Correspondence

EDITED BY KIRIAKOS XENITIDIS and COLIN CAMPBELL

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A role for psychedelics in psychiatry?

I read with interest the editorial ‘Can psychedelics have a role in psychiatry once again?’ (Sessa, 2005). Aside from overcoming current legislative barriers, attention needs to be given to education about known research into this field, a function which this editorial uselessly starts to fulfil.

The concern remains that the image of psychedelics was not shaped by the already existing extensive professional literature, but by the mass media sensationalising the accidents of unsupervised self-experimentation (Grof, 2001). It could therefore be surmised that decisive influences will be a variety of political, legal, economic and mass-psychological factors, rather than the results of current and ongoing scientific research. Interest from the psychiatric community will be paramount if this research information is to be critically reviewed with a view to clinical application.

The difference between psychedelics (entheogens) and other psychotropic drugs is that entheogens work as ‘non-specific amplifiers of the psyche’, inducing an altered or non-ordinary state of consciousness (Grof, 2000). The content and nature of the experiences are not thought to be artificial products of their pharmacological interaction with the brain (‘toxic psychoses’) but authentic expressions of the psyche revealing its functioning on levels not ordinarily available for observation and study. In order to conceptualise this, a vastly extended cartography of the psyche (Grof, 2000), one which challenges our biomedical psychiatric model, is required.

Within psychiatry, entheogen substances (one of several methods of inducing a non-ordinary state of consciousness) could contribute to a powerful form of experiential psychotherapy; an important addition to a psychiatric armamentarium, working with domains of the psyche traditionally ignored in our ethnocentric Western model (Schltiz et al, 2005).

Potential credence for this field depends upon whether we view all non-ordinary states of consciousness as pathological or whether in some cases, some ‘psychotic’ experiences can be seen to have potential value as well as being potentially damaging. There is ongoing interest among mental health professionals in the concept of spiritual emergence as well as the therapeutic power of altered states of consciousness, the subject of a recent 1 day meeting held jointly with the Royal College of Psychiatrists and the Royal Society of Medicine (http://www.rcpsych.ac.uk/college/sig/spirit/index.asp). I would certainly value a continuing debate exploring this area.


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The editorial by Dr Sessa is both timely and encouraging. The almost complete denial, not only by the media but also by the psychiatric establishment, that lysergic acid diethylamide (LSD) and related psychedelics had an important place in the therapy of a wide range of psychoneurotic disorders is astonishing. This clearly has a psychodynamic explanation.

The interest shown during the 1950s and 1960s by the psychiatric establishment in the use of the psycholytic agents is even greater than Dr Sessa indicates. The meeting of the ‘American Psychological Association’ at which the therapeutic use of LSD was discussed was actually held at the Annual Meeting of the prestigious American Psychiatric Association, in 1955, rather than 1951 (Cholden, 1956). Subsequently, the role of psychedelics in therapy was the subject of a number of national and international conferences. Perhaps the most significant of these was held in London in February 1961, when the Royal Medico-Psychological Association, the forerunner of the Royal College of Psychiatrists, devoted the whole of its 3 day quarterly meeting to the subject (Crocket et al, 1963).

Dr Sessa touches briefly on the question of the possible resumption of psycholytic therapy. There have been a number of recent suggestions that this could once more become a possibility. Psychiatrists tempted to enter this field (assuming that the appropriate drugs – LSD, 3,4-methylenedioxymethamphetamine (MDMA), psilocybin – are made legally available to doctors) should bear in mind that the success of psycholytic therapy depended on careful training, not only of the therapist, but also of the nurses and others who formed the therapeutic team. That expertise at one time reached a high level, and all that has been lost. My hope is that research and practice will continue, and that it will be supported by the College.


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Dr Sessa is to be congratulated on his welcome review of research into psychedelic drugs. We are reminded of the hope that these drugs ‘could be for psychiatry what the microscope is for biology or the telescope is to astronomy: an essential tool to explore the parts of the internal world that are usually inaccessible’.
Grof (1975, 1990) has been the most prominent explorer of these inaccessible regions for over 40 years and once research into lysergic acid diethylamide (LSD) became impossible, developed a technique for inducing non-ordinary states of consciousness called ‘holotropic breathwork’. This offers many of the features of the psychedelic state without the need to take a drug. Using insights from the use of LSD and holotropic breathwork in thousands of people, Grof (1975) proposed an extended model of the psyche with psychodynamic, perinatal and transpersonal layers. These are provocative models of mind which challenge existing Western paradigms of consciousness and which probably reinforce mainstream models of mind which challenge existing personal layers. These are provocative extended model of the psyche with sands of people, Grof (1975) proposed an LSD and holotropic breathwork in thou-LSD and holotropic breathwork in thou-

In his stimulating editorial, Dr Sessa gives a history of the enthusiasm for psychedelic psychotherapy that enjoyed a brief flowering following Hoffman’s discovery of lysergic acid diethylamide (LSD) in 1943. Dr Sessa argues that the time may now have come for a reappraisal of the role of such substances in psychiatry. Having myself recently had cause to look at this literature (Edwards, 2005), I find myself somewhat less keen on a reinstatement of this practice.

Within the historical frame one could argue that the proper subject for the case study is the conduct and attitude of the professionals who were the enthusiasts of that time. The tone of the contemporary publications was in general remarkable for a willingness to get ahead of the research evidence, and rush to positive and at times even messianic conclusions. Here are some examples of writings within that genre: ‘These agents have a part to play in our survival as a species.’ (Osmond, 1957); ‘The wonder of LSD is that it can bring within the capabilities of ordinary people the experience of universal love’ (Davidson, 1961); ‘I feel that those on the moving edge of new culture will eventually use these tools in a way that will utterly transform the nature of human consciousness’ (Einhorn, 1971).

What one sees in those kinds of statements is the dubious ambition of therapists to gain possession of chemical magic and exert power over their drugged patients – the therapist as shaman rather than as evidence-based practitioner. But that I’m sure is not Dr Sessa’s intention.


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Author’s reply: I am most grateful for the correspondence regarding my article on psychedelics. Dr Read is right to point out the various techniques for inducing a non-ordinary state of consciousness. As well as the breathwork developed by Grof (1990), humankind has historically used meditation, exercise, fasting, chanting, dancing and even sex to induce transforming internal changes. What all these states have in common is the final goal of increased awareness and a loosening of the ego – facilitating personal exploration and being useful therapeutically to aid psychotherapy. As well as non-drug-induced non-ordinary states of consciousness, psychedelics may have an important role to play – both in psychotherapy and in the scientific study of consciousness.

I agree with Dr Edward’s comments about statements made by some overenthusiastic individuals of the psychedelic movement. Many clinicians of the 1960s (not to mention writers, artists and pop stars) saw LSD as a magic wand, a common panacea to assure ‘better living through chemistry’. It was this attitude that killed genuine scientific study and kept the therapeutic potential of psychedelics shelved for so long.

Psychedelics cannot save the world, but they may have a role to play as adjuncts to the psychotherapeutic treatment of neuroses. We must at least study and research their potential with modern randomised controlled trials. For the hundreds of clinicians and thousands of patients of the 1950s and 1960s that witnessed the safe and effective usage of psychedelics, these substances did appear to be useful (Masters & Houston, 1973). But as a profession we need to distance ourselves from the Timothy Leary-esque, messianic approach to psychedelics, if we are to allow a dispassionate and scientific study of their potential.
I was pleased to read Dr Crowley’s in-depth understanding of the complexity and value of the altered state of consciousness. Thankfully, there are clinicians such as Dr Crowley with the confidence not to dismiss the non-ordinary state of consciousness as mere ‘acute confusion’, but to believe that psychedelics, and non-drug non-ordinary states of consciousness, can inform and enlighten us with new approaches to understanding the mechanisms (and associated pathologies) of the brain. Since the earliest human societies we have sought knowledge and healing from these states – perhaps now this technique can be utilised in a scientific and evidence-based approach to relieve the burden of anxiety disorders for today’s patients.

I am most grateful to Dr Sandison for his kind and supportive words – and thank him for the correction regarding the date of the American Psychiatric Association conference in 1955. I share his astonishment at the medical profession’s inability or unwillingness to embrace the therapeutic potential of psychedelic substances. This shortcoming is augmented by the fact that the hiatus in research over the past 40 years appears to have been for socio-political rather than scientific reasons – and it is those pioneering psychiatrists like Dr Sandison who are right to feel disheartened.

I am enthusiastic, however, at the current re-emergence of interest in this field. There are increasing numbers of randomised controlled trials of psychedelics (largely from the USA) and these may yield results that guide future therapeutic applications (http://www.maps.org; http://www.heffter.org). There is also increasing interest in using psychedelics in consciousness research in the UK (http://www.beckleyfoundation.org).

I do hope that my article, and a forthcoming meeting to be held at the College (contact me at drbensessa@hotmail.com for further details), can help raise awareness of this subject. I also agree with Dr Sandison in his plea for continued support from the College to bring this subject to the attention of doctors in the UK.


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Kraepelinian dichotomy

Craddock & Owen (2005) attribute the proposed demise of the Kraepelinian dichotomy to advances in genetic epidemiology, and rightly emphasise the need to integrate data across multiple domains in large numbers of people. However, it may also be important to use a population-based approach. This involves extra effort but avoids being misled by convenience samples which may not be representative of the population. This is illustrated by Fig. 1 in the editorial of Craddock & Owen which suggests that prototypical schizophrenia and prototypical bipolar disorder are relatively rare in clinical populations. Work in population-based samples suggests that there is an early, insidious-onset psychosis with a poor outcome affecting predominantly men – a ‘neurodevelopmental’ form of schizophrenia which is very close to dementia praecox (Castle et al., 1998). This prototypical form of schizophrenia together with prototypical bipolar disorder accounts for 30% of people with psychosis in a treated prevalence sample, demonstrating the utility of Kraepelin’s division. In our experience affective and non-affective psychoses can be accounted for by these prototypical forms and a further two latent classes which appear to be valid (Murray et al., 2005). Whether such empirically derived classes might provide better phenotypes for genetic studies is as yet undetermined.

Until biological markers are identified, there is perhaps only one way to improve our classification. Large-scale, empirical, population-based studies of psychiatric symptoms, demography, course, treatment response and outcomes are suggested to reclassify these disorders from first principles and provide an atheoretical framework which may capture underlying pathophysiological substrates. Such studies should, as described by Craddock & Owen, integrate both dimensional and categorical approaches but also require a developmental perspective across the life span. The debate about the Kraepelinian dichotomy illustrates the lack of evidence-based diagnostic classification in psychiatry as a discipline. It would be fitting if psychiatric genetics, which has been severely impeded by the lack of a robust nosology, focused the collective will of practitioners to establish the evidence base required for a psychiatric classification which at last reflects nature.


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Authors’ reply: We are in full agreement with Dr Murray regarding the utility of large-scale, population-based studies. These are highly desirable and will, we hope, be facilitated by the recent establishment of the Mental Health Research Network (http://www.mhrn.info) under the auspices of the UK Clinical Research Collaboration (http://www.ukcrc.org). We also agree that longitudinal variables such as course, outcome and treatment response might be key to classification, as Kraepelin supposed. However, although we have not undertaken relevant population studies ourselves, we are not convinced that Kraepelinian dichotomous categories are any more useful in population-based samples than in clinical samples. We find the studies of Van Os and colleagues (e.g. Krabbendam et al, 2004) persuasive that dimensional measures are useful in describing psychosis-related morbidity in the general population and, contrary to the proposition of Dr Murray, we would expect dimensions to be more useful than categories in populations unselected for severe illness.

Finally, we would like to restate and further emphasise our optimism about the likely rate of progress in identifying biological markers that can validate psychiatric diagnoses. Markers (in the form of genetic polymorphisms) have already been identified that challenge current nosology. For example, using the Bipolar Affective Disorder Dimension Scale (which rates affective and psychotic dimensions; Craddock et al, 2004) in a study of over 600 cases each of schizophrenia and bipolar disorder, we have demonstrated that a risk variant within the Neuregulin 1 gene, which has been associated with risk of schizophrenia in several samples (reviewed in Craddock et al, 2005), may confer
specific risk for a form of psychotic illness characterised by features of both mania and mood-incongruent psychosis (Green et al., 2005). Other findings of a similar nature are currently emerging from our own studies and those of other groups, and we anticipate that we are entering a period during which psychiatric research and practice will be placed on much firmer nosological foundations than has been possible in the past.

Declaration of interest
N.C. and M.J.O. are consultants to GlaxoSmithKline and have received grant funding and honoraria from GlaxoSmithKline, AstraZeneca and Lilly.


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CBT for refractory symptoms in schizophrenia
Valmaggia et al (2005) report an interesting randomised controlled trial evaluating cognitive–behavioural therapy (CBT) for refractory psychotic symptoms of schizophrenia resistant to atypical antipsychotic medication. They conclude that patients should not be excluded from psychological help on the grounds that they are too ill to benefit from therapy, and CBT for psychotic symptoms should be available in in-patient facilities.

We feel the conclusions drawn by the authors do not truly reflect their results. Valmaggia et al report that their primary hypothesis was that CBT would be more effective than supportive counselling in reducing auditory hallucinations and delusional beliefs. They used the Positive and Negative Syndrome Scale (PANSS) and Psychotic Symptoms Rating Scale (PSYRATS) to measure outcomes. The post-treatment score on the PANSS positive sub-scale of those receiving CBT was not significantly different from that of the control group. On the PSYRATS no significant effect was found on the delusions. Benefits of CBT were found on the auditory hallucinations scale for physical characteristics and cognitive interpretation but not for emotional characteristics. However, the benefits noticed were not sustained at follow-up. It would have been helpful if the authors had used an a priori definition of what constitutes a clinically meaningful improvement and provided the actual figures for the dichotomous outcome.

Also, if we look at the numbers needed to treat (NNT) calculations, the authors have accurately reported the lack of statistical significance (PANSS positive symptom scale, NNT=8, 95% CI 3–∞; PSYRATS factor 2, NNT=6, 95% CI 2–∞; delusion scale factor 1, NNT=4, 95% CI 2–∞; factor 2, NNT=12, 95% CI 3–∞). The only finding with reasonable confidence intervals seems to be cognitive interpretation on the auditory hallucination scale of the PSYRATS (NNT=3, 95% CI 2–13). The authors also draw our attention to the fact that clozapine is effective in 32% of cases in producing a clinical improvement (NNT=5, 95% CI 4–7; Wahlbeck et al, 1999). They seem to suggest that the figures from the current study reveal the effects of CBT to be similar to clozapine. However, it should be noted that this figure reported by Wahlbeck et al is for global improvement, whereas Valmaggia et al do not give any figures for global improvement and hence in our opinion these results are not comparable. To conclude from these results that CBT could induce a change in psychotic symptoms seems to be overestimating the beneficial effects.

Patients with schizophrenia who are resistant to clozapine form one of the most difficult-to-treat groups. Jones et al (2004) concluded that trial-based data supporting the wide use of CBT for people with schizophrenia or other psychotic illnesses are far from conclusive. The randomised controlled study of Valmaggia et al evaluating interventions in this population is welcome.


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Olanzapine co-therapy in bipolar disorder
Baker et al (2004) report an interesting post hoc analysis from a randomised double-blind, placebo-controlled study evaluating the efficacy of olanzapine co-therapy in patients with bipolar disorder who had adequate responses to valproate or lithium monotherapy (Tohen et al, 2002). The authors describe a secondary analysis assessing response among dysphoric and non-dysphoric patients with bipolar I disorder.

The authors conclude that olanzapine in combination with either lithium or valproate was effective in improving the severity of depressive symptoms coexisting with acute mania. This conclusion is based on statistically significant differences in mean changes in Hamilton Rating Scale for Depression (HRSD) score. However, the authors have not reported the standard deviations for these mean changes. Hence it is difficult to ascertain whether the data are skewed. It is possible that a few patients showing large changes on the HRSD could have skewed the data. It was also puzzling that the authors reported that the difference in the HRSD score between combination and monotherapy groups was larger for dysphoric patients. One would expect participants in the non-dysphoric group to have much lower baseline scores so that there would be less chance of a significant reduction. (The mean HRSD baseline score in the non-dysphoric group was 10.42 (s.d.=5.27) and in the dysphoric group 25.18 (s.d.=4.62).)

We are also of the view that reporting study outcomes in terms of mean changes on a rating scale does not provide meaningful information for clinicians. Reporting results using dichotomous outcome
measures such as ‘improved’ and ‘not improved’ with a meaningful cut-off point defined \emph{a priori} would be helpful. Clinicians would be more interested in outcome measures such as complete remission of symptoms, return to premorbid levels of functioning, etc. To address the question of whether olanzapine is helpful for patients with dysphoric mania it would be helpful to know how many in the olanzapine co-therapy group achieved complete remission and whether there was any statistical difference between groups. It would have been interesting if Baker \emph{et al} had also provided dichotomous outcomes based on the Clinical Global Impression scale for bipolar disorder (CGI-BP; Spearing \emph{et al}, 1997), as this was administered during the course of the trial and data should be readily available.

It is not uncommon to come across reporting of various outcome measures and multiple analysis of a randomised controlled trial. However, whether this adds to clinical knowledge is questionable. We agree with Baker \emph{et al} that it is important to explore the pharmacological options for dysphoric mania as the available options are limited. However, we need more pragmatic outcome measures that are easily understood by clinicians and can be applied in routine practice rather than being lost in multiple analysis. Systematic reviews such as that on the use of olanzapine for mania also highlight the lack of pragmatic outcome measures in the reporting of randomised controlled studies (Rendell \emph{et al}, 2003). We hope future reports of such studies will use outcome measures that are more applicable to the real world.

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\begin{figure}
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\includegraphics[width=\textwidth]{figure}
\caption{Graph showing the comparison between olanzapine and placebo in the treatment of mania.}
\end{figure}

ECT in depression

Schulze-Rauschenbach \emph{et al} (2005) found in their comparison of unilateral electroconvulsive therapy (ECT) and repetitive transcranial magnetic stimulation (rTMS) that these two procedures have similar efficacy in the treatment of major depression. However, the rate of treatment response for ECT in their study was 46\%, well below the figures found in other studies (Medical Research Council, 1965). The authors state that the response rate for ECT might have been higher if a higher dosage had been used, but that this would have increased the risk of side-effects. This argument is misleading, just as comparing a sub-therapeutic dose of amitriptyline and placebo would be. The authors should have compared the incidence of side-effects between treatments, but at therapeutic doses. This comparison would probably have confirmed the prevalent belief that ECT is more effective than rTMS in the treatment of major depression (Aaree \emph{et al}, 2003).


\textbf{British Journal of Psychiatry} (2001)

We started an audit of ECT at our regional psychiatric hospital 1 year ago. So far 23 consecutive patients with treatment-resistant depression, who had an HRSD–17 (17-item version) score of 15 or above (the cut-off used by Schulze-Rauschenbach \emph{et al}), have completed at least six ECT sessions. We observed a 55\% improvement on the HRSD–17: from 24.6 to 11.0 points. The decrease on the self-rated Beck Depression Inventory was 20.1 points (an improvement of 49.9\%). This compares with a decrease of only 7.6 points (24\%) in the ECT group of Schulze-Rauschenbach \emph{et al}. Even more importantly, the remission rate in their study was very low. Using the remission criterion of \emph{≤}7 points on the HRSD–17 (Thase, 2003), only one of their 13 ECT patients (8\%) achieved remission (as shown in Fig. 1). This contrasts with a rate of 43.5\% (10 out of 23 patients) in our study and 74.7\% (189 out of 253 patients) in the CORE study. Four of our patients scored 0 or 1 point at the end of treatment.

There could be at least two reasons for the low response rate in the ECT group of Schulze-Rauschenbach \emph{et al}. First, unilateral ECT is less effective than bilateral ECT, and when used at a simulation intensity of 100–150\% above seizure threshold, it has produced only a 30\% response rate (Sackeim \emph{et al}, 2000). Only four patients in our series and none in the CORE study had unilateral ECT. Second, patients with psychotic depression respond better to ECT (Petrides \emph{et al}, 2001). None of the patients of Schulze-Rauschenbach \emph{et al} had psychotic symptoms, but 13 (56.5\%) in our group and 77 (30.4\%) in the CORE study did. This cannot explain all the difference, as the non-psychotic patients in our group still showed an improvement of 48\% on both HRSD–17 and Beck Depression Inventory scores.

Properly administered bilateral ECT still remains by far the most effective treatment for severe depression.


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Authors’ reply: We welcome the letters of Dr Kirov et al and of Dr Euba who address the important issue of clinical efficacy of electroconvulsive therapy (ECT), which may be greater when bilateral ECT is used instead of unilateral ECT. We have little doubt that this is true, but bilateral ECT is associated with more unwanted effects on cognition than unilateral ECT (National Institute for Clinical Excellence, 2003). This is the main reason why unilateral ECT is still frequently applied, certainly at the beginning of a course of treatment. Some patients experience severe and persistent memory deficits after ECT (see Donahue, 2000). In their systematic review, Rose et al (2003) found that about one-third of patients reported significant memory loss after ECT. One can question the validity of this worrisome figure on methodological grounds, as the studies reviewed by Rose et al used questionnaires instead of neuropsychological assessments. Nevertheless, cognitive alterations can be very disturbing for the patient, and there remains a need to examine this controversial issue further.

In assessing the somewhat lower clinical response obtained in our study compared with others, it should be borne in mind that all our patients were treatment refractory (i.e. they had unsuccessful treatment response to at least two different types of antidepressants, each given in a sufficient dosage range for at least 4 weeks). Patients with resistance to antidepressant treatment are known to have reduced rates of response (Sackheim et al, 2000). For example, less than 30% of those with depression who had failed to respond to one adequate medication trial finally responded to low-dose or moderate-dose right unilateral ECT, in contrast to about 50% who had not received such an adequate antidepressant trial (Sackheim et al, 2000). Thus, the therapeutic effect of ECT in our study was well within the expected range both for the group of patients studied and the type of ECT applied. It should also be noted that participants in the CORE study (Petrides et al, 2001) cited by Dr Kirov and colleagues were about 10 years older on average than patients in our study, and that ECT response rates in the CORE study were higher for older patients.

We have stated quite explicitly that our study was not designed to compare the absolute or relative effectiveness of repetitive transcranial magnetic stimulation (rTMS) or ECT. As outlined in our paper, some preliminary randomised trials suggest that rTMS might be as effective as bilateral ECT in non-psychotic patients but, although the meta-analytic evidence for the clinical efficacy of ECT is strong, the evidence for strong efficacy of rTMS in depression is less conclusive.

Our primary intention was to highlight the continuing need to delineate the cognitive side-effects of ECT in comparison with other treatments. Weighing benefits and side-effects of a specific form of ECT treatment for a specific patient may have to take into account age, prior response to treatments, sensitivity to memory side-effects and other factors. Physicians and patients need better evidence about such side-effects, preferably from randomised controlled trials, but also from audits such as that reported by Kirov et al, to make informed decisions on the use of ECT, particularly as other forms of treatment become available.


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Hospital admission rates and diagnosis

We read with interest the article by Thompson et al (2004) on changing patterns of hospital admission for adult psychiatric illness. Although they acknowledged the limitations of routinely collected admissions data, the authors reported a lower than anticipated proportion of all admissions in the schizophrenia and related psychoses categories and greater than anticipated proportions for depression and anxiety and substance misuse. A further analysis of admissions for substance misuse suggested that this did not include a large number of patients with dual diagnosis and that psychotic disorder secondary to alcohol or drug misuse accounted for around 10% of admissions for substance misuse.

On a variety of indices, Manchester has the highest level of need for mental health services in England (Glover et al, 1999). Using a similar methodology, we have analysed the 2003/4 admissions data for Manchester and found marked differences from the patterns reported by Thompson et al: 42% of admissions in Manchester were for schizophrenia and related psychoses (national average 26%), with only 18% for depression or anxiety (national average 29.6%) and 6.5% for substance misuse (national average 19.1%). Further examination of the admissions for substance misuse in Manchester showed that 57% were for psychoses secondary to alcohol or drug misuse.

Our own earlier analyses of admissions in the north west of England (Harrison et al, 1995) also found marked variation according to diagnostic group and suggested that health districts with higher levels of deprivation admitted a higher proportion of patients with psychotic diagnoses and fewer patients with anxiety and depression. Similarly, the King’s Fund report into London’s mental health (King’s Fund, 1997) argued that a high proportion of admissions for schizophrenia reflected increased need for services. This could explain some of the regional variation in admissions according to diagnostic group reported by Thompson et al and our own recent findings. Admissions for substance misuse may also be influenced by deprivation and availability of in-patient beds, with some areas only admitting patients with secondary psychoses rather than drug or alcohol dependence.
The continued variation in the use of inpatient facilities across England requires further attention, particularly as it suggests that current means of resource allocation do not adequately address the marked impact of deprivation on need for mental health services.


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Obesity and schizophrenia

After reading less than half of 'Metabolic syndrome and schizophrenia' (Thakore, 2005) I checked the Declaration of interest and found the expected link to the pharmaceutical industry. On rereading the whole paper carefully I could not pinpoint a single statement that seemed wrong. However, the uneasy general impression remained that the author attempted to suggest that the metabolic syndrome was rather a result of schizophrenia itself and/or the associated stress or antipsychotic drugs. Therefore, I would like to draw attention to the high probability that patients with schizophrenia were rarely overweight before the advent of neuroleptics. First, Kretschmer (1961) found that 50.3% of 5233 people with schizophrenia had a leptosome (or asthenisch) body build, for which he measured an average waist/hip ratio of 0.67 (74.1/84.7 cm) in men and 0.82 (67.7/84.7 cm) in women. Only 13.7% of 5233 people with schizophrenia were pyknisch, characterised by a strong development of circumference of the intestines (starke Umfangsentwicklung der Eingeweideohlen) and an average waist/hip ratio of 0.97 (88.8/92.0 cm) in men and 0.84 (78.7/94.2 cm) in women. The rest of the schizophrenia sample was classified as athletic, dysphasic or uncharakteristisch (not typical of any of the aforementioned). Among the 1361 people with manic-depressive illness, 64.6% were pyknisch and only 19.2% leptosome. The leptosome body build, which does not seem to indicate a risk of developing the metabolic syndrome, was thought of as typical for schizophrenia.

Second, I asked a student to classify the patients with schizophrenia on old photographs in Bleuler's textbook (1969) as probably underweight, normal weight or overweight, without letting her know the reason. She quite rightly protested that she could not carry out the task with any certainty. However, as she appears rather underweight herself and as most people tend to use themselves as a yardstick, it is unlikely that she underestimated the number of overweight patients with schizophrenia. She classified 25% (5 out of 20) as overweight, 60% (12 out of 20) as normal weight and 15% (3 out of 20) as underweight. Thus, in spite of Thakore's paper, I still think that neuroleptic drugs contribute considerably to the development of obesity and its consequences.

Declaration of interest
None.


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Author's reply: In response to Professor Thiels letter, intra-abdominal fat (IAF) is critical in determining the overall risk of physical morbidity and one does not need to be overweight, or indeed obese in the conventional sense, to have an excess of IAF (Thakore, 2005). For example, patients with melancholic depression, who by definition have usually lost weight, have twice as much visceral fat as matched controls, and have higher mortality rates than the general population (Thakore et al, 1997). Hence, the patients with schizophrenia described by Kretschmer may have been underweight or of normal weight but still have carried excessive amounts of IAF, which would have increased their risk of developing a host of physical problems.

The waist/hip ratio is an indirect anthropometric measure of IAF whose value is greatly influenced by exactly where the tape measure is placed. Using a direct measure of IAF, computed tomographic scanning, we have shown in two separate studies that first-episode drug naive non-obese patients with schizophrenia have over three times as much IAF as matched controls (Thakore et al, 2002; Ryan et al, 2004). The amounts of IAF in both of these samples were far in excess of what one would see in simple obesity, but were similar to what one might observe in patients with Cushing's syndrome. There is little doubt that most of the widely used neuroleptics (old and new) cause weight gain. Yet, using computed tomographic scanning, an acknowledged gold standard, we have shown that there is no significant increase in IAF with two commonly used atypical antipsychotics (Ryan et al, 2004). Therefore, we should be asking questions such as what has a greater physical impact on patients with schizophrenia – the illness, with all of its associated stress and poor lifestyle choices, or the medications used to control symptomatology?

Declaration of interest
J.H.T. has in the past received unrestricted educational grants from Bristol-Myers Squibb, Eli Lilly and Pfizer but is currently receiving no funding from pharmaceutical companies.


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Zero tolerance of violence

Behr et al (2005) rightly draw attention to the advantages of those with various forms of mental disturbance, in some circumstances, being held to be accountable for their actions (see also Smith & Donovan, 1990; Prins, 2002, 2005: chapter 2). However, their comments concerning the degree to which alcohol and other drugs may totally erode criminal responsibility need slight qualification. It is of course true that, in general terms, the ingestion of alcohol and other drugs not only does not excuse culpability, but may in fact exacerbate it. There are, however, instances where specific intent has to be proved (as for example in homicide), where the ingestion of such substances may negate full responsibility (Homicide Act 1957, Section 2). In addition, the unknowing ingestion of alcohol, for example ‘spiking’ someone’s non-alcoholic beverage with alcohol, may be held to exclude responsibility. The law on this whole topic is somewhat complicated, and has, from time to time, led to some equivocal decisions in the higher courts.

One hundred years ago

The First Belgian Congress of Neurology and Psychiatry

On Sept. 28th and 29th there was held at Lierre, in connexion with the International Exhibition which is now in progress in the city, the first Belgian Congress of Neurology and Psychiatry. The opening meeting took place in the buildings of the university, where M. de Latour, Director-General of the Ministry of Justice, received delegates from France, Germany, Holland, Switzerland, Turkey, and Roumania. Dr. Glorieux began the formal business of the Congress by delivering an address dealing with the first paragraph (p. 209) should read: It processes the reward value and/or affective valence of environmental stimuli, assesses the future consequences of the individual's own actions (response selection) and inhibits inappropriate behaviours (response inhibition; Bechara & Damasio, 2002; Krawczyk, 2002; Fan et al, 2003).