References

DEVOOGD, T. J. (1987) Androgens can affect the morphology of mammalian CNS neurons in adulthood. *Trends in Neuroscience*, **10**, 341–342.

GESCHWIND, N. & GALABURDA, A. M. (1985) Cerebral lateralisation I, II, and III. *Archives of Neurology*, **42**, 428–459, 521–552 and 634–654.

IVERSEN, L. L., IVERSEN, S. D. & SNYDER, S. H. (1983) *Handbook of Psychopharmacology Vol 17*. New York: Plenum Press.

KANDEL, E. R. & SCHWARTZ, J. H. (1985) *Principles of Neural Science (2nd edn)*. New York: Elsevier.

SIR: While laying no claim to specialist knowledge in either genetics or virology, a position no doubt shared by the majority of psychiatrists, I find Dr Crow's remarks on the causes of schizophrenia rather baffling (Crow, *Journal*, October 1987, **151**, 460–465). His grounds for revising the exogenous virus theory seem plausible, although available knowledge of viral infiltrations of the CNS appears to already provide adequate grounds for dismissal. His new theory evades simple misgivings, but if the circumstantial evidence is examined the leap of faith required will be seen to be commensurate.

Dealing first with transposable elements, transposons have not been demonstrated in vertebrates, let alone man, whereas Alu inversion segments, similarly mobile, are widespread on the human genome and not so far associated with any illness. Retroviruses are known to be capable of vertical transmission, but also of horizontal transmission and in some cases neoplastic changes, two capacities that even the most ardent advocate could not credit to a schizophrenia retrovirus. Without these abilities replication and survival must be problematic, especially given the sub-fertility of the chosen host.

Perhaps there is a case for an analogy to human oncogenes, similar to viral material and incorporated on the human genome with beneficial effects, presumably on cell growth and differentiation with which their products are thought to be associated, offsetting the occasional clinical cancer. This is unlikely, for several reasons. Schizophrenia is common, and occurs at optimal reproductive age. There are no animal models, unlike the case with oncogenes. It is difficult to see any selective advantage: the relatives of schizophrenics do not have any distinctive qualities, except perhaps the traits of schizophrenia in attenuated form – hardly advantageous except under exceptional conditions such as social isolation. Dr Crow mentions the growth of certain factors that enhance hemispheric differentiation as possibly advantageous. If he means growth of the neural systems thought to mediate schizophrenia, then this theory has nothing better to offer than current polygenic theories presumably also focused on such systems.

The theory is at a disadvantage compared with polygenic theories when activation of the virus is considered. The oncogene implicated in Burkitt's lymphoma is known to be activated by two environmental stimuli: chronic antigenic stimulation from the malaria parasite and the Epstein Barr virus. The brain is well protected from viruses, immune complexes, and mutagens in general when compared with extracerebral cells in every one of which the virogene must be present if present at meiosis. The notion that the virogene is activated by other genes is not borne out by the monozygotic twin pair concordence rates unless a massive rate of mutation in significant genes (and no others) is postulated. This seems rather unlikely.

Thus Dr Crow asks of his virogene certain nonpareil capabilities, stretching the definition of the words 'virus', 'virogene', etc. much as a clever science fiction writer adapts topical scientific concepts for creative effect. True, my information comes from perusal of library textbooks (Emery, 1985; Wetherall, 1985) and is probably outdated; the parent sciences are constantly throwing up new marvels which will probably become grist to further theories. But my distrust of such theories goes beyond their inherent unlikeliness. In compressing the natural history of schizophrenia into the imperceptible transactions of genes, virogenes, and mutagens, squeezing out the role of brain tissue and the environment that it works on, there is a real danger of a *reductio ad absurdum*, symmetrical to the equally reductionist environmental theories of the 1960s.

Indeed, it is tempting to see Dr Crow's and similar theories and the Scheff/Lidz/Cooper axis as opposing keystones in the overarching false antitheses of nature and nurture. The opposition is more precise even than that; 1960s theorists strove to exclude medical concepts, Dr Crow strives to exclude everything but. To the majority who work or live with patients with schizophrenia, unfamiliar with genetics but knowing that the environment is somehow important, these theories must indicate that it is us, not their charges, who are out of our wits.

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References

EMERY, A. (1985) *Medical Genetics*. Edinburgh: Churchill Livingstone.

WETHERALL, D. (1985) *The New Genetics and Clinical Practice*. Oxford: Oxford University Press.