Transactions of the Korean Nuclear Society Spring Meeting
Chuncheon, Korea, May 25-26 2006

Quantitative Evaluation of PET Imaging with I-124 Labeled Dopaminergic Radiotracer in Small Animal Study

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1. Introduction

SPECT imaging with I-123 labeled radiotracer has been a useful tool in investigating *in vivo* dopaminergic neurotransmission. Although there has been big achievement in development of small animal SPECT system, there is limitation in practice to evaluate pharmacokinetics of dopaminegic system of small animal uisng I-123 labeled radiotracer and dedicated SPECT imaging with high-resolution, due to the lower sensitivity of SPECT than that of PET. In this study, we examined the applicability of PET imaging with I-124 labeled radiotracer to pharmacokinetic evaluation of dopaminergic system in rat study.

2. Methods

2.1 PET Acquisition

IPT that is a well-known dopamine transporter[1,2], was employed in this study. Rat (n = 4, age: 14 ± 2 weeks, weight: 211 ± 15g) under anesthesia by isofluorane gas (~1.5%) was placed on bed of microPET-R4 scanner (CTI Concorde Microsystems, TN). Radiochemical purity of I-124 labeled IPT was checked with HPLC. I-124 IPT (37~120 MBq/0.5mL) was injected through tail vein to rat. Immediately after a bolus injection, PET emission list data was acquired for 3 hours. A transmission scan to get attenuation correction factor, was performed during 30 min, prior to the injection of I-124 IPT, using an external rotating point source of Ge-68.

2.2 PET Image Reconstruction

The acquired emission list data was sorted to temporally framed 3-dimensional sinograms (10 min × 18 frames) and reconstructed to dynamic images using Fourier rebinning (FORE) and 2-dimensional ordered subseet expectation maximization (OSEM) algorithms with attenuation corrections.

2.3 Kinetic Analysis

On the reconstructed dynamic images, regions of interest (ROIs) were placed to get time-activity curves (TACs) of striatum (STR) and cerebellum (CBL), respectievely. The both TACs were used in kinectic analysis with reference-tissue based Logan plot[3], to obtain quantitative value of distribution voloume ratio (DVR) of striatal region. The value of binding potential (BP) at transient equilibrium state[4] was estimated using equation of (STR – CBL)/CBL.

3. Results

On the reconstructed I-124 IPT image, the radioactivity distribuiton on STR regions was clearly diffrerentiated from background including CBL region (Fig. 1), and the contrast between specific (STR) and non-specific regions was improved with time. The specific activity (STR-CBL) in striatal region was increased with time, due to the rapid activity decrease of cerebellum region, compared to that of striatal region (Fig. 2). Therefore, this temporal change resulted in significant increase of specific binding ratio (STR/CBL) with time (Fig. 3), which was similar with that reported in human SPECT studies[2]. Using TACs of both STR and CBL regions, non-invasive Logan ploting could be achieved and get value of DVR of striatal region. The values of DVR obtained from Logan's plot was 2.05 ± 0.27, and showd high correlation (r > 0.95) with the BP values.

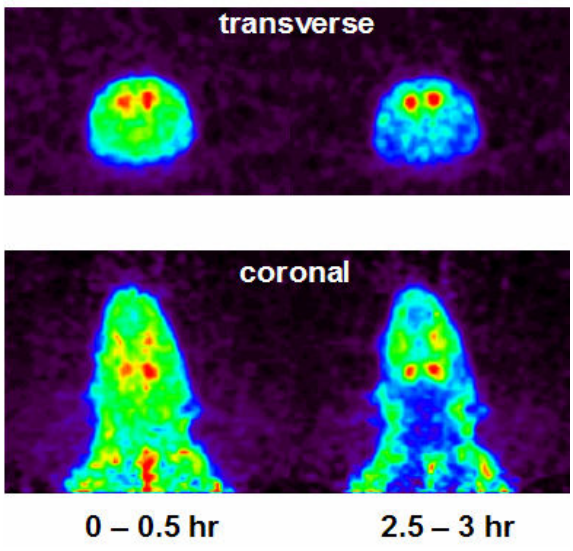

Figure 1. Uptake distribution of I-124 IPT and regional change with time in a rat brain.

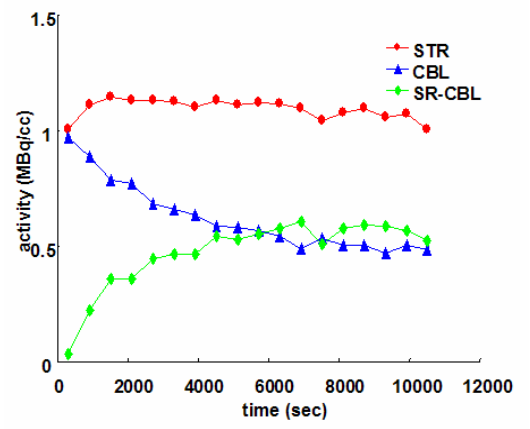

Figure 2. The changes of regional activities of both STR and CBL regions, and specific activities (STR-CBL) in striatal region, with time after injection of I-124 IPT.

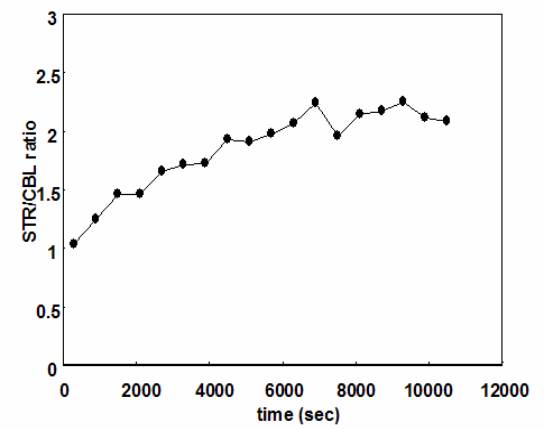

Figure 3. Change of specific binding (STR/CBL) ratio of I-124 IPT with time in striatal region.

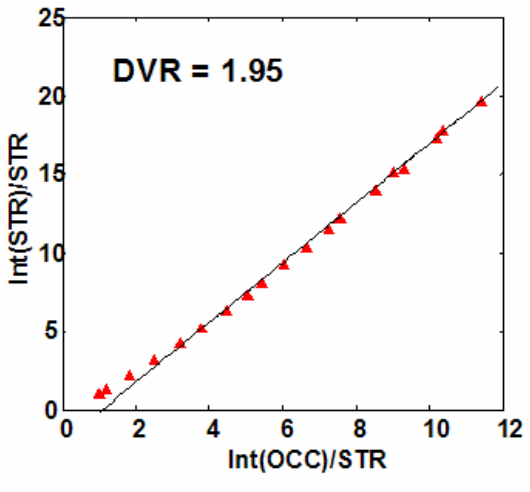

Figure 4. Result of kinetic analysis to get distribution volume ratio (DVR) using noninvasive Logan's graphical method.

4. Conclusion

We found that the quantitative evaluation of pharmacokinetics of I-124 labeled dopaminergic radiotracer is possible, and therefore small animal PET imaging with I-124 labeled radiotracer could be useful in pre-clinical study for disease model evaluation or new drug development, prior to SPECT study using I-123 or I-125 labeled radiotracer.

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