# Important new TCP review

I would like to draw attention to this significant paper by Sven Ulrich and his co-authors for this useful and significant paper on TCP [1].

For this initial rapid response comment, I make no apology for citing the abstract of the paper in its entirety

PURPOSE: We conducted a comprehensive meta-analysis of the comparison of tranylcypromine (TCP) and tricyclic antidepressants (TCAs) in the treatment of depression because such work is lacking in medical scientific literature. METHODS: Literature was searched for studies of TCP controlled by TCAs in multiple databases and in reviews of TCP and monoamine oxidase inhibitors. The natural logarithm of the odds ratio (logOR) and the pooled logOR according to a fixed effect model were calculated for the numbers of responders and nonresponders. RESULTS: A total of 227 studies of TCP were found including 75 controlled studies of TCP-monotherapy. Twelve of 23 studies of TCP monotherapy and TCAs were excluded for several reasons (duplicates, safety studies, retrospective, cross-over), leaving 11 prospective and parallel controlled studies of TCP monotherapy versus TCAs (6 randomized double-blind). One study was excluded from the meta-analysis because of low quality of study design according to the Food and Drug Administration guidelines of studies of antidepressant drugs and high risk of bias according to the Cochrane's tool. Two studies with equal efficacy of TCP and TCAs in continuous endpoints did not provide dichotomous response data. A pooled logOR of 0.480 (95% confidence interval, 0.105-0.857, P = 0.01) resulted for the remaining eight studies in the primary meta-analysis, which favors TCP significantly over TCAs (test for heterogeneity: capital HA, Cyrillic = 8.1, df = 7, P > 0.3, not heterogenous; I = 13.6%, heterogeneity not important). The result is robust with respect to inclusion of hypothetical response data of the 2 studies with continuous data only: pooled logOR, 0.350 (95% confidence interval, 0.028-0.672, P = 0.03). Visual inspection of forest plots and subgroup analysis suggest that superiority of TCP over TCAs is determined by 2 studies in psychomotor-retarded (anergic) depression.

CONCLUSIONS: Tranylcypromine and TCAs have an equal antidepressant effect in a mean sample of depressed patients with mixed psychomotor symptoms. Tranylcypromine might be superior to TCAs in depression with predominant psychomotor retardation.

## Concerning side-effects, the studies they reviewed indicated:

> Significantly lower frequencies occurred in TCP treatment compared with amitriptyline with P < 0.05 or better for tremor, dry mouth as a single reaction, and anticholinergic reactions as a group in one study.25 Significantly higher frequencies resulted for TCP treatment compared with nortriptyline with P < 0.05 or better for dizziness, insomnia, and overexcitement in another study.26 Diastolic (mean values of 77.8 and 88.0 mm Hg, respectively, P < 0.001) and systolic (mean values of 115.6 and 129.3 mm Hg, respectively, P < 0.001) blood pressure...
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> Tranylcypromine was superior to TCAs in terms of a significantly lower frequency of tremor, constipation, and blurred vision. Tricyclic antidepressants were superior to TCP in terms of a significantly lower frequency of insomnia.

I would also add the comment that the huge advantage of less sexual side-effects does not come out in this analysis for the simple reason that most of the studies making comparisons did not make proper enquiries about sexual side-effects. If you don't look you won't see!

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## Concerning effectiveness in relation to the TCAs

> The primary meta-analysis of the comparison of TCP and TCAs as presented in Figure 1 **revealed superiority of TCP over TCAs**. This is an astonishing result in light of the history of discussion of this topic presented previously.

In my opinion this is only astonishing to people who read (and rely on) papers rather than having actual clinical experience of treating patients. That experience makes it perfectly obvious that TCP is superior to TCAs and other antidepressants.

Concerning efficacy for the 'anergic' symptom profile (i.e. more severe 'biological' depression)

> Superiority of TCP over TCAs in psychomotor-retarded (anergic) depression is in agreement with the pharmacological profile of TCP.

I am pleased, but not surprised, by that conclusion. This is yet further compelling evidence that attaining improvement in these sorts of illnesses requires a drug that significantly elevates dopamine.

I have repeatedly expressed the view that carefully evaluated clinical opinion and experience is superior to many, if not most, drug trials. This review highlights that the superiority of TCP in anergic depression relates to a relatively small number of studies were the total number of patients treated is a fraction of the number of patients I have treated in my career.

One does not need a double-blind trial to recognise that a patient with severe retarded depression has got better, gone home, and gone back to work within a month of starting TCP — despite the fanfare and pseudoscience, it is that simple. See (*inter tot alia*) the Professor's story

Almost the only drugs that raise dopamine are MAOIs.

### References

1. Ulrich, S., et al., *Efficacy and Adverse Effects of Tranylcypromine and Tricyclic Antidepressants in the Treatment of Depression: A Systematic Review and Comprehensive Meta-analysis.* J Clin Psychopharmacol, 2020. **40**(1): p. 63-74.