

ECT Dosing by the Benchmark Method

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Abstract

Background: The methods used to select ECT stimulus dose have no basis in physiology and are incomplete. They are not related to the quality of the ECT seizure, such as its intensity or its generalization through the brain. These methods are not substantially individualized and do not guide the dose along the course. A rational system is described that does not have these shortcomings. **Method:** On the basis of the axioms that higher dose produces greater effect, and meaningful physiological measurements reflect efficacy, the principle to guide ECT dosing is that diminished physiological intensity indicates decreased treatment quality. **Results:** The corresponding strategy for dosing begins with a strong stimulus at the first ECT treatment. The measured resulting physiological effects should be intense, and these serve as benchmarks. At later treatments the electrical stimulus dose is gradually adjusted to approximate the lowest dose that produces physiological effects that are near these benchmarks. Smaller physiological effects suggest increase in stimulus dose. **Conclusions:** This method uses physiological measurements in a manner analogous to blood drug levels in pharmacotherapy. A strong first-ECT stimulus typically has a dose 3.5 to 4 times age with bilateral or 5 times age with unilateral electrodes at 0.5ms pulsewidth and 30-70 Hz; wider pulsewidths necessitate higher dosage. Recent studies suggest that peak seizure heart rate and several computer-processed EEG aspects are suitable physiological measurements to use in this method. The use of peak heart rate requires no special EEG equipment or EEG training (German J Psychiatry 2002; 5: 1-4)

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Introduction

In selecting the dose to use in electroconvulsive therapy (ECT) treatment, the goal is effectiveness and avoidance of overdose side-effects. The usual motivation to administer ECT is need for its efficacy. Although side-effects are only temporary and a secondary consideration, patient and staff morale are high when noticeable side-effects are rare. A rational method to set the stimulus dose should help to minimize side-effects.

The "Benchmark Method" is a rational method for ECT dosing. It accounts for the wide individual variations among patients, and it is based on the principle that higher electrical doses generally produce larger changes, including

physiological, therapeutic, and adverse effects. In other words, for suitably selected physiological measurements, physiology corresponds to the amount of therapeutic benefit. Generally, clinically effective ECT produces strong physiological effects, while weak physiological effects indicate weak treatment.

Accordingly, a goal for the ECT stimulus is to produce physiological effects of about the same size as accompany an effective ECT, for that same patient. These physiological effects are a representative, or proxy, for efficacy. In contrast, there is no relationship between the weakest possible ECT (i.e., seizure threshold) and effective ECT, and no reason for one. Similarly, there is no relationship between seizure threshold and a logical ECT dose, but only the absence of a relationship; a recent review describes the relevant details (Swartz 2001).

The Benchmark Method guides the ECT dose with physiological measurements, using ordinary equipment. In this method larger physiological effects are analogous to higher drug doses in pharmacotherapy, with more rapid response. With the Benchmark Method, values of suitable physiological effects that accompany an effective ECT represent its efficacy, and are goals for every ECT. The method begins by establishing personal benchmarks for physiological measurements, with each patient. The method is more complete when it includes several physiological effects that are at least partially independent of each other. Still, a single sensitive "target measurement" may suffice. In specific, the peak heart rate during the ECT seizure (peak HR) has shown clear sensitivity; patients who showed higher peak HR relative to their personal benchmark required fewer ECTs (Swartz 2000). The peak HR will be referred to as the target measurement to illustrate the method, but other physiological effects (e.g., EEG measurements) might sometimes be useful with it or instead. The Benchmark Method has four steps.

The Benchmark Method Step-by-step

1. At the first ECT a stimulus dose is selected to produce an intense seizure. For bilateral electrode placements such as bitemporal, bifrontal, or LART (Swartz, 1994) a dose (in mC) of 3.5 to 4 times age (%Energy or expected joules = 70-80% of age) usually suffices for this. This is because a dose of 2.5 times age virtually always induces seizure (Petrides and Fink, 1996), and small dose additions rapidly increase seizure intensity with bilateral ECTs. For unilateral placement the mC dose would be about 5 times age (%Energy = age). The first ECT is usually especially vigorous (Krystal et al., 1996), which makes useful benchmarks easier to obtain at ECT#1. The goal is not mere seizure occurrence, but vigor. This plan is opposite to giving a stimulus near seizure threshold to produce a weak seizure, per the "stimulus titration" method (Sackeim et al., 2000).

2. Measure baseline HR and peak HR during the seizure. Common digital ECG monitors and pulse oximeters display HR continuously, which facilitates this measurement. Some ECT instruments report peak HR. The peak HR at the first ECT becomes the initial benchmark. A peak HR that exceeds it at a later ECT supersedes it. In a recent study of 24 patients the benchmark HR over the course of ECT ranged from 121 to 190 bpm, with a median of 151 bpm (Swartz 2000). If peak HR is only 10 bpm above baseline, or less, there is a problem. Either the seizure is weak and unsuitable to produce benchmarks, or HR acceleration is blocked, pharmacologically or physiologically. Several medications diminish HR acceleration, e.g., the anesthetic propofol, beta-blockers, calcium channel blockers. If peak HR cannot rise much above baseline other physiological measurements should be used instead.

3. When using a type of bilateral ECT consider a lower dose at the second treatment. Dose reduction is a stronger consideration when potential adverse effects are more important than urgency; for such cases the mC dose with bilateral ECT might be decreased to about 2.5 times age (i.e., %Energy = half age). Dose reduction with unilateral ECT is a potential consideration for patients at high risk for problematic adverse effects, e.g., those with cerebrovascular disease.

4. At the second and following ECTs measure peak HR. If it is within 6 bpm of the benchmark the efficacy is probably maximal. When efficacy is maximal the dose is not too low, and a small dose decrease (25-50 mC) can be considered. If peak HR is 6 to 12 bpm below benchmark the efficacy is probably moderate; consider a small dose increase, e.g., by 25 mC. If peak HR is at least 12 bpm below benchmark, efficacy is probably low; consider a moderate dose increase, e.g., by 75 mC. If there are no signs of seizure consider a large dose increase, e.g., by 100-125 mC.

This fourth step is repeated with each ECT. It helps regulate dosage along the ECT course, that is, when to increase or decrease and by how much. About half of patients—particularly elderly men—show increasing seizure threshold along the course (Coffey et al., 1995); their dosage needs reconsideration repeatedly. The use of EEG measurements (instead of peak HR) is not completely understood, specifically the amount of change large enough to indicate a dose increase. Still, *prima facie* considerations suggest that a result within 5% of the benchmark is generally good, while a result more than 25% below the benchmark seems deficient. Conversely, if a useful dose increase does not elevate a specific physiological effect, measurement of that effect might have little value for that patient.

The steps are summarized in Table 1.

Table 1. Summary of Benchmark Method Steps

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| - At ECT #1 use a high-dose stimulus to produce a clearly effective treatment |
| - Take the resulting physiological measurement as the benchmark, e.g., peak seizure HR |
| - At later ECT sessions try to decrease the electrical dose, while maintaining the physiological effect near the benchmark, e.g., peak HR within 6 bpm of benchmark |
| - If the physiological effect falls substantially below the benchmark, increase the electrical dose. If the benchmark is surpassed it is superseded by the higher result |

Interpretation of Observations

Any sign of seizure weakness at the first ECT suggests that this ECT is not suitable to produce good benchmarks.

Common signs of weakness include little if any tonic motor activity, such as only clonic activity (Cronholm and Ottosson, 1960), motor duration under 18 sec (Swartz and Larson 1989), indistinct postictal EEG suppression (Nobler et al. 1993), and peak HR under 120 bpm (Swartz, 2000). Another sign of weakness is absence of high-amplitude low-frequency waves with superimposed high frequencies (Swartz, 1995), except when EEG electrodes are located symmetrically, e.g., above the two eyes. Unfortunately, this commonly-used symmetrical EEG placement causes cancellation of low-frequency waves. If at least one sign of seizure weakness occurs at the first ECT, consider increasing the dose by 75 mC and looking for new benchmarks.

To be useful, the physiologic target measurement should meet two particular expectations. It should be sensitive to stimulus dose, e.g., larger with higher doses. It should also be sensitive to efficacy, e.g., larger with greater efficacy. Of course, sensitivity to dose and efficacy represents sensitivity to seizure intensity. In turn, seizure intensity refers to seizure spread through the brain as well as amplitude. Accordingly, distinctions in ECT seizure intensity are easier to detect at greater distances from the stimulus electrodes. This means that physiological effects at greater distances from the stimulus electrodes are generally more sensitive to stimulus dose and treatment efficacy. Conversely, measurements of brain regions near the stimulus electrodes are relatively insensitive, so that only large differences are detectable. The same conclusion follows the slightly different perspective that important gradations in seizure intensity are most noticeable in brain areas where intensity is weakest.

Indeed, none of a wide range of EEG phenomena recorded from electrodes located about 5 cm from the stimulus electrodes showed sensitivity to doubling of stimulus dose, while peak HR was sensitive (Swartz 2000). That is, 5 cm between stimulus and EEG electrodes is too close. In contrast, the site for peak HR effect is relatively far from the stimulus electrodes. This site is the right medulla, the brain area that mediates cardioacceleration. Logically, then, EEG electrodes are best located more than 5 cm from the nearest stimulus electrode; sensitive configurations await determination.

Besides peak HR, physiological effects that have shown some sensitivity to stimulus dose or electrode placement (and by implication stimulus dose) include prolactin and cortisol release. Several EEG measurements including seizure amplitude and postictal suppression have shown some sensitivity to dose or efficacy, although this sensitivity was at the lowest significance ($p < .05$) and it reached saturation at low efficacy (Nobler et al. 1993). Such saturation is analogous to a serum drug assay that reaches its maximum limit well below minimum therapeutic level; only the most severe deficiencies can be detected, and therapeutic adequacy cannot be assessed.

Some patients might show little physiological effect but respond anyway; this can happen if the physiological effect

is blocked. In this case other physiological effects should be used instead. Other patients might show intense physiological effects but deny benefit from treatment; this can result from concurrent conditions that resist ECT, e.g., post-traumatic stress disorder. Still other patients might show a peculiarly high physiological result not approached later; this should be dismissed as a peculiarity. For example, a 75 year old depressed woman showed a peak HR of 184 at ECT #1, which is extraordinarily high for age. The peak HR was 170 at ECT #2, a more realistic benchmark value; peak HRs ranged from 163 to 166 at ECTs #2 through #5.

Previous Methods

Close matching to individual patient physiology is an unusual virtue of the Benchmark Method. Other methods do not consider individual variations with regard to other patients of the same seizure threshold or age.

Just as basic is that previous methods identify only an initial dose; this is a double omission. First, the initial dose is only an estimate. It can be too weak or unnecessarily strong for the individual patient; an assessment is needed and consideration given to adjustment. Second, ECT itself is anticonvulsant and stimulus dose increases can be needed along the course, and frequently with some patients. One method took similarity to the weakest (threshold) seizure to suggest stimulus increase (Krystal et al. 2000). This is analogous to dosing lithium through serum lithium level similarity to the lowest detectable level (e.g., 0.1 meq/L)-the relationship is weak and unreliable.

The fixed dose method was used in comparison between unilateral and bilateral ECT at a high dose of 378 mC (Abrams et al., 1991). A fixed dose of 403 mC was more effective in unilateral ECT than the threshold multiple method at 2.25 multiple (McCall et al., 2000). The fixed dose method is most applicable to unilateral ECT because the side-effects of moderate overdosage are usually mild. Still, about one third of ECT responders remit with low-dose unilateral ECT, while others relapse quickly after high-dose unilateral ECT and should have responded better to a bilateral placement (Sackeim et al., 2000).

In setting the dose proportional to age, the rationale is that the dose needed to induce an effective seizure rises with age. This rationale is probably true but has not been specifically verified; it is related to the rise in seizure threshold with age only by analogy. In the "full-age method" for unilateral ECT %Energy (or expected joules) is set to patient age; this equals setting mC to age times five. The "half-age method" uses a dose half this, and is most applicable to the various types of bilateral ECT (Petrides and Fink, 1996).

The rationales for the seizure threshold multiple method are that dosage must exceed threshold and higher dosage produces larger effects. Unfortunately, the relationship

between dosage-over-threshold and clinical effect is not known for individuals, but it must be known to apply the seizure threshold to treatment (Swartz 2001). Physiological measurements should be able to provide details about this relationship, but there is no reason for the resulting method to be better than the Benchmark Method, and so there is no rationale to measure seizure threshold.

Clinical Case Example

To illustrate, here is how the Benchmark Method was used with a 58 year old depressed man who received ECT with LART electrode placement. At ECT #1 a 202 mC dose gave a seizure with peak HR (PHR) of 128; this is the benchmark. At ECT #2 a 302 mC dose produced seizure PHR=118; this PHR suggests increase in the dose for two separate reasons. First it is 8% under benchmark. Second it is generally low. At ECTs #3 and #4 a 328 mC dose produced PHRs of 123 and 109; the latter suggests dose increase. At ECT #5 a 353 mC dose gave PHR=115, suggesting increase. At ECTs #6 and #7 a 454 mC dose produced seizure PHRs of 126 and 120; the latter led to dose increase. At ECTs #8 and #9, with 504 mC dose, PHRs were 134 and 135, and the course concluded with remission.

Limitations

Peak HR cannot be used with the Benchmark Method in patients whose cardiac disease or medication blocks essentially all HR elevation with ECT. Nevertheless, only partial attenuation of HR elevation does not necessarily prevent its use in ECT monitoring. HR elevation can be diminished by the anesthetic agent propofol and by beta-blockers and calcium-channel blockers. Propofol and some beta-blockers weaken the ECT seizure, a drawback to their routine use. Labetalol or esmolol administration to prevent post-ECT hypertension is an occasional consideration for elderly patients. Diseases that can interfere with HR elevation at ECT include dysfunctions of the cardiac conduction system, e.g., bundle branch blocks and nodal blocks. Such dysfunctions tend to follow cardiovascular disease, acute MI, stroke, electrolyte disturbances, and elevated intracranial pressure. Nevertheless, little is known about the nature of effects by drugs and diseases on peak HR. These HR effects are not necessarily stronger than effects by CNS drugs and conditions on the EEG, which include the suppression of alertness into unconsciousness by anesthesia.

The Benchmark Method and its use with peak HR are based on a study in which higher average peak HR relative to benchmark HR was associated with fewer ECTs in the course (Swartz, 2000). Because the data from this study guided the formulation of this method, independent testing

would require new data. A new data collection might compare the clinical outcome for patients whose stimulus dose produces a mean peak HR within 6 bpm of benchmark against another group whose dose produces a mean peak HR of 12-18 bpm below benchmark. Such a comparison would require controlling for influences by age, stimulus electrode placement, and subtype of major depression. Another study might compare the clinical outcome with use of benchmarks based on different physiological measurements, such as peak HR and EEG postictal suppression. Still another study might compare a group treated by the Benchmark Method against a group treated by a different method, but it is not plain what a good alternative should be.

Disclosure

Dr. Swartz has equity interests in Somatics, LLC, a manufacturer of ECT instruments.

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