ELECTRO CONVULSIVE THERAPY: THE CONCEPT OF DOSE

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Electroconvulsive Therapy (ECT) is simply too effective to ignore in cases without an alternative or to resign to as a treatment of last resort. While ECT is synonymous with psychiatry it is unfamiliar when not routine in most cases. That electricity is used to induce a therapeutic seizure is a complicated factor since there is familiarity with the concept of medication dose but not with the concept of electrical ECT dose. Unfamiliarity with the concept of ECT dose may negatively affect its use and familiarity with the concept may improve the general attitude towards ECT practice.

THE ARTICLE WILL OUTLINE THE CONCEPT OF ECT ELECTRICAL DOSE IN MILLI-COULOMBS (MC) AS ANALOGOUS TO MEDICATION DOSE IN MILLIGRAMS (MG). FOR ILLUSTRATIVE PURPOSES REFERENCE IS MADE TO THE *THYMATRON SYSTEM IV* DEVICE USED IN SOUTH AFRICA.

A colleague reported that a family member from an engineering background asked *"What is the ECT dose given?"* Firstly one answer could be the frequency of ECT per week where usually twice a week is done to minimize side effects (three a week being used for a more rapid effect) or the total number of treatments until the treatment plateau is reached. But secondly the more relevant dose question is the actual dose for an individual ECT treatment. The ECT dose readout on the *Thymatron System IV* is as a % where 100% is 504 mC where the mC indicates total charge of electrical current. Electrons in an electrical current flow like water and in this analogy the total volume is up to 504 mC (100%) spread over and up to the full 8 seconds. If electrical current is analogous to water flowing in a drip, then like an IV drip the restricted total possible current is 504 mC in the IV fluid bag. The limitation of the total current is analogous to the limited current of an electric fence compared to unlimited current in the case of the electrical mains. The total current is fixed to a low 0,89A. Further this current dose is delivered in a physiological way linked to the physiology of the excitable tissue and the qualities of the dose are further outlined.

The device gives the dose not as a fluctuating sine wave but in brief bursts of electrical activity which is both more effective physiologically and also results in fewer side effects. More effective physiologically is a large number of brief stimuli per second (such as 20 per second) which is possible by limiting the time for each stimulus (to 0,5ms).

The original sine wave with a pulse width of 8.33-10ms alternating current induced unconsciousness but the excess energy (as only the peak had an effect) contributed to side effects. Since anaesthesia became available there was a change to lower amplitude and shorter pulse (1ms and 0,5ms) width with fewer side effects. Rectangular pulses with a brief pulse width (0,5ms - 2ms) reduced the dose required (with a lower seizure threshold) with

fewer side effects and maintained efficacy. Electrical silence between the pulses are much longer than the pulses when current briefly flows.

The current is used to start a synchronous electrical discharge, analogous to a Mexican wave in a football stadium, in the brain excitable tissue. The muscles of the jaw will however also be stimulated directly (not through the neuromuscular junction) irrespective of suxamethonium use, causing a supra-physiological jaw muscle contraction, so the teeth and especially crowns must be protected during the treatment stimulus.

The body has two kinds of excitable tissue: muscle to move and nervous tissue to decide where to move to. Animals have more sodium than plants and ions in solution are the basis for the electrical conduction of water and are involved across cell membranes in the physiology of electrical action potentials. Action potentials are based on ion channel polarity and there is a physiological range which is utilized with respect to the ECT stimulus. This means that the electrical stimulus is not constant but intermittent. There are more gaps between the stimuli than electrical stimuli while the ECT treatment is given.

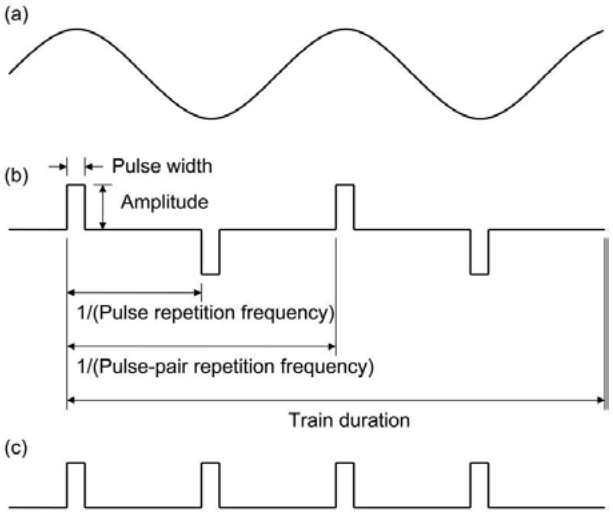

Diagram 1: Examples of ECT stimulus waveforms: *(a) sine wave, (b) bidirectional rectangular pulses with indicated parameter definitions and gaps between stimuli, (c) unidirectional rectangular pulses*

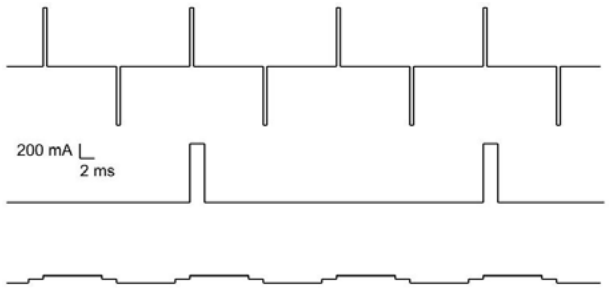

Diagram 2: Three ECT stimulus trains all with a total charge of 3.2 mC and widely different parameters: *[Vertical axis: current in milli-amps; Horizontal axis: duration in milli-seconds; total dose is the area under the curve]*

Top - Bidirectional: 3.2mC = 0,8A x 0,5ms x 2 x 100Hz x 8pulses
Middle - Unidirectiona 3.2mC = 0,8A x 2ms x 25Hz x 2pulses
Bottom - Bidirectional 3.2mC = 0,05A x 8ms x 2 x 50Hz x 8pulses

The time per second with the intermittent electrical stimulus flowing is shorter overall than the time with current not flowing. That is analogous to a drip being switched on and off 100 or 160 times a second (50 or 80 Hz; double the readout frequency since it is a biphasic wave).

A shorter duration with respect to a narrower pulse width (the duration of each brief stimulus) has been shown to reduce side effects. The previous *Thymatron System DG* delivered a pulse width of 1ms while the current *Thymatron System IV* delivers as standard a 0,5ms pulse width (with the option of a 0.25 or 0.3 ms pulse width, with the latter having some favour).

PHYSIOLOGICALLY THE LOWER LIMIT OF USEFULNESS BASED ON NEURONAL PHYSIOLOGY IS 0.2MS AS A PULSE-WIDTH.

An ECT treatment stimulus is therefore an intermittent electrical current with a physiological effect sufficient to trigger the synchronous cortical electrical discharge (analogous to a soccer stadium Mexican wave, which must circle the soccer stadium) for a duration of 25 seconds.

The total volume of current in the analogous drip bag is therefore limited by the % setting of the dose. This conceptually makes ECT closer to a low current electrical fence which is intermittent. An ECT device intermittent charge is limited to a total current of 0.9A up to a total volume of 504 mC whereas a kettle is a constant 15A with an unlimited total current in mC.

The total charge is described by the formula:

Charge (as a % of 504mC) = 0.5ms x Hz x 2 x duration in seconds x 0.9A

Dose = Pulse width in milli-seconds x Hz (Hertz or number per second) x 2 (as a biphasic wave) x Time in seconds x Amps in mC.

ALL ARE ADJUSTABLE EXCEPT THE FIXED AMPS WHILE THE PULSE WIDTH IS SPECIFIED BY THE SPECIFIC PROGRAM CHOSEN. THE PULSE WIDTH AND FREQUENCY RANGES ARE BASED ON NEURO-PHYSIOLOGY TO MAXIMISE THE ELECTRICAL NEURONAL STIMULATION EFFECTS.

The equation describes the relationship between the different dose components. Changing one parameter determines changes and determines the others for a set dose. Many different parameters add up to the same total charge or dose. If the dose increases and the pulse width and Amps do not change then what changes is only the Hz frequency (per second) and the total duration (up to a maximum of 8 seconds).

The seizure threshold is lower for a shorter pulse width and low frequency. An increased dose automatically receives a higher frequency and the electrical device adjusts the parameters automatically according to the total dose to be given.

The best stimulus is therefore the lowest adequate dose to get an observed generalized bilateral seizure.

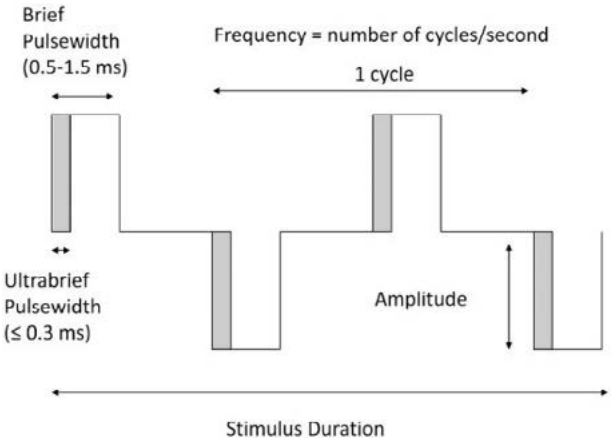

Diagram 3: Relationships between the dose parameters. *Dose (charge) = (current amplitude) x (pulse width) x 2 x (pulse pair frequency) x (train duration)*

In pharmacotherapy the dosage is described in mg

In ECT the summary of dose was the total energy later superseded by the total charge in mC

Dose (charge) = (current amplitude) x (pulse width) x 2 x (pulse pair frequency) x (train duration)

Two identical options for total dose with different parameters

50.4mC (10%) = 0,9A x 0,5ms x 2 x **10Hz** x **5.6s**
50.4mC (10%) = 0,9A x 0,5ms x 2 x **20Hz** x **2.8s**

50.4mC (10%) = 0,9A x **0,5ms** x 2 x 30Hz x **1.87s**
50.4mC (10%) = 0,9A x **0,25ms** x 2 x 30Hz x **3.73s**

Usually the low dose program with a pulse width of 0,5 milliseconds is selected, the program then adjusts the other parameters automatically.

7 automatic stimulus programs or adjust manually:

- DGx (previous Thymatrom DGx = 1ms pulse width);
- LOWEST, lowest charge rate;
- LOW 0,25 (varies frequency to maximise duration), above 50% frequency is 70-140Hz;
- LOW 0,5 (varies frequency to maximise duration);
- INTERMIT (intermittent bursts of 4 unidirectional quarter sine wave pulses repeated at 6hz) - no comparative studies;
- 2xLP, lowest possible pulse width 0,5-1ms;
- 2xDOSE

10% = 50.4mC = 0,9A x 0,5ms x 2 x 10Hz x 5.6s
20% = 100.8mC = 0,9A x 0,5ms x 2 x 20Hz x 5.6s
30% = 151.2mC = 0,9A x 0,5ms x 2 x 30Hz x 5.6s
40% = 201.6mC = 0,9A x 0,5ms x 2 x 30Hz x 7.47s
50% = 252mC = 0,9A x 0,5ms x 2 x 40Hz x 7s
60% = 302.4mC = 0,9A x 0,5ms x 2 x 50Hz x 6.72s
60% = 302.4mC = 0,9A x 0,5ms x 2 x 60Hz x 5.6s
60% = 302.4mC = 0,9A x 0,5ms x 2 x 70Hz x 4.8s
80% = 404.2mC = 0,9A x 0,5ms x 2 x 60Hz x 7.47s
100% = 504mC = 0,9A x 0,5ms x 2 x 70Hz x 8s

Electrical seizures stop when the subcortical structures are activated to result in cortical suppression by subcortical grey matter. This is probably the mechanism accounting for the efficacy of ECT and conversely the comparable lack of equivalent efficacy found for other brain stimulation procedures which has a more localised cortical effect.

Subcortical versus cortical activation is seen in the spike and wave decreasing frequency (slowing) in the second half of the seizure as the amplitude increases. This slowing and increasing amplitude is seen both with epileptic seizures and therapeutic ECT seizures and is associated with the termination of the seizure. This is usually abrupt with post-ictal electrical suppression, analogous to football stadium crowd fatigue after the Mexican wave. Seizure threshold correspondingly is then elevated with often a need to increase treatment dose through the ECT course.

THE ADEQUACY OF THE TREATMENT IS DEMONSTRATED BY PATIENT IMPROVEMENT IRRESPECTIVE OF ALL ELSE BUT THIS IS NOT ROUTINELY THE CASE AFTER A SINGLE TREATMENT.

Features of an adequate therapeutic seizure are then useful, indicated by the EMG/EGG having a of duration over 25 seconds (with the EMG often 10 seconds or so shorter than the EEG). A clear peak heart rate from the sympathetic response to a seizure. On the bilateral EEG a progression from rapid polyspike and to slower δ 3Hz spike and wave with post-ictal suppression.

A lot to think about in a short time but for the sake of brevity, as an aid a one-page summary is provided.

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ONE PAGE ECT PRACTICAL REGISTRAR ORIENTATION REFERENCE

Thymatron system IV: Constant current 0,9A, limited to 450V

Stimulus programs: DGx; LOWEST; LOW; LOW 0,5; INTERMIT; 2xLP; 2xDOSE

Dose (charge) = (current amplitude) x (pulse width) x 2 x (pulse pair frequency) x (train duration)

1. **CHECK INFORMED CONSENT.**
2. **SWITCH ON MACHINE: do not unplug the recording and treatment cables from the machine, the connections are vulnerable to damage if not inserted in the correct orientation.** To see current program: press flexi-dial button and keep depressed (to print out the current program: press **flexi-dial button** then **stop/start button**).
3. **CHECK PROGRAM SELECTED** Usually used is LOW 0,5ms pulse width program
4. **RECORDING CONNECTIONS (no EEG recording if attached incorrectly): Clean skin** sites for left and right EEG leads with **hibitane in alcohol** (or soap & water) or you will not get a reading due to skin resistance and the very low EEG voltages (ECG voltages are much higher) **AND** depending on the stick-on electrodes used, can put a very small drop of electrode gel (not ultrasound or lubricating gel as this does not contain ionic salts) under the stick-on EEG electrodes.

a. **CONNECT FIRST EEG PAIRED RED/BLACK RECORDING LEADS FOR LEFT HEMISPHERE**

b. **SECOND EEG RED/BLACK LEADS** (to check seizure

is bilateral) for right hemisphere. Apply these four EEG leads above EACH EYEBROW and over each MASTOID PROCESS (over bone behind the ear, not on the neck); with same bilateral red/black lead orientation (both foreheads black or red leads) for left and right hemispheres. This provides good contrast as the frontal areas are relatively high amplitude & the mastoid bone is relatively inactive electro-physiologically. Do not put one lead onto the L and R forehead as two prefrontal EEG leads cancel each other out, so harder to read.

c. **EMG:** brown, long to reach leg, requires an independent person to monitor. (Neutral on front of the tibia, other over calf muscle)
d. **ECG:** attach paired cardiac red/black leads 8cm apart above and below heart
e. **SINGLE GREEN "EARTH LEAD" TO A SHOULDER**
5. **THEN PRESS FAR LEFT YELLOW IMPEDANCE BUTTON** (below the readout screen) to start baseline (EEG and heart rate) and **immediately** release. When finished it will display **BASELINE (=OF EEG AND ECG)**
6. **CONNECT DISPOSABLE TREATMENT ELECTRODES TO THE TREATMENT CABLE**
7. **APPLY THE BI-TEMPORAL TREATMENT ELECTRODES (or right unilateral position (RUL) position),** use electrode/defibrillator gel to lower impedance over hair under the treatment electrodes
8. **PUSH YELLOW BUTTON AND KEEP PRESSING TO CHECK IMPEDANCE <3000 (0=short circuit; >3000= no connection)**
9. Can hold treatment electrodes in place (keep gel off fingers) during the treatment
10. **PRESS STOP/START BUTTON TO PRINT OUT A SHORT 5-10 SECOND STRIP** so that post ictal suppression can be checked visually afterwards.
11. **AS CLINICALLY INDICATED SET DOSE ON THE DIAL AS A%** in 5% increments of 504mC (100%), turn and then turn back to display % in mC); SEIZURE THRESHOLD DOSE TITRATION: 5/10/20/40/80/100 for <50 yrs (for >50yrs 10/20/40/80/100); HALF AGE DOSE TITRATION for bilateral start with half age % and full age % for RUL and titrate as needed. Can reset for 2x dose (200% = 1008mC) when only 10% dose increments are possible which limits the pulse width and frequency possible.
12. **ANAESTHETIC, limb isolation for EMG, HYPERVENTILATE (decreases seizure threshold)**
13. Insert teeth bite guard (or airway; gauze; rubber tubing etc), **SUPPORT JAW CLOSED** (anaesthetist) **/ RECHECK IMPEDENCE <3000**
14. **ADMINISTERING TREATMENT DOSE: keep pushing the TREATMENT YELLOW BUTTON (UNDER THE PLASTIC COVER) UNTIL the tone ENDS.** The full pulse width train duration is up to **8 seconds** and the button must be kept depressed THROUGHOUT, releasing the button early **STOPS** the stimulus train. AUDIBLE SEIZURE WILL THEN SOUND (volume on back of machine). The printout will run automatically, use start/stop button to STOP the printout when the seizure stops
15. **INDICATORS OF AN ADEQUATE SEIZURE: SYMPTOMATIC TREATMENT RESPONSE** irrespective of EEG record / facial flush / **PEAK HEART RATE SYMPATHETIC RESPONSE** to seizure / **EEG SEIZURE DURATION OF 25 SECONDS** or more (17s if propofol was used; etomidate or ketamine have longer seizures) / **EEG PROGRESSION FROM POLYSPIKE TO SLOWER δ 3Hz SPIKE AND WAVE; POSTICTAL SUPPRESSION INDEX >87%**
16. **DECIDE IF RESTIMULATION IS REQUIRED** (after at least 20s)
17. **TO REPRINT** (if paper runs out halfway: FLEXIDIAL→DATA OUT→REPRINT)
18. **COMPLETE THE MHCA form 48** & decide on DOSE for next treatment