

# Antipsychotics: psychiatry's biggest idea

COMMENTARY ON... MEET THE RELATIVES<sup>†</sup>

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## SUMMARY

Clinical psychiatrists working today owe a great deal to the discoveries of the pharmaceutical industry since 1953, especially in relation to antipsychotic drugs. Yet patients need still better antipsychotics with greater efficacy and fewer side-effects. We should not let nostalgia cloud our judgement.

## DECLARATION OF INTEREST

J.C. has provided advice and lectures at meetings sponsored by the manufacturers of several antipsychotics.

'Sexual intercourse began  
In nineteen sixty-three  
(which was rather late for me) –  
Between the end of the Chatterley ban  
And the Beatles' first LP'

Annus Mirabilis: Philip Larkin (1922–1985)<sup>‡</sup>

In a similar sense, psychiatry began in nineteen fifty-three, between the reports about chlorpromazine in France and the validation of John Cade's discovery of the antimanic effect of lithium in nineteen fifty-four. This was not too late for Professor Owens or for me; we ourselves were too late to witness the actual introduction of antipsychotics, but we have spent our professional lives in an era dominated by developments in neuroscience and therapeutics. We have lived through the elucidation of the mechanisms of action of antipsychotics, and of dopamine as a neurotransmitter.

Owens (2012a,b, this issue) regrets the loss of the concept of ataraxy, and that little attention has been given to understanding its neural basis. However, this affective 'detachment', or 'indifference', which was unique and distinct from sedation, may be what is now described as the effect of antipsychotics to reduce 'incentive salience', a vital aspect of emotion dependent on dopamine function (Berridge 1998).

The distinction between classes of 'typical' and 'atypical' antipsychotics is unfashionable, but the words are embedded in our language and we need

to share a meaning. This was addressed by Kerwin (1994): 'clinical atypicality would be defined by the low propensity to produce extrapyramidal side-effects and tardive dyskinesia relative to typical drugs like haloperidol and chlorpromazine'. This definition avoids the old/new dichotomy, allowing some older drugs to be included, but preserves the usefulness of the class distinction.

It is useful to note that Owens has recanted his earlier teaching that anticholinergic drugs should be used only if (or when) extrapyramidal side-effects occur, but now recommends their routine use for starting anyone on haloperidol. In countries where patients are treated exclusively with older antipsychotics, it appears that 'Parkinsonism is as prominent a risk as ever' only with the older typical antipsychotics. This is also the conclusion of independent meta-analyses (Leucht 2011).

Although the atypicals share no other quality than this, they do show individual differences in efficacy as well as side-effects. The statement that 'Most clinicians would now accept the American view that in terms of efficacy (and, post-CATIE, effectiveness too) all antipsychotics are comparable' (Owens 2012a) contrasts with experience with clozapine and meta-analyses of the newer drugs, which shows small but real superiority in efficacy for some new drugs over older ones (Cookson 2008a; Leucht 2011).

The differences are more striking when the treatment of mania is analysed. A multi-treatment meta-analysis (Cipriani 2011) confirms the impression from individual randomised controlled trials (Cookson 2008b) that no atypical antipsychotic is superior in efficacy to haloperidol in mania and some are distinctly inferior.

The history of the discovery of chlorpromazine is informative (and often asked about in the Royal College of Psychiatrists' Membership examination, the MRCPsych). Most accounts give credit to the pharmaceutical industry (Paul Charpentier, the chemist who synthesised it, and Simone Courvoisier, the pharmacologist who named the drug Largactil<sup>®</sup> for its diversity of pharmacological and potential clinical actions)

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<sup>†</sup>See pp. 323–336 and 337–350, this issue.

<sup>‡</sup>The poem 'Annus Mirabilis' is published in *Philip Larkin: The Complete Poems*, Edited by Archie Burnett, Faber & Faber Ltd, 2014. Extracts from the poem appear with kind permission of Faber & Faber.

and to the clinicians (Henri Laborit, a surgeon with particular interest in anaesthesia, and the psychiatrists Professor Jean Delay and Dr Pierre Deniker). We should remember, as the professional historian Edward Shorter (1997: p. 250) put it:

‘Although Rhône-Poulenc had not identified chlorpromazine as an antipsychotic, it was company scientists who had systematically designed the compound and tested it on animals. The drug’s discovery owed nothing to serendipity.’

Owens and I have seen the efforts of the pharmaceutical industry to improve the quality of antipsychotics available to our patients and to extend the indications for these drugs. Given his concerns about neurological side-effects it is surprising that Owens gives industry little credit for developing the newer drugs. Indeed, the widespread distrust of the motives and products of the industry bodes ill for the future of psychiatry (Kendall 2011). New drugs are staggeringly expensive to develop, and no organisation apart from the pharmaceutical industry will fund them. It is tempting to convey our disappointment in the pharmaceutical industry in the way of a jilted lover, who suddenly realises that the beloved was interested not just in their higher aspirations but in their money and says they will never trust a suitor again.

We shall certainly need better psychotropic drugs, including antipsychotics. Unless we

appreciate the advances that have been made in drug treatments, we shall feel, like Philip Larkin:

‘So life was never better than  
In nineteen sixty-three’.

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