ECT: a controversial but effective treatment

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Until proven otherwise, ECT remains the most effective somatic clinical therapy available for the treatment of severe depression, particularly if melancholic or psychotic features are present, and also in the treatment of post-partum psychosis.[1] Administered correctly it is a safe procedure with mortality rates (1/15,000 procedures), little above those for general anaesthesia.

In the report of the Inspector of Mental Hospitals for the years 1999-2001, it was noted that a total of 1,116 patients received ECT in Ireland, with considerable regional variation.[2] The variation in the use of ECT around the country, a variation that has also been demonstrated in the UK, suggests that there is still uncertainty about the use of ECT among psychiatrists and may also reflect a lack of clarity in the guidelines for the use of ECT.

While some argue that this regional variability suggests ECT is being over-prescribed in some areas, it also begs the question as to whether any patients are being deprived the opportunity to receive ECT, given that ECT is more commonly prescribed in private hospitals.[2]

How is it therefore that such an effective treatment for a psychiatric condition associated with so much suffering and anguish is an on-going topic of controversy? Cardioversion, a similar medical procedure to ECT, is used by cardiologists to treat certain unstable cardiac arrhythmias, except that in cardioversion the electrodes are placed over the heart (instead of over the head in ECT). But there is no stigma associated with cardioversion.

Background

Contrary to recent claims[3] ECT originated in the 1930s when it was noted that patients with schizophrenia improved after having epileptic seizures. Ladislas Meduna in Hungary induced a seizure in a catatonic schizophrenic patient by injecting camphor in oil in 1934. After eight induced seizures, the patient showed signs of recovery and remained well until Meduna left Hungary in 1939.[4] In his paper on the use of ECT in schizophrenia, Meduna noted that ECT was most effective in those who had been sick for only a few years.[5]

The induction of seizures by electrical means was subsequently developed in 1938 in Italy by Ugo and Cerletti.[6]

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Nowadays, ECT should be administered in a dedicated fully equipped ECT suite (waiting room, treatment room, recovery room) with an anaesthetist in attendance. Following the administration of an intravenous short-acting sedative anaesthetic and the administration of a short-acting muscle relaxant, the fasting patient is given a brief electric current of a certain stimulus intensity either to both sides of the head (bilateral) or to the non-dominant side of the head (unilateral). A modified seizure is induced which typically lasts between 20-60 seconds.

The patient is oxygenated manually until normal breathing resumes, typically within a couple of minutes as the anaesthetic wears off. Most people are up and about within 30 minutes to two hours. A course of ECT usually consists of four to 12 treatments, given two or three times a week, depending on the age of the patient and their response to ECT.

ECT: a proven therapy

A number of studies suggest that major depression effects 2%-5% of the population at any one time. Furthermore, the Global Burden of Disease, an assessment of mortality and disability from diseases and injuries in 1990 suggests that major depression was the fourth leading cause of disease burden in the world. This measure is based on a measure of disability-adjusted life-years which takes into account the effect of disability and mortality.[7]

The most recently published UK guidelines on the use of ECT were compiled by the National Institute for Clinical Excellence (NICE) in the UK.[8] These guidelines were based on two surveys commissioned by the UK department of Health and a Cochrane review on the use of ECT in schizophrenia.[9]

Two recent surveys commissioned by the Department of Health in the UK were systematic reviews of the available literature, one on the safety and efficacy of ECT in depression,[10] mania and schizophrenia and the other a review of surveys of patients attitudes to ECT.[11]

On the basis of these extensive surveys, NICE has recommended that ECT be used to achieve rapid and short-term alleviation of severe symptoms, when an adequate trial of other treatments has failed or when the condition is considered to be potentially life-threatening. These guidelines apply only to people suffering from severe depression, catatonia or a severe and prolonged manic episode.

The study focusing on ECT and depression examined all randomised controlled trials that compared ECT with sham ECT and ECT with pharmacological treatment for depression. It also examined data on the short and longterm effects

of ECT on cognitive functioning and mortality.

It concluded that ECT is an effective short-term treatment for depression and is more effective than pharmacotherapy. It also concluded that while the information available on the cognitive effects of ECT is limited, there are temporary changes in memory associated with treatment and that further research is necessary into to the long-term effects of ECT on memory.

The study that looked at the use of ECT and schizophrenia concluded that there is no evidence to refute the use of ECT in schizophrenia and that there is some evidence to support its use in people with schizophrenia in combination with pharmacological treatment where there has been only a partial response to medication alone. This large meta-analysis of the literature also concludes that the research base on the use of ECT in people with schizophrenia is still inadequate.

Rose concluded in her review[11] that further study is needed which takes into account measures of outcome which are valued by patients. She notes that clinician-led research tends to favour ECT more than patient-led research and that there remain considerable concerns about the effect on memory of ECT.

There is some evidence to suggest that ECT may have a clinical role to play in the treatment of delirium, atypical psychosis and a variety of the schizophreniform disorders which will not be reviewed here.[12] Two conditions in particular where ECT is effective are worthy of further consideration due to their clinical importance.

Neuroleptic malignant syndrome (NMS) is a rare and idiosyncratic illness which carries a high mortality. Two studies suggest that ECT may be of benefit in NMS.[13,14] Secondly, the consequences of maternal depression have been increasingly studied in the last few years and the effects of maternal depressive symptoms in mothers at any time but particularly pre-natally is a risk factor for the child's well-being.[15]

While there are only a few well-controlled trials in the literature on the use of ECT in both these conditions, the knowledge that response to ECT is rapid and that a number of case studies suggest that it is safe and well tolerated in these populations,[16] argues in favour of further research into the use of ECT when the potential effects of the illnesses are particularly devastating both for mothers and for their offspring.

ECT: the controversy

ECT unfortunately suffers from the particular stigma associated with psychiatric practice, magnified by the early days of ECT, where the seizures were unmodified. Two enduring myths are frequently conjured up in this regard.

The first is the image of the patient receiving ECT being held down, or indeed strapped down while the seizure was being induced, with the widely held notion that this was in order to stop the patient running away. It was actually a humane preventive measure to avoid the common pre-muscle relaxant era complication of dislocated joints including shoulder and hip, as well as fractures during the seizure.

The second enduring myth is that ECT is painful, immortalised in the Jack Nicholson grimace which filled the movie screen while ECT was dramatised during the movie *One Flew over the Cuckoos Nest.* The ECT grimace is not however the consequence of pain, but of bilateral contraction of the masseter muscle following the electrical stimulus.

Patients, mental health advocates and researchers should focus their attention on some real and unresolved issues associated with ECT. Firstly, how does it work, and secondly what are the real adverse effects, and specifically what about cognitive side-effects.

There is an abundance of recent data relating to the mechanism of action of ECT which is outside the scope of this editorial. Suffice to say at this point that a greater understanding of the workings of ECT has led to new and exciting focused brain antidepressant technologies including transcranial magnetic stimulation, deep brain stimulation and vagal nerve stimulation, all of which have the advantage of not requiring a general anaesthetic or the use of electrical current as used in traditional ECT.[17]

Moreover, although the mechanism of action of ECT is uncertain and for many years it was used empirically, this approach is not without precedent in medicine. The classical example of that is the use of digitalis to treat heart failure. The use of digitalis was first described by William Withering in 1785 in his treatise on the uses of foxglove, *An Account of the Foxglove and Some of its Medicinal Uses with Practical Remarks on Dropsy and Other Diseases.* For many years the mechanism of action of digitalis remained a mystery, although it has now been elucidated. To this day, digoxin has an important role in the treatment of heart failure.[18]

Despite claims that ECT is associated with an increased mortality articulated by some, a number of observational trials have reported the opposite. In their review, the UK ECT group identified four studies which looked specifically at the issue of mortality and ECT. These were non-randomised cohort studies and three of these showed a reduced overall mortality associated with ECT[19-21] and one other trial showed no difference.[21]

Whilst some anti-ECT advocates have claimed that ECT may cause 'brain damage' a small number of brain imaging studies that have prospectively scanned patients before and after ECT[23,24] have not showed any change in brain structure before or after ECT. In their review of the literature, Devanand *et al* could find no evidence that ECT causes brain damage, either in structural imaging studies or post-mortem studies.[25]

Given that we now know much more about ECT than we did 20 years ago, so too do we know more about the side-effects. For example up until the late 1980s the concept of varying seizure thresholds between individuals was not factored into the prescription of ECT. The consequent introduction of dose titration as part of a more tailored approach to ECT delivery has more than likely benefited patient antidepressant response and reduced the side-effect profile.[26]

Short-term memory disruption has always been a problem associated with ECT, much more so with bilateral ECT treatment. Results from US studies over the past decade using unilateral treatment with the correct dosing strategy[27,28] are sufficiently compelling for this treatment modality to be given greater consideration as a first line ECT strategy in Ireland, particularly in older people with declining cognitive reserve. Greater research attention is required on ways to reduce early relapse rates, and indeed maintenance ECT is particularly effective in this regard.[29]

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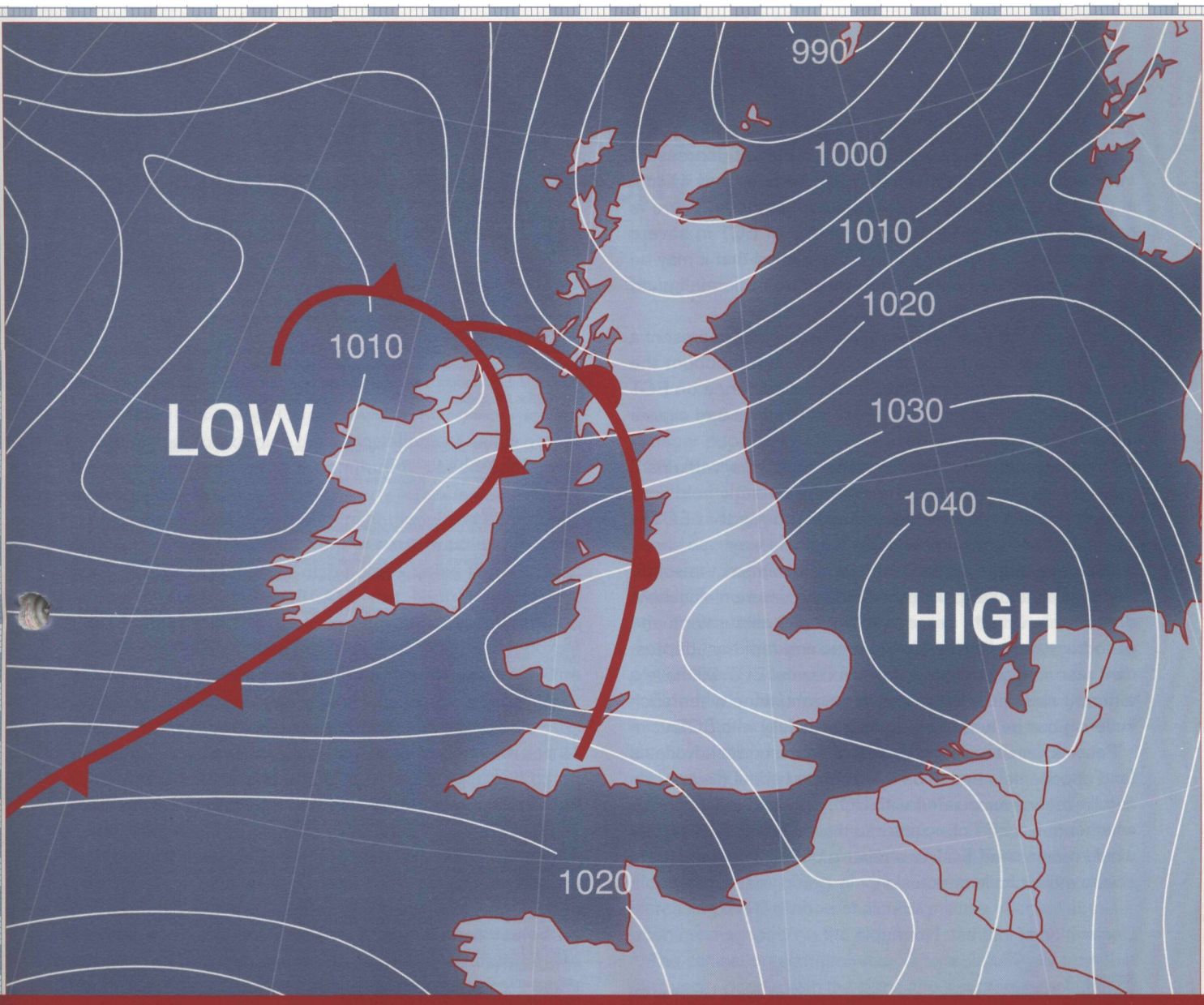

Lamictal improves the forecast for depression in bipolar disorder

The effective management of depression (compared to mania) has been identified as the greatest unmet need in patients with bipolar disorder[1]. Lamictal addresses that need.

In the largest ever placebo-controlled clinical trial in bipolar disorder Lamictal significantly delayed the onset of depressive episodes, often by more than a year[2,3].

Lamictal is well tolerated, with no need for blood monitoring and it has a well established safety profile as a treatment in epilepsy. It does not stimulate or induce a switch to mania[2-6].

With Lamictal, you have a vital new way to exercise control.

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Lamotrigine for **bipolar** disorder

Abbreviated Prescribing Information: (See SPC for full prescribing information): Lamictal Tablets: Pale yellow tablets, containing 25mg, 50mg, 100mg, 200mg lamotrigine. Lamictal Dispersible Tablets: White tablets containing 2mg, 5mg, 25mg, 50mg, 100mg, 200mg lamotrigine. **Uses:** Lamictal is licenced for the prevention of mood episodes in patients with bipolar disorder, predominantly by preventing depressive episodes. **Dosage and Administration.** Dosage in monotherapy: - *Adults (over 18 years of age):-* The initial Lamictal dose in monotherapy is 25 mg once a day for two weeks, followed by 50 mg once a day for two weeks. Thereafter, the dose should be increased to 100mg in Week 5. The usual maintenance dose to achieve optimal response is 200 mg/day given once a day or as two divided doses. However a range of 100-400mg was used in clinical trials. **Dosage in add-on therapy:-** *Adults (over 18 years of age):-* Initial dose in those taking enzyme-inducing AEDs is 50mg once a day for 2 weeks, followed by 100mg/day in 2 divided doses for 2 weeks. The dose should be increased to 200mg/day given as two divided doses in week 5. The dose may be increased to 300mg/day in two divided doses in week 6. The usual maintenance dose to achieve optimal response is 400 mg/day gi ven once a day or as two divided doses which may be given from week 7. For patients taking sodium valproate, the initial dose is 25mg every alternate day for the first two weeks, followed by 25mg once a day for 2 weeks. The dose should be increased to 50mg once a day (or in two divided doses) in week 5. The usual maintenance dose is 100 mg once daily or in two divided doses. However the dose may be increased to a maximum of 200mg once daily or in two divided doses depending on clinical response. *Children with bipolar disorder (less than 18years):* Safety and efficacy of lamotrigine in bipolar disorder has not been evaluated in this age group. *Use in the elderly :>65years:* No dosage adjustment required. Use in hepatic / renal impairment. **Contra-indications :** Known hypersensitivity to lamotrigine; **Precautions and Warnings:** There have been reports of adverse skin reactions which have generally occurred within 8 weeks of starting Lamictal therapy. Majority of rashes are mild and self limiting, but serious life threatening skin rashes including Stevens Johnson syndrome and to xic epidermal necrolysis have been reported. Rash appears to be associated with high initial doses of Lamictal, exceeding recommended dose escalation and concomitant use of valproate. Withdraw Lamictal if rash appears, unless clearly not drug related. Rash has also been reported as p art of a hypersensitivity syndrome including fever, lymphadenopathy, facial oedema and blood and liver abnormalities. This syndrome may rarely lead to disseminated intravascular coagulation and multiorgan failure. Fever and lymphadenopathy with no evident rash may be an early manifestation of the syndrome - discontinue Lamictal if no alter native aetiology established. Possibility of a suicide attempt is inherent in bipolar disorder, close supervision of high-risk patients is recommended. **Interactions:** Anti-epileptic agents (e.g. carbamazepine, phenobarbitone, primidone and phenytoin) may increase metabolism. Sodium valproate may reduce Lamictal metabolism. In patients taking carbamazepine there have been reports of CNS events following introduction o f Lamictal which usually resolve when dose of carbamazepine is reduced. **Side Effects:** Headache, tiredness, skin rash, nausea, dizziness, drowsiness, irritability, blurred vision, tremor and insomnia have been commonly reported. Other adverse events reported include diplopia, arthralgia, back pain, agitation, conjunctivitis, dizziness, dro wsiness, GIT disturbances, aggression, confusion and hallucination. Lupus-like reactions have been reported very rarely. Movement disorders and haematological abnormalities have been reported. Hepatic dysfunction has been very rarely reported. Stevens Johnson Syndrome, Toxic Epide rmal Necrolysis, Hypersensitivity Syndrome and other CNS disorders have been rarely reported. See SPC for full details. **Pregnancy and Lactation:** Insufficient data. Balance benefits against risks. **PA numbers :** Lamictal Tablets 25mg, 50mg, 100mg, 200mg: (PA 17/99/ 1-4) Lamictal Dispersible Tablets 2mg: (PA 17/99/10) Lamictal Dispersible Tablets 5mg, 25mg, 50mg, 100mg, 200mg: (PA 17/99/ 5,6,7,8,9). **Legal category:** POM. **PA Holder:** Wellcome Ireland Ltd., Beech Hill Office Campus, Clonskeagh, Dublin 4. Drug Classification: S1B. Full prescribing information available on request from GlaxoSmithKline, Stonemason's Way, Rathfarnham, Dublin 16. Tel.:01 4955000. **Date of preparation:** August 2003.

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Conclusion

ECT is a particularly useful and valuable antidepressant treatment strategy when correctly administered and when it is used in specifically indicated circumstances. There is particular evidence to support the use of ECT in severe depression and a growing body of evidence that it may be useful in other conditions such as neuroleptic malignant syndrome.

The most recent guidelines on the use of ECT represent a considerable advance in that they take into account the largest body of systematically reviewed evidence on ECT and, importantly, they incorporate users views and experience.

There remain very considerable problems with ECT, however. Not least among these is the strongly held view among some professionals and user groups that ECT is 'inhumane' and possibly 'damaging in some way'.

Clinicians at the clinical coal face who witness the suffering, anguish and despair associated with severe melancholic depression, with its associated cognitive disruptions and distortions, followed by the dramatic and rapid antidepressant response associated with successful ECT will have a different slant on what is and is not inhumane when such suffering can be ameliorated so successfully with ECT.

Patients, families, user groups and mental health advocates (and opponents) need to be fully informed about the benefits and limitations associated with ECT. The acid test might be whether or not ECT clinicians and their academic colleagues would recommend ECT to a relative of theirs suffering from severe melancholic depression.

Declaration of interest: None

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