Ocular involvement occurs frequently at all stages of amyotrophic lateral sclerosis: preliminary experience in a large Italian cohort

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108° CONGRESSO NAZIONALE
Società Italiana di Fisica

125 YEARS SIF 1897-2022
SOCIETÀ ITALIANA DI FISICA
Italian Physical Society

JCN Open Access ORIGINAL ARTICLE
pISSN 1738-6586 / eISSN 2005-5013 / J Clin Neurol 2021;17(1):96-105 / https://doi.org/10.3988/jcn.2021.17.1.96

Ocular Involvement Occurs Frequently at All Stages of Amyotrophic Lateral Sclerosis: Preliminary Experience in a Large Italian Cohort

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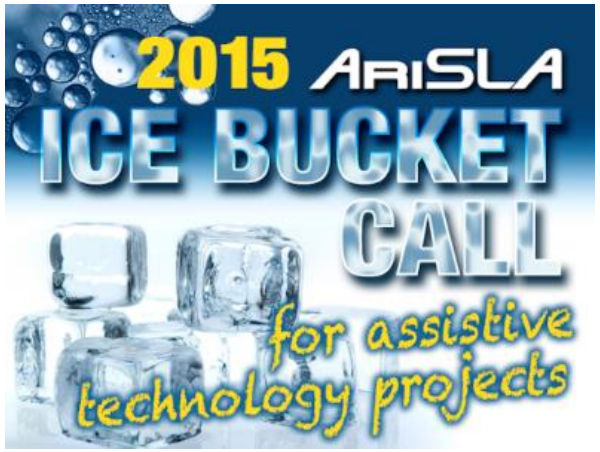
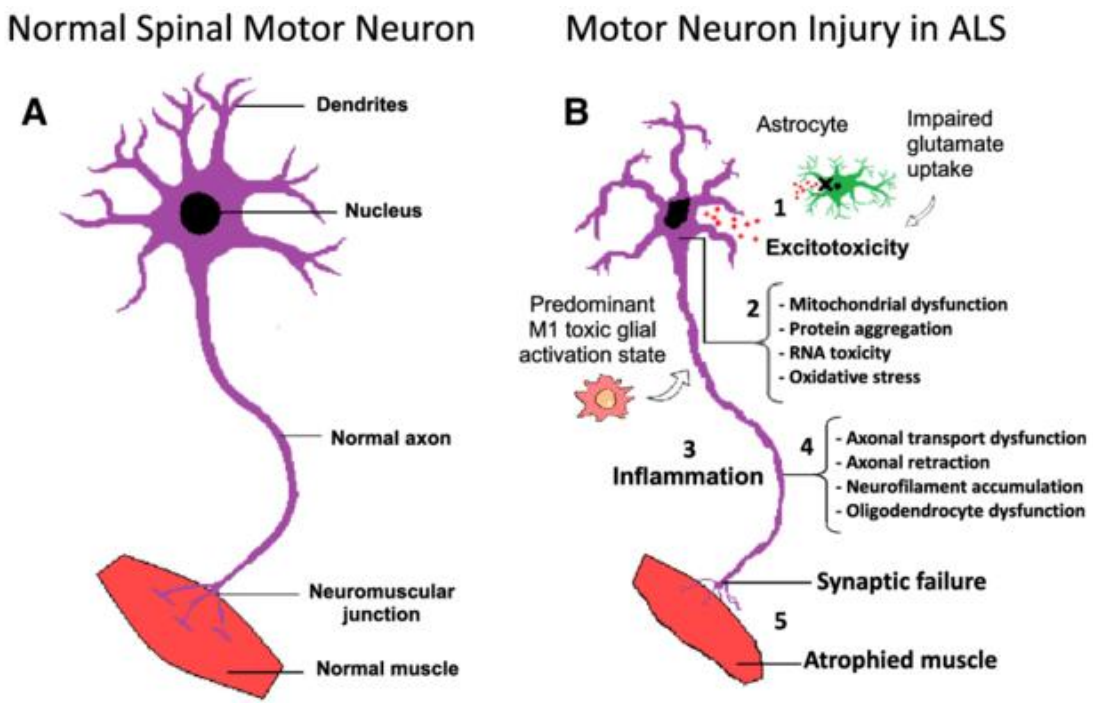


Introduzione

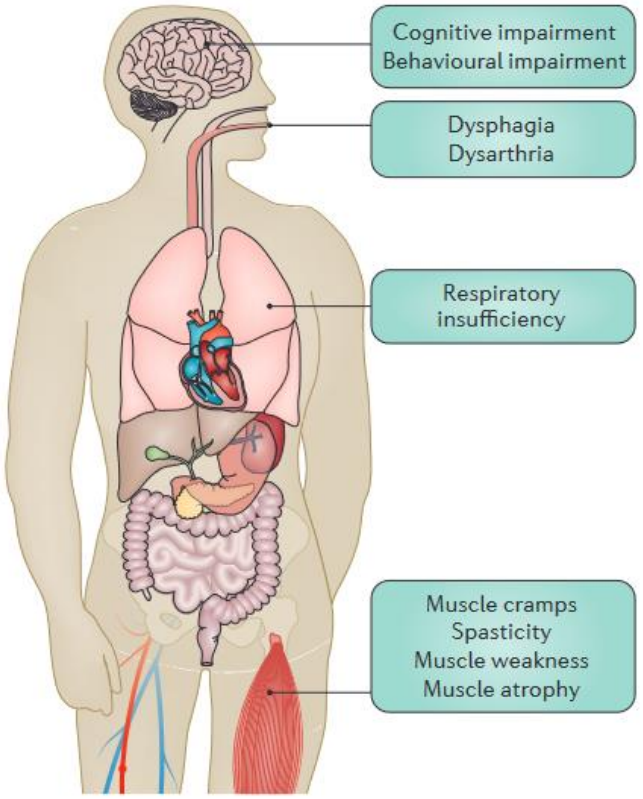


Ciervo, Y. et al, Molecular Neurodegeneration (2017)

"Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease, is characterized by the **degeneration of both upper and lower motor neurons,** which leads to **muscle weakness and eventual paralysis.**"

Hardiman, O. et al., Nat Rev Dis Primers (2017).

Introduzione



Hardiman, O. et al., Nat Rev Dis Primers (2017).

Early Stages of ALS

- Muscle weakness
- Muscle twitching (fasciculation)
- Muscle cramping
- Fatigue
- Poor balance
- Slurred speech

Middle Stages of ALS

- More severe muscle weakness
- Paralysis in some muscles
- Difficulty in swallowing
- Difficulty in eating/chewing
- Breathing issues
- Bouts of uncontrollable laughter or crying (pseudobulbar affect)

Late Stages of ALS

- Paralysis in most muscles
- Extremely limited mobility
- Inability to speak
- Inability to breath without assistance
- Inability to eat without assistance
- Inability to drink without assistance

www.mda.org

Introduzione

Brain Sci. 2022 Apr 11;12(4):489. doi: 10.3390/brainsci12040489.

Eye Movement Abnormalities in Amyotrophic Lateral Sclerosis

Xintong Guo [1 2], Xiaoxuan Liu [1 2], Shan Ye [1 2], Xiangyi Liu [1 2], Xu Yang [3], Dongsheng Fan [1 2 4]

Affiliations + expand

PMID: 35448020 PMCID: PMC9026966 DOI: 10.3390/brainsci12040489

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Abnormal Oculomotor Functions in Amyotrophic Lateral Sclerosis

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Oculomotor Function in Amyotrophic Lateral Sclerosis: Evidence for Frontal Impairment

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R. J. M. Lane, MD, FRCP, L. Henderson, DSc, and C. Kennard, PhD, FRCP, FRCOphth

J Neurol (2010) 257:1134–1140
DOI 10.1007/s00415-010-5478-7

ORIGINAL COMMUNICATION

Slow saccades in bulbar-onset motor neurone disease

Colette Donaghy · Ralph Pinnock · Sharon Abrahams ·
Chris Cardwell · Orla Hardiman · Victor Patterson ·
R. Canice McGivern · J. Mark Gibson

Introduzione

RESEARCH ARTICLE

Eye Movement Deficits Are Consistent with a Staging Model of pTDP-43 Pathology in Amyotrophic Lateral Sclerosis

Martin Gorges[1], Hans-Peter Müller[1], Dorothée Lulé[1], Kelly Del Tredici[2], Johannes Brettschneider[3], Jürgen Keller[1], Katharina Pfandl[1], Albert C. Ludolph[1], Jan Kassubek[1], Elmar H. Pinkhardt[1]*

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Eye-tracking in amyotrophic lateral sclerosis: A longitudinal study of saccadic and cognitive tasks

Malcolm Proudfoot, Ricarda A.L. Menke, Rakesh Sharma, Claire M. Berna, Stephen L. Hicks, Christopher Kennard, Kevin Talbot, and Martin R. Turner
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RESEARCH ARTICLE

Association of Clinically Evident Eye Movement Abnormalities With Motor and Cognitive Features in Patients With Motor Neuron Disorders

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Neurology® 2021;97:e1835-e1846. doi:10.1212/WNL.0000000000012774

Introduzione

Anomalie nelle saccadi, inseguimenti e fissazione oculare

Oftalmoplegia (rara) in pazienti in ventilazione invasiva.

Donaghy et al., Journal of neurology, neurosurgery, and psychiatry, 2011

Obiettivi

- Raccolta dati optometrici di pazienti affetti da SLA in diversi stadi della patologia

- Trovare eventuali correlazioni fra dati optometrici e dati clinici:

  (i) valutazione dello stato funzionale

  (ii) funzione cognitiva

  (iii) stadio della malattia

Pazienti e metodi | Dati più significativi

DATI CLINICI

- **STATO FUNZIONALE:** Amyotrophic Lateral Sclerosis Functional Rating Scale–revised (Alsfrs-r)
- **COGNITIVO:** Edinburgh Cognitive and Behavioural ALS Screen (ECAS)
- **STADIO DI MALATTIA:** Milano-Torino staging (MiToS)
- Utilizzo di eye-tracking communication device (**ETCD**) (> 4ore/giorno).

DATI OPTOMETRICI

- Questionario sintomi oculari
- Motilità oculare (broad H test, saccades and pursuits test, near point of convergence);
- Errore refrattivo e Best Corrected Visual acuity (BCVA);
- Valutazione presenza foria/tropia;

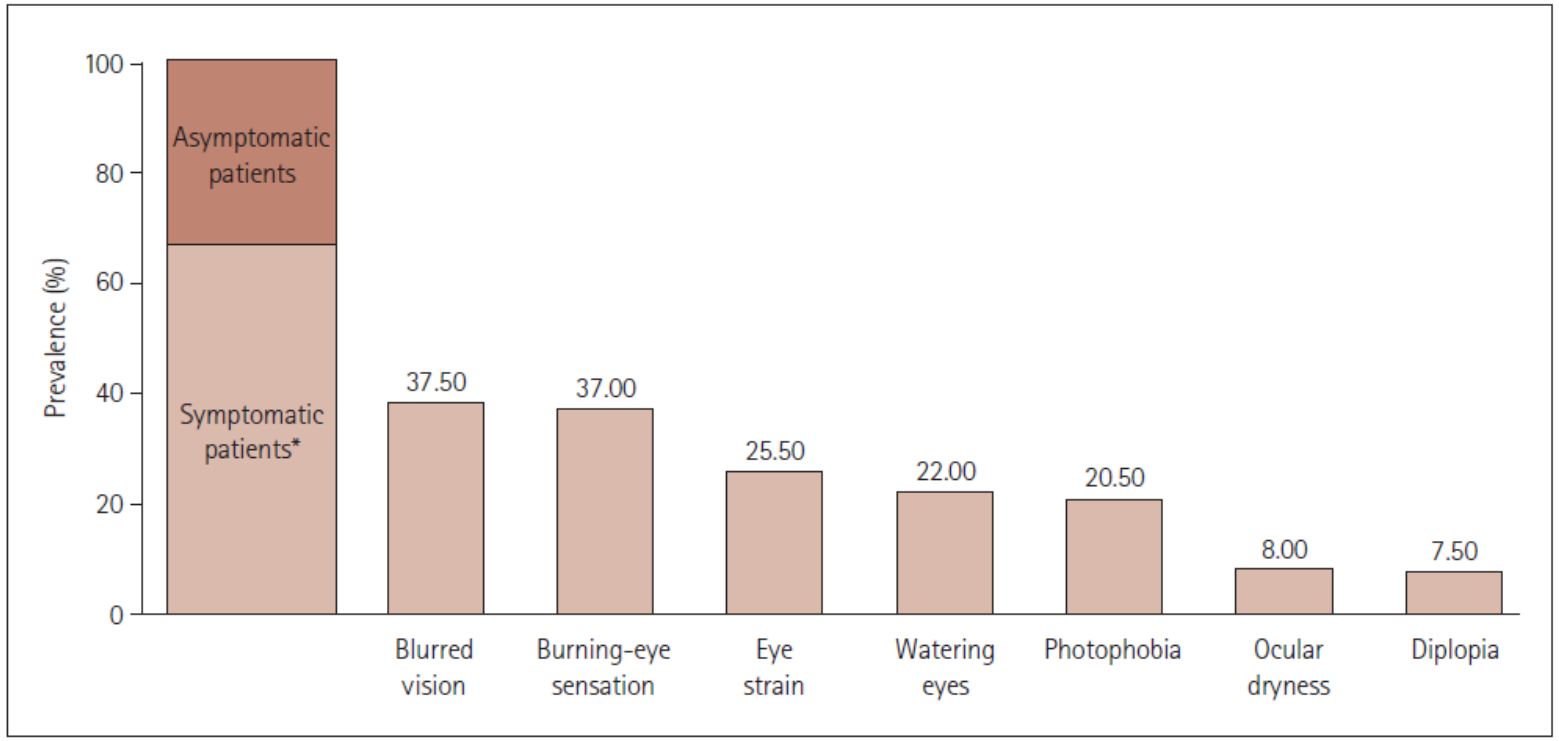
Pazienti e metodi

Studio trasversale
Coorte di 200 pazienti

Table 1. Description of the study cohort

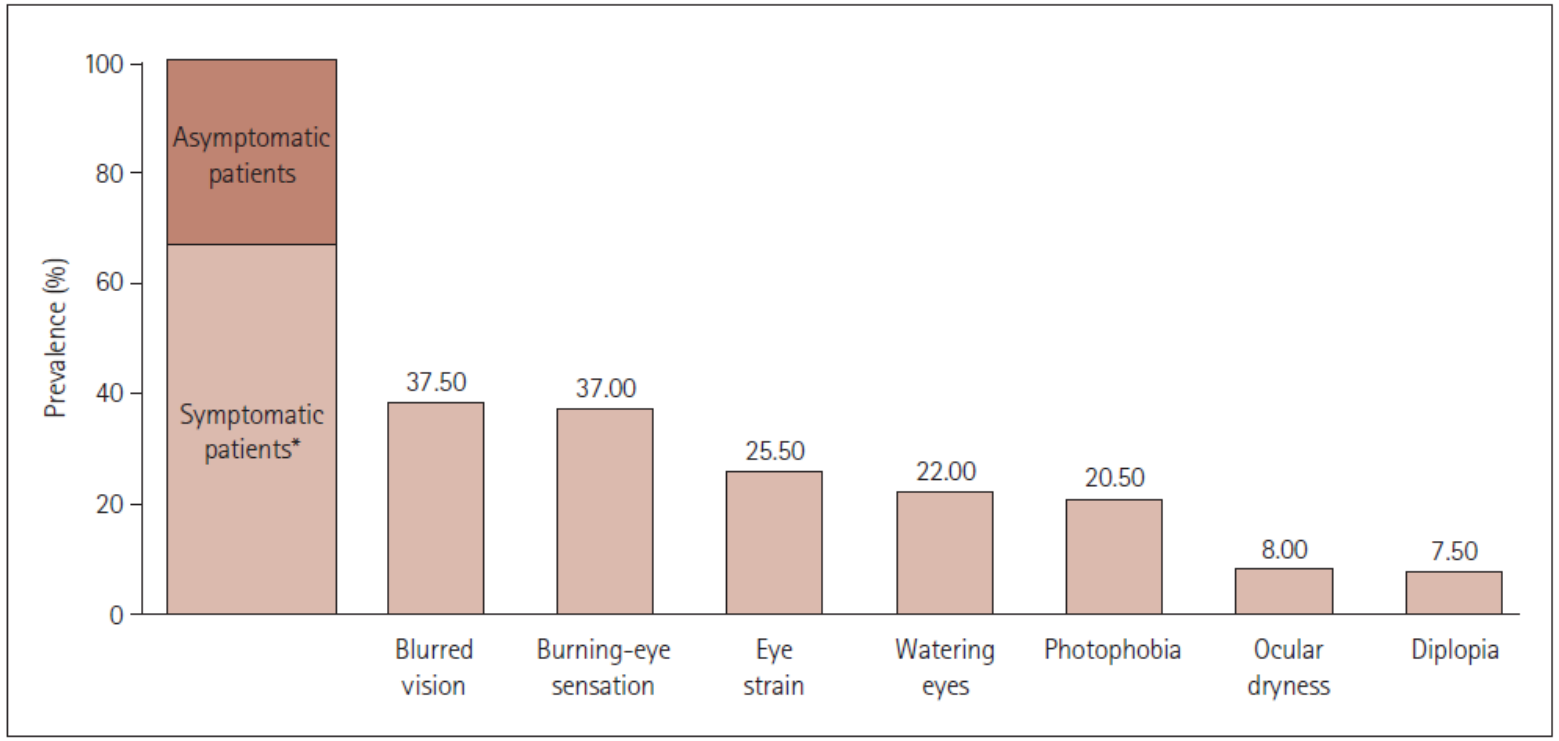
Demographic and clinical characteristics	Values
Age at evaluation, years	63.99 [55.26–70.71]
Disease duration, months	42.90 [21.93–82.73]
Diagnostic delay, months	12.17 [7.07–21.37]
Disease progression rate, ALSFRS-r score unit/months	0.50 [0.26–0.89]
Sex, male	118 (59)
C9ORF72 expansion	5 (3)
Site of onset, bulbar	38 (19)
EEC, definite	34 (17)
NIV at evaluation	92 (46)
IV at evaluation	9 (5)
PEG at evaluation	31 (16)
Ocular device used	
ETCD user	23 (12)
Functional features	
MiToS	
0	50 (34)
1	34 (23)
2	32 (21)
3	15 (10)
4	18 (12)
Missing	51
ALSFRS-r	
Total score	29 [18–36]
Bulbar-subscale score	10 [6–12]
Spinal-subscale score	11 [4–15]
Respiratory-subscale score	10 [3–12]
Cognitive assessment	
ECAS total score	105.00 [92.00–115.00]

Risultati | Frequenza dei sintomi oculari



Distribution of ocular symptoms. *Symptomatic patients include both mildly and severely symptomatic groups.

Risultati | Dati optometrici e utilizzo ETCD



Distribution of ocular symptoms. *Symptomatic patients include both mildly and severely symptomatic groups.

Optometric findings	Number of ETCD user, *n* (%)	*p*	
		Univariate analysis	Multivariable analysis*
Symptoms		<0.0001	0.0006
Asymptomatic	3 (5)		
Mildly symptomatic	1 (2)		
Severely symptomatic	19 (26)		

Risultati

Sintomi oculari, stato funzionale e stadio di malattia

Functional features	Scores by symptoms			Univariate analysis	Multivariable analysis†
	Asymptomatic patients	Mildly symptomatic patients	Severely symptomatic patients	*p*	*p*
ALSFRS-r bulbar-subscale	11 [7–12]	10 [8–11]	8 [3–10]	0.0003	0.0016
ALSFRS-r spinal-subscale	12 [8–17]	12 [8–16]	7 [0–12]	0.0001	0.0004
ALSFRS-r respiratory-subscale	11 [5–12]	11 [3–12]	6 [2–11]	0.0007	0.0006
ALSFRS-r total	33 [24–38]	31 [22–37]	19 [9–31]	<0.0001	<0.0001
MiToS>1*	16 (33%)	12 (27%)	37 (66%)	0.0054	0.0008
	No blurred vision	**Blurred vision**		***p***	***p***
ALSFRS-r bulbar-subscale	10 [7–12]	9 [3–11]		0.0124	0.0143
ALSFRS-r total	31 [22–36]	26 [12–36]		0.0351	0.0075
	No eye strain	Eye strain		***p***	***p***
ALSFRS-r bulbar-subscale	10 [7–12]	8 [2–10]		0.0002	0.0002
ALSFRS-r spinal-subscale	12 [7–16]	8 [0–11]		<0.0001	0.0003
ALSFRS-r respiratory-subscale	11 [5–12]	5 [2–10]		<0.0001	0.0002
ALSFRS-r total score	31 [23–38]	18 [9–27]		<0.0001	<0.0001
MiToS>1*	36 (33%)	29 (67%)		0.0002	0.0002
	No burning-eye sensation	**Burning-eye sensation**		***p***	***p***
ALSFRS-r bulbar-subscale	11 [8–12]	8 [2–10]		<0.0001	0.0002
ALSFRS-r spinal-subscale	12 [9–17]	6 [0–12]		<0.0001	<0.0001
ALSFRS-r respiratory-subscale	11 [5–12]	6 [2–11]		0.0012	0.0027
ALSFRS-r total	32 [24–38]	19 [9–31]		<0.0001	<0.0001
MiToS>1*	29 (31%)	36 (63%)		0.0002	<0.0001
	No watering eyes	**Watering eyes**		***p***	***p***
ALSFRS-r spinal-subscale	12 [8–16]	9 [0–15]		0.0038	0.0125
ALSFRS-r respiratory-subscale	11 [3–16]	6 [1–11]		0.0021	0.0045
ALSFRS-r total	31 [22–38]	22 [8–32]		0.0015	0.0036
MiToS>1*	35 (33%)	21 (64%)		0.0020	0.0032
	No photophobia	**Photophobia**		***p***	***p***
ALSFRS-r bulbar-subscale	10 [7–12]	6 [2–9]		<0.0001	0.0003
ALSFRS-r spinal-subscale	12 [7–15]	4 [0–12]		0.0026	0.0405
ALSFRS-r respiratory-subscale	10 [4–12]	4 [1–10]		0.0043	0.0037
ALSFRS-r total	30 [22–37]	17 [4–29]		0.0001	0.0008
MiToS>1*	45 (37%)	20 (69%)		0.0022	0.0056

Data are *n* (%) or median [interquartile range] values.
*Comparison between patients who lost up to one function and patients who lost multiple functions, †*p* value adjusted for sex, disease progression rate, disease duration, and diagnostic delay.
ALSFRS-r: Amyotrophic Lateral Sclerosis Functional Rating Scale–revised, MiToS: Milano-Torino staging.

Risultati | Motilità oculare e stato funzionale

Functional features	Scores by optometric findings		Univariate analysis	Multivariable analysis*
	Abnormal saccade head movements	**Normal saccade head movements**	***p***	***p***
ALSFRS-r bulbar-subscale	9 [5–11]	10 [8–12]	0.0026	ns
	Abnormal pursuit head movements	**Normal pursuit head movements**	***p***	***p***
ALSFRS-r bulbar-subscale	9 [6–11]	10 [8–12]	0.0256	ns
	Abnormal eye movements (Broad-H test)	**Normal eye movements (Broad-H test)**	***p***	***p***
ALSFRS-r bulbar-subscale	7 [2–11]	10 [7–12]	0.0292	ns
	Abnormal NPC	**Normal NPC**	***p***	***p***
ALSFRS-r bulbar-subscale	8 [3–10]	10 [7–12]	0.0003	0.0040
ALSFRS-r total	25 [8–33]	30 [21–37]	0.0123	0.0389

Data are median [interquartile range] values.
*p value adjusted for sex, disease progression rate, disease duration, and diagnostic delay.
ALSFRS-r: Amyotrophic Lateral Sclerosis Functional Rating Scale–revised, NPC: near point of convergence, ns: not significant.

Risultati | Motilità oculare e cognitivo

Cognitive assessment	Scores by optometric findings		Univariate analysis	Multivariable analysis*
	Abnormal saccade accuracy	**Normal saccade accuracy**	***p***	***p***
ECAS total	95.0 [84.0–108.0]	111.0 [103.0–117.0]	<0.0001	0.0010
	Abnormal saccade head movements	**Normal saccade head movements**	***p***	***p***
ECAS total	96.0 [85.0–105.0]	111.0 [102.0–116.0]	0.0006	0.0105
	Abnormal pursuit accuracy	**Normal pursuit accuracy**	***p***	***p***
ECAS total	98.0 [85.0–111.0]	111.0 [103.5–116.5]	0.0027	0.0290
	Abnormal pursuit head movements	**Normal pursuit head movements**	***p***	***p***
ECAS total	96.0 [84.0–108.0]	111.0 [102.0–116.0]	0.0019	0.0202
	Abnormal eye movements (Broad-H test)	**Normal eye movements (Broad-H test)**	***p***	***p***
ECAS total	84.0 [69.0–99.0]	108.0 [96.0–115.0]	0.0246	0.0210

Data are median [interquartile range] values.
*p value adjusted for sex, disease progression rate, disease duration, and diagnostic delay.
ECAS: Edinburgh Cognitive and Behavioural ALS Screen.

Conclusioni

- Dal punto di vista clinico emerge la necessità di una **presa in carico «visiva»**, considerata la diffusa sintomatologia oculare, con una particolare attenzione ai pazienti che utilizzano ETCD.
- **Anomalie nella motilità oculare** sono significativamente associati alla presenza di **deficit cognitivi** e maggiormente presenti in pazienti con **compromissione bulbare**.

Quesiti in sospeso:

- Studio longitudinale
- Messa a punto di un questionario strutturato sui sintomi

Ringraziamenti

Andrea Lizio
Lucia Catherine Greco
Stefania Bona
Giordana Donvito
Silvia Tavazzi
Elena Carraro
Nicola Ticozzi
Barbara Poletti
Valeria Ada Sansone
Christian Lunetta

CENTRO CLINICO NEMO

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Grazie per l'attenzione