

LONGITUDINAL ASSESSMENT OF FRONTAL COGNITIVE IMPAIRMENT IN PATIENTS WITH MOTOR NEURON DISEASE

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INTRODUCTION

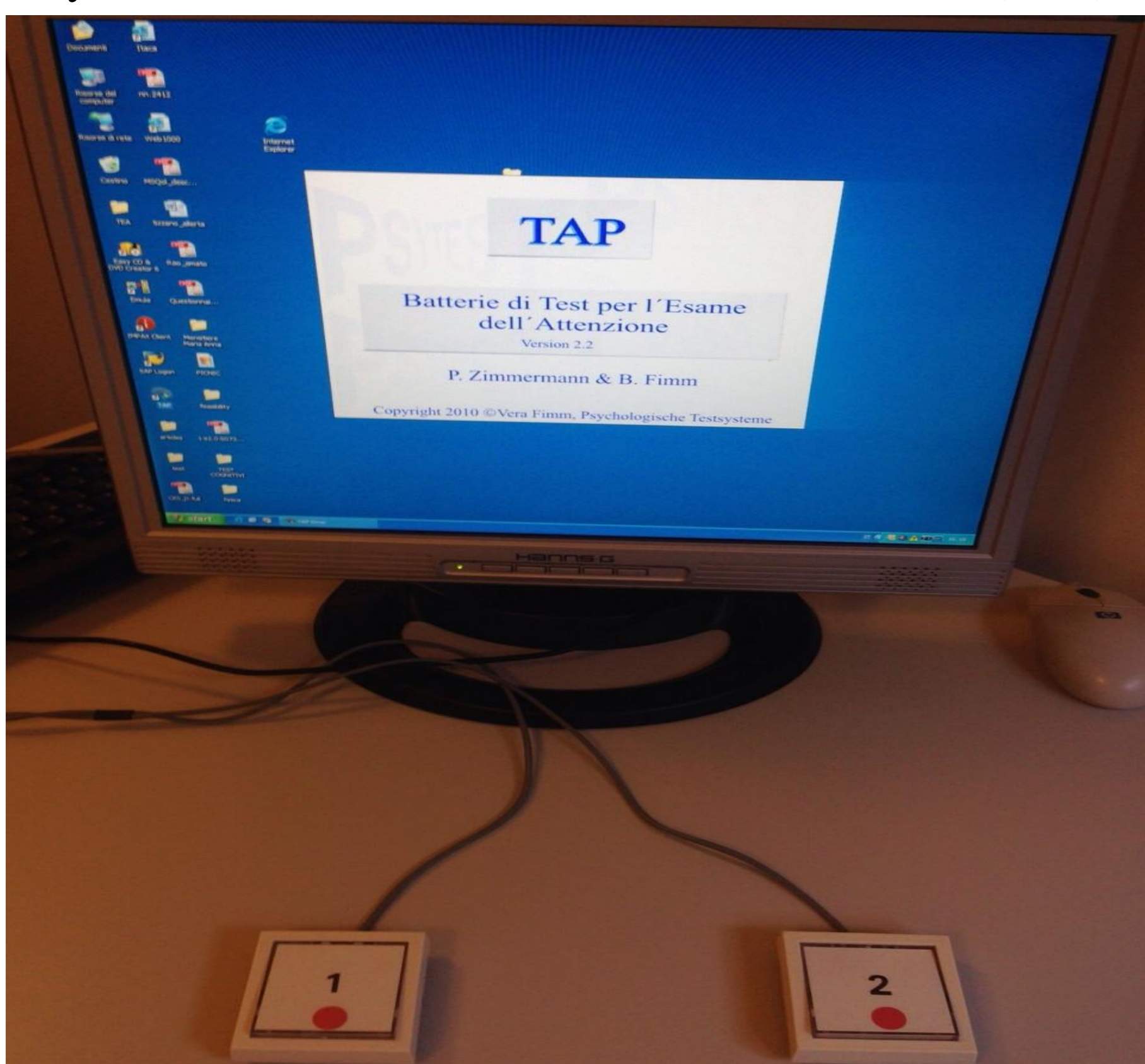
- ✓ Motor neuron disease (MND) is now widely recognized as a multi-system pathology. Despite the prominence of motor symptoms, indeed, up to 50% of MND patients also manifest a broad range of neuropsychological deficits.
- ✓ Cognitive impairment in MND seems to be mainly characterized by deficits on tests of executive function.
- ✓ Due to progressive verbal and physical disability, it is often difficult to investigate cognitive domains in MND, especially in advanced stages of the disease.
- ✓ The majority of cognitive studies of MND are cross-sectional and little is known about the longitudinal course of cognitive disturbances in these patients.

OBJECTIVE

- ✓ To test the progression of frontal cognitive impairment in patients with MND, accounting for the effect of progressive verbal and/or physical disability.

MATERIALS AND METHODS

- ✓ 28 non-demented sporadic MND patients were studied.
- ✓ Among the MND patients: 46% classic ALS; 35% predominant UMN; 19% predominant LMN.
- ✓ Mean disease duration: 18 months ± 13.
- ✓ All patients were followed prospectively with clinical and neuropsychological evaluations every 3 and 6 months, respectively, for a maximum follow up of 24 months.
- ✓ Cognitive assessment was performed using the MMSE, verbal fluency tests and the Test of Attentional Performance (TAP).



Test of Attentional Performance (TAP) program version 2.2 (P. Zimmermann and B. Fimm)

- ✓ Performance accuracy and speed were evaluated for alertness (intrinsic and phasic components), divided attention, sustained attention, behavioral control and interference tendency (using the stimulus-reaction incompatibility paradigm).
- ✓ Longitudinal linear models were used to analyze clinical and cognitive variable changes over time and the relationship between baseline clinical features and cognitive decline.

RESULTS

BASELINE

- ✓ At baseline, general cognition and fluency domains were not impaired in our MND cases (MMSE: 28.25 ± 0.47; phonemic fluency: 29.93 ± 9.91; semantic fluency: 39.44 ± 11.18).
- ✓ Using the TAP battery, we found that: phasic and intrinsic alertness were impaired, respectively, in 80% and 83% of patients; 76% of patients showed altered sustained attention; behavioral control was impaired in 57% of patients; interference tendency was impaired in 48% of patients.

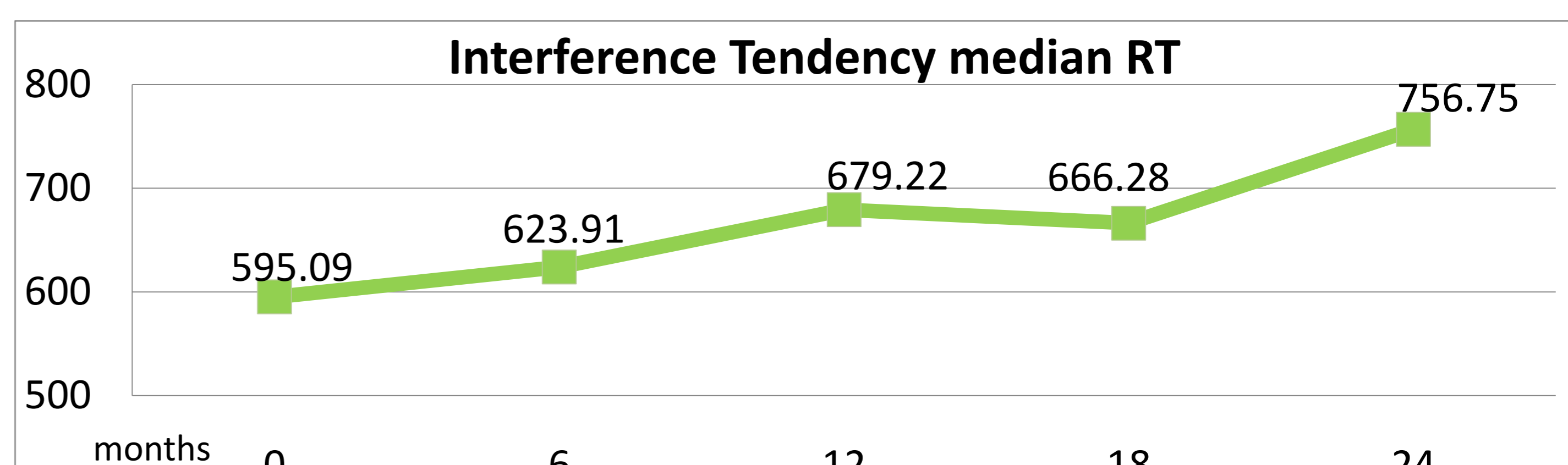
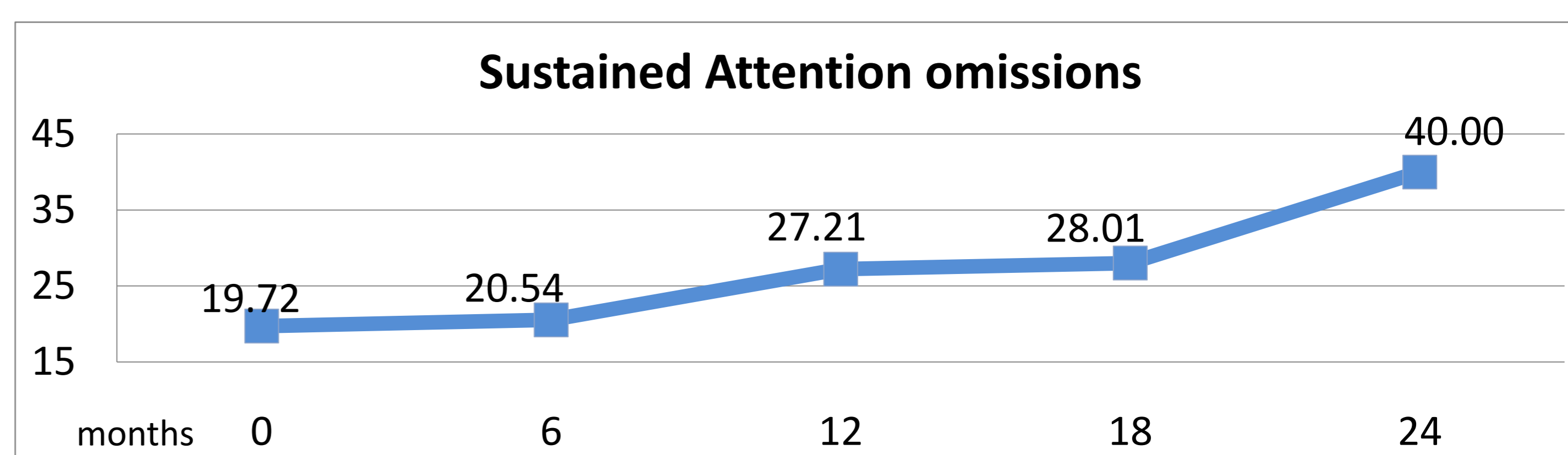
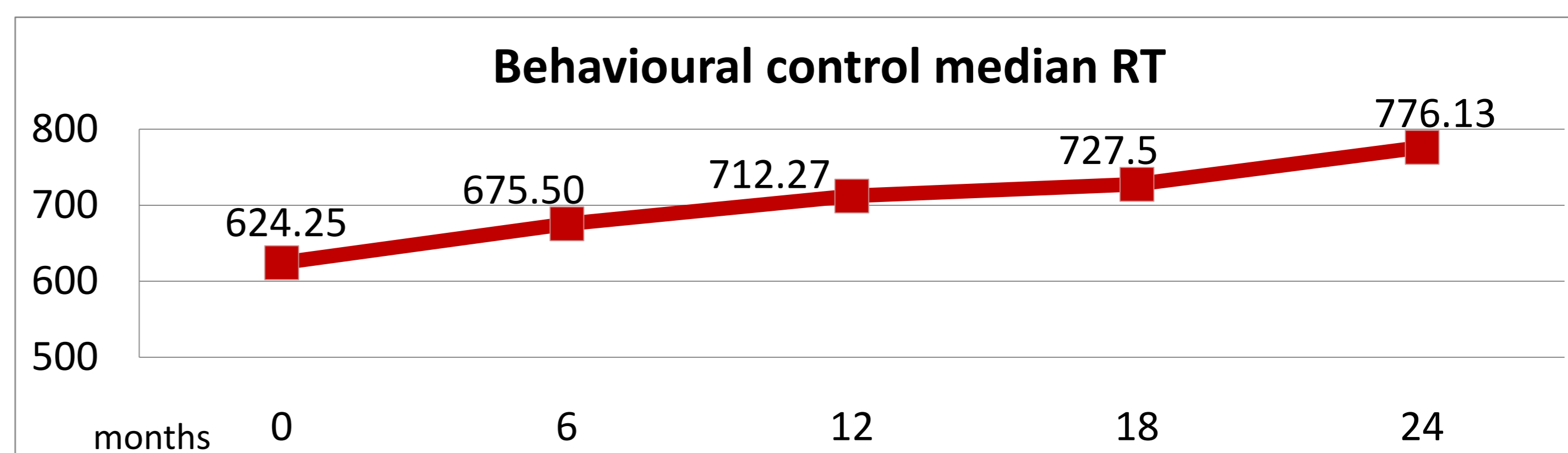
RESULTS

FOLLOW UP

- ✓ MND patients showed a progressive worsening of motor disability and global cognitive functions over time (table).
- ✓ The TAP showed a significant decrease over time of sustained attention performance accuracy as well as behavioral control and interference tendency performance speed (table and figures).
- ✓ The progressive cognitive deterioration was independent of baseline motor features.

	Baseline mean ± SD	Mean % change baseline-month 24 ± SE	p
ALSFRS-R score	40.08 ± 1.36	-32.49 ± 7.16	<0.001
Total MRC score	105.38 ± 2.88	-27.78 ± 5.36	<0.001
ALS Severity Scale – bulbar speech score	8.73 ± 0.39	-12.28 ± 11.54	<0.001
ALS Severity Scale – swallow score	8.96 ± 0.36	-11.81 ± 7.99	<0.001
ALS Severity Scale – lower extremity score	7.42 ± 0.40	-31.65 ± 11.74	<0.001
ALS Severity Scale – upper extremity score	7.38 ± 0.42	-49.53 ± 11.68	<0.001
UMN score	9.42 ± 1.03	7.30 ± 22.72	<0.001
MMSE	28.25 ± 0.47	-0.75 ± 5.26	0.04
Sustained attention (total omissions)	19.72 ± 1.91	130.39 ± 85.76	0.001
Behavioral control (median RT)	624.25 ± 104.23	17.10 ± 10.33	<0.001
Interference tendency (median RT)	595.09 ± 40.93	23.21 ± 7.63	0.001

Abbreviations. ALSFRS-R: ALS Functional Rating Scale-Revised; MMSE: Mini Mental State Examination; MRC: Medical Research Council; RT: reaction times; UMN: Upper Motor Neuron.



CONCLUSIONS

- ✓ Longitudinal analyses using computerized-based, sensitive executive measures revealed a progressive cognitive decline in MND patients, which appeared relatively early in the course of MND and is not associated with baseline motor disability.
- ✓ Cognitive deterioration in MND encompasses both executive performance accuracy and speed.

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