Impaired cardiovascular control in amyotrophic lateral sclerosis: correlation with clinical parameters

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by motor and extra-motor neuron loss. Several autonomic nervous system (ANS) disturbances have been observed in ALS. Although an altered cardiovascular neural response to orthostasis has been described in ALS patients, the comparison of the response with an healthy control group has not been studied so far. In addition, no clear correlation between specific ANS abnormalities and ALS clinical characteristics has been found.

Aim: To compare the response to tilt test in ALS patients with age-matched controls and to correlate the results of power spectral analysis of heart rate and systolic arterial pressure variability with patients' clinical features.

Methods: We studied 52 ALS patients and a control group of 16 healthy subjects. Clinical evaluation included: Revised ALS Functional Rating Scale (ALSFRS-R) score, its bulbar subscore and the rate of disease progression (RDP), calculated as the difference between two ALSFRS-R scores at two different evaluation times.

ECG, non-invasive arterial pressure and respiratory signals were acquired in supine position (REST) and during head up tilt test (TILT) at 75° for 10 minutes.

Means, μ_{RR} and μ_{SAP}, and variances, σ^2_{RR} and σ^2_{SAP}, of RR interval (RR) and systolic arterial pressure (SAP) time series were calculated. Parametric power spectral analysis RR and SAP time series provided the indices of cardiac sympathetic (LF_{RR}) and vagal (HF_{RR}) modulation and of sympathetic vasomotor control (LF_{SAP}).

Linear correlations between clinical markers and time domain and power spectral indices were calculated (Pearson correlation coefficient, r).

Results: At rest, ALS patients were more tachycardic than controls and showed a lower σ^2_{RR}. During TILT μ_{SAP} was lower in ALS patients compared to controls. During tilt, μ_{RR} decreased in both groups. LF_{RR} tended to increase in controls, as expected, but not in ALS patients. HF_{RR} physiologically decreased during TILT in controls and in ALS patients. The physiological increase of σ^2_{SAP} and LF_{SAP} during the orthostatic challenge was present only in controls (Table 1).

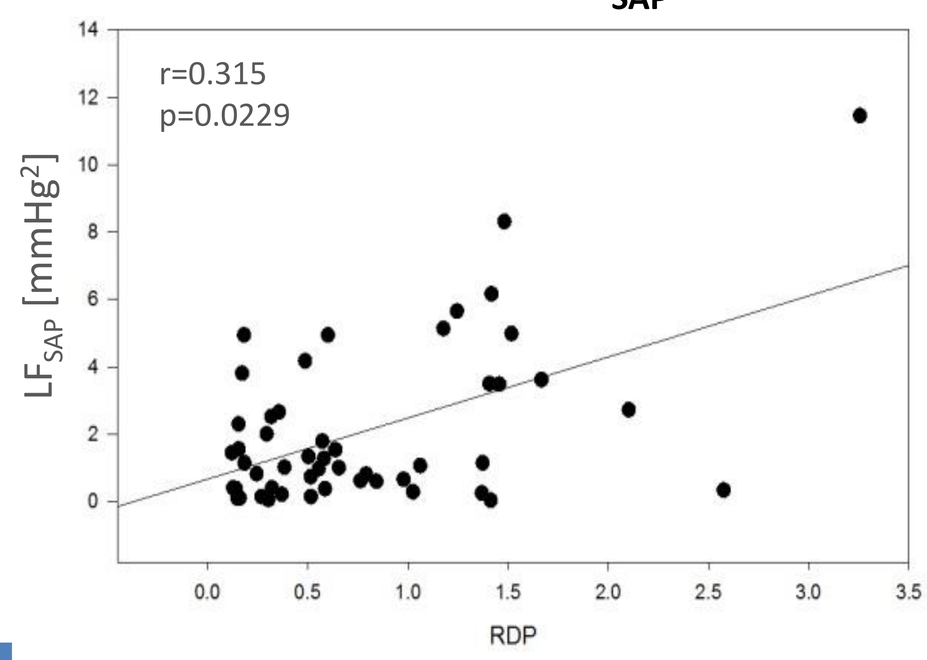
RDP was the only clinical feature that correlated to power spectral indices: a significant positive correlation between RDP and LF_{SAP} was found (Fig.1)

Table 1. Results of the comparison of ALS patients and healthy controls at REST and during TILT

Index	REST		TILT	
	Controls	ALS patients	Controls	ALS patients
μ_{RR} [ms]	899±158	814±127#	797±157*	712±123*#
σ^2_{RR} [ms^2]	1354±1032	703±734#	1141±877*	427±443*#
LF_{RR} [nu]	59±19	55±25	67±23	52±31
HF_{RR} [ms^2]	176±172	153±256	94±122	52±69*
μ_{SAP} [mmHg]	124±17	118±16	131±34	111±29#
σ^2_{SAP} [mmHg^2]	31±15	16±15	44±25*	24±47#
LF_{SAP} [mmHg^2]	8±9	2.5±5	25±32*	5±12#

* p<0.05 REST vs. TILT; # p<0.05 controls vs. ALS patients

Figure 1. Positive correlation between RDP and LF_{SAP}



Conclusions: ALS patients showed an altered response to the orthostatic challenge in comparison with a control group. The impairment was more evident in the vascular control than in the cardiac one. In addition, ALS patients with faster disease progression, were characterized by increased cardiovascular sympathetic modulation directed to the vessels compared to patients with slower disease progression.