BJPsych | The British Journal of Psychiatry (2011) 198, 333–335. doi: 10.1192/bjp.bp.110.086207

Editorial

Has psychopharmacology got a future?

Philip J. Cowen

Summary
Fifty years ago pharmacological discoveries transformed psychiatry but progress since then has been relatively slow and there is unease about the role of industry. Despite this, the possibilities of pharmacological treatment have improved in recent years but exploiting developments for the benefit of patients requires psychotherapeutic skill as well as a high level of scientific knowledge.

Declaration of interest
P.J.C. has been a paid member of boards that have advised different drug companies on the development of antidepressant drugs. In the past 3 years these companies have included Eli Lilly, Lundbeck and Servier. P.J.C. has also received remuneration for scientific advice given to legal representatives of GlaxoSmithKline.

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Last year, AstraZeneca and GlaxoSmithKline announced cessation of research activity in the field of psychiatric drug development. To some who deprecate the use of drugs to help people with psychological problems this will be welcome news. For if psychiatric disorders are best regarded as social constructs, related to issues of personal narrative and social exclusion, the use of pharmacological treatment can be seen as incoherent and harmful. Other commentators, although highly critical of current psychopharmacology, allow that drug treatment may have a role in some clinical situations.[1,2] Overall. the majority of practitioners would probably agree that better drug therapies would be helpful. Why has it been hard to achieve this goal?

The development of modern pharmacological treatments for bipolar disorder, depression and schizophrenia in the middle of the last century was an extraordinary story of chance discovery and brilliant clinical observation. Those who have recounted the various discoveries so well appear to believe that the effect of these medicines for patients was generally beneficial.[3,4] Since then, however, further progress has been slow because we lack reliable knowledge of the neurobiological basis of the conditions we treat. The notion that discovery of relevant genes would be a spur to current drug development looks to have been premature, and although neuroimaging provides fascinating and plausible accounts of the pathophysiology of psychological disturbance, knowledge of the relevant neural networks has not readily mapped onto pharmacological discovery. In terms of new drug design it has therefore been necessary to build on what we already know, which inevitably limits true innovation.

Is it the fault of industry?

As with other branches of medicine it is difficult at present to see how new drugs could be developed for clinical use without the support of the drug industry and yet many see the industry as part of the reason for our lack of progress. Drug companies stand accused, for example, of overpromoting drugs for the management of spurious disorders such as 'social anxiety' and 'major depression'.[4] At the same time, inconvenient data that question efficacy and safety are suppressed while leading members of the profession are financially induced to market dubious agents to their colleagues. It must be noted that these accusations are by no means restricted to psychiatry, although perhaps our field is more vulnerable to the charge of illness creation because of the limitations of psychiatric diagnosis.[3,4]

Collaboration between academics, clinicians and industry is more likely to produce better drugs than if industry works in isolation. However, an influential strand of current opinion sees such collaboration as inevitably corrupting. A *BMJ* correspondent, noting the publicly declared industrial conflicts of interest of eminent members of a National Institute for Health and Clinical Excellence (NICE) panel advising on thromboebolism, asked, 'Are these guidelines worth the paper they are written on?'[5] A recent working party of the Royal College of Physicians concluded that the current stand-off is unhelpful. We need to decide whether or not to encourage industrial collaboration and if so what the mechanisms should be.[6] At the same time it is important for industry to rebuild its relationships with professionals and patients by adopting a radically more open and honest scientific and marketing culture. It is also helpful to recognise that conflicts of interest are universal, not just financial, and particularly in psychiatry, extend to matters of ideology, politics and religion.[7,8]

Perception of psychopharmacology

Pharmacological treatments for psychiatric disorders have a poor image both inside and outside psychiatric services. Public perception is probably influenced by stigma (a flagship BBC current affairs programme referred to antidepressants as 'happy pills')[9] and the coverage of selective serotonin reuptake inhibitors by the *BMJ* at one point became so deranged that the journal achieved the difficult feat of having to apologise publicly to Eli Lilly.[10] Within the mental health profession pharmacological treatment has been associated with paternalism, insensitivity to personal and social context and lack of psychotherapeutic skill. Richard Bentall contrasts drug treatment and psychotherapy in the context of placebo-controlled trials, 'Warmth, kindness and the installing of hope . . . are intrinsic elements of psychotherapy, but not of drug treatments'[2] (those of us who have experienced Kleinian psychotherapy may not necessarily share this view). At a recent meeting of the Faculty of Academic Psychiatry, a speaker showed a slide of donkeys to illustrate the profession in relation to its use of atypical antipsychotic drugs. In this context it is perhaps understandable that taking psychotropic medication may add to a patient's sense of stigma.[11]

A contributory element to this antipathy is probably the fact that, unusually in medical practice, psychotropic drugs (mainly

antipsychotic agents) are sometimes given coercively to people who decline treatment. With the decrease in medical paternalism and the lessening of professional trust this feels increasingly uncomfortable, particularly since the available drug treatments are of limited effectiveness and have unpleasant side-effects. Nevertheless, many of us will have treated patients who, although reluctant to receive antipsychotic medication, posed less risk to their families and the public when taking it. Only a fraction of psychotropic drug treatment is given in this way. However, because of the critical ethical importance of the issue there needs to be much more debate about the justification and practice of coercive pharmacological treatment in psychiatric practice.

Psychopharmacology in psychiatry

Most prescribing of psychotropic drugs occurs outside specialist psychiatric practice. Do we need psychiatrists to prescribe medication at all? Pharmacological treatment of most conditions is broadly straightforward, supported by NICE guidelines, and perhaps could be carried out by general practitioners and appropriately trained nurses. Having once subscribed to this view I now believe that a fairly sophisticated knowledge of pharmacology is helpful in providing individual patients with the best treatment and at the same time resisting irrational marketing claims. Recently, for example, in a penitential commentary, Tyrer & Kendall called for the terms 'first-generation and second-generation antipsychotic' to be abandoned.[12] But for many years it has been clear that these terms do not describe meaningful pharmacological distinctions.[13] It is important that prescribers be aware, for example, that amisulpride is very different pharmacologically from olanzapine (and in what way) but not very different at all from sulpiride.[13] When prescribing antipsychotic drugs we should collaborate with patients to find the best treatment for a particular person in a particular situation. An expert knowledge of pharmacology is part of this.

In the same way, the pharmacological treatment of bipolar disorder is now rather complicated with several additional drugs available for different stages of illness. Interestingly, some of these drugs, for example, quetiapine and lamotrigine, were introduced first for other indications, showing that clinical discovery of useful treatments is still important in psychopharmacology. Careful trials of different medications can sometimes lead to meaningful benefits which patients have the right to explore if they wish. To achieve this, patients need to collaborate with clinicians who are knowledgeable and skilled in the safe use of rational treatment combinations.[14]

Is progress possible?

Psychopharmacology may have a golden past,[4] but does it have a future? Pharmacological treatment is better now than when I trained in psychiatry. The greater variety of drugs means that, with care, it is more often possible to find a treatment that is acceptable and helpful to an individual patient. Less toxic, better-tolerated antidepressants are useful, and clozapine has been another important clinical discovery. Between the blandishments of industry and the antipathy of critics, psychopharmacology has made some incremental progress. From where might future advances come and what are the obstacles?

Psychiatry is a field where it is still possible to make important clinical discoveries by investigating drug therapies developed for other medical purposes. The fact that we know relatively little about the neurobiological basis of our disorders does not mean that useful treatments cannot be found and of course novel therapies can stimulate interesting pathophysiological research. In this respect the current regulatory and economic barriers confronting independent clinical trials are a worry.[6] Would the pharmacological discoveries that transformed psychiatry be possible today? In the meantime, developments in pragmatic trials and meta-analyses are important in enabling us to use the tools we have as well as possible.[15] However, trials do not necessarily help us find the right treatment for individual patients. Despite the promise of pharmacogenetics, the goal of scientifically based personalised pharmacological treatment is still elusive, remaining almost totally reliant on the combined experience and expertise of patient and doctor.

One reason for the disappointing output of innovative compounds from industry – despite enormous investment – has been over-reliance on animal models of psychiatric disorders, which have always been of doubtful validity. From this viewpoint the development of human models of disorders using, for example, neuropsychological paradigms and studies of people at high risk of illness looks more promising[16] and might enable better selection of the new drug candidates, which will eventually result from growing knowledge of genetic mechanisms and novel cellular signalling pathways. There is also definite progress in understanding the neural systems involved in psychiatric disorders and how current drug therapies and psychological treatments interact with them.[17] This information could be valuable in assessing potential therapeutic benefits of new pharmacological and psychological approaches.[16]

Psychopharmacology is important to many patients, can be difficult to manage safely and effectively, and is controversial. The best way to secure the future of the discipline is to ensure that psychiatrists who prescribe have a deep understanding of the relevant clinical science as well as the ability to assess clinical trials of whatever provenance in a critical yet balanced way. In terms of individual treatment, initiation of medication with a follow-up appointment several weeks hence, perhaps with a different clinician, is not the way to use medicines successfully. Like psychotherapy, successful prescribing in psychiatry requires a collaborative and reflective clinical relationship characterised by continuity as well as warmth, kindness and hope.

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First received 23 Aug 2010, final revision 3 Jan 2011, accepted 17 Jan 2011

Acknowledgement

I thank the *Journal* reviewers for their helpful comments on an earlier version of this paper.

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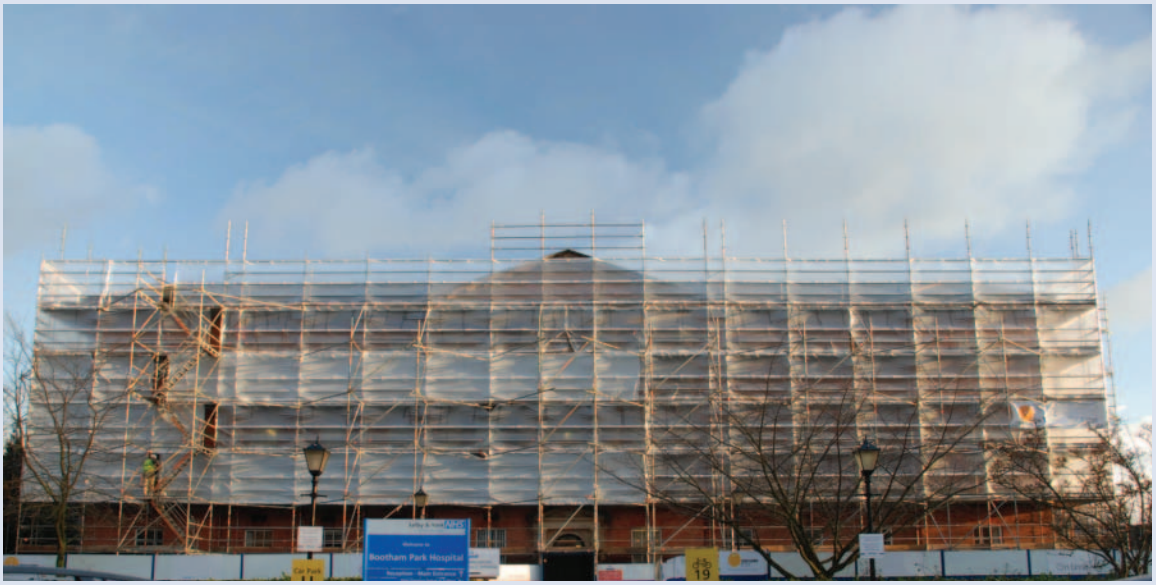
psychiatry in pictures

Shrink-wrapped asylum

Jeff Clarke



The imposing façade of Bootham Park Hospital in York, shrouded behind builder's plastic during repairs to the roof (above), and (below) as it more usually appears. Bootham Park is the oldest purpose-built psychiatric hospital in England which is still used for its original purpose, providing 21st-century services in an 18th-century building.

Although the times and terminology (right) may have changed – until 1904 the building was called the York Lunatic Asylum – the need for skilled and compassionate care and treatment for people with mental illness remains the same.

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The British Journal of Psychiatry (2011) 198, 335. doi: 10.1192/bjp.198.5.335

https://doi.org/10.1192/bjp.bp.110.086207 Published online by Cambridge University Press