

# PARC News

Portland Alcohol Research Center Newsletter

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## To Seek or Not to Seek, That is the Question



Center Scientific Director **Christopher Cunningham**, Ph.D. (Professor and Interim Chair, Behavioral Neuroscience, OHSU) recently received a MERIT award from the National Institute on Alcohol Abuse and Alcoholism (NIAAA) to continue his investigation of the learning and motivational processes underlying ethanol-seeking behavior.

The RO1 grant, "Modulation of Alcohol Reinforcement," was converted to a MERIT award toward the end of its 11<sup>th</sup> year of continuous funding. This award virtually guarantees an automatic renewal of the project for another 5 years when the current 5 years of funding runs out at the end of year 15. In addition, this well-deserved award was a complete surprise to Cunningham, who has established himself as an expert on the motivational effects of drugs of abuse as well as the involvement of specific physiological and neurochemical systems in the mediation of drug reward.

Trained as an experimental psychologist, Cunningham accepted a position as an Assistant Professor in the Department of Medical Psychology (currently Behavioral Neuroscience) at Oregon Health Sciences University (OHSU) in 1977 following one year of postdoctoral training at Yale University and one year of teaching at Indiana University. At that time, Cunningham was one of two faculty members in the department who were conducting alcohol

research. As his graduate and post-doctoral training was in the field of animal learning and motivation, with an emphasis on Pavlovian conditioning, Cunningham's initial studies focused on the effects of ethanol on anxiety and fear or conflict-based behaviors. During this time he also developed conditioned place preference and conditioned taste aversion as two animal models for assessing the motivational properties of ethanol and other drugs of abuse. He was among the first to study ethanol-induced place conditioning in rats, and was the first to demonstrate that ethanol produced a conditioned place aversion in rats in 1979. In the early 1990s, Cunningham was the first to report that mice exhibited a conditioned place preference to ethanol. Overall, Cunningham's efforts "set the stage" for alcohol researchers by providing additional measures for assessing the rewarding effects of ethanol.

The underlying goal of the research conducted by Cunningham is to understand the behavioral and neurobiological processes that

contribute to the etiology, maintenance, elimination and relapse of drug-seeking behavior. His MERIT award has been evaluating the contribution of learning associated with the pairing of environmental stimuli with ethanol's rewarding or aversive effects. In a series of elegant experiments, Cunningham has determined that certain ethanol-predictive stimuli can impact ethanol's motivational effects and thereby direct ethanol-seeking behavior. The presentation of certain paired vs. unpaired stimuli also can elicit physiological responses that differ in anticipation of, or in response to, drug administration. As PI of a component of the Portland Alcohol Research Center, Cunningham is using gene-mapping strategies to identify and localize genes relevant to the rewarding or aversive effects of ethanol. Since the late 1980s, Cunningham also has been involved in various funded contracts from the National Institute on Drug Abuse to conduct place-conditioning studies following administration of morphine, methamphetamine and cocaine. He is currently collaborating on a gene-mapping project for opioid analgesia and reward. Collectively, Cunningham is utilizing his behavioral expertise to understand the different motivational aspects of drugs of abuse as well as mechanisms contributing to drug-seeking behavior. He believes that his behavioral approach complements the molecular strategies utilized in other laboratories.

*(cont. page 2)*

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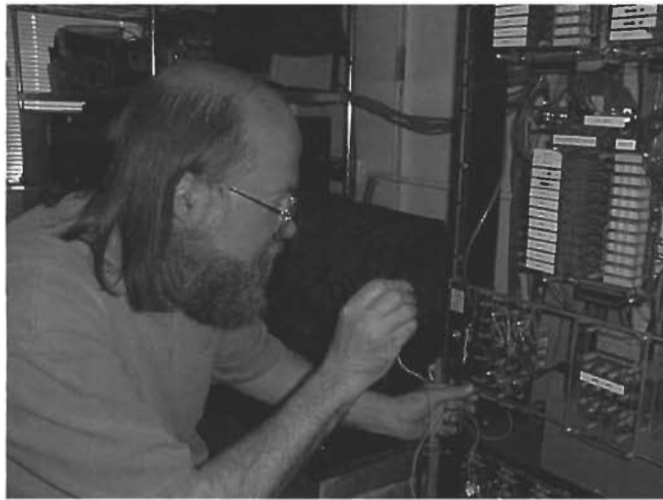
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Cunningham, cont.

ries. "Since we are ultimately trying to understand behavior, the behavior of interest must be well understood in an intact animal in order for neurochemical or molecular manipulations to be relevant."



For more than twenty years, Cunningham has been an active participant in the teaching and training programs of graduate students and postdoctoral candidates, serving on more than 60 Master's thesis or Ph.D. dissertation advisory or examination committees. His participation in administrative activities at OHSU is equally impressive, occurring at all levels (i.e., University, School of Medicine, Department of Behavioral Neuroscience). Most notably, as interim chair of the Department of Behavioral Neuroscience since 1996, Cunningham has been a strong leader and departmental advocate during the restructuring and reorganization of

departments at OHSU. In a department with limited resources, Cunningham has successfully fostered a collaborative spirit among faculty and maintained a high level of productivity within the department. He admits that he "enjoys the facilitatory interaction," which he sees as one benefit of his role as interim chair.

The Department of Behavioral Neuroscience has benefited/thrived under Cunningham's leadership and from his strong commitment toward improving conditions within the department. As an example of his support to junior faculty, Cunningham initiated a policy on faculty mentoring in 1996. In addition to providing a written annual review to junior

faculty by the departmental promotion and tenure committee, junior faculty were assigned a faculty mentor and encouraged to meet annually to discuss progress and identify goals. As interim chair, Cunningham also met with each junior faculty member and mentor to discuss the annual written review and any general issues related to career development. When asked why he felt it was important to initiate a policy on faculty mentoring, Cunningham answered, "When I first came to OHSU as an Assistant Professor, I was the only junior faculty member in the department. Now, with so many Assistant Professors in our department, it seemed only natural to nurture the junior faculty." Clearly, other departments are recognizing the wisdom of Cunningham's words as the School of Medicine's policy on promotion and tenure has recently been revised to include annual reviews for all Assistant Professors.

As the chair search for the Department of Behavioral Neuroscience is underway, Cunningham's future role as leader of the department is uncertain. Regardless, he is, and will continue to be, an integral and valued member of the department. The new chair of Behavioral Neuroscience will have a very tough act to follow.

## Selected Recent Publications

Buckman JF, Meshul CK, Finn DA and Janowsky A. Glutamate uptake in mice bred for ethanol withdrawal severity. *Psychopharmacology* 143:174-182, 1999.

Chester JA and Cunningham CL. Baclofen alters ethanol-stimulated activity but not conditioned place preference or taste aversion in mice. *Pharmacol. Biochem. Behav.* 63:325-331, 1999.

Chester JA and Cunningham CL. GABA-A receptors modulate ethanol-induced conditioned place preference and taste aversion in mice. *Psychopharmacology* 144:363-372, 1999.

Crabbe JC, Phillips TJ, Buck KJ, Cunningham CL and Belknap JK. Identifying genes for alcohol and drug sensitivity: Recent progress and future directions. *Trends Neurosci.* 22:173-179, 1999.

Crabbe JC, Wahlsten D and Dudek BC. Genetics of mouse behavior: Interactions with laboratory environment. *Science* 284:1670-1672, 1999.

Davies DL, Bolger MB, Brinton RD, Finn DA and Alkana RL. *In vivo* studies suggest novel sites of action for ethanol. *Psychopharmacology* 141:339-350, 1999.

Demarest K, Hitzemann B, Phillips T and Hitzemann R. Ethanol-induced expression of *c-Fos* differentiates the FAST and SLOW selected lines of mice. *Alcoholism: Clin. Exp. Res.* 23:87-95, 1999.

Finn DA and Crabbe JC. Chronic ethanol differentially alters susceptibility to chemically-induced convulsions in Withdrawal-Seizure Prone and -Resistant mice. *J. Pharmacol. Exp. Ther.* 288:782-

790, 1999.

Ryabinin AE, Wang Y-M and Finn DA. Different levels of *Fos* immunoreactivity after repeated handling and injection stress in two inbred strains of mice. *Pharmacol. Biochem. Behav.* 63:143-151, 1999.

Ryabinin AE, Wang Y-M, Freeman P and Risinger FO. Selective effects of alcohol drinking on restraint-induced expression of immediate early genes in mouse brain. *Alcoholism: Clin. Exp. Res.* 23:1272-1280, 1999.

Wood RD, Shen EH, Chester JA and Phillips TJ. Ontogeny of ethanol-induced locomotor activity and hypothermia differences in selectively-bred FAST and SLOW mice. *Pharmacol. Biochem. Behav.* 62:339-347, 1999.

## Scientist Update

**Tamara Phillips, Ph.D.**

(Professor and Vice-Chair, Behavioral Neuroscience, OHSU) was hosted by Oregon State University to give the Alcohol and Public Health lecture in April, 1999. Phillips spoke on the "Genetic Basis of Alcoholism." In May Phillips gave an invited seminar at Scripps Research Institute in La Jolla, CA, entitled, "Genetics of Ethanol Preference Drinking. She also gave an invited presentation at the First International Meeting of the Behavioral Pharmacology Society and European Behavioural Pharmacology Society in Boston, MA, entitled, "Sensitization and Other Behavioral Effects of Drugs in Knockout Mice."

**Chris Cunningham, Ph.D.** was an invited discussant at the "Rat Model Priority Meeting," which was sponsored by NIH in May, 1999. He participated in a symposium (Role of Conditioning in Ethanol Reinforcement: Neurochemical and Behavioral Studies) at the annual meeting of the Research Society on Alcoholism (RSA) in June, 1999 and spoke on "Place Conditioning and the Neurobiology of Ethanol's Motivational Effects." In August of this year, Cunningham attended the FASEB Summer Research Conference on "Biological Vulnerability to Alcoholism and Drug Addiction in Copper Mountain, CO. His invited presentation was entitled, "Genetic Applications in the Study of Drug and Alcohol Abuse." Cunningham also attended the joint meeting of the Behavioral Pharmacology Society and European Behavioural Pharmacology Society in Boston, MA and participated in a symposium entitled, "Behavioral Pharmacology of Alcohol." He spoke on "Conditioned Stimulus Effect Produced by Ethanol Reinforcement."

**Andrey Ryabinin, Ph.D.** (Assistant Professor, Behavioral Neuroscience, OHSU) organized a symposium (Ethanol and the Central Nucleus of the Amygdala) at the recent RSA meeting, during which he

gave a talk entitled, "Selective Effects of Alcohol on Expression of Immediate Early Genes in Extended Amygdala and Hippocampus." In August of this year, Ryabinin gave an invited presentation entitled, "ITF Mapping After Drugs of Abuse: Pharmacological Versus Perceptual Effects" at the conference "Inducible Transcription Factors in the Brain" in Rydzyna, Poland, a satellite meeting of the Annual Meeting of the European Society for Neuroscience.

**Deborah Finn, Ph.D.** (Assistant Professor, Behavioral Neuroscience, OHSU) was an invited participant in a symposium (Neurosteroids and CNS function) at the Neurochemistry Winter Conference in Soelden, Austria in March, 1999. She spoke on the "Rewarding Effects of Allopregnanolone and Interaction with Ethanol Drinking Behavior." Later that month, Finn was invited to speak about "Neurosteroid Modulation of Ethanol Withdrawal Severity" to the Department of Pharmacology and Neuroscience at Dundee University in Dundee, Scotland. In June 1999, Finn participated in the lead symposium (Diverse Effects of Neurosteroids) at the International Behavioral Society annual meeting in Nancy, France and talked about the "Influences of Neuroactive Steroids on Seizure Activity." During the same month, Finn also gave an invited presentation entitled, "Genetic Differences in Ethanol Withdrawal Severity: Modulation by Neurosteroids" at the Institut de Transgenose in Orleans, France.

**John Crabbe, Ph.D.** (PARC PI, Professor, Behavioral Neuroscience, OHSU) was appointed to the Board of Scientific Counselors at NIDA and to the Scientific Advisory Board of the Waggoner Center for Alcohol and Addiction Research. Crabbe gave numerous invited presentations over the past year. In January of this year, Crabbe spoke on "QTLs for Effects of Alcohol and Drinking Preference" at the USA-Chile-Canada Workshop on

"Genetic Factors in Alcoholism" in Santiago, Chile. Later that month, Crabbe participated in the Workshop on the Genetics and Neurobiology of Addiction, which was sponsored by the Zaffaroni Foundation in San Francisco, CA. He was invited by the Genetics Program at Duke University Medical Center to speak about the "Use of Genetic Animal Models to Study Substance Abuse Vulnerability Genes" in March and spoke about "Searching for Alcohol and Drug Susceptibility Genes" to the Department of Pharmacology at the University of Colorado, Boulder, in April, 1999. Crabbe was an invited participant at the "Strain Characteristics Database Summit" that was sponsored by the Jackson Laboratory in Bar Harbor, ME in May. Crabbe also spoke on "Mouse Neurogenetics of Substance Abuse" at NIDA in June of this year.

## Awards

**Michele Grubb, Ph.D.** received an individual post-doctoral NRSA from NIDA to study "Mesolimbic GABA-ACh Interactions in Cocaine Reward" in the laboratory of **Gregory Mark, Ph.D.**

**Kaitlin Browman, Ph.D.** received an individual post-doctoral NRSA from NIAAA to continue her studies on "Serotonin Mechanisms in Ethanol and Thermoregulation" in the laboratory of **John Crabbe, Ph.D.**

**Stephen Boehm** received a pre-doctoral NRSA from NIAAA to study "GABA-B Modulation of Ethanol's Locomotor Stimulant Effects in Mice" in the laboratory of **Tamara Phillips, Ph.D.**

**Amy Beadles-Bohling** was recently awarded a 3 year pre-doctoral NRSA from NIAAA to conduct research on the "Analysis of the Kappa-Opioid System in Ethanol Withdrawal" in the laboratory of **Kristine Wiren, Ph.D.** Bohling also won second prize for her oral presentation entitled, "Analysis of Prodynorphin Expression in Withdrawal Seizure-Prone and Withdrawal Seizure-Resistant Mice" at the 1999 Student Research Forum.

# PARC Sponsored Research Seminars

*February 1999*

Paul Gresch, Dept. of Psychiatry & Behavioral Neurosciences, Wayne State University, "Regulation of striatal tachykinin gene expression: Role of serotonin 2A/2C receptors."

Maureen Hahn, Dept. of Psychiatry & Behavioral Neurosciences, Wayne State University, "Role of the neurokinin 1 receptor in stress-induced activation of the rat locus coeruleus."

John C. Fentress, Ph.D., Dept. of Psychology, Dalhousie University, Halifax, Nova Scotia, "Developmental neurogenetics of mammalian movement."

*April 1999*

Igor Ponomarev, Dept. of Behavioral Neuroscience, OHSU, "Genetic association between chronic ethanol withdrawal severity and acoustic startle parameters in WSP and WSR mice."

*May 1999*

Irwin Lucki, Ph.D., Dept. of Psychiatry and Pharmacology, University of Pennsylvania, "Antidepressants: Distinct mechanisms or final common pathway?"

William T. Greenough, Ph.D., Dept. of Psychology, Psychiatry & Cell and Structural Biology, Beckman Institute, University of Illinois, "Behavioral, structural and molecular facets of synapse plasticity."

Christopher L. Cunningham, Ph.D., Dept. of Behavioral Neuroscience, OHSU, "A top-down look at bottoms up."

Katherine Hill, Dept. of Psychology, Kansas State University, "Naltrexone treatment and alcohol palatability."

*June 1999*

Robert Hitzemann, Ph.D., Dept. of Psychiatry & Behavioral Neuroscience, Stony Brook State University of New York, University Hospital and Medical Center, "Detection, mapping and fine mapping of the genes for acute ethanol response."

Nancy Zahniser, Ph.D., Dept. of Pharmacology & Neuroscience, University of Colorado Health Science Center, "Regulation of the dopamine transporter: What can expression systems tell us about brain and behavior?"

*July 1999*

Abraham Palmer, Dept. of Pharmacology, University of California at San Diego, "Differential autonomic and behavioral responses to startle stimuli in inbred rat strains: Possible implications for hypertension and schizophrenia."

Heather S. Hain, Dept. Behavioral Neuroscience, OHSU, "Quantitative trait loci analysis of baseline nociceptive sensitivity and morphine-induced antinociception in the writhing assay."

Wim Crusio, Ph.D., Research Director, Behavioral Neurogenetics, CNRS, Orleans, France, "Hippocampal mossy fibers and radial maze learning abilities in inbred mice."

*September 1999*

Douglas Wahlsten, Ph.D., Department of Psychology, University of Alberta, Edmonton, Alberta, Canada, "Absence of the corpus callosum: Genes, environment, and a third source of developmental errors."

*October 1999*

Angelo Contarino, Ph.D., Scripps Research Institute, "Anxiety-like behavior and cognitive performance of CRF-R1 knock-out mice."

Rueben Gonzalez, Ph.D., Dept. of Pharmacology, College of Pharmacy, University of Texas at Austin, "Neurochemical analysis of the mechanism of ethanol effects on the brain reward system."

Jennifer Loftis, Dept. of Behavioral Neuroscience, OHSU, "Cocaine administration alters the expression of NMDA receptor subunits and neuronal nitric oxide synthase with regional and withdrawal-time specificity."

*November 1999*

NIDA/NIAAA Training Program Annual Retreat

Adena Svingos, Ph.D., Dept. Neurology & Neuroscience, Weill Medical College of Cornell University, "Cellular sites for kappa opioid receptor modulation in limbic forebrain regions."

Heather Hood, Dept. Behavioral Neuroscience, OHSU, "Epistatic interactions between quantitative trait loci affects the genetic predisposition for physical dependence on pentobarbital in mice."

*December 1999*

Ivan Jeanne Weiler, Ph.D., Dept. of Psychology, Psychiatry & Cell and Structural Biology, Beckman Institute, University of Illinois, "Does Fragile X mental retardation protein play a role in synaptic protein synthesis?"

Anna Y. Klintsova, Ph.D., Dept. of Psychology, Psychiatry & Cell and Structural Biology, Beckman Institute, University of Illinois, "Fetal alcohol exposure and prospects for intervention: Lessons from animal models."

PARC News  
Published to disseminate information on alcoholism research and the mission of the Center, which is to identify genes and to explore mechanisms underlying neuroadaptation to alcohol administration.

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