PET IMAGING OF DOPAMINE TRANSPORTERS IN THE HUMAN BRAIN IN HEALTH AND PARKINSON'S DISEASE WITH [F-18]β-CIT-FP

Sang Eun Kim *, Yearn Seong Choe, Seung Jun Oh, Joon Young Choi, Dae Yoon Chi, Gyeong-Moon Kim*, Yong Choi, Byung-Tae Kim

Departments of Nuclear Medicine and Neurology*, Samsung Medical Center

The N-fluoropropyl analog of β-CIT [2β-carbomethoxy-3β-(4-iodophenyl) tropane], β-CIT-FP, has been labeled with F-18 and shown to bind to the dopamine (DA) transporters with faster kinetics in nonhuman primate brain (Lundkvist et al., 1996). We report the successful application of [F-18]β-CIT-FP to image DA transporters in the living human brain in health and Parkinson's disease (PD). [F-18]β-CIT-FP was prepared by N-alkylation of nor-β-CIT (2 mg) with 1-bromo-3-[F-18]fluoropropane (2 drops of DMF/CH3CN, 140°C, 15 min). 1-Bromo-3-[F-18]fluoropropane was readily obtained in 55-70% yield from a reaction of 3-bromopropyl triflate with [F-18]fluoride (THF, 90°C, 2 min). Three healthy subjects and three PD patients were injected i.v. with [F-18]β-CIT-FP and 27 sequential PET images were acquired for 120 min. The tracer demonstrated high brain uptake (10% of the injected dose at 9 min postinjection). Brain activity was highly concentrated in the striatal area. In the healthy subjects, striatal activity peaked within 30 min and remained at similar levels for the rest of the study, with a mean specific (putamen or caudate–cerebellum)-to-nonspecific (cerebellum) binding ratio of 6.7 (putamen) or 7.0 (caudate) at equilibrium. The activity in the thalamus, a region known to contain a high density of serotonin transporters, showed an earlier peak at approximately 15 min and a rapid washout thereafter. The mean (thalamus–cerebellum)/cerebellum ratio at peak thalamic specific binding was 0.9. Frontal and cerebellar activity showed similar patterns, exhibiting an early peak within 10 min and rapid washout, followed by stable levels between 80 min and 120 min postinjection. In the PD patients, striatal activity peaked earlier (within 15 min) at reduced levels compared to the healthy subjects, followed by a significant washout. A greater reduction in uptake occurred in the putamen than in the caudate, with lateralized differences in striatal uptake. The mean specific binding ratios in the putamen and caudate were reduced to 20% and 47% of the healthy subject mean, respectively. The activities in the thalamus, frontal cortex, and cerebellum revealed similar patterns to those from the healthy subjects. These preliminary results in humans demonstrate that [F-18]β-CIT-FP has faster brain kinetics and a high in vivo selectivity for the DA transporters. In addition, they suggest that [F-18]β-CIT-FP may be an in vivo marker for the loss of striatal DA terminals in PD. Therefore, it should be an alternative PET ligand for imaging DA transporters in the human brain in health as well as disease.