Correspondence

EDITED BY MATTHEW HOTOPF

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Evolutionary psychology revisited

Dr Abed’s (2001) reply to my letter (Lucas, 2001) prompted me to contact Professor Steven Rose, one of the authors I cited (Rose & Rose, 2000), to check that I had not fundamentally misunderstood his position. It seemed to me unlikely that a neuroscientist would be, in Abed’s words, “effectively in the camp that views the mind as a tabula rasa” (Abed, 2001). These are Professor Rose’s comments:

‘Dr Abed both mistates the arguments of those of us who are critical of the claims of evolutionary psychology and is over-anxious to absolve its protagonists from charges of biological determinism. First, neither Professor Hilary Rose nor I, as the two editors of Atlas, Poor Darwin (Rose & Rose, 2000), are evolutionary biologists. I am a neuroscientist whose research interest lies primarily in learning and memory and she is a sociologist of science. No neuroscientist could ever suggest that the mind was a Lockeian tabula rasa. As all my own writings make clear, any understanding of the human mind and brain needs to locate its structure and workings in the context of evolution and development, as well as social, cultural and technological history. For that matter, nothing the population geneticist Richard Lewontin has ever written could, to my knowledge, justify Abed’s assertion concerning him and I would challenge Abed to find any quote which would support this assertion.

‘In terms of evolutionary psychological theory, I dispute the claim made most strongly by evolutionary psychology’s spokesperson the architecture of the human mind was laid down in the Pleistocene and there has not been evolutionary time for any major change to occur. Cavalli-Sforza (2000), for one, has recently surveyed the substantial evidence of significant post-Pleistocene genetic change under selection pressures. ‘Returning to Dr Abed’s reply to Dr Lucas, if it is not biologically deterministic to claim that humans possess innate ‘cheat detector’ modules or that men are innately programmed to prefer sex with younger women with specific hip: waist ratios, and women sex with older men preferably with symmetrically shaped bodies which guarantee better orgasms – I am not sure what is. And I cannot believe that Abed quotes as a respectable source Thornhill & Palmer’s (2000) claim that rape is an evolutionarily adaptive male strategy – that melange of scorpion fly data and human anecdote, so broadly condemned by the academic community.

‘Finally, Abed parrots the attack made in Cosmides and Tooby’s straw-person invention of what they call the standard social science model’ that they argue dominates sociology. As Hilary Rose points out in Atlas, Poor Darwin, there is little in European sociology which conforms to such a caricature. What is at stake is the autonomy of the social sciences as research fields from the imperialistic claims of an overly reductive biology at the hands of these new evolutionary fundamentalists. If evolutionary psychology were, as Abed claims, a hypothesis-driven empirical science’, there would be little to complain about. Indeed, both biologists and social scientists should welcome it. The problem is that what currently passes for evolutionary psychology is little more than an untestable bunch of anecdotes based upon a priori ideological convictions.”

I think further comment from me would be superfluous.


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Placebo response in antidepressant trials

The recent editorial by Gavin Andrews (2001) omitted some important considerations on the discussion of placebo response in clinical trials of antidepressants. These include the obligations of regulatory authorities in the appraisal of new treatments, numerous research-specific factors that contribute to the placebo response in a research environment, and the contribution of the scales currently employed as primary efficacy measures in depression trials to test the null hypothesis.

The demand by regulatory authorities for placebo-controlled trials in the evaluation of antidepressant therapies is supported by data published by Paul Leber, former Director of the Neuropharmacologic Products Division of the US Food and Drug Administration. Leber (1989, 1991) cited research studies where the antidepressant test agent was as effective as an already-approved active control medication, but in five of the six studies he cited, both were inferior to placebo. Given the notoriously poor sensitivity and interrater reliability of the Hamilton Rating Scale for Depression (HRSD), the usual primary efficacy instrument in US antidepressant clinical trials, this is not surprising to investigators who use the HRSD on a day-to-day basis. However, based on Leber’s evidence alone, if regulatory agencies move toward the Declaration of Helsinki (World Medical Association, 2000) mandated non-inferiority trials as a basis for approving new drugs, then it is only a question of time before regulatory approval is given to drugs that very well might be less effective than placebo. The regulatory approval of an inferior-to-placebo drug would ultimately be harmful to the large number of patients who would take this ineffective drug, in part being persuaded to do so on the basis of regulatory agency assurance of its efficacy. As all drugs have some side-effects in some patients, regulatory agencies must be able to affirm that a drug has been demonstrated to be better than ‘nothing’ (i.e. placebo) in conditions where ‘nothing’ has demonstrated benefits.

Andrews’ summary of the mechanisms of placebo response in antidepressant clinical trials also omits several important considerations. Spontaneous remission of depression time, the natural fluctuations of a chronic illness, and the encouragement that comes with being treated were the only factors he cited as contributors to placebo response. He does not cite the anxiety-lowering effect of receiving of a definitive diagnosis from a trusted expert physician in a clinical trial, and the increased sense of mastery and control that comes from patients’ greater understanding of their illness as a result of the more unhurried
and usually very extensive evaluation that occurs in clinical research practice compared with standard medical practice. He does not consider that these aspects of placebo response might be inherent in the environment of clinical trials, but are not generalisable to day-to-day general or psychiatric practice (although these differences are difficult to assess quantitatively). Other factors of the placebo response in clinical research are potentially amenable to change. These include potentially unhelpful-to-research, overly encouraging behaviours of those conducting the clinical trial, and false, overly optimistic patient assumptions and expectations about their outcome in the research trial, leading to inaccurate reporting of symptoms and thereby excessive response in those patients randomised to placebo. It is likely that increased efforts in patient and investigator education about how both patients and study site staff can be helpful in forming a productive research alliance and not generate ‘wishful thinking’ and the overly positive responses that might accompany it, is needed to reduce the costly, wasteful number of failed trials caused by excessive placebo response. In response to this need, I have recently proposed PREECT (Patient and Rater Education about Expectations in Clinical Trials), a two-component approach to the problem (Zimbioff, 2001). Briefly, the first component focuses on ensuring that clinical trial participants understand that they are entering a research alliance – not receiving regular medical care. The second component involves education of study site staff. Both anecdotal feedback and data lend support to the contention that PREECT reduces placebo response rates and, thus, could ultimately reduce the numbers of patients needed in placebo-controlled trials to achieve sufficient power to test the null hypothesis. Further exploration and validation of the PREECT approach would benefit patients and researchers involved in antidepressant trials, and would reduce the likelihood of an excessive placebo response.

Finally, a critique of the scales used as primary efficacy measures needs to be considered. This in itself is a thesis. The very fact that regulatory authorities in the USA are collaborating with researchers on tackling this issue lends support to its importance as a consideration in appraising this topic.


Cannabis regimes

We read with interest MacCoun & Reuter’s (2001) report on evaluating alternative cannabis regimes. In The Netherlands, drug policy is a topic of great interest. A scientific evaluation of policy regimes would be highly appreciated. MacCoun & Reuter’s paper illustrates this, however, is not an easy job.

As the authors stress, cross-national scientific evaluations are hampered by a lack of comparability due to methodological differences. Nevertheless, many studies summarised in their Table 1 are not methodologically comparable. MacCoun & Reuter compare the results of Dutch school surveys with those of population surveys in the USA. However, school surveys yield higher prevalence figures of substance use than population surveys do (Grooer et al., 1997). Furthermore, the age group “approximately 18” from the Dutch school survey is compared with the 18-year-old age group in the American national study. In The Netherlands schooling is compulsory until the age of 15–16 years, so 18-year-old high school students cannot be considered as representative of all 18-year-olds in our country. Among high school students aged 12–18 years we saw an increase in cannabis use in 1984–1996, but this had stabilised in 1999. The arguments that the rise may be associated with the coffee shop model and with a phenomenon the authors describe in terms of commercialisation and glamourisation do not quite convince us.

(a) The increase in cannabis prevalence coincides with a supposed increase in the number of coffee shops but this does not prove a causal relationship.

(b) About 80% of Dutch municipalities have no coffee shops at all (Bielemann & Goeree, 2000). Less than half of cannabis consumers purchase the drug in a coffee shop – the majority obtains it elsewhere (from a friend, a private house, on sale on the street, courier services and take-away services).

(c) The authors do not present clear definitions of the concepts commercialisation and glamourisation. Coffee shops must adhere to the so-called AHOJ-G criteria, which include no advertising. The Public Prosecution Department proclaimed deviation from these criteria a nationwide criminal prosecution policy in 1991.

(d) The increase in cannabis use in the USA seems to have taken place much earlier than in Europe. The authors do not offer a plausible explanation for this trend but indicate the importance of non-policy factors.

(e) Countries with a high prevalence of drug use are more likely to experience a downward trend than countries with low prevalence figures. This is now the case in Europe: an ongoing increase in countries with previously low use levels, and stabilisation or even decline in countries with previous high prevalence figures, both in general population studies and in school surveys, confirm the tendency towards convergence (European Monitoring Centre for Drugs and Drug Addiction, 2000; Hibell et al., 2000). In the UK cannabis use among students was significantly lower in 1999 than in 1995, while in France cannabis prevalence increased steeply, although there are no coffee shops in France. In The Netherlands, among students between 1996 and 1999, not only cannabis use but also use of ecstasy, cocaine, heroin and amphetamines stabilised (de Zwart et al., 2000).

Clearly, trends in drug use are influenced by a complex interplay of factors.


**Over-representation of Black people in secure psychiatric facilities**

I read with great interest Lelliot *et al* (2001) survey of patients from an inner-London health authority in medium secure psychiatric care. In particular, the authors set out to compare Black and White patients and found statistical differences which they dismiss. The scores on the Health of the Nation Outcome Scales and compound variables of clinical behaviour and social function differed between Black and White patients, but Lelliot *et al* comment that these may not be clinically significant.

If statistically significant findings on scales used in the study need not be explained, then the instruments cannot be considered valid to address the third aim of the study, to compare Black and White patients. Black patients were significantly more morbid on a number of clinical, social and behavioural variables, including affective symptoms, activities of daily living, problems with living skills, relationship problems and other mental or behavioural problems of self-harm and overactive and aggressive behaviour. Why should Black patients with less severe psychopathology or aggressive behaviour continue to find themselves in medium secure units?

There are two possible explanations. One is non-engagement with treatment options in less secure environments. It is known that Black patients are more likely to abscond from in-patient units (Falkowski *et al*, 1990) and that they are increasingly dissatisfied with each consecutive in-patient admission (Parkman *et al*, 1997).

An alternative explanation is that Black patients are perceived to be more dangerous despite lower ratings of psychopathology (Cope, 1990; Lewis *et al*, 1990). Lelliot *et al* unfortunately dismiss important findings as clinically insignificant. These very findings warrant further research and exploration and such work may well deliver a better understanding of why Black people are over-represented in secure psychiatric facilities.

**Evidence-based psychiatry**

Lawrie *et al* (2001) have touched upon the core problem of evidence-based psychiatry by raising the most relevant questions. Although the evidence-based medicine movement began in 1992 (Sackett *et al*, 2000), it was not until the Royal College of Psychiatrists introduced a Critical Review Paper to the MRCPsych Part II examination in 1999 that clinicians suddenly realised the problems of not knowing enough about critical appraisal of scientific papers.

Brown & Wilkinson (2000) assert, “Psychiatrists should be able to evaluate published literature both in terms of its scientific validity and its clinical relevance”. Why – to be able to practise evidence-based psychiatry, or to help trainees pass their exam? In a Scottish survey Lawrie *et al* (2000) discovered that senior psychiatrists found the time required to search and appraise the literature as the greatest barrier to practising evidence-based psychiatry. Would they be able to practise better if they had enough time, for instance 60 minutes per day? I do not know how to search for the best evidence to answer this question. I have recently read the recommended books (Brown & Wilkinson, 2000; Sackett *et al*, 2000), and I have also attended a few evidence-based medicine workshops. When my patients and trainees ask real-life clinical questions, I often get lost. Is this the beginning of my age-related cognitive impairment? Or is it just because I am such a busy clinician that I do not have time and need to take evidence-based psychiatry seriously? But how can we help our trainees? What about our own revalidation? We cannot really fudge the issue any more if we want to remain effective trainers.

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**Effects of schizophrenia on patients’ relatives**

Tennakoon *et al* (2000) stated that their study is ‘one of the first’ to investigate burden among caregivers of people with first-episode psychosis. Their paper was published 13 years after our paper which covered much the same ground (The Scottish Schizophrenia Research Group, 1987) and which they did not mention.

We found, using the General Health Questionnaire (GHQ), that 24 (77%) of 31 main caregivers were categorised as ‘psychiatric cases’; this compares with 12% of caregivers in the Tennakoon *et al* study, which also used the GHQ. However, the relatives in our study were interviewed during the first week of the patients’ first admission to hospital, and before the patients received antipsychotic medication. Tennakoon *et al*’s patients could have been ill for up to 2 years and received up to 12 weeks of antipsychotic drugs – hardly ‘first-episode’.

In our 5-year follow-up study (The Scottish Schizophrenia Research Group, 1992), 14 of the 19 relatives who were still living with the patient were reassessed; 6 (43%) were still categorised as ‘cases’, using the GHQ. We concluded that a patient’s illness had a considerable and continuing effect on his or her relatives.

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Lawrie et al (2001) have raised the question, 'Whose responsibility?' Clinicians intimidated by the practical concepts of evidence-based psychiatry need to respond by expressing their difficulties and asking for time and resources to guide them through its complexities. Easy access to summaries of evidence may be the short-term solution, but the science of evidence-based psychiatry has to be mastered to continue practising the art of medicine. It's our responsibility.


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Reintroduction of clozapine after diagnosis of lymphoma

The atypical antipsychotic clozapine has been shown to be of value in some patients with treatment-resistant schizophrenia. The drug is now only used with careful blood monitoring after fatalities were noted in the early 1970s when the drug was initially released. Alvir et al (1993) estimate the incidence of agranulocytosis to be about 0.9% at 1 year. The following case demonstrates that a patient may suffer blood dyscrasias for reasons other than the known effects of clozapine and that the drug can be successfully reintroduced with a coexistent haematological malignancy.

A patient with a history of treatment-resistant schizophrenia was started on clozapine. After several months she developed asymptomatic agranulocytosis. On admission, investigations were normal apart from a bone marrow biopsy which showed agranulocytosis and mild myeloblastic changes attributed to an acute drug effect. Clozapine was ceased and short-term treatment with granulocyte colony-stimulating factor appeared to be successful.

The patient's mental state deteriorated after treatment with chlorpromazine and quetiapine. During her subsequent psychiatric admission, fevers were noted and a further general hospital admission was arranged. She was found to have severe hypercalcemia and hyperphosphataemia and reported bone pain. Bone marrow aspirate revealed a diffuse large B-cell lymphoma, which was treated with intensive combination chemotherapy over three cycles.

The patient was initially managed with haloperidol and diazepam. Relatively large doses of these medications were used to provide sedation during the initial phases of chemotherapy. After discussion with the patient, her relatives and the treating haematology team, it was decided to reintroduce clozapine seeking better antipsychotic control. The drug was restored with good effect and continued, despite very significant neutropenia secondary to the chemotherapy.

The case illustrates that clozapine can be ceased because of suspicions that it has lead to agranulocytosis while an underlying more sinister cause is not immediately detected. Subsequently, the drug was reintroduced with good antipsychotic effect in a patient who was severely medically ill.


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Stigma and ineffective legislation

Further to Haghight (2001), I would like to point out that the impact of stigmatisation is what it was when Goffman was developing his thoughts on stigma.

The impact of the Human Genome Project potentially reveals boundless information that is stigmatising to both individual and family, in terms of employment, education and insurance. Although Haghight refers to legislation in this area to prevent such discrimination, existing law provides little confidence in these burgeoning areas. The UK Disability Discrimination Act 1995, specifically referring to physical or mental impairment, provides little but deficiencies in the setting of discrimination against a propensity of developing a disorder in the future. Discrimination against such individuals would not be deemed unlawful. Amendments regarding this issue were discussed in both Houses of Parliament but not implemented (Nuffield Council on Bioethics, 1998). In contrast, a number of states in the USA have prohibited the use of information about employees' genetic characteristics by employers (Yesley, 1997).

In insurance, clients who have undergone genetic tests will be required to inform insurance companies of these. Proposals to avoid the unfair use of genetic information by insurance companies were announced in November 1998. Such a scheme relies on a voluntary rather than legal framework between the Department of Trade and Industry and the Human Genetics Advisory Committee (Clarke, 1995). This may do little to allay fears that an essentially profit-making business is being expected voluntarily to operate an ethical code of practice.

We may find that genetics provides a potential source of stigmatisation. As yet, the UK has few legal safeguards in place to protect individuals, who increasingly will have to manage this information carefully, rather as the 'discreditable' Goffman wrote of. Rather than legislation providing 'institutional support', the present situation serves only to propagate, in the public eye, a vision of a 'genetic underclass' (Clarke, 1995). An underclass where the stigmatising scars are invisible but their devastating effects on individual freedom are all too apparent.


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