George Breese, Ph.D.

Affiliations
Professor, Psychiatry and Pharmacology; Head, Neuropharmacology Laboratory, Bowles Center for Alcohol Studies; Member, Neuroscience Center; University of North Carolina at Chapel Hill School of Medicine

Education and Training
Ph.D., Pharmacology, University of Tennessee, Memphis, 1965; M.S., Pharmacology, 1961, and B.S., Pharmacy, 1959, Butler University, Indianapolis; Postdoctoral Fellow in Pharmacology at NIMH, National Institutes of Health, Bethesda, MD, 1966-68.

Awards
Distinguished Alumni Award from Butler University, 2005
ASPET Award for Experimental Therapeutics, 2001.

Recent Publications


Website

The Director’s Column
Fulton T. Crews, Ph.D.
Director
Bowles Center for Alcohol Studies

George Breese is the kind of pharmacologist who loves to make discoveries that help people. Although most agree that epileptic seizures kindle, George looked at kindling as a fundamental process involving long-term alterations that change brain function. He first discovered that alcohol withdrawal seizures kindle like epileptic seizures. Then he explored whether kindling could occur with negative affect, a vague term that encompasses anxiety, dysphoria, bad feelings, depression and loss of interest in social interaction. This might seem a small step, but the basis of the seizure kindling hypothesis was that the seizure caused such major adaptations in the brain that the next seizure was more likely. Most animal drinking models do not show seizures during withdrawal. George proposed that loss of alcohol (withdrawal) is the key element rather than the seizure itself.

In collaboration with David Overstreet and Darin Knapp, George found that subtle measures of negative affect, like social interaction, change during alcohol withdrawal in rats. The unexpectedly delicate piece was that this subtle social interaction measure showed increased intensity and duration (kindling) with multiple drinking-abstinence episodes, but without any seizures. This is particularly exciting in part because it now relates to a more clinical situation.

Relapse during recovery from alcoholism is associated with anxiety, craving, stress and other factors that can be explored using this model. The discovery that stress can kindle a rabbit drinking bout by increasing the negative affect that can induce relapse is very exciting, because it is one of the first instances that couples stress and alcohol use in the brain. George is working hard to identify these adaptations and show how they can be reactivated by stress, drinking or other stimuli that might trigger relapse.

Pharmacological study of agents that can prevent the “kindling” or activation of the negative affect response give insight into its mechanisms, as well as providing potential therapeutic approaches to help prevent relapse. This kind of translational work is just what George loves to do. In fact, he proposed a “high-risk-high-gain” clinical trial that will be headed by Dr. J.C. Garbutt, a center faculty member. Funded by donations to the Center for Alcohol Studies, the trial will include safe and approved drugs not currently used in alcohol recovery, but used to reduce negative affect-anxiety. The hypothesis is that factors which trigger the kindled negative affect induce relapse and that drugs shown to block the kindled response in animals will block the response in humans, thereby preventing relapse. We are all excited about this translational effort and hope it will be successful in helping people maintain their abstinence. This approach might also delineate new and innovative ways to treat addiction.

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Figure. Schematic representation of the contribution of kindling to the etiology of alcoholism. Adapted from Breese et al. Psychopharmacology 2005; 178: 367-380.
Fulton Crews Receives 2006 Bowles Lectureship Award

On April 24, Bowles Center for Alcohol Studies (BCAS) Director Fulton Crews, Ph.D., received the Bowles Lectureship Award for his work in alcohol research. Established in 1996 by the family of Hargrove Skipper Bowles, the Award honors distinguished researchers who have made significant contributions to our understanding of the causes, prevention and/or treatment of alcoholism and alcohol abuse. Crews is the ninth researcher to receive the award and the first from UNC.

William L. Roper, M.D., MPH, dean of the UNC School of Medicine and CEO of UNC Health Care, presented the award plaque to Crews during the event on campus. Both Roper and National Institute on Alcohol Abuse and Alcoholism Director Ting Kai Li, M.D., spoke to a packed room about Crews’ accomplishments.

“This award has been given to some of the most eminent scientists in the world today,” said Roper. “Fulton Crews has long been a leader on this campus, and it’s a pleasure to see him recognized for his national and international leadership in the field of alcohol.”

Dr. Crews has led the center to a level of considerable renown,” said Li. “It is a joy to be able to help honor him here today. I can’t think of anyone more deserving of this award.”

The award presentation was followed by an hour-long seminar by Crews entitled, “Neurobiological Changes During Alcohol Dependence and Recovery.”

Crews, a UNC-CH professor of pharmacology and psychiatry, has lead the field in understanding the neuretotoxic effects of alcohol on the brain, including cell death and inhibition of neurogenesis. In his 12 years as BCAS director, Crews has established the Center as a world leader in molecular medical research on the mechanisms of alcoholic pathology in the brain, liver and fetus.

“This award is particularly special because it comes from my colleagues. Knowing the others who have received this award and the impact of their work, it’s really an honor to be recognized as part of that group,” said Crews.

Breese Laboratory Advances Kindling Model as Framework for Understanding the Behavioral Pathology of Alcoholism

John T. van Zandt II, son of the Texas blues and folk musician Townes van Zandt, describes the years before his father’s death from alcoholism in 1997 at the age of 52:

“...It was a miserable time. He became so uncontrollable because of his alcoholism that I had to ration his intake to keep him from convulsing and at the same time not too drunk to play. I had to be a chemist of sorts... He blew every third gig and maybe three in a row and we’re talking great American music halls where people just get up and walked out when he never played a note... and we were just wondering how much worse it could get. The answer was plenty worse... A couple of years before he died, he went into treatment 14,15 times, to serious hospital with the full detox... mandatory treatment to keep him from dying through withdrawals.

Breese uses animal models to study mechanisms and manifestations of alcohol withdrawal. Breese and his laboratory have advanced the kindling hypothesis by demonstrating that kindling, once thought to underlie only motor aspects of alcohol withdrawal, also appears to underlie affective aspects of alcoholism and alcohol withdrawal. They have also shown that kindling, formerly considered to operate mainly in advanced, severe alcoholism, may begin very early during the course of alcoholism and, in fact, may be a crucial process underlying development of alcohol dependence.

The alcohol withdrawal syndrome is manifested by negative affect, including symptoms such as anxiety and agitation, in addition to motor symptoms such as convulsions. Breese hypothesized that negative affect might be sensitized (kindled) in the way that alcohol withdrawal seizures are. Working with colleagues Drs. Darin Knapp and David Overstreet, he modeled repeated withdrawals from alcohol by exposing rats to three 5-day regimens of alcohol-containing diet with two days of abstinence between each regimen. They found that rats exposed to repeated withdrawals showed more negative affect in two tests of anxiety-like behavior than rats exposed to only...