metabolism and schizophrenia. In their effort to summarise a complicated field some detail was lost, which leads to the false impression that the original cytosolic phospholipase A_2 gene study (Hudson *et al*, 1996) was not replicated. A brief review of the literature supports cytosolic phospholipase A_2 as a candidate gene for schizophrenia.

Cytosolic phospholipase A_2, unlike many other phospholipase A_2 enzymes, possesses a number of properties which suggest an important role in cellular signal transduction in schizophrenia: migration to the membrane when activated by a variety of signals such as changes in intracellular calcium concentration; specificity as to the fatty acid at the second carbon of the phospholipid moiety that initiates production of prostaglandins and other lipid-based messengers; regulation by dopamine and glutamate (neurotransmitters implicated in schizophrenia).

Our original genetic study into cytosolic phospholipase A_2 in schizophrenia was in fact two separate analyses (Hudson *et al*, 1996). Initially, an association-type study compared 65 patients with schizophrenia with matched healthy controls and found an association between a marker near the cytosolic phospholipase A_2 gene and schizophrenia. Spurious results may arise with association-type studies and, therefore, we undertook a haplotype relative risk study of 44 families including a proband with schizophrenia, which resulted in the same positive association. A more recent study employing a second marker actually within the intron of the cytosolic phospholipase A_2 gene also found an association between cytosolic phospholipase A_2 and schizophrenia (Peet *et al*, 1998). Again, a haplotype relative risk study of 50 families replicated this finding (Wei *et al*, 1998). Other studies (Price *et al*, 1997) employing association strategies on smaller sample sizes have not replicated our findings.

The majority of genetic data and biochemical data to date suggest the cytosolic phospholipase A_2 gene on chromosome 1 plays a role in increased vulnerability to schizophrenia. The precise determination of the specific phospholipase A_2 enzyme(s) involved in schizophrenia may well prove critical in the development of lipid-based strategies for improved treatment of schizophrenia.

Hudson, C. J., Kennedy, J. L., Gotowiec, A., *et al* (1996) Genetic variant near cytosolic phospholipase A_2 associated with schizophrenia. *Schizophrenia Research*, **21**, 111–116.

Peet, M., Ramchand, C. N. & Lee, J. (1998) Association of the Ban I dimorphic site at the human cytosolic phospholipase A2 gene with schizophrenia. *Psychiatric Genetics*, **8**, 191–192.

Price, S., Fox, H., St Clair, *et al* (1997) Lack of association between schizophrenia and a polymorphism close to cytosolic phospholipase A2 gene. *Psychiatric Genetics*, **7**, 111–140.

Walker, N. P., Fox, H. C. & Whalley, L. J. (1999) Lipids and schizophrenia. *British Journal of Psychiatry*, **174**, 101–104.

Wei, J., Lee, K. H. & Hemmings, G. P. (1998) Is the cPLA2 gene associated with schizophrenia? *Molecular Psychiatry*, **3**, 480–481.

C. Hudson Department of Psychiatry, Stratford General Hospital, 90 John Street South, Stratford, Ontario, Canada N5A 2Y8

Hallucinatory assumptions

Sir: Feinberg & Guazelli (1999) constructed an elaborate theory of subcortical motor system dysfunction to explain schizophrenia. Whether or not it explains some symptoms, it certainly cannot explain schizophrenic auditory hallucinations for two fundamental reasons: non-verbal auditory hallucinations occur in many disparate non-psychotic states, and complex verbal auditory hallucinations occur in all psychoses.

Feinberg & Guazelli divided auditory hallucinations into four broad classes, despite conceding that there can be phenomenological overlap, and that such a classification was oversimplified. If Occam is right, as he usually is, then this scheme is overcomplicated. The literature on musical auditory hallucinations (Gordon, 1997) is quite clear that their basic phenomenology is similar, whether these occur in psychosis, delirium, ear disease, mysticism, intoxication, fever, etc. A simple common explanation was offered, namely inner-ear hyperirritability. However, one does not have to accept this explanation to realise that there must be some unitary mechanism for the production of auditory hallucinations, although of course their interpretation will vary enormously depending on psychiatric, religious or medical context. Anyone arguing that voices have nothing to do with music needs to show that these auditory hallucinations have different causes. If anyone knows of any diseases, risk makers or risk markers associated with verbal but not non-verbal auditory hallucinations (music, noises, tinnitus), please could they let me know, as I cannot find any. Feinberg & Guazelli cite Kraepelin's 1919 book which has detailed descriptions of all sorts of simple and complex auditory hallucinations in schizophrenia.

Verbal auditory hallucinations can become particularly complex in schizophrenia when associated with loss of insight or incorporated in delusional systems. Peralta & Cuesta (1999) convincingly showed that first-rank symptoms, particularly voices, are just as common in six other psychoses as in schizophrenia. Hence, Feinberg & Guazelli's theory, however plausible for schizophrenia, is a non-starter for explaining auditory hallucinations, since it cannot explain first-rank symptoms in non-schizophrenic psychoses. All other psychological theories specific to schizophrenia are equally suspect, especially linguistic ones which, in addition, make no attempt to explain non-verbal auditory hallucinations.

Feinberg, I. & Guazelli, M. (1999) Schizoprehnia – a disorder of the corollary discharge systems that integrate the motor systems of thought with the sensory systems of consciousness. *British Journal of Psychiatry*, **174**, 196–204.

Gordon, A. G. (1997) Do musical hallucinations always arise from the inner ear? *Medical Hypotheses*, **49**, 111–122.

Peralta, V. & Cuesta, M. J. (1999) Diagnostic significance of Schneider's first-rank symptoms in schizophrenia. Comparative study between schizophrenic and non-schizophrenic psychotic disorders. *British Journal of Psychiatry*, **174**, 243–248.

A. G. Gordon 32 Love Walk, London SE5 8AD

Amiodarone and psychiatric symptoms

Sir: The pharmacokinetics of the class III antiarrhythmic amiodarone make it unlikely that its withdrawal was the reason for the dramatic clinical improvement observed within one week in the patient described by Ambrose & Salib (1999).

Amiodarone, a highly lipophilic drug, is extensively distributed into tissues, with a half-life as long as 100 days. Its therapeutic effect can last in excess of one month after withdrawal of long-term oral therapy (Latini *et al*, 1984).

If amiodarone is implicated in triggering psychiatric symptoms, then I would propose that the benefits of stopping this agent might not be observed until many weeks or even months after withdrawal of therapy.

Ambrose, A. & Salib, E. (1999) Amiodarone-induced depression. *British Journal of Psychiatry*, **174**, 366–367.

https://doi.org/10.1192/bjp.175.2.191a Published online by Cambridge University Press