CTAC R&D PROGRAM SUMMARY

CTAC's R&D program supports both demand and supply reduction efforts to reduce illicit drug use in America.

Demand Reduction

CTAC, in collaboration with the National Institute on Drug Abuse (NIDA), has created a niche for developing and installing advanced technology that enables innovative substance abuse research across the nation. This collaboration ensures that advances in the design of neuroimaging and genetics instrumentation enable concept-driven paradigm shifts in science. Just as X-ray crystallography enabled Watson and Crick's discovery of the double helix, advanced neuroimaging instrumentation and facilities to image the living brain likely hold the keys to unlock knowledge about the effects of substance abuse on the brain.

The creation of a comprehensive representation of how the brain forms, functions, and falters will help reduce drug addiction (and other neurological disorders) as both a public and individual health problem. Thoroughly understanding the changes that occur on a cellular, molecular, circuit and behavioral level within individuals in an addicted state will enable researchers to develop truly effective preventative and treatment measures. Identifying individual genetic variations that confer risk (or resistance) will help society provide more effective and targeted prevention and education efforts. Likewise, knowing the precise changes will allow for specific regimens targeting the particular brain pathways that have been distorted by the substance of abuse.

Novel non-invasive neuroimaging instrumentation allows scientists to penetrate the deepest regions of the brain. These scientists aim to unveil the detailed underlying mechanisms that answer how drugs act in the brain, how addictive states transpire, and which treatment and prevention efforts are most effective. With CTAC support, many of the nation's finest substance abuse research centers are being equipped with the most modern neuroimaging facilities available to reveal the brain with a depth, clarity, and delineation previously unavailable.

Figure 2 shows the location of the CTAC-supported substance abuse research centers that have received leading-edge neuroimaging facilities or medical instrumentation through this CTAC program. These institutions have all agreed to focus on drug abuse research and train the next-generation of researchers to continue the advancement of our knowledge.

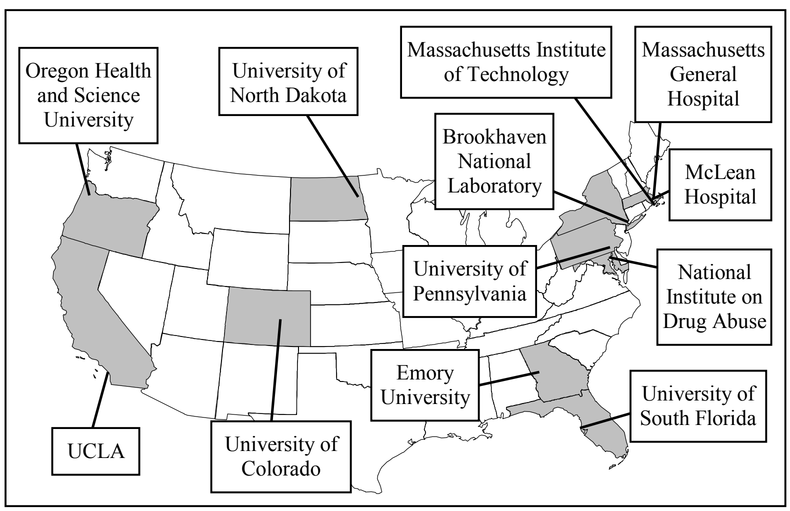

Figure 2. Locations of CTAC Demand Reduction Infrastructure Technology Initiatives

Projects Becoming Operational During 2002

McLean Hospital's Brain Imaging Center in Belmont, Massachusetts has begun using a high field (4-Tesla) functional Magnetic Resonance Imaging (fMRI) / Magnetic Resonance Spectroscopy (MRS) scanner for clinical assessments of drug addicts. This system provides a spectroscopic means to measure the drug chemistry and metabolism in the brain. McLean Hospital scientists are using these MRS capabilities to study the neurochemical changes associated with acute and chronic use of alcohol, marijuana, cocaine, and heroin, in addition to attracting new post-doctoral fellows to focus their efforts on drug abuse research. McLean's MRS experience will enable them to develop better treatment assessments, dubbed "surrogate markers." Such markers are already used in clinical trials of multiple sclerosis, HIV dementia, and other neurological diseases.

An Institutional Research Protocol was approved for the Massachusetts General Hospital (MGH) in Boston, Massachusetts allowing the MGH research team to use the powerful 7-Tesla fMRI to obtain human images. Receiving protocol approval allows researchers to move forward with a research program to examine the brain reward circuitry that mediates drug addiction and characterizes the temporal dynamics when presented with a drug. Doing so will require a multi-site, national effort with the collection of thousands of scans comparing the addicted and naïve brains. The MGH team is forming collaborative relations with other institutions with specialized capabilities in genetics and allied fields to further empower their research to develop neuroimaging technology as a clinical tool for the diagnosis and prognostic determination of treatment for substance abuse disorders.

In early April, the University of Pennsylvania held the ribbon cutting for a new high resolution Positron Emission Tomography (PET) camera making breakthrough use of Gadolinium Ortho-Silicate crystal detectors. This crystal type has demonstrated improved signal-to-noise ratio, increased image contrast, and higher count-rate capability compared to standard sodium iodide crystals. Those improvements over the PET systems are expected to significantly advance the output of Pennsylvania's research into craving and its possible controls. Patient studies in 2003 will validate the imaging protocol, modeling and quantitative analysis of neuroreceptor studies by imaging brain activity resulting from cue-induced cocaine craving.

NIDA's Intramural Research Program (IRP) applied the advantages of a head-only fMRI over those of typical whole-body machines in a multidisciplinary approach to drug abuse research. IRP-based scientists will interact with medication development and treatment researchers to test clinical efficacy of new potential medications. The selected 3-Tesla unit provides an increased signal-to-noise ratio through advanced techniques.

Research Triangle Institute has completed tests with human subjects using the PET system and associated radiotracer chemistry lab at the NIDA Intramural Research Program (IRP) in Baltimore. Researchers conducted quantitative analyses of brain activity using bolus Oxygen-15 to measure regional cerebral blood flow in abstinent drug abusers and healthy control subjects performing standardized cognitive tasks. Researchers aim for differences between the two groups in cognitive abilities and their neuroanatomical correlates to be used by clinicians to extrapolate treatment responses based on the underlying dysfunction seen through the tested vulnerability factors/markers.

Projects Continuing in 2003

At UCLA's Crump Institute, an ultra-high resolution small animal PET facility was installed at the main campus in the Sepulveda Veteran's Administration Medical Center. This state-of-the-art MicroPET center will be co-located with the Vervet monkey colony. The facility will consist of the MicroPET relocated from the main campus with associated biomedical cyclotron and radiochemistry equipment. This new facility will enable scientists to use the well-defined lineage of the Vervet monkey colony in non-human primate studies to link biochemical events to the specific genes critical to brain reward functions. This facility will also have the capability to evaluate therapeutic compounds and will provide a platform for training future scientists in addiction research.

A high-field fMRI will enable scientists at Oregon Health and Science University to study the effects of performance enhancing anabolic steroids and other drugs in the adolescent brain. Several advanced techniques will be employed with the machine. Magnetic Resonance perfusion and tensor imaging will be used to learn more about the effects of methamphetamine and cocaine in humans and in developing monkeys. MR arterial spin labeling will be used to examine the relationship between anxiety and depressive behaviors and the risk for drug dependence.

The University of Colorado Health Sciences Center will use a 3-Tesla fMRI to study prevention efforts in adolescents just beginning drug abuse, and how brain function is altered during cocaine and amphetamine-induced states. This tool will radically help researchers determine the brain abnormalities associated with inherited risk for substance abuse in conduct-disordered adolescents.

Massachusetts Institute of Technology is exploring improved imaging methods using conventional single photon emission computed tomography (SPECT) technology based on the use of innovative processing algorithms, particularly coded aperture. Researchers are building a prototype system with sub-millimeter resolution to upgrade existing gamma camera technology with limited three-dimensional information available through laminography.

The Drug Evaluation Network System (DENS) is a data backbone with analysis software used to collect and track "treatment entry" data on addicts. DENS is helping addiction researchers compare treatment outcomes across treatment modalities. The system incorporates the standardized Addiction Severity Index (ASI) screening and assessment system. This project has already yielded a database rich in detail from over 35,000 patient records enrolled in 21 treatment programs. The DENS website tracks treatment program data from clinics in major cities, including Philadelphia, Chicago, Los Angeles, New York and Miami. The European Union is now interested in using the ASI with DENS. A planning meeting in early 2003 in Stockholm, Sweden is being held to discuss how best to implement DENS in Europe.

In January 2003, a new exhibit on the dangers of addiction opened at the Arizona Science Center in Phoenix. Visitors to this exhibit learn about the latest research on brain function before and during addiction. The exhibit, comprised of two four-sided kiosks, includes a range of multi-sensory interactive experiences and computer-based media to introduce teens and parents to groundbreaking research on the dangers of addiction and how it can be treated and prevented. Visitors to the exhibit can view a simulated PET scan machine to see the effect drugs have on the human brain.

Videos featuring testimonials of young addicts now in recovery show the emotional and spiritual costs of using illicit drugs. Ideally, this presentation will not only warn students away from drugs but also inspire young people to pursue careers in the field of addiction research. If this prototype science museum exhibit is successful, it can be replicated for use in other science museums across the country.

University of Arizona is conducting a study to reduce adolescent substance abuse relapse through the treatment of sleep disturbance. This project focuses on developing an effective, multi-component, group treatment of sleep disturbance and daytime sleepiness for adolescents who have completed treatment for substance abuse. Sleep problems occur in association with and during withdrawal from a variety of substances and lead to increased likelihood of reuse, poor school and work performance, absenteeism, and increased depression. The treatment of sleep disturbance promises to reduce these risk factors and reduce the likelihood of relapse.

New Projects Starting in Late 2002 or Early 2003

University of North Dakota at Grand Forks will install a MicroPET facility to validate the use of the Weaver mutant mouse as a suitable model to study individual dopaminergic systems involved in drug addiction. This technology dedicated for substance abuse research is also devoted to training Native American students to participate in such research.

Genetics researchers at the Roskamp Institute of the University of South Florida in Tampa are using recent developments in microarray technology to investigate blood gene expression to classify characteristic fingerprints produced by specific drugs. This ability to profile changes in RNA across the human genome will enable the production of detailed genomic and proteomic models of responses to drug challenges by serial analysis of gene and protein expression/ modification. Coordination between CTAC sites will subsequently correlate these models with neuroimaging of use, abuse, and addiction. This program will generate a standard procedure for using microarray technology to obtain unique patterns from peripheral blood samples from a large, well-characterized sample. The DNA of identified genes will be analyzed to determine any genetic variation, indicating any possible susceptibilities to substance abuse. Comparing the differences of the genes will enable inferences among those encoding predisposition to drug abuse (trait), or response to drug exposure (state). The researchers will then create easily useable customized RNA and DNA arrays to test for the presence of these trait or state markers.

Brookhaven National Laboratory (BNL) is using MR microscopy and molecular modeling to establish a preclinical high-resolution MicroMRI. This 9.4-Tesla 20-centimeter bore diameter MRI will become part of the NIDA Regional Neuroimaging Center at BNL. The MicroMRI technology will enable the researchers to non-invasively measure changes in brain morphology, brain function, and brain neurochemistry in rodents. A MicroMRI instrument will make studies possible in the rodent model pertaining to the functional and structural changes in response to drugs while monitoring their temporal response.

A superconducting magnet system for use in high-resolution magnetic resonance in-vivo spectroscopy will be installed at the NIDA IRP in Baltimore, Maryland in early 2003. This high field machine is also at 9.4-Tesla, but with a 31-centimeter bore diameter, other primate species will be available for future testing.

Supply Reduction

CTAC works with the national drug control agencies in the development and evaluation of technology to interdict drug shipments and to disrupt drug trafficking organizations. The following development projects are either complete or are being evaluated by federal law enforcement agencies (LEAs) for use in the field.

Tactical Technologies

Tactical technology development efforts to support the law enforcement officer performing daily operations include projects to improve knowledge management through information sharing across networks, data mining, tracking and surveillance, internet analysis, and communications interoperability capabilities.

The integration of real-time location and tracking systems with database records of current and past criminal associations will give law enforcement new tools for strategic and tactical planning and execution of drug-related criminal investigations. A scalable information tool, Crystal, is being developed in conjunction with the Rockland County (NY) Narcotics Task Force to enable agencies to organize and present criminal and case-related information with real-time positional data from tracking and surveillance management systems. Users can visually link suspected criminal activity under surveillance to a geographic / historic positional background.

CTAC, in conjunction with DEA, also supports the development of a digital radio system for use in an advanced body wire device. The digital radio features will provide increased capabilities in terms of security (low probability of detection) and intelligence gathering compared with earlier analog devices.

In addition, CTAC supports the development of low-cost handheld sensors to detect cocaine methylbenzoate vapors. These sensors are based on a combination of sensitized metal ion luminescence and molecular imprinting. Molecularly imprinted polymers are synthetic polymers designed to selectively bind to a certain molecule. Optical fibers coated with ultraviolet LED's then detect the binding of the target molecule. Ten handheld units will be available for testing by the spring of 2003.

Decoder technology is being developed to enable law enforcement agencies to monitor mobile telephone communications across the various provider and vendor technologies. This technology should be available in early 2003.

A VHF tactical repeater technology is being developed with deployment planned for spring 2003.

Wireless Communications Interoperability

A statewide wireless communications interoperability architecture was designed for Colorado in fiscal year 2001. This architecture facilitates communications across the dissimilar and incompatible wireless networks of federal, state, and local agencies within the state. Engineers from the U.S. Naval Space and Naval Warfare Systems Center - San Diego (SPAWAR SSC-SD) evaluated two system configurations for this architecture – one capable of interfacing up to 24 agencies for larger operations and a second configuration designed for smaller operations involving five or fewer agencies.

The project had two phases:

- *Phase I: Denver Metro.* In the Denver metropolitan area, SSC-SD engineers installed a fixed interoperable system that makes use of the existing radio-antenna area coverage of local area LEA participants. Portable interoperable systems were also deployed for those drug task forces operating outside the range of the existing towers. Participating LEA resources were provided complete training on use of these systems. This phase was completed and a major demonstration held during August 2001.
- *Phase II: Statewide Deployment.* SSC-SD Engineers conducted surveys of radio spectrum coverage and an inventory of existing infrastructure equipment for six selected locations throughout Colorado. SSC-SD engineers then installed interoperable communications systems at a host organization for each site and provided location-specific training to LEA resources with responsibility for operating each system. CTAC worked with participant LEAs to establish protocols and procedures for linking the deployed systems to create a statewide communications interoperability capability. Participant LEAs displayed this statewide capability to law enforcement officers from across the country at a major demonstration held at Castle Rock, Colorado in August 2002.

In fiscal year 2002, communications interoperability systems were installed in six regions including Denver, Colorado Springs, Durango, Grand Junction, Larimer County, and Pueblo. The installation of a seventh system has begun in Steamboat Springs.

Drugged Driving Initiatives

Last year, the University of Utah Center for Human Toxicology conducted an evaluation of Point of Collection Test (POCT) devices with an emphasis on those devices using saliva. In coordination with the National Highway Traffic Safety Administration (NHTSA), CTAC is collaborating with the British Home Office and European Union for further testing and evaluation of POCT devices in the United Kingdom and Europe. The tests will be a continuation of the original Roadside Testing Assessment (ROSITA) with an anticipated start date for the testing phase to be in the first quarter of calendar year 2003.

CTAC also supports the development of an ion selective electrode designed by the Naval Research Laboratory to detect drugs in various matrices such as saliva and sweat in field settings. A prototype device has been constructed.

Test and Evaluation Support

SPAWAR SSC-SD manages CTAC's tactical technology testbed project. This testbed examines tactical technologies that will become part of an overall system architecture of law enforcement current and future counterdrug systems. SSC-SD has testbeds in San Diego, New York, Baltimore and Oklahoma City. Each testbed has a different set of tactical support technologies.

CTAC also sponsors test and evaluation activities with the federal drug control agencies. For example, the U.S. Customs Service uses a Community Test and Evaluation Center (CTEC) that has been relocated from North Carolina to the Patuxent Naval Air Station in Maryland. Less than lethal technologies for boat-to-boat interdiction were developed by Customs engineers and tested at CTEC last year.