Office of National Drug Control Policy
Counterdrug Technology Assessment Center (CTAC)

Counterdrug Technology

Advanced Systems to Help Law Enforcement and Medical Science in the Struggle Against Drug Crime and Abuse

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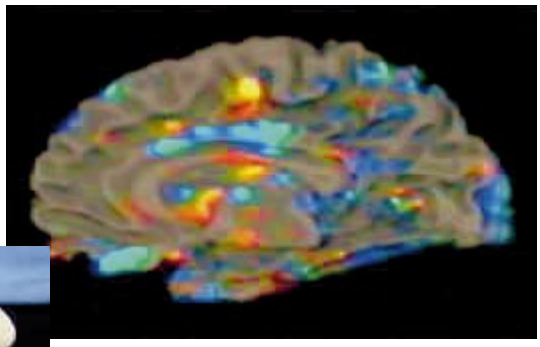
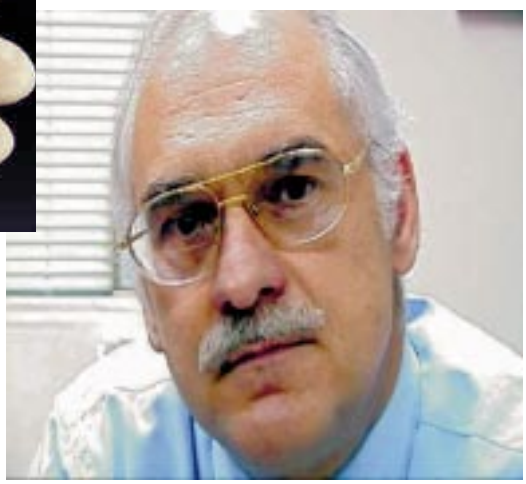
Unlocking Mysteries Deep in the Brain that Block Prevention and Treatment

It is inside the brain that cocaine triggers euphoria and along with it, for some, a terrible craving that leads to the destruction of job, family, and self. Inside the brain is where Dr. Michael Kuhar's development will act if it is successful. His efforts—including the recent CTAC-sponsored phase—to create anticocaine medication span 15 years and have encompassed the testing and evaluation of some 500 chemical compounds. A dozen of the best of the 500 were administered to rats and then the best two of the 12 were chosen to be given to monkeys. In the Yerkes Primate Center at Emory University, Atlanta, Kuhar and his team are at the cusp of what could be a major breakthrough. "These two compounds have been injected into primate subjects thousands of times with no observable side effects and the subjects stop performing the tasks required to receive the cocaine, strongly suggesting that these medications eliminate the desire for the drug.

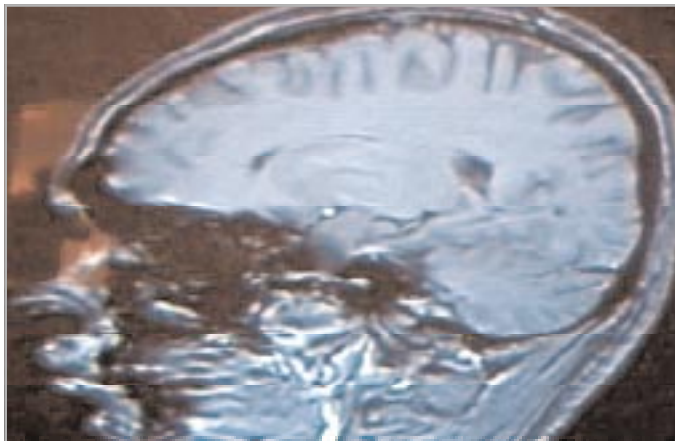




When we move into human subject trials, we will be watching very closely not only for evidence of effectiveness but against negative side effects including toxicity." The scientific community is closely watching Kuhar's pioneering work. A new pharmaceutical company focused solely on creating substances to heal drug abusers is negotiating to license and further develop Kuhar's compounds. Licensing by a company is essential for bringing new medications to market. There is reason to believe that if Kuhar (photo above) and Landry both succeed, then their drugs could be used together to help cocaine addicts. Both researchers have done remarkable work, but it would be a mistake to assume that effective, safe anticocaine medication will be available soon; there's lots more testing before that day arrives—if it ever does.

Much of CTAC's research and development budget supports bold new efforts to obtain crucial information for the demand reduction side of the National Drug Control Strategy. In direct pursuit of that goal, CTAC is funding the construction of brain imaging centers to learn everything we can about the interactions of drugs of abuse as they enter the brain, and ways to block those destructive effects. Research institutions receiving these state-of-the-art scanners promise to give top priority access to scientists who are working right now on drug abuse questions and to train the next generation of brain researchers to focus on drugs of abuse.

A massive, CTAC-sponsored Functional Magnetic Resonance Imaging machine, powered by a 7-Tesla coil magnet seen under construction in photos (left)—has been installed at Massachusetts General Hospital. It's the most



powerful brain scanner in the world, according to Dr. Bruce Rosen (top right), who directs the use of the new FMRI. The hospital's chief clinician on this project, Hans Breiter, M.D. (above), sees the enormous machine's equally huge mission as, "Mapping the neurochemistry of human behavior itself and creating a virtual stethoscope for treatment professionals, ultimately allowing them to easily, reliably measure the effectiveness of everything they do on behalf of their patients." Other CTAC-supported advanced neuroimaging system installations are complete or scheduled at NIDA in Baltimore, Brookhaven National Laboratory on Long Island, University of Pennsylvania in Philadelphia, Harvard's McLean Hospital outside Boston, and at UCLA.

Neuroscientists working on drug abuse today routinely discuss the role in cocaine dependence of a brain area called the nucleus accumbens. But it wasn't until 1997 that Dr. Edythe London (in lab coat, photo right) of the National Institute on Drug Abuse, was able to visualize—with high resolution—the function of this nucleus in the human brain of a cocaine addict by using a state-of-the-art Positron Emission Tomography (PET) scanner sponsored by CTAC for use at NIDA's Addiction Research Center in Baltimore. The PET instrument at NIDA will now be used by Dr. Diana Fishbein under CTAC sponsorship to conduct basic research leading to better management of recovering

addicts. Today, Dr. London is based at UCLA where her new work focuses on methamphetamine dependence. The photos (right) show a young woman in a UCLA treatment research program, who consented to brain scanning, an interview and to be photographed. She told Dr. London that she believes her years of doing meth have damaged her brain, resulting in changed behavior.

Dr. London hopes that this line of study will result in new knowledge leading to the development of effective medications and behavioral therapies for people whose lives are being destroyed by meth. Also at UCLA, investigators at the Crump Institute on Molecular Imaging are bringing state-of-the-art techniques to bear on the problem of drug abuse from another unique perspective. With CTAC's sponsorship, Dr. Simon Cherry and his colleagues are developing a small PET scanner with resolution fine enough to literally see gene expression in discreet nuclei of a monkey brain. This new instrument will allow injection of DNA and selective probes that can alter gene expression in specific monkey brain regions critical to the reward effects of cocaine and other abused drugs. The effects of such genetic manipulations on brain function will be studied at the molecular level with PET, and ultimately can be related to drug abuse behaviors in nonhuman primates. For the first time, the links between drug abuse and brain function will be linked to the expression of certain genes that can then be monitored externally. While this may sound like science fiction, it is excitingly real and feasible and the implications for the development of counterdrug medications for humans could be breathtaking.