P24

Progressive supranuclear palsy phenotyping: a data-driven approach from the PSP-NET

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Introduction: Progressive supranuclear palsy (PSP) is an atypical parkinsonism diagnosed according to the Movement Disorder Society (MDS) criteria [1]. On the basis of expert opinion, different phenotypes have been identified [1]. However, phenotype attribution is often difficult and complex hierarchical rules are needed to overcome the frequent overlapping. Moreover, a data-driven approach to describe PSP phenotyping has not been explored yet.

Objective: To identify PSP phenotypes with unsupervised machine learning algorithms.

Methods: Three hundred eighty-one patients from the Italian PSP-NET supported by Fondazione LIMPE [3] were assessed by the PSP rating scale [4] and the Montreal Cognitive Assessment [5]. All records were systematically combined to obtain pre-specified PSP feature scoring and used as variables for a two-step cluster analysis. One-way ANOVA and Chi-squared test were used to determine differences among clusters in disease duration and MDS phenotype distribution.

Results: Four different clusters were found. Cluster 1 (n=70) presented prominent axial impairment, postural instability and oculomotor dysfunction. Cluster 2 (n=84) had mild PSP features with prominent appendicular involvement. Cluster 3 (n=131) presented major frontal and language impairment, with partial levodopa response. Cluster 4 (n=96) had freezing of gait with partial levodopa response. No significant differences were found in disease duration and MDS phenotype distribution among clusters (p=0.397 and p=0.8, respectively).

Conclusions: Four clinical clusters based on PSP clinical features have been identified. Interestingly, they do not completely overlap with classical MDS phenotypes. We hypothesize that specific combinations of features, each with a different weight, have a prominent role in the definition of phenotypes. As such, a simple hierarchical phenotype attribution may not represent the best solution to assign PSP phenotypes [1-2]. Nonetheless, this is a preliminary analysis and further studies are needed to define the reproducibility and the clinical significance of the proposed clusters.

References:

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