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RADIOTRACERS IN PETT: STRATEGIES FOR IN VIVO RECEPTOR ACTIVITY, SCHIZOPHRENIA, AND ALZHEIMER'S DEMENTIA STUDIES.

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The application of radiotracers labeled with positron emitters to probe brain biochemistry coupled with Positron Emission Tomography as the assay device has opened new vistas for studying brain and heart biochemistry in normal and disease states (7). The choice of tracer is paramount since it must be amenable to biomodeling and useful as a probe for a particular function or biochemical pathway in vivo. Questions to be addressed include: (A) Criteria for choice of tracer and label to be used; ^{11}C, ^{13}N, ^{15}O or ^{18}F. (B) Nuclide production method and synthetic strategy for a particular radiotracer. Emphasis will be on carbon-11 and fluorine-18 (4). (C) Dynamic studies of neuroleptic drugs in baboons. (D) The Test-Retest paradigm for task and drug intervention studies. (E) Application to Alzheimer's Disease, Chronic Schizophrenia and other disorders.

The preparation of the radionuclide to be used is usually carried out in-house because of the short half-lives involved; ^{11}C= 20.4 m, ^{13}N = 9.96 m, ^{15}O = 2.07 m, ^{18}F = 109.7m. The half-life of fluorine-18 is sufficiently long to allow transport and use within a 800-1200 km radius. Methods of production are readily available: $^{14}N(p,\alpha)^{11}C$, $^{16}O(p,\alpha)^{13}N$, $^{13}C(p,n)^{13}N$, $^{14}N(d,n)^{15}O$, $^{15}N(p,n)^{15}O$, $^{18}O(p,n)^{18}F$, $^{20}Ne(d,\alpha)^{18}F$. These radiotracers can be converted on stream, or with 5 to 10 min delays post irradiation, to the labeled precursors necessary for synthesis (7). All too often a synthesis is conceived and effected with little consideration of the use to which it is to be put. This is particularly evident in the neuroleptic and radioligand-for-receptor study areas. The specific activity achievable, the time course of the study, and the metabolic fate of the e.g., neuroleptic, must be considered before a synthetic procedure is chosen. Fluorine-18 is perhaps one of the most useful radionuclides but its position in the compound must be carefully chosen so as not to add to the complexity of probing a specific biochemical pathway.

The specific activity problem becomes painfully evident when considering the neuroleptics and much effort has been directed to syntheses leading to NCA (no-carrier-added) or CF (carrier free) compounds (4,6). While the use of ^{11}C-labeled spiperone has certain advantages in human experimentation relative to dose and multiple intervention and has been effectively used in baboons (1) the use of ^{18}F-labeled spiperone prepared via a new facile NCA synthesis has shed new light on receptor activity in the live baboon brain when studied over an eight hour period (2). Using ^{18}F-spiperone SA $\cong 2 \times 10^4$ Ci/mmole (factor of ~ 100 dilution from CF), a one compartment system with a driving function as model, blocking agents such as butaclamol and ketanserin, assay of the live adult female baboon striatum over the 8 hr period, and assay of the parent compound in plasma, it is apparent that residence times in the living tissue and those estimated from in vitro tritium data are at variance. Occupancy rises to a maximum for ^{18}F benperidol and ^{18}F haloperidol after ~ 25 minutes and for ^{18}F spiperone after ~ 75 minutes, but the striatum concentration of ^{18}F-spiperone and benperidol remain nearly constant over an eight hour period whereas ^{18}F haloperidol concentration starts falling almost immediately to half its

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