the rats on first exposure to the apparatus show highly active swimming, headshaking, diving and defaecating frequently. With prolonged exposure, and particularly during the 5-min test on the second day, the vigorous activity declines, being interspersed with phases of immobility of increasing duration.

We do not, however, agree with their conclusion that the rats are merely making an adaptive response to a stressful situation which is unrelated to a state of lowered mood. Although it is evident that the rats do adapt to the situation in that their initial agitated behaviour rapidly subsides, we see no reason to exclude *a priori* the possibility that they may at the same time also be feeling depressed. Three lines of evidence would support this latter proposition. First, it is known that exposure to inescapable traumatic situations can induce symptoms of depression in man and higher animals[3,4]. Second, our results show that a variety of clinically effective antidepressant drugs selectively decrease immobility whereas other drug classes do not[1,2]. Finally, we have shown that immobility is also reduced by nonpharmacological treatments such as electroconvulsive shock and deprivation of REM sleep[2], procedures which are generally accepted to be effective in the treatment of human depression[5,6]. A further point with which we disagree is the assumption of Hawkins *et al.* that for immobility to represent despair, it should be maintained once adopted. It seems to us more reasonable to expect the animal to oscillate between attempts to escape and immobility, with immobility predominating as the inescapability of the situation becomes more apparent, which is what both we and Hawkins *et al.* observe.

In general, we do not claim to have produced a model of human clinical depression in the rat. Nonetheless, our results encourage us to believe that our procedure provides an animal model of at least some aspects of depressed mood which is readily amenable to experimental manipulation.

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1. Porsolt, R. D., Le Pichon, M. & Jalfre, M. *Nature* **266**, 730–732 (1977).
2. Porsolt, R. D., Anton, G., Blavet, N. & Jalfre, M. *Eur. J. Pharmac.* **47**, 379–391 (1978).
3. Seligman, M. E. P. *Helplessness: on Depression, Development and Death* (Freeman, San Francisco, 1975).
4. Harlow, H. F. & Suomi, S. J. *Behav. Biol.* **12**, 273–296 (1974).
5. Turek, I. S. & Hanlon, T. E. *J. nerv. ment. Dis.* **164**, 419–431 (1977).
6. Vogel, G. W. *Archs gen. Psychiat.* **32**, 749–761 (1975).

Effect of osmolarity on quantal size

VAN DER KLOOT reports[1] that he was unable to detect an amplitude change in miniature end plate potentials as a result of the imposition of osmotic changes in the incubation medium of the nerve–muscle preparation. He argues that his failure excludes a release mechanism depending on the free acetylcholine (ACh) in the cytoplasm because the change in osmolarity should have changed the terminal volume which should then have changed the free ACh concentration. This would have been then detectable as a change in the amplitude of the miniature end plate potential.

Unfortunately, he did not measure the change in the terminal volume so we have no idea how successful his procedure was in overcoming the various compensatory mechanisms for maintaining cell volume.

More critically, he neglected to measure the free ACh concentration. The factors which control this are unclear but it is certain that the concentration of free transmitter can change significantly in response to functional demands within five seconds[2]. The activity of choline acetyltransferase in neuromuscular junction terminals is sufficient in appropriate conditions to synthesise (or degrade; it is fully reversible) the whole transmitter store within the 20-s period it took him to change the osmolarity and repenetrate the muscle[3].

I am afraid we are no further forward unless Van der Kloot can supply direct evidence that the free ACh concentration changed in the way he thinks it did.

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1. Van der Kloot, W. *Nature* **271**, 561–562 (1978).
2. Israel, M. *et al. J. Neurochem.* **28**, 1259–1267 (1977).
3. Marchbanks, R. M. in *Synapses* (eds Cottrell, G. A. & Usherwood, P. N. R.) 81–101 (Blackie, Glasgow, 1977).

VAN DER KLOOT REPLIES—The changes in the volume of frog motor nerve terminals in hypertonic solutions were described by Clark[1]. The nerve terminals surely shrink appreciably in hypertonic solutions.

The experimental demonstration of a swift mechanism for the homeostasis of free acetylcholine in nerve terminals, operating over massive changes in concentration, like that proposed by Marchbanks, would be of substantial interest in itself and certainly, as I pointed out in my report, could account for the observations within the framework of the gated channel hypothesis for quantal acetylcholine release. The major problem that would remain is how the diffusion of charged acetylcholine cations through membrane channels could be independent of the potential across the membrane.

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1. Clark, A. W. *J. cell. Biol.* **40**, 521–538 (1976).

Use of ADTN to define specific ^{3}H-spiperone binding to receptors in brain

THE report of Leysen *et al.*[1] concerning the binding of the relatively new radiolabel ^{3}H-spiperone to both dopamine (DA) and 5-hydroxytryptamine (5-HT) receptor sites suggests that caution is needed in using this radioligand for DA receptor binding

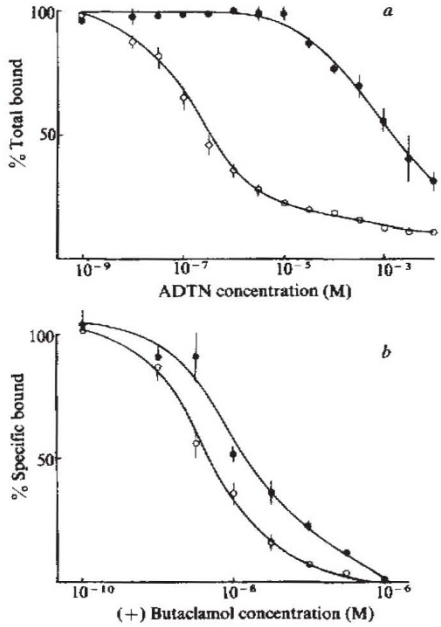

Fig. 1 Effect of ADTN (*a*) and (+)-butaclamol (*b*) on the binding of ^{3}H-spiperone in rat brain striatal (○) and medial frontal cortex (MFC) (●) homogenates. Tubes contained 0.50 nM and 0.25 nM ^{3}H-spiperone for the medial frontal cortex (MFC) and striatum, respectively, these represented the K_d values of saturable binding sites in the two brain regions. Each point represents the mean ± s.e.m. of 4–10 determinations from 2–5 separate experiments. In *a*, the results are expressed as % of total ^{3}H-spiperone binding, corrected for filter blanks. In *b*, results are expressed as % of 'specific' ^{3}H-spiperone binding, defined as that displaced by 1 μM (+)-butaclamol.

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