Review Article

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Response Predictors in ECT: A discussion about Seizure Threshold

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Abstract
Electroconvulsive Therapy (ECT) has been in use since 1938 and remains one of the most important and controversial treatments. The National Institute of Clinical Excellence in UK specifically recommends considering ECT as an option in treatment of severe depression (when life threatening and a rapid response is needed or when other treatments have failed), moderate depression (not responding to multiple treatments), catatonia and a prolonged and severe manic episode. For ECT to have a therapeutic response, it is now recognised that a generalised tonic-clonic seizure is essential. The degree by which the stimulus intensity exceeds the seizure threshold is an important determinant of both therapeutic effectiveness and cognitive side effects. This article attempts to discuss the significance of estimating the seizure threshold and the practical ways of lowering it, to reduce the side effects during the course of the treatment.
Keywords : ECT, Electroconvulsive Therapy, Seizure Threshold
Abbreviations: ECT: Electroconvulsive Therapy

Introduction

The use of convulsive therapy for psychiatric conditions evolved after its first use by Meduna using camphor in 1934, and by 1938, Cerletti and Bini had documented the use of electricity to induce convulsions and therapeutic benefit. The technique has been extensively modified by the addition of muscle relaxants and general anaesthesia. Electroconvulsive Therapy is now an important and effective treatment option for certain severe neuropsychiatric disorders.

Most developments and changes in the practice of ECT have been driven to reduce the adverse effects and not by the need to make it more efficacious. The aim is to induce a generalised tonic-clonic seizure with a sufficient dose to maximise efficacy but not too high to reduce cognitive side effects. The newer brief-pulse, constant-current, square-wave machines are more efficient in inducing seizure than the older sine-wave, constant-voltage machines.

Between January and March 2002, there were nearly 12800 ECT administrations in England to 2300 individuals [1]. The National Institute of Clinical Excellence currently recommends that ECT is only used to achieve rapid and short term improvement of severe symptoms after an adequate trial of other treatment options have proved inefficient and/or when the condition is life threatening as in people with severe depression, catatonia or prolonged/severe manic episode[2]. The newer guidelines on depression suggest that ECT be considered as a treatment option in moderate depression when it has failed to respond to multiple treatments[15]. It has been noted from the observation of the users' experiences that the cognitive impairment often outweighed their perception of any benefit after ECT treatment.

It has been recognised that the induction of a generalised tonic-clonic seizure is necessary to achieve a therapeutic response and a number of studies demonstrate superiority of ECT over Sham ECT. It is also noted that administration of an electrical stimulus that fails to induce a seizure and immediate termination of a seizure after induction does not result in clinical improvement. Stimulus which just about produces a generalised tonic-clonic seizure may not ensure therapeutic potency, but the degree to which the stimulus intensity exceeds the Seizure Threshold is an important determinant of the therapeutic effectiveness. Unfortunately, this also corresponds to the cognitive side effects[3].

Seizure Threshold

Seizure Threshold is emphirically defined as the minimal electrical dose that induces generalised tonic clonic seizure activity. Boylan et alfound that greater that 40% of individuals had an initial seizure threshold of less than 50mC with unilateral electrode placement[4] and Scott and Dykes and Sakheim concluded that for bilateral ECT, this was around 7%[5,9].

Standard fixed doses continue to be used in UK, and this can result in a dose which is several times the seizure threshold, contributing to acute and long term cognitive side effects without any additional benefits of clinical efficacy. It is also associated with a greater risk of missed or partial seizures that have no therapeutic effect.

There is a great deal of variability between seizure thresholds in different individuals. Many factors influence it and Box 1 summarises them. Seizure threshold is generally higher in older men than younger women. Electrolyte imbalances, particularly, hyponatremia and hypocalcaemia can lower the seizure threshold. It is important for the clinician to consider these before starting the course of ECT.

Box 1: Factors influencing Seizure Threshold

- Individual characteristics
  - Increases with age
  - Higher in men
  - Increases with increase in skull density
  - Higher for bilateral electrode placement
  - Electrolyte imbalances
- Seizure Threshold increases during course of ECT
- Medication increasing Seizure Threshold
  - Anticonvulsants, Benzodiazepines, Hypnotics, Anti-arrhythmics
- Medication decreasing Seizure Threshold
  - Antidepressants, Antipsychotic, Lithium, Theophylline
- Anaesthetic Induction agent
  - Increased: Propofol & Barbiturates
  - Decreased/minimal effect: Methohexital, Etomidate, Ketamine
- Machine characteristics
  - Brief-pulse, constant-current, square-wave output better

Initiation of a course of Electroconvulsive Therapy treatment should routinely involve the estimation of the seizure threshold by gradual dose titration (Stimulus dosing) and then treatment by using the supra threshold doses. Once seizure threshold is determined a dose of 1.5 to 2 times the seizure threshold for bilateral ECT and at least 2.5 to 3 times the seizure threshold for unilateral ECT may provide the best balance of clinical efficacy and cognitive side effects[3]. This is supposed to be a better practice compared to the fixed dose method used to initiate the ECT treatment.[6]

Missed Seizure

An adequate electrical dose will manifest as generalised tonic, followed by clonic activity of skeletal muscle, accompanied by a typical seizure pattern on EEG. The absence of both is deemed a missed seizure[7].Pippard's audit of ECT practice showed that in nearly 22% of ECT treatments, there was either no seizure or a brief seizure.

Box 2: Causes for Missed Seizure

- Low stimulus intensity
- Excess impedance
- Premature stimulus termination
- Excess Anaesthetic Agent
- Increase of seizure threshold by ECT
- Other factors increasing seizure threshold

The causes of Missed Seizures are summarised in Box 2. Missed seizures may be due to faulty technique leading to insufficient stimulus intensity, excess impedance or premature stimulus termination. Individual patient factors such as electrolyte imbalances, particularly dehydration and hypercarbia can lead to missed seizures. A common reason for raised seizure threshold is the administration of high dose of anaesthetic induction agent [5]. Propofol, the most commonly used agent for ECT increases seizure threshold and also decreases the seizure duration. Use of alternatives like Methohexital, Etomidate or Ketamine may be successful as they either have minimal or no effect on seizure threshold and may increase the seizure duration.

During the course of treatment seizure threshold usually rises and this may lead to missed seizures. In addition to delaying the improvement, missed seizures cause more irritability and restlessness[10]. By measuring the seizure duration during the course of ECT missed seizure could be anticipated and appropriate steps can be taken. Some of the effects of a missed seizure are listed in Box 3.

Box 3: Consequences of Missed Seizure

- Anxiety
- Headache
- Confusion
- Lethargy
- Tiredness

A missed seizure should prompt monitoring and correction of electrolyte imbalance if any. Seizure activity during the ECT procedure is affected by medication as well. Administration of seizure threshold increasing drugs should be reviewed and where possible stopped or reduced. If the treatment is for depression, consider using tricyclic drugs which lower the seizure threshold and augment ECT.

The maximum dose deliverable by the ECT machines is restricted in some countries and this may be inadequate due to very high seizure threshold in a few individuals. The US Food and Drug Administration restrict the maximum output of ECT machines to 576 millicoulombs compared to the Royal College of Psychiatrists which has recommendeda maximum output charge of 1200millicoulombs[8]. While higher electric doses may be able to induce generalised seizure activity, the cognitive side effects are also increased[11]. Therefore attempts must be made to decrease the seizure threshold to minimise these side effects.

Seizure Threshold Lowering Techniques

The aim of ECT treatment is to induce a generalised seizure activity; failure to do so makes the treatment session ineffective and of no therapeutic benefit. If a patient does not have generalised tonic-clonic seizure after a stimulus it is important to wait for at least 20 seconds after a non-seizure and at least 45 seconds after a partial/focal seizure prior to restimulating. Using appropriate techniques to avoid like low stimulus intensity, inappropriate application of electrodes, premature stimulus termination, etc are important[6].

Charter and Simpson established the use of hyperventilation immediately before the application of the electrical stimulus and it has been shown to enhance seizure duration[12]. Sleep deprivation safely reduces the seizure threshold and also

increases the seizure duration[13]. Caffeine prolongs the seizure duration, but has no effect on the seizure threshold[14].

Conclusions

ECT remains the most maligned and misunderstood of psychiatric treatments. Whilst it has no doubt, successfully saved many lives and provided relief from the abyss of depression, proving its efficacy, the thrust of recent developments have been towards minimising the side effects. Adequate training and supervision of trainee psychiatrists will be essential to raise the standards of ECT administration techniques and skills.

Being aware of the significance of seizure threshold and ways to lower it, as an alternative to electric dose increase may address to some extent, the concerns about cognitive difficulties.

Competing Interests
None declared
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