Behavioural correlates of attentional function in ALS patients

Maher Zoubi [1,2], Marcel Daamen [2], Patrick Weydt [1,2], Xenia Kobeleva [2, 3]

1 University Hospital Bonn, Department of Neurodegenerative Diseases and Gerontopsychiatry, Bonn, Germany
2 Clinical Research, DZNE Bonn, Bonn, Germany
3 University Hospital Bonn, Department of Neurology, Bonn, Germany

Background

Past studies demonstrate a significant genetic, pathophysiological and clinical overlap between amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) and report cognitive impairment in up to 30% of ALS patients [1]. Although executive impairment and difficulties in verbal fluency in ALS have been shown in several studies [2], impairments of attentional control have not been extensively examined so far. The aim of this work was to test our hypothesis that even ALS patients without clinical evidence of cognitive dysfunction show behavioural attentional deficits performing a modified version of the Attention Network Test (ANT) [3] (see Figure 1).

Methods

In total, n=51 participants took part in the behavioral study and underwent a neuropsychological screening using the Edinburgh Cognitive Assessment Screen (ECAS) [4]. A cohort of 25 ALS patients (13 ♂, 12 ♀), were matched with 26 controls.

In a modified version of the ANT [5], our study participants were shown arrowheads with three difficulties (congruent, incongruent easy, incongruent hard).

Statistical analysis included a comparison of absolute reaction times and relative reaction time changes (e.g. cue > no cue [alerting effect], incongruent > congruent [executive effect], hard > easy targets [conflict effect]) as well as of ECAS performance.

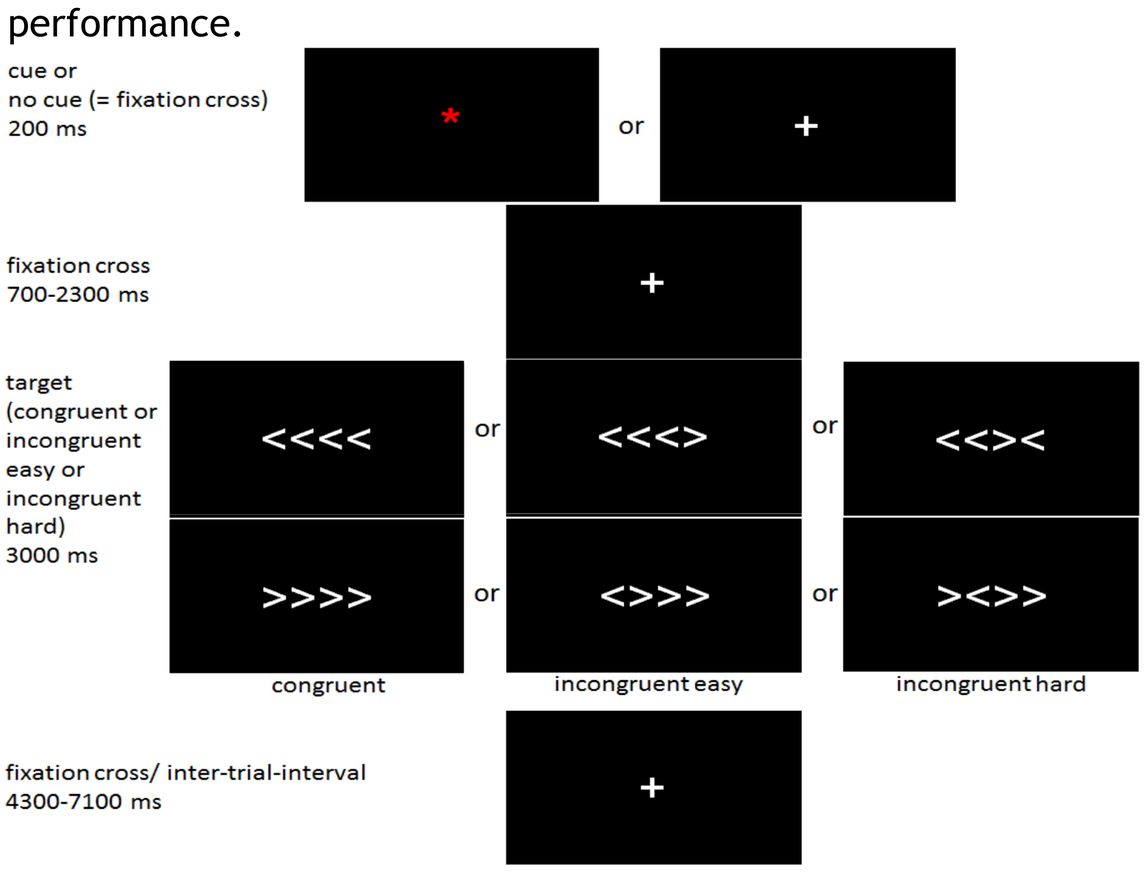

Figure 1: Study design of the modified Attention Network Test

Results

There were no significant differences in age and education between ALS patients and controls. Also there was a comparable neuropsychological performance in both groups as assessed by the ECAS (p = 0.475, Table 1).

In the behavioral task both groups had intact alerting, executive and conflict effects as indicated by the differences between reaction times to targets (Figure 2). ALS patients had significantly longer absolute reaction times (p = 0.013) but the relative reaction times for the alerting, executive and conflict effect did not differ between groups (p > 0.505). In our cohort all ALS patients achieved an ECAS total score above the required cut-off.

	ALS (n=25)		Controls (n=26)		p-values
	mean	SD	mean	SD	
DEMOGRAPHICS					
Age	59.24	8.53	57.77	6.45	0.439
Education [years]	14.44	2.85	16.29	3.08	0.031
Duration since onset [months]	33.26 (n=23)	26.07 (n=23)	-	-	-
CLINICAL VARIABLES					
ALS-FRS-R	36.42 (n=19)	5.84 (n=19)	-	-	-
Progression rates [48-ALS-FRS/duration in months]	0.533 (n=17)	0.455 (n=17)	-	-	-
NEUROPSYCHOLOGY					
Language	27.42*	1.40*	27.46	0.86	0.203
Fluency	19.67*	2.93*	20.54	2.00	0.222
Executive function	37.92*	5.48*	38.00	6.03	0.960
Memory	16.63*	4.07*	17.00	2.74	0.702
Visuospatial function	11.67*	0.72*	11.88	0.43	0.188
TOTAL					
ALS specific score	84.71*	7.93*	86.04	7.59	0.547
ALS non-specific score	28.29*	3.87*	28.88	2.80	0.536
Total score	112.83*	10.83*	114.64	8.21	0.475

* n=24

Table 1: Demographics, clinical variables and results of ECAS in patients and controls

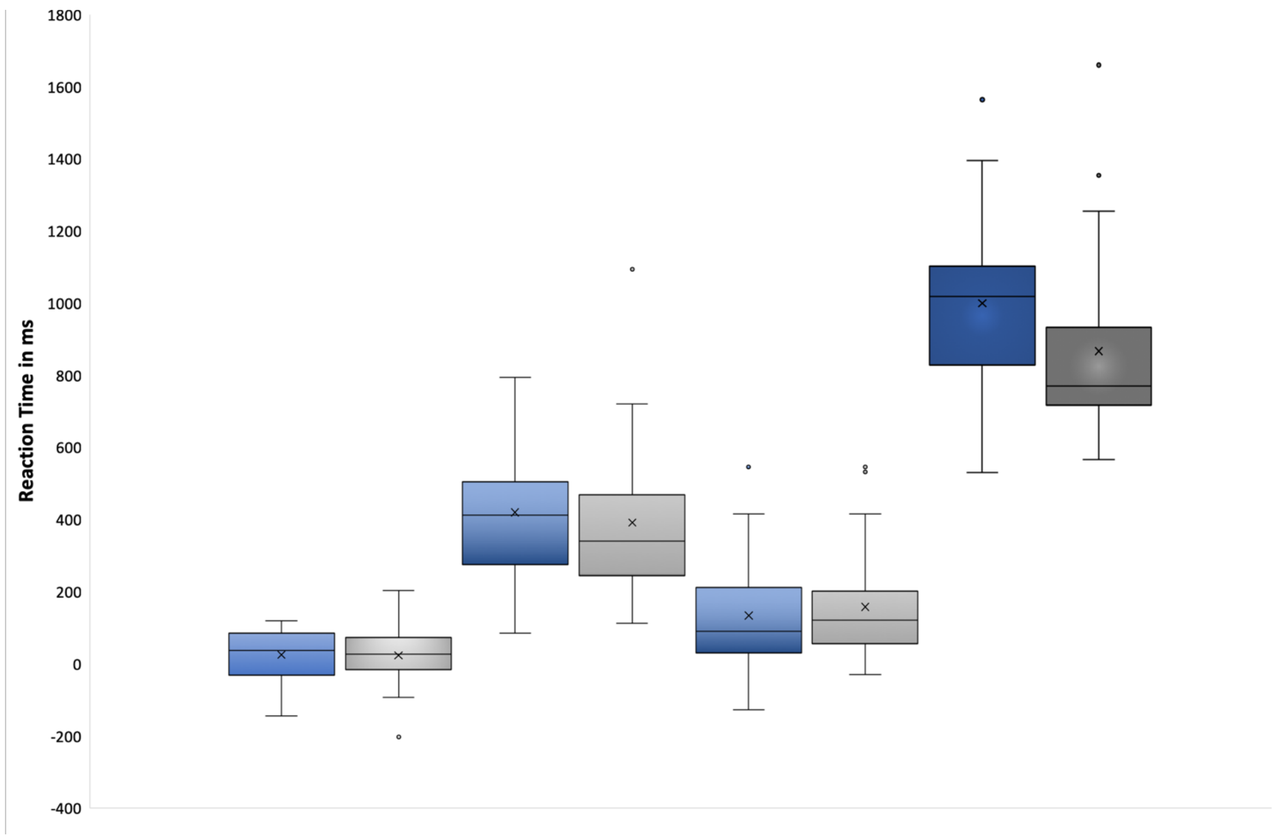

Figure 2: Alerting effect, executive effect, conflict effect and mean reaction time in patients and controls

Discussion

As ALS patients are facing an impairment of motor function, we did not take the absolute reaction times into account but focused on relative reaction times (executive, conflict and alerting effect). In both groups we found alerting, executive and conflict effects, as indicated by a modulation of the reaction times by task condition. However, significant differences of attentional-executive performance between patients and controls could not be shown. This is either caused by the absence of a difference between the two groups regarding attentional control functions (which is consistent with the non-impaired global cognitive performance in the ECAS) or may be due to methodological limitations such as sensitivity of the task and selection bias.

Our future analysis will concentrate on association with clinical variables (disease duration, age of onset, clinical impairment) and brain activations using functional MRI to detect subclinical abnormalities, and we are planning to recruit more ALS patients with cognitive or behavioral abnormalities as well as ALS-FTD.

References

[1] Rippon GA, Scarmeas N, Gordon PH, Murphy PL, Albert SM, Mitsumoto H, et al. (2006): An observational study of cognitive impairment in amyotrophic lateral sclerosis. Arch Neurol. 63: 345–52.
[2] Beeldman E, Raaphorst J, Klein Twennaar M, de Visser M, Schmand BA, de Haan RJ (2016): The cognitive profile of ALS: a systematic review and meta-analysis update. J Neurol Neurosurg Psychiatry. 87: 611–9.
[3] Fan J, McCandliss BD, Fossella J, Flombaum JI, Posner MI (2005): The activation of attentional networks. NeuroImage 26:471–479
[4] Abrahams, S., Newton, J., Niven, E., Foley, J., & Bak, T. H. (2014). Screening for cognition and behaviour changes in ALS. Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 15, 9-14
[5] Firbank M, Kobeleva X, Cherry G, Killen A, Gallagher P, Burn D, Thomas A, O'Brien J, Taylor JP (2016): Neural Correlates of Attention-Executive Dysfunction in Lewy Body Dementia and Alzheimer's Disease

Acknowledgements

This work is supported through a DZNE project funding (BN037) and a travel grant from the AlleLiebenSchmidt initiative.