

55

2'-IODOSPIROPERIDOL: A NEW RADIOPHARMACEUTICAL FOR SPECT STUDIES OF DOPAMINE RECEPTORS. H.Saji, T.Tokui, Y.Kuge, A.Saiga, A.Yokoyama, I.Nakatsuka*, M.Okuno*, A.Yoshitake*, K.Torizuka**. Fac. of Pharma. Sci. & Sch. of Med. *Sumitomo Chemical Inc., **Fukui Medical College.

The usefulness of 11-C and 18-F labeled butyrophene compounds for the detection of dopamine receptors (DAR) constitutes a field of great interest. Being aware of the prompt availability of 123-I, our effort was directed to the development of butyrophenes iodinated at the ortho position of the p-fluorobutyrophene moiety, postulated as the position causing lower alteration in receptor binding environment. Various iodinated butyrophenes were synthesized from corresponding amine compounds by the Sandmeyer reaction. The radiolabeling easily carried out by radioiodine exchange reaction. Among synthesized compounds, the 2'-iodospiroperidol (ISP) showed the highest affinity for DAR by the vitro binding assay. On the other hand, this compound showed relatively low affinity for serotonin receptor. The in vivo biodistribution and macroautoradiographic studies were compatible with results obtained in the in vitro study, showing higher accumulation in the striatum than in other brain regions. Thus, the 2'-ISP is a promising candidate for SPECT study of DAR, provided the 123-I becomes readily available.

57

RADIOPHARMACEUTICALS AS AMINO ACID METABOLISM MARKER (7). BASIC STUDY FOR PANCREAS FUNCTION DIAGNOSIS USING L-[S-METHYL-C-11]-METHIONINE. Y.Fujibayashi, K.Kawai, K.Matsumoto, H.Saji, A.Yokoyama, K.Torizuka. Faculty of Pharm. Sci. & School of Med., Kyoto Univ. Kyoto & Fukui Medical College, Fukui.

C-11-natural amino acids (AA) have been evaluated as pancreas imaging radiopharmaceutical. L-[S-methyl-C-11]-Methionine (S-methyl-Met), an easy and rapidly synthesized amino acid is already in use in clinical studies. It will be soon become available in our hospital and the AA metabolic rate measurement for functional diagnosis using compartment model analysis was considered of interest. For function diagnosis, we studied the metabolic retention system of S-Met in pancreas. As a first approach, clinically applicable FDG-type 3-compartment model was used. Upon the analysis of the radioactivity in pancreas and its protein fraction, great discrepancy of calculated data from the observed data was visualized. The causal being assigned to the considerable amount of low molecular weight metabolites (LMWM), confirmed by TLC of 5 % TCA soluble pancreas fraction. Upon the assignment of a compartment for the LMWM, the model fitted well to observed data. Thus the present results indicated the difficulty of FDG-type 3-compartment model analysis in S-methyl-Met study and the necessity to estimate the participation of Met specific metabolic pathway along with protein synthesis.

56

¹⁸F-LABELLED PHENYLALANINE AND TYROSINE - SYNTHESIS AND FUNDAMENTAL STUDY FOR THE AVAILABILITY. M.Murakami, K.Takahashi, H.Sasaki, E.Hagami, H.Iida, I.Kanno, S.Miura and K.Uemura. Research Institute for Brain and Blood Vessels-AKITA, Akita.

Amino acids labelled with positron emitting nuclide is a useful for the measurement of protein synthetic rate. At present, carbon-11 labelled amino acid is popular, but its physical half life is thought to be short for sufficiently long lasting data acquisition. Therefore, we tried the fluorination of phenylalanine and tyrosine. The fluorination with ¹⁸F-F₂ and ¹⁸F-AcoF was compared to obtain ¹⁸F-phenylalanines. L-phenylalanine in CF₃COOH trapped ¹⁸F-AcoF more effectively than ¹⁸F-F₂. The main product was 2-¹⁸F-phenylalanine (28.4 ± 18.5 %) when ¹⁸F-AcoF was used as a reagent. Lower radiochemical yield of ¹⁸F-phenylalanines and significant formation of by-products were observed in the case of ¹⁸F-F₂. Similarly, 3-¹⁸F-tyrosine was obtained with good yield (28.8 ± 4.1 %) when ¹⁸F-AcoF was used as a precursor.

In the rat brain, about 30 % of radioactivity was fixed in macromolecules and most of free radioactivity was existed as amino acids at one hour after 2-¹⁸F-phenylalanine injection. In the case of 3-¹⁸F-tyrosine, significant amount of radioactivity existed as keto-acids. Catecholamine fraction had negligible radioactivity in both cases.

58

RADIOPHARMACEUTICALS AS AMINO ACID METABOLISM MARKER (8). THE EFFECTS OF LABELED POSITION OF C-11-METHIONINE ON ITS METABOLIC BEHAVIOR. K.Kawai, Y.Fujibayashi, K.Matsumoto, Y.Yonekura, H.Saji, A.Yokoyama, K.Torizuka. Faculty of Pharm. Sci. & School of Med. Kyoto Univ. Kyoto & Fukui Medical College, Fukui.

L-[S-methyl-C-11]-Methionine (S-methyl-C-11-Met) accumulation in pancreas has been considered as reflecting the protein synthesis function in clinical studies, however as previously shown, this represents part of the agent metabolic pathway. In order to study the influence of labeled position on the metabolic selectivity followed S-methyl-C-11-Met, three different labeled L-Met, S-methyl-Met, L-[1-C-14]-Methionine (1-Met) and L-[3,4-C-14]-Methionine (3,4-Met) were selected and the mice biodistribution was surveyed. Pancreatic accumulation of S-methyl-Met and 3,4-Met was higher than 1-Met, but protein incorporation (5 % TCA insoluble fraction) in pancreas was, in S-methyl-Met and 3,4-Met, 50-66 % of the accumulated radioactivity at 30-60 min. post i.v., while an increase to 90 % was detected in 1-Met. This result suggested the presence of catabolism to C-14-CO₂, easily released from pancreas cells. Therefore 1-C-11-Met accumulation reflects mainly the protein synthesis. S-methyl-Met showed also high potentiality as amino acid metabolism marker especially if co-administered with 1-C-11-Met.