Reviewer's report

Title: Hyperintense putaminal rim at 1.5T: prevalence in normal subjects and distinguishing features from multiple system atrophy

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Reviewer: Hedok Lee

Reviewer's report:

This MR imaging study aims to evaluate HPR conspicuity as a diagnostic marker for MSA using T2W and DTI at 1.5T. Two experienced neuroradiologists diligently performed detailed evaluation on many variables across a respectable sample size (N=130), and the results indicate that HPR is also prevalent (39%) among neurologically normal subjects. The conspicuity does not dependent on age, gender, and laterality, extending the implication of the study across a broad spectrum of HPR diagnosis. The authors suggest utility of HPR continuity, putaminal atrophy, and MD, as useful diagnostic markers in discriminating the three groups, though generalizability is limited by small sample sizes for some outcome variables. Overall these findings may be promising and suggest additional features that can enhance clinical diagnosis of MSA, pending replication and expansion of findings.

Major Compulsory Revisions

1. Generally, the results and discussion sections are too long and unfocused, spending too much space on detailed results that can better be listed in tables. The discussion contains lengthy explanations for a histological basis of HPR. I would suggest a tighter focus on diagnostic utility.

2. Blindness was arranged for the patients, but it is unclear what information the raters received. Were they aware that MSA was one of major groups and diagnostic concerns ? Also, when the normals were reviewed, were the raters aware that these were all normals ? These two points render the blindness very weak. Clarify this in the method section.

3. Contrary to a previous study (Ref 9), this study finds high HPR prevalence among neurologically normal subjects, but a care should be taken in the interpretation of the actual number (39%). Absence of sensitivity and specificity figures at both 1.5T and 3.0T limits a fair comparison between the two field strengths and undermines the reliability of the number. Further, ambiguous blindness of the raters and absence of inter-rater reliability (see Ref 11), can distort the interpretation. This should be discussed in the discussion.

4. As is the case with most of the published studies (Ref 9~12), relying on T2-weighted image instead of T2 (transverse relaxation time) probably contributes to inconsistency across studies. Contrast between putaminal
hypo-intensity and HPR, for example, can depend on the choice of echo time (TE), affecting raters ability to score HPR conspicuity. Quantifying T2 in HPR, may mitigate a potential systematic bias across the studies. Consider adding this point in the discussion.

5. The study suggests continuity and length of HPR as useful diagnostic markers for discriminating the groups, but it’s not clear how the authors decided to use 2mm as a threshold. First, in-plane resolution of the study is 1.02x0.47mm, hence detection of 2mm would translate to only ~4 voxels at most which is not easily discernible. Second, the continuity and length of HPR depend on the angulation of the image plane. The paper appears to indicate that only a single image slice (at the foramen of Monro level) was evaluated for HPR conspicuity. Unless all images were taken in a standardized plane as described in Ref 11, several adjacent slices need to be evaluated for HPR length and continuity as well. Clarify these points in the method and discussion sections.

Minor Essential Revisions

1. In the abstract, MSA patients (which?) had significantly higher (not larger) MD values.
2. Background should be shorter.
3. In the methods, provide MRI magnet manufacture.
4. In the methods section first paragraph, it’s unclear why consent was waived for patients. Do the authors mean that consent was not required because the scans were clinically acquired and not research?
5. In the methods section, there is no mention of the number of subjects being scanned with DTI. Figure 5 clearly does not have 10 MSA-P patients.
6. In the visual analysis section, a lot of redundancy between Table1-2 and the text. Reduce it substantially.
7. Comments on table 2. Express values in % and provide p-values. In normals, there are 13 males and 11 females which don't add up to the total of N=39. In “hypo-intensity of nearby putamen (anterior half)”, the number of MSA-C does not add up to 18. It’s 17 in the table. In “hypo-intensity of nearby putamen (posterior half)”, the numbers of all 3 groups do not add up. Check these numbers.
8. In the discussion, “Imaging at 3T allows acquisition of images with smaller pixel sizes” is an inaccurate statement. Higher field strength enhances overall signal to noise ratio (SNR) but the image resolution is dictated by an imaging gradient strength.
9. “An improved signal-to-noise-ratio” should be “An improved contrast-to-noise-ratio”
10. Whenever mentioning MSA, the authors should specify whether they mean C, P, or both.
11. MD values of the normal putamen should be quantitatively compared to previous literature.
12. Table 1 legend should specify that it refers to healthy controls

13. In Figure 5 high mean values in MSA-C and MSA-P are determined by outliers. These distributions raise questions about the nature of the patients and the reasons for this heterogeneity. Repeat the same statistical analysis without those outliers.

14. Report ANOVA result with F, df, and P-value

15. In the discussion, “0.66 x 0.41 mm, whereas that in this study was 1.02 x 0.47 mm” provide slice thickness of both studies.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests