Hobart talk, Oct 24th 2023. RANZPsych.

MAOIs: indications, usage, and interactions

The talk itself concentrates general aspects and principles. Details are here in key references for those who wish to understand more about the substantive evidence and to study in greater depth.

Supplementary information & resources

References, numbers as in PPT slides from the talk

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Comments and further information

The important purpose of starting my talk by noting the flaws and difficulties with RCT research is to get things in proportion and to emphasise that clinical experience is epistemologically just as valid as supposedly 'evidence based medicine' and RCTs — that is an important message. Do not allow yourself to be bullied into following the guidelines. It is not possible to make optimal decisions about the individual treatment of patients if one set of evidence (RCTs) is overvalued relative to many other types of evidence, especially when it is falsely perceived as a 'gold standard'.

Note that the opinions and sources I discuss and cite are from eminent mainstream academics, not Mavericks and eccentrics. John Ioannidis is an exemplar.

John Ioannidis Dsc is a colossus, he is Professor, of Medicine, Epidemiology and Population Health, Biomedical Data Science, and Statistics, at the Meta-Research Innovation Center at Stanford. He has written many articles pointing out the faults in research and methodology in medicine which are essential reading. I mentioned especially, 'Why most published research findings are false' [1], 'Lies, Damned Lies, and Medical Science' [2], 'The Mass Production of Redundant, Misleading, and Conflicted Systematic Reviews and Meta-analyses' [3], Cochrane crisis: Secrecy, intolerance and evidence-based values [4] — but I could have given many other similar examples of his work.

Usage and history: I encourage especially younger practitioners to familiarise themselves with the history of how these drugs have been used. This has been written about extensively especially the eminent professor of the history of psychiatry in Toronto, Edward Shorter. Vincent & I published a paper with him covering some of this and giving references [5], and there are several commentaries on my website that are relevant.

It is especially important to understand that ~90% of RCTs are industry funded and they form the basis of 'EBM' and guidelines. There is a strong argument that this distorts the whole process of clinical decision-making for individual patients since RCTs and guidelines do not tell us about individuals. We have written a specific paper relevant to that [6].

Causality. I draw particular attention to the number of eminent people in recent decades who have made powerful statements about the limitations of scientific methodologies relating to RCT studies — as Pearl said [7], 'Science is nothing without causality' and **RCTs contribute nothing to understanding causality [or mechanisms]**.

Ashcroft [8], of RCTs, 'autonomous of the basic sciences…blind to mechanisms of explanation and causation'

Solomon [9],, 'Emphasis on EBM has eclipsed other necessary research methods in medicine'

Berwick [10], 'we have overshot the mark with EBM';

Sir Michael Rawlins said, in his Harveian Oration [11], '*the notion that evidence can be reliably placed in hierarchies [as all guidelines do] is illusory … Yet the technique has important limitations of which four are particularly troublesome: the null hypothesis, probability (P-values), generalisability, and resource implications.*'

NB. The famous, but disordered and unpleasant, statistician Fisher was largely responsible for P-values. Understanding how flawed that idea is, and how vehemently he was against Bayesian ideas, leads to a deeper understanding of statistics; Baye's theorem remained in the shadows because it had played a essential role in cracking the Enigma code (Allan Turing) and information about it was restricted under the official secrets acts, both in North America and the UK. That impeded the adoption of Baye's theorem in science, which, long ago, would have gone at least part-way to overcoming the problems caused by P values — I've written a separate commentary about this on the website — that details the **widespread opinion, among statisticians, that P-values were the worst thing ever to happen to medical science**. The fact that they are still so dominant is the greatest condemnation of the poor quality and inappropriateness of most scientific methodology. As the renowned Oxford statistician Altman states [12] '*abuse of statistical tests… have been decried for decades, yet remain rampant*'.

An illustration of this ignorance of methodology, statistics, and P-values is given by Charles Beasley, a 'bigcheese' at Eli Lilly, and the architect of the multi-billion dollar success of fluoxetine and derivatives; almost every paper he has ever published has been about that drug: he admitted in court that he knew little about statistics — he failed to respond to a public criticism I made of his views here. In checking the link I was reminded of the witty tag I gave to this comment, '*P-hunting: The illogical in pursuit of the indefensible*' (cf. Oscar Wilde)

… then there is the **RCT death-blow of Simpson's paradox** which invalidates most RCT trials [13-17], about which one should be informed. See Fenton [13] for a quick primer: he demonstrates simply and clearly how Simpson's paradox has serious implications that invalidate almost all RCTs that demonstrate small differences — that is all the trials relating to antidepressants. Note that almost all RCTs are conducted with complete disregard to the existence of, and difficulties caused by, this paradox — this is because most of those involved in designing these trials have insufficient knowledge of scientific logic, methodology, and statistics.

The Helsinki declaration states that, *de facto*, badly conducted research cannot be ethical!

PTR group papers

The full list of papers that my group has published about MAOIs (about 20) is available here and there are a number of commentaries on my website in this section, some of which have been the basis of subsequently published peer-reviewed papers.

Pharmacologic properties: keys refs [18-20].

Interactions: a good overview paper is our recent CME orientated one in Psych Annals [21], because it explains why interactions are much easier to understand than most sources would have you believe — that references many of the key papers I have written.

They have been **over 100 reviews of ST since the turn of the millennium**: the vast majority of them have contained substantial amounts of misinformation and exhibited serious misconceptions about ST: this critique [22] that we published only a month or two ago, of a recent ST review paper, is a useful exercise in understanding how such reviews are misconceived, see also here.

Papers supporting MAOI superior efficacy. Lastly, since so many of you will encounter colleagues who decry the evidence for the effectiveness of MAOIs in biological depression, it is helpful to be aware of a number of recent key papers summarising the evidence for their superior effectiveness [20, 23-29]. Over the decades of my professional life the opinion of experienced psychopharmacologist about drugs has consistently proved to be more helpful than the results of RCTs. Therefore I recommend you consider joining my International MAO Expert Group where

you will have access to the opinions of many internationally eminent psychopharmacologists; a quick look at the link to the group will help you appreciate how many eminent persons are involved.

It is important to understand that RCTs are not the 'gold standard', that various other types of experimentation and evidence are just as epistemologically valid, and that the erosion of confidence in clinical judgement and clinical experimentation has severely dented the confidence of clinicians in their own opinions, such that large sections of the profession now eschew treatments that are not "in the guidelines".

BP guide to MAOI titration

Using postural BP drop to guide MAOI titration, Gillman, Ken. 'MAOIs - Blood Pressure'. PsychoTropical Research, 13 Nov. 2002. Direct URL: https://www.psychotropical.com/wp-content/uploads/9.1-MAOI_BP-Instructions.pdf

MAOIs in Bipolar depression (versus reuptake inhibiting Ads)

Many experienced clinicians consider TCP to be the drug of preference for depression in those who are bipolar. Key refs: [23, 30-33]

A suggested treatment pathway to consider

Charlie, Page and link

Join the maoi roundtable

Link

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