its inheritance on the supposition that 'schizophrenia results from defects in a pathway a→b→c→ brain function'. The timing of, and the substrate for, the activity of such a gene are subject to a myriad of possible modulations, from the coincidental development of the rest of the organism, and from environmental factors. The final expression of the gene as schizophrenia could depend upon this quite as much as the details of the inheritance of the gene itself.

SLACK, J. M. W. (1989) Peptide regulatory factors in embryonic development. *Lancet*, *i*, 1312.
WIESEL, T. N. (1982) The postnatal development of the visual cortex and the influence of the environment (Nobel Lecture). *Bioscience Reports*, **2**, 351–377.

CHRIS HOLMAN

Bridgewater Hospital
Eccles
Manchester M30 0RL

SIR: We were interested to read the paper by Roberts & Claridge (*Journal*, April 1991, **158**, 451–456) and appreciate the new approach in giving a genetic model with a dimensional view of schizophrenia. The authors have given interesting analogies of eye colour in *Drosophila*, and thrombin formation. Most of the ideas were centred around the percentage production of active protein and the examples were towards less than normal amounts of the resulting proteins.

They also gave another example wherein it is supposed that schizophrenia results from defects in a pathway of brain function. A complete mutation in the gene controlling a step of this pathway would result in a phenotype, the failure of development of brain function being manifest as schizophrenia.

We agree with this proposition, but want to look at it from another angle. Instead of postulating that the altered genes on one or more chromosomes produce an end effect of reduction in the amount of protein (for example an enzyme of a pathway), we can say that the end result of the mutation on a single gene acting on its own or the mutations on several genes acting in union would cause an increase rather than a decrease in the amount of protein (again an enzyme). We can cite the example of acute intermittent porphyria where the activity of the hepatic delta-amino laevulinic acid synthetase is increased several fold (Dewar, 1988). Another example is Huntington's chorea in which it has been shown that there are increased dopamine concentrations in parts of basal ganglia (Gelder *et al*, 1989). This possibility of increase in protein would be in conformity with the dopamine hypothesis where the dopamine-like effect is supposed to be increased. What we mean to say is that, under the given circumstances, it is also possible that the pathology can be explained by overproduction of proteins – say to 200% (not only to less than 40% as stated in the paper). So in this example, if 200% explains development of schizophrenia, 150% may explain a schizotypal state. The authors gave the example of thrombin formation and cited haemophilia as a pathological entity resulting from a block of any step in the pathway. We feel that hypercoagulability is a suitable example that can be given from our view of increased protein formation. As we have already mentioned, this approach seems to be much closer to the dopamine hypothesis.

DEWAR, A. J. (1988) *Companion to Psychiatric Studies, 4th edn* (eds R. E. Kendell & A. K. Zeally). Edinburgh: Churchill Livingstone.
GELDER, M., GATH, D. & MAYOU, R. (1989) *Oxford Textbook of Psychiatry, 2nd edn*. Oxford: Oxford Medical Publications.

RAMAMOHAN VELURI
ANGELA MOHAN

St Brendan's Hospital
Dublin 7, Ireland

V. T. GREENE

Royal College of Surgeons in Ireland
Dublin 2

Sibling sex and bulimia nervosa

SIR: Lacey *et al*'s data on the siblings of patients with bulimia nervosa (*Journal*, April 1991, **158**, 491–494) led them to conclude that all-female sibships were significantly over-represented. This conclusion is based on dubious statistical reasoning. Only female bulimics were included in the study, and the authors have underestimated the impact that this will have had on the likelihood of all-female sibships. For example, in the case of a sibship of two (i.e. the female proband and just one brother or sister), the authors claim that the expected proportion of all-girl sibships is one-third. This is a surprising claim since having a brother and having a sister should be equally likely (provided one ignores the slight excess of boys in the general population), leading to an expected proportion of one half. The authors' expectation that chance alone will result in bulimic women having strikingly more brothers than sisters seems no better founded than the expectation that normal women will typically have more brothers than sisters, or that normal men will typically have more sisters than brothers.

R. GOODMAN

Department of Child and Adolescent Psychiatry
Institute of Psychiatry
London SE5 8AF