ECT: Scientific methodology gone wrong

Abstract

Evidence based medicine, via the vehicles of randomized controlled trials, meta-analysis, and guidelines, has achieved a hegemony in all spheres of medical research, practice, insurance reimbursement, clinical practice auditing, and administration that is unwarranted from its credentials in relation to its weak foundations in basic sciences, methodology, and epistemology. This commentary argues that the resultant inherent denigration of both other scientific methodologies, and clinical science expertise, elucidates the pronounced, repetitive, and controversy-generating divergences of opinion about treatment effectiveness that are starkly evident between experienced clinicians and 'RCT-ologists' concerning treatment modalities such as ECT and the use of MAOI drugs. This divide is explicated in the context of the current debate concerning the conspicuous effectiveness of ECT, as decisively adjudged by experts after decades of clinical experience world-wide, contrasted with the hotly debated equivocal, but widely divergent, results from RCTs and their subsequent meta-analyses.

I argue that because RCTs are divorced from basic sciences and causality, they have emasculated themselves of the power to act as productive techniques of investigation in clinical scenarios: in contrast, clinical science using non-RCT methods, and 'bed-side' observation, are directly to do with causality and individually tailored treatment response, and thus have distinct theoretical and practical advantages. I conclude that it is time for the prolonged hegemonic reign of RCTs (and EBM) to be critically reevaluated because it has led to a methodological monoculture and investigational tunnel vision, divorced from science and causality.

Introduction

See also related YouTube video discussion and here 'Why the effects of ECT (& MAOIs) cannot be assessed with RCTs alone'

Nothing extenuate; nor set down aught in malice; Shakespeare

There is little room for doubt that ECT is an effective treatment for cases of serious depression, as is vehemently attested to, over decades, by clinicians with experience in the field from around the world (this commentary does not discuss its use in other conditions). It is under-used by some and mis-understood by others, even after all these years [1-18].

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The context of this commentary, and the reasons I am commenting about ECT (I am not an ECT expert), is:

First; its effectiveness is again being questioned by **psychology** researchers, which will cause some patients and their families, serious distress, and concern.

Second; the assessment of the efficacy of ECT with a standard RCT is an apposite instance of inappropriate and inadequate methodology and therefore a good starting point for a reconsideration of epistemology and methodology.

Third; speaking as an MAOI expert, it is my experience that a proportion people are given ECT without an adequate trial of drug treatment; **particularly, they are not offered an MAOI prior to being offered ECT**. Others are not given ECT when it might be life changing.

Fourth: I suggest that a trial of an MAOI before ECT is strongly indicated and much preferred by most of the patients whom I have treated; however, it is rarely mentioned, never mind discussed. That represents sub-optimal knowledge and clinical practice.

I am not an expert concerning the latest research on the clinical mechanisms of action of ECT, nor the optimal mode of administration.

This commentary is focused on scientific methodology in order to foster an understanding of the divergence of opinions about ECT and is about the value and applicability of different scientific methodological approaches. That may also help in understanding my rationale for considering MAOIs before embarking on a course of ECT.

These considerations elucidate the puzzle of why, with many treatments, there is such a conspicuous gap between the opinions of experienced clinicians world-wide and the pontifications of guidelines which are all based on RCTs — these considerations apply to MAOIs as much as they do to ECT.

MAOIs and ECT may be an 'odd couple', but they walk hand-in-hand, in that they illustrate the widest divisions between 'clinical opinion' and RCTs.

I am sure that if more clinicians used MAOIs before giving ECT, they would become as convinced that MAOIs work for severe melancholic depression, as they already are that ECT works; despite the uncertainties caused by RCTs.

Clinicians who dogmatically assert that ECT definitely works, no matter what the findings of RCTs might appear to be, are correct in being confident in their opinion — this commentary aims to foster an understanding of why that is an epistemologically valid position.

The above dismissive phrase 'pontifications of guidelines' is not me being supercilious and opinionated; it is a serious criticism that reflects opinions expressed by others more eminent than me, like John Ioannidis who has called them:

'**Impregnable strongholds of expert-based insolence and eminence-based innumeracy.**'

That is a pulsating red flag that anyone claiming to be informed about science and its methodologies needs to be informed about.

Background

Sed quis custodiet, ipsos custodes

Juvenal

A recent review (2019) by Read, Kirsch et al. [1],* which opines there is insufficient RCT evidence of the effectiveness of ECT to justify its use, was one factor that triggered the updating of this commentary, which I first posted some years ago. One of the co-authors of this review is a veteran of placebo research, **Irving Kirsch** (aged 77), who has already stimulated much thought and reconsideration, and some angst, with his criticisms of antidepressant drug trials; that grew out of his interest in hypnosis and the placebo response, which have been a large part of his research career [2-4]. Some regard his criticisms as cogent.

*It may be noted that this paper has been published in an obscure journal (Kirsch himself is one of the members of the editorial advisory board — that fact is not mentioned in the disclosures at the end of the paper). The J of 'Ethical Human Psychology and Psychiatry' is the 'house journal' of the organisation that a well-known critic of drugs & ECT in psychiatry, Dr Peter Breggin (now aged 85), launched as the official J of the center that he founded, the '**International Center for the Study of Psychiatry and Psychology**'. That journal has had a low, and steadily decreasing, impact factor over the last 20 years. The modest status of the members of the editorial board, and the disciplines from which they come, would cause one to have doubts about their suitability and competence to judge and find referees for a paper such as this, and one would wonder exactly who the referees of this paper might have been and whether any of them had expertise in statistics.

Since this is a (potentially) important paper by authors who would be regarded as having some degree of eminence (Kirsch is at Harvard), one would normally expect it to be published in a highly cited mainline journal. The fact that this is not the case makes me wonder why, and whether it was submitted to such journals unsuccessfully. Submission of rejected papers to a cascade of decreasingly prestigious journals is a relatively common occurrence; unfortunately, readers are never made aware of the adverse comments that might have been made by previous referees for other journals. That is in itself an insult to the such referees, whose trouble and contribution is unrecognised and consigned to the rubbish bin.

My commentaries have a widespread readership of non-medically experienced readers: therefore, an analogy may help an understanding of the problems with the validity of a criticism by non-medically qualified psychologists, like Read et al. If a surgeon wrote criticizing some surgical procedure one would not have much trouble assuming there might be some substance to what was said; if a physiotherapist published such a criticism one might examine it with a rather more critical eye, especially if it was published in a journal about physiotherapy, not in a journal of

surgery. If a sports coach criticized a surgical technique one would probably not read it at all.

Read and Kirsch's review and Bentall's comments center around, and highlight, the difficulties with **Evidence based medicine (EBM)** (as represented by the ubiquitous **Randomised Controlled Trial (RCT), on which they rely exclusively** in advancing their opinions — these gentlemen are psychologists and have a lesser knowledge and experience of ECT and medical science generally, and particularly that relating to serious depressive illnesses — that comment is not intended to be dismissive of their views, but rather to indicate for general readers 'where they are coming from': they are offering opinions, and supposing expertise, in an area of science and practice of which they are not an integral part, and in which they have no formal qualifications. That suggests there are likely to be important aspects of this subject about which they are uninformed.

In stridently repudiating the effectiveness of ECT, and berating those who use it, these psychologists are coming from outside of the field and challenging a large body of expertise and knowledge, accumulated over a long time. If their challenge to the status quo is to be taken seriously it needs to have considerable substance, perhaps more than yet another re-hashed analysis of decades-old ECT studies (cf. Ioannidis and the 'plague of meta-analyses'). It is disingenuous that they refer to this decades-old material as 'new evidence'.

Whilst such external comment about various disciplines can have value, it can also be narrowly focused and misleading.

I am sure Read, Kirsch and Bentall will be accused of being ultracrepidarian:

> 'You might think that [Mattie]... I could not possibly comment'.
>
> Ian Richardson, The House of Cards BBC 1990

The above Latin tag about 'who guards the guardians' is frequently used because it expresses a commonly encountered and fundamental difficulty in debates.

Who gets to decide what constitute the legitimate techniques and subject matter admissible to the address the question at hand?

That is a difficult and consequential problem the EBM-community has not overcome, indeed, has hardly addressed. This is especially pertinent because **EBM operates outside the general sphere of scientific knowledge** — that is to say it does not demean itself by consideration of evidence derived from basic science, animal experiments, clinical practice, or Bayesian prior probability (see below).

One can take the view that the very phrase 'EBM' is self-contradictory, since EBM specifically ignores most scientific knowledge and evidence.

For instance, RCTs and EBM would be just us comfortable with a meta-analysis of whether people who see aliens experience them as predominantly green, or predominantly blue — the reality or meaningfulness of the subject matter is utterly irrelevant (cf. parapsychology research).

It is helpful to clarify why this is relevant to the ECT (and MAOI) issue: exactly how are the criteria are set, concerning what is an acceptable type, method, or quality of study? how are these studies assessed and dealt with? **and most importantly of all, how have clinicians become bamboozled* into believing the incorrect notion that the only acceptable evidence is an RCT?**

*Bamboozled is a word that Samuel Johnson wanted to exclude from the English dictionary! I am so glad he failed; it is a wonderful word. The sort of word you can roll around your mouth like a draught of fine wine.

These considerations are crucial influencing factors on the result of any meta-analysis. That is even more so when the differences being looked for are small. Thus, differences between different meta-analysis in which particular studies were deemed admissible, or inadmissible, for consideration can and do change the conclusions reached.

An eminent researcher has stated that the publication of meta-analyses has become a plague in the medical literature. There are now more meta-analyses about antidepressants than there are original studies of individual antidepressant drugs, as Ioannidis shows in '*The Mass Production of Redundant, Misleading, and Conflicted Systematic Reviews and Meta-analyses*' [5] — that remarkable fact illustrates my point; you can select which ever one supports the view you favour. And, I hardly need to repeat, they are generally done by people purporting to be experts in EBM and meta-analysis, who I am sure, like Read, Kirsch, and Bentall would all argue, convincingly and sincerely, that they have used objective criteria to select the particular studies they included and excluded — most of these authors have no formal statistical training, and the publishing journal probably has no expert statistics reviewer. Only 30% of papers published in 'top' medical science journals actually have a statistical review by an expert [6] and it can be safely assumed that lesser journals are even less likely to have had any expert statistical review — and it is likely that would include the Read Kirsch paper.

One of my old acquaintances was an early publisher in the field of meta-analyses of drug trials. When I contacted him a little while ago he expressed regret that he had ever bothered with meta-analyses, because he now felt that they produced results that were

unhelpful or unreliable (he expressly asked me not to mention his name in my writings) — as I have said repeatedly, 'you cannot make a silk purse out of a sows ear'.

The review and epistemology

Read, Kirsch, and their erstwhile collaborator, Bentall will be considered by some to be emotive and hyperbolic; in their own words '…**so appalling that ECT cannot be scientifically or ethically justified**' and 'the dwindling number of psychiatrists still using ECT are doing so **outside the parameters of science in general* and evidence-based medicine in particular**' — that is a sweeping generalisation in which there is no precise meaning — I would describe it as a weak attempt to sound magisterial; others might label it as pompous bloviation. It betokens emotion rather than logic. They all give the impression of having assumed that RCTs constitute the entirety of the scientific enterprise. That is a mistake, a huge mistake. A racehorse with blinkers on does not represent the entire equine species.

*That is a tellingly mistaken and hyperbolic comment precisely because RCTs divorce themselves from 'science in general' and are an 'atheoretical' technique.

I am not sure they have applied the same standards, or skepticism, to the claim that ECT impairs memory (that is not synonymous with the wording they also use, which is the more emotive term 'brain damage'), as they have to the contention that it confers no benefit on mood — again indicating that emotion overly influenced their logic; cf. '*Given the* ***high risk of permanent memory*** *loss … use should be* ***immediately*** *suspended …whether there really are any significant benefits against which the* ***proven**** *significant risks can be weighed.*'

*Nothing in the science is proven.

Also, as referenced below, there is a considerable body of work suggesting improvement in brain structure and function after ECT: I have not double-checked, but I do not think they have cited any of those studies.

Most of us have forgotten most of the things that have happened to us in the past, I don't think that means we have all got brain damage [7].

It is a perturbing contradiction that so many eminent and experienced scientists and doctors from around the Western world, who have produced guidelines, which recommend ECT, are doing so using the same EBM as Read et al. are invoking to say that they are culpably wrong — thus vividly exemplifying the deficiencies of this sometimes self-contradictory, inevitably blinkered, and frequently fallible, fashion of EBM.

The above perspective will enable the general reader to understand why world-wide experts in this field are likely to view their

statements as an example of hubris; *'Given the high risk of permanent memory loss and the small mortality risk, this longstanding failure to determine whether or not ECT works means that its use should be immediately suspended.*' … coupled with their conclusion, '*uncritical acceptance of that research by psychiatry's meta-analyses, and its professional bodies, all of which endorse ECT as an effective and safe treatment, is a sad indictment of all involved, and a grave disservice to the public.*'

This division of views about ECT, which is not helped by the polarized RCT-dominated approach of Read et al. and Bentall, is substantially related to misunderstandings concerning the epistemological validity of different forms of evidence, whereby the **RCT is given undue precedence over other methodologies** in medicine — from animal research on one hand to clinical observation on the other. This elevation of the status of RCTs to a supposed 'Gold standard' has a meagre scientific basis, as has been stated by a number of eminent scientists over the years; furthermore, **EBM is RCT-centric, to the point of being methodologically crippled**. It is a restrictive and blinkered approach that has little to do with what science is about (i.e. causality).

Crucially, from a practical empirical viewpoint, **EBM has conspicuously failed to demonstrate its own success in achieving its main objective of improving patient treatment outcomes**, notwithstanding almost slavish adoption by much of the medical community, who may feel threatened with censure for not following 'clinical practice guidelines' which are often inappropriate and do not suit individual patients. There are various other serious problems exacerbated by EBM across all medical-care delivery platforms, including insurance, administration, clinical auditing etc. and 'the exploitation of EBM by commercial interests, and … narrowing the research agenda' [8].

Recognition of the deficiencies of EBM

I have written extensively about this previously; here, I will garner the support of some heavy guns and give a brief snapshot of the various eminent scientists who have, over many years, discussed views supporting what I am saying about the deficiencies, faults, and limitations of RCTs and EBM — one interesting paper, from more than 20 years ago [9], presaged the issues, '*Problems in the "evidence" of "evidence-based medicine*". Since then, EBM has not been analysed or judged by its own precepts and has failed to demonstrate that it improves patient treatment outcomes.

RCTs do not, and cannot, address causality. Science is nothing without causality (cf. Pearl).

Repeat after me: Science is nothing without causality.

Opinions of note

Ashcroft [10] writes that EBM is, 'autonomous of the basic sciences…blind to mechanisms of explanation and causation'

Pearl (the Turing prize-winner) pioneer of modern causation thinking, has said 'Causality is the key: there is no way of doing science without causality, it is the *sine qua non* for all understanding and progress' [11-13].

Solomon states [14]; 'Emphasis on EBM has eclipsed other necessary research methods in medicine, even those methods necessary for its own development and application. Clinical research requires an engagement with basic theory (e.g. physiological, genetic, biochemical) and a range of empirical techniques such as bedside observation, laboratory and animal studies.'

Berwick, the founder of the leading organization for quality improvement in healthcare (an EBM-centric organisation), says 'we have overshot the mark with EBM and created an **intellectual hegemony** that excludes other important research methods from recognition.' [15] — thank you Berwick, I have used similar words myself in a previous commentary.

Sir Michael Rawlins in his Harveian Oration [16] argued that: 'the notion that evidence can be reliably placed in hierarchies [as all guidelines do] is illusory … striking effects can be discerned without the need for RCTs*… the findings of RCTs should be extrapolated with caution.' Of RCTs he says, 'Yet the technique has important limitations of which **four are particularly troublesome:** the null hypothesis, probability, generalisability, and resource implications.'

*He agrees with **Sir Austin Bradford Hill** (of fame in the smoking-cancer saga) who long ago expressed the opinion that statistics and randomisation were unnecessary unless the effects being sought were small.

If that does not persuade you to think twice about RCTs, and EBM's claims and dominance, then your credibility as a scientific thinker should be called into question.

'Ego requiem meam doleat.'

Read's review & Bentall's comment

The comments and criticisms of Read & Bentall are pertinent to key points about the nature of scientific methodology and the relative merits of other methodologies, other than simplistic RCTs — on which evidence-based medicine perches, like an elephant on stilts.

However, Read et al. and Bentall evince little evidence of taking account of the above considerations. An untutored external

observer of the debate could be forgiven for being seduced into the erroneous position of supposing that there is no other knowledge or methodology relevant or applicable, other than the RCT.

I have written about the poor quality of scientific investigation in medicine and the limitations of evidence based medicine elsewhere — I sympathize with Read's views about poor RCTs, even though they are only one part of a bigger picture. EBM has problems (EBM and RCTs are pretty much synonymous), especially because the nature of the gathering of the RCT evidence, and the baggage of the sponsors who do most of it, almost always limits its objectivity and the way it can be generalized or extrapolated to the average patient: that introduces even more difficulties and uncertainties over and above any poor methodology and measurement techniques that may be utilized.

Doing good science is not easy, especially for doctors who generally have a relatively elementary grounding in scientific methodology, logic, and statistics; but clinging mindlessly to the life-raft of EBM is not an adequate solution.

It is a fundamental and elementary misconception about scientific reasoning and methodology to conclude that because RCTs are imperfect, or inconclusive, that therefore there is inadequate evidence to support the use of ECT, or any other treatment.

In the blog of the Council for evidence-based psychiatry (CEP) one of Read's previous ECT co-authors [17], Bentall (who describes himself as 'an experienced* clinical trialist'), comments on Read's paper, essentially endorsing the view that there is inadequate (RCT) evidence for the effectiveness of ECT and castigating the psychiatric fraternity for their lack of understanding of EBM.

*Experience and knowledge are not synonymous. Many weeks ago, I asked him if he had any suggestions for better methodologies that could be used, but he has remained silent on that issue.

Incidentally, Bentall's comment is titled, '*ECT is a classic failure of evidence-based medicine*', but he did not formulate his wording carefully: I do not suppose that he intended to imply, as he has done, that it is an illustration of how EBM itself is a failure.

One must concede there is a lot of second-rate RCT methodology in medicine generally, and the psychiatric fraternity are among the worst disciplines — but, as an aside, psychologists are the last people who should start throwing stones from inside their glass houses; their discipline is riddled with execrably poor science [18-20]. There are strange folk such as Daryl Bem [21], with his ridiculous work postulating 'time-reversed causality' — I shall not

devote space to this champion of intellectual masturbation, you can read the story here (it is entertaining):

https://replicationindex.com/2018/01/05/bem-retraction/

An important point (I have elaborated on this elsewhere) is that the fashion for RCTs has obscured other methodological approaches which are valuable. EBM's obsession with RCTs also fails to take account of our extensive knowledge of biology, evolution, physiology, genetics, pharmacology, and the other sciences that make up the foundations of medical science. Although such subjects may be less likely to capture the attention of psychologists (as far as I am aware psychology degrees do not have significant basic science content), they nevertheless form an important foundation from which rational therapeutics emerges. Knowledge from the basic sciences greatly increases the confidence underlying various forms of medical treatment. Treatment modalities and outcomes cannot be assessed in isolation and without taking account of that pre-existing science and knowledge. To do so is to exhibit ignorance and hubris.

This wider and deeper consideration of science helps to resolve the difficulty of withholding a treatment [ECT] which is rightly regarded as likely to be **life-saving in some instances, and valuable in some serious depressions.**

Pearl and the 'Do operator'

My opinion about the need to consider other methodological approaches is supported by the work of the 2011 Turing-award-winner, Judea Pearl. He has advanced scientific methodology with a set of techniques that involve [*inter tot alia*] manipulating an important variable in the equation, the 'do operator' [13].

I am not sufficiently well informed about the totality of Pearl's work to understand it in depth, and certainly not well enough to explain it cogently to others. Those interested may consult original material and other sources of explanation of this inchoate field.

However, I think I have grasped enough to suggest that a better trial methodology can be accomplished by doing (for instance) a trial of ECT that manipulates Pearl's 'Do operator'. For instance, where some of the initial treatments are inactive, or differently active, treatments — there are various ways of doing that — and using that 'Do operator' to establish that the timing of the changes and improvement subsequent upon treatment varies accordingly. An attempt has been made recently to consolidate the cause-and-effect relationship with a 'dose-effect' study using EEG parameters [22]. This is a powerful methodology; it should be possible to harness Pearl's techniques in such a scenario and

thereby design better trials that minimise or avoid the ethical conundrums that are perceived.

This is close to what has already been done in 'observational' studies (and good clinical practice) and is what makes those clinicians who are good scientific observers confident that ECT works.

There are frequent cases where, in the course of normal clinical practice, ECT has been delayed for one reason or another. The frequency with which improvement occurs in a discrete and predictable timescale after the initiation of treatment is difficult to explain, except by invoking a causal role for the effect of the main intervention, i.e. the induction of fits by an electrical current (as opposed to the other attendant changes which might represent non-specific effects, I prefer to avoid the term 'placebo effect' which is an inadequately conceptualised and defined notion).

If the improvement after such interventions occurred evenly, or randomly distributed over a non-specific timeframe of a month or two, that would indicate the evidence was insufficient to substantiate a cause-effect relationship: however, since the time interval to improvement occurs, determined by when the course of 'fit-induction' has started, in a defined and relatively narrow time-frame, it is difficult to come to any other conclusion than that there is a cause-effect relationship between induction of a fit and clinical improvement.

The same logic about how improvement follows a discrete predictable time course applies to drug treatment, where improvement is evident, to appropriately astute observers, within 5 to 10 days [23]. When people ask me how long it takes for MAOIs to start working my answer is, 'it depends on the astuteness of the observer and on what they focus their observations.' If on the other hand no improvement occurs for 2 to 4 weeks and then subsequently gradual improvement occurs, there is less sound reason to ascribe that to a treatment-effect. Such improvement is likely to be a non-specific effect (I prefer not to use the word placebo). In such cases it is logical, if the situation is stable, to reduce, or even cease, the treatment to see if a worsening of the condition occurs.

Next, we have the phenomenon of relapse after cessation of treatment — far from disproving effectiveness, that further substantiates the cause-effect nexus, because most of these patients when given maintenance ECT improve again, and then relapse if the interval between treatments is extended too much. You do not have to be Einstein to realize that this 'treatment-no treatment' linked to 'improvement-relapse' pairing much strengthens the supposition of a cause effect relationship.

Practicalities

Current best statistics indicate that about 50% of people relapse within six months of a successful course of ECT, **which leaves 50% who stay well**. There is insufficient space here for a discussion of how evidence strongly indicates that psychomotor retardation and CORE symptoms predict an even higher success rate for ECT [24-31].

That constitutes a valuable intervention modality when one is considering a serious illness with a substantial mortality, which causes a great deal of suffering over a prolonged period, including sometimes-irreversible deterioration in work and family circumstances, and is sometimes unresponsive to many attempts at both psychological and drug treatment.

I have had occasional difficulty in suppressing an air of knowledgeable condescension when listening to psychologist colleagues, whom I have treated as patients, who have been restored to wellness by such treatments as MAOIs and ECT, having previously been desperately frustrated at their failure to benefit from CBT.

My advice was, in general, that if you were well enough to do CBT then you were not seriously depressed, and if you were seriously depressed then you would not be cognitively or motivationally able to do CBT.

I would go as far as to say that is a practical test of whether a person needs primarily medical treatment, or primarily psychological treatment.

I should record here that I actively disliked giving ECT; it entailed getting up at an ungodly hour in the morning to do it before the surgeons started on their general surgery list, it was a treatment patients were sometimes disquieted about, and it involved all the palaver of consent procedures and making sure all the family were comfortable with it. The financial recompense to me was poor and it often incurred burdensome added costs for patients.

Also, a key issue, that non-medical contributors fail to take into account, is that although it may be an aesthetically unpleasant treatment, that is a completely irrelevant consideration: serious surgery is an aesthetically unpleasant exercise, but you do not say that you want to do an emergency operation because it is messy and smelly.

Therefore, I was disinclined and disincentivised to use ECT: however, I did it occasionally, because it was medically indicated — I doubt that I gave half a dozen courses of ECT in my whole private practice career: I would not want any patient, or patient's family, to discount the dramatic benefit it can confer as a result of the somewhat hyperbolic comments of these psychologists who

(like most psychologists) probably have little (or no) firsthand experience in the field. Ultracrepidarian.

I would always offer and advise a course of an MAOI before considering ECT: because of that policy I rarely needed to give ECT; most patients got better with the MAOI.

However, that is another story — in most western countries few people referred for ECT have been offered and MAOI beforehand, which in my view is not just illogical, but also sub-optimal practice.

Astonishingly, and regrettably, most guidelines and discussions on ECT do not even mention MAOIs.

Anyone who encounters a doctor who refuses to discuss ECT or dismisses it 'out-of-hand' — and the same goes for MAOIs — has met a person who neither understands serious depression, nor the life-saving and life-changing benefits that may be conferred by MAOIs and ECT. In such circumstances it would be advisable to seek a second opinion from someone experienced in the treatment of serious depression. Worryingly, the 'psycho-pharmacologically competent' sub-species of psychiatrist seems to be becoming increasingly rare.

The Brain Damage question

Read et al. have put some emphasis on the occurrence of brain damage, although they use the term carelessly and synonymously with memory impairment. They go on to say; '*Sadly, the severity and significance of the brain damage and memory loss is rarely studied.*' This is contradicted by recent research and reviews, such as Gbyl's meta-analysis which included thirty-two studies (not exactly '*rarely studied.*') **with 467 patients and 285 controls** [32], and concluded '*The MRI studies do not support the hypothesis that ECT causes brain damage; on the contrary, the treatment induces volume increases in fronto-limbic areas.*'

A useful paper and review by Anderson et al. has become available since the initial posting of this commentary which contains an excellent summary of the situation with appropriate references; '*Cognitive function after electroconvulsive therapy for depression: relationship to clinical response*' [33], this would not have been available to Read et al.

Anderson et al. concluded, *'We found no evidence for persistent cognitive deficits occurring as a result of ECT and were able to provide evidence of the importance of remission on the degree of improvement of subjective memory and some aspects of neuropsychological test performance up to 4 months after ECT.'*

There is much other work [34-37] strongly suggesting that there is no evidence that ECT adversely affects brain structure or causes brain 'damage' — quite the opposite would appear to be the case.

There is now good evidence that ECT reverses area specific changes, including atrophy, that seem to be associated with severe depression. This is an expanding area of research because new ultra-sensitive imaging technologies are continuing to produce better data, suggesting probable **improvements in brain volume, structure and connectivity after ECT**; this is attested to by a host of recent studies [32, 38-50].

Opinion and Conclusion

There is little doubt among researchers and clinicians concerned with ECT that it is a safe and effective treatment **for severe depression,** when that has not responded to other appropriately sequenced treatments: chronic depression engenders a higher risk of morbidity and mortality than ECT.

A great number of experienced and intelligent researchers in many countries have been researching and working with ECT over decades; so, however much one might sympathise with the criticisms of Read et al. about the less than ideal quality of research studies, it is easy to see how criticisms from such psychologists, with only peripheral experience, expertise and knowledge in this complex area, will be seen by many as hubristic and incompletely informed.

I have written extensively about the mediocre quality of research concerning drugs and other treatments in psychiatry. It is disappointing that, well into the third millennium, such deficiencies exist in the quality of the research underpinning important treatments — therefore the Read et al. critique, irrespective of one's agreement or disagreement with particular details, has positive aspects. Hopefully it will play a part in stimulating some overdue and methodologically better studies.

Such studies should utilize the latest advances in scientific methodology (cf. Pearl) and use techniques other than RCTs.

It would be an advance if all ECT could be documented in a central database and reviewed and followed up appropriately: indeed, that would be true for many other procedures used in medicine.

I would suggest consideration of a course of an MAOI before embarking on ECT.

Although ECT can be an effective treatment for severe depression, therapeutic resolve should not be lessened if it fails; patients may subsequently respond to appropriate regimes

designed for refractory cases [51]. Whether clinicians consciously adopt this negative 'last resort' view or not, they do tend to behave as if it were true; if a patient remains ill after ECT it is my experience that doctors give up on drug treatment.

Finally; the science is clear in showing that RCTs (and hence EBM) are 'autonomous of the basic sciences and blind to mechanisms of explanation and causation' and that 'causality, is the *sine qua non* for all understanding and progress'. RCTs have little to do with the basic sciences and causality and repeatedly demonstrate that A>B>C>A — after which you disappear up your own fundament: **it is like Penrose stairs with drugs**.

It is time to break free of the hegemony of RCTs which for too long have been an albatross around the neck of sensible clinical science: clinical science using non-RCT methods, and 'bed-side' observation, are directly to do with causality and individually tailored treatment response and have distinct advantages; when harnessed to Pearl's 'do operator' they can be expected to lead to useful progress.

Finally, it is useful for general readers to appreciate that great caution is required when reading opinions by some authors, especially those from outside of the relevant field of study – it is difficult to regard what Read et al. have written as anything other than exhibiting poor objectivity, poor scholarship, and poor probity.

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