Correspondence

EDITED BY KIRIAKOS XENITIDIS and COLIN CAMPBELL

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Cognitive–behavioural therapy for bipolar disorder

Dr Lam (2006) comments on our study (Scott et al, 2006a), the largest randomised controlled trial (RCT) of psychological treatment for bipolar disorder conducted so far. We respond as follows.

(a) Dr Lam seems to misinterpret the nature and purpose of pragmatic trials. It is not a matter, as he suggests, simply of appropriate outcome measures, which should be a feature of all trials. Pragmatic trials are intended to test therapies in the practical circumstances of everyday clinical settings, using large multicentre samples (Hotopf et al, 1999). Most previous trials of therapies for bipolar disorders were single-centre efficacy studies designed to try out new interventions in specialist services or where the originator worked.

(b) Dr Lam comments on the number of cognitive–behavioural therapy (CBT) sessions received. We believe that 20 sessions with 2 boosters is as many as is practical in most National Health Service (NHS) settings. That patients attended about 14 of the sessions offered is frustrating but reflects clinical reality and is remarkably similar to the attendance achieved in Dr Lam’s own study (Lam et al, 2003: average 13.9 sessions, s.d. = 5.5).

(c) Our analysis strategy was determined before inspection of the data under the scrutiny of a trial steering committee appointed by the Medical Research Council. Dr Lam confounds several issues and recommends an actuarial analysis that is fundamentally incorrect in the context of an RCT (ICH Harmonised Tripartite Guideline, 1999). In an intention-to-treat analysis, the date of randomisation determines the start of the clock and everyone who is randomised is analysed; it is wrong to delay the inclusion of any participant in the analysis until they are asymptomatic. We also reported in the text on the issue he raised, namely that there was no difference in time to next bipolar episode or mean severity of symptoms in the sample who were in acute bipolar episode at baseline, not in acute bipolar episode at baseline or the whole sample.

(d) Dr Lam suggests it was inappropriate to include in our study individuals who were in a current episode or not on mood stabilisers. However, given that RCTs of therapy for mental disorders are usually undertaken with participants who are currently symptomatic, we believe it is important and informative to explore the potential effects of therapies commenced in the acute phase of bipolar disorder. Furthermore, in Judd et al’s (2002) 12-year follow-up it was shown that individuals with bipolar disorder spend 50% of their time with syndromal or sub-syndromal symptoms of mood disorder, predominantly depression. Not receiving or not adhering to recognised mood stabilisers is a similar well-documented issue in 20–50% of individuals with bipolar disorders (Scott & Colom, 2005). Our sample thus reflects the realities of clinical practice.

(e) It is standard practice in RCTs to control for design variables and also to pursue additional analyses that control for potential confounders (Schulz & Grimes, 2005). None of our analyses failed to converge, a common consequence of multi-collinearity.

(f) Dr Lam points out that a median split of a continuous variable can lose information. In fact, this was the reason why we looked for a trend across four groups as shown in Fig. 4 (p. 318).

Previous studies of psychological therapies have mostly involved more selected populations at relatively lower risk of relapse. In those circumstances CBT appears beneficial. Our study used a mixed patient sample; many were high-risk or currently symptomatic. We designed the trial in this way to address an issue not explored so far in any other psychological therapy study, namely whether the treatment would be effective in all patients who might be considered for it. Patients were only excluded if participation was unfeasible or unethical.

Our findings indicate that 22 sessions of CBT may not be effective for most people seen in NHS general adult psychiatry settings. In our lower-risk subgroup, similar in characteristics to Dr Lam’s sample (Lam et al, 2003), CBT may be very helpful. The clinical implications are that for a stable, lower-risk population, early in their history of bipolar recurrences, CBT should be considered as an adjunctive treatment option to further enhance their outcome. For high-risk, complex cases, other forms of therapy should be considered, such as those targeted at medication adherence or relapse prevention, before considering CBT. These recommendations are consistent with the results from published meta-analyses and other findings on psychological therapies in bipolar disorders (Scott & Colom, 2005; Scott et al, 2006b).


Scott, J., Colom, F. & Vitea, E. (2006b) A meta-analysis of adjunctive psychological therapies compared...
We suggest that this trial could not have been conducted in a high-income country but may have been conducted in India because regulatory requirements could be fulfilled there. The use of a placebo when an effective treatment exists – and other elements of the study as mentioned above – goes against the Helsinki guidelines and those of the Indian Council of Medical Research (2000). Finally, publication of such studies in a leading journal such as the *British Journal of Psychiatry* gives credibility to unethical medical research and practice and is a matter of serious concern.

**Declaration of interest**

The authors are editors of the *Indian Journal of Medical Ethics* and have previously written or spoken on the need for ethical approval to proceed with certain drug company practices, including sponsored research.


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Although it is encouraging to see the *Journal* take an active role in redressing ‘editorial racism’ as discussed in a previous editorial (Tyrer, 2005), there is a need to ensure that promotion of positive discrimination does not exacerbate the problem.

We feel that a recently published randomised double-blind placebo-controlled trial of risperidone performed in India illustrates the dangers inherent in such a policy (Khanna *et al*, 2005). The report had a number of serious shortcomings, which included omission of crucial details of the process of randomisation, interrater reliability and the measures taken to ensure masking. However, the most worrying aspect of the trial was the use of a placebo in the control group and the apparent absence of any ethical approval to proceed with this study. What was the justification for denying severely unwell and vulnerable patients access to appropriate treatment? Why was there no discussion about the ethical dilemmas associated with this study?

We support the *Journal* policy of combating editorial racism by promoting positive discrimination in the instructions to referees. However, the *Journal* must not relinquish its responsibilities as the official journal of the Royal College of Psychiatrists by failing to act as final arbiter for the quality (including the ethics) of the *Journal’s* content.


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With a sample size of 290 patients the report by Khanna *et al* (2005) buttresses the data about efficacy of atypical antipsychotics in the treatment of acute mania, but the article also raised the following concerns.

One of the sites had to be withdrawn from the study after enrolling three participants because of concerns about data quality. However, the data from these individuals were still included in the safety analyses. We are of the opinion that if there were concerns about the data from one particular site, then that site should have been excluded from any further analyses.

We also have concerns about the legitimacy and validity of the informed consent obtained from 145 patients with acute mania and a mean Young Mania Rating Scale score of 3.75 to be enrolled in the placebo arm of a clinical trial. Article 4 of the World Medical Association Declaration of Helsinki (World Medical Association, 1989) states that biomedical research involving human participants cannot legitimately be carried out unless the
importance of the objective is in proportion to the inherent risk to the participant. Delayed treatment of acute mania is associated with considerable acute and long-term morbidity from both illness and its secondary consequences (Post, 2000). Randomising a patient with acute mania to the placebo arm of a 3-week trial leads to considerable delay in treatment.

In this trial 145 patients with acute mania were assigned to the placebo arm. We consider it unethical and inhumane to treat 145 patients with acute mania with placebo. All future trials concerning the efficacy of a medication for acute mania should use an arm with one of the proven medications as a comparator and not include a placebo arm.


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Authors’ reply: Dr Srinivasan et al are in error when they state that this trial (Khanna et al, 2005) could not have been conducted in a high-income country. Johnson & Johnson conducted this trial in India at the same time as two trials in other countries (including the USA) as part of a global effort to obtain registration for risperidone monotherapy in bipolar mania. (Hirschfeld et al, 2004; Smulevich et al, 2005). Quality investigators and sites were chosen and approval from research ethics boards and participant consent were obtained at each site.

We categorically reject the implication that a clinical trial in India is medically inferior or ethically suspect. The investigators and sites in India were comparable in scientific quality and adherence to ethical guidelines to their peers globally. Any suggestion to the contrary is unwarranted, and fosters prejudice by creating a distorted perception of Indian clinical scientists and centres of research.

Below are our responses to the other questions raised by Dr Srinivasan et al:

Why was a placebo used?

Placebo-controlled trials expose the lowest number of patients to a potentially ineffective (new) treatment, while also providing valid data on adverse events attributable to the treatment.

How did patients give their informed consent during an episode of acute mania?

In this study, patients or a family member provided informed consent as required in the protocol. Patients with psychiatric illness, including mania, can give informed consent: capacity to consent or withhold consent is not automatically lost because of illness.

Where were the trial sites? Who were the participants? What were the adverse events? How were seven patients from the placebo group lost to follow-up?

The study was conducted at eight sites in India, as reported in the Journal article (page 229); participants were those experiencing an acute exacerbation of symptoms of mania and are described in Table 1 (page 231); adverse events are reported on pages 232–233; as in all clinical trials, a few participants could not be contacted at follow-up. In this study, 3% of participants were lost to follow-up, which is in line with previous studies of mania (Sachs et al, 2002; Yatham et al, 2003).

Was the wash-out period medically and morally justified?

Stable patients who were responsive to their current medication were not enrolled in this trial. Patients who were enrolled were symptomatic despite their current medication (suggesting that they were not responsive to the treatment) or because they had spontaneously discontinued medication. In order to successfully assess the trial medication, it was necessary that they discontinue their current suboptimally effective medication. This is scientifically and ethically justifiable.

Do the authors who are not drug company employees have any competing interest to declare?

The two authors who were not Johnson & Johnson employees had no conflict of interest related to this study.

Was the trial conducted according to the Declaration of Helsinki? Why did the authors cite the 1989 revision of the Declaration and not a more-recent revision?

The trial was conducted in accordance with the principles originating in the Declaration of Helsinki. Reference to the 1989 version of the document was made since this was a commonly cited version at the time the study preparations were underway (1999–2000).

Drs Murtagh and Murphy refer to ‘serious shortcomings’ in our report. These are said to include omitting crucial details of the process of randomisation, interrater reliability and masking. In addition, ‘the most worrying aspect of the trial was the use of a placebo in the control group and apparent absence of any ethical approval to proceed with this study’.

There were no such ‘shortcomings’ in the trial itself but not all methods were detailed in our report. On page 229, we wrote, ‘Randomisation was stratified by the presence or absence of psychotic features at baseline, manic or mixed episode, and by treatment centre. After randomisation and the initiation of treatment (baseline), patients remained in hospital for at least 7 days’. On page 230, we wrote, ‘Investigators were trained in the use of each of these instruments and certification was required for those administering the YMRs’. Furthermore, page 229 states, ‘Signed informed consent was obtained for all participants and the study was conducted according to the Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects, in the 1989 version of the Declaration of Helsinki’. The study had the approval of national and local research ethics boards. These are standard descriptions of such procedures and are similar to those provided in many published reports of clinical trials.

A placebo control was necessary to establish the effects of medication because people with mania manifest response to placebo which is of variable magnitude. The true efficacy of risperidone in this trial was incontrovertibly established over and above the effects observed with placebo.

Similarly, the safety of risperidone can only be appropriately assessed in the context of adverse events in the placebo arm. Furthermore, patients could be withdrawn from the study and treated in an open-label
manner at any time. The appropriate use of placebos in clinical trials for bipolar disorder has recently been reviewed by Vieta & Carné (2005), who point out that the regulatory agencies (Food and Drug Administration, European Agency for the Evaluation of Medical Products) and consumer associations support their use to ensure that ineffective drugs are not authorised for this condition.

Basil et al question why data from a site that was withdrawn because of concerns about data quality were included in the safety analyses. It is a conventional procedure in clinical trials to omit efficacy data but not safety data from such sites. They also question the ‘legitimacy’ of the informed consent obtained from the patients. It is our experience that patients with severe illness are capable of giving their informed consent to participate in a trial. Capacity to consent is not automatically lost because of a symptom score on the Young Mania Rating Scale.

Basil et al question the ethics of including a placebo arm in the trial. A placebo group was included because patients with mania generally show a high and variable placebo response, making it difficult to identify their responses to an active medication. Placebo-controlled trials are valuable in that they expose the fewest patients to potentially ineffective treatments. In addition, inclusion of a placebo arm allows a valid evaluation of adverse events attributable to treatment vs. those independent of treatment. For these reasons, regulatory agencies (Food and Drug Administration, European Agency for the Evaluation of Medicinal Products) and the consumer associations support the use of placebo controls (Vieta & Carné, 2005).

Most (83%) of the placebo patients had been receiving treatment for bipolar disorder for at least 30 days before being hospitalised for the treatment of severe acute mania. This indicated that their current treatments were not adequately treating their symptoms and illness. Thus, as expected, a high response to placebo was shown by these patients. Significant improvements vs. baseline were seen on each of the efficacy measures in patients receiving placebo or risperidone. For example, improvements in YMRS total scores at week 3 end-point were −10.5 (s.e. = 1.3) in patients receiving placebo and −22.7 (s.e. = 1.1) in patients receiving risperidone (P < 0.001 vs. baseline in both groups). The proportion of placebo patients whose severity of illness (Clinical Global Impression scale) was rated as ‘not ill’, ‘mild’, or ‘very mild’ increased from 1% at baseline to over one-third (37%) at end-point (the increase was from 0% to 72% in the risperidone group).

Declaration of interest
B.L., F.G., M.E. and M.K. are employees of Johnson & Johnson Pharmaceutical Research and Development, which supported the study.


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Editor’s reply: We thank our correspondents for pointing out an important issue that we need to address more assiduously in our reviews of papers. We agree fully that the British Journal of Psychiatry needs to ensure that a greater policy of openness towards low- and middle-income countries is not accompanied by any lowering of ethical standards.

However, there are clear divisions of opinion here. When the protagonists for each of these make their eloquent arguments, it may seem strange that any should remain rather uncomfortably on a rickety fence when the alternative certainties are so much more inviting. Well, we are still wobbling because we feel it is right to wobble. The two sides of this argument, put crudely, are (a) it is unethical to exploit patients in low-income countries for studies that would never be allowed to proceed in rich countries, and (b) research performed for a global scientific community has to provide general evidence, not specific to one group or country, and so worldwide efficacy studies are necessary.

Drs Murtagh & Murphy, basil et al, and Srinivasan et al all allege, directly or indirectly, that the patients in India have been selectively exploited for research purposes and this is fundamentally unethical. Patel (2006) also asks whether there is a personal financial aspect to the trial that has been undeclared. The allegation that ‘this trial could not have been conducted in a high-income country but may have been conducted in India because regulatory requirements could be fulfilled there’ (Srinivasan et al) is a serious charge.

However, the case for the trial is also strong. Although Basil and his colleagues suggest that ‘all future trials concerning the efficacy of a medication for acute mania should use an arm with one of the proven medications as a comparator’, regulatory bodies such as the Food and Drug Administration insist on at least two placebo-controlled studies that demonstrate superiority of the index drug over placebo in order to get a licence approved. Although one may criticise the Administration for this requirement, it is scientifically unimpeachable and is a general one for drug treatments. A very similar trial has also been carried out in the USA in which risperidone was also compared with placebo treatment (Hirschfeld et al, 2004) (and which should have been disclosed with the paper of Khanna et al, 2005). The findings suggest that when risperidone is licensed for the treatment of mania it is possible to argue that both these positive trials represent an advance in patient care. A subsidiary argument, a practical one not always well-received in ethical circles, is that participation in a research study can, and should be, a proper and ethical way of providing good patient care, exemplified by the recent comments of Phillips et al.
(2005): ‘the clinical treatment of young people identified as being at high risk of developing a psychotic disorder, particularly the use of neuroleptics, should be provided only in the context of a research trial, where standards of informed consent and monitoring are highest’.

Nevertheless, there remain worries about trials in poorer countries. Ethical committees often do not have the same level of independence as they do elsewhere, financial inducements may lead to covert or overt pressures, and there is even sometimes a nationalistic element (e.g. if country X can recruit 100 patients, we must not recruit fewer than 200). This somewhat macho mentality may be behind comments such as that by Khanna et al (2005) that the symptoms of mania in the patients seen were ‘substantially more severe than those of patients with bipolar disorder participating in trials elsewhere’, implying that only countries that can be successful in persuading these ‘difficult’ patients to take part should be chosen.

We note that the Indian Council of Medical Research has now decided to audit clinical trials systematically to ensure that national recommendations are followed (Mudur, 2005) and the outcome of this will be followed closely. For our part, we have made changes to our refereeing procedure, and have been asking assessors to examine more closely the ethical aspects of papers that are submitted. We shall also be using our new group of international editors (in the case of India this will be Dr Vikram Patel) to advise on ethics both generally and with regard to specific papers, attempting as much as possible to take account of the need for ‘autonomy, beneficence, non-maleficence and justice… and care ethics’ summarised by Bloch & Green’s (2006) recent paper.


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Antiparkinsonian prescription and extrapyramidal symptoms

Park et al (2005) cite the results of clinical trials as evidence supporting their hypothesis that the use of antiparkinsonian drugs in schizophrenia is an indication of extra-pyramidal symptoms (EPS). This may be true for clinical trials (most of which include young adults with no comorbidity) but may not hold true for their observational study, in which other factors such as prescribing habits and comorbidity may affect the reason for prescription of antiparkinsonian drugs. As the mean age of their sample was 48.6 years, which falls within the range in which Parkinson’s disease often develops, some patients could have been receiving antiparkinsonian drugs for the illness per se. Although this is mentioned as a limitation of the study, it has an adverse impact on the central hypothesis. Since decrements and increments in antiparkinsonian medication followed expectations from changes in antipsychotics (Tran et al, 1997), the results could well reflect the prescribing pattern of the general practitioners (GPs) rather than be true evidence for the presence of EPS.

One of the main limitations of the study is the lack of data regarding the reason for switching antipsychotics. As it is mandatory to submit data of all major illnesses (presumably including Parkinson’s disease), any indication for prescribing or altering medication and any adverse drug reaction to the General Practice Research Database (GPRD; Walley & Mantgani, 1997), the data could have been provided and would have helped in the interpretation of the results. Furthermore, during the period studied more than 400 GPs provided data to GPRD but data from only 266 were analysed. It is not clear why the data from some GPs were excluded.

Park et al (2005) classified their study population as those switched from typical to atypical antipsychotics (TA group) and those switched from typical to different typical antipsychotics (TT group). However, when we add up the total figures provided (3% and 99% were receiving atypicals and typicals respectively in 1992, which changed to 47% and 70% in 2000), it appears that some patients were receiving a combination of both classes of antipsychotics. This could have influenced the trend for prescribing antiparkinsonian drugs.

Nevertheless, antiparkinsonian drug prescribing is only a marker of EPS and


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Authors’ reply: We agree with the comments of Grover & Kulhara on the lack of information about the specific reasons for the prescription of antiparkinsonian drugs in our observational study. We have stated that such prescribing might have been influenced by factors other than the occurrence of EPS. However, previous naturalistic studies have shown that the use of antiparkinsonian medication was highly correlated with clinical indices of EPS when patients were prescribed antipsychotics (Barak et al, 2002; Bobes et al, 2003; Montes et al, 2003). In addition, the sudden change in the incidence of antiparkinsonian drug use following introduction of atypical antipsychotics in the entire population (not just among patients who switched type of antipsychotic therapy) makes it unlikely that physician prescribing habits were a strong alternative explanation for our findings.

Since we observed the same patients over time in the analysis of drug switching, changes in antiparkinsonian drug prescribing following the switch could be explained by the differential effects of antipsychotics on EPS.

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cannot perfectly reflect the incidence of EPS. Owing to the limitation of our data set (which did not include indications for prescriptions), we cannot exclude the possibility that some patients may have been prescribed antiparkinsonian medication because they had Parkinson’s disease, not because they had EPS caused by antipsychotics.

Grover & Kulhara question why we included only 266 GPs in this study. We selected from the GPRD only those patients who had been diagnosed with schizophrenia between 1992 and 2000. Therefore 6336 patients who met those requirements and their 266 general practices were included in the study.

Grover & Kulhara raise the possibility that patients might have taken both classes of antipsychotics simultaneously. We examined the effects of switching antipsychotics on antiparkinsonian drug prescribing by classifying patients into two groups. We defined the TA group as patients who had been prescribed typical antipsychotics with no atypical antipsychotic use before the switch, completely stopped typical antipsychotics and subsequently switched to atypical antipsychotics, with no typical antipsychotic use for at least 2 years after the switch. The TT group included patients who were prescribed one typical antipsychotic (e.g. chlorpromazine) then switched to a different typical antipsychotic (e.g. haloperidol), and who never received an atypical antipsychotic during the study period. Therefore, by definition, no patients in our study were receiving a combination of both classes of antipsychotics.


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Treatment of borderline personality disorder

Fonagy & Bateman (2006) hypothesise that a more benign course of borderline personality disorder may partially result from a reduction in iatrogenic harm. They describe people with borderline personality disorder as having ‘hyperactive attachment systems’ which interfere with the therapeutic relationship and treatment. They describe ‘treatment’ as being psychosocial treatment or psychotherapy, and attachment figures as therapists.

Many people with borderline personality disorder do not receive psychotherapy but do have contact with psychiatric services – casualty assessments, out-patient contact with generic services, brief crisis admissions and sometimes even prolonged admissions. I am curious as to Fonagy & Bateman’s view on the nature of attachments that people with borderline personality disorder have with psychiatric institutions, especially when contact with individual workers may be inconsistent. Fonagy & Bateman give advice about how to encourage ‘mentalisation’ in the context of psychotherapy in order to avoid potential iatrogenic damage but give no advice for other clinical settings.

Clinical teams are well aware of how people with borderline personality disorder may unconsciously ‘engineer’ situations to re-enact disturbed early life experiences. Now Fonagy & Bateman suggest that although teams are aware of this situation further damage may be done. A ‘helpful’ intervention may deprive the patient of using or developing other more useful strategies. Fonagy & Bateman suggest that an ‘inquisitive and flexible’ approach may be useful. The challenge is therefore how this approach should be applied to how clinical teams within institutions respond to people with borderline personality disorder.


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Authors’ reply: We share Dr Mountain’s concern that this group of patients is often inadequately managed. Our primary aim in pointing to the iatrogenic consequences of psychotherapy was to illustrate the dangers of intensive interventions or those with poorly defined boundaries. The same concerns for iatrogenic consequences apply to institutional involvement because this is often disrupted by frequent staff changes. Separations and losses of this kind are also iatrogenic. They activate patients’ attachment systems, leading them to make unproductive attempts to restabilise their sense of self. Moreover, interactions with institutions often occur at times of personal crisis when the attachment system is already stimulated. Concerns about the patient’s state of panic and about reduced mentalising may lead to hospital admission. However, this can become iatrogenic in itself because emotionally charged interactions with staff and other patients may further destabilise the patient, leading them to self-harm or threaten suicide, prolonging hospital admission. We and others (Paris, 2004) recommend that the level of risk for self-harm of patients admitted to hospital should be assessed and documented daily. If there is no reduction in risk, alternative management of the patient in the community should be implemented.

Although patients may seem to be enacting past experiences in their interactions with clinical teams, in our view it is not useful to consider these as hapless repetition of past patterns or as acts that respond to or compensate for past hurts; rather they should be viewed as the only solution available to restore a sense of integrity, continuity and coherence. The provision of a highly integrated model of psychiatric care in a structured institutional environment that aims to offer consistent, coherent and thoughtful psychological care with a relationship focus, organised in a patient-oriented flexible manner with individualised care plans, is likely to be most helpful. Out-patient treatment, discharge from an in-patient unit or referral following a casualty visit should be considered in
this context if services are to present a stable and coherent view of the patient's subjective world that may be adopted (internalised) as part of the self-image of the patient's mind. In our view this is the critical change in the treatment of borderline personality disorder.

**Declaration of interest**

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Neurobehavioural characteristics and relapse in addiction

The systematic review by Dom et al (2005) of studies using behavioural decision-making tasks and/or neuroimaging techniques to investigate orbitofrontal cortex functioning in substance use disorders was comprehensive. Our research article ‘Risk-taking on tests sensitive to ventromedial prefrontal cortex dysfunction predicts early relapse in alcohol dependency’ (Bowden-Jones et al, 2005) was published simultaneously and, because of its relevance to the review, we considered it important to bring it to readers’ attention.

We not only used most of the neuro-psychological tests mentioned by Dom et al but, more importantly, rated participants on both the Rogers Cambridge Gamble Task (RCGT; Rogers et al, 1999) and the Iowa Gambling Task (IGT; Bechara et al, 1994), and on the Barratt Impulsivity Scale and two personality scales: the Structured Clinical Interview for DSM–III–R (Spitzer et al, 1989) and the Dimensional Assessment of Personality Pathology–Basic Questionnaire (Livesley & Jackson, 2002).

The 21 participants in our study were in-patients in a residential detoxification unit and we were therefore able to carry out tests at 21 days post-detoxification in the knowledge that they had been substance-free during that period. They were followed up for 3 months post-discharge.

The six patients who relapsed early were significantly younger and more prone to the Barratt Impulsivity Scale, they sampled significantly more cards from the bad decks on the IGT and consistently risked more points across all odds on the RCGT. Hence people who had recently undergone detoxification were more likely to relapse within 3 months if they made more choices on a gambling task in which the immediate reward was large but the long-term consequences were disadvantageous.

It is unlikely that these findings reflect alcohol-induced brain damage because these people showed no impairments on a memory test sensitive to the early stages of dementia and on tests of dorsolateral prefrontal cortex functioning, which is particularly affected by long-term alcoholism.

Our results are consistent with the hypothesis that a dysfunctional orbitofrontal prefrontal cortex mediates the inability to resist the impulse to drink. This may lead a person to relapse after treatment despite the ultimately deleterious effects and despite the many hours of psychological input associated with a rehabilitation programme.

Relapse after detoxification is an area in need of further research. If it has a biological basis we need simple tests that are able to predict vulnerability to relapse and treatment programmes which are able to identify those patients at greater risk.


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Authors’ reply: The findings of Bowden-Jones et al (2005) add to the accumulating evidence that impairments on decision-making tasks are an important characteristic of people with substance use and possibly other addictive disorders. The finding that those alcohol-dependent people that performed poorly on behavioural tasks were at higher risk of relapse is a nice demonstration of the ‘myopia’ for the future that is reflected by poor task performance. This is in line with other recent studies, including that of Goudriaan et al (2006), which showed that relapse among gamblers was associated with behavioural (but not self-reported) measures of impulsivity. Furthermore, Paulus et al (2005) reported that methamphetamine-dependent people with low prefrontal activation during a decision-making task relapsed significantly more frequently than those with greater activation. Together with the results of Bowden-Jones et al (2005), these findings represent an important new line of investigation.

Identification of distinctive neurobehavioural characteristics may allow detection of those people with addictions that are more vulnerable to relapse. Neurobehavioural (endophenotypic) characteristics may prove to be better for the identification of high-risk patients than traditional clinical (phenotypical) variables.


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