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ABSTRACTS

Meeting of Division 28 of the American Psychological Association
Psychopharmacology and Substance Abuse

INVITED ADDRESSES

A1

PHYSIOLOGICAL, SUBJECTIVE AND REINFORCING EFFECTS OF ILLICIT AND LICIT DRUGS IN HUMANS

Hendreé E. Jones, Johns Hopkins University School of Medicine, Baltimore, MD

A series of studies investigated the subjective, physiological and reinforcing effects of stimulant drugs including cocaine, nicotine and caffeine. The first study used cocaine abusing volunteers trained to discriminate between orally administered placebo and cocaine capsules (100 mg/70 kg). Following acquisition of the discrimination, the reinforcing effects of cocaine were determined in two experiments. Results from both experiments show that context can influence cocaine self-administration. Another study compared the subjective and physiologic effects of oral versus i.v. cocaine and found that compared to oral administration, i.v. cocaine is a more potent reinforcer. A subsequent study examined the subjective, physiologic and reinforcing effects of i.v. cocaine and nicotine. Overall, although both cocaine and nicotine increased subjective ratings of drug effect, rush, good effects, liking, high and stimulated, only nicotine increased ratings of bad effects and jittery. At doses that produced comparable ratings of drug effect (e.g., 40 mg/70 kg cocaine vs. 1.5 mg/70 kg nicotine), cocaine produced significantly greater good effects while nicotine produced greater bad effects. A further study examined the effects of i.v. caffeine and nicotine under oral caffeine maintenance and abstinence conditions and found an enhancement of nicotine's effects under oral caffeine maintenance conditions. Taken together, these studies provide a greater understanding of the processes involved in stimulant drug abuse and have implications toward the development of treatment and prevention strategies for stimulant drug abuse.

A2

INDIVIDUAL AND STRAIN DIFFERENCES IN SENSITIVITY TO OPIOIDS

Drake Morgan and Mitchell Picker, Dept. of Psychology, Univ. of North Carolina at Chapel Hill

These experiments provided an analysis of some of the behavioral and pharmacological effects of opioids with varying degrees of intrinsic efficacy at the μ opioid receptor. After determining the relative intrinsic efficacy of various μ opioids using the irreversible antagonist β-FNA in a drug discrimination procedure, the interactions between several of these drugs were examined in an antinociception procedure. These studies demonstrated the role of intrinsic efficacy and the intensity of the nociceptive stimulus in determining the drug effect. Higher efficacy opioids produce antinociception regardless of stimulus intensity, whereas the antinociceptive effects of intermediate efficacy drugs are evident using low intensity stimuli, but not high intensity stimuli. Very low efficacy drugs failed to produce antinociception at all intensity levels. When a drug that produced no effect alone was combined with a higher efficacy drug, a competitive antagonism was observed. When two drugs that produced antinociception were combined, additive effects between the drugs were observed. When butorphanol (i.e. an intermediate efficacy opioid) was combined with morphine, it produced both an enhancement of morphine's effect at the low intensity, and an antagonism of morphine's effects at the high intensity, in the same animal at essentially the same time. A role for intrinsic efficacy and stimulus intensity in the expression of differential sensitivity to opioid effects across strains of rats and among individuals within a particular strain of rats was then examined. We replicated the differential sensitivity between strains and between individuals reported in the literature (i.e. 2-3 fold differences in sensitivity) with higher efficacy opioids. When these animals were tested with lower efficacy opioids and/or at higher stimulus intensities, larger individual and strain differences emerged. For example, there was a 3-fold difference in sensitivity to the discriminative stimulus effects of morphine across individual Long-Evans rats, whereas there was a >1000-fold difference in sensitivity to the low efficacy opioid nalbuphine. With regards to strain differences, Lewis and F344 rats show less than a 3-fold difference in sensitivity to morphine. In contrast, F344 rats showed maximal effects at low doses of butorphanol, whereas Lewis rats failed to show any effects at doses 560 times higher. Together these data demonstrate that there are profound differences to the antinociceptive and discriminative stimulus effects of μ opioids across rat strains or among individuals within a particular strain.

A3

DEPRESSION, SEROTONIN, AND SMOKING

Bonnie Spring, Ph.D., ABPP, University of Illinois at Chicago and Hines Hospital, Hines, Illinois

Cigarette smoking is more prevalent in those with a history of depression (~49%) than in the general population (~27%). Four studies examined whether alterations in brain serotonergic function may contribute to the high comorbidity between depression and nicotine dependence and have implications for helping depression-prone smokers to quit.

Study 1 compared the response to tryptophan depletion of 60 currently nondepressed adult smokers and nonsmokers who were classified as depression-prone or not as a function of whether they possessed or lacked a personal and familial history of recurrent depression. Depression-prone participants became dramatically more depressed ($p<.001$) after depletion, especially if they were also smokers. Dysphoria after depletion correlated $r=.74$ with dysphoria after 48 hours of verified abstinence from smoking. Moreover, all depression-prone subjects relapsed to smoking within 5 days of the quit period, whereas 40% of non-prone subjects remained abstinent one month later ($p<.05$). I conclude that depression-prone smokers respond similarly to serotonin deficiency and nicotine withdrawal, showing dysphoria that predicts relapse to smoking.

In Study 2, 989 nondepressed smokers from 16 sites were treated with placebo, 30 mg or 60 mg fluoxetine plus 9 sessions of individual behavioral therapy to quit smoking. Niaura, Spring, Borrelli & Hedeker found that the 60 mg but not the 30 mg dose of fluoxetine enhanced cessation in comparison with placebo. Fluoxetine's effect on smoking cessation was more modest than effects found in trials of antidepressants with greater catecholaminergic action.

Study 3 showed that fluoxetine's effect also differed somewhat in nature. Among 253 non-depressed smokers, fluoxetine selectively benefitted the cessation efforts of smokers who displayed some subclinical depressive symptoms ($p<.05$), contrasting with other investigators' findings for bupropion and nortriptyline.

In a subsample of 98 individuals, Study 4 demonstrated that fluoxetine dose-dependently prevented an increase in dysphoric mood in the initial week after nicotine withdrawal ($p<.05$).

Findings suggest that, in depression-prone people, acute serotonergic deficiency triggers a mood state that mimics the one accompanying nicotine withdrawal and that predicts cessation outcome. The antismoking action of the serotonergic agent, fluoxetine appears to be selective and partially mediated by its effect on depression, apparently differing from the action of more highly catecholaminergic quit smoking aides.

A4

NICOTINIC MODULATION AND COGNITION-ENHANCING DRUGS

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Using event-related functional magnetic resonance imaging (fMRI) during eyeblink classical conditioning in the 400 ms delay paradigm, we observed activation in the hippocampus in previously-conditioned human subjects in trials with conditioned responses (CRs) and in trials with unconditioned responses (URs) alone. This result parallels results from electrophysiological recording in the CA1 region of the hippocampus in rabbits during eyeblink conditioning. The neural circuitry for eyeblink classical conditioning is similar in non-human mammals and humans. Whereas the cerebellum ipsilateral to the conditioned eye is essential for this form of associative learning, the hippocampus can affect the rate of learning. We demonstrated that the cognition-enhancing drug, nefiracetam is effective only when the hippocampus is intact, and we feel that nicotinic modulation occurs via the hippocampus. The septo-hippocampal cholinergic system is of demonstrated involvement in eyeblink conditioning. It was this cholinergic involvement that led us to condition patients with Alzheimer's disease (AD). Patients diagnosed with probable AD are profoundly impaired in CR acquisition, making eyeblink conditioning a useful model system for preclinical trials of cognition-enhancing drugs. Initial pharmacological manipulations tested in this model system were muscarinic. Disruption of muscarinic receptors with scopolamine injections impaired acquisition of CRs in rabbits and eliminated pyramidal cell activity in the hippocampal CA1 region in conjunction with CRs and URs. Subcutaneous scopolamine injections in humans also impaired acquisition of CRs. Blockade of nicotinic cholinergic receptors with mecamylamine injections impaired acquisition of CRs in young adult rabbits, and both nicotine (0.25 mg/kg) and the nicotinic drug, GTS-21 (0.5 mg/kg) reversed learning deficits resulting from mecamylamine administration. In older rabbits that are impaired in the acquisition of CRs, 15 daily sc injections of GTS-21 (0.5 and 1.0 mg/kg) ameliorated learning deficits. Daily injections of GTS-21 did not cause receptor up- or down-regulation in the cortex. In a test of retention, 17 days after 15 daily injections of 0.5 mg/kg GTS-21, drug-treated older rabbits produced four times as many CRs as vehicle-treated older rabbits. We also have evidence that some other cognition-enhancing drugs with demonstrated efficacy in the rabbit eyeblink conditioning model system such as nefiracetam and galanthamine are modulating nicotinic cholinergic receptors.

SYMPOSIA

From Symposium 1: Alcohol and Other Drug Involvement: A Behavioral Genetic Focus

A5

NICOTINE ADDICTION AS A COMPLEX GENETIC TRAIT: OVERVIEW OF CURRENT FINDINGS AND FUTURE CHALLENGES

Gary E. Swan, Ph.D., Center for Health Sciences, SRI International (formerly Stanford Research Institute), 333 Ravenswood Ave., Menlo Park, CA 94025

This presentation will provide an up-to-date overview of research on the genetics of nicotine addiction. Results from twin studies, genetic association studies, and genetic linkage studies will be reviewed. Several issues confronting researchers in this area will be discussed including: 1) The definition of the phenotype, in this case, nicotine addiction, is subject to some debate. For genetic epidemiologic studies, is it better to use broad or narrow phenotypic descriptions, behavioral or physiological? Several examples exist from the literature on complex psychiatric disorders, where the definition of the phenotype has presented difficulties for cross-validation of genetic association studies. On the other hand, the success stories behind BRCA1 and ApoE ε4 are due, in part, to the use of a refined phenotype (early vs. late age of onset). What can we use from these examples to inform future genetic studies of nicotine addiction?; 2) Most of the available evidence on genetic involvement in nicotine addiction comes from fairly straight-forward behavioral genetic studies of twins. While heritability estimates are usually reported in a univariate context, we also know that nicotine addiction shares phenotypic and genotypic covariance with alcohol consumption and depression. What advances in behavioral genetic methodologies may be of use in clarifying which of the plethora of nicotine addiction indices show genetic influences, share or don't share genetic covariance with other addictive phenotypes, and are or are not stable over time?; and, 3) Khoury, Ottman, and others have recently called for an increased emphasis on the study of gene-environment interactions in the study of complex diseases. Several examples exist from the cancer and neurological arenas where demonstrable, nonlinear interactions exist between genes and environment to dramatically increase risk for illness. How might future studies of nicotine addiction be designed to enhance the probability of detecting such interactions? Conclusions: 1) It is clear from the available evidence that the underlying genetic substrate for nicotine addiction is quite complex; 2) This complexity will impact the design and size of future genetic studies; 3) The possible influence of gene-environment interactions raises several scientific and ethical issues for the correct interpretation of results from genetic studies of nicotine addiction.

A6

ALCOHOL INVOLVEMENT: GENETIC RISK AND PROTECTIVE FACTORS WITHIN ETHNIC GROUPS. Tamara L. Wall, University of California, San Diego, La Jolla, CA and Veterans Affairs San Diego Healthcare System, San Diego, CA

Candidate genes of the alcohol metabolizing enzymes, alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH), have been shown to be associated with various alcohol-related behaviors. Data suggest that individual variability in level of response to alcohol is a genetically influenced trait and an important biological phenotype in etiological theories of alcoholism. Findings will be reviewed from three different ethnic groups with widely varying patterns of alcohol use and alcohol-related problems: Asian Americans, Jewish Americans, and Native American Indians. Asian Americans, as a whole, have high rates of abstinence and low rates of alcoholism. Genetic polymorphisms of ADH and ALDH are both associated with decreased alcohol consumption and lower rates of alcoholism among Asians. Results suggest that the mechanism by which these genetic variants influence alcohol-related behavior may be, in part, through the intensity of response to alcohol and may be mediated by increased levels of acetaldehyde. Asians with these genetic variants who do drink, however, may experience more severe alcohol-related sequelae at relatively lower doses. Compared to other religious and ethnic groups in the United States, Jewish Americans have low rates of abstinence and low rates of alcoholism. An ADH polymorphism has recently been identified in Jews, and similar to Asians, this variant appears to be protective in the development of alcohol-related behaviors. It is also possible that this variant acts by influencing level of response to alcohol. Finally, although there is variability both among and between tribes, Native Americans, as a group, have high rates of abstinence and high rates of alcoholism. Results indicate that Native Americans do not have genetic variants of ALDH and do not have heightened sensitivity to alcohol as some previous research suggested. Rather, data indicate that Native American men, particularly those with greater degrees of Native American heritage, may be less sensitive to alcohol's effects, a biological phenotype that has been associated with an increased risk for alcoholism. This research was supported by National Institutes of Health grants R29AA11257, R01AA10201, K02AA00269, P50AA07611, and M01RR00827.

From Symposium 2: Regional Variability in Psychostimulant Use: New and Important Findings

A7

PREVALENCE OF PSYCHOSTIMULANT USE IN VIRGINIA: DEVELOPMENTAL AND SCHOOL HEALTH IMPLICATIONS. **Gretchen B. LeFever, Ph.D.**, Margaret S. Villers and Ardythe L. Morrow, Center for Pediatric Research, Norfolk, VA, glefever@chkd.com

Background: Based on a limited number of regional studies of psychostimulant use, ADHD is estimated to affect 3-5% of children. Methylphenidate distribution rates suggest that ADHD prevalence may vary up to six-fold across states. **Objective:** Estimate the prevalence and impact of ADHD in Virginia. **Methods:** Prevalence of ADHD medication use in schools was determined by review of nursing records of students in grades 2-5 in District A (N=5,765) and District B (N=23,967), and by parent report among students in 3 elementary schools in District C (N=1,032, 63% return rate). In District C, parents were also asked to report on ADHD medication use at home and ADHD diagnosis. **Results:** Prevalence of ADHD medication use in school was similar across districts and up to 90% of students received psychostimulants. The rate of ADHD diagnosis was substantially higher than the rate of ADHD medication administration in school, because only 52% of diagnosed students received medication in school. Overall, 17% of students were diagnosed with ADHD. Compared to other students, ADHD students were 3-7 times more likely to receive special education, to be expelled or suspended from school, to repeat a grade, and to be frequently absent from school (P values <.01). Parent report indicated that 40% of ADHD students experienced problems of depression and that 25% of ADHD children were receiving anti-depressant medication in addition to psychostimulant medication. In one district, young-for-grade students were 21 times more likely than other students to be medicated for ADHD (63%, P<.01). **Conclusions:** ADHD prevalence in southeastern Virginia appears to be 3-6 times higher than the national estimate. Additional research in regions with high and low distribution of methylphenidate is needed before determining a national prevalence estimate of ADHD. ADHD may be underestimated if studies rely exclusively on school record or Medicaid methylphenidate prescription data. ADHD children are at substantial risk for adverse education and social outcomes. School policies may place young students at risk for being perceived as having a disorder, rather than experiencing developmental appropriate attention and control problems. The large number of children treated for ADHD, lack of a diagnostic test for ADHD and adverse outcomes experienced by children establishes ADHD as an important public health problem.

A8

STIMULANT TREATMENT IN MARYLAND PUBLIC SCHOOLS

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School nurse headcounts of public school students receiving medication treatment for hyperactivity and inattentiveness have been performed in Baltimore County, Maryland since 1971. In April, 1997, 4.8% of all of its public school students (4954/103,222) were receiving medication for ADHD, an increase from 4.1% in 1995.

In April, 1998, the Maryland State Department of Education initiated a school nurse headcount of all its public school students to determine the number receiving one or more doses of medication for the treatment of ADHD during school hours. Of the 806,465 students in the system, 20,050 (2.46%) received methylphenidate (Ritalin®) and 3,721 (0.46%) received other medications for ADHD. If an estimated 20% received medication only at home, 3.65% of all Maryland public school students were receiving medication then for this disorder.

Other findings of interest were: 1) special education students received methylphenidate in school at a rate over 6 times that of regular education students (8.7% vs. 1.36%). In fact, of all Maryland public school students receiving methylphenidate during school hours, 45% had a special education individual educational plan. 2) African-American and Hispanic students were receiving methylphenidate at approximately one-half the rate of their Caucasian counterparts. 3) the male-female ADHD medication gender ratio was relatively similar for secondary school students (4.3:1) compared to the ratio for elementary school students (3.5:1). 4) there was a 5-fold difference in the prevalence of methylphenidate treatment between the Maryland county with the highest rate compared to the one with the lowest rate. 5) nurse practitioners were the prescribers for 9.2% of the youths in Maryland receiving methylphenidate.

A9

FACTORS THAT INFLUENCE THE PREVALENCE OF STIMULANTS FOR THE TREATMENT OF YOUTHS WITH ATTENTIONAL DISORDERS

[1]JM Zito, [2]Safer, DJ, [1]dosReis, S, [1]Gardner, J, [3]Johnson, RE, [3]Lynch, F, [3]Boles, M
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Objective: This NIMH-funded study examines the demographic and clinical factors that influence the rate of stimulant use for the treatment of US youths with attentional problems.

Method: Data sources include Medicaid populations from two states (MCD-1 and MCD-2) and a staff model HMO population (HMO). Medicaid administrative claims data and HMO prescription dispensing records were organized for a 10 year interval (1987-1996). Prevalence is defined as 1 or more prescription claims or records during a study year per 100 enrolled individuals.

Results: Age (<5, 5-9, 10-14, 15-19 years), gender, geographic and, where available, ethnicity-specific prevalence data illustrate substantial variations based on patient and geographic factors. Key findings include: 1) 5-14 year olds are the most common stimulant-treated youths: 1996 prevalence of 6.9% (MCD-1); 8.0% (MCD-2) and 4.1% (HMO); these rates were 5-10 times (MCD-1), 7-19 times (MCD-2) and 3-11 times (HMO) greater than their older and younger counterparts, respectively; 2) 10 year increased use was most dramatic for 15-19 year olds: 6.1-fold (MCD-1), 4.4-fold (MCD-2) and 25-fold greater (HMO). Unexpected 10 year increases occurred among preschoolers, particularly those 2-4 years old. Gender ratios reveal a trend for increased utilization among girls, a change that is consistent with criteria changes in the Diagnostic and Statistical Manual (DSM). Ethnicity, and diagnostic differences are also pronounced.

Conclusion: Time trends for total and selected specific prevalence rates illustrate the increased stimulant medication utilization for the treatment of attentional disorders in the US in recent years. The wide range of reported prevalence of stimulant treatment of youths reflects important concerns. Among these concerns are increased duration of use (more adolescents) and very early use (preschoolers) despite the absence of long-term effectiveness data and lack of efficacy and safety data among preschoolers. Outcome studies in the usual practice setting should be undertaken to help to establish the effectiveness, continuity and complexity of drug treatment and the extent of multimodal therapies.

From Symposium 3: Applications of Behavioral Economics to Addictive and Other Health Behaviors

A10

BEHAVIORAL ECONOMICS OF PHYSICAL ACTIVITY AND EATING

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Behavioral economics provides a valuable conceptual and methodological framework for exploring individuals' choices among weight-related behaviors such as being physically active versus sedentary and eating high-fat, low nutrient dense versus more healthy foods. People are faced with numerous activity and caloric intake decisions on a daily basis. Research suggests that such qualities as individual differences, environmental factors, and alternative characteristics can impact people's choice to be physically active or to eat. In addition, such influences affect individuals' decision on what, when, and how much to eat and when, where, and in what way to be physically active. These choices have consequences for energy balance, weight and obesity status, and ultimately overall health.

Understanding the factors that influence activity and food choice has the potential to improve interventions for the modification of weight-related behaviors in a time when obesity prevalence, and particularly a sedentary lifestyle, among the population is rising. Evidence from behavioral economics research could inform interventions from the individual-based to community level. Findings from behavioral economic studies of weight-related behaviors provide hope for initiating behavior change in favor of higher energy expenditure and lower caloric intake. For example, recent evidence suggests that sedentary activities are not necessarily completely substitutable and individuals choose to be more physically active in order to get access to more preferred sedentary activities. A review of the behavioral economics literature as it pertains to weight-related behaviors will be presented, along with possible future directions for translating laboratory findings for intervention development and further exploration of factors (e.g., genetic predisposition) that may be influencing activity and food choice.

From Symposium 4: Combined Pharmacological and Psychological Treatment Strategies for Mental Disorders

A11

COMBINED PHARMACOTHERAPY AND PSYCHOTHERAPY FOR UNIPOLAR DEPRESSION

Jeremy W. Pettit, Zachary R. Voelz, and Thomas E. Joiner, Jr.
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There is currently much debate, disagreement, and uncertainty concerning the most effective treatment available for unipolar depression. Those favoring a primarily biological view of the disorder provide cogent arguments that medications are the best way to deal with the disorder. Those favoring a primarily environmental view argue convincingly that psychotherapies render the best results when treating depression. In the middle are those who believe that both sides have strengths and weaknesses, and view depression as a disorder involving biological, environmental, and internal factors. This group maintains that both pharmacotherapy and psychotherapy are effective ways to treat unipolar depression. The remaining task is to determine which approaches are most efficacious under a given set of circumstances (e.g., particular subtypes of depression), and whether combinations of psychological and pharmacological treatments alleviate and prevent depression better than either therapy administered singly.

The purpose of this presentation is to briefly review the empirical evidence relevant to combined psychotherapy and pharmacotherapy for unipolar depression, and discuss the relative merits of combined therapies in the treatment of depression. We will comment on the various pharmacotherapies and psychotherapies most commonly employed when dealing with unipolar depressive episodes, then discuss combined therapy in more detail.

Based on the results of empirical studies on combined treatment over the past decade, we conclude that combined treatment may have modest superiority over either pharmacotherapy or psychotherapy alone. In addition, combined treatment appears to be most effective when treating individuals with more severe levels of depression.

From Symposium 5: Harm Reduction: Offering Humane and Pragmatic Care to Substance Abusers

A12

HARM REDUCTION: OFFERING HUMANE AND PRAGMATIC CARE TO SUBSTANCE ABUSERS

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U.S. approaches to the drug problem emphasize reducing the drug supply through interdiction and imposing criminal penalties for drug use, possession, and trafficking. Like Prohibition before it, the current U.S. War on Drugs has had only limited positive impact on drug use and related problems, while producing negative effects ranging from increased drug-related incarceration rates (especially among minorities) to under-funded treatment programs to failing to curb HIV infection among injection drug users. Conspicuously absent in American drug control policies are adequate efforts to help those with drug-related problems, which is an important part of an overall HIV/AIDS prevention strategy. Few substance abusers enter formal treatment, which tends to be stigmatizing and dominated by intensive, abstinence-oriented programs that are better suited for the minority of substance abusers with more severe problems.

Several developed countries have pursued a different approach to the drug problem known as harm reduction, which is a public health approach aimed at reducing the harmful consequences of substance use and other high risk behaviors for the user and the community. Although abstinence remains a long-term goal, any change that reduces harm or the risk of harm is encouraged and accepted, even if it falls short of abstinence. Harm reduction interventions are varied in purpose and scope (e.g., providing drug treatment on demand with minimal delays, free needle exchanges to reduce HIV transmission, methadone maintenance and other pharmaco-substitutes), but they share a goal of attracting more substance abusers into helping environments and providing them with services that better match consumer need. Growing scientific evidence supports the positive effects of harm reduction programs, including reducing HIV infection, but they remain controversial in the U.S. If the approach is to continue to develop, substance abuse professionals and scientists would benefit from education about harm reduction principles and interventions and about relevant organizational, policy, and legal issues.

A13

THE ORIGINS AND PRINCIPLES OF HARM REDUCTION

Mary E. Larimer
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Harm reduction is founded on a set of principles and strategies designed to reduce or minimize the harm to oneself and others associated with ongoing addictive behaviors. Beginning with the Dutch approach to drug problems in the 1960s, the concept spread internationally in an attempt to deal with the overwhelming AIDS crisis in the 1980s and has now developed into an approach that can be applied to many different high-risk behaviors. Harm reduction differs from other approaches in many respects, primarily through an emphasis on compassion, acceptance, pragmatism, and partnership.

The first basic principle of harm reduction is that it serves as a public health alternative to the moral/criminal and disease models of drug use and addiction. Second, harm reduction recognizes abstinence as an ideal outcome, but accepts alternatives such as moderation and controlled use that reduce harm. Third, rather than being a "top-down" policy promoted by drug policy-makers, harm reduction has emerged primarily as a "bottom-up" approach based on addict advocacy. Fourth, in addition to promoting low threshold access to services by not requiring abstinence and by not criminalizing the addicted person, harm reduction programs attempt to reduce harm by degrees, viewing addiction on a continuum of severity rather than as an all-or-nothing phenomenon. Finally, harm reduction approaches are client-centered and collaborative, with the direction and pace of change determined by the client's preferences and abilities.

A14

HEALTH CARE ORGANIZATION AND POLICY ISSUES IN PURSUING HARM REDUCTION

Jalie A. Tucker
Auburn University, Auburn, AL

Harm reduction programs have largely emanated from the addict and addict counselor communities with a goal of reducing risk and providing low threshold, drug-related services to substance abusers. Expanding these grass-roots efforts requires coordination of drug-related initiatives among stakeholders with diverse agendas (e.g., service providers, consumers of services, police, and the government) that span community, health care, legal, and drug policy arenas. Critical considerations in an expansion of services include: (1) Offer a range of interventions that match the heterogeneity of substance-related problems and consumer needs and preferences. This would involve community outreach, lowering intervention thresholds, making treatment available on demand with minimal delays, and relaxing the abstinence requirement for services. (2) In the health care system, coordinate and integrate substance abuse and other behavioral health services with medical care, especially primary care, and offer brief interventions to substance abusers with mild to moderate problems and referrals to specialized care to those with more serious problems. (3) Achieve parity of insurance coverage. Medical care is better covered than substance abuse and mental health care, which creates disincentives for utilization and increases demand for public drug treatment, which is in limited supply while private slots go unused. (4) Eliminate mandatory drug sentencing laws for simple drug possession, scale back the War on Drugs, and increase funding for prevention and treatment, including in the prison system.

This complex agenda highlights the interdisciplinary issues involved in harm reduction and points to multiple health services research questions related to increasing help-seeking, treatment engagement, and retention. A root impediment that will be difficult to resolve is the longstanding tendency in the U.S. to stigmatize substance abuse and to segregate interventions for it outside of mainstream health care.

A15

EVALUATING TREATMENT ON DEMAND FOR DRUG USERS IN SAN FRANCISCO

James L. Sorensen, Joseph Guydish, James P. Kahn, and Alice Gleghorn
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To address the critical drug problem in San Francisco, in 1996 the Board of Supervisors and Mayor joined in making a commitment to provide treatment to active drug users upon request. Labeled "Treatment on Demand," this movement attracted widespread support because of its potential to increase access to treatment, change the city's capacity to treat drug use, and reduce the costs to the community that accompany drug problems.

To develop a strategic plan for treatment on demand, the city convened a diverse 40-member Planning Council. The plan that emerged represents a striking departure from traditional treatment models in calling for a continuum of integrated services, ranging from harm reduction to holistic client-centered approaches to abstinence-based interventions.

Evaluating the Treatment on Demand initiative presented intriguing issues for researchers. A partnership emerged between university and city health department research teams, with a goal of producing an objective and reliable assessment of the effects of the Treatment on Demand initiative. Rigorous assessment of the project impact normally would employ a randomized design, with individual clients and organizations being assigned to either the Treatment on Demand or a standard practice control condition. In the current context, however, where change was implemented throughout the system beginning at one point in time, randomized designs were not feasible. Instead, the evaluation entailed an interrupted time series analysis that contrasted a 2-year pre-intervention period (Fiscal Years 1995-96 & 1996-97) with a 4-year intervention period (FY 1998-99 through 2001-02) and focused on detecting changes in access to treatment (e.g., decreased waiting lists, reaching more individuals from under-served groups), treatment capacity and utilization of services (e.g., increased treatment slots, decreased repeat detoxifications), and cost outcomes (e.g., savings to society from decreased crime). The project illustrates the multiple stakeholder collaboration required for effective harm reduction.

A16

IMPLEMENTING HARM REDUCTION IN URBAN COMMUNITIES

Imani P. Woods
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America's urban communities tend to experience the worst examples of drug-related morbidity and mortality. These drug-related outcomes are a direct result of the ready availability of drugs in many urban communities and the lack of positive alternatives to drug-taking and drug distribution, especially among youths. America's collective suffering from HIV and AIDS, family dislocation, and drug-related crime are disproportionately borne by urban residents, especially by persons of color. These problems typically take place in a context characterized by other grave social, economic, and health-related problems and are compounded by racial discrimination, poor educational outcomes, barriers to health and social services, and an absence of opportunities for gainful employment.

The drug-related problems of urban communities thus are inextricably intertwined with other community issues and needs and must be addressed as such. Harm reduction strategies offer an approach to addressing these challenging and urgent public health priorities in urban communities. A logical sequence of program development is needed that involves identifying basic individual and community needs, community engagement, raising awareness, and mobilizing residents in order to begin and sustain a successful harm reduction effort in depressed communities. Preparing communities for an alternative educational experience is a key component, and of major concern are issues related to race and class. Race issues, in particular, can make or break a good program design, and providers must delicately address neighborhood concerns.

From Symposium 6: An Empirical Look at Gender Issues and Cocaine

A17

SEX DIFFERENCES IN COCAINE USE: EPIDEMIOLOGIC FINDINGS FROM THE 1996 NATIONAL HOUSEHOLD SURVEY ON DRUG ABUSE

Howard D. Chilcoat, Henry Ford Health Sciences Center, Detroit, MI

Epidemiologic studies have found that males are more likely to use cocaine than females, but little is known about the nature of this sex difference. This report explores sex differences in cocaine use, using data from the 1996 National Household Survey on Drug Abuse (NHSDA). The NHSDA uses a multistage probability sample to provide estimates of drug use for the United States household population age 12 years and older. In 1996, the NHSDA interviewed 18,269 respondents. Males were more likely than females to have ever used cocaine (12.9% versus 8.0%), to be current users (i.e., in the past year) (2.5% versus 1.3%), and to experience problems related to use in the past year (1.7% versus 0.8%). However, among those who ever used cocaine, there was no sex difference in cocaine problems. Results from survival analysis indicate that the onset of cocaine use is similar for males and females through adolescence but that the sex difference in cocaine use emerges in early adulthood. These results were reflected in a comparison of the age-specific prevalence of cocaine use by sex. Prevalence of cocaine use was higher for adolescent (12-17 years old) girls than boys (2.3% and 1.6%, respectively). For ages 18 years and older, males were more likely than women to have used cocaine and the magnitude of the sex difference in prevalence of cocaine use increased with increasing age. In addition, the magnitude of the sex difference varied by race/ethnicity. CONCLUSION: These findings suggest that the observed sex differences in cocaine use outcomes might be explained by sex differences in initiating cocaine *use* rather than sex differences in vulnerability to *problems* once exposure to cocaine has occurred.

A18

GENDER DIFFERENCES IN TREATMENT OUTCOME FOR COCAINE DEPENDENCE

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Gender differences in demographics and drug use characteristics were examined among 185 males and 73 females who sought treatment at a university-based research clinic. A subset of 85 males and 40 females who received the Community Reinforcement Approach (CRA) plus vouchers treatment for cocaine abuse were compared on selected measures of treatment outcome. A greater proportion of men than women were employed full-time (63 vs. 42, $p<.01$), and had never married (53 vs. 39, $p<.05$). With regard to cocaine use severity at treatment intake, men reported spending more money per week on cocaine ($p=.05$), and a greater proportion of men received prior treatments for cocaine abuse (55 vs. 40, $p<.05$). With regard to other drug use, men reported more cannabis and alcohol use in the last 30 days, and more years of regular cannabis and alcohol use ($p<.05$). Greater proportion of men than women were also cannabis dependent (28 vs. 4, $p<.01$) or cannabis and alcohol dependent (18 vs. 1, $p<.01$). With regards to adverse consequences of cocaine use, more women experienced depression, low energy, and unwanted sexual relations, while men experienced more paranoia, and were more likely to report having physically harmed someone ($p<.05$). Women had higher BDI scores than men ($p<.01$), while men scored higher on the MAST ($p<.05$). With regard to treatment outcome, no gender differences were found in either treatment retention or cocaine abstinence achieved during treatment or during follow-up timepoints. Though more commonalties were revealed than differences, these data suggest that men may have greater severity of other drug use and dependence at intake. Moreover, men and women respond equally well to the CRA plus vouchers treatment for cocaine dependence.

From Symposium 7: Substance Abuse and Impulsivity: Delay Discounting Investigations

A19

IMPULSIVITY IN CURRENT, FORMER, AND NONSMOKERS OF CIGARETTES

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Recent research indicates individuals who abuse heroin and alcohol show more extreme discounting of delayed outcomes. The present experiment examined delay discounting in current, former, and nonsmokers of cigarettes with matched demographic characteristics. The subjective value of delayed hypothetical monetary rewards was determined in a psychophysical titration procedure. Participants indicated their choice of immediate and delayed rewards. The amount of the immediate reward was adjusted until the indifference point was found. This process was repeated at each of 7 delays ranging from 1 week to 25 years. The hyperbolic decay model (Mazur, 1987) was fit to data from each participant to yield a derived discounting rate (k). Median discounting rates for current smokers were higher than rates for former and nonsmokers. Rates for former and nonsmokers did not differ. This result confirms the reduced sensitivity to delayed outcomes found in other drug-dependent populations and implicates foreshortening of the temporal horizon as a pervasive feature of drug addiction. Interestingly, these characteristics could be a reversible result of drug abuse, as indicated by the similar discounting rates of former and nonsmokers.

A20

A ROLE FOR DELAY-DISCOUNTING IN CONTINGENCY-MANAGEMENT BASED SUBSTANCE ABUSE TREATMENT PROGRAMS?

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A popular behavioral intervention for the treatment of a variety of substance abuse disorders is Voucher Based Reinforcement Therapy (VBRT). In this therapeutic procedure patients receive vouchers for providing evidence that they have engaged in a specified behavior. When such evidence is provided the patient receives a voucher with a certain monetary value. In order to exchange a voucher the patient selects a good or service they desire and the clinical staff approves and carries out the transaction. This transaction can take some time to carry out, and an exchange delay of varying duration is introduced. Given the basic work on delay-discounting it would be expected that the reinforcing efficacy of a voucher would decrease as this exchange delay increased. Differences in exchange delay may help to account for some of the variability in the efficacy of VBRT programs. We present both clinical and laboratory data examining this issue. First we will consider data on preference between money and vouchers for patients enrolled in a VBRT program. The majority of the patients report preference for money over vouchers and this preference is consistent across a variety of voucher and money values ($0.50 - $32.00). These data suggest a general preference for a reinforcer with a short exchange delay (money) to one with a potentially longer exchange delay (vouchers). In the laboratory, we have adapted a laboratory analog of a VBRT program to examine the effects of reinforcer magnitude and immediacy. Abstinent cigarette smokers made repeated choices between puffs on a cigarette (drug analog) and points worth a variety of monetary values (voucher analog). The time at which these points could be exchanged for money varied from the end of the session to three weeks. Longer exchange delays and lower magnitude reinforcers increased the number of choices for drug.

From Symposium 8: Human Behavioral Pharmacology: Laboratory and Clinical Studies

A21

SIGNS AND SYMPTOMS OF MARIJUANA WITHDRAWAL: AN OUTPATIENT STUDY

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The clinical relevance of marijuana withdrawal has not been established. Eight heavy marijuana smokers participated in a 16-day ABAB, outpatient study comprised of a Baseline (smoking-as-usual) Phase, a Marijuana Abstinence Phase, a Return to Baseline (smoking-as-usual) Phase and a second Marijuana Abstinence Phase. Between-condition comparisons indicated that marijuana users experienced significantly increased aggression, sleep difficulty, anger, craving, strange dreams, and decreased appetite during periods of abstinence compared to periods of regular marijuana smoking. Examination of individual participants' data showed large individual differences in reports of withdrawal symptom severity. These findings replicate and extend previous reports of marijuana withdrawal experienced during inpatient studies. The marijuana withdrawal syndrome appears to consist of affective and behavioral symptoms similar to those commonly experienced during withdrawal from most substances of abuse. Additional research is needed to further establish the reliability and clinical significance of such symptoms and their potential influence on cessation attempts.

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A22

BEHAVIORAL ECONOMICS OF CIGARETTE SMOKING: CONDITIONED REINFORCEMENT EFFECTS?

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In two experiments progressive-ratio responding of cigarette-deprived smokers was reinforced with puffs on nicotin-containing or de-nicotinized cigarettes. In the first experiment, the two types of cigarette were available independently in one phase and concurrently at selected ratio values in a second. In a second experiment, the effects of alternative reinforcement (i.e., money) on demand for both cigarette types are being examined A behavioral economic analysis revealed similar measures of reinforcing efficacy for the two cigarette types when presented alone. This finding suggests that the conditioned reinforcing effects of smoking the de-nicotinized cigarettes played an important role in cigarette consumption. Cigarette preference in a choice situation and, at least tenatively, sensitivity to competition by alternative reinforcers appear to be determined in part by nicotine content.

A23

d-AMPHETAMINE INCREASES CHOICE OF CIGARETTE SMOKING VERSUS MONETARY REINFORCEMENT

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Psychomotor stimulants such as *d*-amphetamine and cocaine previously have been found to increase the frequency and rate of cigarette smoking, but it is unclear whether this is due to non-specific rate-increasing effects or a specific increase in the reinforcing effects of smoking. In the present study, we examined the effects of *d*-amphetamine (0, 7.5, 15 mg/70 kg) on choice between smoking two cigarette puffs versus obtaining a monetary reinforcer ($0.25 per choice). Ninety minutes after drug or placebo administration, thirteen male and female subjects had 3 hours in which to make 20 smoking vs. money choices. Each subject received each dose twice, in counter-balanced order. *d*-Amphetamine dose-dependently increased smoking choices (placebo: 4.2 ± 0.6; 7.5 mg/70 kg: 4.7 ± 0.6; 15 mg/70 kg: 5.7 ± 0.6 choices) and decreased latency to first smoking choice. Expired breath carbon monoxide (CO) levels showed corresponding dose-related increases. In separate sessions, *d*-amphetamine increased ad lib smoking (placebo: 2.8 ± 0.4; 7.5 mg/70 kg: 3.5 ± 0.5; 15 mg/70 kg: 3.8 ± 0.6 cigarettes) and CO levels. In addition to its effects on cigarette smoking, *d*-amphetamine significantly increased heart rate and systolic, diastolic, and mean arterial blood pressures. *d*-Amphetamine also increased subjective measures of stimulant effects, including "feel drug effect", "feel good effect" and "feel energetic". These results provide evidence that *d*-amphetamine increases the relative reinforcing effects of cigarette smoking.

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POSTERS

A24

CONDITIONED MORPHINE WITHDRAWAL: REARING INDICATES WITHDRAWAL, NOT EXPLORATION

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Several studies have demonstrated that contextual cues previously paired with morphine elicit withdrawal signs in the absence of the drug. One sign, rearing, may indicate exploration rather than withdrawal. Rats for which the environment is paired with drug are sedated and explore it less than the controls which are undrugged. During the withdrawal test, the environment is more novel for the paired rats than the unpaired rats. In the present study, exploration was equated in these groups by physically restraining them during conditioning. During the withdrawal test, the rats which had morphine paired with the contextual cues displayed more rearing. This result suggests that rearing indicates conditioned withdrawal.

A25

REINFORCING EFFECTS OF ALCOHOL ON MEMORY CONSOLIDATION IN SOCIAL DRINKERS.

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SEVERAL STUDIES DOCUMENT THE RETROGRADE FACILITATION OF MEMORY BY ALCOHOL, BUT THE MECHANISMS RESPONSIBLE FOR THIS CURIOUS EFFECT ARE UNKNOWN. SOCIAL DRINKERS (HEALTHY MEN AGED 18-30; N=151) TOOK PART IN EXPERIMENTAL PARADIGMS INVOLVING EITHER INCIDENTAL OR INTENTIONAL LEARNING OF EMOTIONALLY SALIENT VERBAL STIMULI. ALCOHOL OR PLACEBO (1.0 V. 0.1 ML/KG) WAS CONSUMED AFTER LEARNING; MEMORY WAS TESTED, SOBER, 24 HR LATER. RESULTS SUGGESTED THAT ALCOHOL ENHANCED INCIDENTAL LEARNING OF POSITVE AND NEGATIVE STIMULI, LIKELY BY FACILITATING THE BIOLOGICAL PROCESSES UNDERLYING MEMORY CONSOLIDATION (NOT MERELY BY REDUCING INTERFERENCE). FURTHER, ALCOHOL ENHANCED INTENTIONAL LEARNING OF POSITIVE (BUT NOT NEGATIVE) STIMULI, AND THIS EFFECT WAS PROBABLY LINKED TO ALCOHOL'S REWARDING PSYCHOMOTOR STIMULANT PROPERTIES ON THE RISING LIMB OF THE BLOOD-ALCOHOL CURVE. MEMORY PROCESSES ARE CENTRAL TO ALCOHOL'S REINFORCING EFFECTS.

A26—AWARD WINNER (PREDOCTORAL)

EFFECTS OF ALCOHOL ON RISK-TAKING DURING SIMULATED DRIVING

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Alcohol use has been identified as the most important factor contributing to the occurrence of severe to fatal automobile crashes. Several prior studies that have examined the direct effects of alcohol on risk-taking driving maneuvers have produced negative results. However, the expectation of alcohol in these studies has resulted in significant driving impairment. The present design studied the direct effects of alcohol with a simulated driving lane-choice task in which participants gained points by driving through either a narrow lane or a wide lane. The lanes were marked by cones. Participants received a larger point reward for driving through a narrower lane (+5) than a wider lane (+3). A narrow lane attempt was considered a "risk move" because of the greater likelihood of hitting a cone. Penalties of varying severities (-1, -3, and -5) were incurred for each cone hit. To maximize motivation across all participants, bonus compensation was reserved for the participant with the highest point total. The study used a placebo-controlled, randomized, double-blind, within-subject design to determine whether or not risk-taking increases within the ascending limb of the blood alcohol curve. Eight adult male volunteers participated in the study. With placebo, as predicted, subjects made fewer risk moves as the cone penalty point values increased. After consuming alcohol (0.03, 0.05, and 0.08 g/kg) the participants' risk-taking did not significantly differ from risk-taking with placebo. While alcohol did not directly affect driving performance, the effects of alcohol expectancy in this paradigm are worthy of future study.

A27—AWARD WINNER (DOCTORAL)

GENETIC INFLUENCES ON EPS LIABILITY: HALOPERIDOL'S EFFECTS ON INBRED MICE. Stephen C. Fowler, Troy J. Zarcone, and Elena Vorontsova, University of Kansas, Lawrence, KS 66045

Extrapyramidal side effects (EPS) were modeled in two inbred strains (BALB/c and C57BL/6) and one outbred strain (CD-1) of mice by assessing the effects of a range of doses of haloperidol (0.08-1.28 mg/kg, ip, 45 min) on arrest of movement during the course of operant behavior. Immobility or microcatalepsy was defined in terms of the maximum dwell time in the reinforcement dipper well for each session. The C57BL/6 strain exhibited the greatest amount of microcatalepsy, and the BALB/c strain the least, with the CD-1's being higher than the Balb/c's but near them. Microcatalepsy was significantly reversed in all three mouse strains by the muscarinic anticholinergic trihexyphenidyl (1.0 mg/kg). The C57BL/6 mice expressed a pronounced microcatalepsy sensitization effect but the Balb/c mice did not. The data suggest that genetic factors importantly influence susceptibility to EPS-like effects of neuroleptics. Also, the C57BL/6 mice may provide an especially sensitive animal model for detecting EPS liability before antipsychotic drugs reach the clinic. Supported by MH43429.

A28

DSM-IV AXIS I AND II COMORBIDITY AMONG PREGNANT SUBSTANCE-DEPENDENT WOMEN

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Substance use during pregnancy is a serious public health and treatment concern, further complicated by high rates of comorbid psychopathology. This study examined the prevalence of DSM-IV Axis I and Axis II disorders among 123 pregnant drug-dependent treatment-seeking women. Participants ranged in age from 20 to 39 years old (M = 30.2; SD = 3.7) with an average education of 11 years (SD=1.6). Eighty-seven percent of subjects were African-American, 95% were single or never married, 94% unemployed, and 61% received methadone maintenance. Consistent with previous research, results indicated overall high prevalence of non-substance Axis I disorders (50%) and Axis II personality disorders (26%). Drug abuse severity and psychosocial problems (medical, employment, legal, and family/social) on the Addiction Severity Index were positively associated with higher rates of Axis I and Axis II disorders. Lower age of first substance use (alcohol, opioids, cocaine and cannabis) was significantly correlated with greater antisocial criteria endorsement. These findings pose important questions regarding the etiology of such comorbid conditions, including differentiation of primary versus secondary diagnoses. Assessment of comorbidity in pregnant drug-abusing women also has implications for prevention and treatment. Individualized and intensive psychotherapy for dually-diagnosed pregnant women may be warranted.

A29

RACIAL DIFFERENCES IN ADOLESCENT SUBSTANCE ABUSE

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Analysis of epidemiological data from the University of Michigan's annual Monitoring the Future study, are analyzed to examine the racial differences in adolescent substance use. The data were accessed through the Substance Abuse and Mental Health Data Archive of the United States Department of Health and Human Services. The analyses were conducted on 12,500 students from the 1995 data set. Logistic regression analyses were conducted to determine odds ratios, confidence intervals, and probability levels for use of substances (dependent variable) by white and black students (contrast variables). A dichotomous variable was created to indicate the presence or absence of substance use for the logistic regression analyses. Results of the logistic regression analyses show that white students are more likely to use all drugs, including alcohol and cigarettes. Issues of trust and the subsequent responses to highly personal and legally explosive issues surrounding substance use could be a factor in mediating African American self reported use. For example, African Americans constitute 40% of the all drug arrests and one-third of all drug convictions nationwide, yet the make up only 13 % of the population- this social reality may influence African American's feelings of trust when asked to disclose substance use by the MTF survey. Further research is needed to explore issues regarding the context or setting of self-report rates of substance use as this relates to and perhaps mediates differential reporting among African American and White adolescents. Finally, while the differences in use between the races need to be interpreted cautiously, these differences, which may deviate from the public opinion, could have an important role in informing public perception, attitudes, and policy regarding adolescent substance abuse.

A30

MODELING RELATIONS AMONG TEMPTATION, EFFICACY, AND DRINKING DURING TREATMENT

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The purpose of this presentation was to investigate within-treatment temptation to drink, efficacy to abstain from drinking, and drinking intensity, and how these variables influence post-treatment drinking. Participants in the current study were a Project MATCH subsample of 238 outpatients (25% females, 8% minorities, M age = 40.61, SD age = 10.41), and 280 aftercare patients (19% females, 15% minorities, M age = 43.85, SD age = 11.70) who completed Client Session Reports (brief measures of efficacy, temptation, and drinking) at 4 critical time periods and a drinking intensity post-treatment measure. As predicted, the proposed model demonstrated relatively stable relations among temptation, efficacy, and drinking quantity over time for both outpatients and aftercare patients. This finding indicates that during the process of change, shifts in within-treatment temptation, efficacy, and drinking are comparable whether one is struggling to achieve and to maintain abstinence (outpatients) or attempting to remain abstinent (aftercare patients). Surprisingly, when temptation, efficacy, and drinking were assessed during the final session, they were related minimally to overall 4- to 15-month post-treatment drinking. For aftercare patients, however, drinking just prior to the end of treatment predicted 4- to 15-month post-treatment drinking. This finding suggests that individuals who entered aftercare mostly abstinent are more at risk for long-term drinking if report a "slip" during the final treatment week. Overall, temptation was the best predictor of drinking during follow-up for both groups.

A31

EXPECTANCIES OF ALCOHOL IN GREEK-LETTER ORGANIZATIONS

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A large proportion of college students experience problems related to alcohol use (Engs & Hanson, 1986). These problems may be particularly common among members of fraternities and sororities (Kuh & Arnold, 1993). One approach to reducing drinking among college students has been successful by focusing on changing alcohol expectancies (Darkes & Goldman, 1993; 1998). The purpose of the present work was to identify expectancies unique to the Greek population that could be targeted in expectancy-based drinking reduction programs for this high-risk population. Although a factor unique to the Greek population was identified, the "Alcohol Can Enhance or Impede Social Behavior" AEQ-A subscale (Christiansen, Goldman, & Inn, 1982) accounted for more variance in drinking behavior than any of the scales derived specifically for the Greek population.

A32

METYRAPONE ATTENUATES INCREASED PHENCYCLIDINE (PCP) INTAKE PRODUCED BY FOOD-RESTRICTION

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The present experiment sought to investigate whether metyrapone, an inhibitor of glucocorticoid synthesis, would attenuate the increased drug intake typically observed following food restriction. Five adult male rhesus monkeys administered 0.25 mg/ml PCP and water from two drinking spouts under concurrent FR16 schedules of reinforcement during daily 3-hr sessions. Feeding conditions alternated from food-satiated (400 g/day) to food-restricted (75 g/day) on a weekly basis. Monkeys underwent an ABA treatment design to assess the effects of metyrapone (30 mg/kg) versus saline administration on PCP consumption under both satiated and restricted feeding conditions. Food restriction significantly increased the consumption of PCP in all monkeys during baseline assessment. Compared to placebo, metyrapone significantly decreased the consumption of PCP under food-restricted, but not food-satiated, conditions. Thus, metyrapone administration selectively attenuated the effects of food restriction. These data demonstrate that metyrapone reversed the restriction-induced increase in PCP intake, and when taken together with previous reports, support the hypothesis that glucocorticoids may mediate the reinforcing value of abused drugs.

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A33

HEROIN AND 6-MONOACETYLMORPHINE PARTIALLY MIMIC THE STIMULUS EFFECTS OF COCAINE

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Despite the prevalence and detrimental consequences of combined cocaine-heroin ("speedball") abuse, relatively little is known about the pharmacological mechanisms underlying this form of polydrug addiction. Previous studies using drug discrimination techniques, a proposed model of the subjective effects of drugs, have shown that prototypical *mu* opioid agonists (e.g., morphine, fentanyl) can enhance the discriminative stimulus (DS) effects of cocaine when administered in combination, yet do not consistently mimic the DS effects of cocaine when administered alone. The present study examined the effects of heroin and its active metabolite 6-monoacetylmorphine (6-MAM) in squirrel monkeys trained to discriminate intramuscular injections of 0.3 mg/kg cocaine from saline under a fixed-ratio 10 schedule of food presentation. Cumulative doses of cocaine (0.03-0.3 mg/kg) engendered dose-related increases in drug-lever responding, reaching nearly 100% accompanied by little change or an increase in the rate of responding. Cumulative doses of heroin (0.003-0.1 mg/kg) and 6-MAM (0.01-0.3 mg/kg) also engendered dose-related increases in drug-lever responding, reaching a maximum of approximately 80% in 3 of 4 subjects and accompanied by pronounced decreases in response rate. Pre-treatments with the opioid antagonist naltrexone (0.003-0.3 mg/kg) surmountably antagonized the cocaine-like DS effects of heroin and 6-MAM, resulting in dose-dependent shifts to the right in the opioid dose-response functions. Schild analyses revealed *in vivo* apparent pA_2 values of 8.4 for heroin and 8.0 for 6-MAM, with slopes of the regression lines of −1.1 and −1.4, respectively. The results show that heroin and 6-MAM partially mimic the DS effects of cocaine, but only at doses that markedly suppress rate of responding. The partial cocaine-like DS effects of heroin and 6-MAM may be mediated via *mu* opioid mechanisms as suggested by surmountable antagonism by naltrexone and Schild analysis. (Supported by USPHS grants DA00499, DA11928, and RR00168).

A34

ADHERENCE TO ANTIRETROVIRALS AMONG INDIVIDUALS WITH HIV/AIDS IN METHADONE MAINTENANCE.

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New medications and combination therapies for HIV are often followed by complex schedules and instructions, creating problems with adherence. Preliminary data suggest that HIV+ individuals in methadone maintenance may have difficulty with a crucial element of adherence: knowledge about their prescriptions. This study investigated adherence to antiretrovirals in a proposed sample of 18 patients. The sample consisted of 18 HIV+ patients from the methadone maintenance program at San Francisco General Hospital. Adherence data was collected during the baseline phase of a pilot project aimed at increasing medication adherence. When self-reported data were compared with the recommended prescription requirements for individual antiretroviral medications, 11% of the patients were inaccurate in their dosage requirements, 44% were inaccurate in reporting the scheduling requirements, and 56% were inaccurate in reporting the special dietary instructions for their protease inhibitors (PI). Patients reported taking 82% of their PI doses yesterday; however, only 40% of doses were taken according the medications' scheduling requirements and 26% were taken according to the special dietary instructions (i.e., "take with food"). Although patients reported relatively good adherence to PI doses, their inability to attend to the medications' scheduling and dietary instructions may contribute to sub-therapeutic outcomes, leading to possible drug resistance. Patients must know how to correctly take their medications in order to adhere to their prescribed regimens. Thus, adherence should be measured in various ways to help researchers better understand the difficulties patients experience.

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