

and international networks of academic centres and in keeping them active, although the outcome of these endeavours has not always been worthwhile. A similar effort should be made in all those research fields which are consistently regarded as promising by academic centres at the national or international level. These networks could also be used for exchange programmes involving residents and researchers.

Finally, the specific skills needed to interact effectively with families, administrators, journalists and the legal system should become a formal component of postgraduate training and continuing medical education. Academic psychiatrists tend to be seen by such counterparts as a competent and reliable source of information, but their performance when they are asked to provide an expert opinion or advice is not

always brilliant, which contributes to the deterioration of the image of our profession. We should learn from our own mistakes and train ourselves and our young colleagues in the art of being convincing and effective partners and communicators.

## References

- Maj, M. (2007) Physical illness and access to medical services in people with schizophrenia. *International Journal of Mental Health* (in press).
- Martindale, B. (2005) The European psychiatrist and inter-organisational co-operation. *World Psychiatry*, 4, 61–63.
- Thornicroft, G. & Tansella, M. (2002) Balancing community-based and hospital-based mental healthcare. *World Psychiatry*, 1, 84–90.

### THEMATIC PAPERS – INTRODUCTION

# Ethno-psychopharmacology

David Skuse

Behavioural and Brain Sciences Unit, Institute of Child Health, London WC1 1EH, UK, email d.skuse@ich.ucl.ac.uk

**H**ow we judge in what way, with what potential side-effects, our patients respond to medications designed to help them recover from their psychiatric disorders is informed by experience, scientific knowledge and guesswork. The rapid movement of populations around the world, usually voluntary but sometimes driven by other motives or exigencies, means that many psychiatrists are increasingly frequently faced with providing treatment for individuals who come from cultures about which they know little. Determining the characteristics of the illness itself can prove challenging in such circumstances, as this can be influenced by cultural differences in, for example, the degree of somatisation of symptoms. In this issue, we link three papers, each of which provides a different viewpoint on the way in which the effectiveness of pharmacological treatment for psychiatric problems could be influenced by the ethnic background of the patient.

There are several factors that must be taken into consideration in making decisions about medication that depend on the ethnic origins of the patient. Perhaps the one that is attracting most attention at present concerns their genotype. We have known for decades that certain enzymes involved in drug metabolism vary in their efficiency, systematically by ethnic origin. Every medical student knows that a high proportion of people from the Far East cannot metabolise alcohol efficiently and that they have unpleasant side-effects from the consumption of alcohol – a reaction that greatly reduces the risk of alcoholism. In recent years we have discovered not only the genetic basis of the difference in enzymatic activity with respect to alcohol metabolism but also critical enzymatic systems that play a role in the metabolism of lipophilic drugs, which cannot be easily eliminated

from the body by means of excretion. They are usually biotransformed to more hydrophilic compounds, which are easily removed by the renal system.

Many drugs we use in psychiatric practice are metabolised by the cytochrome P450 (CYP) system. The CYP system consists of a number of different enzymes and the classification of these involves the following nomenclature: the CYP{number}{letter}{number}\*{number} groups. The first number refers to a group of compounds that have high (> 40%) protein sequence homology. There is then a letter which refers to subfamilies that have greater than 55% homology. The second number refers to members of subfamilies that are encoded by a particular gene. Finally, there is a number following the \* which represents specific alleles of that gene. The cytochrome P450 system differs in its genetic profile by ethnic group, and hence the efficiency of its component enzymes in terms of drug metabolism.

The P450 system is involved in the metabolism of many lipophilic drugs, but from the perspective of psychiatrists the most intensively studied have been the selective serotonin reuptake inhibitors (SSRIs), which serve both as substrates and as inhibitors of these enzymes. For example, both paroxetine and fluoxetine are potent inhibitors of CYP2D6 and therefore they have the potential to increase the plasma concentrations of antipsychotic medications metabolised by this enzyme. Polymorphisms of CYP2D6 can either greatly increase the rate of drug elimination or decrease drug metabolism, and the proportions of populations that fall into one or other of these categories varies considerably with ethnicity. Do we need to genotype our patients before prescribing medications, such as the SSRIs, that interact with this enzymatic system? Should we be purchasing the

Roche Amplichip CYP450, now approved for use in both the USA and the European Union? An editorial in the *BMJ* (17 April 2007) provides a critical review of the evidence and concludes that the relationship between P450 genotype and antidepressant action is tenuous: there are just so many other metabolic and other factors that also influence drug concentrations.

In our thematic section in this issue, Pedro Ruiz summarises the variable response of broadly defined ethnic groups to psychopharmacological agents. Although he

defines the role of the cytochrome P450 system as potentially relevant, we do not yet know exactly how important it is in relation to these well established differences. Edmond Pi and Weiguo Zhu discuss the relevance of genetic variants and their associated enzymes to the treatment of Far Eastern and Asian patients. Finally, Tarek Okasha emphasises the importance of other cultural influences which may interact with genetic vulnerability, such as support from families and the community, and the faith the patient places in the psychiatrist and in God.

## THEMATIC PAPERS – ETHNO-PSYCHOPHARMACOLOGY

# The role of ethnicity in psychopharmacology

**Pedro Ruiz MD**

President of the American Psychiatric Association; Professor and Vice Chair of the Department of Psychiatry and Behavioral Sciences at the University of Texas Medical School at Houston, 1300 Moursund Street, Houston, Texas 77030, USA, email [pedro.ruiz@uth.tmc.edu](mailto:pedro.ruiz@uth.tmc.edu)

The association between ethnicity and pharmacology has been reported in the medical literature for several decades. However, the relationship between ethnicity and psychopharmacology has become widely recognised only in the last two or three decades. The large-scale migration which started after the Second World War, at first to the USA and more recently to other higher-income countries, as a result of globalisation, has greatly contributed to the attention and focus given to these migrant groups. In this context, these migrant groups primarily comprise ethnic and racial minority groups. This article briefly reviews the relationship between ethnicity and psychopharmacological agents.

## The foundation

The foundation of the relationship between ethnicity and psychopharmacology is based on three major principles (Ruiz, 2005):

- *Pharmacogenetics*. This mechanism focuses on the genetic and environmental factors that influence the functions of enzymes in the organism. Some of these enzymes act on psychopharmacological agents. Some persons are poor metabolisers and others are extensive metabolisers.
- *Pharmacokinetics*. This mechanism addresses the fate and distribution of pharmacological agents in the organism. It consists of four basic processes: absorption, distribution, biotransformation and excretion.
- *Pharmacodynamics*. This mechanism pertains to the interaction between receptors and pharmacological agents. The substances that bind with these receptors can be exogenous or endogenous.

Besides these three biological principles, we must also take into consideration non-biological factors, which can

also influence the relationship between ethnicity and psychopharmacology (Pi & Gray, 1998). These factors are all related to culture and include: diet, placebo effect, prescription patterns, stress, compliance factors, consumption of herbs, climatic effects, and so on.

Additionally, we must acknowledge the role of the cytochrome P450 enzymatic system in this regard (Ruiz, 2002). These enzymes are under genetic control, but certain isozymes can be induced by specific substrates, such as phenobarbital, ethanol and steroids. They can also be inhibited by certain drugs which are potent competitive inhibitors of these enzymes, such as cimetidine and ketoconazole (Pi & Gray, 1998). The genetic polymorphism demonstrated by the CYP enzyme system leads to individuals being classified as extensive metabolisers or poor metabolisers. Table 1 shows which CYP subsystems primarily affect what types of psychopharmacological agent.

## Asian populations

Of the different ethnic groups, the Asian populations are among the most studied with respect to ethno-psychopharmacological differences (Pi & Gray, 1998). Studies have shown that Asian patients require lesser amounts of the following psychopharmacological agents than do the Caucasian population to achieve similar results: neuroleptics (haloperidol, clozapine), lithium and tricyclic antidepressants (clomipramine, desipramine).

Similarly, Asian populations have been shown to be more sensitive to psychopharmacological agents and, thus, to have more severe side-effects than Caucasian populations. This is another confirmation that Asian populations need lower dosages of psychopharmacological agents than the Caucasian population.