Correspondence

EDITED BY MATTHEW HOTOPF

Psychiatrists can cause stigma too

The Royal College of Psychiatrists' campaign to reduce the stigma of mental illness needs to examine the role that we play in maintaining stigma as well as reducing it. The negative attitudes of members of the public (Crisp *et al*, 2000) towards people with mental illness were mirrored by some psychiatrists (Farrell & Lewis, 1990). The latter authors found that psychiatrists held significantly more negative attitudes towards patients with a prior history of alcohol dependence. This included the view that they would not like these patients in their clinics. Similar findings apply to other groups of patients. Lennox & Chaplin (1996) surveyed the attitudes of Australian consultant psychiatrists. They found that 39% agreed with the statement 'personally I would prefer not to treat patients with learning disability and mental illness'.

The very nature of our job can be powerfully stigmatising in a way that cannot be underestimated. While engaging in debate with the public via the media and other means to inform and change attitudes, performing our clinical duties can have exactly the opposite effect. A Mental Health Act assessment at a patient's residence can be a cause of tremendous stigma to the patient and the family. This is especially so because of the highly visible involvement of the ambulance and police services whose help is often essential. It is against such almost routine community experiences that a broader national campaign has to compete.

Another very real source of stigma may be the side-effects of the medications that we prescribe. People with schizophrenia may not appear any different to the general public. However, side-effects such as drooling and tardive dyskinesia immediately point out an individual as being socially undesirable. Obesity, often a result of antipsychotic treatment, has been described as being seen as unattractive and unlikeable and has been linked with impaired employment and education opportunities (Crandall, 1994).

Psychiatrists have a clear duty to reduce stigma at the individual level. We must be prepared to identify and challenge our own prejudices and attempt to modify our clinical practice. Consideration also needs to be given to how we can carry out Mental Health Acts assessments, potentially the most stigmatising event that any family with a member with mental illness will suffer.

Crandall, C. S. (1994) Prejudice against fat people: ideology and self-interest. *Journal of Personality and Social Psychology*, **66**, 882–894.

Crisp, A. H., Gelder, M. G., Rix, S., *et al* (2000) Stigmatisation of people with mental illnesses. *British Journal of Psychiatry*, **177**, 4–7.

Farrell, M. & Lewis, G. (1990) Discrimination on the grounds of diagnosis. *British Journal of Addiction*, **85**, 883–890.

Lennox, N. & Chaplin, R. (1996) The psychiatric care of people with intellectual disability: the perceptions of consultant psychiatrists in Victoria. *Australian and New Zealand Journal of Psychiatry*, **30**, 774–780.

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Stigmatising pharmaceutical advertisements

The general public holds stigmatising attitudes toward those with mental disorder, with schizophrenia being rated as highly associated with dangerousness and unpredictability (Crisp *et al*, 2000). The authors mention that health professionals may share some of these views. After reading their article, I was struck by a number of pharmaceutical advertisements elsewhere in the same issue of the *Journal*, that appeared to perpetuate a negative image of schizophrenia. My curiosity thus stimulated, I performed a cursory lunchbreak study examining the portrayal of people with mental disorder in pharmaceutical advertising in three recent issues of international psychiatric journals (Table 1). It was notable that all the advertising for antidepressants had positive imagery. Indeed this was also largely true for the 'other' category, with only one negatively rated advertisement.

By contrast, three out of five advertisements for antipsychotic medications in this *Journal* were negative. One was particularly striking, a fearful young man peering through a door, his house covered in foil. The copy included the following: "His parents have to withstand torrents of verbal abuse. And Constant threats of violence". This small sample also suggests that there may be international variations in advertising in the field; what underlies this is unclear. It is intriguing, however, that the British advertising mirrors the attitudes of surveyed householders.

Table 1 Pharmaceutical advertisements in three psychiatry journals

	British Journal of Psychiatry, July 2000	*American Journal of Psychiatry*, June 2000	*Australian and New Zealand Journal of Psychiatry*, June 2000
Antidepressants			
No. advertisements	2	5	5
No. rated as negative	0	0	0
Example of imagery			Smiling woman
Antipsychotics			
No. advertisements	5	3	2
No. rated as negative	3	0	0
Example of imagery	Wan young woman, dishevelled hair	Family photos of happy family	Attractive young woman putting lipstick on
Other			
No. advertisements	1	5	0
No. rated as negative	0	1	
Example of imagery		Smiling children (advert for stimulants)	

How can we expect the general public to have a rational and informed approach to people with schizophrenia when learned journals accept advertisements that promote a product through negative stereotyping? Perhaps our willingness to allow this to happen is in accord with work in the field which suggests that health professionals may have even more negative attitudes to mental disorder than the general public (Jorm *et al*, 1999). A public campaign to combat stigma is undoubtedly important, but perhaps we should be prepared to examine our own beliefs about serious mental illness as a prelude to changing attitudes in society at large.

Crisp, A. H., Gelder, M. G., Rix, S., *et al* (2000) Stigmatisation of people with mental illnesses. *British Journal of Psychiatry*, **177**, 4–7.

Jorm, A. F., Korten, A. E., Jacomb, P. A., *et al* (1999) Attitudes towards people with a mental disorder: a survey of the Australian public and health professionals. *Australian and New Zealand Journal of Psychiatry*, **33**, 77–83.

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Serum cholesterol and parasuicide

Garland *et al* (2000) reignited the various controversies on the role of cholesterol in psychiatric disorders. The methodology used was similar to those in previous studies (Asberg *et al*, 1976) which did not control for the substances used in parasuicide. This may affect the levels of the chemical or metabolites being researched. Garland *et al* (2000) did not mention the methods used in those parasuicides and whether they would have affected serum cholesterol.

Engelberg (1992) and Block & Edwards (1987) held contrasting views on the relationship between cholesterol and serotonin uptake. The work by Heron *et al* (1980) used to support the hyposerotonergic function caused by low cholesterol appeared flawed. The serotonin site labelled by Heron *et al* (1980) is not the uptake site (Hawton *et al*, 1993), and therefore changes in brain serotonin content cannot be explained on the basis of their data. Furthermore, the serotonin stored within brain cells is not accumulated from blood but synthesised *in situ* from L-tryptophan.

Plasma cholesterol is in a dynamic state, entering the blood complexed with lipoproteins that keep it in solution and leaving the blood as tissues take up cholesterol. High-density lipoprotein (HDL)-cholesterol that transports circulating cholesterol to the liver for clearance plays a crucial role. Excess HDL can result from excess alcohol (Parkes *et al*, 1989). This increases the amount of cholesterol transported peripherally, causing low serum cholesterol. Alcohol, drugs and poisons are usually involved in parasuicides (Asberg *et al*, 1976) and low cholesterol level may therefore be due to ethanol misuse or poisoning. It is unlikely that cholesterol would provide the needed answers to parasuicide. It would only reduce this complex human behaviour to a 'matter to mind' paradigm.

Asberg, M., Traskman, L. & Thoren, P. (1976) 5-HIAA in the cerebrospinal fluid: a biochemical suicide predictor? *Archives of General Psychiatry*, **33**, 1193–1197.

Block, E. R. & Edwards, D. (1987) Effect of plasma membrane fluidity on serotonin transport by endothelial cells. *American Journal of Physiology*, **253**, 672–678.

Engelberg, H. (1992) Low serum cholesterol and suicide. *Lancet*, **339**, 727–729.

Garland, M., Hickey, D., Corvin, A., *et al* (2000) Total serum cholesterol in relation to psychological correlates in parasuicide. *British Journal of Psychiatry*, **177**, 77–83.

Hawton, K., Cowen, P., Owens, D., *et al* (1993) Low serum cholesterol and suicide. *British Journal of Psychiatry*, **162**, 818–825.

Heron, D. S., Shinitzky, M., Herschkowitz, M., *et al* (1980) Lipid fluidity markedly modulates the binding of serotonin to mouse brain membranes. *Proceedings of the National Academy of Sciences of the USA*, **77**, 7463–7467.

Parkes, J. G., Hussain, R. A. & Goldberg, D. M. (1989) Effect of alcohol on lipoprotein metabolism. I. High density lipoprotein binding. *Clinical Physiology and Biochemistry*, **7**, 269–277.

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Transcranial magnetic stimulation: asymmetrical excitability and depression

Maeda *et al* (2000) have succeeded in demonstrating the interhemispheric asymmetry of motor cortical excitability in major depression, using transcranial magnetic stimulation (TMS). This is an important finding that raises questions not only about the pathophysiology of major depression, but also about the state or trait nature of the results.

In discussing possible explanations for this functional asymmetry the authors consider the activity of inhibitory interneurons between cortical output cells, as proposed by Wasserman *et al* (1996), but it is not clear whether this mechanism is thought to act within the hemisphere being stimulated. The role of transcallosal inhibitory mechanisms has been demonstrated in schizophrenia (Davey *et al*, 1997; Boroojerdi *et al*, 1999) and is likely to be relevant to understanding asymmetrical motor thresholds in depression. In support of this view, Menkes *et al* (1999) hypothesised that depression is associated with decreased left hemisphere excitability with respect to the right hemisphere. They successfully showed that inhibitory low-frequency repetitive TMS applied to the right frontal lobe produced a significant antidepressant effect, in contrast to exciting the left frontal lobe by means of fast-frequency repetitive TMS, the antidepressant effects of which have been known for some years.

Furthermore, Maeda *et al* report mean motor thresholds in the depression group of 41.13% for the left hemisphere and 37.63% for the right hemisphere, and in the healthy group of 48.29% for the left hemisphere and 52.7% for the right hemisphere. This gives a mean motor threshold of 39.38% for the depression group and 50.50% for the controls, which suggests important differences in both absolute threshold and laterality between the groups. Any changes to either of these parameters in subjects recovered from depression, and possibly in their first-degree relatives, not only promises new insights into the pathophysiology of depression, but also may provide clues about the most elusive object, a biological marker for depression.

Boroojerdi, B., Töpper, R., Foltys, H., *et al* (1999) Transcallosal inhibition and motor conduction studies in patients with schizophrenia using transcranial magnetic stimulation. *British Journal of Psychiatry*, **175**, 375–379.

Davey, N. J., Puri, B. K., Lewis, H. S., *et al* (1997) The effects of antipsychotic medication on electromyographic responses to transcranial magnetic stimulation of the motor cortex in schizophrenia. *Journal of Neurology, Neurosurgery and Psychiatry*, **63**, 468–473.

Maeda, F., Keenan, J. P., Pascual-Leone, A. (2000) Interhemispheric asymmetry of motor cortical excitability in major depression as measured by transcrannial magnetic stimulation. *British Journal of Psychiatry*, **177**, 169–173.

Menkes, D. L., Bodnar, P., Ballesteros, R. A., *et al* (1999) Right frontal lobe slow frequency repetitive transcranial magnetic stimulation (SF r–TMS) is an effective treatment for depression: a case–control pilot study of safety and efficacy. *Journal of Neurology, Neurosurgery and Psychiatry*, **67**, 113–115.

Wasserman, E. M., Samii, A., Mercuri, B., *et al* (1996) Responses to paired transcranial magnetic stimuli in resting, active and activated muscles. *Experimental Brain Research*, **109**, 158–163.

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Child abuse and the clinical course of drug misuse

Charnaud & Griffiths (2000) in response to the finding of increased psychiatric symptoms in female drug users by Marsden *et al* (2000) postulate that this finding may be a sequela of earlier child abuse. It is interesting to note the high incidence of childhood sexual abuse found in their study population based in Cornwall. In a Dublin sample, the level of sexual abuse for both males and females was considerably lower (21%). However, the effects of abuse appeared to have a significant influence in subsequent clinical progression of substance misuse. Those patients with a history of sexual abuse in the past had a significantly younger mean age of first opiate use (16.7 years *v.* 19.1 years for those without a history of sexual abuse) (Browne *et al*, 1998). The duration of drug misuse was also considerably longer (mean 10.8 *v.* 8.4 years).

We would support the suggestion of Charnaud & Griffiths (2000) that the evaluation of previous history of sexual abuse can predict the best plan of treatment for these patients. We would suggest that the long-term clinical progression of sexually abused drug misusers is that of more rapid progression to intravenous drug misuse with all the prognostic features that this implies.

Charnaud, B. & Griffiths, V. (2000) Drug dependence and child abuse (letter). *British Journal of Psychiatry*, **177**, 84.

Marsden, J., Gossop, M., Stewart, D., *et al* (2000) Psychiatric symptoms among clients seeking treatment for drug dependence. Intake data from the National Treatment Outcome Research Study. *British Journal of Psychiatry*, **176**, 285–289.

Browne, R., Keating, S. & O'Connor, J. (1998) Sexual abuse in childhood and subsequent illicit drug abuse in adolescence and early adulthood. *Irish Journal of Psychological Medicine*, **15**, 123–126.

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Apolipoprotein E, Alzheimer's disease and Down's syndrome

We read with interest the article by Deb *et al* (2000) apparently demonstrating findings contrary to our own (Prasher *et al*, 1997). Overall, we agree with the findings by Deb *et al*, although clarification on several important points is required.

The principle reason why we did not find a statistically significant association (at the 5% significance level) between apolipoprotein E (ApoE) ε4 and Alzheimer's disease in adults with Down's syndrome was because at that time there was a much smaller sample size of adults with Down's syndrome and dementia available for meta-analysis (102 subjects previously included compared to 158 in Deb *et al*'s report). The three additional reports included in Deb *et al*'s meta-analysis are of significantly larger samples. However, even with this greater number of subjects available for meta-analysis the power remains at 76%. Given the proportions of ε4 in the groups with and without dementia in the Deb *et al* paper, for a power of 90%, a minimum of 224 adults with Down's syndrome and dementia are required to demonstrate statistical significance at the 5% level. Furthermore, the ε4 allele frequency in the different studies varies from 5.9% to 33.4% in subjects with dementia (Deb *et al*, 2000) and therefore future studies are still required if an association between ApoE ε4 genotype and Alzheimer's disease in adults with Down's syndrome is to be established.

Deb *et al* are incorrect to exclude the study by Wisniewski *et al* (1995) because "they diagnosed Alzheimer's disease on the basis of neuropathological findings alone". Wisniewski *et al* (1995) made a diagnosis of dementia (not Alzheimer's disease) by a clinical assessment alone "as judged by the physician following the patient". However, the inclusion of this study in the present meta-analysis makes little difference to the findings by Deb *et al* (2000) as only one person with an ε4 allele was present.

The increase in risk of developing dementia in adults with Down's syndrome (odds ratio 2.02) appears to be less than that in populations with no learning disability where it can be increased by as much as 30 times for people with two copies of the ε4 allele (Swartz *et al*, 1999). From the allele frequency given by Deb *et al* (2000) the diagnostic accuracy of ApoE ε4 for adults with Down's syndrome and dementia is of some clinical value. The sensitivity is 18% (95% CI 13.5–22%) and specificity 90% (95% CI 88–92%). The absence of an ε4 allele strongly suggests the absence of Alzheimer's disease. ApoE genotyping in the Down's syndrome population may possibly be used to screen for dementia.

We conclude, as previously (Prasher *et al*, 1997), that the presence of an ε4 allele is neither sufficient nor necessary to cause Alzheimer's disease but ApoE ε4 genotype does have a role to play in the presentation of Alzheimer's disease in adults with Down's syndrome. The effect is, however, 'overwhelmed' by the excessive amyloidosis due to the triplication of the amyloid precursor gene.

Deb, S., Braganza, J., Norton, N., *et al* (2000) *APOE* ε4 influences the manifestation of Alzheimer's disease in adults with Down's syndrome. *British Journal of Psychiatry*, **177**, 468–472.

Prasher, V. P., Chowdhury, T. A., Rowe, B. R., *et al* (1997) ApoE genotype and Alzheimer's disease in adults with Down's syndrome: meta-analysis. *American Journal on Mental Retardation*, **102**, 103–110.

Swartz, R. H., Black, S. E., St George-Hyslop, P. (1999) Apolipoprotein E and Alzheimer's disease: a genetic molecular and neuroimaging review. *Canadian Journal of Neurological Sciences*, **26**, 77–88.

Wisniewski, T., Morelli, L., Wegiel, J., *et al* (1995) The influence of Apolipoprotein E isotypes on Alzheimer's disease pathology in 40 cases of Down's syndrome. *Annals of Neurology*, **37**, 136–138.

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Authors' reply: We thank Drs Prasher & Haque for their interest in our paper and are pleased that they agree with our conclusions. It is quite obvious that the difference in findings in the meta-analysis between our study and Prasher *et al*'s study was due to the inclusion of data in our study that were not available at the time of Prasher *et al*'s study. According to our calculation, our meta-analysis has 92% power (95% CI 88–96%) at the 5% level. However, traditional power calculation is not applicable in this case because instead of simply adding allele frequencies among all studies, we have used the computerised version of the Woolf (1995) method of meta-analysis that takes account of each study individually. Also, because of the varied nature of studies included in the meta-analysis we did not feel it appropriate to calculate specificity and sensitivity in the traditional way.

It was not stated in Prasher *et al*'s (1997) paper which 31 patients (15 with and 16 without dementia) out of 40 patients with Down's syndrome, presented in Wisniewski *et al*'s (1995) study, were included in their meta-analysis. The age of death of patients reported in Wisniewski *et al*'s study ranged widely between 15 and 69 years. They mentioned at the bottom of their table that "The presence of dementia is defined as a deterioration of competence, as judged by the physician following the patient". No detail

about diagnosis was mentioned in the text and no patient over age 30 had an ε4 allele. For these reasons we chose not to include this study in our meta-analysis. However, as Prasher & Haque point out inclusion of this study would have made little difference to our findings.

Whereas Prasher & Haque rightly suggest that further research is needed to clarify the role of ApoE ε4 in Alzheimer's disease in people with Down's syndrome, we were surprised to see that they have recommended ApoE genotyping as a possible screening test for dementia in this population. This will be totally inappropriate at this stage considering the uncertain relationship between Alzheimer's neuropathology and ApoE genotype in people with Down's syndrome, as we mentioned in the last paragraph of the Discussion in our paper.

We agree with Prasher & Haque that the presence of ε4 allele is neither necessary nor sufficient for the development of Alzheimer's disease.

Woolf, B. (1995) On estimating the relation between blood group and disease. *Analysis of Human Genetics*, **19**, 251–253.

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Chronic fatigue syndrome and depression

I found MacHale *et al*'s (2000) discussion of their results confusing. According to the abstract and methods, they screened their patients with chronic fatigue syndrome (CFS) to exclude those with depression. Then they examined this group further using a standardised psychiatric interview (Schedule for Affective Disorders and Schizophrenia), in order to "exclude subjects with current psychiatric illness, with a particular emphasis on depression". The data from the Hamilton Rating Scale for Depression are difficult to interpret given the number of illness-rated items, but the scores did not indicate a significant degree of depression either. So, having excluded "subjects with depression or anxiety", why did the authors claim in their discussion that "the main limitation of the present study is that our CFS subjects had high levels of depression"?

If this is correct, why was their depression not picked up by the three measures? Why were these patients not excluded from the research as stated by the authors or, funds permitting, used as a comparison group (Costa *et al*, 1995; Fischler *et al*, 1998)? How depressed were the 10 patients on antidepressants and, if these were not effective, could their suboptimal treatment have contributed to their ongoing fatigue?

I was also baffled by the authors' suggestion that the thalamic hyperperfusion may reflect "increased attention to motor and cognitive tasks". What were the patients doing? The abstract states that the scans were conducted at rest. If the subjects had just completed a battery of cognitive tests, why did the authors not check to see whether the data available supported their hypothesis (Fischler *et al*, 1998)?

If this paper was subjected to peer review, why did no one query the selective discussion of the findings and the misrepresentation of the literature on CFS and psychopathology?

Costa, D. C., Tannock, C. & Brostoff, J. (1995) Brainstem perfusion is impaired in chronic fatigue syndrome. *Quarterly Journal of Medicine*, **88**, 767–773.

Fischler, B., Flamen, P., Everaert, H., *et al* (1998) Physiopathological significance of ^{99m}TcHMPAO SPECT scan anomalies in chronic fatigue syndrome: a replication study. *Journal of Chronic Fatigue Syndrome*, **4**, 15–30.

MacHale, S. M., Lawrie, S. M., Cavanagh, J. T., *et al* (2000) Cerebral perfusion in chronic fatigue syndrome and depression. *British Journal of Psychiatry*, **176**, 550–556.

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Authors' reply: As explained in the method section, the potential participants were screened by excluding those scoring above case threshold in the Hospital Anxiety and Depression (HAD) scale, a self-rating scale that does not require a detailed interview. The remaining participants were then interviewed using the Schedule for Affective Disorders and Schizophrenia to further exclude any current mental illness.

First, in the discussion we say: "The main limitation of the present study is that our CFS subjects had high levels of depression: almost half were on psychotropic medication and five had a previous history of depression". "Had high levels of depression" is defined by what follows after the colon. There is, therefore, no contradiction. Participants were not currently depressed, but some were receiving antidepressant medication and some had previously been depressed.

Second, regarding that point made relating to our comment that "thalamic overactivity in CFS (and depression) may, therefore, reflect increased attention to motor and cognitive tasks . . .". The perceived contradiction is that participants were at rest during uptake of the tracer, i.e. not currently engaged in motor or cognitive tasks. It is clearly speculative that increased thalamic activity at rest will also mean increased thalamic activity during tasks. What was implied, however, was that increased baseline or resting activity of the thalamus may be an underlying brain marker that is related to patients being more attentive to motor and cognitive activity, as they occur.

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