Molecular imaging reveals marker of neurodegenerative disease

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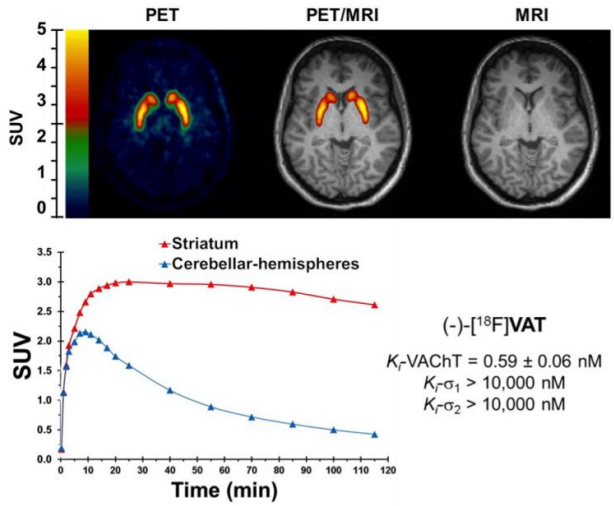

Figure 1. PET study of (-)-[^{18}F]**VAT** in a healthy human subject. PET (top left), PET/MRI (top middle) and MR (top right) images; time-activity curves (bottom) for striatum (red triangles) and cerebellar-hemispheres (blue triangles).

Figure 1 is a PET study of (-)-[F-18]VAT in a healthy human subject. PET (top left), PET/MRI (top middle) and MR (top right) images; time-activity curves (bottom) for striatum (red triangles) and cerebellar-hemispheres (blue triangles). Credit: H. Jin, X. Yue, X. Zhang, J. Li, H. Yang, Z. Tu, Radiological Science, Washington University, St. Louis, Mo.; H. Flores, M. Karimi, J.S. Perlmutter, Department of Neurology, Washington University School of Medicine, St. Louis, Mo.; S.M. Parsons, Department of Chemistry and Biochemistry, University of California, Santa Barbara, Santa Barbara, Calif.

Brain researchers have been working for years on targeting a cellular process involved in neurodegeneration and cognitive dysfunction. A specialized molecular imaging agent does the job by binding to a transporter of the neurotransmitter acetylcholine, a major mediator of the central nervous system, say presenters at the 2015 Annual Meeting of the Society of Nuclear Medicine and Molecular Imaging (SNMMI).

Scientists first realized in the 1980s that the biomarker known as the vesicular acetylcholine transporter (VAChT) was involved in the loss of certain nerve cells called cholinergic neurons, which happen to be plentiful in the cerebral cortex and other areas of the brain. Acetylcholine works as either an excitatory or inhibitory medium, depending on the environment. It is the inhibition of cholinergic neurons that has been the focus of recent studies. After several setbacks, researchers are evaluating a positron emission tomography (PET) imaging agent that follows the eventual breakdown of neurons, leading to problems with cognition.

"A potent and selective PET tracer for VAChT could be used to quantify the loss of cholinergic neurons and assess the effect of that loss on cognitive impairment in patients with Alzheimer's disease, Parkinson's disease, Huntingtons disease and other neurodegenerative disorders," said Hongjun Jin, PhD, lead author of the study and a researcher from the department of radiological science at Washington University in St. Louis, Mo.

PET is an ideal imaging system for VAChT because it is capable of imaging physiological processes at the cellular and molecular level. The scan is preceded by an injection of a radiotracer comprising a very small amount of radioactive material and a molecular compound that seeks out the targeted biochemistry, in this case the VAChT via an inhibitory pathway.

For this preclinical rodent and primate study, a small group of rats and cynomolgus monkeys underwent PET imaging with the investigational imaging agent (-)-[18F]VAT. Results of the research showed encouraging biodistribution, and exposure did not exceed acceptable limits. Uptake of the agent was highest in the striatum of the brain. The agent is not yet approved for widespread use, but this study shows that the radiotracer is stable, safe and able to visualize the VAChT.

"Molecular imaging of this presynaptic marker would be a valuable tool in not only preclinical investigations of cholinergic neurons and the biological mechanisms underlying cholinergic neurotransmission but also dystonia, a movement disorder. It may even provide insight into the biochemistry of drug abuse," said Jin.

A human trial is already underway. With further validation, this noninvasive method of VAChT imaging could be used to monitor the efficacy of cholinergic therapies in neurodegenerative disease.

More information: Scientific Paper 4: "A promising F-18 labeled PET radiotracer (-)-[18F]VAT for assessing the VAChT in vivo"

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