Genuine genetics or conceited convenience?

Alper and Natowicz[1] are to be congratulated on their thoughtful critique in *TINS* of the committed genetic reductionism of much current neuroscientific thinking on the causes of mental disease. The danger is that such a dogmatic geneticism can both misdirect research and blind one to more probable non-genetic explanations. As the authors imply, there are few patterns of distribution of a trait in a population to which a genetic model cannot be fitted, given appropriate assumptions about partial penetrance and incomplete dominance. I had thought that the dramatically higher incidence of diagnosis of schizophrenia in the children of black–white parents in the UK than in either the black- or white-parental population was one phenomenon where a transparently plausible social explanation rooted in the racism of the host society would defeat genetic ingenuity. Not so: a distinguished behavioural geneticist, presented with the data, needed only a few moments thought before offering as an explanation assortative mating; that is, it is people with schizophrenic personalities from either black or white populations who are most likely to have sexual relationships across the colour divide! Alper and Natowicz speculate on the reasons, internal to science, as to why this strong preference for genetic explanations exists, but I assume they would not wish to exclude the broader social and ideological framework of societies in which great disparities of wealth, status and power occur on the basis of class, race and gender [Rose, S. P. R., Lewontin, R. C. and Kamin, L. (1984) *Not in our Genes*, Penguin].

No biologist would wish to deny the existence of many behaviourally manifested conditions for which genetic causations exist; some of them might indeed mimic disorders caused by purely phenotypical or developmental contingencies [early onset senile dementia of the Alzheimer type is one striking example (for review see Ref. 2)]. Geneticists refer to phenotypic conditions which seem to mimic genetically caused ones as 'phenocopies', thereby making clear their commitment to genetic primacy in explanation. I suggest the use of the term 'genocopy' to describe those conditions, such as schizophrenia and Alzheimer's, where disordered genes might be strongly implicated in a subset of those with the condition, thus mimicking a more general non-genetic set of causes.

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References

1 Alper, J. S. and Natowicz, M. R. (1993) *Trends Neurosci.* 16, 387–389
2 Mullan, M. and Crawford, F. (1993) *Trends Neurosci.* 16, 398–403

Histochemical localization of nitric oxide synthase in the CNS

In a recent article, which we enjoyed very much, Murphy *et al.*[1] reviewed the synthesis of nitric oxide (NO) in CNS glial cells. Among other results, they showed, using NADPH-diaphorase histochemistry, that nitric oxide synthase (NOS) is localized in cultured astrocytes and microglia. (Recently, it has been shown that NADPH-diaphorase is NOS and that this fully accounts for NADPH-diaphorase histochemistry[2].) However, in that article, and others on the same and related subjects[3], there has been a historical misconception, because it has never been mentioned that in the late 1950s and early 1960s histochemists had already described the NADPH-diaphorase activity not only in the brain (for example, in neurons, glial cells, cerebral blood vessels, meninges, ependyma, gliomas and other brain tumours) and in other organs (for example, in retina, heart, liver and intestines), but also in cultured rat astrocytes, oligodendrocytes, capsular satellite cells and Schwann cells[4]. Therefore the recent descriptions could be classified as a 'rediscovery'. Interestingly, the early histochemists observed NADPH-diaphorase activity in glial cell cultures that were not treated with bacterial endotoxin (lipopolysaccharide) or with combinations of cytokines while Murphy *et al.*[1] emphasized that NADPH-diaphorase activity was not apparent in untreated glial cell cultures. However, it is difficult to comment further on this difference because 'early' histochemists did not detail the intensity and incidence of NADPH-diaphorase activity in cultures and in tissues. The early histochemists described a weak staining reactivity in astrocytes in human, rat and rabbit brains[5] (see Fig. 1B), and a more intense staining reactivity in reactive and neoplastic astrocytes[5–8] and in reactive macrophages or microglia[6] or Schwann cells[9]. Murphy *et al.*[1] also stressed that the NO-producing capacity of oligodendrocytes is not yet known. Previously presented facts, and current results from our laboratory (Fig. 1A), show that oligodendrocytes and other glial cells can also express NADPH-diaphorase/NOS, and probably synthesize NO.

We suppose that one of the reasons that current investigators have failed to notice these results is that until recently the nature and function of the enzyme responsible for the NADPH-diaphorase activity remained a mystery[2]. Furthermore, the name of the enzyme has gone through several changes [for example, triphosphopyridine nucleotide (TPN)- or TPNH-cytochrome c reductase; TPNH- or NADPH-tetrazolium reductase; TPNH- or NADPH-dehydrogenase; NADPH:(acceptor) oxidoreductase; TPNH- or NADPH- or $NADPH_2$-diaphorase (E.C. 1.6.99.1.); endothelium-derived re-