

We have never suggested that, in Zimbabwe, spiritual causes are unrelated to depression. This would be a ridiculous assertion for a culture which holds life to be controlled by the spirits of one's dead ancestors. However, in trying to counteract taboos among the public about psychological disorder it was useful to distinguish between depression and the most well known and feared form of mental illness, akin to the Western category of acute psychosis, which is viewed as caused by a specific form of alien spirit possession.

Neither was it suggested that management guidelines developed in Harare could simply be transported elsewhere. The point of health systems research is that the process of involving local people is the model. We cannot understand why this process could not be used in rural areas to generate appropriate interventions.

Patel found three-quarters of attenders with conspicuous morbidity to be turning to traditional care providers. We welcome his call for their involvement in treatment programmes. Analysis of our cases drawn from a population sample (in preparation), shows only one-fifth had consulted traditional healers, with most turning to family members or the church. Some of the poorest had also struggled to pay for private doctors, operating outside the government clinics. Successful intervention programmes need to take into account the variety of agencies that people choose to turn to.

LUTZ, C. (1985) Depression and translation of emotional worlds. In *Culture and Depression: Studies in the Anthropology and Cross-Cultural Psychiatry of Affect and Disorder* (eds A. Kleinman & B. Good). Berkeley: University of California Press.

MELANIE ABAS

*Institute of Psychiatry
London SE5 8AF*

JEREMY BROADHEAD

*Maudsley Hospital
London SE5 8AZ*

GERTRUDE KHUMASLO-SAKATUKWA

*Department of Psychiatry
University of Zimbabwe*

Chromosomal aberration and bipolar affective disorder

SIR: Craddock & Owen (*BJP*, April 1994, 164, 507–512) state that no literature review has suggested an increased rate of bipolar disorder to be associated with the possession of an extra X chromosome. However a recent review (Everman & Stoudemire, 1994) does reach this conclusion.

Reporting a patient with bipolar disorder and previously undiagnosed Klinefelter's syndrome, Everman & Stoudemire state that this is the 14th recorded instance of such an association and note three other cases of bipolar illness in individuals with other X chromosome excesses (two with XO/XX/XXX mosaicism and one with XXX syndrome). Two of their cases are included in Craddock & Owen's table 1 but a further 15 (13 with cytogenetic confirmation of an extra X) are not. The addition of these cases makes the ratio of X chromosome relative to autosomal abnormalities more impressive, in agreement with Everman & Stoudemire's conclusion that there is some support in cytogenetic studies for a theory of X linkage.

If both bipolar disorders and schizophrenia (Crow, 1988; DeLisi *et al.*, in press) are found in excess in individuals with an extra X chromosome this adds support to the concept of a continuum of psychosis (Crow, 1986) with a single genetic locus on the X, perhaps counter-balanced by one on the Y chromosome.

CROW, T. J. (1986) The continuum of psychosis and its implication for the structure of the gene. *British Journal of Psychiatry*, 149, 419–429.

— (1988) Sex chromosomes and psychosis: the case for a pseudo-autosomal locus. *British Journal of Psychiatry*, 153, 675–683.

DELISI, L. E., FRIEDRICH, U., WAHLSTROM, J., *et al.* (1994) Schizophrenia and sex chromosome abnormalities. *Schizophrenia Bulletin* (in press).

EVERMAN, D. B. & STOUDEMIRE (1994) A bipolar disorder associated with Klinefelter's syndrome and other chromosomal abnormalities. *Psychosomatics*, 35, 35–40.

T. J. CROW

*Medical Research Council
Watford Road
Harrow HA1 3UJ*

Genetics, chance and dysmorphogenesis in schizophrenia

SIR: McGuffin *et al.* (*BJP*, May 1994, 164, 593–599) emphasise the prominence of the genetic contribution to schizophrenia and examine in detail four hypotheses as to the relative roles of genes and environment in the origins of the disorder. In evaluating their fourth and most radical hypothesis, they argue that apparently 'non-genetic' components may be random changes in gene structure and expression, but fail to note an earlier formulation thereon that also relates importantly to contemporary perspectives of schizophrenia as a neuro-developmental disorder.

That chance may in part determine differences in brain development, even in the face of genetic

identity, is credited to Goodman (1991). However, Kurnit *et al* (1987) have argued previously that chance plays a major role in the occurrence of many developmental perturbations that cluster in families but recur less frequently than expected for simple Mendelian traits; these authors argue that for dysmorphic disorders showing non-Mendelian patterns of inheritance, randomness is intrinsic to morphogenesis such that a stochastic [probabilistic] single gene model can generate continuous liability curves very similar to those postulated by multifactorial-polygenic threshold models thereof. Given the weight of evidence that in schizophrenia the primary aetiopathophysiological process is one of disturbance(s) in early cerebral morphogenesis (Waddington, 1993), we have speculated that these formulations as to the role of chance in the genetic regulation of development may be relevant to the disorder (Waddington *et al*, 1994). Thus, to the extent that the entry of schizophrenia to the ranks of dysmorphic disorders is sustained, such theorising assumes a particular relevance for the continuing debate on the relative roles of 'genes v. environment' in its origins. There would still remain fundamental questions concerning not only the nature and timing of these early (genetically programmed, stochastic or other) dysmorphic events in schizophrenia but also the process(es) by which they might result in the evolution of psychotic symptoms and determine overall course of illness.

GOODMAN, R. (1991) Growing together and growing apart: the non-genetic forces on children in the same family. In *The New Genetics of Mental Illness* (eds P. McGuffin & R. Murray), pp. 212–224. Oxford: Butterworth-Heinemann.

KURNIT, D. R., LAYTON, W. M. & MATTHYSSE, S. (1987) Genetics, chance, and morphogenesis. *American Journal of Human Genetics*, **41**, 979–995.

WADDINGTON, J. L. (1993) Schizophrenia: developmental neuroscience and pathobiology. *Lancet*, **341**, 531–536.

—, O'CALLAGHAN, E., YOUSSEF, H. A., *et al* (1994) The neurodevelopmental basis to schizophrenia: beyond a hypothesis? In *Schizophrenia—An Integrated View* (Eds R. Fog, J. Gerlach, R. Hemmingsen, *et al*. Copenhagen: Munksgaard (in press).

JOHN L. WADDINGTON

*Royal College of Surgeons in Ireland
St. Stephen's Green
Dublin 2, Ireland*

SIR: In his criticisms of our paper (McGuffin *et al*, *BJP*, May 1994, **164**, 593–599), Eagles' (*BJP*, August 1994, **165**, 266) comments show a profound misunderstanding both of what we were trying to say and of some of the papers he cites. Of course it is possible that twin studies do not on their own allow an accurate estimate of the magnitude of the genetic effect in schizophrenia, and that one

possible source of error is that the prenatal environment is more similar in monozygotic (MZ) than dizygotic (DZ) pairs. However, as we pointed out, the evidence for an aetiological role for obstetric complications (whether pre-, peri- or post-natal) is extraordinarily difficult to interpret and suggests at most a very small effect. Indeed the incidence of schizophrenia is not markedly greater in twins in spite of their preponderance of early adverse events. Eagles describes us as using "clever formulae" to estimate heritability (with the implication that cleverness is somehow reprehensible). In fact the underlying principles are simple and straightforward with heritability estimated as double the difference between the MZ and DZ correlations.

Eagles goes on to quote the results of a family study by Kendler *et al* (1993) which he believes "used a preferable genetic method" (not, we think, a claim which Kendler and co-workers would make). He seems to believe that the results of this paper contradict our own findings. Kendler *et al* (1993) reported a comparatively low rate of schizophrenia in the parents of schizophrenics and described the likely explanation of this in terms of the diminished reproductive rates associated with schizophrenia. A more useful indicator of the familiarity of schizophrenia was that 9.2% of siblings of schizophrenics were affected compared with 0.5% of controls. This translates to a sibling correlation in liability of about 0.48 (± 0.04). Since siblings share half of their genes, heritability can be roughly estimated by doubling the sibling correlation, i.e. a heritability of schizophrenia of about 96%. Simply doubling the sibling correlation runs the risk of over-estimating heritability since this approach ignores non-additive genetic effects and shared environment. Nevertheless the results are not markedly different from our own estimate of a maximum heritability of 89%.

Lastly, Eagles find it counter-intuitive that part of the aetiology of schizophrenia may be explained by random events. We described a number of genomic phenomena that can decrease the resemblance within pairs of relatives and gave examples of where these have been demonstrated in other diseases. Although strictly speaking not all such phenomena are stochastic they would all normally be interpreted as 'non-genetic' but yet would be completely undetectable by traditional epidemiological methods designed to investigate environmental factors in disease.

We are sorry that Eagles finds all this so perplexing and can only suggest that a read of a recent primer (e.g. McGuffin *et al*, 1994) will help remedy his present confusion.