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116
[C-11]FLUDIAZEPAM: BENZODIAZEPINE RECEPTOR MAPPING AGENT

Synthesis of [C-11]fludiazepam (FDZ) and its biodistributions in rats and a dog were investigated as basic studies of benzodiazepine receptors with positron emission tomography.

[C-11]FDZ was synthesized by the reaction of norFDZ with [11C]I and purified by HPLC. In rats, [C-11]FDZ accumulated in order of adrenal > small intestine > liver > spleen. In other organs including the brain, high incorporation just after the injection and rapid clearance were observed. Autoradiogram of the brain showed relatively high uptake in the cortex. Two treatments with antagonist of benzodiazepine, RO 15.1788, 15 min before and 15 min after the injection of [C-11]FDZ were performed for estimating specific accumulation. Regional cerebral uptakes were reduced to be 50%-90% by the posttreatment except for the thalamus and hypothalamus, but the effect of pretreatment is small. Uptake in the adrenal was enhanced, but uptakes in other organs were not significantly influenced. In PET studies of a dog brain, similar treatments showed relatively high accumulation in the cortex. Since RO 15.1788 has little physiological effects on the human, there is a possibility that these treatments were applied to human studies with PET.

117
EFFECTS OF BENZODIAZEPINES TO THE KINETICS OF C-11 RO15-1788 IN NEUROLOGICAL PATIENTS

Ten patients of functional neurological disorders receiving benzodiazepines were studied with C-11 RO15-1788 and positron emission tomography. In those patients, the cortex: blood ratios 20 minutes after injection, which is thought to be and index of receptor binding potential, were lower than those in normal volunteers without any drug. The result suggest that some of benzodiazepine receptor were occupied by benzodiazepines, which the patients had taken.

Two patients were studied twice when they had taken no medicine and when they had taken benzodiazepines for the treatment. The brain uptake of C-11 (Dose/ml) was observed in some parts of the brain. The cortex: blood ratios of RO 15-1788 significantly declined with advancing age. Old blood flow scanning was carried out for each subjects either just before or after the PET images anatomiically.

Region of interest (ROI), circular and 16 mm x 16 mm size, was set on each functional images and the average values within each ROIs were evaluated.

In whole brain, only rCMRO2 showed significant decline with advancing age, but, other parameters did not. Regionally, significant reduction of rCMRO2 with age was observed in some parts of the cerebral cortex and the basal ganglia.

118
CEBREAL BLOOD FLOW AND OXYGEN CONSUMPTION DURING AGING — QUANTITATIVE ANALYSIS USING O-15 LABELLED GAS INHALATION METHOD.

Positron emission tomographic (PET) study provides the regional functional information of the human brain such as cerebral blood flow and oxygen metabolism. In the present study, regional cerebral blood flow (rCBF), regional cerebral metabolic rate of oxygen (rCMRO2), and regional cerebral blood volume (rCBV) were measured using O-15 labelled gas inhalation method and HEADTOME-III in 22 normal volunteers (17 males and 5 females) whose age were ranged from 26 to 64 years old. The measurement was performed at resting state in the supine position with eyes and ears open, and plain X-ray CT scanning was carried out for each subjects either just before or after the PET images anatomiically.

Region of interest (ROI), circular and 16 mm x 16 mm in size, was set on each functional images and the average values within each ROIs were evaluated.

In whole brain, only rCMRO2 showed significant decline with advancing age, but, other parameters did not. Regionally, significant reduction of rCMRO2 with age was observed in some parts of the cerebral cortex and the basal ganglia.

119
BRAIN METABOLISM IN CEREBRAL INFARCTION STUDIED WITH [11C-1-PYRUVATE. F. Yokoi et al.
T. Hara, M. Ito, R. Iizuchi and K. Shigeno. National Center for Nervous,Mental and Muscular Disorders, Tokyo. National Nakano Chest Hospital, Tokyo, Tzu-Nirayama Onsen Hospital, Shizuka.

We examined eight patients with cerebral infarction using PET scanner. Quantitative measurements of cerebral blood flow (CBF), cerebral metabolic rate of oxygen (CMRO2), and oxygen extraction fraction (OEF) with 18O continuous technique were conducted according to Frackowiak et al. A dose of 30-40 mCi of 11C-l-pyruvate was injected intravenously, and immediately afterwards the PET scan started. Images were obtained with the count collected at consecutive 5-minutes periods until 25 min after the injection. After PET study was finished, the patient underwent X-ray CT examination next.

The early PET images closely resembled the images of CBV and CMRO2, both of which were decreased in the area where XCT indicated low density. In the fresh 5 cases, the late images with C-1-pyruvate demonstrated increased intensity in the cerebral ischemic region. In the relatively old 3 cases, the late images were still low in the ischemic region.

The extraction of 11C-l-pyruvate - 11C from blood and cerebral clearance of its metabolic product should be rapid in well-oxygenated brain tissue but the radioactivity in ischemic region should accumulate as result of entrapment in the 11C-lactate produced.

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