energy criterion to a brittle body of idealised geometry. However, it has been shown recently[3] that the Kendall theory could be improved, and brought into complete agreement with the Griffith theory, if allowance were made for the restraint to the free lateral movement inevitably experienced by the brittle body during compression. Assuming the lateral restraining force to be a small fraction, α, of the axial compression, F, and following exactly Kendall's[1] procedure and notation, the cracking force is

$$F = \frac{1}{(1 - w/d + 8\alpha c/d)} \left(\frac{2ERd}{3}\right)^{1/2} \quad (1)$$

where c is the crack length.

The force at the transition from cracking of the brittle body to its gross yielding under the platen is given by the solution to the quadratic

$$\frac{1}{Yd}\left(\frac{F}{b}\right)^2 - \frac{F}{b}(1 + 8\alpha c/d) + \left(\frac{2ERd}{3}\right)^{1/2} = 0 \quad (2)$$

In particular, if the particle size is reduced to a critical value

$$d_{crit} = \frac{32ER}{3Y^2(1 + 8\alpha c/d)^4} \quad (3)$$

cracking becomes impossible. Equations (1)–(3) differ from their counterparts in Kendall's paper by the presence of the very crucial term $8\alpha c/d$.

Based on my experimental data[3] and that of Kendall[4], I have argued that the restraining force would be very small especially if the size of the body is reduced. In fact, a value of α between 1/100 and 1/200 seemed most appropriate.

For the model material (polystyrene) tested by Kendall[1] the c/d ratio in equation (3) for all samples was 1.25. Equation (3) suggests that for $\alpha = 1/200$ the transition from brittle to ductile behaviour of polystyrene could be expected at a size of 3.69 mm as opposed to 4.48 mm predicted by Kendall's theory. The experimentally observed value was 3.6 mm (ref. 1). Expression (3) clearly is in better agreement with experimental data. Likewise, equation (3) predicts a crushing limit of around 0.85 μm for calcium carbonate which is also in close agreement with the average particle size of 0.8 μm to which calcium carbonate is reduced after prolonged milling.[1].

B. L. KARIHALOO

Department of Civil Engineering, University of Newcastle, New South Wales 2308, Australia

1. Kendall, K. *Nature* **272**, 710–711 (1978).
2. Griffith, A. A. *Phil. Trans. R. Soc.* **A221**, 163 (1920).
3. Karihaloo, B. L. *Proc. R. Soc.* (in the press).
4. Kendall, K. *Proc. R. Soc.* **A361**, 245–263 (1978).

Agonist regulation of α-adrenergic receptor numbers

THERE have recently been several reports which indicate that agonist-induced desensitisation of cells might be explained, at least in part, by reductions in the number of receptors exposed at the surface of target cells; the evidence has been particularly clear for β-adrenergic receptors. Thus, it is not surprising that studies have been designed to see whether agonist-induced desensitisation of cells to α-adrenergic stimulation might be explained in a similar way. Two reports have now described fairly rapid agonist-induced decreases in α-receptor number[1,2], and another described a modest rise in α-receptor number in animals treated for several weeks with reserpine to induce supersensitivity[3].

In their report, Cooper *et al.*[2] seemed to consider that the observed reduction in receptor number provided an adequate explanation for the desensitising effects of agonists; no other mechanisms were apparently considered. However, this position is untenable, as their main observation was that a 50% decrease in receptor number in adrenaline-treated platelets (assessed by dihydroergocryptine binding) was accompanied by an essentially complete loss of two cellular responses to the same agonist (aggregation and 5-hydroxytryptamine secretion).

Surely, this must mean that only a small proportion of the desensitising effect of agonist treatment can have been mediated through the change in receptor number? Most of this desensitising effect was presumably a result of some event which was brought about by receptor activation but which did not involve any changes in the number of exposed receptors. This is hardly surprising, as there is much evidence which indicates that in other tissues, especially smooth muscles, changes in receptor numbers are not likely to be the main mechanism whereby increased or decreased exposure to agonists brings about changes in cell sensitivity to those ligands which act at Ca^{2+}-mobilising receptors[4–6] (of which the α-adrenergic receptor is one type[7]). These alternative mechanisms for changes in sensitivity may not be as conceptually simple nor as well understood as the changes in receptor number, but they cannot be ignored when the available data are incompatible with an explanation based solely on changes in receptor number.

ROBERT H. MICHELL

Department of Biochemistry, University of Birmingham, PO Box 363, Birmingham, UK

1. Strittmatter, W. J., Davis, J. N. & Lefkowitz, R. J. *J. biol. Chem.* **252**, 5478–5482 (1977).
2. Cooper, B., Handin, R. I., Young, L. H. & Alexander, R. W. *Nature* **274**, 703–706 (1978).
3. U'Pritchard, D. & Snyder, S. H. *Eur. J. Pharmac.* **51**, 145–155 (1978).
4. Fleming, W. W., McPhillips, J. J. & Westfall, D. P. *Ergebn. Physiol.* **68**, 55–119 (1973).
5. Carrier, O. *Fedn Proc.* **34**, 1975–1980 (1975).
6. Fleming, W. W. *Rev. Neurosci.* **2**, 43–90 (1976).
7. Jones, L. M. & Michell, R. H. *Biochem. Soc. Trans.* **6**, 673–688 (1968).

ALEXANDER AND HANDIN REPLY—Michell is correct, of course, in stating that agonist-induced desensitisation of physiological responses might not be explainable on the basis of a 40–50% decrease in receptor number, as determined by ligand binding with ^{3}H-dihydroergocryptine (DHEC), an α-adrenergic antagonist. It was not our intention to imply that this was the sole explanation for adrenaline-induced desensitisation in the platelet. However, we do not agree "that only a small proportion of the desensitising effect of agonist treatment can have been mediated through the change in receptor number". Since submission of our paper, there has been a report on the desensitisation of β-adrenergic receptors showing that the percentage of receptors identified by agonist binding is decreased to an extent considerably greater than the 35% decrease in receptor number determined by antagonist binding. These data suggest that agonists and antagonists bind different forms of the β-adrenergic receptor[1]. It has been reported that α-adrenergic agonists and antagonists bind to distinct states of the α-adrenergic receptor and that ^{3}H-DHEC may label both the agonist and antagonist state[2–5]. If most of the decrease in ^{3}H-DHEC binding in platelets preincubated with (−)adrenaline represents changes in the putative agonist state, then the observed decrease in receptor number may be sufficient to explain most of the α-adrenergic agonist-induced desensitisation in platelets. This possibility requires further investigation using both agonist and antagonist binding assays.

The references on denervation supersensitivity may not be relevant to our work on desensitisation. In fact, it has recently been reported that α-adrenergic receptors in rat cerebral cortex increase after chronic reserpine treatment, suggesting that an increase in receptor number may contribute to post-junctional supersensitivity[6].

R. WAYNE ALEXANDER
ROBERT I. HANDIN

Peter Bent Brigham Hospital, Boston, Massachusetts 02115

1. Wessels, M. R., Mullikin, D. & Lefkowitz, R. J. *J. biol. Chem.* **253**, 3371–3373 (1978).
2. Greenberg, D. A. & Snyder, S. H. *Molec. Pharmac.* **14**, 38–49 (1978).
3. Peroutka, S. J., Greenberg, D. A., U'Prichard, D. C. & Snyder, S. H. *Molec. Pharmac.* **14**, 403–412 (1978).
4. U'Prichard, D. C., Charness, M. E., Robertson, D. & Snyder, S. H. *Eur. J. Pharmac.* **50**, 87–89 (1978).
5. Miach, P. J., Dausse, J. P. & Meyer, P. *Nature* **274**, 494–497 (1978).
6. U'Prichard, D. C. & Snyder, S. H. *Eur. J. Pharmac.* **51**, 145–155 (1978).

0028–0836/79/0278—0864$01.00

© Macmillan Journals Ltd 1979