PET Imaging Agents for a4b2 Nicotinic Receptors

https://neurodegenerationresearch.eu/survey/pet-imaging-agents-for-a4b2-nicotinic-receptors/

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Country

USA

Title of project or programme

PET Imaging Agents for a4b2 Nicotinic Receptors

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 871,720.18

Start date of award

01/06/2007

Total duration of award in years

8

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Bioengineering... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Lung... Neurodegenerative... Neurosciences... Prevention... Substance Abuse... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): Nicotinic ?4ß2 receptors have been implicated in a number of pathophysiologies and are being studied extensively. At University of California-Irvine (UCI), we have several major programs that would gain from imaging nicotinic receptors. These include: 1) Program in neurodegenerative disorders; 2) Program on studies related to nicotine dependence; 3) Program in the early detection of lung cancer, and 4) Neurobiology of learning and memory. During the previous funding period we have successfully taken a new imaging agent, 18F-Nifene to human studies. 18F-Nifene, which has high affinity for ?4ß2 receptors, had no adverse effects in the healthy subjects, showed rapid brain uptake with ratios of thalamus to corpus callosum reaching 3 in 45 mins. A scan time of 45 mins is considered optimal. Both thalamic and extrathalamic receptors were clearly visualized in the human brain. The high ratios in specific brain regions and short scan time suggest 18F-Nifene to be amongst the most suitable agonist as a PET imaging agent for ?4ß2 receptors in humans. Therefore, our goals in this renewal NIH application are to complete the brain human studies with 18F-Nifene. Brain distribution of 18F-Nifene will be evaluated in normal volunteers in a test-retest paradigm to establish reproducibility and imaging methodology for quantitative analysis. Human radiation dosimetry studies will be carried out using a PET/CT scanner on 6 subjects. A second goal of the study is to evaluate effects of nicotine in healthy subjects in order to assess the degree of 18F-Nifene displacement in various brain regions, including corpus callosum. Sensitivity of 18F-Nifene to cigarette smoking will also be assessed, in order to evaluate its usefulness in tobacco dependence studies. A third goal of the proposal is to complete the preclinical development of a novel PET/SPECT agent Niofene which is a putative antagonist for this receptor and can be radiolabeled with fluorine-18 for PET or iodine-123 for SPECT studies. The availability of an agonist and antagonist will allow comparative studies of this receptor system in various disorders. The fourth goal of this application is to evaluate if 18F-Nifene is able to detect changes in the receptors in postmortem brains of Alzheimer’s and Parkinson’s disease patients using autoradiographic methods. This will help in translation of the use of 18F- Nifene in PET studies of neurodegeneration as well as other CNS disorders.

Lay Summary

PUBLIC HEALTH RELEVANCE: Development of human imaging methods for nicotinic receptors will help understand several brain disorders, such as Alzheimer’s disease, Parkinson’s disease, learning and cognition as well as tobacco dependence and lung cancer. This grant application has the potential for efficient diagnosis, treatment planning and therapeutics development for these diseases.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A