Correspondence

EDITED BY MATTHEW HOTOPF

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Personality disorder: agency and responsibility

Much of the published reaction to the government’s Reforming the Mental Health Act (Department of Health, 2000) has been ethically in tune, focusing upon whether it might be justifiable to detain people with personality disorders who have yet to commit a criminal offence. An implication has been that it is perhaps unreasonable to ask psychiatrists to treat the behaviours associated with personality disorders prior to conviction. However, an alternative view might be that, in these proposals, psychiatry is being hoist with its own petard.

At both the psychodynamic and biological ends of the specialty’s spectrum there are research findings which suggest that personality disorder is a legitimate concern of psychiatry. Psychotherapists (particularly in the context of a therapeutic milieu) claim to be able to treat personality disorders. Neuroscientists report organic correlates (e.g. implicating prefrontal cortex). Hence, if one takes the evidence at face value, personality disorders are brain disorders amenable to psychotherapeutic intervention. Why should not a democratically elected government, concerned for the safety of its citizens, ask psychiatrists to do what we say we can do: treat mental disorder? After all, we detain other patients without them having to commit an offence.

Of course, the problem is that commentators from within the psychiatric profession either do not believe such findings or they do not wish to bear their consequences. Both the psychodynamic and biological accounts of personality disorder, if indiscriminately applied, appear to diminish personal responsibility. If personality disorder justifies mitigation in the forensic setting, then large numbers of people in society are walking about with a trump card, to be played should they ever go to court. This is not fanciful: there are many sophisticated patients who can effectively use this card to their short-term advantage in their dealings with members of community mental health teams. These individuals have carte blanche to commit immoral acts, an excuse, a reason (i.e. their personality disorder), and if they should murder or maim, it is the health professional who will be held to account. It has never been more important for the discipline of psychiatry to establish a coherent and consistently applied approach to agency and responsibility in the context of personality disorder.

Parenthetically, it is worth noting that there are severe limitations at both ends of the spectrum referred to above. The evidence that psychotherapeutic interventions treat personality disorder seems often to emerge from institutions with a vested interest in demonstrating success. While I do not question the integrity of the researchers concerned, perhaps their papers should include ‘declarations of interest’. Also, the applicability of their findings to the real world seems limited: violent subjects with comorbid substance misuse are rarely accepted for psychotherapy lest they act out. On the biological side, despite the demonstration of correlates with psychopathy, it has to be admitted that these findings have yet to differentiate cause from effect. We have good evidence that when children learn a musical instrument, then they change the structure and function of motor regions in their brain. Might not discovering, learning and practising immoral conduct affect other brain regions similarly?

Aristotle may have pre-empted us:

“We learn how to make by making, men come to be . . . harp-players by playing the harp: exactly so, by doing just actions we come to be just”


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Revisiting evolutionary psychology and psychiatry

At the risk of prolonging this non-meeting of minds, I must respond to the comments by Abed (2001) and Ayton (2000), passed on to me by Dr Lucas. No biologist could fail to agree with the great geneticist Theodosius Dobzhansky when he argued that nothing in biology makes sense except in the light of evolution – a point made at length in, for instance, my book Lifelines (Rose, 1998). However, we must distinguish between testable and untestable evolutionary speculations, and between determining and enabling conditions.

Despite Abed’s assertion, I find it difficult to imagine what type of empirical study could reveal whether or not “the human psyche or mind [was] formed primarily during the Pleistocene”, although quite clearly evolutionary processes have both enabled and limited humans in their creation of the wide variety of psychic, social and cultural styles evident in the world around us. But what determines our mental states and actions is for most useful purposes better understood by examining proximal causation rather than distant generalisation. And I am extremely surprised to find a psychiatrist, of all disciplines, adopting the cognitivist style of referring to the ‘architecture’ of the human mind as if this rigid, blueprint-evoking metaphor could encompass the richness of evolutionarily, developmentally, socially and culturally shaped mental experience.

Ayton (2000) suggests that there has been some sort of conspiracy in psychiatry to ignore biology. I am not a psychiatrist, but like any other scientist, I endeavour to defend the truth as I see it, while recognising that all our perceptions of such truths are formed within the metascientific context within which all living humans are embedded.


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The editorial by Abed (2000) and the subsequent correspondence cause me considerable concern as someone interested in the
Chromosome 22q11 deletion and brain tissue composition

We thank Eliez & Blasey (2001) for their kind comments about our paper (van Amelsvoort et al., 2001). However, we disagree that our paper implied that Eliez et al. (2000) reported relatively smaller frontal lobe volumes and would like to draw their attention to the following. Normal brain maturation is accompanied by a reduction in cortical grey matter volume and an increase in white matter volume. Myelination typically progresses from posterior to anterior brain regions and occurs relatively late in frontal regions (where it continues into adulthood). Also, the maturational process from adolescence into adulthood is associated with a net volume reduction in frontal regions (Giedd et al., 1999; Sowell et al., 1999), and a volume increase as Eliez & Blasey (2001) suggest. Consequently, we interpreted the relatively larger frontal lobe volumes found by Eliez et al (2000) in children and adolescents with velo-cardio-facial syndrome (VCFS) as compared with controls as possibly being caused by a relative delay in onset of ‘maturational’ grey matter reduction in VCFS. Our finding of a regional increase in volume of frontal grey matter and decrease in frontal white matter, in the absence of a difference in total frontal lobe (grey and white matter) volume, supports this interpretation and suggests that subtle differences in tissue composition occur which may reflect a delay in maturational processes (van Amelsvoort et al., 2001). Moreover, white matter abnormalities have been reported in VCFS and abnormal myelination could partially explain the abnormal, or delayed, maturational process. Future studies using longitudinal designs across this age span, and newer techniques such as diffusion tensor imaging, should be able to address this issue.


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Long-term potentiation and changes seen in depression

Reid & Stewart (2001) review evidence for a neurobiological basis of depression and it is suggested that brain plasticity plays a major role. These plasticity changes involve neuronal atrophy, neurogenesis, dendrite involution and formation, and long-term potentiation (LTP). Electroconvulsive therapy (ECT) and antidepressants enhance LTP and, as Reid & Stewart imply, the benefits (and adverse effects) of such treatments may be due to an enhancement or saturation of LTP. We question whether abnormal LTP per se is a critical neurobiological path to the changes seen in depression. We support the view that alterations in structural plasticity, as opposed to LTP, are more critical. Antidepressants, ECT, depression and stress can all modulate neuronal structure and LTP has been shown to be abnormal in models of depression and stress, but it does not follow that abnormal LTP is a prerequisite for these states, even though LTP is accepted to be important in, for example, associative learning.

In studies where LTP has been shown to alter neuronal structure, the increase in synaptic efficacy (assayed electrophysiologically) occurs within seconds to minutes but the earliest detected structural changes take at least 20 minutes (Yuste & Bonhoeffer, 2001). This time frame also does not correlate with the time required for the effects of antidepressant treatment (including ECT) – structural changes correlate better. Furthermore, although LTP is associated with morphological changes, these do not necessarily contribute to the potentiation (Yuste & Bonhoeffer, 2001). This casts doubt on the notion that the alterations in LTP are critical to the pathophysiological mechanism. We support the notion that the primary pathology is due to maladaptive neuronal structural change (Vaidya & Duman, 2001). The most likely reason why LTP can be affected by stress and depression,


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or by treatments for depression, is because such stimuli activate neuronal molecular signalling pathways. These pathways overlap with each other and with the signalling pathways that lead to dendritic structural changes.


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Authors’ reply: It was kind of Drs S. H. & R. Zaman to take an interest in our paper. In their thoughtful response they draw attention to the time course of LTP induction (seconds to minutes), and point out that this does not correlate with the time required for the effects (presumably, clinical response) of antidepressant treatments. The key issue is not the speed with which LTP induction itself occurs, which is unchanged by stress or antidepressant treatments (Stewart & Reid, 1993). It is rather the time course of changes induced in the regulation of LTP by antidepressant treatments (the so-called ‘metaplasticity’ referred to in our paper) that is important. This develops gradually, requiring at least six spaced ECT treatments for maximum effect (Stewart et al., 1994) or 14 days of fluoxetine treatment (Stewart & Reid, 2000). Interestingly, the effects of ECT on the degree to which LTP can be induced are detectable even 40 days after the end of a course (Stewart & Reid, 2000). These periods each correlate very nicely with antidepressant response, with the last described also mirroring the time course of relapse after successful ECT treatment in humans without antidepressant prophylaxis. Changes in excitatory post-synaptic potentials are seen, however, immediately after a single electroconvulsive application in experimental studies (Stewart et al., 1994), but they are smaller and more transient than those seen after a series of applications. This also accords with clinical observation: severely ill patients receiving ECT often show clear but transient responses after the first treatment in a course.

Of course, these are electrophysiological observations, and they may be mediated by ultrastructural neuronal changes. In this sense, we agree with the subtle point being made by Zaman & Zaman. Our aims are to draw together rather than disaggregate structural and functional phenomena. That is why we used the term connectivity in the review to refer to both functional and ultrastructural (e.g. dendritic) changes underlying the plasticity of neuronal connections, which we wished to distinguish from more gross effects such as cell death or proliferation. The fact that “molecular signalling pathways” to “dendritic structural changes” and to LTP overlap is precisely why we classed them together as candidate contributors to the neurobiology of depressive disorder. They may be dissociable, as Zaman & Zaman point out, but this is not in itself evident for or against the role of the regulation of LTP in affective disorder.

In any event the functional (electrophysiological plasticity) and structural changes (microanatomical plasticity) described in our review are each associated in reciprocal fashion with stress and antidepressant treatments, respectively – neither structural nor functional changes have been shown to have a causal role in depressive disorder. It does not allow that either phenomenon is a prerequisite for depressive states.


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Leptin and antipsychotic drugs

There is growing interest in the role of leptin in excessive body weight gain during antipsychotic drug treatment. Herrán et al’s (2001) paper is an important contribution to the field. Among other interesting findings they demonstrated that the functioning of the leptin system is preserved during antipsychotic drug administration. However, it is not “the first study analysing the effects of chronic antipsychotic medication on serum leptin levels”, since other authors have published relevant data for humans and rats (Baptista et al., 2000; Lacruz et al., 2000; Melkerson et al., 2000).

An important finding by Herrán et al was that olanzapine- and risperidone-treated patients displayed the highest and lowest leptin levels, respectively, “even after controlling for BMI”. This may support the contention that olanzapine is promoting a deleterious metabolic profile. That finding also prompts speculation that other mechanisms besides body weight gain could be involved in leptin elevation during antipsychotic treatment.

We have proposed elsewhere that insulin may be one of these additional mechanisms. Insulin is a powerful stimulus for leptin synthesis and secretion. Female rats with sulphide-induced obesity unexpectedly displayed normal serum leptin (and insulin) levels (Lacruz et al., 2000). In addition, serum leptin and insulin levels correlated positively in healthy people and antipsychotic-treated patients (Baptista et al., 2000, 2001). As olanzapine strongly stimulates appetite, it may promote insulin (and leptin) secretion, with relative independence from body weight gain. Surprisingly, Herrán et al reported that treatment with clozapine (another agent with strong appetite-stimulating properties) was associated with leptin levels similar to those found in haloperidol- and phenothiazine-treated patients (in spite of a higher body weight gain). If it were possible for Herrán et al to furnish the information, readers would benefit from knowing (a) the insulin levels in these patients; (b) a comparison of leptin levels between clozapine-, olanzapine- and risperidone-treated patients and their specific matched controls; and (c) the gender distribution in these treatment groups. If olanzapine- and risperidone-treated subjects display higher and lower leptin levels, respectively, than their controls, and if the gender distribution is similar in the three treatment groups, an additional important contribution will have been brought to the field of psychopharmacology.


Gender differences in treatment response to antidepressants

Parker (2001) expertly reviews the evidence for efficacy and effectiveness of different classes of antidepressants. In particular, he addresses the issue of whether selective serotonin reuptake inhibitors (SSRIs) are less efficacious in melancholia; reviews effectiveness studies; examines why there is a discordance between efficacy studies and clinical observation; and reviews the implications of differential effectiveness.

An additional important area that should be considered is that of gender differences in treatment response to antidepressants. Recent evidence has arisen to suggest that women may have a better response to SSRIs and men a better response to tricyclic antidepressants (Kornstein et al., 2000). As depression is approximately twice as common in women than in men, gender differences of this nature are important and should be considered when reviewing this area. The reasons for this difference may be related to the effects of female sex hormones on serotonergic neurotransmission and in particular on the function of the 5-HT1A receptor (Young et al., 1993). The evidence for gender differences in treatment response to antidepressant is not definitive (Kornstein et al., 2001; Quitkin et al., 2001) and further studies are needed to fully establish the validity of this notion. However, there are potentially important implications, and in the future clinical management strategies may take account of gender differences in treatment response.

World psychiatric literature

Patel & Sumathipala (2001) have provided an interesting survey of the country of origin of papers published in six psychiatric journals over a 3-year period. Only 6% of the literature was published from non-Euro-American countries. Unfortunately, the authors equate this low representation with the state of international research in psychiatry and these inferences are amplified by two accompanying commentaries (Leftf/Cheng, 2001).

It has been repeatedly shown that use of journals’ impact factors to infer the actual citations of individual papers or investigators is misleading (Fava & Ottolini, 2000). Further, both the authors of and the commentators on the study have failed to cite the research evidence available in terms of international trends (Fava & Montanari, 1998). Such evidence is based on the National Science Indicators on Diskette developed by the Institute for Scientific Information. All journals listed in Current Contents under the heading of Psychiatry were included in the database. The number of papers published per year, their citations, and the number of citations received per paper published were reported. Even though North America and the European Union rule the psychiatric arena, the picture is rather different from the one portrayed by Patel & Sumathipala. In the most recent survey of world psychiatric literature (Fava et al., 2001), limited to the journals included under the heading of Clinical Psychology and Psychiatry in Current Contents (Clinical Medicine), an impressive growth in impact from Latin America was documented. Fortunately, the progress of international psychiatric research is not confined to the six journals selected for the analysis by Patel & Sumathipala. None the less, many of their comments are valid and useful.


Error in Andrews et al (2001)

Dr Meadows and colleagues have drawn our attention to a wrong and misleading sentence in the Method section of Andrews et al (2001a). We conclude the sub-section on assessment (p. 146) by saying “Perceived health need was based on the UK Survey of Psychiatric Morbidity questions”. This sentence should read: “Perceived health need was based on work by Meadows et al (2000a). Similar concepts were used by the UK Survey of Psychiatric Morbidity questions”.

We apologise for this omission and draw readers’ attention to Meadows et al (2000b) for a more complete discussion of the development of the Perceived Need for Care Questionnaire. This is a reference we have used in subsequent papers (e.g. Andrews et al., 2001b).


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One hundred years ago

**Lunacy in Scotland**

The forty-third annual report of the General Board of Commissioners in Lunacy for Scotland consists of 18 sections and 4 appendices.

**Number of insane persons**

On January 1st, 1901, there were 15,899 insane persons in Scotland, of whom 2,395 were maintained from private sources, 13,458 by parochial rates, and 46 at the expense of the State. Since 1858 the number of lunatics under the jurisdiction of the Board has shown a total increase of 10,075, or 173 per cent. The increase of the population during the same period has been 42 per cent. The proportion of pauper lunatics per 100,000 of population shows an almost steady increase since 1858, and at the beginning of this year, attained its highest figure of 308, as against the next highest – 304, which was attained last year. During the last 27 years the proportion of private patients to population remains practically the same. The whole number of voluntary patients admitted into asylums in 1900 was 84. The Commissioners continue to be of opinion that it is a useful provision of the law which permits persons who desire to place themselves under care in an asylum to do so in a way which is not attended with troublesome or disagreeable formalities.

**REFERENCE**

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Researched by Henry Rollin, Emeritus Consultant Psychiatrist, Horton Hospital, Epsom, Surrey
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S. A. Spence
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