275–276). I agree that this is an important topic. Among the 7887 men in the two lipid-lowering drug trials mentioned (Lipid Research Clinics Program, 1984; Frick *et al*, 1987), there was an excess of 17 coronary deaths in patients assigned to placebo as compared with those assigned to the drug, but there was an excess of 13 violent deaths in those assigned to the drug. Since there was an excess of 8 other deaths in the drug groups, there were overall 4 more deaths in the drug than in the placebo groups.

Thus lipid-lowering drugs are not saving lives. At best they are merely changing the cause of death. It is therefore of major importance that they should not be causing side-effects which may change the quality of life for patients and those close to them. Death is an extreme outcome of violent or impulsive behaviour. Drugs which increase violent deaths are also likely to produce greater increases in milder forms of violence, leading to more aggression at home and at work, more abuse of spouses and children, and generally more unhappiness.

There is other evidence, not mentioned by Drs McLoughlin & Clarke, which supports the relationship between violence and lowered cholesterol levels. Virkkunen, a forensic psychiatrist from Finland, was the first to draw attention to this when he noted unusually low blood total cholesterol levels in men who had committed violent and impulsive crimes, including murder (Virkkunen, 1983). He then went on to study aggressive children and found a similar relationship there (Virkkunen & Penttinen, 1984).

This is a potentially serious problem in view of the likely rapid increase in the numbers of men taking lipid-lowering drugs, and the likely lack of attention which will be paid to violence as a possible side-effect. It deserves serious investigation by psychiatrists concerned with aggressive behaviour.

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Paradoxical intervention

SIR: Adshead *et al* (*Journal*, December 1988, **153**, 821–823) describe the use of paradoxical intention in a non-compliant ritualiser. It is assumed in the report that the patient relapsed after initial improvement with behaviour therapy because she did not comply with instructions given. The paradoxical intervention (which took the form of 'masterly inactivity' being formally recommended by the psychiatrist) produced a successful outcome, but the authors drew attention to the discomfort experienced by both the patient and the treatment team concerned.

Paradox is a useful therapeutic technique (Cade, 1979). However, it is not a single prescriptive act or magic formula. Paradox is part of a therapeutic programme requiring a sensitive adjustment to the patient's needs and a recognition of the importance of the patient's attitudes to the problem, the treatment, and the therapist (Fisch *et al*, 1982). For best results, improvement should be greeted with caution, puzzlement, and an (apparent) acceptance that the patient's recovery is due to factors other than the therapist and the intervention.

This flexible and understated response is hard for eager therapists to apply, but often serves to avoid the reactions described in this interesting report.

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The near-death experience

SIR: In their thorough and timely review of the near-death experience (NDE), Roberts & Owen (*Journal*, November 1988, **153**, 607–617) note that the dissociative anaesthetic ketamine can reproduce many of the features of the NDE. Several recent discoveries in neuroscience suggest a physiological explanation for at least some NDEs which involves a ketamine binding site in the brain.

Like its congener phencyclidine (PCP, 'angel dust'), ketamine can bind to a site on the N-methyl-D-aspartate (NMDA) receptor (Sonders *et al*, 1988). Many of the substances which bind to this site are also powerful dissociative hallucinogens. There has been an enormous increase in research activity involving the NMDA receptor, as it has been shown

to be implicated in excitotoxic brain damage, epilepsy, learning and memory, and possibly psychosis (Barnes, 1988).

The neurotransmitter at NMDA receptors is probably L-glutamate, an excitatory amino acid which may kill the neuron if present in excess ('excitotoxicity'). Blockade of the receptor by ketamine can prevent this damage, which occurs in ischaemia, epilepsy, and other conditions (Barnes, 1988). Thus an endogenous blocking agent would have neuroprotective properties. An endogenous agent, which has been labelled 'alpha endopsychosin' (Quirion *et al*, 1984), has in fact been discovered for the PCP site. It is thus possible that a flood release of alpha endopsychosin could serve the function of reducing excitotoxic damage in the ischaemic brain, for example in the situation of a cardiac arrest. A by-product may be a temporary, dissociative hallucinogenic effect on consciousness. This is a more specific version of Carr's (1981) theory concerning the secretion of psychoactive peptides in stressful situations. However, while the endorphins, as suggested by Carr, may play a role in the NDE, they are not usually regarded as potent hallucinogens, unlike many of the substances active at the PCP binding site.

A further matter to consider is the possible role of this site in the formation and retrieval of memory. In his discussion of the psychological bases of the NDE, Siegel (1980) suggested that memories may normally be suppressed by a mechanism which acts as a gate to data from the outside. If this external input is decreased (as occurs in the patient who has had ketamine) while awareness remains, stored perceptions are released and may be dynamically organised. Blockade of NMDA receptors, by ketamine or perhaps alpha endopsychosin, suggests a neural substrate for the 'gate' of the sensory deprivation theory – i.e. it closes the 'gate' to external input so that old memories come to the fore instead, a feature of some NDEs.

In conclusion, the NDE is an entity of considerable interest and it may be of some value to apply the recent explosion of knowledge in neuroscience to our attempts to understand the phenomenon. Elucidating the properties of the endopsychosins, and the development of substances which are more specific for the PCP site (ketamine also binds to several other sites), may be of some value in this attempt.

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Affective 'switch mechanisms'

SIR: The notion of "switch mechanism" in affective disorders (Carney *et al*, *Journal*, January 1989, **154**, 48–51) is a challenging one, with both theoretical and clinical applications. I am sceptical about the conclusion that because "S-adenosyl methionine enters the CSF, is linked with CSF 5HIAA and folate metabolism, and influences prolactin" these "suggest an effect on dopamine metabolism" and the "dopamine system should be further explored".

I do agree that the dopamine system is an important neurotransmitter in the study of affective disorders, but I do not see the results of these open trials as being sufficient to highlight solely the role of dopamine and not serotonin if we have to concentrate on either.

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What's so special about two years anyway?

SIR: One of the most important criteria to be taken into account when assessing a patient for psychosurgery is that all reasonable treatments should have been tried and failed. In other words, the patient needs to have a treatment-resistant illness, usually depression, and some describe this as chronic depression. I was therefore interested in Dr Scott's review article with the title 'Chronic depression' (*Journal*, September 1988, **153**, 287–297).

Dr Scott accepts the definition of chronicity, previously suggested by others, as "symptomatic nonrecovery for a period of two or more years". She goes on to consider the factors that may relate to chronicity, which include – among others – the illness (length of episode, course, symptom profile, etc), treatment, family and personal history, and personality.