Analysis of I[123]-Ioflupane SPECT intensity iso-surfaces to assist the diagnosis of Parkinsonism

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Introduction

Parkinson's Disease (PD) is a progressive neurological disorder that affects the motor system. It is related to the destruction of pigmented neurons in the *substantia nigra* by triggers that are still unknown.

As PD is characterized by a marked reduction of dopaminergic neurons in the striatal region, images like SPECT I[123]-Ioflupane give us a quantitative measure of the spatial distribution of the transporters in the *striatum*.

Known fact: A healthy control subject (HC) is expected to present the *striatum* region highly illuminated and approximately homogeneous.

Hypothesis: A direct comparison between regions with the same intensity values in I[123]-Ioflupane SPECT images could be a good predictive factor for Parkinson's Disease progression.

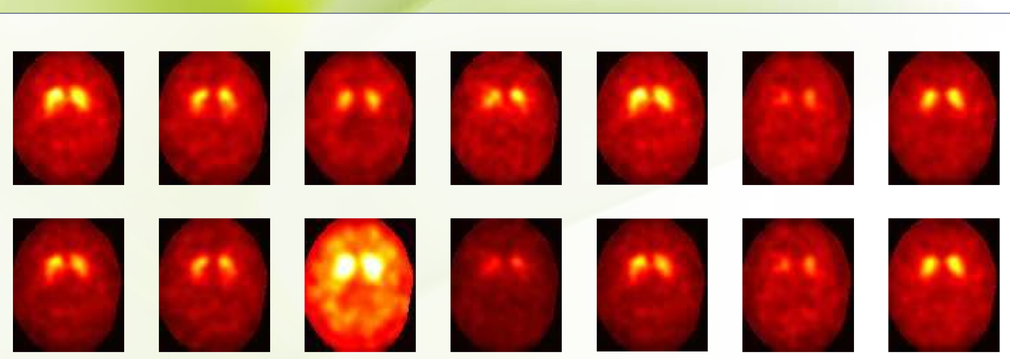

Figure 1 - Examples of I[123]-Ioflupane SPECT images once applied spatial normalization.

Materials & Methods

For this work, we have made use of 388 SPECT images (194 from HC subjects and 194 from patients with PD) from the **Parkison's Progression Markers Initiative (PPMI)** dataset available at www.ppmi-info.org.

1. Image Preprocessing

Spatial normalization - All SPECT images have been spatially registered using the SPM (Statistical Parametric Mapping) tool **SPM12**. After being co-registered and averaged, each cerebral image presented a dimension of 79x95x78 voxels and a voxel size of 2x2x2 mm. See Figure 1.

Intensity normalization - The procedure performed was based on the use of **α-Stable distributions** described in [1]. Mathematically, this procedure uses a linear transformation as presented in expression (1) where γ^* and μ^* represent the mean of γ (dispersion) and μ (location) parameters, respectively, computed for the database.

$$Y = \left(\frac{\gamma^*}{\gamma}\right) X + \left(\mu^* - \frac{\gamma^*}{\gamma}\mu\right) \quad (1)$$

2. Generating a reference map

To get a realistic model of reference for all patients, we have averaged the DaTSCAN maps of all HC subjects. This template map will be used to define its max and min intensity values and reference points required later.

3. Iso-surfaces

If I_{max} and I_{min} correspond to the max and min intensity values of the template image, we can split this difference into N parts defining N intensity levels, a_i with i=0,1,2,...,N−1, as expressed in (2).

$$a_i = I_{min} + i\frac{I_{max} - I_{min}}{N} \quad (2)$$

These intensity levels, a_i, can be used to determine, for each subject j, the shape of the region whose voxels exceed this intensity value through the use of the **Lewiner marching cubes algorithm** [2]. This algorithm iterates across the volume, looking for regions which cross the level of interest a_i. If such regions are found, triangulations are generated and added to an output mesh. The final result is the set of vertices and triangular faces as depicted in Figure 2.

5. Morphological features extraction

Labelling $I_{i,j}$ as the region from subject j whose voxels have an intensity level above a_i, each surface presents a set of features that can be obtained afterwards.

For this work we have included: Area; Center of Mass (CoG) of the voxels inside $I_{i,j}$; distances (min, max, mean and std) from the vertexes which conforms the contour of the layer and the CoG obtained using the template at the same intensity level; Euler characteristic number; orientability and sphericity of the region; volume and number of vertexes and faces of the polyhedron.

6. Classification and Cross-validation strategy

Once all features were computed, they have been used as input of a **linear SVM classifier**. Validation has been carried out using a ***k*-fold** validation strategy schema.

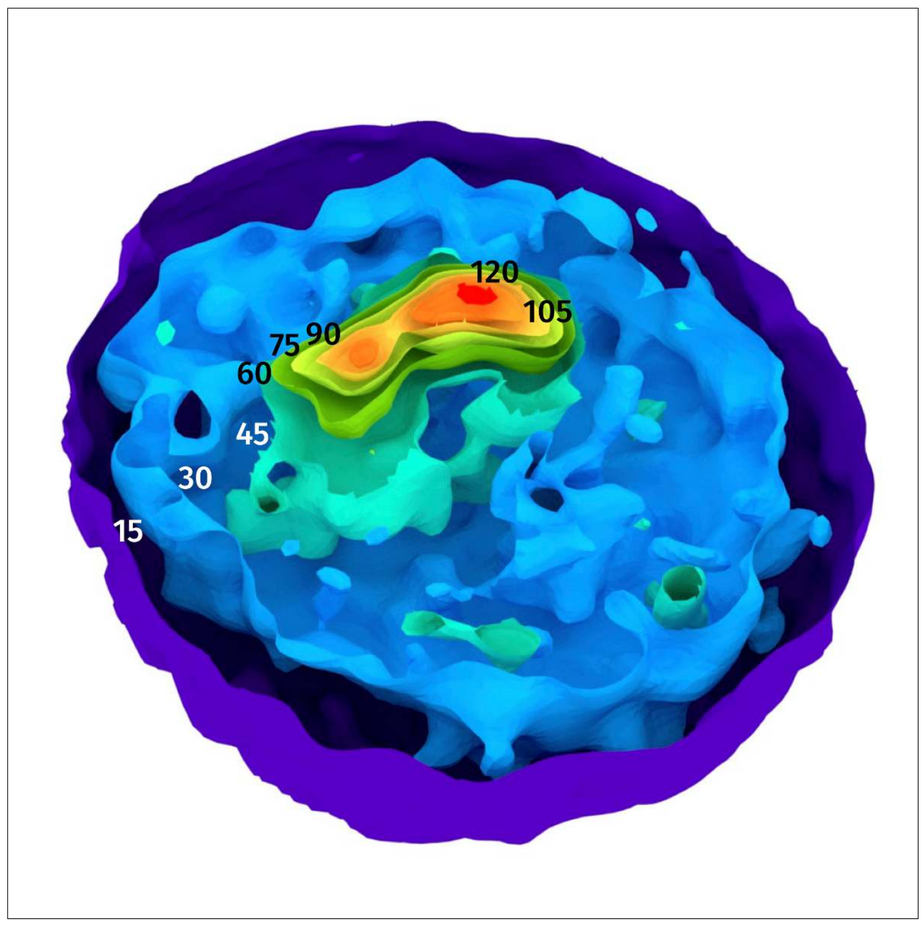

Figure 2 - Examples of 3D iso-surfaces obtained from a subject. Axial view including striatum area.

Results

For this work, we have defined several experiments considering different brain areas for classification: full *striatum* area, only left hemisphere, only right hemisphere and mixing all of them (full *striatum* + left hemisphere + right hemisphere). *Striatum* volume was calculated using the template including both *caudate nucleus* and *putamen* areas and it contains a total of 44,126 voxels. Preliminar results obtained from all experiments are summarized in Figure 3.

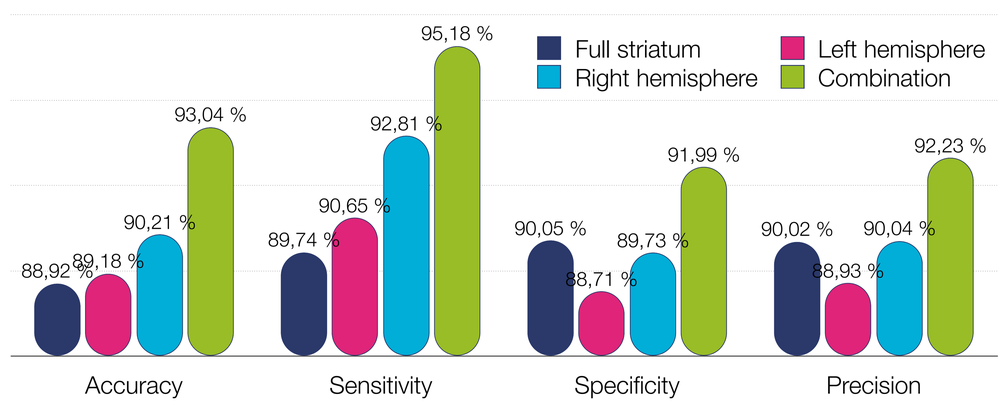

Figure 3 - Classification results.

Conclusions

Known fact: Since medical science has begun to consider neuroimaging as the reference test in the diagnosis of neurological disorders like Parkinsonism, its diagnostic has become easier and more accurate.

Strengths: This work presents two significative strengths: A reduction in computational costs and the study how quick dopaminergic transporters decrease in the *striatum*. As expected, the caudate nuclei and putamen volumes are significantly reduced in the PD cohort compared to controls. However, we have also seen a slight difference between results considering only the right or left hemisphere. This difference is seems to be similar to current state-of-art [3].

Conclusions: These preliminary results, with an averaged accuracy about 93% when combining Full+Left+Right cases, have evidenced that further investigation of iso-surfaces may be needed for Parkinsonism. We expect that inclusion of new morphological features and the comparison of different intensity levels would give us more information about prognosis and evolution of the disease.

References

[1] D. Salas-Gonzalez, et. al., "Linear intensity normalization of FP-CIT SPECT brain images using the α-stable distribution", NeuroImage, vol. 65, no. C, pp. 449-455, 2013.

[2] T. Lewiner, et. al., "Efficient Implementation of Marching Cubes' Cases with Topological Guarantees", Journal of Graphics Tools, vol. 8, no. 2, pp. 1-15, 2003.

[3] C. Owens-Walton, et. al., "Striatal changes in Parkinson disease: An investigation of morphology, functional connectivity and their relationship to clinical symptoms", Psychiatry Research: Neuroimaging, vol. 275, pp. 5-13, 2018.

Informed consents to clinical testing and neuroimaging prior to participation of the PPMI cohort were obtained, approved by the institutional review boards (IRB) of all participating institutions. More info, visit: www.ppmi-info.org/data.