Neuropsychological comparison between PLS and Predominant Upper Motor Neuron ALS at first evaluation in a tertiary ALS Center

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Introduction and objective

Primary lateral sclerosis (PLS) is a slowly progressive upper motor neuron syndrome, and its diagnosis remains clinical after exclusion of mimic conditions.
Differentiation of PLS from predominant upper motor neuron ALS (PUMN-ALS) is a significant challenge in the early phase of both disorders.
Our aim was **to determine the cognitive/behavioral profile of PLS patients at the time of their first visit to an ALS center and compare it with that of PUMN-ALS patients.**

Methods

We evaluated patients later diagnosed with **definite PLS** according to established criteria. At their initial visit to the ALS center, they underwent **comprehensive neuropsychological testing. Propensity score matching** (age, sex and years of education) was used to **compare their scores with those of healthy controls (HC) and PUMN-ALS patients, in a 1:2 ratio.**

Results

We included **32 PLS patients, 64 PUMN-ALS patients and 64 HC.**

	PLS N=32	PUMN-ALS N=64	HC N=64	p-value PLS vs PUMN-ALS	p-value PLS vs HC
Age at test (years, SD)	60.5 (8.5)	60.0 (12.1)	60.3 (8.3)	0.85	0.98
Education (years, SD)	10.2 (3.6)	10.8 (4.2)	11.0 (4.0)	0.49	0.34
Sex (female)	16 (50.0%)	32 (50.0%)	32 (50.0%)	1	1
Onset to test time (months, SD)	24.6 (19.5)	19.5 (16.2)	N/A	0.18	N/A
Site of onset (spinal)	29 (90.6%)	61 (95.3%)	N/A	0.93	N/A
ΔALSFRS-R (points/month, SD)	0.38 (0.30)	0.73 (0.54)	N/A	0.002	N/A

Table 1. Comparison of demographic and clinical characteristics of PLS, PUMN-ALS and HC. N/A: not applicable.

Cognitive/behavioral impairment was identified in **1/3 of PLS and PUMN-ALS** patients:

- no significant differences in categorial distribution between PLS and PUMN-ALS (p=0.15);
- **tendency for less pronounced behavioral and more pronounced cognitive impairment in PLS.**

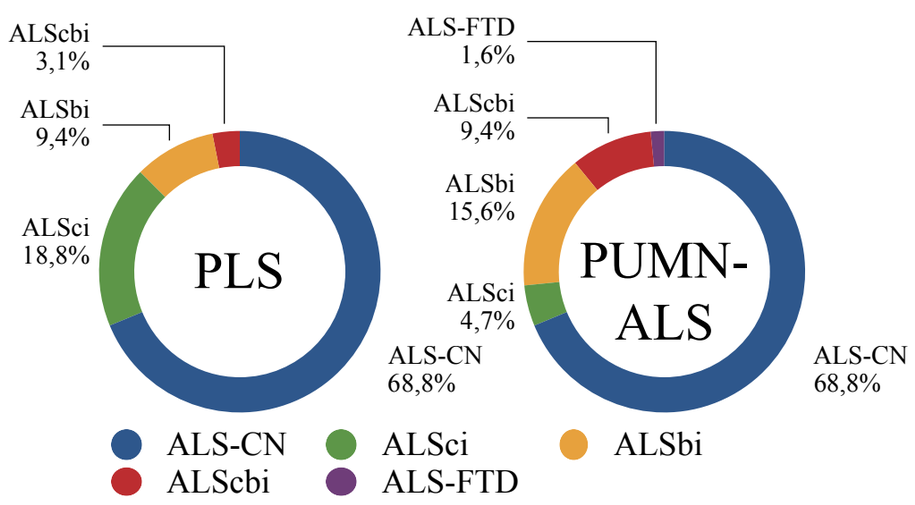

Table 2. Comparison of the cognitive classification of PLS and PUMN-ALS.

PLS patients showed **poorer multidomain performance compared to HC** and performed **similarly to PUMN-ALS** patients.

	PLS vs HC	PLS vs PUMN-ALS
MMSE	**PLS<HC**	**PLS<PUMN-ALS**
FAS	**PLS<HC**	NS
CAT	NS	NS
FAB	NS	NS
Digit Span FW	**PLS<HC**	NS
Digit Span BW	**PLS<HC**	NS
TMT A	NS	NS
TMT B	NS	NS
TMT B-A	NS	NS
RAVL-IR	**PLS<HC**	NS
RAVL-DR	**PLS<HC**	NS
BSRT-IR	NS	NS
BSRT-DR	NS	NS
ROCF-IR	**PLS<HC**	NS
ROCF-DR	**PLS<HC**	NS
Clock	NS	NS
CPM47	**PLS<HC**	NS
SET-IA	NS	NS
SET-CI	NS	NS
SET-EA	NS	NS
SET-GS	**PLS<HC**	NS
HADS-A	**PLS>HC**	NS
HADS-D	**PLS>HC**	NS
ECAS Language	NS	NS
ECAS Verbal Fluency	NS	**PLS<PUMN-ALS**
ECAS Executive	NS	**PLS<PUMN-ALS**
ECAS Memory	NS	NS
ECAS Visuospatial	NS	NS
ECAS ALS-specific	NS	**PLS<PUMN-ALS**
ECAS ALS-nonspecific	NS	NS
ECAS total score	NS	**PLS<PUMN-ALS**

p-value≤0.001
p-value≤0.01
p-value≤0.05

Table 3. Comparison of scores. PLS vs HC and PLS vs PUMN-ALS. NS: not statistically significant.

Conclusion

A substantial proportion of PLS patients exhibit cognitive/behavioral impairment at their first ALS center visit.
The cognitive/behavioral profile of PLS closely resembles that of PUMN-ALS, although there could be a trend for less behavioral and more cognitive impairment in PLS.

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References

1. Turner MR, Barohn RJ, Corcia P, et al. Primary lateral sclerosis: consensus diagnostic criteria. J Neurol Neurosurg Psychiatry. 2020;91(4):373-377.
2. Strong MJ, Abrahams S, Goldstein LH, et al. Amyotrophic lateral sclerosis - frontotemporal spectrum disorder (ALS-FTSD): Revised diagnostic criteria. Amyotroph Lateral Scler Frontotemporal Degener. 2017;18(3-4):153-174.
3. de Vries BS, Rustemeijer LMM, Bakker LA, et al. Cognitive and behavioural changes in PLS and PMA:challenging the concept of restricted phenotypes. J Neurol Neurosurg Psychiatry. 2019;90(2):141-147.
4. Maranzano A, Poletti B, Solca F, et al. Upper motor neuron dysfunction is associated with the presence of behavioural impairment in patients with