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POSTER PRESENTATION

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TV-L1 Ordinal Logistic Regression Reveals New Morphometric Patterns Related to Parkinsonian Symptom Severity: An ENIGMA-PD study

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Abstract

Background: Parkinson's disease (PD) is heterogeneous, both phenotypically and in terms of temporal progression. The Hoehn and Yahr (HY) scale is a well-established PD staging approach, and identifies 5 stages of the disease. Morphometric effects in deep gray matter regions of the brain associated with HY stages are complex; a recent large-scale ENIGMA-PD study showed higher local subcortical volumes in early HY stages relative to controls, followed by a precipitous decrease after stage 2 [1]. This finding motivates a closer look at fine-level morphometry beyond gross volume measures. Here, we developed and applied a novel machine learning algorithm to reveal the subcortical shape signatures of HY staging.

Method: We computed shape features in 7 bilateral subcortical regions [2] based on T1-weighted MRI data from 2,322 PD subjects and 1,207 controls from 20 ENIGMA-PD cohorts (HY stages in **Table 1)**. We developed a sparse, spatially coherent (total variation/TV-L1) ordinal linear logistic classifier [3] to predict HY stages with a single linear model. We applied the model to vertex-wise medial thickness features. We optimized regularization parameters for balanced recall (sensitivity) and precision using a 4-fold cross-validation grid search. Very low numbers of HY4 and HY5 samples necessitated merging stages 3-5 into one category. For comparison, we also trained 4 binary TV-L1 logit models on the same features [4], discriminating (1) PD-Control; (2) HY1-HY2; (3) HY1-HY345; (4) HY2-HY345, using ROC area-under-the-curve (AUC) evaluation.

Result: Across-stage mean out-of-sample precision and recall were 0.43, and 0.393, respectively (chance=0.33). **Table 2** shows the confusion matrix and precision/recall for each HY stage. All models' linear coefficient maps are displayed in **Figures 1,2.** Binary classification ROC-AUC was 0.66 for PD-Control, and ranged from 0.62 to 0.73 for HY prediction (**Figure 2**).

Conclusion: We developed an ordit machine learning model for morphometric shape-based ordinal classification of disease stages, training it for Parkinson's Disease Hoehn and Yahr stage prediction on a large MRI collection. Performance was substantially above chance. Model weight maps indicate early increased thalamic thickness, followed by a complex thinning pattern associated with later HY stages.

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Table 1. Sample characteristics in ENIGMA-PD.

Sample	Size	Age (mean ± SD)	% Female
PD patients (all)	2322	63.4 ± 9.7	34.8
Controls	1207	59.5 ± 12.4	44.7
HY1	436	59.5 ± 9.9	39.5
HY2	1047	64.5 ± 9.1	32.5
HY345	339	65.6 ± 9.9	41.0

Table 2. Average ordinal regression performance in classifying HY stages using subcortical shape features, based on out-of-fold evaluation. "Recall" here means the fraction of all subjects with the true HY stage as given. "Precision" means the fraction of all subjects with the predicted HY stage as given. Standard Recall and Precision values are in bold italics.

		Predicted HY1	Predicted HY2	Predicted HY345
Confusion Matrix	True HY1	124	293	19
	True HY2	182	791	73
	True HY345	31	261	47
Recall	True HY1	***0.284***	0.672	0.044
	True HY2	0.174	***0.756***	0.070
	True HY345	0.091	0.770	***0.139***
Precision	True HY1	***0.368***	0.218	0.137
	True HY2	0.540	***0.588***	0.525
	True HY345	0.092	0.194	***0.338***

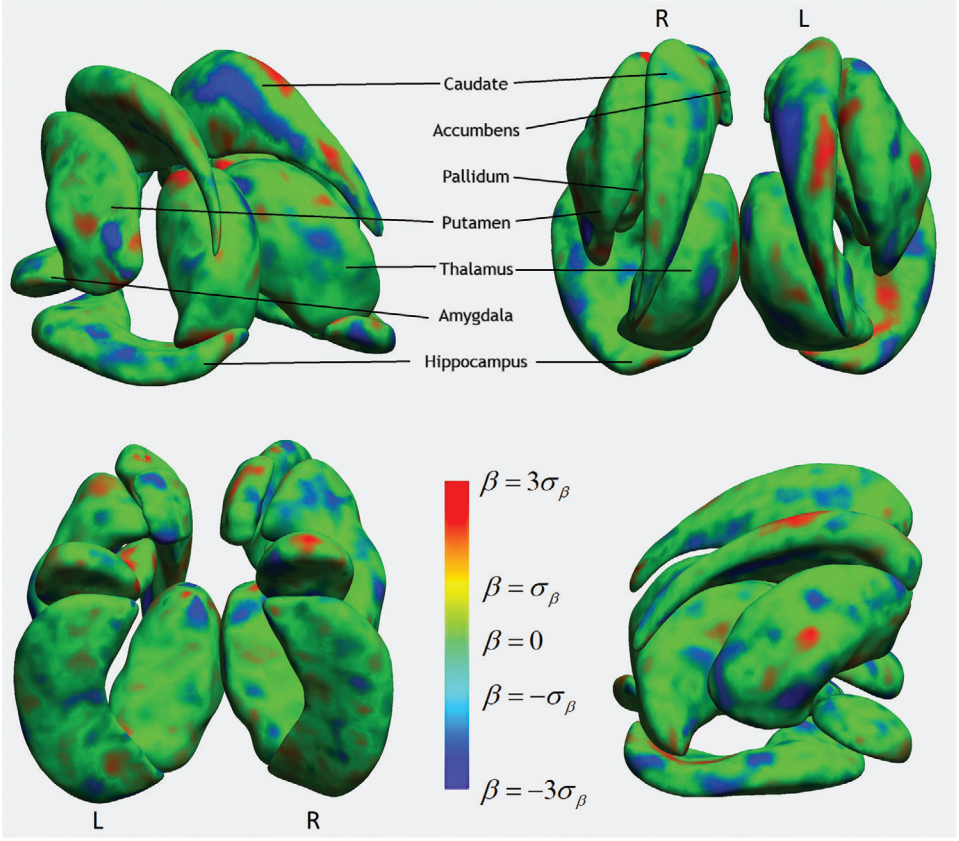

Figure 1. Coefficient (beta) maps of the ordinal linear Hoehn and Yahr stage model, distinguishing 3 categories (HY1, HY2, and HY345). Increased thickness in the positive (warm-colored) regions and decreased thickness in negative (cool-colored) regions increases likelihood of being classified at a later HY stage. Regional deformation of the bilateral caudate, putamen, and thalamus appear to be the most important discriminators in the binary classifications. The ordinal classification shows subtle, but dispersed effects across all structures.

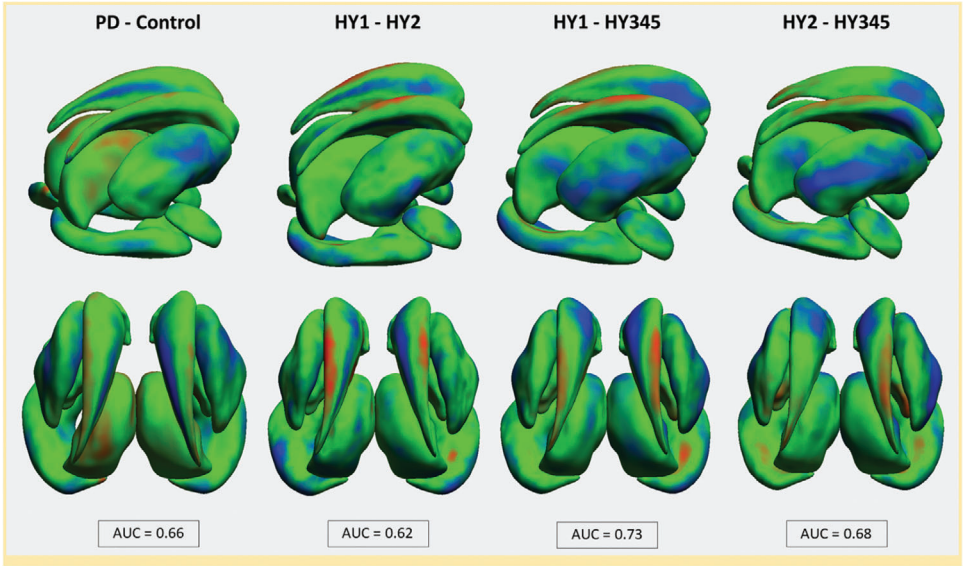

Figure 2. Coefficient maps showing the contribution of all vertices to the differentiation of PD patients from controls and for HY prediction in binary classifiers. Expansion (i.e., thicker; red) and compression (i.e., thinner; blue) of the surfaces are shown for patients relative to controls, or for higher stages relative to lower stages.