DBI serum levels in ALS patients correlates with behavioural dysfunction

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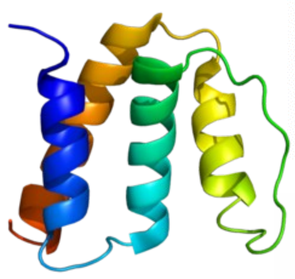
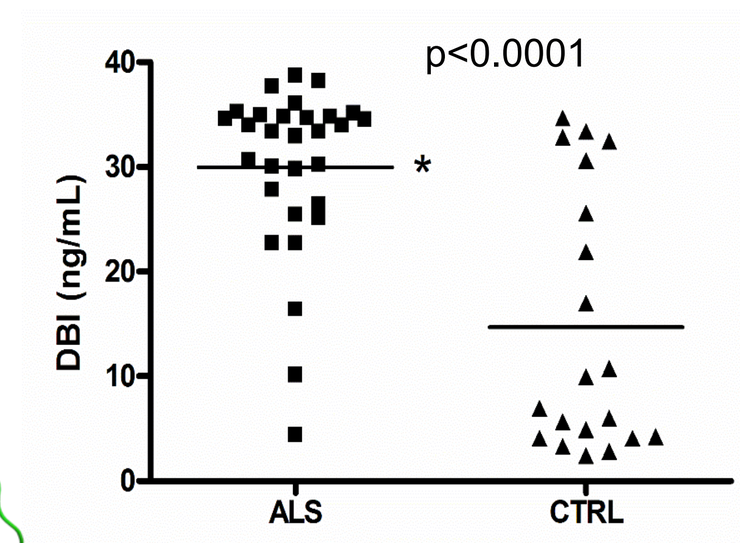
Amyotrophic Lateral Sclerosis (ALS) patients express significant cognitive (ALSci) and behavioral (ALSbi) dysfunctions, ranging from minor alterations to a frank frontotemporal dementia (ALS-FTD), with a minority of patients fully expressing both phenotypes. The presence of cognitive and/or behavioral affection is associated with a worse disease course; hence, the importance of identifying suitable biomarkers for recognition of ALSci or ALSbi subgroups, in order to establish specific strategies of treatment and management (i.e., NIV or nutritional strategies). **Diazepam binding inhibitor (DBI)** is an endogenous inverse agonist of GABA-A receptor and a direct agonist of the peripheral benzodiazepine receptor, which is involved in initiating the biosynthesis of neurosteroids. Both of these actions have been variously linked to cognitive, behavioral and/or mood disorders.

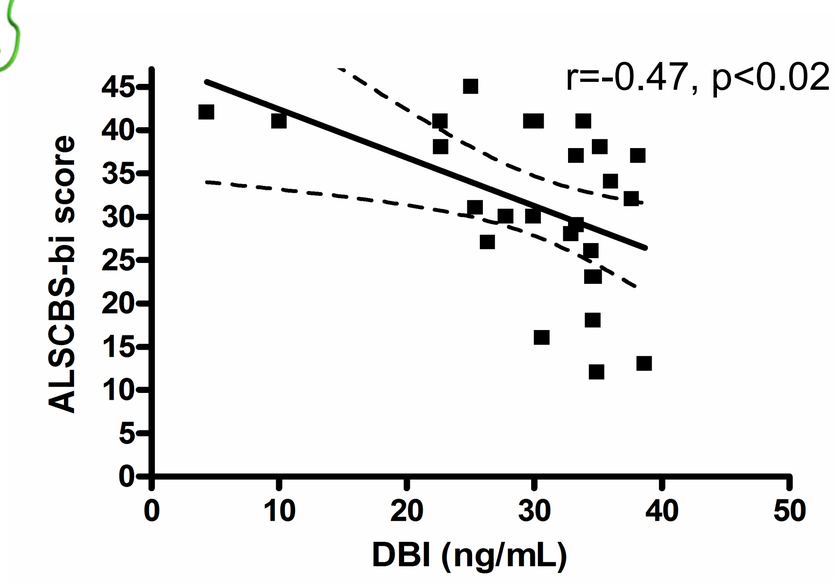
Materials and Methods: In this exploratory case-control study, we assessed DBI serum levels by ELISA in 30 ALS outpatients and in 20 healthy matched controls (CTRL), assessing a putative relationship between DBI levels and cognitive, behavioral and mood status in ALS patients. See **Table**.

	ALS n=30	**CTRL** n=20
Sex, M (%)	19 (63.3%)	12 (60%)
Age, years	61.5 ± 9.7 (42-75)	62.7 ± 12.5 (39-86)
Education, years	10.6 ± 4.8 (3-19)	11.0 ± 3.8 (3-19)
ALSFRS-R, score	30.3 ± 8.9 (18-47)	---
Disease duration, months	48.6 ± 39.6 (7-161)	---
DPI	0.51 ± 0.33 (0.06-1.39)	---
Body weight, kg	69.3 ± 11.3 (42-89)	---
BMI	25.0 ± 2.9 (17.5-31.9)	---
FVC%	69.3 ± 23.4 (15-102)	---
FAB, corrected score *	14.5 ± 3.4 (3.8-18)	>13.4
ALSCBSbi, score *	31.3 ± 9.5 (12-45)	---
BDI, score *	11.8 ± 7.4 (1-35)	≤9

Results: ALS patients showed a two-fold increase in DBI serum levels compared to CTRL ($p<0.0001$). Furthermore, DBI serum levels were increased in ALSbi patients compared to ALSnon-bi ones (+25%, $p<0.03$) and a significant negative correlation was found between serum DBI levels and ALSCBS-bi scores ($r=-0.47$, $p<0.02$). Conversely, neither cognitive nor mood status significantly correlated with DBI serum levels.







Discussion: Increased DBI serum level might represent a suitable biomarker for stratifying ALS patients according to the severity of behavioral deficit, potentially proposing selected management strategies.

Conclusions: Extended studies on serum and/or CSF DBI might improve our understating concerning biological determinants of behavioral affection associated to ALS.

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