ALCOHOL AND
DRUG ABUSE
INSTITUTE

Biennial Report
1999-2001

Warren G. Magnuson Health Sciences Center
University of Washington
ALCOHOL AND DRUG ABUSE
INSTITUTE

BIENNIAL REPORT
1999-2001

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# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Message from the Director</td>
<td>4</td>
</tr>
<tr>
<td>Research</td>
<td></td>
</tr>
<tr>
<td>Intramural (Grants and Contracts)</td>
<td>6</td>
</tr>
<tr>
<td>Extramural (ADAI Small Grants Program)</td>
<td>9</td>
</tr>
<tr>
<td>Library and Information Services</td>
<td>18</td>
</tr>
<tr>
<td>Research Dissemination</td>
<td>18</td>
</tr>
<tr>
<td>Fiscal Reports</td>
<td>20</td>
</tr>
<tr>
<td>Appendices</td>
<td></td>
</tr>
<tr>
<td>History of Small Grants Funding</td>
<td>25</td>
</tr>
<tr>
<td>Small Grants Scientific Review Committee</td>
<td>27</td>
</tr>
<tr>
<td>Small Grants Final Review Committee</td>
<td>28</td>
</tr>
<tr>
<td>Publications by ADAI Researchers</td>
<td>29</td>
</tr>
<tr>
<td>ADAI Researchers and Staff</td>
<td>33</td>
</tr>
</tbody>
</table>
A MESSAGE FROM THE DIRECTOR
1999 - 2001

The past biennium has seen continued growth for the Alcohol and Drug Abuse Institute (ADAI). This has been reflected in the continued research productivity of the Institute’s Research Scientists, our move into new office space, and the award of a major grant from the National Institute on Drug Abuse.

New projects initiated by Institute Research Scientists have been funded by both federal and non-federal sources. The primary sources of our federal funding continue to be the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the National Institute on Drug Abuse (NIDA). The bulk of the non-federal funding has come from the State’s Division of Alcohol and Drug Abuse (DASA), the Juvenile Rehabilitation Administration (JRA), and the Washington Institute for Mental Illness Research and Training. Additional funds were received from the Robert Wood Johnson Foundation. The increased level in grant support during the biennium reflects the ongoing success of our Research Scientists in obtaining external funding. The research supported by these funds is diverse, ranging from social psychological studies of alcohol’s influence on women’s perception of risk for date rape, to a study evaluating interventions to get “street youth” to seek care for alcohol, drug, and other psychosocial problems, to the clinical evaluation of combined behavioral and pharmacological treatments for alcohol dependence. Articles published in peer-reviewed journals and book chapters authored by Institute Research Scientists have contributed to better understanding of factors contributing to substance use and abuse, the negative social and physical consequences experienced by both adults and adolescents from this abuse, and methods that can facilitate behavior change and improve treatment outcomes among substance abusers.

In the last Biennial Report, concerns about the Institute’s space shortage were raised. Our two houses on campus were fully utilized at the time. In addition, a number of projects were housed off-campus in proximity to subject recruitment sites, while others were off-campus due to lack of space in the main ADAI offices. A goal had been to find both short- and long-term solutions to our space limitations. I am pleased to say that these concerns have been addressed, though not without some complications along the way. For a period of time beginning in the summer of 2000, we expected that ADAI would be forced to relocate because Sound Transit, the regional transportation authority, planned to build a University District Station for its light rail system on the site of our Institute offices. Working with the University’s Capital and Space Planning Office and the Real Estate Office, replacement space was located in the University District Building, located on NE 45th Street between 11th and 12th Avenues. Sound Transit agreed to pay for costs associated with remodeling, moving, and leasing of the space. With only a month before our scheduled move, Sound Transit was found to have significant financial problems because of cost overruns on the proposed light rail system. Sound Transit told the University to discontinue any proposed moves of programs and individuals; thus our hope for new space was initially dashed. However, it was felt that the proposed move made good sense from a number of perspectives. Keeping this goal in mind, negotiations with the University led to their willingness to relocate the Institute into the University District Building, assuming the costs of remodeling and moving and defraying a portion of the space lease. The Institute moved into its new location in June of 2001. The move brings together most of the Institute’s projects and staff under one roof, allows for future growth, and provides the library the space it needed to display its full collection and provide patron work space. While still adjusting to the transition, the outcome of the move seems positive overall. To say the least, it has been a “moving experience!”

A major element in both the Institute’s growth and its need for additional space was the award of a five-year, $11 million grant from the National Institute on Drug Abuse to become a Regional Research and Training Center (RRTC) in the National Drug Abuse Treatment Clinical Trials Network (CTN). The goal of the CTN is to move empirically supported substance abuse interventions, both behavioral and pharmacological, into community based treatment programs. A related goal is to generate ideas from
community practitioners about issues in their experience that could be developed into research protocols, assuring clinical relevance of the research being conducted within the CTN. It is seen as a collaborative, bi-directional process that is meant to “bridge the gap” between substance abuse research and practice. Each of the 14 Regional Research and Training Centers is expected to have an administrative core, a data management unit, a cadre of researchers having expertise in substance abuse treatment, and a group of at least five affiliated community-based treatment programs. Our Center has eight treatment programs affiliated with it, ranging from Yakima to the east, Vancouver to the south, Bremerton to the west, Everett to the north, with four programs in the Seattle-King County area. We are in the midst of developing the data management unit, which will be a resource not only to our RRTC but also to other Research Scientists at the Institute and substance abuse researchers at the University. We are also in the process of developing research concepts that can be evaluated further for development into research protocols. The concepts initially considered for development reflect both areas of interest to UW researchers and identified areas of need by community based treatment providers. These include the best methods to train counselors in motivational interviewing skills, the benefit to dual disordered clients to have psychiatric evaluation and medication management integrated into substance abuse treatment compared to a more typical referral out for such services, and interventions for methamphetamine abusers that takes into account the degree of cognitive impairment associated with abusing methamphetamine.

It is our hope that the accomplishments of the Institute’s programs and its Research Scientists are reflected in the details of this report and are reflective of the continued growth and vibrancy of ADAI within the research community at the University of Washington, the State, and the nation.
Funding of intramural research at the Institute reached a new high during the 1999-2001 biennium, led by an award from NIDA making ADAI the center for the Washington Node in the National Drug Abuse Treatment Clinical Trials Network (CTN). Other new and continuing studies were underway during this time, with federal funding from the National Institute on Alcohol Abuse and Alcoholism and the National Institute on Drug Abuse; state funding from the Washington State Division of Alcohol and Substance Abuse, Juvenile Rehabilitation Administration, and Washington Traffic Safety Commission; funding from King and Kitsap Counties; private foundation funding from the Robert Wood Johnson Foundation and the Alcohol Beverage Medical Research Foundation; and the ADAI Small Grants Program. As in previous years, collaborative work with colleagues outside of ADAI remains an important Institute goal; many of the studies listed below involve researchers in other UW departments and at other universities. A list of previously funded, continuing projects follows the new projects.

Summaries of New Projects

Alcohol and Rape Risk ≈ P.I., Jeanette Norris, Ph.D.

Sexual assault by acquaintances is a serious problem for young women. Approximately one in four experiences either rape or attempted rape, the overwhelming majority of which are committed by acquaintances. Alcohol consumption by the victim, assailant, or both is involved in more than half of these assaults. One key element of sexual assault is early perception of risk, which enables a woman to respond effectively and extricate herself from the situation before it escalates. In assessing risk and responding to it, women make a series of primary and secondary cognitive appraisals. Primary appraisals are those directed specifically to acknowledging and assessing the level of risk in a particular situation. Secondary appraisals involve weighing the ability to respond effectively against psychological barriers. A woman's own alcohol consumption and her perception of the assailant's consumption can affect this cognitive appraisal process. The proposed project, funded by NIAAA, will investigate alcohol's psychological and expectancy effects on cognitive appraisals and responses to sexual assault. It will employ theoretical models of cognitive appraisal and coping and response conflict related to alcohol consumption.

Descriptive Study of TASC Felony Services in Washington State ≈ P.I., Linda Brown, RN, Ph.D.

Treatment Alternatives to Street Crimes (TASC) Felony Services programs were developed in the early 70s in response to a growing recognition of the relationship between drug abuse and crime, and the potential of treatment to reduce drug-related crime. TASC programs were designed to provide services to drug dependent, adult felony offenders that would facilitate community based treatment, decrease drug abuse, criminal activity and incarceration, and link the criminal justice system and drug treatment systems. In Washington state, responsibility for TASC programs, which began with federal and then state law enforcement funding, moved to the state Division of Alcohol and Substance Abuse Services in 1998. This DASA-funded study will describe TASC Felony Services in six counties of Washington in order that DASA may more completely evaluate the organization and functioning of TASC programs.

Descriptions will include the philosophy, mission and goals, and the organization of each program; program relationships with their respective communities and the criminal justice system; and an overview of the services provided to include examination of several specific aspects. Similarities and differences among the programs and the issues they each face will be identified and examined.
Driver Improvement Study  ≡  P.I., Dennis M. Donovan, Ph.D.

An area of growing public concern is aggressive driving or "road rage," a set of behaviors which may range from swearing under one’s breath at another driver who has irritated you to running another car off the road or some other form of overt violence. Relatively little is known about those individuals who are involved in the more overt road rage incidents, however it appears that they share a number of personality, attitudinal, and behavioral characteristics with other high-risk drivers, including drivers convicted of DUI. Previous studies have shown that drivers with multiple non-DUI violations are at increased risk for being arrested and convicted for drinking and driving and that they may also be more prone to aggressive driving and road rage. This study, funded by the Washington Traffic Safety Commission, has two main objectives: 1) determine the relationship among drinking behavior, driving aggression, and driving behaviors through self-reports collected from an anonymous survey among participants in the Department of Licensing Driver Improvement Program and from the general driving population; and 2) develop, implement, and evaluate a new driver improvement program designed to reduce the likelihood of alcohol-impaired driving and driving aggression.

Evaluation of the Adolescent Treatment Enhancement Projects  ≡  P.I., Megan Rutherford, Ph.D.

Funded by King County Mental Health, Chemical Abuse & Dependency Services Division, on Evaluation of the Adolescent Treatment Enhancement Project, this project will implement enhanced treatment capacity for 200 adolescents who are involved in the juvenile justice system, or who are at high risk for involvement, and who are members of one of five special populations: Hispanic/Latino, Asian, African-American, Native American, or sexual minority. The purpose of the project is to increase the number of youth from these special population groups who are offered effective treatment as an alternative to juvenile justice sanctions. The project will document the contribution of increased attention and resources to outreach and engagement-focused case management to increased treatment referrals, enrollment, engagement and retention for the special populations served. It will demonstrate that such young people can be offered treatment in lieu of juvenile justice sanctions with positive outcomes. It will further demonstrate the benefit of explicitly providing multicultural alliance and leadership opportunities for these young people and the degree to which these measures can improve treatment retention and recovery.

Kitsap Outcome Evaluation  ≡  P.I., Megan Rutherford, Ph.D.

This project will expand the previous outcome evaluation study for the Kitsap County Adult and Juvenile Court, to include a process evaluation for juvenile drug court and an outcome evaluation for adult drug court. The outcome evaluation will assess the clients’ reduction in recidivism, reduction in substance use, improvement in other areas of life functioning, and the relationships of these outcomes to the structure of the treatment and court program.

National Drug Abuse Treatment Clinical Trials Network – Washington Node  ≡  P.I., Dennis Donovan, Ph.D.

In January 2001, the Institute received an $11 million five-year grant from NIDA to join the CTN as the Washington Node, one of fourteen state and regional nodes throughout the country. ADAI and UW researchers from many disciplines will form the node’s Regional Research and Training Center (RRTC), which will collaborate with community-based treatment centers.

The NIDA CTN has as its primary purpose the development, implementation, and evaluation of behavioral and pharmacological therapies for drug abuse, targeted at treatment as delivered in real world settings. It will integrate behavioral and pharmacological research as a means of informing policy, therapy development, and the evaluation process, with a goal of contributing meaningfully to the
improved effectiveness of new and promising therapies developed within the larger Clinical Trials Network.

Eight clinical programs have been identified for inclusion in the Washington Node. These programs have been selected to represent a range of patient populations, with respect to ethnic background and primary drugs of abuse. Many of these populations, such as Native Americans and methamphetamine abusers, are currently underrepresented in other Nodes in the CTN. The eight programs also represent a variety of treatment modalities and geographic locations throughout the State of Washington.

**Road Rage**  
**P.I. Dennis M. Donovan, Ph.D.  =  Project Director: Brent Baxter, Ph.D.**

Funded by the Washington Traffic Safety Commission, this project will study the timely issue of "Road Rage" or aggressive driving. Researchers will analyze the Aggressive Drivers Apprehension Team (ADAT) database of aggressive driving arrests and compare it with both statewide and regional databases of the general driving population. This will allow them to compile a profile of aggressive drivers and to propose a set of interventions aimed at reducing aggressive driving. Such interventions could potentially be implemented by the State's court system or Department of Licensing.

**SSI Battelle**  
**P.I. Gary B. Cox, Ph.D.**

Funded by DASA, this project has two primary aims: 1) to estimate the impact of the Contract with America Advancement Act (which terminated the Social Security Administration’s Disability Insurance (DI) and Supplemental Insurance SSI) benefits for persons diagnosed with substance abuse problems; and 2) to estimate based on findings from AIM 1) the economic impact of the benefits termination on federal, state, and local government resources for the people denied these benefits as a whole and in subgroups. ADAI will be responsible for building and documenting the analytic database that will be used in determining outcomes for former recipients of these benefits.

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### Continuing Projects from Previous Years

- **Alcohol Use and Decompression Sickness in Recreational Divers**  
  P.I., Barbara C. Leigh, Ph.D., M.P.H.

- **Attrition While Awaiting Drug Treatment (Project START)**  
  P.I., Dennis M. Donovan, Ph.D.  
  Project Director, David Rosengren, Ph.D.

- **Chemical Dependency Disposition Alternative (CDDA)**  
  P.I., Megan Rutherford, Ph.D.

- **Computer Modeling of Alcohol Services Research Data**  
  P.I., Gary B. Cox, Ph.D.

- **Enhancing Recall of Sexual and Drug Injection Partners**  
  P.I., Devon D. Brewer, Ph.D.

- **HIV, Hepatitis, STD and Reproductive Health Risk Behaviors among Female Seattle Methamphetamine Users**  
  P.I., E. Michael Gorman, Ph.D., M.S.W., M.P.H.
Implicit Cognition and HIV Risk Behavior in Drug Users
  P.I., Barbara C. Leigh, Ph.D., M.P.H.

Interviewer Factors in the Elicitation of HIV Risk Networks  [still going as of July 99?]
  P.I., Devon D. Brewer, Ph.D.

Methadone Maintenance in Primary Care
  P.I., Joe Merrill, M.D.

Motivational Enhancement to Reduce Risk of Street Youth
  P.I., Peggy L. Peterson, Ph.D., M.P.H.

Outcome Analyses of Persons in Chemical Dependency Treatment
  P.I., Brent L. Baxter, Ph.D.

Neuronal Mediation of Ethanol-Induced Taste Aversions
  P.I., Todd Thiele, Ph.D.

NW High Intensity Drug Trafficking Area Drug Court Evaluation
  P.I., Gary B. Cox, Ph.D.

Pharmacological and Behavioral Therapies with Alcoholics
  P.I., Dennis M. Donovan, Ph.D.

SSI Project Evaluation
  P.I., Gary B. Cox, Ph.D.

Substance Use and Predictors of Risk Behavior
  P.I., Barbara C. Leigh, Ph.D., M.P.H.

Treatment Outcomes of DASA Clients
  P.I., Molly Carney, Ph.D.
EXTRAMURAL RESEARCH

ADAI's Small Grant Program supports research in all areas of alcohol and drug abuse by making research funds available to University of Washington faculty. Monies to support this program come from state Initiative 171 funds. Awards are made twice yearly through a peer review process and are based on scientific merit and relevance to the field of alcohol and drug abuse. The principal goal of the Small Grants Program is to stimulate new research by providing initial funding to new investigators and to promising pilot projects, which may be ultimately developed into full research studies with outside grant support. Since its inception, the Small Grants Program has awarded 308 grants to UW researchers, totaling over $2,825,000 dollars.

During the 1999-2001 biennium, the Small Grant Scientific Review Committee and the Final Review Committee reviewed four rounds of applications. Researchers from twelve University schools and departments submitted a total of 33 proposals during this period; of these, fifteen were awarded funding. Total funding for ADAI Small Grants during this two-year period totaled $284,505, an increase of 2.4% over the previous biennium (and the highest level of funding ever allocated for this program).

At the initial review meeting, each application received a detailed review by at least two members of the Scientific Review Committee, a careful discussion of scientific merit by the full committee, and then a vote on the grant's overall merit. Written comments and documentation of the committee's discussion were presented to the Final Review Committee, which chose the top grants to receive funding. For both funded and non-funded applications, anonymous comments of the reviewers were returned to the investigators to provide constructive feedback.

Grants Awarded October 1999:

Utilities for Mental Health Outcomes among Individuals with Co-occurring Substance Use Disorders and Schizophrenia. Dan Kivlahan, Ph.D., Associate Professor, Psychiatry and Behavioral Sciences ($15,251)

Substance use disorders are a significant problem among individuals with schizophrenia, and are associated with deleterious consequences including poor treatment adherence, high institutionalization costs, poor psychosocial functioning and treatment outcome. Because this population is so difficult and expensive to treat, it is important to identify treatments that are cost effective. Cost-utility analysis (CUA) is a widely used method that incorporates measures of effectiveness and importance of different outcomes. To conduct CUA studies, health utilities must be measured. Preliminary literature indicates that it is feasible to measure mental health utilities among individuals with schizophrenia; however, no studies have tested the feasibility of this methodology with individuals with co-occurring schizophrenia and substance use disorders.

The objective of this study is to determine the feasibility of measuring mental health outcome utilities among individuals with co-occurring substance use disorders and schizophrenia. This effort is consistent with Veterans Affairs efforts to identify cost-effective, patient-centered care. Veterans who have a diagnosis of schizophrenia and substance use disorders will be invited to participate in this study. We will determine whether it is feasible for participants to complete the measurement of utilities using a state-of-the-science multi-media computerized assessment. We will identify inconsistencies in responses, and whether symptom severity (schizophrenia and substance use) is associated with frequency of making inconsistent responses and repairing inconsistent responses. If this method is shown to be feasible with this sample, we will report the variability of utility values obtained, in preparation for future studies. If this approach is not feasible, we will better understand the limitations of this methodology and identify the limits of generalizing utility weightings derived from individuals with these co-occurring conditions.
Barriers to Care and the Impact of Delaying Treatment for Injection Drug Use-Related Soft-Tissue Infections.  **Joseph O. Merrill, M.D., M.P.H., Acting Instructor, Medicine, and Research Scientist, Alcohol and Drug Abuse Institute** ($19,824)

**Background:** Soft tissue infections are common medical complications in injection drug users and result in significant morbidity and medical costs. Injection drug users' delay in seeking care may alter the natural history of soft tissue infections and lead to adverse health outcomes and increased health care utilization. While previous studies have identified a number of barriers to care in this population, none has evaluated how these barriers impact the natural history and health outcomes of soft tissue infections.

**Purpose:** The aims of the proposed study are to determine the clinical features and natural history of soft tissue infections and evaluate reasons for delay in seeking care among injection drug users. We will also evaluate the impact of delaying care on health outcomes and health care utilization.

**Method:** The proposed study will use cross-sectional interviews and medical record reviews of injection drug users with soft tissue infections who seek care at the Harborview Medical Center Emergency Department. Descriptive statistics will be used to characterize the clinical features and natural history of soft tissue infections. Linear regression will be used to evaluate the association of potential barriers to care with a delay in seeking care. Logistic regression will be used to identify factors, including delay in seeking care, that predict hospitalization in this setting.

**Significance:** Identification of barriers to care that result in delayed treatment and adverse health outcomes for injection drug users will allow development of rational programs to improve the medical care of this underserved population. This study will also provide pilot study data for a future randomized control trial to study interventions that reduce barriers to care and ultimately improve the health status of injection drug users.

Relationship of Substance Use, Psychiatric Symptoms, and Social Networks in Persons with Severe Mental Illness at High Risk for Violence.  **Richard Ries, M.D. Professor, Psychiatry and Behavioral Sciences, and Medical Director, Outpatient Psychiatry and Dual Disorders Program, Harborview Medical Center** ($19,994)

Co-morbid alcohol and drug disorders occur in 40-80% of the severely mentally ill (SMI). Use of substances by this population can result in homicidal violence as evidenced by several high profile cases headlined in the media. Although tragic, these relatively uncommon events overshadow the more customary violence associated with addiction in this population, which includes the focus of this proposal: non-lethal physical assaults, verbal threats, and victimization. Numerous publications document the strong relationship between substance use and violence in the severely mentally ill, yet the almost exclusive reliance on cross-sectional and epidemiological approaches makes it difficult to understand the complex relationships between substance use and violence.

To date there have been no longitudinal prospective investigations examining 1) how alcohol and drug use affects the recurrence of violence in high-risk SMI individuals; 2) how substance use influences psychiatric symptoms and violence in the SMI; and 3) how factors, such as social network composition, influence substance use and violence in these individuals. Such studies are necessary before more focused preventive and treatment initiatives can be developed for this high-risk population. However, before a larger study can be undertaken to examine these questions, a small pilot project is needed to evaluate some key issues including the 1) enrollment and longitudinal retention rates in this difficult to engage population; 2) enrollment and longitudinal retention rates of significant others; and 3) concordance in key risk factors for violence gathered from subjects, significant others, and clinical case managers. Building on experience from our NIDA funded representative payee study of a dually diagnosed SMI population, this project will provide in-depth information about effective ways to engage these high-risk individuals that can be used in future clinical research studies.
Additional Endogenous Agonists for the Cannabinoid Receptor in Brain.  **Nephi Stella, Ph.D., Assistant Professor, Pharmacology**  ($19,370)

Marijuana and hashish are prevalent drugs of abuse in western society. Delta-9 tetrahydrocannabinol (the active ingredient) activates cannabinoid receptors, producing both psychotropic and therapeutic effects. A current line of research in molecular pharmacology is focused on the mechanism of action of delta-9 tetrahydrocannabinol, with the objective of identifying a new generation of cannabinoid based medicines that lack side effects, tolerance and/or addiction properties. Cannabinoid receptors are normally engaged by endogenous agonists, the endocannabinoids. To date, one substance found in brain fulfills the necessary criteria to be considered an endocannabinoid. The aim of this proposal is to identify and characterize additional endocannabinoids in brain, results that would be pivotal in designing efficient cannabinoid-based medicines.

**Grants Awarded March 2000:**

The Reinforcing Effects of Alcohol: Is Dopamine Required?  **Michelle D. Brot, Ph.D., Research Assistant Professor, Orthodontics**  ($19,938)

It is widely believed that dopamine (DA) is a critical neurotransmitter in mediating the reinforcing properties of drugs of abuse, yet in the case of alcohol, there are many other neurotransmitters that have been implicated in its rewarding effects (e.g. GABA, serotonin, glutamate, opiates). These studies will test whether DA in particular is required for self-administration of alcohol. This will be assessed using DA-deficient (DA-/-) mice and wild-type (WT) controls, which will be trained to orally self-administer alcohol. Mice will be exposed to alcohol gradually by implementing the sucrose-fading methodology, in which they are first habituated to drinking water from the tube, then sucrose is introduced into the water, then the drug is added to the sucrose solution, and finally the sucrose is faded out. Following the training period, when sucrose has been entirely faded out and the mice are consuming pure drug solution, a preference test between water and alcohol will determine whether the mice find alcohol rewarding.

The results will be compared among DA-/- groups, and ad lib drug-consuming WT group, and a yoked control WT group that will have been provided with the same drug dose as the DA-/- mice consumed each day. Because DA-/- mice consume very small volumes in the absence of DA, it is necessary to have an accurate way to measure the amount consumed. This is feasible using a lickometer, which counts the actual number of licks the mouse makes to each substance. The hypothesis is that if DA is critical for alcohol's rewarding or addictive properties, then DA-/- mice will not prefer drinking alcohol to water. Alternatively, DA-/- mice might show a similar (high) preference ratio for alcohol compared to that of the control WT groups if DA does not play an important role in the reinforcing effects of alcohol.

Integrating Clinical Practice Guidelines for Smoking Cessation Into Primary Mental Health Care for Veterans with Posttraumatic Stress Disorder.  **Miles McFall, Ph.D., Associate Professor, Psychiatry and Behavioral Sciences**  ($20,000)

**Introduction:** Most veterans with posttraumatic stress disorder (PTSD) who smoke do not follow through with treatment upon referral to a smoking cessation specialist. Treatment of these patients is complicated by the fact that anxiety and depression may be exacerbated by quit attempts and increase risk for relapse to smoking. Therefore, referral to smoking cessation clinics may constitute suboptimal intervention for veterans with PTSD who smoke. This project aims to (a) determine the feasibility of integrating smoking cessation into primary mental health care for veterans with PTSD and (b) gather preliminary data showing superior outcomes from an integrated care approach, compared with referral to a smoking specialty clinic.

**Method:** This randomized controlled clinical trial will use a 2-group design and an intention-to-treat analysis. Patients admitted to a Veterans Affairs (VA) PTSD clinic will be randomly assigned either to integrated care for PTSD and tobacco use administered by mental health clinicians (n=25), or to usual care for smoking provided by a specialized Smoking Cessation Clinic (n=25). After subjects receive five
sessions of smoking cessation treatment, smoking outcomes will be assessed at weeks 8, 16, and 24. Effects on psychiatric and functional status will be measured at week 24. Exit interviews and review of documentation provided by clinicians will verify that interventions were implemented. **Analysis Plan:** Point-prevalence of smoking abstinence and other dichotomous measure of smoking outcomes will be analyzed by x2 tests and odds ratios. Continuous measures of smoking outcomes and psychiatric and functional status will be analyzed using t-tests. A primary goal of analysis is to establish that our effect size estimate (11% minimum difference between conditions) is realistic, for computing power analyses supporting subsequent clinical trials. **Significance:** Demonstrating the feasibility and efficacy of an integrated approach to smoking cessation for mentally ill veterans will potentially improve access to, and compliance with, smoking cessation treatment for this large population. It will also provide a new model for intervention that addresses dynamics between nicotine dependence and psychiatric symptoms.

**Predictors of Symptom Severity in the Alcohol Withdrawal Syndrome: Testing a Patient Self-Report Screening Instrument.**  
*Joseph P. Reoux, M.D., Assistant Professor, Psychiatry and Behavioral Sciences* ($19,198)

Appropriate management of alcohol withdrawal syndrome (AWS) is a critical challenge facing addiction treatment providers. Non-optimal management can result in serious medical complications or unnecessary utilization of costly services such as hospitalization. While many patients experiencing AWS require little medical management, others experience emergent conditions such as delirium treatments (DTs). A history of DTs helps identify patients at high risk for complicated AWS, however most patients have not had previous DTs and predicting the severity of the AWS or the intensity of medical monitoring needed for these patients is less well delineated. Given evidence that inpatient management is not necessary for all patients with AWS, treatment programs increasingly offer outpatient detoxification. Empirically tested predictors of the course of AWS are needed to identify patients most appropriately managed in the outpatient setting. While instruments exist to guide treatment by monitoring the severity of active withdrawal symptoms (i.e. CIWA-Ar), no assessment tool is available to predict which alcohol dependent individuals will require close monitoring and medical intervention for their AWS. The intent of this project is to evaluate the validity of a brief patient self-report screening instrument to predict whether or not the severity of AWS in alcohol dependent patients will need medication to manage the AWS as indicated by an accepted threshold score on the CIWA-Ar. An effective screening instrument would assist treatment providers in making more efficient and cost effective decisions about management of AWS.

**Grants Awarded October 2000:**

**Role of P-glycoprotein in Human Opioid Pharmacodynamics.**  
*Evan D. Kharasch, M.D., Ph.D., Professor, Anesthesiology* ($20,000)

There is considerable clinically significant and largely unexplained inter- and intra-individual variability on the dose-effect relationship for opioids. Although pharmacokinetic differences exist and account for some of this variability, inter- (and possibly) intra-individual differences in pharmacodynamics (blood concentration-CNS effect relationship) are substantially greater. Nevertheless, the mechanism of such differences is poorly understood. The drug efflux pump P-glycoprotein (Pgp), located on the luminal surface of endothelial cells in the brain, is an integral component of the blood-brain barrier and regulates drug access in the CNS. It was recently discovered that opioids such as morphine, fentanyl, and methadone are substrates for P-gp in vivo. In animals, P-gp is a major determinant of opioid CNS access and pharmacodynamics. However the role of P-gp in therapeutic/addicting opioid CNS access and pharmacodynamics in humans is totally unknown. The aim of this investigation is to test the hypothesis that opioids (specifically morphine and fentanyl) are substrates for human brain P-gp, and that P-gp is a major determinant of opioid pharmacodynamics and clinical effect. A recently identified human brain P-
gp inhibitor will be used as an in vivo probe to test this hypothesis in a series of clinical studies measuring blood opioid concentrations and CNS effects. Using a randomized, double-blind, placebo-controlled, balanced crossover design, we will evaluate the clinical effects (pupil diameter change and subjective self-assessment of sedation, energy level, confusion, clumsiness, anxiety, and nausea) and arterial blood concentrations of morphine and fentanyl after inhibition of P-gp or control. The hypothesis will be tested by comparing clinical effects and pharmacodynamic parameters (EC50 and ke0 determined by pharmacokinetic-pharmacodynamic modeling) with and without P-gp inhibition. Verification of the hypothesis will yield the first report of P-gp determination of therapeutic / addicting opioid CNS access and pharmacodynamics, and will spawn an entire field of human investigation regarding mechanisms of opioid effect, variability, toxicity, tolerance, and addiction.

Teensmart / Informa-T /Ayuda-T: Exploring the Acceptability and Feasibility of Conducting an Internet Web-Based ATOD and Sexual Risky Prevention Intervention for Latino Adolescent Youth and their Families. Catherine Strachan Lindenberg, RN, Dr.P.H., Associate Professor, Family and Child Nursing ($14,609)

This project will assess the acceptability and feasibility of a theory-driven, empirically based, bilingual, web-based, Youth Risk and Resilience Multi-Scale Profile (YMSP, and a 10 module psycho-educational Risk and Resilience curriculum, for Latino youth and their families. The measures and the prevention curriculum, based on the Social Stress Model for Substance Abuse and Other Risk Behavior Prevention, are designed to promote protective factors (personal competence, and positive family support and peer influence) and prevent or reduce alcohol, tobacco and other drug use (ATOD) and risky sexual behaviors (RSBs) among Latino youth and their families. A voluntary sample of 20 Latino high school adolescent boys and girls from Cleveland High School and their parents will participate in this pilot study. Adolescents will pilot test the self-administered bilingual web-based YMSP and the Risk and Resilience Prevention Curriculum. Both qualitative (focus groups with adolescent boys and girls and parents) and quantitative research methods (self-administered web-based questionnaires) will be used to achieve the pilot study objectives. Findings from this pilot study will support the future development of a NIH sponsored R01 grant proposal to conduct a randomized field trial to assess the efficacy of this web-based bilingual adolescent telehealth prevention intervention to reduce and/or prevent ATOD and RSBs among Latino teens.

The Effect of Viral Mediated Overexpression of 5-HT 1B Receptors in Rat Nucleus Accumbens on Cocaine Sensitization. John Neumaier, M.D., Ph.D., Assistant Professor, Psychiatry and Behavioral Sciences ($19,962)

Drug addiction involves many adaptations in brain function, including sensitization, tolerance, and withdrawal. For example, cocaine induces changes in the function of neurotransmitters and their receptors, neuronal circuitry, and complex behaviors of rats and other research animals; many of these animal observations have been confirmed in studies of brain function of addicted humans. These changes are likely to account for the physical and psychological processes that lead to the abuse of psychoactive drugs; elucidating these mechanisms may offer us insights into more effective treatments for addiction. Similarly, manipulations of various neurotransmitter systems may modulate the acute and long-term effects of cocaine on brain function. For example, central 5-HT 1B serotonin receptors modulate cocaine's actions, but the available data is complex and sometimes contradictory. It is our hypothesis the axon terminal 5-HT1B receptors, contained within nucleus accumbens neurons that project to the ventral tegmental area, disinhibit dopamine transmission and contribute to several important effects of serotonergic drugs on cocaine related behaviors. However, the 5-HT1B receptor has been technically difficult to manipulate in a single neuron population. We propose to use viral mediated gene transfer to increase 5-HT1B expression in nucleus accumbens neurons, allowing the hypothesis to be addressed directly. Our preliminary data indicate that overexpression of 5-HT1B receptors in these neurons alters
the rewarding and aversive properties of cocaine. We propose to test whether selectively increasing 5-HT1B receptor expression in nucleus accumbens neurons will sensitize (enhance) the biochemical and behavioral responses of rats to acute and subchronic cocaine administration as measured by cFOS expression, delta-cFosB expression, and cocaine-induced hyperactivity. The results may suggest a role for 5-HT1B receptors in cocaine addiction, leading to redefined neurobiological models for drug addiction and improved therapies for its treatment.

The Role of Specific Neuropeptide Y Receptors in Neurobiological Responses to Ethanol and Diazepam.  
**Todd Thiele, Ph.D., Research Scientist, Psychology and Alcohol and Drug Abuse Institute ($19,728)**

Little is known about the role that modulatory neuropeptides play in ethanol-seeking behavior. One promising candidate is neuropeptide Y (NPY), a 36 amino acid neuromodulator that is distributed widely throughout both the peripheral and central nervous systems. Genetic linkage and neurochemical analyses or rats that were selectively bred for alcohol preference indicated the NPY may be involved with high alcohol consumption in these rats. Consistent with this hypothesis, we have found that NPY knockout mice drank significantly more ethanol, and recovered from ethanol-induced sedation significantly sooner, than wild-type littermate mice. On the other hand, transgenic mice that overexpress NPY drank more ethanol and were more sensitive to the sedative effects of this drug. These data provide direct evidence that ethanol consumption and resistance are inversely related to NPY levels in the brain. This project will address the following questions: (A) Which specific NPY receptor(s) are involved in regulating the effects of NPY on sedation caused by high doses of ethanol and locomotor activation caused by low doses of ethanol? To address this question, we will assess ethanol-induced sedation and ethanol-induced locomotor activation in mice with targeted gene disruption of NPY Y1, Y2, or Y5 receptors. (B) Are NPY receptor(s) involved in regulating sedation caused by high doses of diazepam and locomotor activation caused by low doses of diazepam? We will assess diazepam-induced sedation and diazepam-induced locomotor activation in mice with targeted gene disruption of Y1, Y2, or Y5 receptors to determine if the NPY system modulated neurobiological effects of another abused drug. Determining how NPY acts to influence responses to ethanol is critical to a complete understanding of the neurobiological mechanisms that determine alcohol use and abuse. Such knowledge will be useful for the development of pharmacological treatments targeted at preventing excessive alcohol intake.

**Grants Awarded March 2001:**

**Alcohol and Sexual Disinhibition among College Students.**  
**William George, Ph.D., Associate Professor, Psychology ($20,000)**

Alcohol-related sexual risk-taking is a problem among American college students. Potential risks of intoxicated sex include sexual assault, STD/HIV transmission, and unplanned pregnancy. However, little is known about how alcohol may engender sexually risky behavior. Alcohol has long been popularly assumed to disinhibit sexual expression, but the mechanisms behind this phenomenon have not been rigorously examined. Current theory suggests that people become more sexual after drinking because they expect such an effect; however, numerous studies have shown that cognitive functioning is impaired at higher doses of alcohol, such that expectancies may not be so influential over behavior. Our overarching hypotheses are as follows. Alcohol expectancies determine post-drinking sexual behavior only at low doses of alcohol. At higher doses, alcohol expectancies are less influential over behavior because cognition is impaired. Post-drinking sexual behaviors at higher doses of alcohol are determined by more primitive cognitive structures, termed implicit attitudes. We plan to measure implicit and explicit attitudes in 160 undergraduate men and women. Subjects will be administered no alcohol or a low or high dose of alcohol. Executive cognitive function will be measured before and after the beverage administration. After the beverage administration, subjects will be asked to look at sexually explicit images on a computer screen. The amount of time spent looking at each image (“sexual interest”) will be covertly recorded. In addition, subjective measures of sexual arousal will be made. We hypothesize that sexual interest and arousal will be a function primarily of implicit sexual attitudes among cognitively-
impaired intoxicated subjects, of alcohol expectancies among less-cognitively-impaired subjects, and of explicit sexual attitudes among sober subjects.

A Parametric Examination of the Effects of 60-Hz Magnetic Fields on Ethanol Consumption in the Rat. Henry Lai, Ph.D., Research Professor, Bioengineering ($19,315)

The focus of the proposed research stems from concerns about the biological and health effects of exposure to magnetic fields in our environment. Magnetic fields are emitted from all electrical household appliances and machines in occupational settings. Millions of people are being chronically exposed to these fields. There is evidence from our laboratory and others that exposure to magnetic fields below the national and international magnetic field exposure guidelines causes an increase in activity of endogenous opioids in the brain of rats. Since opioid activity in the brain has been associated with an increase in ethanol consumption, we propose to investigate whether acute exposure to magnetic fields can enhance ethanol-drinking behavior in the rat. The initial challenge is to identify specific magnetic field exposure parameters that interact with variables that influence ethanol consumption. This study proposes to investigate the effects of two variables on ethanol consumption in the rat, the intensity of magnetic field (0.0 mT (sham), 0.05 mT, 0.1 mT, and 0.5 mT) and the delay (30, 60, and 120 min.) between exposure and access to 10% ethanol (v/v). Twelve groups of animals will be matched based upon a 14-day two-bottle ethanol preference test given prior to the magnetic field exposure sessions to determine the amount of any lasting ethanol preference changes. Finally, if effects on ethanol consumption are observed in the parametric study, two studies will be run using the most efficacious parameters of magnetic field exposure. The first experiment will determine whether the effects of magnetic exposure are specific to ethanol by measuring changes in water intake following exposure. In the other experiment, animals will be given an opioid antagonist prior to magnetic exposure to determine the involvement of endogenous opioid systems on magnetic field-induced ethanol intake.

Normative Feedback Intervention Project. Mary E. Larimer, Ph.D., Research Assistant Professor, Addictive Behaviors Research Center, Psychology, and Psychiatry and Behavioral Science. ($17,323)

An estimated 44% of college students nationwide report periodic heavy drinking episodes with about half of these engaging in multiple heavy drinking episodes on a monthly basis. Given the established relations among heavy drinking and academic, legal, interpersonal and health problems, identification of effective, low-cost interventions for this population represents an important endeavor.

Interventions designed to correct misperceived drinking norms have recently demonstrated efficacy for addressing heavy drinking among college students. Unfortunately, individual brief interventions that include normative feedback have typically not been designed in a way that allows unique evaluation of this component. The proposed research seeks to evaluate the unique impact of personalized normative feedback on drinking patterns and associated problems among heavy drinking college students. In addiction, the motivational mechanisms underlying the efficacy of normative influence in alcohol interventions will be explored in detail.

Participants will include 300 heavy drinking University of Washington students who will be randomly assigned to intervention conditions. After completing a baseline computer assessment, participants in the intervention condition will receive personalized normative feedback highlighting actual drinking norms and the discrepancy between their drinking behavior and typical student drinking practices. Follow-up assessments will take place at three months and six months post-baseline.

The goals of this project are to assess the effectiveness of a personalized normative-feedback alcohol intervention, assess the role of motivation in this process, and to lay the foundation for a larger study examining the unique contribution of brief intervention components.
Alcohol and Executive Cognitive Functioning: Influences on Men's Judgments and Self-Reported Likelihood of Engaging in Sexual Assault.  Jeanette Norris, Ph.D., Senior Scientist, Alcohol and Drug Abuse Institute  ($19,993)

Alcohol consumption is consistently implicated in men's sexual assault of women. "Alcohol myopia" is theorized to facilitate sexual assault by narrowing a drinker's attention to a subset of environmental and internal cues. The mechanisms underlying this myopic response are not well understood. One possible mechanism through which alcohol might facilitate sexual assault is by physiological impairment of executive cognitive functioning (ECF). ECF includes "higher-order" mental abilities, such as self-regulation, and the ability to use cues in the environment and within oneself to adaptively adjust behavior. Research has documented that alcohol intoxication disrupts ECT, and that it may serve as an underlying etiological mechanism for the alcohol-aggression relationship. However, no study to date has applied this reasoning to alcohol-related sexual assault. By disrupting ECF, alcohol may decrease men's ability to accurately perceive situational cues related to a woman's refusal for sex. One study will investigate whether ECF might mediate differences between intoxicated and sober non-problem drinking college men's judgments of sexual assault and their subsequent self-reported likelihood to pursue sexual intercourse in the face of a woman's refusals. In addition to alcohol consumption, the proposed study will vary two contextual variables thought to affect men's responses: female story character alcohol consumption and prior consensual sexual intercourse in a sexual assault analogue.
LIBRARY AND INFORMATION SERVICES

The ADAI Library continues to serve the University community of researchers and students, as well as treatment professionals, policy makers, and students from other colleges and universities in the state and Northwest region. Web and e-mail access have increased the number and geographic distribution of researchers, students, and practitioners who contact library staff for assistance. The ADAI Library provided more 2500 books, chapters, and articles to its patrons during the biennium, and loaned another 1000 items to libraries in the Northwest and nationally via interlibrary loan.

Library facilities were significantly improved when the Institute moved into new offices in June 2001. In its prior location, the collection could not fit into one space and the library had been forced to divide the collection into two separately housed sections, which was inconvenient for both staff and patrons. It was also difficult to find shelf space for new acquisitions, so older materials were regularly discarded to make room for current books and journals, a practice that undermined the integrity and historical value of the library collection. The reading/work space for patrons was limited and competed with other Institute functions, as did office space for library staff.

In its new location, the Library has been able to integrate the entire collection, as well as make space for future growth. Patron workspace is now separate from other Institute functions, and patrons now have access to two public access computers for searching the ADAI Library catalog, accessing other databases on the Internet, and e-mail. Library staff now have office space separate from the shelving and patron work areas.

Continued development of the ADAI web page is another role for Library & Information staff. During the biennium, the Grants & Funding Resources page was enhanced to provide more comprehensive information about funding sources for alcohol and drug research. Bibliographies and several online publications by ADAI Researchers were added to the site as well.

RESEARCH DISSEMINATION

Conferences & Workshops:

In November 1999, the Institute helped to organize and co-sponsor a regional Town Meeting with the National Institute on Drug Abuse (NIDA), which brought together over 600 participants involved in drug abuse treatment, research, and policy. Understanding Drug Abuse and Addiction: Myths vs. Reality was a daylong series of presentations on state-of-the-art addiction treatment and research. ADAI assisted NIDA in the planning and publicity for the meeting, and several ADAI Scientists and Research Affiliates made presentations or held poster sessions. Highlights are published on the web at: [http://165.112.78.61/TownMeetings/Seattle/Seattle.html](http://165.112.78.61/TownMeetings/Seattle/Seattle.html).

The following January 2000, ADAI and the drug policy organization The Lindesmith Center, collaborated on organizing and hosting an international conference on Preventing Heroin Overdose: Pragmatic Approaches. This two-day meeting attracted a national and international audience of more than 400, and generated considerable local public and press attention. Abstracts from the presentations are published on the web at: [http://depts.washington.edu/adai/conf/heroin.htm](http://depts.washington.edu/adai/conf/heroin.htm).

ADAI also helped to support a 2-day training for Washington state substance abuse treatment providers on evidence-based treatment interventions, as part of national study looking at how substance abuse treatment programs learn about new ideas in the field and adopt them. Research-Based Interventions to
**Improve Treatment Outcomes** was hosted by the Northwest Frontier Addiction Technology Transfer Center in Portland on April 23-24, 2001, in Federal Way, and featured D. Dwayne Simpson of Texas Christian University. A PowerPoint slide summary of the training can be downloaded from [http://www.ibr.tcu.edu/posters/posters.html](http://www.ibr.tcu.edu/posters/posters.html) under the title “Report on NF-ATTC/TCU Workshop in Seattle.”

**Lectures:**


*Addiction: Highjacking the Brain, Winter 2001 Lecture Series.* Speakers were:
  - Akira Horita, Ph.D. (Pharmacology) *The Brain’s Reward System*
  - David Scratchley, Ph.D. (Seattle University) *Stimulants: Physical and Behavioral Effects*
  - Matthew Gardner. (Mercer Island Youth Center) *Stimulants and the Juvenile Justice System*
  - Jennifer Sayers, Ph.D., (Psychology) *Emotional Regulation Techniques*

This was the latest in a series of public lectures on Addiction and Brain, funded by a NIDA Science Education grant to the School of Nursing, Susanna Cunningham, Ph.D., Principle Investigator. ADAI has helped to identify speakers, publicize the series, and arrange for continuing education credits for attendees. [http://www.son.washington.edu/centers/addiction/](http://www.son.washington.edu/centers/addiction/)


In addition, ADAI research and library staff made presentations at numerous state and national professional conferences.
FISCAL REPORTS

[Data for this section is derived from the UW Office of Research Annual Reports of Awards and Expenditures for the periods July 1, 1999 – June 30, 2001.]
ADAIR Grant and Contract Awards for Biennial Fiscal Years 1992-2001

ADAIR Direct Expenditures for Biennial Fiscal Years 1988-2001
Indirect Costs Received by the University
from ADAI Grants and Contracts
for Biennial Fiscal Years 1992-2000
APPENDICES
## ADAI SMALL GRANTS

### History of Funding by Department

1973 through June 30, 2001

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TOTALS                              | 605                | 308             | $2,825,730         

*Research Scientists from the Alcohol and Drug Abuse Institute were not allowed to apply for Small Grants before the October 1997 funding period.*
## SMALL GRANT SCIENTIFIC REVIEW COMMITTEE
### 1999-2001

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<td>John S. Baer, Ph.D.</td>
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<td>Christopher M. Bernards, M.D.</td>
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<tr>
<td>C. June Strickland, Ph.D.</td>
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