Prophylaxis of depression in older people

I read with interest the recent article by Wilson et al (2003). On the basis of a randomised, double-blind placebo-controlled trial, they conclude that sertraline is not effective in preventing recurrent episodes of depression. However, I would like to make certain observations.

First, looking at Table 2 (p. 494), we find that the number of patients remaining in the study at 100-week follow-up is 15 in the sertraline group and 12 in the placebo group. These numbers are too small to draw any major conclusions. Also, looking at the same table, we find that at 4-week follow-up there were six recurrences of depression in the placebo group compared with only two in the sertraline group; that is, the sertraline group had significantly fewer recurrences of depression in the first 4 weeks of prophylactic therapy.

Second, I would like to make an observation about statistical significance. Again looking at Table 2, we find that the number of cumulative recurrences were fewer in the sertraline group than in the placebo group at all points of the maintenance phase over 2 years. Even though these numbers did not reach statistical significance, they are clinically significant. This opinion is based on two reasons: first, for a physician, prevention of even one case of recurrence is important and satisfying; second, from a community and financial perspective, sertraline prophylaxis has been found to be more cost-effective than treating each new episode of depression with dothiepin (Hatzizandreou et al, 1994). If Wilson et al had included an analysis of treatment costs (including the cost of treating episodes of recurrent depression) in both the groups, it might have made interesting reading.

Third, as Wilson et al pointed out, failure to increase the dose of sertraline at the earliest signs of recurrence contributed to the greater number of recurrences observed in their study. There should have been provision to increase the dose of sertraline as and when the clinical situation demanded it. After all, a significant number of patients do require a daily dose in excess of 50 mg sertraline (Suri et al, 2000), a dose that was used to treat almost three-quarters of the patients in this study.

In conclusion, the data presented by Wilson et al are insufficient to suggest making any changes in the current practice of prescribing sertraline for treatment and prophylaxis of depression in older people.


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Author’s reply: In response to Dr Kumar’s comments there are some important issues that need addressing. First, Dr Kumar introduces his letter in saying that we conclude that sertraline is not effective in preventing recurrent episodes of depression. This is not the case. We only stated that there is no evidence that sertraline has a prophylactic efficacy when used at the dose that achieved remission.

Second, we agree that if we had conducted an end-point analysis on the 27 subjects who completed the 100-week follow-up, then the study would have been relatively meaningless. We conducted a survival analysis on 113 subjects. This is a well-founded and recognised method of analysis of this type of study.

Third, we concur with Dr Kumar in that the prophylactic management of recurrent depression is critical. We do not advocate treating each episode as a new episode when prophylactic management is indicated. However, we do make the point that preventive techniques should be based on evidence of efficacy and effectiveness.

Dr Kumar suggests that we should have adopted a protocol that enabled increase in dose ‘when the clinical situation demanded it’; presumably when we thought a patient was experiencing the early stages of a recurrence. This misses the point of the paper. Our study (which is of a power similar to or greater than equivalent studies in this field) shows that the dose of sertraline required to achieve remission does not have prophylactic efficacy. This is important, as what evidence there is suggests that therapeutic doses of dothiepin (Old Age Depression Interest Group, 1993), nortriptyline (Reynolds et al, 1999) and citalopram (Klysner et al, 2002) do have prophylactic efficacy. The implications for guidelines concerning the long-term management of older people with depression are self-evident.

Dr Kumar has failed to present arguments that undermine our conclusions. There is no evidence that the dose of sertraline required to achieve remission has prophylactic efficacy. The 8.4% reduction in risk of recurrence (over 100 weeks) that it offers is unlikely to instil clinical confidence in prophylactic efficacy when evidence indicates that other drugs for which the dose does not need to be changed are available.

Declaration of interest
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Liaison psychiatry and older adults

Lloyd & Mayou (2003) argue cogently for the development of liaison psychiatry, or ‘psychological medicine in general hospitals’ as they prefer it. Their arguments would carry more weight with commissioners if they included the mental health needs of older people. Two-thirds of general hospital beds are occupied by people aged over 65 and it is obvious to anyone visiting a general medical ward that the majority of ‘bed-blocking’ is caused by older people with dementia, depression and prolonged delirium. The epidemiology, together with demonstrably poor coordination of services, is highlighted in a recent report, partly commissioned by the Faculty of Old Age Psychiatry of the Royal College of Psychiatrists (Holmes et al., 2002).

The time is now ripe for old age psychiatrists to take their multi-disciplinary skills and experience of community support into general hospitals to enable earlier discharge of so-called bed blockers. Liaison psychiatrists could develop their services (and sub-speciality status) more quickly and comprehensively if they worked more closely with old age psychiatry colleagues clinically, and within the Royal College of Psychiatrists.


As a mentor after I took up post in Edinburgh, Bob Kendell impressed on me his view that liaison psychiatrists were ‘ambassadors of psychiatry’ in the general hospital. He pointed out that, for most hospital specialists, liaison psychiatrists would be the only psychiatrists they were likely to encounter – so we had to be available, approachable, helpful, practical, considerate and sensible; we had to be good clinical psychiatrists and we had to resolve problems rather than cause them.

That does not mean liaison psychiatrists cannot bring special skills to the workplace, but it does imply that such skills have to be welded to basic clinical nous and rapport with colleagues. The significance of this is increased in a world in which we tend to be more valued by physicians than fellow psychiatrists – perhaps increasingly so as psychiatry becomes focused on severe and enduring mental illness, and other forms of disability, suffering and resource demand are marginalised.

Next, I made the leap from mental health to general hospital management when trusts were first mooted (without understanding the implications – it just felt right), and this turned out to be a fortuitous decision. Liaison psychiatry at the Infirmary rapidly expanded as I planned with medical colleagues solutions to the clinical problems we faced: some funds came through the Trust Improvement Programme and some from individual directorates seeking to purchase consultant sessions. I do not believe this initiative would, or could, have happened had I remained with the mental health unit. Now the rest of Scotland has progressed as the Executive’s intentions have been made good – notably, with the appointment of four consultant liaison psychiatrists and 10.5 liaison nurses in Glasgow.

The consequences of going with the acute trust have been far-reaching. Psychiatry is not regarded as an alien speciality – we are seen as assets. We understand the environment and the pressures and we respond to the needs that arise rather than pursue a purist agenda. Crucially, we appreciate that what the acute hospital requires primarily from its psychiatric service lies in the areas of rapid assessment, immediate management and optimal resource usage rather than the proven areas of effectiveness that are highlighted as the rationale for spending on liaison psychiatry.

As a tangible illustration of our significance and role, the department of psychological medicine in Edinburgh’s new Royal Infirmary has not been located up some back alley or on the top floor. We are sited on the ground floor near the hospital’s front door because we are recognised as a key constituent in the modernisation agenda that has swept through acute medical care in the hospital. Without ‘going native’ I doubt that much of this progress would have occurred – so seek to make this management leap rather than sticking with tried and trusted strategies that have been found wanting.


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Adverse events following neurosurgery

Matthews & Eljamel (2003) gave an excellent overview of the controversial field of neurosurgery for mental disorders (NMD). I agree with them that ‘the accumulated literature on neurosurgery for mental disorder remains highly unsatisfactory’ but would like to point to some recent evidence.

Matthews & Eljamel state that ‘there is surprisingly little evidence’ to support the occurrence of adverse personality change. In my opinion, some of the literature suggests otherwise. Herner (1961) noted that in a group of 116 capsulotomy cases, frontal lobe deficit syndrome was obvious at follow-up in 30%. In the anxiety group, 40% and 13%, respectively, had adverse events of mild and of modest severity. In another study (Kullberg, 1977), capsulotomy caused ‘some personality changes in the majority of the patients’. Adverse events in those studies included fatigue, emotional blunting, emotional incontinence, indifference, low initiative, disinhibition and impaired sense of judgement.

In a very recent study (Ruck et al., 2003), 26 anxiety patients who had undergone bilateral theromcapsulotomy were followed up after a mean of 13 years. Psychiatric methods included symptom rating scales and neuropsychological testing. To
avoid bias, ratings were done by psychiatrists not involved in patient selection and postoperative treatment. Seventeen of 23 patients alive at long-term follow-up were seen in person and relatives were interviewed. The reduction in anxiety ratings was significant both as 1-year and long-term follow-up. Seven patients were, however, rated as experiencing significant adverse events, the most prominent symptoms being apathy and dysexecutive behaviour; also neuropsychological performance was significantly worse in these patients. I therefore agree with Matthews & Eljamel that we must continue to evaluate the efficacy and safety of NMD.

Declaration of interest

C.R. has participated in numerous educational events sponsored by pharmaceutical companies and has been a consultant for Pfizer.


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Authors’ reply: Rück makes reference to a series of studies reporting personality change following anterior capsulotomy, including his recent review of 26 patients undergoing thermal capsulotomy for anxiety (Rück et al, 2003). He raises interesting questions about the prevalence of personality change following certain (if not all) neurosurgical procedures for mental disorder, and such questions remain, we believe, essentially unaddressed by previous research. Rück’s rate of apparent personality change following anterior capsulotomy is comparatively high at approximately 30% of patients. This rate is higher than those rates reported in earlier literature, which suggest rates of up to 10% for stereotactically subcuate tractotomy (Ström-Olsen & Carlisle, 1971; Goktepe et al., 1975) and 2% for stereotactic cingulotomy (Dougherty et al., 2002). However, 24% of patients undergoing limbic leucotomy had transient apathy which resolved fully (Montoya et al., 2002).

In addition to the lack of uniformity of measurement across studies, another key difference may lie in the fact that many of the larger studies included patients with a variety of diagnoses, including depressive disorder, obsessive–compulsive disorder (OCD) and anxiety disorder. In fact, non-OCD anxiety disorders made up a small percentage of most of the studies cited above, whereas Rück’s study sample comprised entirely patients diagnosed with non-OCD anxiety disorder.

The lesions of anterior capsulotomy disrupt the continuity of the fronto-striatal–pallidal–thalamic circuits which are believed to be dysfunctional in OCD (Modell et al., 1989). Important connections between the orbitofrontal cortex, anterior cingulate regions and the thalamus also lie in the anterior part of the internal capsule and are thought to play an important role in the pathogenesis of major depressive disorder (Tekin & Cummings, 2002).

Most psychiatrists, neurologists and neurosurgeons would probably predict high rates of serious psychopathology — including personality changes — if such lesions were made within ‘healthy brains’. If the existing literature can be considered reliable, including the report of Rück and colleagues, it is quite remarkable that the reported rates of significant frontal psychopathology are so infrequent. Hence, three possibilities (at least) must be considered:

(a) that neuropsychological and personality screening for frontal impairment has been grossly inadequate in almost all studies;
(b) that the deleterious effects of frontal surgery on patients with chronic intractable affective disorders may be minimised because the target brain structures are already dysfunctional, perhaps with important frontal functions being undertaken by non-frontal structures (such plasticity of mammalian brain function is plausible, see e.g. Kolb & Gibb, 1993);
(c) different forms of psychiatric disorder may be associated with different risks of adverse consequences following NMD; for example, thermal capsulotomy for non-OCD anxiety disorders may present a higher risk of frontal psychopathology than capsulotomy for OCD or depression.

In reality, the true picture may represent a combination of influences from these three factors. What is clear is that all NMD must be accompanied by detailed prospective audit with comprehensive evaluation of ‘frontal’ neuropsychology and personality functioning.

Declaration of interest

K.M. has received payment for lectures on the management of depression from various pharmaceutical companies.


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Neuroscience and psychodynamics

I was taken by surprise to read a positive article concerning psychoanalysis. In response I would like to make some comments on facts and their interpretation, the individual and his or her context and the impossible relationship between mind and brain.
I agree that psychoanalysts can have an interesting dialogue with neuroscientists, but it oversteps the mark to conclude that consciousness (and unconsciousness) can be explained by the working of the brain. There is an interaction between a working brain and its context. In this sense I agree with Hobson’s (2003) comments on the two directions of causality, but there is more to be considered: consciousness and unconsciousness are not explained by this interdependence.

The neuroscientific concept of the ‘mirror neuron’ is merely an interpretation, and one that for me is no more than a false explanation, or at least a tautology. To call a neuron firing during the execution and observation of the movements of another person a ‘mirror neuron’ is, of course, an interpretation of the two simultaneous phenomena. To say more on this matter we need an interpretation by the subject himself or herself. When Hobson writes that minds mirror one another, that statement does not tell us anything about self-consciousness.

In considering the interaction between one person and another in relation to identity and self-consciousness, the mirroring stage plays an important role. However, as investigators we remain outsiders. To learn about the subjective experience of mirroring we need the interpretation of the subject. This interpretation will include the symbolic function of human beings (i.e. the potential to recall a reality by a word) and goes beyond the imitation (mirroring) of words. Of course, the subject hears the spoken words from the other within the context. But there is more than just the repetition of the word of the other. This is what is referred to as the hole in the being, or the gap between the thing and the word (as Hegel, Heidegger and Sartre postulated). When we consider the subject as a thing among other things, then something very strange happens when the subject names him- or herself; a hole is then made in the person’s own being. This is what is referred to as alienation: ‘The human being has a special relation with his own image – a relation of gap, of alienating tension’ (Lacan, 1988).

There is always a gap between the spoken word and the thing for speech to exist, but once the subject speaks, he actualises the gap again and again. What then can be the relation between the mind and the brain? Nowadays the neurosciences are popular, so it is quite accepted to say that the psychic functions are epiphenomena of the brain. For me this statement is much too simplistic. It does not take into account that there is a fundamental difference between a word and the thing it describes. As mirroring needs a distance between the two objects, so it is a fortiori necessary that there is a distance between the symbolic and the material. The distance between word and thing creates a suspense in which symbolic function tries to bridge that gap. Interpretation is one of these metaphorical bridges.

Since there is a fundamental gap between symbol and thing, between thought and matter, it is impossible to explain the mind as a product of the functioning brain. Thoughts are not the excreta of neurons. In this sense the (un)conscious can not be found in the neuron. Explaining the mind as a product of the brain is a metaphor, and a bad metaphor.


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One hundred years ago

Psychopathology in prisons

The philosophic doctrine that our actions are free is generally based on the conscious-ness of freedom; and in its legal aspect on the sense of accountability or responsibility. That this consciousness of freedom exists is a psychological fact, and therefore a psychological examination of the conviction, an analysis of this psychological phenomenon, is a necessary preliminary to the philosophical inquiry.

It may be contended that the question of a transcendental ego or noumenal will behind, superior to the law of causation and capable of free choice, is not legitimately within the domain of psychology; but it is manifest that if psychology, in unfolding and genetically explaining the phenomena of volition, prove that this mode of consciousness does not necessitate any such idea of a transcendental will, that in fact this sense of freedom may and does accompany actions which are absolutely determined, the psychological foundation is taken away from the doctrine of free will. This task Professor Hoche of Freiburg has set himself to accomplish. He is frankly a determinist, entirely at variance with the Kantian doctrine of a self-determining will. He affirms that the observations of psychopathology must be taken into account in the normal psychology, because the mental activities of the insane do not differ intrinsi-cally from those of the so-called normal, but only in degree; and that, moreover, there exist all gradations from the sane to the insane.

Now, the feeling of freedom exists in many forms of mental disease, particularly and to a high degree in mania, as to whose unfreedom of volition no doubt can exist, and this feeling of freedom, Dr. Hoche contends, is related to the central emission of motor impulses.

In the next place, the observations of psychopathologists show that in the empiric character much greater differences exist in permanent, deeply-seated, elementary qualities than is customarily recognized by theoretic psychology. The value, therefore, of conclusions based on the hypothesis that
in all men there are certain psychical processes, particularly within the region of the emotions, which are for all men identical, is thus at once nullified, and with these necessarily, Dr. Hoche says, conclusions founded on the belief in an ever and everywhere present conscience. The conscience, says the author, exhibits the same variations as do other emotions. With the insane the conscience wastes, or it is subject to objectively unfounded fluctuations. Also in neurotic and borderland cases this variability of conscience is found.

The clear parallelism in fact between material and mental processes does not permit of such a distinction as that the principle of causality holds good only for the material and not for the mental side of these processes.

The practical importance of these doctrines lies in its relation to the penal treatment of that large class of male-factors – and only those with an intimate acquaintance with prison populations know how surprisingly large this class is – who are neither of normal mental and physical make-up nor actually insane, degenerates, hereditarily-burdened individuals, or, to use the prison term, the weak minded. A system of graduated punishments is, Dr. Hoche says, futile, and punishment at all unreasonable, and for these he would substitute individual treatment decided by the medico-psychological examination, and some form of sequestration so as to render them harmless to society.

We believe that those who have had experience in dealing with prisoners in this country would be very much disposed to agree with Professor Hoche on the ground that the separation of weak-minded from ordinary prisoners would conduces to better management of the latter class. Dr. Hoche has had wide experience in such matters, is the author of the important work on forensic psychiatry already reviewed in our pages, and his views deserve the most serious gravest consideration.

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