Epilepsy Drug Stops Nicotine's Addictive Effects in Animals; Also Shows Promise in Animals for Treating Cocaine Addiction

Smokers who want to kick the habit may find powerful help from a European epilepsy drug that already has shown promise in treating cocaine's effects in animals, U.S. Secretary of Energy Bill Richardson announced at a press conference at DOE headquarters in Washington, D.C., on Wednesday, December 2.

The same research team published today in the journal Synapse by scientists from BNL, St. John's University, New York University School of Medicine and the Albert Einstein College of Medicine showed that drugs related to the epilepsy drug—known as vinyl-GABA, or GVG—looks very promising in preventing nicotine's addiction effects in animals. In animals, it prevented the dramatic changes in brain chemistry and behavior brought on by cocaine or nicotine (see Bulletin, August 7, 1998).

The new paper shows that GVG does the same for nicotine. And, the dose needed to block nicotine's effects was about one-tenth to one-twentieth the dose currently used to treat epilepsy in humans. Upcoming clinical trials will determine the dosage needed in humans. According to Alan Leshner, Director of the National Institute on Drug Abuse within the National Institutes of Health, “This study confirms the importance of the brain's GABA system as an important target for potential anti-addiction medications like GVG. It also emphasizes that there is likely a common brain mechanisms underlying addiction to all drugs and gives hope that we can develop a single medicine to use in treating addiction, whatever the primary addicitve drug.”

The evidence is so strong that the scientists think GVG might work better and have fewer side effects than other stop-smoking treatments available today. It is not addictive, is not based on nicotine, and has been used safely in Europe by epileptic children for more than a decade.

“Of all the addictive drugs that exist, nicotine is the most frequently abused drug in the world, and every smoker who has tried knows how hard it is to quit,” said BNL's Stephen Dewey, the lead author on the paper. “Never shown in animals that the proper dose of GVG can stop nicotine’s addictive effects entirely.”

The team's research also suggests that GVG may work against a variety of other addictions.

“We are gaining confidence that this approach could offer hope to all addicts, from smokers and alcoholics to hard-core heroin and cocaine users,” said team member Charles Ashby of St. John's University.

Added coauthor Jonathan Brodie of New York University (NYU), “Since the same brain chemistry changes may be common to all addictions, it follows that a single well-aimed strategy, combined with a person's desire to quit, could assist in defeating them all.”

To show whether GVG can be as effective in humans as it is in animals, clinical trials are now being planned at institutions in Europe, Canada and the United States.

Though GVG is not currently approved in the U.S. to treat epilepsy, U.S. institutions can apply to conduct clinical trials under investigational new drug protocols from the U.S. Food & Drug Administration.

The research grew out of cooperative work to understand the brain's chemical messengers, called neurotransmitters, and the effect of addictive drugs on the balance of those chemicals in the brain. One neurotransmitter, in particular, called dopamine, plays a central role in the sensations and behaviors associated with all drug use.

The GVG results on cocaine were published after more than a decade of investigation that started when Dewey and NYU's Brodie looked at the way brain cells "talk" to one another, especially in people with schizophrenia. Soon after receiving encouraging results with cocaine, the team began testing GVG against other addictive substances. Work on alcohol, heroin, morphine, amphetamines, and methamphetamine is nearing completion.

Tobacco's Addictive Hook

The researchers looked at how different doses of GVG changed nicotine's ability to alter brain dopamine levels in rodents and primates.

This used sophisticated imaging techniques to measure dopamine concentrations in the brains of both nicotine-addicted rodents and those that had never been exposed to nicotine. And they performed brain scans on female baboons given intravenous nicotine.

“Nicotine doubles the brain's dopamine levels, sending a rush of pleasure and a signal that you should smoke more often and over again,” said Dewey. “But, in an appropriate dose of GVG taken before nicotine exposure can completely block nicotine's effects on brain dopamine.”

GVG increases the levels of another brain chemical, GABA, which decreases dopamine production. So, GVG prevents nicotine from causing dramatic changes.

Studying the Behavioral Effects

As any smoker will attest, nicotine addiction is not just a matter of the mild rush caused by smoking. The mere sight or smell of cigarettes, or a smoker's hangout, can bring on a craving.

This kind of behavioral effect is what makes quitting smoking so hard. So, Ashby and his colleagues tested (continued on page 2)
Research at BNL Into Addiction

In 1987, BNL became the first research institution to position emission tomography (PET) and other medical imaging techniques to investigate the brain mechanisms underlying drug addiction. Since then, Lab researchers and their collaborators at other institutions have probed the mysteries of how drugs such as nicotine (see story, page 1) and cocaine affect the brain and how they lure a person into the cycle of use and abuse that is addiction. Much of this research has used medical imaging techniques of ever-increasing sophistication. BNL scientists were pioneer developers of PET technology and radiotracer drugs, the movement of which in the brain is tracked by PET scans. Brookhaven chemists were the first to make a radiotracer incorporating a cocaine that could be used for addiction studies. They also developed a fluorine-labeled compound now used in hospitals and research institutions worldwide to make images of brain function and diagnose cancer.

Attention Lab employees, facility-users, retirees, and guests: Wednesday, December 8, is the last day to register for Front Page, a Web page development workshop on Wednesday, December 8, at noon in Berkner Hall, sponsored by the Employee Assistance Program (EAP) of the Occupational Medicine Clinic. The lecture is open to all.

A third example of addiction research at Brookhaven showed that smokers have high levels of a brain enzyme which breaks down brain chemicals involved in pleasure and reward. This result suggested that something other than nicotine may play a role in tobacco addiction. Among the drugs being studied at BNL are alcohol, cocaine and related drugs, heroin and opiates, and marijuana.

Research at BNL has encouraged changes in diet, exercise and smoking, and it has assembled an array of drugs and surgeries.

The technique is called conditioned-place preference, or CPP. “Not only could GVG keep addicted animals from returning to the nicotine-associated place, but also some of these rats did not show nicotine-seeking behavior even after having been exposed to nicotine.” — Kara Villamil

The Psychology of Coronary Artery Disease has been identified: emotions. Disease of the coronary arteries is the leading cause of death in the United States. The Division of Contracts & Procurement (DCP) has established a help desk to answer inquiries related to agency form and procurement questions. To reach the help desk, phone Ext. 3432, fax Ext. 5521 (for a “Front Page Help Desk”), or e-mail dcphelp@bnl.gov.
BNL Blood Drive
Lab Director Gives Blood; Why Not You?

Last spring, Laboratory Director John Marburger took time out of his busy workday to donate blood during one of BNL’s many blood drives. Though this was his first time donating blood at the Lab, Marburger was not too nervous about it. He was an active donor at the State University of New York at Stony Brook.

Regardless of where one donates, the benefit of giving blood is the same: It saves lives. In fact, the contribution of one pint by one person can save
approximately five lives — lives of friends, family members, and neighbors. “Here is one way to use this tool, so that we are truly part of our community,” said Marburger.

The next on-site opportunity for Lab employees, facility-users and guests to give blood is during BNL’s fall blood drive, on Tuesday and Wednesday, December 8 & 9 from 9:30 a.m. to 3 p.m. in the Brookhaven Center.

The Lab makes work time available to employees so they can give blood during the on-site drives. “Brookhaven tries to make donating blood as easy and convenient as possible,” says Blood Drive Chair Susan Foster. Human Resources Division will “Wave” employees to take the time to undertake this simple act of generosity.

Those who give are people who are in good health between the ages of 17 and 76 who have donated blood in the past 56 days. To make an appointment, contact Foster at 226-0826, or Ext. 2888, with your name, extension, and preferred date and time.

BNL Toy Drive

Until December 18, help make the holidays, and even the New Year, more joyous for the local community by participating in Brookhaven Town’s annual Toy Drive. Bring new, for infants through teenagers, to the BERA Sales Office, Berkner Hall, Tuesday through Friday, 8 a.m. to 5:30 p.m.

For more information, call Andrea Dehler, Ext. 3347, or M. Kay Dellimore, Ext. 2873.

Calling All Carolers

The BNL Choral Group will present its annual holiday concert in the cafet-eria at 7 p.m., December 15, date to be announced. All employees and re- tirees who sing in tune are warmly welcome to join the group.

Rehearsals will be held from noon to 1 p.m. in Berkner Hall auditorium as follows: Monday, December 7; Thursday, December 10; Tuesday, December 15; and Thursday, December 17.

For more information, call Kara Villamil, Ext. 5658, or Liz Seubert, Ext. 2346.

Defensive Driving

The Environment, Safety & Health Services department will offer a six-hour defensive driving course in two 3-hour sessions beginning the first week of December. The course is open to everyone and is designed for the driver who has never taken a course or one who wishes to review defensive driving practices.

The course will be taught by a Metropolitan Life instructor and is open to BNL employees, retirees, BNL facility-users, and their family members. Completion of the course is a requirement for use of the on-site Lab garages.

For more information, call Peter Doherty, Ext. 6702.

Additional Volunteers

In the November 6 brookhaven Bulletin article entitled, “BNL employees volunteer work for Habitat for Humanity, a nonprofit organization dedicated to providing safe, affordable housing in partnership with low-income families,” the names of two employees were inadvertently omitted from the list of volunteers. They are Susan Cuevas and Paul O’Connor.

Stony Brook Opera Ensemble Performs 12/10

Everyone who attended last year’s magnificent performance at BNL of the Stony Brook Opera Ensemble will be eager to attend their new presentation of “An Evening of Opera Scenes” in Berkner Hall on Thursday, December 10, at 8 p.m. Open to the public, the event is free, but donations will be gratefully accepted to help fund future concerts.

As before, promising graduate music students from the State Univer-sity of New York at Stony Brook will perform the concert. They will present Amahl and the Night Visitors, Giancarlo Menotti’s Christmas opera for children, as well as highlights from famous operas, including the garden scene from Gounod’s Faust, the quintet from Bizet’s Carmen, the second act of Massenet’s Manon, and the final scene from Bellini’s Romeo and Jui...
OPEN RECRUITMENT - Opportunities for Laboratory employees and outside candidates.

MK7131. MANAGER, RADIATION PROTECTION SERVICES DIVISION - Requires a BS in health physics or related discipline, an advanced degree preferred, certification as a health physicist by the American Board of Health Physics, and substantial experience in radiation protection activities including at least five years of progressive management experience in radiation protection at DOE-regulated facilities and NRC-regulated facilities. In addition, must have proven track record and DOE recognition for developing, implementing, and managing a comprehensive radiation protection program. Requires an understanding of the principles of radiological physics, radiation detection and monitoring, radiation effects, and radiation management. Requires the ability to develop, implement, and coordinate radiation protection technical support services to line, facility, and project managers, and for the assurance of compliance, internal and external customer satisfaction, and budget constraints. Requires, Safety and Health Quality Directorate.

MK7830. SCIENTIST - (reposting) Requires a Ph.D. experience in instrumentation development for accelerators, experience in high-vacuum technology, knowledge of the interface of accelerator systems, with beam-line operations, and demonstrated capability of balancing on cross-disciplinary projects and establishing independent research programs. Strong mechanical background preferred. Under the direction of E. Johnson, National Synchrotron Light Source Department.

MK7650. SCIENTIST - Requires a Ph.D. and research experience in the area of on-line/DAQ in a large high-energy or nuclear physics experiment. Experience in the area of on-line/DAQ in a large high-energy or nuclear physics experiment. Will work within STAR, a large detector at the Relativistic Heavy Ion Collider which is designed to study relativistic heavy ion and polarized proton interactions. The on-line software project encompasses run control, on-line monitoring, configuration management, and on-line data bases. Under the direction of T. Hallman, Physics Department.

MK7492. POSTDOCTORAL RESEARCH ASSOCIATE - Requires a Ph.D. in organic chemistry or related discipline, and experience in synthesis, organic chemistry, and mass spectrometry. Will be involved in the broad area of environmental organic chemistry and organo-gold chemistry; specific areas of research include formation of gold macro-molecules from biologic precursors, humic substances, metal-organic matter interactions in soils and sediments, and characterization of metallothioneins and related metal-binding biochemicals from bacteria. Under the direction of A. Vairavamurthy, Department of Applied Science.

MK7644. POSTDOCTORAL RESEARCH ASSOCIATE - Requires a Ph.D. in organic geochemistry or related discipline, experience in sulfur and nitrogen geochemistry, and the ability to use state-of-the-art, chromatographic and spectroscopic instrumentation, including GC-MS and LC-MS. Will primarily be involved in research of sulfur geochemistry aimed at a fuller understanding of the geochemical mechanism of sulfur incorporation into sedimentary organic matter, and the role of sulfur in sterile preservation and diagenesis of organic matter in marine sediments. Under the direction of A. Vairavamurthy, Department of Applied Science.

NS7728. PROGRAMME/ANALYST POSITION - Requires an MS degree or equivalent experience in computing related fields, several years' experience in C programming and data-base programming using Oracle, Dbase, and working with engineers, physicists, and other programmers to define data-base requirements and assist in the implementation of a control system for the Spallation Neutron Source Project. Alternating Gradient Synchrotron Department.

NS7718. ENGINEERING POSITIONS - Requires a BS/MSEE or a minimum of five years’ experience in the design of analog circuits, feedback systems, power electronics, power supplies, and solid-state converter technology. Experience in multi-kilowatt power supplies and fast-paced power techniques is plus. Alternating Gradient Synchrotron Department.

NS7721. ENGINEERING POSITIONS - Requires a BS/MSEE or a minimum of five years’ experience in the design and development of instrumentation systems. Experience in sophisticated instrumentation design, low-noise radio-frequency circuit design, and computer interfacing is required. Alternating Gradient Synchrotron Department.

NS7388. PROGRAMMER/ANALYST POSITIONS - Requires an MS degree or equivalent experience in computing related fields, several years' experience in C programming and data-base programming, and working with engineers, physicists, and other programmers to define data-base requirements and assist in the implementation of a control system for the Spallation Neutron Source Project. Alternating Gradient Synchrotron Department.

NS7389. PROGRAMMER/ANALYST POSITIONS - Requires a bachelor's degree in computer science or related field, four to six years' programming experience, proficiency in any two of the following: VB, C++, Java, Script, C++, C, Fortran, COBRA, or PeopleSoft. Excellent communication skills. Working knowledge of network, Unix, SUN, and Microsoft Windows environments, and experience in developing, implementing, and managing a comprehensive radiation protection program. Requires the ability to develop, implement, and coordinate radiation protection technical support services to line, facility, and project managers, and for the assurance of compliance, internal and external customer satisfaction, and budget constraints. Requires, Safety and Health Quality Directorate.

D07461. TECHNICAL POSITION - Requires a BS in telecommunications technology or equivalent. Familiarity with network technology is desirable, including cable, cable bonding, network protocols, token rings, loop, switches, and diagnostic tools. Additional responsibilities include the design, development, and maintenance of systems, which includes development of software and operating systems, and the ability to use state-of-the-art, chromatographic and spectroscopic instrumentation, in the design of alternate circuitry, a plus. Requires the ability to develop, implement, and coordinate radiation protection technical support services to line, facility, and project managers, and for the assurance of compliance, internal and external customer satisfaction, and budget constraints. Requires, Safety and Health Quality Directorate.

D04412. PHYSICIST/ENGINEERING POSITION - Requires a BS degree or equivalent, and a thorough knowledge of digital logic concepts. Familiarity with high-speed analog circuitry and if techniques are desirable. Requires the ability to use various types of test equipment. Requires the ability to use various types of test equipment. Requires the ability to use various types of test equipment. Requires the ability to use various types of test equipment.