The role of T1-Weighted MRI Radiomics in Progressive Supranuclear Palsy Phenotypes

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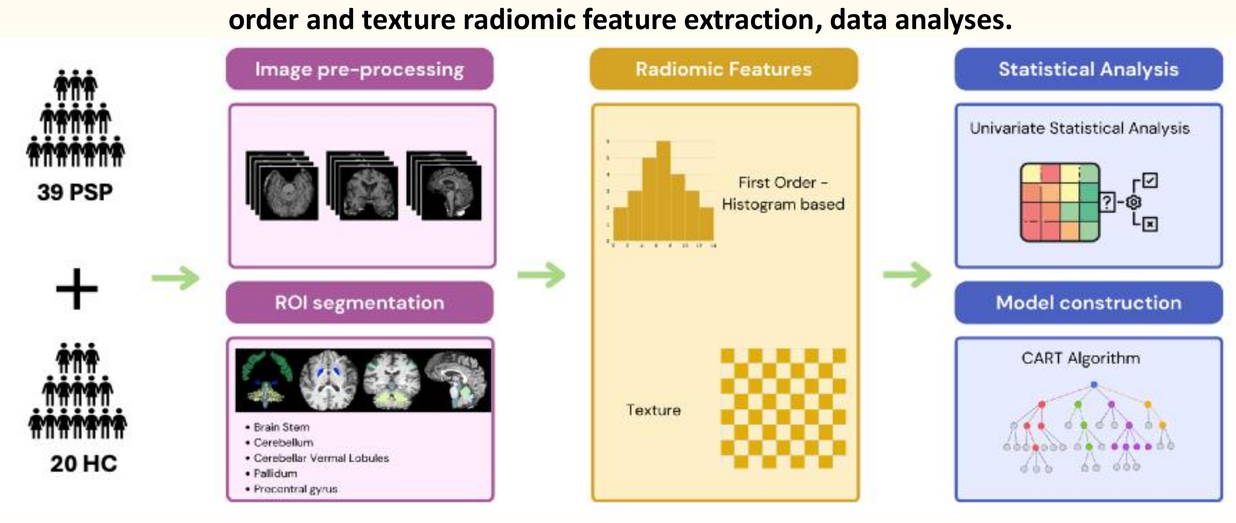
Introduction: Progressive supranuclear palsy (PSP) is a neurodegenerative tauopathy comprising multiple clinical phenotypes, including the classical Richardsons's syndrome (PSP-RS) and other variant forms (vPSP)[1-2]. Despite advances in conventional neuroimaging, current diagnostic tools show limited sensitivity to subtle phenotypic differences.

Objectives: This study aimed to assess the utility of radiomic features extracted from T1-weighted MRI for differentiating PSP from healthy controls (HC) and for supporting phenotypic classification.

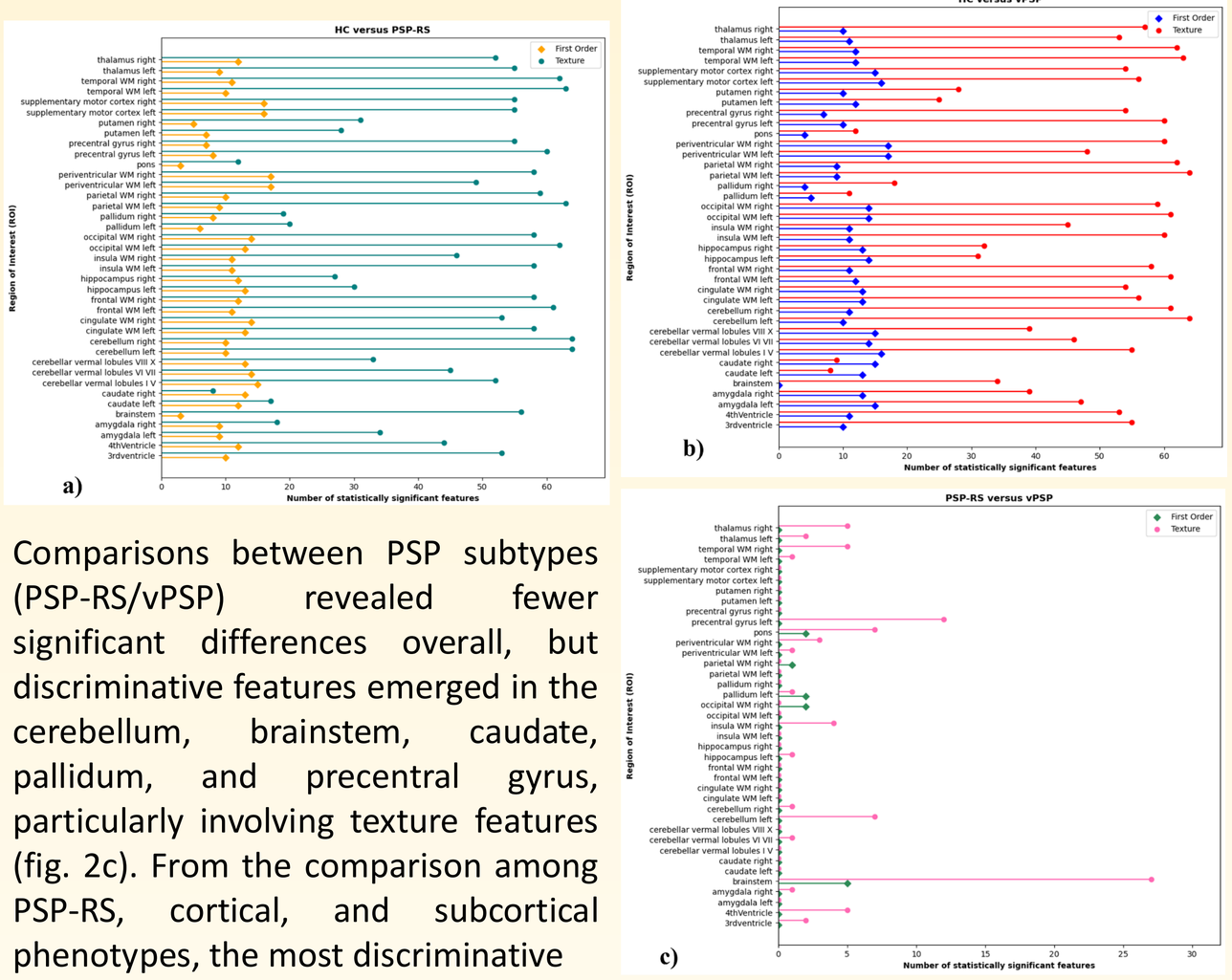
Materials and Methods: We enrolled 39 PSP patients fulfilling the 2017 MDS diagnostic criteria and 20 healthy controls (HC) at the Center for Neurodegenerative Diseases, University of Salerno. Exclusion criteria were MRI contraindications or poor image quality. Demographic and clinical data included age, sex, disease duration, phenotype, LEDD, PSP-rating Scale, Schwab and England scale, and MoCA. All subjects underwent 3T MRI with a 3D T1-weighted MPRAGE sequence. Images were pre-processed with bias correction, skull stripping, and intensity normalization, and then segmented into cortical and subcortical regions using 3D Slicer. Based on available evidence, 21 regions of interest (ROIs) per hemisphere, known to be most affected in PSP, were selected for radiomic analysis. From each region, 86 radiomic features were extracted, including 18 first-order and 68 texture metrics. Radiomic features were compared between HC and PSP, and across PSP subgroups (PSP-RS, cortical, subcortical) using Kruskal–Wallis tests with post hoc correction. A CART model was applied to identify the most discriminative features, using stratified five-fold cross-validation to reduce overfitting; model performance was evaluated by accuracy and AUROC as measures of classification ability (fig. 1).

Figure 1. Study workflow: Image pre-processing, region of interest segmentation, first-order and texture radiomic feature extraction, data analyses.



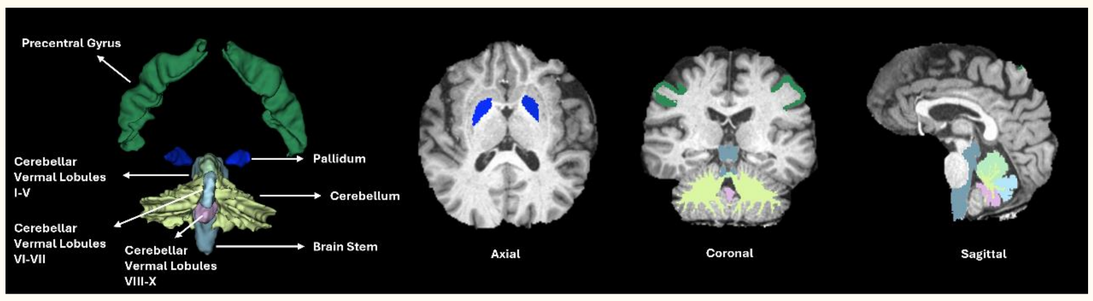
Results: We included 39 PSP patients (mean age 69.3 ± 6.6 years, 36% female) and 20 HC (mean age 67.7 ± 4.4 years, 30% female), matched for age and sex. MoCA scores were significantly lower in PSP compared with HC ($p<0.001$). Within the PSP cohort, 97% had a Probable diagnosis; 19(49%) patients were classified as PSP-RS and 20 (51%) as vPSP, including 8 cortical and 12 subcortical variants. No differences were in demograhic and clinical data among various PSP subgroups. Radiomic analysis showed that, across most ROIs, texture features outperformed first-order metrics in discriminating between groups. Almost all features were significantly different when comparing PSP-RS with HC, with the thalamus, temporal white matter, supplementary motor cortex, putamen, and precentral gyrus bilaterally most consistently affected (fig 2a). In vPSP compared to HC, additional involvement of the cerebellum was evident (fig 2b).

Figure 2. Bar plots representing the number of statistical significance radiomic features for each ROI in multiple comparison. a) HC versus PSP-RS; b) HC versus vPSP; c) PSP-RS versus vPSP.



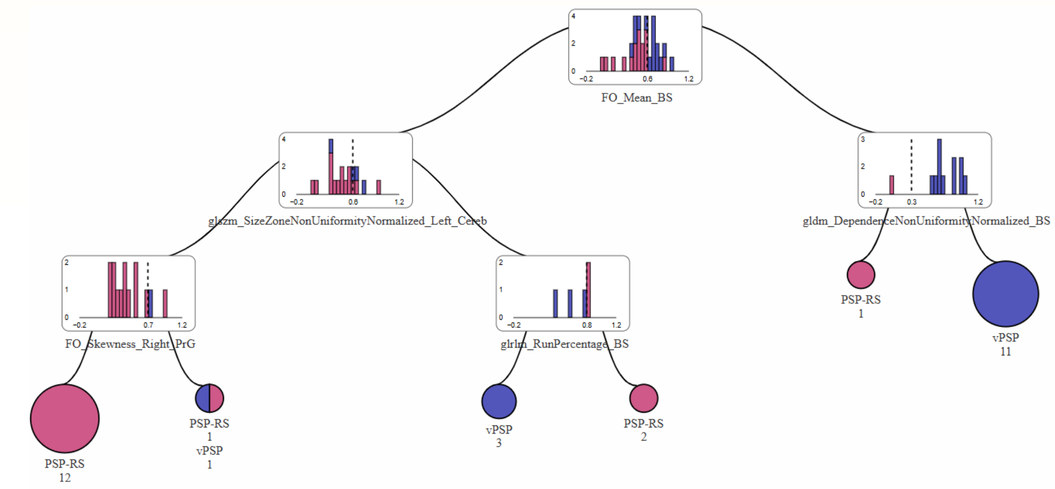
Comparisons between PSP subtypes (PSP-RS/vPSP) revealed fewer significant differences overall, but discriminative features emerged in the cerebellum, brainstem, caudate, pallidum, and precentral gyrus, particularly involving texture features (fig. 2c). From the comparison among PSP-RS, cortical, and subcortical phenotypes, the most discriminative regions of interest were identified and used to generate the 3D representation (fig. 3).

Figure 3. Brain regions identified as most significant for distinguishing PSP using 3D modelling and MRI views



Finally, a CART model was developed to separate PSP-RS from vPSP, using brainstem and cerebellar features as main decision nodes (fig.4). The model reached an accuracy of 0.66 and an AUROC of 0.64, indicating moderate discriminative performance.

Figure 4. Decision tree for the classification of samples into PSP-RS and vPSP groups. The bar graphs at each node show the distribution of features for PSP-RS (in red) and vPSP (in blue), the dotted line shows the threshold value for each variable while the terminal circles represent the final classification, proportional to the number of samples in each group.



Conclusions: These results suggest that radiomics may be complementary to clinical assessment and traditional imaging, for improvement of diagnostic precision and phenotypic stratification in PSP.

Bibliography: 1) G. U. Höglinger et al., Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria, Movement Disorders, 2017, Jun;32(6):853-864. 2) Costanza Pavone et al., Longitudinal clinical decline and baseline predictors in progressive supranuclear palsy, Parkinsonism Relat Disord, 2023, Febr;107:105290.