nol or the ability to block an ethanol discrimination. The results from these ongoing series of studies indicate that the discriminative effects of ethanol are mixed, emanating from action at several neurotransmitter systems. In particular, agonists of the GABA/benzodiazepine ($GABA_A$) receptor complex, uncompetitive antagonists of the *N*-methyl-D-aspartate (NMDA) glutamate receptor complex, and agonists of the serotonin-one ($5\text{-}HT_1$) receptor subtype substitute for the discriminative stimulus effects of ethanol in a dose-dependent manner. In addition, antagonists of the serotonin receptor subtype designated $5\text{-}HT_3$ block the discriminative stimulus effects of ethanol. However, the sensitivities of these receptor systems to ethanol do not appear to be uniform. For example, rats trained to discriminate relatively low doses of ethanol generalize completely to agonists of the $5\text{-}HT_1$ receptor system, whereas rats trained to discriminate higher doses of ethanol show no generalization to these agonists. An opposite effect is seen with NMDA antagonists, where rats trained with high doses of ethanol show better generalization to these antagonists compared to rats trained with lower doses of ethanol. Thus, the relative contribution of each receptor system to the discriminative effects of ethanol is dependent upon the dose of ethanol the animal was required to discriminate. Taken as a whole, the data demonstrate that ethanol is a mixed stimulus, composed of discriminable effects at multiple, differentially sensitive receptor systems. This complex nature of the discriminative stimulus effects of ethanol leaves open the possibility of several avenues for pharmacologically blocking or altering the subjective effects of ethanol, including those subjective effects that reinforce the consumption of ethanol.

BUSPIRONE AS AN ADJUNCT TO RELAPSE PREVENTION IN ANXIOUS ALCOHOLICS. H. R. Kranzler, T. F. Babor, F. Del Boca and J. Brown. University of Connecticut School of Medicine, Storrs, CT.

Sixty-one anxious, alcohol-dependent (DSM-III-R) subjects were enrolled in a 12-week trial of buspirone or placebo, combined with weekly relapse prevention psychotherapy. Prior to entering the study, both groups drank on an average of 67% of days. Buspirone-treated subjects drank an average of 6.1 drinks per day, while placebo-treated subjects drank an average of 8.6 drinks per day ($p < .05$). Of the 31 buspirone-treated subjects, 26 (84%) completed the treatment phase, compared with 15 of 30 (50%) of the placebo-treated subjects ($p < .005$). At the end of the active treatment period both groups reported that they had drunk infrequently. Though the groups did not differ with respect to the average duration of abstinence from the time that treatment was initiated (6.4 weeks), the average time to first heavy drinking episode (i.e., 5 or more drinks in a day) was greater ($p = .05$) for buspirone-treated patients (9.5 weeks vs. 7.4 weeks). However, with 6-month followups having so far been completed on more than half of study subjects, greater group differences are becoming apparent: buspirone-treated subjects reported drinking on an average of 11% of days, consuming 2.3 drinks per drinking day. At followup, placebo-treated subjects reported drinking on 40% of days, consuming an average of 6.1 drinks per drinking day. There was a significant difference ($p < .005$) for number of drinking days, though number of drinks per drinking day was not different ($p = .29$). There was no between-group difference in Hamilton Anxiety Scale (Ham-A) scores at baseline or during treatment; by week 4 Ham-A scores went down significantly (from about 21 to about 8) and remained at that level for both groups. Ongoing data analysis will aim to identify the process by which the delayed treatment effect occurred.

NALTREXONE AND COPING SKILLS THERAPY FOR ALCOHOL DEPENDENCE. Stephanie S. O'Malley,* Adam Jaffe,* Grace Chang,† Richard S. Schottenfeld,* Roger Meyer‡ and Bruce Rounsaville.* *Yale University School of Medicine, New Haven, CT, †Harvard University, Cambridge, MA, and ‡University of Connecticut Alcohol Research Center, Farmington, CT.

Ninety-seven alcohol-dependent patients were treated for 12 weeks in a double-blind, placebo-controlled study evaluating naltrexone and two psychotherapies in the treatment of alcohol dependence. Patients were randomized to receive either naltrexone or placebo and either coping skills/relapse prevention therapy or a supportive therapy designed to support the patient's own efforts at abstinence without teaching specific coping skills. Naltrexone proved superior to placebo in measures of drinking and alcohol-related problems. Almost twice as many naltrexone-treated patients as compared to placebo-treated patients remained continuously abstinent during the study. In addition, patients on naltrexone consumed one-third the amount of alcohol and relapsed at half the rate of placebo-treated patients. Interactions between medication and the type of psychotherapy were also found. Time to first drink was longest for patients treated with naltrexone and supportive therapy. In contrast, patients who received naltrexone and coping skills therapy initiated drinking at a rate similar to placebo-treated patients. One hypothesis for this finding is that discussion of the abstinence violation effect in the coping skills/relapse prevention therapy may have undercut the patient's initial commitment to abstinence. For those patients who initiated drinking, however, patients who received naltrexone and coping skills therapy were the least likely to relapse. The results suggest that naltrexone is an effective pharmacological adjunct to the treatment of alcoholism. In order to maximize treatment outcome, the patient's commitment to abstinence should be encouraged. In addition, treatment focused on the development of new coping skills may further reduce the risk of relapse and enhance the quality of the individual's life. (Supported in part by NIAAA grant AA-P50-03-510.)

PHARMACOTHERAPY AND RELAPSE PREVENTION COUNSELLING WITH ALCOHOLICS. Helen M Annis. Addiction Research Foundation, Toronto, Canada.

Within cognitive-social learning theory, a critical distinction is drawn between treatment strategies aimed at "initiation" versus "maintenance" of behavior change. It is proposed that this distinction provides a theoretical framework for the use of pharmacological agents in the treatment of alcohol and drug abuse. Pharmacological agents can be powerful in initiating a change in consumption, but if patients externally attribute the cause of their improvement to the drug, maintenance of improvement following withdrawal of the drug is likely to be poor. Counselling procedures, on the other hand, that are designed to promote self-attribution for change in drinking/

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-