Correlation between dopamine synthesis and cell-level structure in human striate body using diffusion tensor imaging and positron emission tomography with L-[β-^{11}C]DOPA

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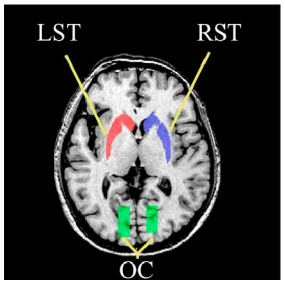
Introduction The central dopaminergic system is of great interest in the pathophysiology of neuropsychiatric diseases such as Parkinson's disease and schizophrenic disorder. To assess the endogenous dopamine synthesis, a presynaptic function, carbon-11 labeled L-DOPA (L-[β-^{11}C]DOPA) is used as a radioactive tracer for positron emission tomography (PET) [1-3]. A PET study has reported that the dopamine synaptic rate varied among individuals [2]. A possible reason for the variability is differences between cell-level structure. It is widely thought that the results of diffusion tensor imaging (DTI) reflect water motion restricted by cell-level structure. In this study, PET with L-[β-^{11}C]DOPA and DTI were measured on the same group of volunteers to assess the relationship between dopamine synthesis and cell-level structure in the striate body, which includes the dopaminergic neuron rich putamen and caudate nucleus. The relationship between parameter estimates (eigenvalues, λ_1, λ_2 and λ_3; mean diffusivity, MD; fractional anisotropy, FA; and dopamine synthesis ratio, R) and age was also analyzed because age-related decrease of cell number can affect the water motion and dopamine synthesis.

Methods This study was approved by the Ethics and Radiation Safety Committees of our institute. Eight men (age:22-69 years, right-handed) were recruited and written informed consent was obtained. PET and MRI were acquired using a Siemens ECAT Exact HR+ PET system and Philips Intera 1.5T system, respectively. The PET scan lasted a total of 64 minutes and 23 images were acquired over that time at intervals of between 1 and 5 minutes. DTI was acquired using single-shot EPI with SENSE parallel-imaging and b-values of 0 and 700 s/mm^2 in six non-collinear directions. The detailed scanning, experimental and reconstruction parameters were the same as those used in references [1] and [4] for PET and DTI, respectively. A T1-weighted (T1W) image was also acquired with a GRE sequence and used for spatial registration of the PET and DTI images and determination of regions-of-interest (ROIs). A ROI was defined for both the left and right striate bodies (LST and RST) on individual T1W images (Fig. 1a). Thereafter, morphological erosion by a 3D 6 nearest-neighbor structuring element was applied [5], because the selected ROI may be affected by the partial-volume effect, especially at the edge pixels (Fig. 1b). A ROI was also defined for the occipital cortex (OC) on the T1W images and used as a reference region when calculating the dopamin synthesis ratio because there is little irreversible binding in that area. The DTI parameters were estimated with FDT in the FSL software package [6]. The PET and DTI images were spatially co-registered to the T1W images using SPM 8 (Wellcome Trust Centre for Neuroimaging, London). The time-activity carves (TACs) were obtained by averaging the radioactivity over the ROI for each PET image. Then, R was calculated by the following equation [3]: $R = \int_{t_1}^{t_2} C_i(t)dt \,/\, \int_{t_1}^{t_2} C_i^{'}(t)dt$,where the integration interval [t_1, t_2] is [29, 64] minutes, C_i and $C_i^{'}$ are the TACs of the LST or RST and OC, respectively. The diffusion parameter estimates in LST and RST were also calculated after averaging across each ROI. The relationship between R and the DTI parameter estimates were evaluated with Spearman's correlation coefficient.



(a) ROIs on T1W

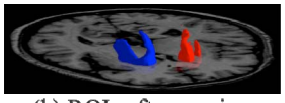

(b) ROIs after erosion

Fig. 1. ROIs.

Results and Discussion Acquired images and the TACs of a typical subject are shown in Fig. 2. While no statistically significant correlation was found between age and the MD or R in either striate body, there was a significant negative correlation between R and MD in the LST (Fig.3, ρ=-0.81, p=0.02). A partial correlation coefficient controlling for age also showed a negative correlation between R and MD, however, it was not statistically significant (ρ =-0.7, p=0.08). While the effects of aging cannot be completely ignored, the correlation between R and MD indicates that the more water motion is restricted, the more dopamine is synthesized in the left striate body. Assuming that water motion is related to cellularity, the dopamine synthesis may depend on the density of dopaminergic neurons. PET/MRI combined measurements can contribute to the investigation of neuropsychiatric diseases involving malfunction of dopaminergic neurons.

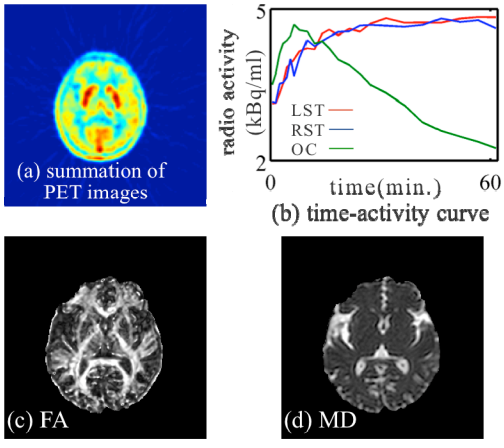


Fig. 2. Results from a typical subject.

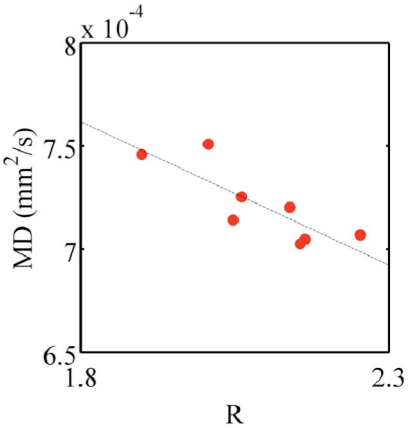


Fig. 3. Scatter plot of the LST dopamine synthesis ratio R vs MD for all subjects.

References [1] Nucl Med Commun, 27: 723-731 (2006), [2] Life Science, 79: 730-736 (2006), [3] Ann Nucl Med, 21: 355-360, (2007), [4] NeuroImage, 23: 208-219 (2004), [5]CVGIP, 54: 252-258 (1992), [6] NeuroImage, 31: 1445-1452 (2006)