ENCALS

Dynamic Bayesian networks for stratification of disease progression in ALS

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INTRODUCTION

Progression rate is quite variable in ALS, implying different times for medical interventions. Thus, new tools for profiling disease progression can be useful for promoting quality of life and prolonging survival.

OBJECTIVE

To apply Dynamic Bayesian networks (DBNs) to determine the relative influence of clinical and demographic variables on the disease progression rate.

METHODS: We included 1214 patients from our database, who were stratified in 3 groups according to ALSFRS-R rate of decay, into: slow, average, and fast progressors (SP, AP, FP), and then analyzed their 1st and 2nd year of follow-up.
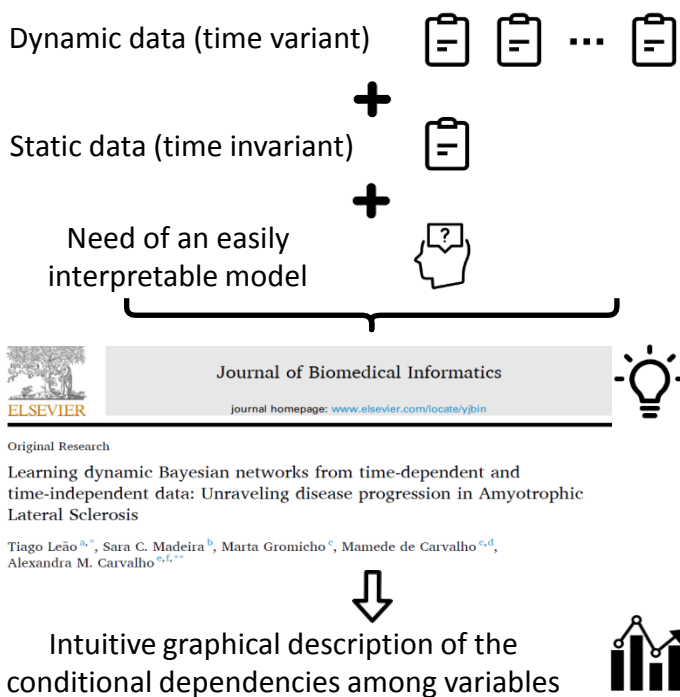
Static Variables	Discretization
Gender	1: male; 2: female
Body mass index (BMI)	1: [0,20[; 2: [20,25[; 3: [25,30[; 4: [30,+1[
ALS Familial history	1: yes; 2: no; 3: unknown
Age at onset	1: [0;30[; 2: [30,50[; 3: [50,70[; 4: [70;+1[
Disease duration	1: [0,6]; 2:]6,12]; 3:]12,18]; 4:]18,36]; 5:]36;+1[
Diagnostic category	1: definitive; 2: probable; 3: possible; 4: PMA
Onset form	1: spinal; 2: bulbar; 3: respiratory/axial; 4: mixed; 5: FTD
C9orf72 HRE	1: yes; 2: no; 3: unknown
Dynamic Variables	**Discretization**
ALSFRS	1: {0,. . .,11}; 2: {12,. . .,23}; 3: {24,. . .,35}; 4: {36,. . .,40}
ALSFRS-R subscores	1: {0,...,3}; 2: {4,...,7}; 3: {8,...,11}; 4: {12}
Forced vital capacity (FVC)	1: [0,40[; 2: [40,60[; 3: [60,80[; 4: [80,100]
Max. inspiratory pressure (MIP)	1: [0,40[; 2: [40,60[; 3: [60,100]
Max. expiratory pressure (MEP)	1: [0,40[; 2: [40,60[; 3: [60,80[; 4: [80,100]
Phrenic nerve response amplitude	1: [0; 0,4[; 2: [0,4;+∞[
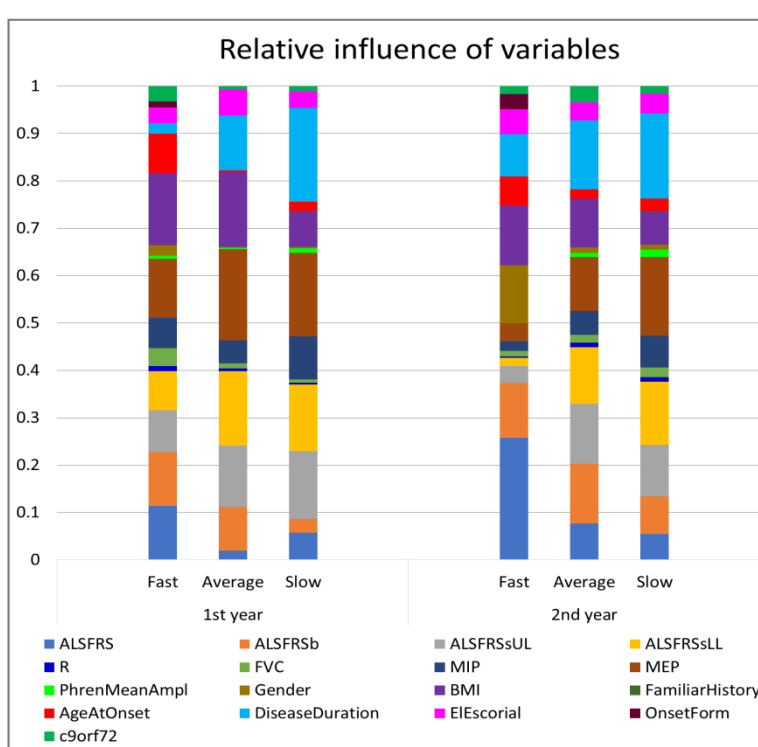
RESULTS

- Disease duration and BMI have higher influence than other static variables.
- BMI has less influence on SL while disease duration has less influence on FP.
- Disease duration is the variable that better differentiates the 3 groups.
- Gender, onset form and familial history of ALS have little influence on all groups.
- Age of onset has medium influence and only on FP.
- MEP is the respiratory test with the highest influence on all groups.
- The ALSFRS score has greater influence on FP than on AP or SP.
- The bulbar sub-score has some influence on FP and AP, but little on SP.
- The sub-scores that evaluate limb function have greater influence on AP and SP.
- The respiratory sub-score has little influence on all groups.

Figure and table: Relative influence of each variable in each progression group in their 1st and 2nd year of follow-up.

	ALSFRS-R questions													FVC	MIP	MEP	Phrenic ampl	Gender	BMI	Familial History	Age at onset	Disease Duration	Diagn category	Onset form	C9ORF72 HRE
1st year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	R1	R2	R3												
Fast	17.34	3.45	2.25	6.42	9.87	5.62	4.98	2.97	8.51	1.04	0.80	0.24	0.72	0.40	2.01	6.26	0.16	1.44	13.16	0.08	3.45	2.01	2.89	0.16	3.77
Average	6.87	1.42	1.72	2.16	10.82	7.24	1.34	2.76	17.46	1.57	1.34	0.07	0.52	0.37	1.79	17.16	0.00	0.00	13.66	0.07	0.37	7.54	3.28	0.00	0.45
Slow	6.34	1.30	1.30	2.67	7.33	7.87	1.68	3.51	16.04	1.07	1.38	0.46	0.53	0.23	7.33	14.90	0.15	0.15	4.51	0.92	1.38	16.58	1.99	0.00	0.38
2nd year																									
Fast	31.27	5.06	4.68	9.87	2.53	2.15	2.41	0.51	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.76	0.00	4.94	10.51	0.00	11.77	5.70	4.81	0.89	1.90
Average	18.18	3.24	2.29	9.25	8.77	6.40	2.61	4.03	10.67	1.26	0.47	0.47	0.55	0.16	1.19	3.87	0.08	0.63	10.28	0.16	1.98	8.38	3.40	0.40	1.26
Slow	9.10	2.54	1.85	6.25	9.18	7.63	4.86	5.17	11.95	0.85	0.54	0.54	0.62	0.62	2.08	10.33	0.15	1.16	5.24	0.23	2.00	15.57	1.00	0.00	0.54

Considering the ALSFRS-R scale questions (Q) separately:

- Q1 is the most important in FP and Q9 in AP and SP. Q5 and Q6 have intermediate influence on all groups.

CONCLUSIONS

- Disease duration at 1st consultation is a critical marker to distinguish groups defined by the progression rate.
- BMI and Q1 are the most influential markers for FP, and disease duration and lower limb function for SP.
- MEP seems to be a better prognostic indicator of patient´s decline than the FVC or the phrenic nerve amplitude.
- sdtDBNs are a promising predictive and descriptive tool.
- This insightful information can lead clinicians to pay special attention to specific variables when evaluating patients, thus helping to improve prognosis and care.