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Introduction

Isaac Schweitzer

It has often been claimed that modern psychopharmacology began with the discovery of chlorpromazine in 1952. Australian psychiatrists argue that the legitimate date is 1949 with the landmark publication by John Cade detailing a case series of ten manic patients who had responded dramatically to lithium salts. The veracity of this argument is supported by the fact that lithium remains the gold standard for bipolar disorder treatment whereas chlorpromazine use for schizophrenia is rapidly disappearing. The genius of John Cade has recently been further highlighted by conversations I have had with one of the editor's of this volume, Edmond Y. K. Chiu, who was my clinical supervisor during 1977. I was a young psychiatric registrar working in an academic unit in Melbourne, Australia. I have clear recollections of Chiu enlightening me that Asian patients were more vulnerable to experiencing side effects to lithium and tricyclic antidepressants and would often respond well to lower doses than the average Caucasian. Chiu, who was born in Hong Kong, informs me that he learned this from Cade. It was in 1968 when as a trainee psychiatrist he came to work with Cade in Melbourne. On his return to Hong Kong, his treatment of his Chinese patients benefited by improved compliance and response rates, having followed Cade's astute observations of the ethnic differences in drug handling of psychotropics.

Should we therefore credit the birth of the discipline of ethno-psychopharmacology to Cade? There is little doubt that since the introduction of modern-day psychotropic medications, there have been many astute clinicians from around the world who have made similar observations regarding ethnic differences in response and tolerability of psychiatric treatments. We must therefore ask, why if this issue has been recognized for such a long time, has there been relatively little research in this area. Few pharmaceutical companies have embarked on such investigations for their products. Most governmental regulatory requirements do not specify a need

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for such research prior to approving new medications for release. Have we remained ethnocentric in our perspectives – what is good for one is good for all? Does the answer lie in our sensitivity to the dictum that "all men are created equal" and in acknowledging ethnic differences in responses to medication we are somehow challenging this dictum?

The word "ethnicity" is closely aligned with "race" and when racial differences are discussed, associations with white supremacist movements and the like are made; this evokes strong emotional reactions in most of us. The linking of fields such as eugenics and Nazi Germany's extermination program has resulted in this area being largely discarded by the scientific community. These issues are a potential minefield and may have acted as significant barriers to embarking on this area of endeavour. But the fact the science has been abused to justify political persecution in the past should not be a barrier to exploring the field as new findings emerge.

As human beings we share many similarities, we are much more alike than are our differences; over 99% of our genes are the same in all human beings. At the same time we do vary, individually and according to our social groupings. When we live in groups, particularly over many generations, our genes come to be more closely aligned, more likely to share certain similarities and develop differences to other social groups. In addition, our lifestyle, diet and other customs are more closely related. It is such concepts of ethnicity that encompass the essence of ethno-psychopharmacology, as espoused by Keh-Ming Lin, the pioneer and leading proponent of the field and one of the editors of this volume.

Ethno-psychopharmacology is attempting to answer the questions of how culture and genetic differences of natural social groupings of the human race determine and influence response to psychotropic medications. The prefix "ethno" has been chosen as it encompasses both the genetic and cultural differences of social groupings, the concept of race becoming increasingly an obsolete one.

It is interesting to note that despite cultural differences the stigma associated with psychiatric disorder has been universally observed. One form this has taken is the trivialization and minimization of psychiatric conditions; they are frequently dismissed as being mild, unimportant and not serious enough to be worthy of treatment. Several worldwide studies have shown psychiatric disorders to be not only highly prevalent but also amongst the most disabling of illnesses, impacting severely on loss of productivity and reducing quality of life. The Global Burden of Disease Study commissioned by the World Health Organization (WHO) predicts that by 2020, depression will have become the second largest contributor of disease burden worldwide. However, we have made many wonderful psychopharmacological discoveries over the past 60 years. We are now beginning to address those critical issues of how best to make these life-saving discoveries available to all populations. If medicine is to be successful in this endeavour a very thorough understanding of

the influence of culture and genetic variation on societies throughout the world is required.

In this volume, the reader will have access to a practical guide to the current advances in ethno-psychopharmacology with a particular focus on the Asia-Pacific region. Genetic factors that control both pharmacokinetics and pharmacodynamics of psychotropic drugs are subject to marked variation between individuals and ethnic groups. These clinically significant issues are related to genetic polymorphisms in drug metabolism particularly affecting CYP2D6 and CYP2C19. For instance, about 15–30% of Asians are poor metabolizers of CYP2C19 compared to 3–6% of Caucasians and 2–4% of Africans. The deficient genotypes are prevalent in Asian populations. In the case of CYP2D6, about 5–10% of Caucasians are poor metabolizers in contrast to only 1–2% of Asians. However, up to 50% of Asians carry a mutant allele that is an intermediate functioning allele. This gives rise to a high incidence of intermediate metabolizers with reduced metabolic capacity. Pharmacodynamic factors are similarly found to have a significant role in drug response but these have been less studied. Candidate genes related to pharmacodynamic effects include those coding for receptors (dopamine, noradrenaline and serotonin receptors) and drug transporters (serotonin).

Response to pharmacotherapy is multifaceted and involves the interaction of genetic, environmental and cultural factors. Environmental factors play a clinically significant role in determining the pharmacokinetics of psychotropic medications but are often inadequately considered. A range of environmental factors, including dietary factors, herbal medication, concomitant medication and other substances, significantly modifies the expression of the genes influencing pharmacokinetics and pharmacodynamics. Dietary factors, herbal medication, chemicals and pollutants are exogenous agents that may alter the activity of drug metabolizing enzymes particularly CYP2D6, CYP1A2 and CYP3A4. Sociocultural considerations represent a diverse dimension affecting pharmacotherapeutic response. Cross-cultural issues can affect diagnosis, beliefs and expectations concerning treatment, compliance, and placebo effect and can impact upon drug response in ways that may be more potent than biological mechanisms. Furthermore, prescribing patterns of the clinician may often determine the type and the dosage of the medication during treatment initiation and maintenance, which may lead to differences in response.

This volume covers topics including cultural perspectives in psychiatric diagnosis and psychopharmacotherapy, differences in pharmacokinetics and pharmacodynamics of psychotropics, pharmacogenetics of ethnic populations, ethnic variations in psychotropic responses, complementary medicines in mental disorders, attitudes towards psychotropic medications, prescribing practices in Asia-Pacific countries, pharmaco-economic implications, integrating theory and practice, and

future research directions. The aim of this volume is to update the clinicians with important research findings that will influence their clinical practice, as well as providing researchers with a comprehensive overview of contemporary research directions and where the field is heading. This volume challenges clinicians, pharmacologists, geneticists and social anthropologists to continue their explorations in this field and to increase our understanding of the effects of ethnicity on psychopharmacological science and practice.

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Culture and psychopathology

Juan E. Mezzich, M. Angeles Ruiperez, and Helena Villa

Introduction

The traditional Western conceptualization of mental disorders as individual experiences that have little or nothing to do with social, cultural or ethnic components, together with the pre-eminence attained in the study of the human brain over the last decades of the twentieth century, have resulted in an increase in the number of biological or intrapsychic explanations put forward by contemporary psychopathology. In consequence, how sociocultural processes are involved in explaining and understanding psychopathological manifestations is not very clearly defined (Agbayani-Siewert, Takeuchi & Pangan, 1999; Fábrega, 1995).

Nevertheless, parallel to this, there has also been a growing and renewed interest in understanding the role played by culture in mental disorders in order to allow cultural aspects to be included in the conceptualization of psychopathologies, in the light of the results obtained by a large number of research studies (for a review, see López & Guarnaccia, 2005).

This interest in seeking to achieve the integration and interaction of biopsychosocial variables within the explanation of psychopathological behavior represented the beginning of a change of paradigm as regards the explanation of both normal and psychopathological human behavior (Mezzich, Lewis-Fernández & Ruipérez, 2003). This change in paradigm involves accepting the fact that psychic phenomena can be explained on a molecular and cellular level, involving tissues, organs, systems, the organism, the way information is processed, the physical surroundings or the sociocultural context (Cacioppo & Berntson, 1992, 2006; Mezzich *et al.*, 2003; Westen, 2004).

Failing to take the cultural perspective into account can therefore mean that normal variations in the behavior of persons belonging to one culture are seen

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as being pathological from another cultural perspective. This chapter attempts to provide empirical evidence concerning the weight that some of these cultural context-related variables have in the manifestation of mental disorders.

First, we are going to briefly review some of the terms used to refer to ethnic differences and to describe the processes that take place when two or more cultural groups come into contact with each other. Second, we will outline some studies that illustrate how cultural aspects can affect, for example, the prevalence of certain disorders, the different ways symptoms are manifested, how therapeutic aid is sought or the efficacy of different forms of treatment. Cultural aspects can determine the appearance of syndromes that are specific to each culture (culture-bound syndromes) or can affect the manifestation of the symptoms that make up the different mental disorders. We will then show how cultural variations have been incorporated into the different systems of classification. Last, we will also detail the current recommendations on including cultural aspects in the diagnoses of mental disorders.

Some concepts used in transcultural research

Before going on to analyze the importance of taking cultural factors into account in order to correctly identify symptoms and, therefore, to reach a correct diagnosis and apply a suitable treatment, we are going to briefly review some of the terms frequently used to talk about cultural factors, such as race or ethnicity, as well as acculturation. Despite their widespread use both by laypersons and in academic spheres, these terms have rarely been defined and on occasions are even used indistinctly (Adebimpe, 1994).

Culture

This is a term that is widely used with a number of different meanings, with no generally agreed definition having been formulated to date. For example, Allen (1992) made a distinction between seven different uses of the term "culture," i.e., generic, expressive, hierarchical, superorganic, holistic, pluralistic and hegemonic. The most pragmatic use of the term refers to culture as a set of guidelines or formulae that allow intercommunication with the surroundings (MacLachlan, 1997).

Race

This term was initially considered as referring to an unalterable biological category, based on distinguishing groups according to shared genetic characteristics. Yet, the evidence for basing racial categorization on biological grounds is weak and frequently conflictive (Williams, Yu & Jackson, 1997) and biology-based racial classifications (although often thought to be valid and scientific) tend to vary arbitrarily

depending on the social, political and economic climate, as well as on social and cultural prejudices.

Ethnicity

This term is used to refer to a group of persons who share a geographical area, nationality or cultural inheritance (Berreman, 1991), and hence it has been suggested that, as humans, we are not born as members of a particular ethnic group but instead it may be a characteristic that has to be learned. This being the case, socializing oneself within a particular ethnic group will include learning aspects such as language, lifestyles, prejudices, daily activities, values, and so forth (Berreman, 1991).

Human migratory movements, which have led to the mixing of cultures, are another aspect to be taken into account from a cultural perspective. Although these migratory movements have facilitated the progress of humanity, from the individual and group point of view they entail a psychological and social impact that has aroused a great deal of scientific interest. It is therefore important to analyze the processes that take place when various groups of humans come into contact with each other.

Unfortunately, the empirical research that has been conducted in this area has been affected by differences in the methodological rigor and the diversity of theoretical postures employed. Two broad approaches stand out among the different theoretical standpoints: (a) the earlier theories, which posited that being an immigrant always involved marginalization phenomena, and (b) the more modern theories, which conceived immigration experiences in more positive and adaptive terms.

The studies conducted from this latter perspective seek to explain the psychological and social phenomena that are produced during the process in which an individual or group belonging to one ethnic group (generally the minority) must become part of another culture (generally the majority). Psychopathology focuses its attention on analyzing the relation between the process of immigration and the manifestation of psychopathological behaviors. In order to understand such a process two clearly distinct elements must be borne in mind – those that refer to the individual and/or group responses that are produced during the process (acculturation and adaptation) and those that allude to the characteristics of the cultures that come into contact.

Acculturation

Findings from research into psychological acculturation have defined three levels, and claim that psychological changes can range from very easy to very complicated: *non-conflictive psychological acculturation* (when the demands in the process of acculturation are limited to learning new behavioral repertoires that are appropriate

for the new cultural context), *cultural shock* or *acculturative stress* (when the individuals do not find it easy to change their behavioral repertoires and/or acquire new ones, and experience a certain amount of emotional malaise) and *psychopathological disorders* (when the changes in the cultural context exceed the individuals' capacities to cope, either due to their magnitude, the speed with which they come about or other features in the process, which trigger severe psychological problems such as clinical depression and anxiety).

Adaptation

In the broad sense of the term, adaptation refers to the changes that take place in individuals or groups in response to the demands imposed by their surroundings. Recent literature has analyzed the distinction between psychological adaptation and sociocultural adaptation (Berry *et al.*, 2006; Sam *et al.*, 2006; Searle & Ward, 1990; Ward & Kennedy, 1999). Psychological adaptation, on the one hand, refers to the set of internal psychological responses, including a clear personal and cultural sense of identity, good mental health and personal satisfaction in the new cultural context. Sociocultural adaptation, on the other hand, refers to the set of external psychological responses that individuals give in their new cultural context, including skills they need so as to be able to cope with the problems that crop up in their daily activities, especially in the family, social and work areas.

Although empirical studies usually present and explain these two forms of adaptation using the same theoretical assumptions, there are reasons to believe that they are conceptually different. This distinction is made on the grounds that psychological adaptation can be analyzed better within a psychopathological approach whereas sociocultural adaptation would be better dealt with by the social skills theories (Ward, 1996).

Relation between the two cultures

As a result of immigration, many societies become culturally plural. Yet, in most cases the groups do not have the same power (as regards numbers, economy or politics). All plural societies need to address the issue of how the acculturation process takes place, at both the cultural group level and at that of their members.

In order to understand the relations that are established between the dominant group and the non-dominant group, Berry (1997) claims that it is necessary to consider two issues at the same time. First, to what extent is it important to maintain one's cultural identity and its characteristics? And, second, to what extent must immigrants integrate into other cultural groups, thus losing their own original culture?

In addressing these two questions, Berry (1997) considers that four acculturation strategies are generated from the point of view of the non-dominant group, and

these can be represented as the two poles of a continuum: *assimilation* (when the individuals do not want to maintain their cultural identity and seek daily interactions with the dominant culture), *separation* (when the individuals grant an excessively high value to their own culture and at the same time wish to avoid contact with the dominant culture), *integration* (when there is a desire to maintain the original culture and to develop interactions with the host culture) and *marginalization* (when there is little chance or interest to maintain their own culture and little desire to forge relationships with others). Berry's (1997) integration corresponds to the term *biculturality* used to refer to the situation in which individuals identify themselves simultaneously with two cultures that are in contact and are competent in both of them (Cameron & Lalonde, 1994; Szapocznil & Kurtines, 1993) and will only occur in societies that are explicitly multicultural.

At the present time there is no universally accepted research model and thus, in spite of the large number of studies carried out over the past 30 years, the lack of a single conceptual field that is common to all of them makes it difficult to compare their findings and in fact on many occasions the results from these studies even contradict one another.

Thus, some studies conducted to research into biculturalism and psychopathology show that an individual who lives between two cultures can undergo a number of different psychopathological alterations due to the continual need to adapt to each of them whenever the cultural demands require them to do so (Cheng, Lee & Benet-Martínez, 2006). Other studies, however, show that individuals who live in two cultures may experience greater benefits than if they were to live a monocultural lifestyle (Blackledge, 2003). Berry (2006), on the other hand, concludes that the key to enjoying psychological well-being lies in the ability to develop and maintain cultural competencies in both cultures.

In view of the different manifestations of psychopathological behaviors found in diverse groups that cannot be adequately accounted for by factors concerning race, ethnic group or the acculturation process, Agbayani-Siewert *et al.* (1999) put forward a model that allows direct examination of the impact of cultural factors on psychopathological manifestations, while continuing to include structural social factors.

In this line, Hofstede (1980) conducted a transcultural study in which five relevant psychological dimensions were identified empirically in all the cultures that were studied, i.e. power–distance (from small to large), collectivism–individualism, femininity–masculinity, uncertainty avoidance (from weak to strong) and time orientation (from short term to long term).

Thus, analyzing the individualism/collectivism construct as a cultural factor can help to explain why some ethnic groups apparently under-use mental health services and, in contrast, rely on members of the family to provide care in possible

cases of mental illness. Individualism emphasizes autonomy and priority is given to personal goals over those of the group. Collectivists, however, do not generally see personal or individual problems as being important enough to seek professional help because they tend to rely on collective ways of coping as a means of making life changes easier to deal with (Triandis, 1993). Taking the collectivist/individualist construct into account therefore goes beyond racial or ethnic categories, and so it is better able to explain the cultural structures that affect perceptions, expressions and responses to the psychopathology.

Influence of culture on the prevalence and expression of symptoms

Although some forms of psychopathological expression can be universal, cultural aspects can affect the manifestation of certain symptoms and, in consequence, the prevalence of a mental disorder (Alegria, Takeuchi, Canino *et al.*, 2004; Chang, 2002). Thus, at this point we are going to review briefly the studies that have attempted to explain the relation between cultural aspects and the expression of psychological malaise. In these studies it becomes clear that the lack of a single generally agreed theoretical model gives rise to dissimilar results because most of them use either ethnic or racial categories or categories related to acculturation processes (structural factors) to explain how culture shapes the perception and expression of the psychopathology, while offering little information about the role played by cultural factors (Agbayani-Siewert *et al.*, 1999).

One strategy that is commonly used to understand the impact of cultural factors on mental illnesses has been to describe the distribution of mental illnesses among different racial and ethnic categories. Because these early studies were carried out on the emigrant population in the USA in the late nineteenth and early twentieth century, a debate began as to whether the relation between particular ethnic groups and psychopathology was due to the stress caused by emigration itself, to a self-selection of persons who were susceptible to certain psychiatric disorders in emigrants or to factors that were specific to an ethnic group (Collazos *et al.*, 2005).

The consistency of the findings from this early research, as regards the higher prevalence of schizophrenia and lower rates of affective disorders among Afro-Americans, led to suggestions that there was little biological foundation for feelings of sadness and depression in Afro-Americans, in addition to a certain predisposition towards schizophrenia that could be attributed to race (Bevis, 1921). Yet, later reviews of these studies reveal the presence of errors in the methodologies used, such as the low degree of reliability of the diagnoses or failing to take into account other variables that could account for such differences (e.g. age, cultural level, socioeconomic level) (Bell & Mehta, 1980). In a similar way, the fact that