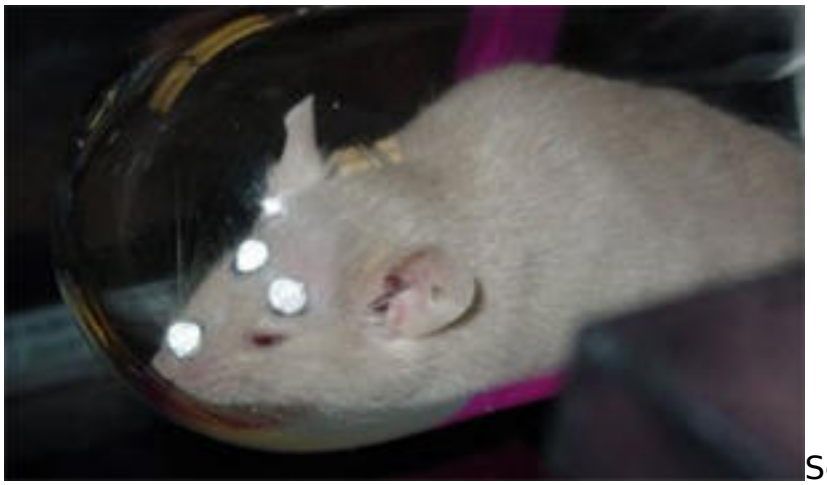
System Provides Clear Brain Scans of Awake, Unrestrained Mice

Kandice Carter, Jefferson Lab



Setting a mouse free to roam might alarm most people, but not so for nuclear imaging researchers from the U.S. Department of Energy’s Thomas Jefferson National Accelerator Facility, Oak Ridge National Laboratory, Johns Hopkins Medical School and the University of Maryland who have developed a new imaging system for mouse brain studies.

Scientists use dynamic imaging of mice to follow changes in brain chemistry caused by the progression of disease or the application of a drug as an effective research tool for developing better ways to diagnose disease and formulate better treatments. In most nuclear imaging studies, laboratory mice are typically drugged or bound in place so that their brains can be studied. However, the results of such research can be tainted by subjecting the mice to such chemical or physical restraints, complicating studies of Alzheimer's, dementia and Parkinson's disease.

But for their nuclear medicine imaging studies, the researchers from Jefferson Lab, Oak Ridge, Johns Hopkins and Maryland used a new system they developed to acquire functional images of the brains of conscious, unrestrained and un-anesthetized mice. The so-called AwakeSPECT system was then used to document for the first time the effects of anesthesia on the action of a dopamine transporter imaging compound in the mouse brain. Such dopamine transporter imaging compounds are used for Alzheimer's, dementia and Parkinson's disease studies.

SPECT is Single-Photon Emission Computed Tomography. In this technique, a radionuclide is injected, where it collects in specific areas of the brain by function. The radionuclide emits gamma rays (single photons) that are collected by a detector in separate scans from many different angles. The scans are combined in an algorithm to produce a three-dimensional image.

"The AwakeSPECT system does regular SPECT imaging of mice. SPECT is a nuclear medicine imaging technique that's used in humans for various types of diagnostic

studies. It's also used in animal studies to facilitate the development and understanding of disease physiology," says Jefferson Lab's Drew Weisenberger, who led the multi-institutional collaboration and directed the SPECT system development effort.

Weisenberger says the AwakeSPECT system uses two Jefferson Lab custom-built gamma cameras to image the radionuclide, as well as a system that processes the data to produce the three-dimensional images. An infrared camera system developed at Oak Ridge National Laboratory tracks movement of the mouse. Finally, a commercially available CT system provides additional anatomical information.

Researchers at Johns Hopkins Medical School, led by Martin Pomper, conducted the first mouse imaging studies with the new system. To prepare a mouse for imaging with AwakeSPECT, it is first tagged with three markers that are glued to its head for the infrared system to track. Once the radionuclide is injected, the mouse can then be imaged as it rests in a homey, burrow-like, clear tube. The beauty of the system is that it doesn't require that the mouse (or potentially people, at a later stage) remain motionless. Two patents have been awarded to Jefferson Lab for the innovative technology associated with this system.

"We developed this system that, while acquiring SPECT images, uses infrared cameras that track the location and pose of the head. We use that information to then computationally remove motion artifacts from our SPECT imaging," he says.

In this recent study published online in The Journal of Nuclear Medicine [1], the researchers showed that AwakeSPECT can obtain detailed, functional images of the brain of a conscious mouse, as the mouse moves around freely in an enclosure.

Researchers also imaged the action of a drug often used to image dopamine transport in the brain, ^{123}I-ioflupane, in awake and anesthetized mice. They found that the drug was absorbed less than half as well in awake mice, showing that the use of anesthetic could potentially confound drug uptake studies.

"We've shown the technology works. Now, you just have to make it a tool that more people will readily use" Weisenberger says.

Weisenberger says the next step is to improve the AwakeSPECT imager by upgrading the infrared tracking system, using newer technology for the SPECT imager, and by making the system more intuitive for animal researchers to operate.

Early funding for the program was provided by DOE's Office of Science, and more recent support has been provided by the National Institutes of Health.

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