

# PSYCHOPHARMACOLOGY RESEARCH IN THE ENGLISH-SPEAKING CARIBBEAN

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## SUMMARY

Ethnic differences in patients' responses to drugs used to treat psychiatric disorders have been increasingly reported. Differences can be found in the English-speaking Caribbean population due to its multi-ethnic composition. With the goal of identifying studies on psychopharmacology and ethnicity, we searched for all abstracts and full papers on clinical psychopharmacology emerging from research in the English-speaking Caribbean published in the West Indies Medical Journal, the Caribbean Medical Journal and Medline. We found no studies focusing on this topic, although there were some which may indirectly imply the existence of such differences. High blood levels of imipramine have been found in Barbadian patients, and the majority of cases of neuroleptic malignant syndrome have been reported in Africans, as well as high levels of CPK. However, the numbers of patients studied have not been large enough to be representative. A significantly higher incidence of alcoholism has also been reported in males of East Indian origin. We concluded there is an urgent need in the region for undertaking this type of research to ensure a more favorable treatment outcome of patients treated with such drugs.

## KEY WORDS

psychopharmacology, ethnicity, English-speaking Caribbean

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## INTRODUCTION

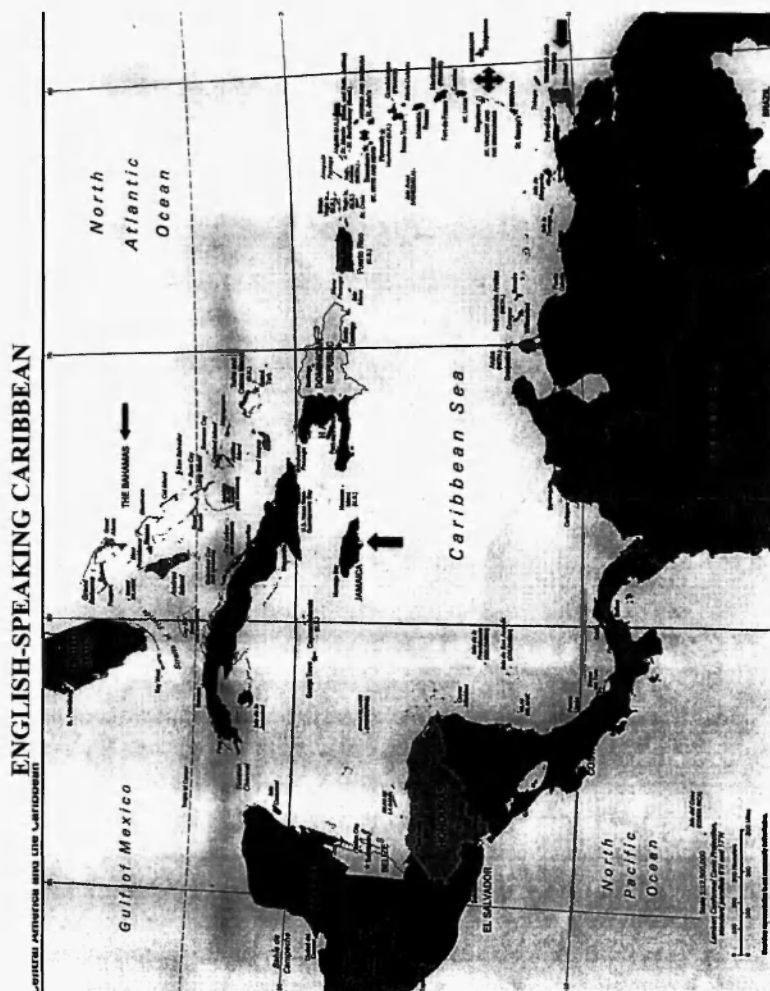
Rapid advances in the field of psychopharmacology have been observed, particularly in the development of studies in humans designed to understand the pharmacokinetics and pharmacodynamics of psychotropic drugs /1/. However, most research in this field has been conducted on Western populations, and the results derived from such research have been accepted and passively transferred by clinicians in other parts of the world /2/. The population of the English-speaking Caribbean (see map) is multi-ethnic with 6 million people composed of approximately 75% of African origin, 20% of East Indian descent and the remaining 5% shared between Europeans, Chinese and Amerindians. There are ethnic population variations within the islands. Jamaica's population is primarily black while that of Trinidad and Tobago and Guyana is approximately equally distributed between Africans and East Indians. Guyana has the largest representation of Amerindians, and Barbados, with a predominantly black population, has the largest proportion of Europeans /3/.

Psychiatrists of this region are routinely seeing a large number of patients of different cultural and ethnic backgrounds. Consequently, research is needed to collate information on ethnic differences in pharmacological response in order to select the proper drug and dosage regime, to predict the possible drug-drug interactions, and, hence, to ensure a more favorable outcome. This is especially relevant for studies on drug metabolism since the efficacy of psychotropic drugs depends in part on the metabolic activity of drug metabolizing enzymes which are genetically determined and depend on ethnic origin.

It was our goal to identify and review studies on psychopharmacology and ethnicity in the English-speaking Caribbean as well as to suggest future directions of psychopharmacology research in the region.

## METHODS

We searched for all abstracts and full papers on clinical psychopharmacology research emerging from research done in the English-speaking Caribbean. Information was obtained from the West Indian Medical Journal, the Caribbean Medical Journal and Medline. All studies on basic psychopharmacology were excluded.



## RESULTS

### 1. Research on clinical psychopharmacology

#### *Studies on drug effects*

Only two studies on drug effects have been published, from Barbados /4,5/. Mahy /4/ reported a pilot study in which the clinical efficacy and blood levels of clomipramine in 11 Barbadians suffering from depression were investigated. In this study, plasma levels of clomipramine were found very high even though patients might have been taking smaller dosages than prescribed. Only six patients completed the study: five whites and one non-white. Three of the five non-completers were black. The reason for withdrawal was the development of side-effects. However, due to the small number of patients, the author did not draw any conclusions about ethnic influences. In the second study /5/, Mahy reported the efficacy of fluphenazine enantate in schizophrenic patients. 85% of the patients included in the study were maintained satisfactorily with a monthly dosage of 25-50 mg, which resulted in a dramatic reduction in the number of days of hospitalization needed in a three-year period.

Although no publications were found on this topic in Trinidad, important trends have been observed. East Indian and Afro-Trinidadians seem to need lower dosages of antidepressants and antipsychotics than British patients. Seldom do psychiatrists in Trinidad attain or maintain a 'usual' therapeutic dosage for effect. The response to antidepressant and antipsychotic drugs is less than six weeks and ECT is seldom indicated.

#### *Studies on adverse effects*

Concerning adverse effects, only one study on tardive dyskinesia (TD) has been reported /6/. In this study Neehall examined 222 psychiatric outpatients on depot fluphenazine decanoate for more than six months. The prevalence rates ranged from 7% for patients with severe TD to 45% for patients with any degree of TD. No sex differences were identified, but the female patients were older than the male patients. Increases in prevalence rates were associated with the combination of an anticholinergic anti-parkinsonian drug and with the

concomitant use of an oral neuroleptic. No attempt was made to identify ethnic differences.

There were three studies which addressed the neuroleptic malignant syndrome (NMS). Beaubrun *et al.* /7/ reported the first case of NMS in a West Indian patient of mixed African descent. Maharajh /8/ studied the effect of high loading and rapid loading dosages of phenothiazines with multiple receptor blockade in the causation of this illness. Mansoor *et al.* /9/ reported the first series (5 cases) of NMS. All patients were of African origin. However, there was no discussion on the possible role of ethnicity. However, interestingly, it has been reported that Africans have a higher level of creatinine phosphokinase than other ethnic groups /10/.

A case of neurotoxicity in a 59 year-old male treated with lithium was reported in 1984 by Mahy /11/. Even though there was very close monitoring of blood lithium levels, the patient developed this side-effect which led to death. The author also reported that fine tremor, lethargy and increased fluid intake were the only side-effects found in 24 in-patients on lithium therapy. In the Caribbean islands, especially in those less developed, there is a severe shortage of trained personnel in the field of psychiatry, and there are even islands with no mental hospitals. In this context, clinical follow-up of patients on lithium therapy is the main source of detection of side-effects.

## 2. Research on substance abuse

### *Alcoholism*

A great deal of research has been devoted to the study of alcoholism by psychiatrists in the region. The themes have included definitions /12/, patterns /13-15/, predisposing factors /16/, identification /17,18/, complications /19-21/, and modalities of treatment and their outcome /22-25/. Nevertheless, only three papers have highlighted the possible role of ethnic differences in incidence rates of alcoholism; these studies were carried out in Trinidad and Tobago /22,26,27/. A high incidence of alcoholism has been found among East Indians. Several hypotheses have been proposed, including genetic polymorphism of the enzymes that metabolize alcohol and of dopamine D<sub>2</sub> receptors, as well as differences in attitudes, values and perceptual constructs as a result of different culturally based experiences /27/. However, this needs further research.

***Drug use and abuse***

Marihuana and cocaine are the two major illicit drugs of abuse in the Caribbean. Some islands have been used for the transshipment of drugs from South to North America, contributing to the availability of these drugs in this region. Tourism is another source of entry of these drugs. Therefore, research based on drug use and abuse has been widely developed.

Because of the high prevalence of marihuana smoking in Jamaica, emphasis has been given to the study of this drug in this country. The drug was first introduced into Jamaica by East Indians. Nevertheless, the heaviest users are Afro-Caribbeans /28/. Similar trends have been observed in Trinidad and Tobago and Guyana.

The role of cannabis in psychiatric disturbance has been reported by several authors /29-31/. The results support the idea of cannabis as a cause of illness or a contributing factor for the modification of existing psychiatric illness. No significant differences were found in developmental outcome between children of marihuana-using and non-using mothers /32/. An increased risk for sexually transmitted diseases among men who smoked marihuana before sex was encountered although it was not possible to determine a cause-effect association /33/. A few review papers on the effects on cannabis on mental and physiological functions were published between 1986 and 1992 /34,35/.

Cocaine use showed a sharp rise in Trinidad and Tobago between the years 1978 and 1985, as evidenced from police records and drug-related hospital admissions /36/. The situation is still prevalent as observed in more recent reports /37-43/.

**DISCUSSION**

There are few but increasing reports suggesting that there are ethnic differences in psychopharmacological response /44-49/. African-Americans are said to achieve better and faster clinical response than Caucasians when treated with tricyclic antidepressants (TCAs) and antipsychotic drugs /50-55/. They have also shown higher average plasma concentrations than depressed Caucasian patients treated with TCAs /56,57/. African-Americans seem to be at greater risk of developing tardive dyskinesia after antipsychotic treatment /58/

and have a higher RBC/plasma ratio of lithium, which may be associated with a greater incidence of side-effects /49/. Evidence suggests there are differences between Asian and non-Asian populations in TCA dosage requirements, in plasma and drug concentrations corresponding to therapeutic and toxic effects, and in the incidence and severity of adverse drug reactions /41,59-62/.

Concerning neuroleptic drugs, several reports have suggested that Asian populations required lower dosages compared to Caucasians /63-65/. Significantly higher plasma levels of haloperidol /66,67/ but a lower ratio of reduced haloperidol to haloperidol has been found in Asian patients than in Caucasians /68/. Korean and Korean-Americans are likely to achieve similar or better response than Caucasians at lower serum levels of clozapine /69/ and schizophrenic patients from Taiwan attain higher serum concentrations of this drug than German patients treated with comparable doses /70/. Asians also appear to be more likely to experience extrapyramidal reactions /61/. Dosages of lithium requirement have been reported to be lower in Japanese patients /71,72/ and the serum levels of lithium appear to be higher in Taiwanese patients than in Japanese, but lower than in American patients /72/. Similar findings have been reported for benzodiazepines /73,74/.

In addition, there is some information in the literature with reference to Hispanic populations. Marcos and Cranco /75/ reported that Hispanics tend to respond to lower dosages of TCAs than Caucasians and that they also develop a greater number of side-effects. In a review by Ramirez /76/, it was suggested that patients from Latin America need less medication than Anglo patients for the treatment of psychiatric disorders.

In a pilot study conducted on clomipramine metabolism in the British population, Allen *et al.* /77/ found significantly high plasma levels of clomipramine among Indian Asians compared to Caucasians. An increased rate of side effects in Indian patients was also found, although it did not reach statistical significance because of the small size of the sample. A higher risk of developing agranulocytosis was reported by Lieberman and Junis in Ashkenazi Jews with schizophrenia /78/.

Recent advances in the field of pharmacogenetics are clearing the way for a better understanding of the biological mechanisms behind the differences in psychopharmacological response in different ethnic

groups. Special attention has been given to genetic factors involved in the metabolism of many psychotropic agents /79/. A central role has been given to psychotropic drug metabolism mediated by the cytochrome P450 microsomal enzyme system. Ethnic differences in drug metabolizing ability have been reported /80/. However, differences in the kinetics of a particular drug among various racial groups may not be due only or at all to genetic differences. Kinetic factors can be also be influenced by socio-cultural or other environmental factors, such as diet, climate, social differences in clinical practice and use of alternative therapies.

We did not find any study in the Caribbean focusing on the possible role of ethnicity in the differences and similarities in the efficacy of treatment methods and/or incidence of adverse effects in patients treated with psychotropic drugs, although the population is composed of different ethnic and cultural groups. However, a few studies have indicated indirectly that these differences may in fact exist. As mentioned above, high plasma levels of clomipramine were reported in a pilot study of Barbadian patients when it was believed that these patients were taking lower doses than those indicated, which were already lower than the usual dose. Although due to the small sample size no conclusion on ethnicity was drawn, it is noticeable that the majority of patients who withdrew from the study were of African origin /4/. Additionally, all patients reported with NMS were also of African origin /7-9/ and high levels of CPK have also been found in this population /10/. Similarly, significantly higher incidence rates of alcoholism and substance abuse have been reported in males of East Indian origin /28/.

The multi-ethnic composition of the English-speaking Caribbean population may suggest that we can indeed expect differences in patients' responses to drugs used to treat psychiatric disorders. There are established ethnic trends in some diseases. Reports have noted an increase of hypertension in Africans, prostate cancer in Africans and myocardial infarction in East Indians. These trends are important since they may suggest that socio-cultural factors of diet, lifestyle, behavior and/or hereditary factors may influence the presentation and consequently the management of diseases in these populations. It is therefore our belief that there is an urgent need in the English-speaking Caribbean to undertake research which considers ethnic factors in the treatment of patients with mental disorders.



## REFERENCES

1. Turner SM, Cooley-Quille R. Sociological and sociocultural variables in psychopharmacological research: Methodological considerations. *Psychopharmacol Bull* 1996; 32: 183-192.
2. Lin K-M, Poland RE, Wan W, et al. The evolving science of pharmacogenetics: Clinical and ethnic perspectives. *Psychopharmacol Bull* 1996; 32: 205-217.
3. CSO Population. Republic of Trinidad and Tobago: Central Statistical Office, 1990.
4. Mahy GE. The effects of clomipramine on depression in Barbadian patients. *West Indian Med J* 1978; 27: 75-80.
5. Mahy GE. Fluphenazine enanthate in a community psychiatric programme. *West Indian Med J* 1975; 24: 61-64.
6. Neehall J. Tardive dyskinesia in outpatients on depot phenothiazine. *West Indian Med J* 1989; 38: 228-233.
7. Beaubrun MH, Patrick AL. The neuroleptic malignant syndrome (N.M.S.) in a West Indian of African descent. *West Indian Med J* 1987; 36: 48-50.
8. Maharajh HD. The effect of high rapid loading and reloading doses in provoking neuroleptic malignant syndrome. *West Indian Med. J* 1988; 37 (Suppl): 44.
9. Mansoor GA, Corbin DO, Edwards CN, et al. Neuroleptic malignant syndrome among acute psychiatric admissions in Barbados. *West Indian Med J* 1992; 41: 15-18.
10. Maharajh HD. CPK levels and neuroleptic malignant syndrome. *Br J Psychiatry* 1989; 154: 885-886.
11. Mahy GE. Neurological sequelae of lithium therapy. *West Indian Med J* 1984; 33: 272-274.
12. Beaubrun MH Alcohol and alcoholism. *Caribbean Med J* 1957; 19: 137-142.
13. Patrick AL, Beaubrun MH, Patrick-Boyd HA. Alcohol consumption patterns in two Caribbean islands: The CAGE questionnaire as a predictor of mortality. *West Indian Med J* 1996; 45 (Suppl 2): 34.
14. Soyibo K, Lee MG. Use of alcohol, tobacco and non-prescription drugs among Jamaican high school students. *West Indian Med J* 1997; 46: 111-114.
15. Grol ME, Halabi YT, Gerstenbluth I, et al. Lifestyle in Curacao. Smoking, alcohol consumption, eating habits and exercise. *West Indian Med J* 1997; 46: 8-14.
16. Beaubrun MH. Factors affecting the incidence and treatment of alcoholism in the Caribbean. *Caribbean Med J* 1975; 36: 40-41.
17. Mansoor GA, Edwards CN. Questionnaire detection of problem drinkers among acute medical admissions. *West Indian Med J* 1991; 40: 65-68.
18. Beaubrun M. The nature of alcohol dependence and its recognition. *Med Digest* 1982; 8: 5-13.
19. Patrick AL, Beaubrun MH, Patrick-Boyd HA. Cardiovascular risk factors and alcohol consumption study of Tobago. *Caribbean Med J* 1996; 41: 4.

20. Beaubrun MH, Thomas C, McFarlane H, et al. Blood alcohol concentrations of motor vehicle accident victims at the Port of Spain general hospital casualty department: A preliminary report. *West Indian Med J* 1986; 35 (Suppl): 55.
21. Francis M, Eldemire D, Clifford R. A pilot study of alcohol and drug-related traffic accidents and death in two Jamaican parishes, 1991. *West Indian Med J* 1995; 44: 99-101.
22. Beaubrun MH. Treatment of alcoholism in Trinidad and Tobago, 1956-65. *Br J Psychiatry* 1967; 113: 643-658.
23. Hosein IN, De Freitas R, Beaubrun MH. Intramuscular/oral lorazepam in acute alcohol withdrawal and incipient delirium tremens. *West Indian Med J* 1979; 28: 45-48.
24. Maharajh HD. Family therapy of alcoholism outcome and evaluation. *West Indian Med J* 1986; 37 (Suppl): 19.
25. Maharajh HD, Bhugra D. Brief family therapy with alcohol-dependent men in Trinidad and Tobago. *Acta Psychiatr Scand* 1993; 87: 422-426.
26. Parasram R. Ethnic differences in reported rates of alcoholism in Trinidad and Tobago. Presented at International Congress on Alcoholism and Drug Dependence, Alberta, August, 1995.
27. Montane LK, Maharajh H. Ethnic differences in the incidence rates of mental disorders in county Caroni, Trinidad. *West Indian Med J* 1998; 48 (Suppl 2): 50.
28. Wray SR, Murthy NV. Review of the effects of cannabis on mental and physiological functions. Justification for an intensive and comprehensive programme for the health of the Caribbean people. *West Indian Med J* 1987; 36: 197-201.
29. Spencer DJ. Cannabis induced psychosis. *West Indian Med J* 1970; 19: 228-230.
30. Beaubrun MH. Psychiatric assessment of 30 chronic users of cannabis and 30 matched controls. *Am J Psychiatry* 1973; 130: 309-311.
31. Knight F. Role of cannabis in psychiatric disturbance. *West Indian Med J* 1991; 40: 120-123.
32. Hayes JS, Lampart R, Dreher MC, et al. Five-year follow-up of rural Jamaican children whose mothers used marijuana during pregnancy. *West Indian Med J* 1991; 40: 120-123.
33. Simeon DT, Bain BC, Wyatt GE, et al. Characteristics of Jamaicans who smoke marijuana before sex and their risk status for sexually transmitted diseases. *West Indian Med J* 1996; 45: 9-13.
34. Wray SR. Drug abuse and mental health. *West Indian Med J* 1986; 35: 1-3.
35. Wray SR, Young LE. Consequences of substance abuse. Future generations at risk. *West Indian Med J* 1992; 41: 47-48.
36. Beaubrun MH. Cocaine update. *Caribbean Med J* 1986; 47: 12-17.
37. Maharajh HD, Dutta A, Gopeesingh SR. Cocaine addiction in Trinidad and Tobago. *West Indian Med J* 1987; 36 (Suppl): 13.
38. Maharajh HD. Therapeutic addictions: The abuse of prescription drugs and other pharmaceuticals in Trinidad and Tobago. *Caribbean Med J* 1989; 50: 27-30.

39. Lewis PD, Hospedales CJ. HIV study of cocaine dependent persons. *West Indian Med J* 1991; 40 (Suppl 1): 25.
40. Singh HN, Maharajh HD, Shipp M. Patterns of substance abuse among secondary school children in Trinidad and Tobago. *Br J Public Health* 1991; 105: 435-441.
41. Hutchinson G, Greenidge C, Lewis P. Sociodemographic features of cocaine dependence. *West Indian Med J* 1992; 46 (Suppl): 67.
42. Maharajh HD. Cocaine and social transformation in Trinidad and Tobago. *Psychiatr Bull* 1997; 21: 184-185.
43. Daisley H, Jones-Le Cointe A, Hutchinson G, et al. Fatal cardiac toxicity temporally related to poly-drug abuse. *Vet Hum Toxicol* 1998; 40: 21-22.
44. Bond WS. Ethnicity and psychotropic drugs *Clin Pharmacol* 1990; 10: 467-470.
45. Lin K-M, Poland RE, Smith MW, et al. Pharmacokinetics and other related factors affecting psychotropic response in Asians. *Psychopharmacol Bull* 1991; 27: 427-439.
46. Mendoza R, Smith W, Poland RE, et al. Ethnic psychopharmacology: The Hispanic and native American perspective. *Psychopharmacol Bull* 1991; 27: 449-461.
47. Pi EH, Wang AL, Gray GE. Asian/non-Asian transcultural tricyclic antidepressant psychopharmacology: a review. *Prog Neuro-psychopharmacol Biol Psychiat* 1993; 17: 691-702.
48. Strickland TL, Ranganath V, Lin K-M, et al. Psychopharmacologic considerations in the treatment of black American populations. *Psychopharmacol Bull* 1991; 4: 441-448.
49. Strickland TL, Lin K-M, Fu P, et al. Comparison of lithium ratio between African-American and Caucasian bipolar patients. *Biol Psychiatry* 1995; 37: 325-330.
50. Overall JE, Hollister LE, Kimbell I, et al. Extrinsic factors influencing response to psychotherapeutic drugs. *Arch Gen Psychiat* 1969; 21: 89-94.
51. Henry BW, Overall JE, Markette JR, et al. Comparison of major drug therapies for alleviation of anxiety and depression. *Dis Nerv Syst* 1971; 32: 655-677.
52. Raskin A, Crook TH. Antidepressants in black and white patients. *Arch Gen Psychiat* 1975; 32: 643-649.
53. Lawson WE. Racial and ethnic factors in psychiatric research. *Hosp Community Psychiat* 1986; 37: 50-54.
54. Silver B, Poland RE, Lin K-M. Ethnicity and the pharmacology of tricyclic antidepressants. In: Lin K-M, Poland RE, Nakasaki G, eds. *Psychopharmacology and Psychobiology of Ethnicity*. Washington, DC: American Psychiatric Association, 1993; 61-89.
55. Strickland TL, Lawson W, Lin K-M, et al. Interethnic variation in response to lithium therapy among African-American and Asian-American populations. In: Lin K-M, Poland RE, Nakasaki G, eds. *Psychopharmacology and Psychobiology of Ethnicity*. Washington, DC: American Psychiatric Association, 1993; 61-89.

56. Ziegler VE, Biggs JT. Tricyclic plasma levels - effect of age, race, sex and smoking. *JAMA* 1977; 238: 2167-2169.
57. Rudorfer MV, Robins E. Amitriptyline overdose: Clinical effects on tricyclic antidepressant plasma levels. *J Clin Psychiat* 1982; 43: 457-460.
58. Glazer WM, Morgesnstern H, Doucette J. Race and tardive dyskinesia among outpatients at a CMHC. *Hosp Community Psychiat* 1994; 5: 38-42.
59. Yamashita I, Asano Y. Tricyclic antidepressants: therapeutic plasma levels in Chinese bipolar patients. *Psychopharmacol Bull* 1979; 15: 40-41.
60. Kleinman A. Culture and patient care: psychiatry among the Chinese. *Drug Ther* 1981; 11: 134-140.
61. Kinzie JD, Leung P, Boehnlein JK, et al. Antidepressant blood levels in Southeast Asians - clinical and cultural implications. *J Nerv Ment Dis* 1987; 175: 480-485.
62. Rosenblatt R, Tang SW. Do Oriental psychiatric patients receive different dosages of psychotropic medication when compared with Occidentals? *Can J Psychiat* 1987; 32: 270-274.
63. Lin K-M, Finder E. Ethnicity and psychopharmacology. Bridging the gap. *Psychiatr Clin N Am* 1983; 18: 635-647.
64. Lin K-M, Poland RE, Nuccio I, et al. A longitudinal assessment of haloperidol dosage and serum concentrations in Asian and Caucasian schizophrenic patients. *Am J Psychiat* 1989; 146: 1307-1311.
65. Lin K-M, Poland RE. Ethnicity, culture and psychopharmacology. In: Bloom FE, Kupfer DJ, eds. *Psychopharmacology: The Fourth Generation of Progress*. New York: Raven Press Ltd., 1995; 1907-1917.
66. Potkin SG, Shen T, Pardes H, et al. Haloperidol concentrations elevated in Chinese patients. *Psychiat Res* 1984; 12: 167-172.
67. Lin K-M, Poland RE, Lau JK, et al. Haloperidol and prolactin concentrations in Asians and Caucasians. *J Clin Psychopharmacol* 1988; 8: 195-201.
68. Jann MW, Chang WH, Davis CM, et al. Haloperidol and reduced haloperidol plasma levels in Chinese vs. non-Chinese psychiatric patients. *Psychiat Res* 1989; 30: 45-52.
69. Matsuda KT, Cho MC, Lin K-M, et al. Clozapine dosage, serum levels, efficacy, and side-effect profiles: a comparison of Korean-American and Caucasian patients. *Psychopharmacol Bull* 1996; 32: 253-257.
70. Lin K-M, Poland RE, Nagasaki G. *Psychopharmacology and Psychobiology of Ethnicity*. Washington, DC: American Psychiatry Press, 1993.
71. Takahashi R. Lithium treatment in affective disorders: therapeutic plasma level. *Psychopharmacol Bull* 1979; 15: 32-35.
72. Yang W. Prophylactic efficacy of lithium and its effective plasma levels in Chinese bipolar patients. *Acta Psychiatr Scand* 1985; 71: 171-175.
73. Kumana CR, Lauder IJ, Chan M. et al. Differences in diazepam pharmacokinetics in Chinese and white Caucasians - Relation to body lipid stores. *Eur J Clin. Pharmacol* 1987; 32: 211-215.
74. Zhang Y, Reviriego J, Lou Y, et al. Diazepam metabolism in native Chinese poor and extensive hydroxylators of S-mephenytoin; interethnic differences in comparison with white subjects. *Pharmacol Ther* 1990; 48: 496-502.

75. Marcos LR, Cranco R. Pharmacotherapy of Hispanic depressed patients: clinical observations. *Am J Psychother* 1982; 36: 505-512.
76. Ramirez LF. Ethnicity and psychopharmacology in Latin America. *Mt Sinai J Med* 1996; 63: 330-331.
77. Alien JJ, Rack PH, Vaddaki KS. Differences in the effects of clomipramine on English and Asian volunteers: Preliminary report on a pilot study. *Postgrad Med J* 1977; 53 (Suppl 4): 79-86.
78. Lieberman JA, Yunis J. HLA-B38, DR4, DQw3 and clozapine induced agranulocytosis in Jewish patients with schizophrenia. *Arch Gen Psychiat* 1990; 47: 945-948.
79. Smith MW, Mendoza RP. Ethnicity and pharmacogenetics. *Mt Sinai J Med* 1996; 63: 285-290.
80. Kalow W. Interethnic variations of drug metabolism. *Trends Pharmacol Sci* 1991; 12: 102-107.

