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.

KARL L. R. JANSEN

Department of Anatomy
University of Auckland Medical School
Private Bag
Auckland, New Zealand

References

BARNES, D. M. (1988) NMDA receptors trigger excitement. *Science*, **239**, 254–256.

CARR, D. B. (1981) Endorphins at the approach of death. *Lancet*, *i*, 390.

QUIRION, R., DIMAGGIO, D. A., FRENCH, E. D., *et al* (1984) Evidence for an endogenous peptide ligand for the phencyclidine receptor. *Peptides*, **5**, 967–978.

SIEGEL, R. K. (1980) The psychology of life after death. *American Psychologist*, **35**, 91–95.

SONDERS, M. S., KEANA, J. F. W. & WEBER, E. (1988) Phencyclidine and psychotomimetic sigma opiates: recent insights into their biochemical and physiological sites of action. *Trends in Neurosciences*, **11**, 37–38.

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.

MAMOUN MOBAYED

St James's Hospital
James's Street
PO Box 580
Dublin 8

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.