times \) **current cubed.** Therefore, 900-mA are substantially more effective than 800 mA, giving \( \sim 50\% \) higher seizure foci dose. Higher current is **desirable with ultrabrief ECT.**

**Swartz 2006, 2011**

---

Charge rate (mC/s) = 2 \( \times \) frequency(Hz) \( \times \) pulse width (ms) \( \times \) current (A)
Phern-Chern Tor, A Bautovich, M-J Wang, D Martin, SB Harvey, Colleen Loo
Sidney/Singapore

A Systematic review and meta-analysis of brief versus ultrabrief right unilateral electroconvulsive therapy for depression

<table>
<thead>
<tr>
<th>Efficacy</th>
<th>Effect size</th>
<th>P</th>
<th>Remission %</th>
<th>P</th>
<th>NNT</th>
<th>No of sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 RCTs + 2 non-RCTs</td>
<td>1.0-1.5 ms &gt; 0.3 ms</td>
<td>0.25</td>
<td>.004</td>
<td>45 v 34</td>
<td>.045</td>
<td>12</td>
</tr>
<tr>
<td>The 4 RCTs only</td>
<td>1.0-1.5 ms ≥ 0.3 ms</td>
<td>.121</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

J Clin Psychiatry 2015;76:e1092-8
Forest plots of efficacy and cognitive tests for brief pulse versus ultrabrief pulse RUL ECT in depression at end of acute ECT course

---

**Retrograde memory**
- Loo 2014
- Mayur 2013
- Sackeim 2008
- Spaans 2013
- Subtotal ($I^2 = 36.3\%, P = .179$)

**Anterograde memory (learning)**
- Loo 2014
- Subtotal ($I^2 = 32.8\%, P = .222$)

**Anterograde memory (delayed recall)**
- Loo 2014
- Sackeim 2008
- Subtotal ($I^2 = 0.08\%, P = .546$)

**Anterograde memory (learning)**
- Galletly 2013
- Sackeim 2008
- Subtotal ($I^2 = 0.0\%, P = .444$)

---

Overall ($I^2=0.0\%, P=0.473$)

---

Favors Brief  Favors Ultrabrief
UBP ECT should not be the standard of care. UBP ECT should be considered in patients in whom avoiding cognitive side effects, even temporary ones, is of primary importance.

- if, in a given patient, a “safer” technique that results in less favorable effects of ECT is selected, the burden of side effects might be heavier.

- a study comparing UBP ECT with the widely used “standard” pulse of 0.5 msec, rather than 1 msec.
### Initial seizure threshold for different pulse width in right unilateral ECT

<table>
<thead>
<tr>
<th>Author, year</th>
<th>0.3 ms</th>
<th>0.5 ms</th>
<th>–</th>
<th>1.0 ms</th>
<th>–</th>
<th>1.5 ms</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loo et al 2007</td>
<td>28 (14)</td>
<td></td>
<td></td>
<td>78 (42)</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Rosa et al 2013</td>
<td>36 (15)</td>
<td>40 (15)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Sackeim et al 2008</td>
<td>22 (8)</td>
<td></td>
<td></td>
<td></td>
<td>70 (27)</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Sienart et al 2009</td>
<td>38 (25)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spaans et al 2013</td>
<td>23 (10)</td>
<td></td>
<td></td>
<td>62 (21)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- might be a **continuum** of increasing efficacy and adverse effects with pulse width
- seizure **thresholds** does not differ between 0.3 and 0.5 ms
- the **number** of treatments in a course with 0.5 ms resembles UB studies
- **0.5 ms** may be considered **ultrabrief**
CASBAS - Clinical and seizure based stimulation

RUL ultrabrief 0.25 v brief 0.5 ms – naturalistic comparison

<table>
<thead>
<tr>
<th></th>
<th>Brief</th>
<th>Ultrabrief</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>162</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>Age at first session</td>
<td>57±14</td>
<td>55±15</td>
<td></td>
</tr>
<tr>
<td>No of sessions</td>
<td>11</td>
<td>13</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean charge per session, mC</td>
<td>444±175</td>
<td>517±159</td>
<td>0.001</td>
</tr>
<tr>
<td>Patients with dose increase %</td>
<td>86</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>Sessions per series with dose increase</td>
<td>3.0</td>
<td>3.7</td>
<td>0.009</td>
</tr>
<tr>
<td>Restimulation %</td>
<td>6.9</td>
<td>6.4</td>
<td></td>
</tr>
<tr>
<td>Switch to LART, %</td>
<td>36</td>
<td>52</td>
<td>0.049</td>
</tr>
</tbody>
</table>

«UBP was a less efficient stimulation than BP»
«Strong clinical improvement in both groups»

Isabelle Brunner and Michael Grözinger (Aachen, Germany)
Brief vs. ultrabrief pulse ECT: focus on seizure quality. Eur Arch Psychiatry Clin Neurosci 2018;268:831-8
Right unilateral ultrabrief pulse ECT (0.25/0.30 ms) combined with venlafaxine, is a rapidly acting and highly effective treatment option for depressed geriatric patients, with excellent safety and tolerability. Response 70%, remission 62%, non-remission 10%, drop-out 28%.

Charles H Kellner et al, New York

*Right unilateral ultrabrief pulse ECT in geriatric depression: Phase 1 of the PRIDE (Prologing Remission In Depressed Elderly) study*

RUL 0.5 ms age, male +5%/female -5%
Age 74. Response 68%, remission 39%
18% increased charge: 366→409 mC

BF 0.5 ms half-age, male +5%/female -5%
Age 76. Response 64%, remission 51%
86% increased charge: 191→356 mC

RUL 0.5 ms age, male +5-10%/female -5-10%
Highly resistant bipolar depression
Age 48. Response 74%, remission 35%
Charge 244 mC

Bjølseth TM et al. J Affect Disord 2015;175:8-17

Kessler U et al 2010. BMC Psychiatry 2010;10:
Epub date 2010/02/25. Schoeyen H, Kessler U et al.
Am J Psychiatry 2015; 172:41-51
MONITORING
# Seizure parameters and outcome – correlations and predictive value

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Seizure duration</th>
<th>EEG</th>
<th>EMG</th>
<th>Short time to high ictal slow waves</th>
<th>Regularity Patterning Stereotypy</th>
<th>(Mid)ictal slow wave amplitude</th>
<th>Inter-hemispheric coherence</th>
<th>Postical suppression</th>
<th>Peak heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Krystal et al 1992/93/95/96/98* (US)</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Nobler et al 1993* (US)</td>
<td>No</td>
<td>No</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>McCall, Farah 1995 (US)</td>
<td>Neg</td>
<td>Neg</td>
<td>Pos</td>
<td>Pos</td>
<td>No</td>
<td></td>
<td></td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Hrdlicka et al 1996 (CZ)</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Folkerts 1996 (D)</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Suppes et al 1996 (US)</td>
<td></td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Gangadhar et al 1997/98/99* (IND)</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Krystal et al 2000 (US)</td>
<td></td>
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<td></td>
<td>Pos</td>
<td></td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Nobler et al 2000** (US)</td>
<td></td>
<td></td>
<td></td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Frey et al 2001 (A)</td>
<td>Neg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Swartz 2002 (US)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pos¹</td>
<td></td>
</tr>
<tr>
<td>Perera et al 2004 (US)</td>
<td>Pos</td>
<td></td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Kho et al 2004** (NL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos²</td>
<td></td>
</tr>
</tbody>
</table>

Pos Neg No: positive, negative and no correlation to outcome. Red: Predictive value  *Manual and computer  **Computer

¹ With anticholinergic  ² Seizure energy index
### Seizure parameters and outcome – correlations and predictive value

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Seizure duration</th>
<th>Short time to high ictal slow waves</th>
<th>Regularity Patterning Stereotypy</th>
<th>(Mid)ictal slow wave amplitude</th>
<th>Interhemispheric coherence</th>
<th>Postical suppression</th>
<th>Peak heart rate</th>
<th>Postictal reorient. time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azuma et al 2007 (J)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos^3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kimball et al 2009* (US)</td>
<td>No</td>
<td>No</td>
<td>Pos</td>
<td>No</td>
<td></td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Combination predictive:</strong> EEG seizure duration + EEG regularity + postictal suppression + age + gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azuma et al 2011** (J)</td>
<td></td>
<td></td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td>Pos</td>
<td>Neg^3</td>
<td></td>
</tr>
<tr>
<td>Abhishekh et al 2013** (IND)</td>
<td></td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos^4</td>
<td></td>
</tr>
<tr>
<td>Bjølseth et al 2016 (N)</td>
<td></td>
<td></td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos</td>
<td></td>
</tr>
<tr>
<td>Minelli et al 2016* (I)</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td>Pos^5</td>
<td>Pos^1</td>
<td></td>
</tr>
<tr>
<td><strong>Seizure Quality</strong></td>
<td>1/0</td>
<td>1/0</td>
<td>1/0</td>
<td>1/0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gálves et al 2017 (AUS)</td>
<td>No</td>
<td>No</td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos^6</td>
<td></td>
</tr>
<tr>
<td>Kranaster et al 2018** (D)</td>
<td>Pos</td>
<td></td>
<td>Pos</td>
<td>Pos</td>
<td></td>
<td></td>
<td>Pos^4</td>
<td></td>
</tr>
<tr>
<td><strong>Seizure Quality Index (SQI)</strong></td>
<td>1/0</td>
<td>1/0</td>
<td>1/0</td>
<td>1/0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brunner, Grösinger* (D) 2018 (D)</td>
<td>1/0</td>
<td></td>
<td>1/0</td>
<td>1/0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Pos Neg No: positive, negative and no correlation to outcome

Red: Predictive value

*Manual and computer
**Computer

^1 With anticholinergic
No anticholinergic
Anticholinergic not mentioned
Postictal suppression index Predictive of threshold increase
## Seizure quality measures

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BT, 4. and 6. session</td>
<td>RUL, 2. session</td>
<td>RUL, all sessions</td>
</tr>
</tbody>
</table>

**Rating:** 1 or 0 for each of five items

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>EMG seizure duration, s</td>
<td>≤ 30/55</td>
<td>≥ 20</td>
<td></td>
</tr>
<tr>
<td>EEG seizure duration, s</td>
<td>&gt; 25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMG/EEG concordance</td>
<td>≤ 0.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Midictal max amplitude, uV</td>
<td>≥ 180</td>
<td>≤ 200/215</td>
<td>&gt; 150</td>
</tr>
<tr>
<td>Coherence/synchronisity, %</td>
<td>± adequate</td>
<td>≤ 98</td>
<td>&gt; 85</td>
</tr>
<tr>
<td>Peak heart rate, b/min</td>
<td>≥ 120</td>
<td>≤ 150/155</td>
<td>&gt; 110</td>
</tr>
<tr>
<td>Postictal suppression, %</td>
<td>≥ 80</td>
<td></td>
<td>good</td>
</tr>
</tbody>
</table>

| SQ Good            | 3.5–5.0                  | SQI ≤ 2 (< 65 yrs)       | ≥ 3 - increase dose if not improved at 6th |
| SQ Medium          | 1.8–3.4                  | predictive of non-response/remission |                                  |
| SQ Poor            | 0–1.7                    | 38.5% responders         | ≤ 2 - restimulate                 |

Where is Laura?
Postictal Reorientation Time (PRT) or Time to Recover Orientation (TRO)*

- Longer PRTs at the first and third treatments **predicted** a more rapid decline and a lower end-point in continuous HRSD$_{17}$ scores
- None of the patients who recovered from disorientation in **less than 5 min** met the remission criterion
- All patients with PRTs of **35 min or more** achieved remission after 12 treatments or less

Tor Magne Bjølseth, Engedal K, Benth JS, Bergsholm, Strømnes Dybedal G, Gaarden TL, Tanum L

*Speed of recovery from disorientation may predict the treatment outcome of electroconvulsive therapy (ECT) in elderly patients with major depression. J Affective Disord 2016;190:178-86*

Stimulus intensity and electrode placement

Postictal reorientation time (PRT) - minutes

RUL threshold (86 mC)

11 ± 7

RUL 2.5 × (175 mC)

21 ± 11

(212 mC)

BT threshold

38 ± 21

41 ± 11

BTCRUL 1.5 × (132 mC)

17 ± 8

RUL 2.5 × (173 mC)

19 ± 11

RUL 6 × (349 mC)

31 ± 13

BT 2.5 × (244 mC)

46 ± 22

800 mA
1.5 ms
20-140 Hz
Max 2 s

Baseline | After 6th Treatment | Immediately after Last Treatment | 1 Week after Last Treatment

800 mA
1.5 ms
20-140 Hz
Max 4 s

Baseline | After Sixth Treatment | Immediately After Last Treatment | 1 wk After last Treatment

Stimulus intensity and electrode placement

RUL threshold (86 mC)

11 ± 7

RUL 2.5 × (175 mC)

21 ± 11

(212 mC)

BT threshold

38 ± 21

41 ± 11

800 mA
1.5 ms
20-140 Hz
Max 2 s


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;57:425-34.
TITRATED MODERATELY SUPRATHRESHOLD VS FIXED HIGH-DOSE RIGHT UNILATERAL ELECTROCONVULSIVE THERAPY

Willian Vaughn McCall, DM Rebuosin, RD Weiner, HA Sackeim

Arch Gen Psychiatry 2000;57:438-44

Postictal reorientation time (PRT) - minutes

<table>
<thead>
<tr>
<th>Electrical dose as a multiple of the seizure threshold (MECTA brief-pulse)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.25x</td>
</tr>
<tr>
<td>14±12</td>
</tr>
<tr>
<td>3-5x</td>
</tr>
<tr>
<td>18±15</td>
</tr>
<tr>
<td>8-12x</td>
</tr>
<tr>
<td>27±17</td>
</tr>
</tbody>
</table>

Antidepressant odds ratio
The Scandinavian liminal titration method

**STIMULATION**
1. Unilateral nondominant with long electrode distance
2. Stimulus duration not prefixed
3. Current interrupted as soon as the clonic contractions shift to the tonic phase, most readily observed in the plantar extension of the great toes

**OBSERVATION**
1. The convulsion usually **ends by degrees**, succeeded by a **comatose** stage from which consciousness is **gradually regained**
2. The dissociative convulsion is followed by **early awakening**
3. The clonic form has no tonic phase, ends abruptly and simultaneously in the whole body, last **only 10 to 20 s**
   
Both have **lower** antidepressant efficacy

---

**Giacomo d’Elia** (1934-), **Jan-Otto Ottosson** (1925-), Gothenburg, **Lizzie Sand Strømgren** (1928-2007), Aarhus

Present Practice of Electroconvulsive Therapy in Scandinavia. *Arch Gen Psychiatry* 1983;40:577-81
Is it time for a return to the Scandinavian liminal titration method?

Börje Cronholm (1913-83)
Jan-Otto Ottosson 1925-
Lizzie Sand Strömgren 1928-2007
Giacomo d’Elia 1934-

d’Elia G, Ottosson J-O, Sand Strömgren L
Present Practice of Electroconvulsive Therapy in Scandinavia
Arch Gen Psychiatry 1983;40:577-81
Adjusting dose to clinical response

Measure clinical response to each treatment and adjust the dose accordingly. This direct method has, remarkably, never been tested. Contrary to popular belief, effects often become manifest quite early – the first week.

- Depression scale 24 h following each ECT
- Sleep: number of hours of each night. REM-sleep
- Weight and food intake daily
- Motor activity level. Motor tapping speed
- Reaction time (and concentration - trail-making test A and B)
- Body temperature (Increased oral temperature correlated to response: Chen, Malmstrom, Nasrallah 2018)

Richard Abrams (Chicago)

*Stimulus titration and ECT dosing. J ECT 2002;18:3-9*
Pupillary response

- Time to Return Of Pupillary response to Light (ROPL) in sec is longer than motor and EEG seizure duration - 34 v 47 v 60 s. 
  *Venkataramaiah et al 2018*

- Constriction ratio - pupillary enlargement. 
  *Shirozu, Murayama, Yamaura 2019*

- Venkataramaiah S ... Thirthalli J (Bangalore). Duration of Pupillary Unresponsiveness to Light: A Physiological Adjunct to Electroencephalography and Motor Seizure Duration Monitoring During Electroconvulsive Therapy. *J ECT 2018;34:e61-64.

Still confused, but on a higher level?

per.bergsholm@gmail.com