subjects, with a one hour interval between injections. To help reduce the effect of residual activity, we gave only 2 mCi in the first injection in two cases, and only 1 mCi in the other case, out of a total injected dose of 5 mCi. The use of only 1 mCi is possible because of the high sensitivity of the Neuro-PET scanner that was used for these studies. A correction for residual activity was included in the phase 2 calculation, which takes into account both the washout of free FDG from the tissue, and the dephosphorylation of trapped FDG. We generally found agreement of about 5% between the two phases, for comparable areas of the brain. Better results may be achieved by increasing the time interval between studies.

(1) M Reivich et al. "The use of 2-deoxy-D-[1-C-11]glucose for the determination of local cerebral glucose metabolism in humans: Variation within and between subjects" J. Cereb Blood Flow Metab 2, 307-319 (1982)

No. 285

SIMILARITIES OF CEREBRAL GLUCOSE METABOLISM IN ALZHEIMER'S AND PARKINSONIAN DEMENTIA

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In the dementia of probable Alzheimer's Disease (AD), there is a decrease in the metabolic ratio of parietal cortex/caudate-thalamus which relates measures in the most and in the least severely affected locations. Since some demented patients with Parkinson's Disease (PDD) are known to share pathological and neurochemical features with AD patients, we asked if the distribution of cerebral hypometabolism in PDD and AD were the same. Local cerebral metabolic rates were determined using the FDG method and positron tomography in subjects with AD (N=23), PDD (N=7), multiple infarct dementia (MID)(N=6), and controls (N=10). The mean par/caud-thal metabolic ratio was decreased significantly ($p<0.0001$) and to the same degree in AD (0.51±.0.15, N=23) and PDD (0.51±0.09, N=7) compared to controls (0.75± 0.06, N=10). In MID, the mean par/caud-thal ratio was normal (0.79±0.09, N=6). In AD and PDD patients, this ratio correlated negatively with both the severity ($r=-0.624$, $p=0.001$) and duration ($r=-0.657$, $p=0.001$) of dementia. The ratio was markedly decreased in subjects with mild to severe dementia (0.46±0.09, N=21) and with dementia duration greater than two years (0.44±0.08, N=18), but the ratio was also significantly decreased in patients with less advanced disease, i.e., when dementia was only questionable (0.64±0.14, N=9)($t=2.27$, $p<0.037$) and when duration was two years or less (0.62±0.13, N=12)($t=2.88$, $p<0.009$). This similarity of hypometabolism in AD and PDD is additional evidence that a common mechanism may operate in both disorders. The par/caud-thal metabolic ratio may be an index useful in the differential diagnosis of early dementia.

No. 286

DETERMINATION OF PATTERNS OF REGIONAL CEREBRAL GLUCOSE METABOLISM IN NORMAL AGING AND DEMENTIA.

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Regional cerebral metabolic rates for glucose (rCMRGlc) were measured using 18F-FDG and positron emission tomography (PET) in 14 patients with probable Alzheimer's disease (AD) ($\overline{age}$=64), 9 elderly controls ($\overline{age}$=61), and 9 young controls ($\overline{age}$=28). PET studies were performed without sensory stimulation or deprivation. Metabolic rates in individual brain regions were determined using an atlas overlay. Relative metabolic rates (rCMRGlc/global CMRGlc) were determined for all subjects. Comparison of young and elderly controls demonstrated significant decreases in frontal metabolism ($p<0.005$) and right inferior parietal (IP) metabolism ($p<0.02$) with normal aging. Patients with mild-moderate AD (MMAD) (n=8) when compared to age-matched controls, showed further reduction in right IP metabolism ($p<0.02$). In MMAD patients also relatively increased glucose metabolism was noted in primary sensorimotor regions bilaterally ($p<0.02$), consonant with the preservation of motor function in degenerative dementia. Patients with severe AD (SAD) (n=6) showed relative increases in calcarine, brainstem, cerebellar ($p<0.01$), and primary auditory ($p<0.02$) metabolism compared to MMAD patients and controls. SAD patients also demonstrated metabolic decrements in left hemisphere language areas ($p<0.01$). This latter finding is consistent with language disturbance observed late in the course of the disease. Our data reveal progressive changes in patterns of cerebral glucose utilization with aging and demential which reflect salient clinical features of these processes.

10:30-12:00 **Room 107B**

RADIOPHARMACEUTICAL CHEMISTRY V: HALOGENS

Moderator: Michael J. Adam, PhD
Comoderator: Leonard I. Wiebe, PhD

No. 287

SYNTHESIS AND EVALUATION OF META-SUBSTITUTED I-122-LABELED DIMETHOXY-N,N-DIMETHYLAMPHETAMINES FOR BRAIN IMAGING STUDIES.

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The positron emitter I-122 (t1/2 3.6 min) was collected from a Xe-122/I-122 generator with a 60% efficiency and incorporated into three meta-dimethoxy-N,N-dimethylphenylisopropylamines (2,4-, 3,5- and 2,6-dimethoxy-N,N-dimethylamphetamines). The speed of direct radiolabeling (3 min, including purification) and high labeling yields (80--90%) have allowed the use of I-122 in brain perfusion studies using positron emission tomography (PET).

The three meta-substituted dimethoxyamphetamine precursors were prepared from the corresponding phenylacetone analogs by reductive amination employing dimethylamine and sodium cyanoborohydride. The ketones were obtained from the appropriate nitrostyrenes by reaction with elemental iron. Direct iodination of the meta-dimethoxyamphetamine precursors was performed at 60°C (pH 1.4) using chloramine-T.

The three meta-dimethoxy-N,N-dimethyl-(I-122)-amphetamine analogs (I-122-DNNA) were injected into dogs and 1 cm brain sections were imaged using the 280 crystal Donner PET. The uptake of the I-122-DNNA compounds was compared to Rb-82 uptake in the dog brain and dynamic PET activity data were obtained 0-20 min post injection of I-122-DNNA. The I-122-DNNA compounds showed rapid uptake (<5 min to reach maximum), good retention (>70% of maximum retained at 20 min) and sharp cerebral/extracerebral tissue contrast (6/1). The feasibility of incorporating I-122 into an extracted brain imaging agent for use with PET has been demonstrated.

No. 288

2-IODODESMETHYLIMIPRAMINE: SYNTHESIS AND EVALUATION AS A FLOW MARKER.

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Desmethylimipramine (DMI) has been shown to have a high extraction and long retention in isolated saline perfused rabbit hearts (Amer. J. of Physiology 245:H707-H712, 1983), suggesting that a gamma labeled derivative of DMI would be useful as a "soluble molecular microsphere" for imaging organ blood flow. DMI was radioiodinated using thallium trifluoroacetate in trifluoroacetic acid, with displacement of the thallium by radioiodine and aqueous potassium iodide. The IDMI was purified by HPLC, and the site of iodination was determined to be the two position on the aromatic ring by NMR. The octanol:H_2O partition coefficient for IDMI was 35, which was greater than for noniodinated DMI, 5. Erythrocyte:plasma partition coefficients (equal volumes of each) for IDMI were 5, 0.1 and 3 for rabbit, dog and human blood respectively. Greater than 90% of the IDMI in the red cell fraction was attached to the membrane. In the plasma phase, 82% co-precipitated with albumin while 16%