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BIOMEDICAL STUDIES OF RADIOBROMINATED NEUROLEPTICS. -BROMPERIDOL AND BROMO-SPIPERONE-

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For imaging dopamine receptors, radiobromi nated neuroleptics, bromperidol(BP) and bromo-spiperone(bromo-SP), were evaluated. Comparison studies were also carried out with H-3-haloperidol(HP), H-3-spiperone(SP), ans C-14-methyl-spiperone(methyl-SP).

Rats were injected with those labeled neuroleptics and, 2 hours later, were killed by decapitation. The brains were removed, and striatum, cortex and cerebellum were dissected for counting radioactivity.

15 to 40 times higher doses of HP or BP were taken up in whole brain than SP, bromo-SP, or methyl-SP.However, these neuroleptics were distributed rather uniformly in brain, which resulted in low striatum to cerebellum or striatum to cortex ratio. On the other hand, although whole brain uptake of SP and its derivatives, bromo-SP & methyl-SP, were low, i.e. 0.04-0.07 %dose, these ligands seemed to be trapped specifically in striatum. In consequence, striatum to cerebellum and striatum to cortex ratios were 2.5-7 and 1.7-2.5 times higher than those of HP or BP, respectively.

In conclusion, for imaging dopamine receptors, SP or its derivatives such as bromo-SP would be a better chice than BP or HP.

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(C-11)LABELED N,N-DIMETHYLETHANOLAMINES AS CHOLINERGIC NEUROTRANSMISSION IMAGING AGENTS : SYNTHESIS AND BIODISTRIBUTION

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Acetylcholine (Ach) is one of the important neurohumoral transmitters. The labeled choline (Ch) derivatives have been used for various studies. But , for the brain imaging study, the labeled Ch derivatives were disadvantageous because they were poorly uptaken in the brain owing to the quaternary ammonium salt structure.

In order to develope the available radiopharmaceuticals for the brain study concerning neurotransmission of Ach, we tried the (C-11)labeling of N,N-dimethylethanolamines such as N,N-dimethylethanolamine (DMEA), O-acetyl-N,N-dimethylethanolamine (O-Ac-DMEA) and O-methyl-N,N-dimethylethanolamine (O-Me-DMEA), which were precursors of Ach and had no quaternary ammonium salt structure in their molecules. These (C-11)labeled compounds were synthesized by the reaction of N-monomethylethanolamine with (C-11)MeI.

In regional distribution study in the rat brain at 30 min after injection by punch sampling procedure, DMEA was relatively highly accumulated in the frontal cortex and posterior cortex.

In PET-study on dog with these three (C-11)labeled compounds, we have also found the relatively high accumulation of DMEA in the frontal cortex and posterior cortex, the high accumulation of O-Ac-DMEA in the muscle and the non-specific accumulation of O-Me-DMEA in the brain.

DMEA is expected to be useful for brain imaging study as positron emitting radiopharmaceuticals.

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Automated Synthesis Of High Specific Activity C11-Ro 15-1788 For PET Studies Of Benzodiazepine Receptors.

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C11-Ro 15-1788 was prepared automatically with high specific activity for in vivo visualization or quantitative analysis of brain benzodiazepine receptor. Yield, radiochemical purity and specific activity of the product ready for an i.v. injection were 276 +/- 76 mCi, 50.8 +/- 7.8 %, 99.3 +/- 0.3 % and 2.9 +/- 0.5 Ci/umol, respectively, on average of latest 3 runs. Required time was around 25 minutes. Each products were enough to carry out successive 3 clinical studies with a PET. All the procedures other than evaporation and filtration at final stage were carried out with a specially designed equipment connected to the central control system for radioisotope production.