drug-taking behavior on the part of clients should help promote maintenance of treatment effects. A combined approach using pharmacological agents (aimed at initiating a change in drinking or drug use) in conjunction with relapse prevention counselling procedures (aimed at fostering internal attribution and maintenance of change) should improve long-term outcome results. A controlled clinical trial was conducted at the Addiction Research Foundation in which 56 alcoholic clients receiving the short-acting alcohol-sensitizing drug, citrated calcium carbimide (Temposil), were randomly assigned to a) a Physician Advice condition in which subjects took the drug within a context designed to reinforce the medical management of their drinking problem; and b) a Relapse Prevention condition in which subjects were instructed to pair use of the drug with planned entry into high-risk drinking situations and to gradually reduce reliance on the drug by developing alternative coping behaviors. As predicted, subjects receiving carbimide in conjunction with relapse prevention counselling showed significant growth in internal attribution for change; whereas those receiving carbimide under more traditional medical management showed no movement toward internality. On measures of alcohol consumption at 6, 12, and 18 months follow-up, there was a trend toward superior maintenance of treatment gains at 18 months posttreatment for subjects who had received relapse prevention counselling. The findings are interpreted as consistent with a cognitive social-learning analysis of the maintenance of behavior change.

DISULFIRAM TREATMENT OF ALCOHOLISM: PAST, PRESENT AND FUTURE. Richard K. Fuller. National Institute on Alcohol Abuse and Alcoholism, Rockville, MD.

Disulfiram (Antabuse®) was introduced in the United States in 1948. Yet its efficacy was controversial due in large part to the methodological problems in the design of clinical trials to evaluate it. These problems included lack of control groups, assignment that was not random in the few studies with comparative groups, lack of blinding, the use of therapists to assess the response to treatment, reliance exclusively on client's self-report, high attrition, only rare attempts to measure compliance with the medication regimen, high attrition, and lack of statistical analysis. This has changed during the past decade, and methodologically sophisticated clinical trials have been done. The results of a multisite Veterans Administration (VA) Cooperative Study of 605 male alcoholics will be presented. These results indicate that disulfiram in conjunction with standard treatment does not achieve more continuous abstinence than standard treatment without disulfiram. However, assignment to disulfiram and counseling resulted in significantly fewer drinking days than counseling without disulfiram in almost half of the men who were not abstinent. Other results from that VA study will be presented: a) The importance of having other sources of information (collateral reports, laboratory tests) in addition to the client's self-report will be demonstrated, and b) the relationship between abstinence and compliance with the medication regimen will be shown. Poor compliance with the medication regimen is the Achilles' heel to disulfiram treatment. Additional studies will be presented which indicate that the supervised administration of disulfiram is beneficial, and this may be an appropriate treatment strategy in the future.

SYMPOSIUM (ETHNIC MINORITY MINICONVENTION)
Interethnic Psychopharmacology: Current Pharmacogenetic, Pharmacokinetic, and Diagnostic Considerations.
Chair: *Tony L. Strickland*, Drew University of Medicine, Madison, NJ.

Discussant: *Matthew V. Rudorfer*, National Institute of Mental Health, Bethesda, MD.

TRICYLIC ANTIDEPRESSANTS AND RBC/PLASMA LITHIUM DIFFERENCES IN BLACK AMERICANS. Tony L. Strickland. Drew University of Medicine, Madison, NJ.

Recent advances in psychopharmacology have facilitated some interesting and provocative interethnic comparisons of pharmacogenetic, pharmacokinetic, and pharmacodynamic differences. Though the majority of existing interethnic psychopharmacology studies include comparisons of Asian and Caucasian patient groups, significant research on blacks is beginning to emerge. Tricyclic antidepressants (TCAs) in blacks appear mediated by significant pharmacogenetic and pharmacokinetic influences, and result in higher plasma TCA levels, faster therapeutic response, though with more toxic side effects compared to whites. Additionally, problems with appropriate diagnosis of mood disturbance in this population continues to be a major issue relative to accurate assessment of the efficacy of TCAs in blacks.

One area where well-controlled studies of pharmacokinetic differences have been fairly consistently demonstrated is with lithium. This literature suggests that blacks have less efficient cell membrane lithium–sodium countertransport ability, and higher RBC/plasma lithium ratios. Differences in the cellular lithium efflux rate in blacks are highly suggestive, though needing to be confirmed by more extensive study.

In general, the psychopharmacology literature on blacks reveals important differential trends along a number of important pharmacogenetic, pharmacokinetic, and pharmacodynamic parameters. Much work remains to clearly delineate these important interethnic differences. Future psychopharmacology studies should control for patient nutritional status, diet, alcohol and other substance abuse. Also, due to historical problems with accurate diagnosis of mood disturbance in blacks, efforts to improve assessment in this area should be undertaken. Finally, we noted few studies of benzodiazepine use in this population. Research relevant to kinetic and dynamic responses to antianxiolytics in black Americans is much needed.

In this presentation, the author will first review and summarize these recent pharmacokinetic and pharmacogenetic research findings on blacks. Next, the author will discuss potential environmental factors related to differential drug responsivity.

ETHNICITY AND PSYCHOPHARMACOLOGY: THE ASIAN PERSPECTIVE. Keh-Ming Lin. Harbor-UCLA Medical Center, Torrance, CA.

The last decade has witnessed substantial progress in our understanding of ethnic differences and similarities between Asians and other ethnic groups in response to various psychotropics. Substantial pharmacokinetic differences have been consistently reported between Asians and Caucasians with haloperidol, diazepam, and alprazolam. Similar comparisons of tricylic antidepressants (TCAs) between these two ethnic groups have led to contradictory findings. In addition to phar-

macokinetics, ethnic differences in protein-binding and in the pharmacodynamics of psychotropics as well as other drugs have also been reported.

Future studies should explore newer assay methods and imaging techniques capable of measuring receptor-drug interactions, in addition to utilizing existing research methodologies to more systematically scrutinize the nature and extent of such differences. They should be designed not only to ascertain differences in drug responses, but also to examine genetic and environmental (e.g., diet, exposure to enzyme inducers) factors that may contribute to these differences. Pharmacogenetic probes could be used in combination with studies examining pharmacokinetic and pharmacodynamic issues for such purposes.

SOCIOECOLOGIC ISSUES IN PSYCHOPHARMACOLOGY: A METHODOLOGICAL CRITIQUE. Samuel Turner. University of Pittsburgh, Pittsburgh, PA.

Ethnic differences in drug absorption, distribution, and metabolism have been clearly demonstrated by numerous authors. The majority of research studies providing evidence for cross-cultural differences in the pharmacokinetic and pharmacodynamic properties of various drugs have compared individuals of Asian descent, and to a lesser extent blacks, to Caucasians. However, few studies have systematically assessed the role of socioecologic factors in relation to kinetic and dynamic responsivity to psychotropics. Specifically, it is well known that nutritional status, alcohol and substance abuse history, and chronic psychological stress are all factors that may directly affect drug metabolism. Additionally, interethnic pharmacokinetic studies on specific psychiatric disorders may vary dramatically as a function of inappropriate diagnosis, as well as from pooling subtypes of similar psychiatric disorders (e.g., major depression) without differentiating them according to first versus second episode, or without consideration for chronicity of illness being evaluated.

The following presentation will discuss some important socioenvironmental methodological factors which have direct influence on metabolic pathways, and hence on any interethnic pharmacokinetic and pharmacodynamic differences observed between ethnic groups studied.

CULTURAL FACTORS IN PHARMACOTHERAPY. William Lawson. University of Arkansas School of Medicine, Little Rock, AR.

Recent advances in pharmacological treatment of mental disorders have greatly improved therapeutic outcomes. However, the majority of these gains have been observed in majority culture populations, while such treatment advances for African Americans and other ethnic groups have not kept pace. Although variations in pharmacotherapeutic outcomes are relevant to all treatment populations, the focus of the present presentation will largely encompass African American populations. It has been observed that some of the disparity in pharmacotherapeutic outcome may be attributed to diagnostic misclassification. African Americans are often overdiagnosed as having schizophrenia and underdiagnosed for a number of disorders that respond to specialized pharmacotherapy including mania, panic disorder, or obsessive compulsive disorder. Moreover, the overprescription of antipsychotics probably contributes to poor compliance, poor outcome, and increased likelihood of neurological complications such as tardive dyskinesia. Additional societal bias probably plays an excessive role in prescribing for African American populations in that they are often treated as a homogeneous undifferentiated mass. Black Americans are more likely to receive "prn" medication in inpatient settings, excessive dosing despite pharmacological evidence that suggests otherwise, and medication to the exclusion of psychological treatment despite a demonstrated need for the latter. Finally, pharmacokinetic and pharmacodynamic differences in response to new pharmacological agents are generally less available to African Americans because this group is often not included in new drug trials. Also, the high cost associated with new agents are often prohibitive. In sum, attitudinal, diagnostic, and pharmacological issues must be addressed to assure more responsible prescribing for African Americans as well as other ethnic groups.

SYMPOSIUM

Contemporary Research in Behavioral Pharmacology

Chair: *Mark Galizio*, University of North Carolina at Wilmington, Wilmington, NC.

Discussant: *Michael Perone*, West Virginia University, Morgantown, WV.

DRUGS AS DISCRIMINATIVE STIMULI. Nancy A. Ator. The Johns Hopkins University School of Medicine, Baltimore, MD.

Work with lorazepam in two-lever food-maintained drug discrimination procedures with baboons and rats found greater specificity in the drug stimulus generalization profile when this drug was used as a training drug compared to studies with other benzodiazepines. That is, animals trained to discriminate lorazepam did not reliably make the drug response in tests with barbiturates, although animals trained to discriminate diazepam, chlordiazepoxide, triazolam, oxazepam, and sometimes midazolam commonly have done so. Characterization of the discriminative stimulus effects of lorazepam included manipulation of species, training dose, and route of administration; drug interaction studies; and tests with a variety of anxiolytics. Time course of the discriminative-stimulus effects of lorazepam and other drugs also has been studied using a multiple session procedure. Other data have been collected with the novel anxiolytic buspirone and specific GABA agonists as training drugs. Taken together, these results have provided information relevant to a number of issues central to interpretation of drug discrimination data, including a) the issue of whether intermediate levels of the drug response in test sessions reflect threshold or partial drug stimulus effects, rather than loss of stimulus control, and b) the extent to which the discriminative-stimulus effects of relatively specific compounds show comparably specific generalization profiles. Such data are relevant both to interpretations of the specificity of the drug discrimination model and to speculation about the extent to which such models can aid discovery of new molecular mechanisms of behavioral action of psychoactive drugs. Furthermore, they can be related to data from self-administration models to determine the extent to which generalization profiles for specific training dugs may be useful for abuse liability evaluations.