

Project: Registration

Due June 21, 2025

Parkinson's disease (PD) is characterized by decease of dopaminergic neurons in the substantia nigra and accompanying motor symptoms. The dopaminergic neurons primarily project to the striatum (containing caudate and putamen), forming the nigrostriatal pathway, which is critical for motor control (Fig. 1). Hence, the loss of dopaminergic neurons can be imaged in vivo by visualizing the dopamine level in the striatum. One way to achieve this is dopamine transporter imaging (DaTscan), a SPECT imaging that shows the density of dopamine transporters (a protein carrying dopamine across neurons) in the striatum of the brain (Fig. 2). This project aims to use a collection of DaTscan images to find how the disease progresses in the striatum.

The dataset contains 3 PD subjects and 9 healthy control subjects. A PD subjects has DaTscans collected at baseline, year 1, 2, 4, with missing data and an MRI image collected at baseline. A healthy control subject has only 1 DaTscan and 1 MRI collected at baseline. Because different subjects have different sizes of the striatum. We need to standardize them to the same space. This can be achieved by registering them to a template. We will do it in the following way:

1. Register all the DaTscans of a subject to his baseline MRI image, i.e., $I_{MRI} \leftrightarrow I_{datscan} \circ \phi_1$ using an affine registration or a rigid registration because they belong to the same person and the structural change over these years could be small. The DaTscans are in the folder ‘data’ with the subfolder name being subject ID. The MRI image is also in the subfolder.
2. Register all the MRI images to a template, $I_{template} \leftrightarrow I_{MRI} \circ \phi_2$. The template is in the folder ‘tpm’ containing tissue probability maps of gray matter, white matter and cerebrospinal fluid (CSF). This registration should be a nonrigid registration (deformable or diffeomorphic).
3. Transform the DaTscans using the composition of transformations, i.e., $I_{datscan} \circ \phi_1 \circ \phi_2$, such that the DaTscans are registered to the template and in the standard Montreal neurological institue (MNI) space.
4. Use the labels from the folder ‘mask’ to identify the region caudate, putamen, occipital lobe in the DaTscans. Normalize the intensity of each DaTscan using the mean intensity in the occipital lobe, i.e. $I_{datscan}(x) \leftarrow$

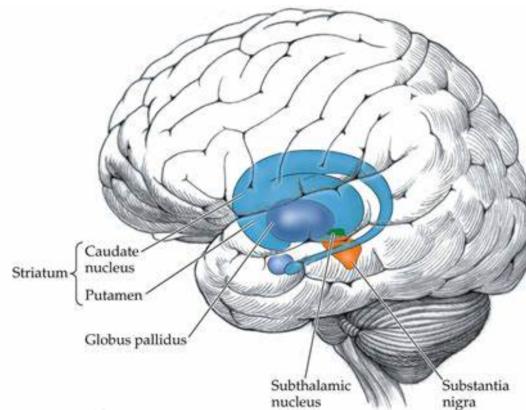


Figure 1: Striatum and substantia nigra.

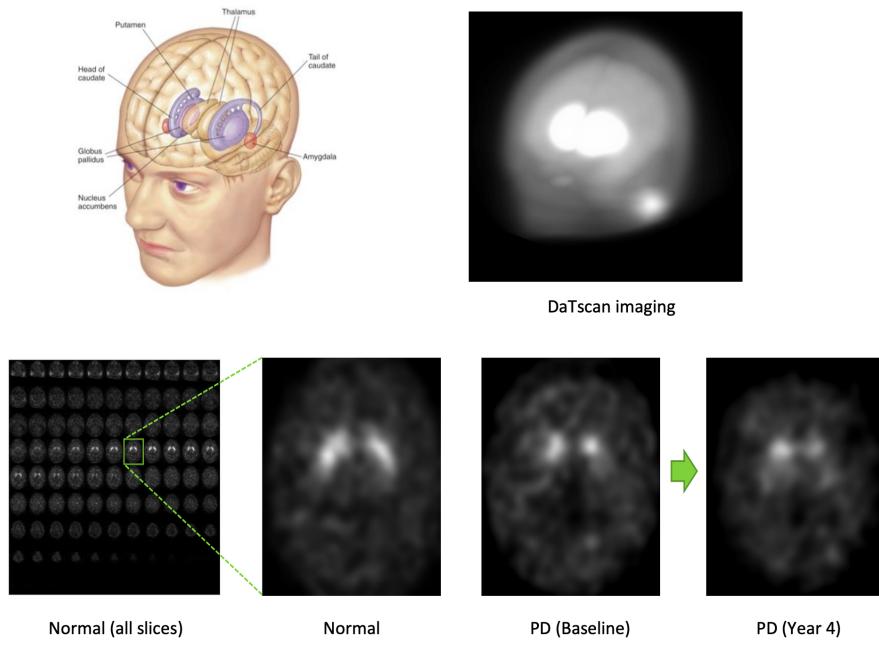


Figure 2: DaTscan.

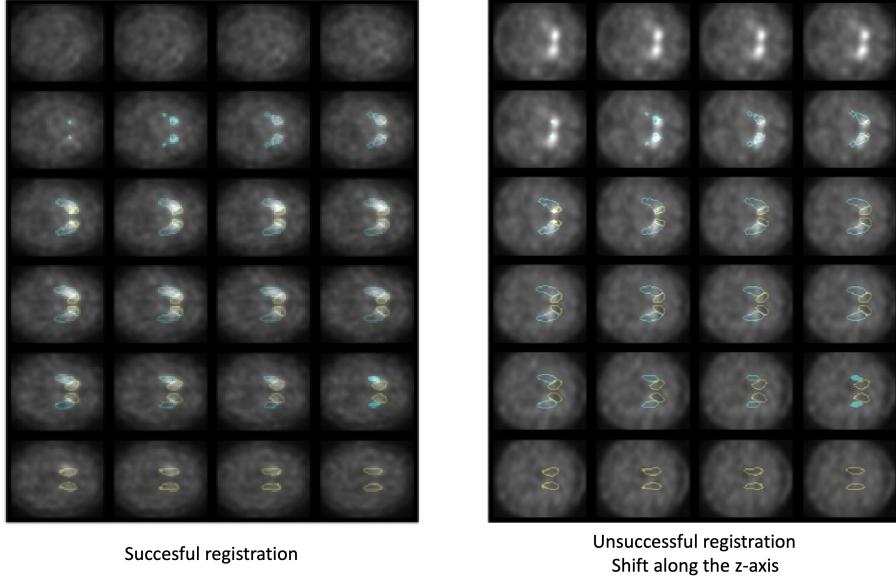


Figure 3: A successful registration case and a failure case.

$(I_{datscan}(x) - \mu_{occ})/\mu_{occ}$ where μ_{occ} is the mean intensity in the occipital lobe. This is because the tracer not only binds to the target (dopamine transporter), it also has off-target bindings. The different effects of tracer remaining in the brain across subjects can be mitigated by this normalization procedure.

5. Visually check if the registration is successful by overlaying the caudate and putamen masks on the DaTscans. Fig. 3 shows a successful case and a failure case.

After registering all the images, we can perform a simple procedure to find how the disease progresses in the striatum. Since the dopamine depletion is irreversible in PD, we can compare the DaTscan signals in the caudate and putamen between PD subjects and healthy controls. Specifically,

1. The affection of PD could start at the left hemisphere or right hemisphere and then invade into the contralateral part. But which hemisphere is affected initially depends on the subject. Therefore, we flip the DaTscans such that the less affected side (brighter side) is always on the left.
2. At each voxel in the striatum (caudate and putamen), compare if the intensities from the PD subjects are significantly different from the intensities from the control subjects. We can use t-test to test this significance and get the t-statistic at each voxel. Whether a subject is in the PD group or in the healthy control group is indicated in the file ‘meta_info.xlsx’.

3. Visualize the t-statistics in the striatum using heat map. This heat map should indicate how the disease progresses in the striatum as the larger the t-statistics, the earlier that the region is affected by the disease.

You can use an existing software package (e.g. SPM) to perform the registration or implement your own algorithm as long as the caudate and putamen are correctly segmented for analysis. A template code for registration with the 2 registration algorithms missing is provided in ‘reg.m’. Once the code is done, write a short report to explain the methods you use for registration and show the results.

Submission: a zip file named by “Your name _ student id” containing code, and the report. Note that the code should be runnable.