Reviewer’s report

Title: Subregional 6-[18F]fluoro-L-m-tyrosine Uptake in the Striatum in Parkinson’s Disease

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Reviewer: Miklos Argyelan

Reviewer’s report:

The authors set out to investigate the AADC activity distribution in the brain of PD subjects. Their choice of radipharmacon, fluoro-L-m-tyrosine, is thought to be a relatively more sensitive indicator of this enzyme by producing greater signal to noise ratio. Their goal was to measure the distribution of AADC which can be used as a proxy to estimate the number of intact dopamine terminals in certain striatal subregions. They also wanted to correlate these measures with clinical data.

Their findings were in complete agreement with earlier findings of presynaptic dopamine label PET/SPECT studies, where they found that dopamine terminals degenerate progressively in dorso-ventral direction, first affecting posterior putamen. Due to the nature of this and because of the floor effect, usually posterior putamen does not correlate with any clinical symptom in moderate and severe PD patients like this population. It is also well known from earlier studies that rigidity dominant patients shows more prominent correlations in their dopamine loss in more ventral striatal regions.

Although this study could replicate these findings, and methodologically perfectly sound, and the number of patients scanned is impressive it lacks any new and interesting findings. The study in itself can confirm earlier findings and could demonstrate the potential that FMT might have in further investigations.

Major considerations

1. Lack of novelty

2. The authors describe their methods as 2D ROI method, where striatum per cerebellum ratios are averaged for several ROIs (if I understand correctly their approach). Given the already acquired MRI images why the authors did not try to define VOIs and use VOI based analysis? I would not require them to recalculate their whole dataset, but in a sample size of subjects (~20 subjects) they could demonstrate that their ROI method provide comparable measures with VOI approach.

3. In results when the correlation between the clinical measures and SCR is detailed the authors did not address the potential need for age correction. They should demonstrate that age correction does not change significantly their results. Presynaptic dopamine measures are subject to 3-5% decrease per decade, if the age range is large, this can affect their measurements, and the potential lack of correlation in elderly.
Minor considerations

1. I am not sure that suspending dopaminergic medications only 6 hours before scanning is enough. How could the authors defend this relatively short interval (usually it is at least 12hr).

2. The authors should consider to describe their image analysis method with more detail. They state in their paper that they coregistered MR and PET images at one point. I suppose this was done through the CT images which they could achieve from the PET/CT scanner, because in dopaminergic PET/SPECT studies the coregistration of the fully anatomical images with the fully functional PET images is not solved.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have no competing interests.