INTRODUCTION and OBJECTIVES

Microglial activation is a biomarker of neuroinflammation
- Previous findings suggest an increase of microglia activation in Parkinson disease [1].
- Binding of [11C]-PBR28, a second generation translocator protein (TSPO) PET marker, is increased in activated microglia.

The objective of this study is to investigate the ability of texture features extracted from regions of interest (ROIs) placed on [11C]-PBR28 images to assess microglial activation: of particular relevance are those metrics that do not rely on the magnitude of the pixel values, as independent of the tracer behavior in the periphery.

METHODS

- **Subjects**
  - Participants included 4 healthy controls (HC) (age 44±16, mean, std, range 24-63 years) and 10 subjects with Parkinson disease (PD) (age 67±14, mean, std, range 42-86 years; disease duration 5±4yrs, mean, std, range 1-10 rs).
  - All subjects were mixed affinity binders (MAB). A 19.7±1.2 μCi dose of [11C]-PBR28 was injected intravenously and dynamic PET scans were performed for 90 minutes.
  - Time-averaged images were calculated from data acquired between 60 and 90 minutes post-injection and were converted to SUV images.

- **ROIs delineation**
  - T1 structural MRI and PET scans were acquired for each subject.
  - Atlas-based ROIs and MRI scans were co-registered to each subject’s PET space.
  - Whole brain white matter, whole brain gray matter and 48 ROIs (Fig 1) were placed on the SUV images.

- **Gray-level co-occurrence matrix and texture features**
  - Gray-level co-occurrence matrix (GLCM) computation
    - 3D-GLCM measures the number of gray-level repetitions (co-occurrences) in a given ROI at a prefixed stepping distance and direction.
    - 13 directions were used to build the 3D-GLCM.
    - Maximum contrast-distance criterion was used to select the optimum distance of nearest neighbor pixels.
  - The statistical properties of the GLCM were calculated from a 1) gray level sampling assessed for each individual separately (IMS) and 2) global max gray level sampling (GMS) where data from all subjects were binned within the same range, thus the same maximum.
    - IMS removes magnitude information between subjects and hence reveals only the spatial distribution difference between groups.
    - GMS includes both magnitude and spatial distribution information.
  - The following Haralick features were estimated as defined in [2,3].

<table>
<thead>
<tr>
<th>Feature</th>
<th>Formula</th>
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<tr>
<td>Energy</td>
<td>$\sum_{i,j} p(i,j)^2$</td>
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<tr>
<td>Contrast</td>
<td>$\sum_{i,j} (p(i,j) - p(i+,j+))^2$</td>
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<tr>
<td>Homogeneity</td>
<td>$\frac{\sum_{i,j} p(i,j)^2}{\sum_{i,j} p(i,j)}$</td>
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<tr>
<td>Entropy</td>
<td>$-\sum_{i,j} p(i,j) \log p(i,j)$</td>
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<tr>
<td>Cluster tendency</td>
<td>$\frac{\sum_{i,j} p(i,j)^2}{\sum_{i,j} p(i+,j+)^2}$</td>
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<tr>
<td>Sum entropy</td>
<td>$-\sum_{i,j} p(i,j) \log (p(i+,j+) + p(i+,j))$</td>
</tr>
<tr>
<td>Dissimilarity</td>
<td>$\sum_{i,j} p(i,j) \log \left( \frac{p(i,j)}{p(i+,j+)} \right)$</td>
</tr>
<tr>
<td>Information</td>
<td>$\sum_{i,j} p(i,j) \log \left( \frac{p(i+,j+)}{p(i,j)} \right)$</td>
</tr>
<tr>
<td>Joint information</td>
<td>$\sum_{i,j} p(i,j)^2 \log \left( \frac{p(i,j)}{p(i+,j+) p(i,j+)} \right)$</td>
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**Metrics selection**
- Variability of each metric as a function of the gray level sampling was used to test for their robustness.
- Correlation of metrics’ outcome to the clinical information
  - The whole brain gray matter was chosen to evaluate GLCM-derived metrics.
  - A comparison of metric outcomes means among the two groups was conducted using Two-sample t-test.
  - A simple linear regression between [11C]-PBR measures and disease duration was calculated.

- **RESULTS**

- **Effect of gray level quantization on Haralick features**
  - Standard 16, 32, 64 and 128 gray level sampling was computed to calculate 3D-GLCM at a distance of 4 pixels and averaged over 13 directions from [11C]-PBR28 images (Fig 2).
  - All used metrics do NOT exhibit a variability with gray level sampling.

- **IMS vs GMS grid based 3D-GLCM computing**
  - IMS reveals the difference in the spatial distribution (Fig. 3 top B) while GMS reveals both spatial distribution and magnitude information (Fig. 3 Bottom B).
  - GMS based GLCMs (Fig. 3 top and bottom D) depict clear difference between HC and PD compared to IMS based GLCMs (Fig. 3 top and bottom C).

- **Pearson correlation between disease duration and texture metrics calculated in whole brain gray matter region.**

- **CONCLUSIONS**

- **GMS_based GLCM-derived metrics enables both information on magnitude and spread of the tracer in defined ROIs.**
- **IMS_based GLCM-derived HARCLUSTERSHADE is a promising metric which has a significant correlation with disease duration without any prior knowledge on tracer concentration magnitude.** The results are thus independent of any modelling or peripheral tracer behaviour.

REFERENCES


Acknowledgments: This work was supported The MJ Fox Foundation, NSERC and PPRI.