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Short Communication

Sleep, Sleep Structure and Sleep Disorders in a Cohort of Patients Affected by ALS

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Abstract

Amyotrophic Lateral Sclerosis is a neurodegenerative disease, mostly due to progressive loss of motor neurons, with poor prognosis. Although motor involvement is predominant, other systems may be altered, and, among these, also sleep. The aim of this study is to evaluate sleep in a cohort of patients affected by ALS. We consecutively enrolled 48 patients, whom underwent to clinical and instrumental evaluation, including a full night video-PSG. They were compared to 15 control subjects. Respect to controls, patients had fragmented sleep, with poor sleep efficiency, higher amount of WASO and N1 sleep stage, and lower percentage of N2 and REM sleep stages, despite they perceived a sleep of good quality. Moreover, 33% of patients underwent video-PSG was diagnosed with OSAS, and 14, 28% with nocturnal respiratory insufficiency. Start NIV early is known to raise QOL, prolong life expectancy, and improve compliance to subsequent 24h NIV and tracheal ventilation. Furthermore, sleep of bad quality is a cardiovascular risk factor. In conclusion, in patients with ALS, instrumental assessment of sleep in early stages of the disease should be mandatory.

ABBREVIATIONS

AASM: American Academy of Sleep Medicine; AHI: Apnea-Hypopnea Index; ALS: Amyotrophic Lateral Sclerosis; ALS-FRS: Amyotrophic Lateral Sclerosis-Functional Rating Scale; ALSSS: Amyotrophic Lateral Sclerosis Severity Scale; BQ: Berlin Questionnaire; CBT: Cognitive-Behavior Therapy; ESS: Epworth Sleepiness Scale; FVC: Forced Vital Capacity; FTD: Fronto-Temporal Dementia; IRLSSS: International Restless Legs Syndrome Severity Scale; NIV: Not-Invasive Ventilation; ODI: Oxygen Desaturation Index; OSAS: Obstructive Sleep Apnea Syndrome; PLMS: Periodic Limb Movement during Sleep; PSG: Polysomnography; PSQI: Pittsburgh Sleep Questionnaire Index; QoL: Quality of Life; RBDSQ: REM sleep Behavior Disorder Screening Questionnaire; RLS: Restless Legs Syndrome; SE: Sleep Efficiency; SL: Sleep Latency; TST: Total Sleep Time; WASO: Wakefulness After Sleep Onset

INTRODUCTION

Amyotrophic Lateral Sclerosis (ALS), also known as Lou Gehrig's Disease or Charcot's Disease, is an adult-onset progressive and fatal neurodegenerative disease, characterized by progressive loss of cortical, bulbar, and spinal motor neurons with consequent painless paralysis of striatal skeletal muscle, dysphagia, dysarthria and respiratory impairment, up to respiratory failure, that is the most common cause of death in ALS, that usually occurs within 3 years after disease onset. So far there is no effective treatment for ALS, and prognosis is always lethal [1-4].

Although motor involvement in ALS is predominant, other systems may be affected [5], and patients often complaint of disturbed sleep. Fragmented sleep and sleep disorders may be early manifestations of ALS [6-8]. Particular attention has been given mostly to sleep disordered breathing, chronic nocturnal respiratory insufficiency and hypoventilation [9] that commonly anticipates the awake respiratory failure, because of the physiologic vulnerability of respiration during sleep; moreover the role of NIV in increasing survival in ALS patients is well known [6-9].

In fact, almost all patients develop respiratory failure during the course of their illness(10), and Miller and colleagues in a evidence-based review published in 2009 [10] indicated that nocturnal desaturations <90% for 1 cumulative minute is a sensitive indicator of early respiratory insufficiency, and that nocturnal oximetry correlates with survival (mean O2 saturation <93 mmHg is associated with mean survival of 7

months vs 18 months when mean O2 saturation is >93 mmHg), and they recommended to consider nocturnal oximetry to detect hypoventilation. They indicated early intervention with NIV as probably effective in prolonging life expectancy, in slowing the decline of FVC and useful in raise quality of life. Moreover, consideration of starting NIV at the earliest sign of nocturnal hypoventilation or respiratory insufficiency may improve compliance for subsequent diurnal NIV and tracheal ventilation [10].

The aim of this study was to investigate sleep characteristics and any sleep disorder in a cohort of Sardinian patients affected by ALS. Sardinian patients affected by ALS present in a very high percentage, a genetic predisposition to develop the disease that is higher than in other Caucasian population, with exception of Scandinavian. Infact, it has been showed by Borghero et colleagues that Sardinian patients affected by ALS carry a mutation of a ALS-related gene in more than 40% of cases; moreover >10% of Sardinian patients without a known mutation showed a familial positive history of ALS or FTD, indicating the possibility of involvement of other new genes [11,12].

MATERIALS AND METHODS

We consecutively enrolled 48 patients affected by ALS (15females, 33 males; mean age 62, 44 years, 11,21 SD), referred to Sleep Disorders Center – University of Cagliari. Diagnosis of definite or probable ALS was made according to the EL-Escorial WFN revised criteria(13,14) at the ALS outpatient service – AOU of Cagliari.

Exclusion criteria were: age < 18 years, pregnancy, patients who denied consent, and severity of the disease as to prevent 1 night in the sleep lab room. All selected patients were eligible to be included in the study. The study was approved by ethical committee (approval no. 2013/3205), and all patients provided the informed consent. Each subject underwent to clinical and instrumental examination.

Clinical evaluation

All patients underwent a thorough history, and a complete general and neurological examination. Functional impairment was evaluated with ALS-Functional Rating Scale (ALS-FRS) [15,16] and with ALSSS (ALS severity scale) [17]. Moreover they answered to specific sleep questionnaire, namely Epworth Sleepiness Scale (ESS) [18,19], Berlin Questionnaire (BQ) [20,21] for risk of OSAS [22], Pittsburgh Sleep Quality Index (PSQI) [23,24], REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ) [25], and in cases of Restless Legs Syndrome (RLS) [26-29], they answered to International Restless Legs Syndrome Study Group Scale (IRLSSS) questionnaire [30]. Control group consisted of 15 healthy age-matched subjects (7 women and 8 men, mean age 60.4 yrs, 10.35 S.D.), without any complaints of sleep, medical and neurological disturbances or disorders.

Instrumental evaluation

All subjects underwent a full-night video-polysomnography (video-PSG), carried out in a standard sound-attenuated sleep laboratory, according to AASM scoring manual [31]. For recording parameters and details see Puligheddu et al. [32], Sleep stages were blindly scored following standard criteria [31,33] by two clinical neurophysiologists expert in sleep medicine (GM and PC).

Statistical analysis

For statistical analysis Prism 7 for Mac OS X - GraphPad softawere was used. For comparison of data between patients and controls Student's t test was used for data with Gaussian distribution, Mann-Withney test was used for data without normal distribution. Gaussian distribution of data was evaluated by means of D'Agostino & Pearson Normality test. Correlation between sleep scoring parameters and ALS-FRS score was evaluated by calculating the Pearson correlation coefficient (Pearson's r). Differences were considered significant when p value were <0.05.

RESULTS AND DISCUSSION

Clinical evaluation

Age and sex of the two groups were not statistically different. Clinical parameters of patients are specified in Table 1. Patients affected by ALS had an average ALS-FRS score of 33.61 ± 8.42, and an average ALSSS score of 30.48 ± 5.43. Mean age at disease onset was 59 years ± 12.40, and mean duration of the disease at time of evaluation was 3.78 years ± 5.34. Five patients had a bulbar type at disease onset; six patients had generalized type at disease onset, while the others had spinal form of ALS at disease onset. Average ESS was below threshold for excessive daytime sleepiness (5.39 ± 3.68), average PSQI was low(8.61 ± 4.43) indicating that patients perceived a good quality sleep, average RBDSQ was 3.98 ± 2.80.Two patients were suspected to have RBD, based on RBDSQ. Two patients, both females, received diagnosis of RLS. None of the patients had cognitive impairment as showed by a comprehensive test battery.

Table 1: Clinical parameters of ALS patients (n=48; 15 females, 33 males).

Parameters	Mean	S.D.
Age (years)	62.44	11.21
Age at disease onset (years)	59	12.40
Disease duration (years)	3.78	5.34
ALS-FRS	30.48	5.43
ALSSS	41.40	11.34
ESS	5.39	3.68
PSQI	8.61	4.43
RBDSQ	3.98	2.80

As demonstrated by sleep questionnaires, patients perceived a good quality sleep.
Based on RBSQ two patients were suspected to have RBD; two patients, both females, received clinical diagnosis of RLS.
Abbreviations: ALS-FRS: Amyotrophic Lateral Sclerosis – Functional Rating Scale; ALSSS: Amyotrophic Lateral Sclerosis Severity Scale; ESS: Epworth Sleepiness Scale; PSQI: Pittsburgh Sleep Questionnaire Index; RBDSQ: REM Sleep Behavior Disorder Screening Questionnaire

Table 2: Sleep scoring parameters of ALS patients and control subjects.

	Patients		Controls		P Value
	Mean	S.D.	Mean	S.D.	
TST (min)	342.71	96.16	423.47	39.64	0.0025
SL (min)	334.23	28.33	9.67	6.68	0.0012*
SE%	69.13	15.78	87.88	8.54	<0.0001
N1%	21.24	9.45	6.81	5.84	<0.0001*
N2%	41.40	11.34	54.16	6.14	0.0001
N3%	22.06	12.33	17.29	7.18	NS
REM%	15.72	7.22	21.73	4.83	0.0039
WASO%	24.84	14.47	10.39	8.09	0.0005

ALS patients showed fragmented sleep with poor sleep efficiency, increased sleep latency, reduction of TST, increased WASO and N1 stage of NREM sleep, and reduced percentage of N2 stage of NREM sleep and of REM sleep stage. There were no statistical differences in percentage of N3 sleep stage between patients and controls.

Abbreviations: TST: Total Sleep Time; SL: Sleep Latency; SE: Sleep Efficiency; N1%: Percentage of Stage N1 of NREM sleep; N2%: Percentage of Stage N2 of NREM sleep; N3%: Percentage of Stage N3 of NREM Sleep; REM%: Percentage of REM Sleep Stage; WASO%: Percentage of Wakefulness after Sleep Onset. *Mann-Whitney Test

Table 3: Correlation between sleep scoring parameters and severity of disease based on ALS-FRS score, by means of Pearson's correlation].

	ALS-FRS vs TST	ALS-FRS vs SL	ALS-FRS vs SE%	ALS-FRS vs WASO%	ALS-FRS vs N1%	ALS-FRS vs N2%	ALS-FRS vs N3%	ALS-FRS vs REM%
Pearson r	0.033	-0.075	0.16	-0.11	0.06	0.36	0.38	0.06
95% CI	-0.27 to 0.33	-0.37 to 0.24	-0.16 to 0.45	-0.40 to 0,2	-0.24 to 0.36	0.07 to 0.6	-0.61 to 0.09	-0.25 to 0.35
P value (two-tailed)	NS	NS	NS	NS	NS	0.0177	0.0118	NS

Assessment of correlation between sleep scoring parameters and ALS-FRS score showed a significant correlation between both N2% and N3% ALS-FRS score, indicating that percentage of both N2 and N3 sleep stages were less in ALS patients with the most severe illness.

Abbreviations: ALS-FRS: Amyotrophic Lateral Sclerosis- Functional Rating Scale; TST: Total Sleep Time; SL: Sleep Latency; SE: Sleep Efficiency; WASO: Wakefulness After Sleep Onset; N%: Percentage of TST of N1 Stage of NREM Sleep; N2%: Percentage of TST of N2 stage of NREM Sleep; N3%: Percentage of TST of N3 Stage of NREM Sleep; REM%: Percentage of TST of REM Sleep Stage; CI: Confidence Interval; NS: Not Statistically Significant

Instrumental evaluation

Sleep parameters for two groups are reported in Table 2. Two patients did not perform video-PSG, despite signed consent, and four patients had a TST<4h, time necessary for reliable cardio respiratory assessment during sleep.

Respect to control subjects, ALS patients showed fragmented sleep with poor sleep efficiency (p<0.0001), increased sleep latency (p=0.0012), reduction of TST (p=0.0025), increased WASO (p=0.0005) and N1 stage of NREM sleep (p<0.0001), and reduced percentage of N2 stage of NREM sleep (p<0.0001) and of REM sleep stage (p=0.0039). One patient had no REM sleep, nine patients had a percentage of REM sleep < 10% of TST, and among these in three it was lower than 4% of TST. There were no statistical differences in percentage of N3 sleep stage between patients and controls. Figure 1 shows three hypnograms with curve of SpO2 of three patients.

Assessment of correlation between sleep scoring parameters, namely TST, SL, SE, WASO%, N1%, N2%, N3%, and REM%, and ALS-FRS score showed a statistically significant positive association between ALS-FRS and percentage of N2 and N3, as the r coefficient was > 0.3 for both N2% and for N3% (respectively p=0.177 and p=0.011). These results indicate that the higher the ALS-FRS score, the higher the percentage of N2 and N3 stages, thus the percentage of both N2 and N3 sleep stages were less in ALS patients with the most severe illness (Table 3 and Figure 2).

Moreover, patients had higher AHI (apnea-hypopnea index) and ODI (Oxygen desaturation index) and they spent more sleep time with SpO2 below 90% respect to controls, which were previously selected with AHI and ODI <5 and mean SpO2 higher than 90%.Five patients were diagnosed with moderate to severe OSAS (11,9%), and 9 with mild OSAS (21,4%). Mean AHI of OSAS patients was (17.34 ± 12.27); mean AHI of all patients was 7.83 ± 10.6).REM-related events were predominant. Average value of mean SpO2 during TST was 94.32% ± 3.17%), mean minimum SpO2 during TST was 84.92% ± 7.29%), and six patients (14, 28%) were diagnosed with nocturnal respiratory failure.

Based on the clinical and polysomnographic diagnosis, the appropriate treatment and follow-up were set. In particular, patients diagnosed with OSAS and/or nocturnal hypoventilation/ respiratory insufficiency were immediately evaluated by pneumologist in order to start the nocturnal NIV, with the aim to raise QOL, prolong life expectancy, and increase compliance to an eventual future diurnal NIV.

How concern PLMS, although they have been previously reported to be increased in ALS patients [34-36], in a previous work [32], in which we performed a much more detailed analysis

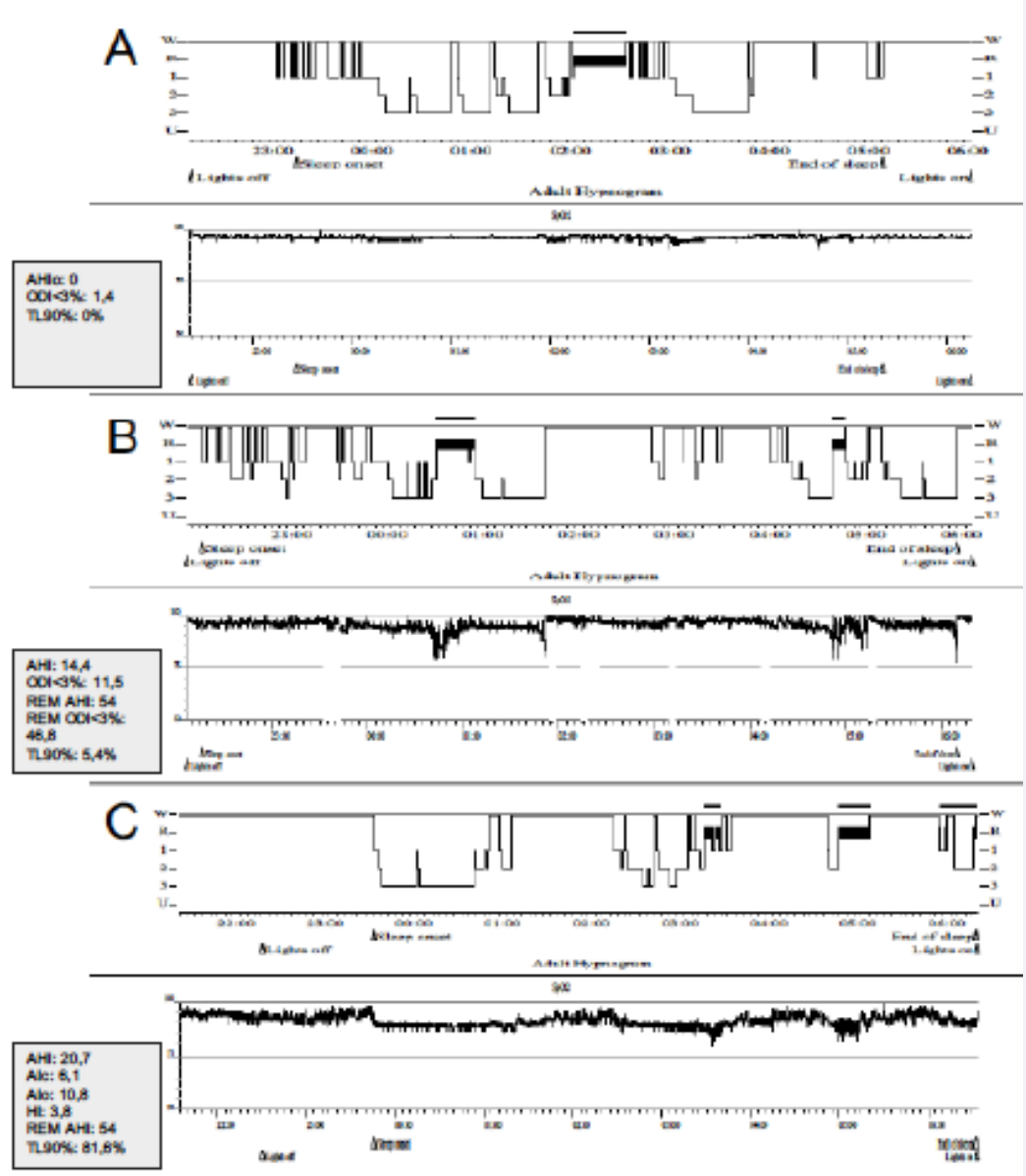

Figure 1 Three examples of hypnograms (up) and profile of SpO2 (down) of three ALS patients, all characterized by a structure of sleep deeply altered.

A. Hypnogram shows long sleep latency, many awakenings, only one complete sleep cycle, and early morning awake. Curve of SpO2 shows some desaturation during REM sleep.

B. Hypnogram shows a deeply altered sleep structure with many awakenings in the first part of the night, a prolonged awakening in the central part, and two complete sleep cycles. Curve of SpO2 shows deep phasic desaturations during REM sleep, not always with return to baseline value.

C. Hypnogram shows prolonged sleep latency, three prolonged awakening in the middle and in the latter parts of the night, and two complete sleep cycles. Curve of SpO2 shows during sleep tonic desaturation, with superimposed phasic desaturations during REM sleep phases.

Abbreviations: AHI: Apnea-Hypopnea Index; AIc: Central Apnea Index; AIo: Obstructive Apnea Index; HI: Hypopnea Index; ODI: Oxygen Desaturation Index; TL90%: Percent Time of TST (total sleep time) spent with SpO2<90%]

of motor activity during sleep [37-39], we did not find any differences between a population of ALS patients and control subjects. We concluded that the association between RLS, PLMS and ALS might be due to the most frequent emergence of RLS/PLMS and also of ALS in advanced age [40-42], and the discrepancy in findings might be due to the different methods of detecting PLMS [32].

CONCLUSION

Sleep in patients affected by ALS may be affected by many disorders, such as immobility, nocturnal cramps, excessive salivation with ineffective cough, circadian rhythm alterations, nocturnal hypoxia and hypoventilation [6]. Moreover also sleep disorders may affects sleep in these patients, namely RLS [40],

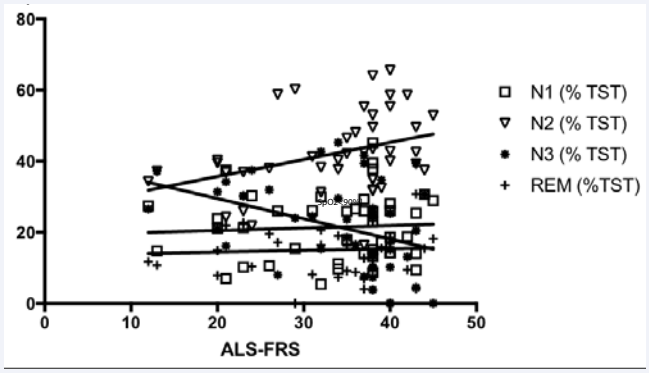

Figure 2 Correlation between sleep scoring parameters and severity of disease based on ALS-FRS score, by means of Pearson's correlation, showed a significant correlation between both N2% and N3% ALS-FRS score, indicating that percentage of both N2 and N3 sleep stages were less in ALS patients with the most severe illness.

PLMS [34-36,41] and RBD [41-44], that, as we discussed in a previous paper [32], may be a casual association due to the most frequent emergence of all these disorders in advanced age.

Results of this study confirm that sleep in patients affected by ALS is altered, with deeply disrupted sleep structure, characterized by lower TST, and SE, and higher SL, increased percentage of N1 sleep stage and of WASO, and reduced percentage of N2 and REM sleep stages. We could hypothesize that reduction up to absence of REM sleep may be a "protective" central mechanism against phasic desaturation and hypoventilation, as also shown by Arnulf [34]. Moreover, we could speculate that impairment of sleep structure, with reduction of SE, and increase of N1 sleep stage and of WASO, observed since the earliest stages of the disease, may be due to several factors, including sleep breathing disorders. On the other hand, the reduction of percentage of N3, that well-correlates with the severity of the illness, make us speculate that in advanced stages of disease neuro degeneration may involve also structures responsible for regulation of sleep.

Despite this marked alteration of sleep structure with poor sleep efficiency, high sleep fragmentation and increased amount of WASO, sleep is not subjectively perceived as altered as it really is by patients. The discrepancy between perceived sleep quality and objective alteration of sleep structure might be attributed to a possible preclinical cognitive disorder. Furthermore the mutual relationship between sleep and cognitive functions in neurodegenerative disorders like Parkinson's disease and Alzheimer Disease is well-recognized [6], instead this interconnection has not been described yet in patients affected by ALS, but it is well-recognized that cognitive impairment in ALS is a negative prognostic factor [45].

Moreover, sleep disorders are associated to daytime impairment, excessive daytime sleepiness, easy fatigue, and in these patients, affected by a neurodegenerative disease characterized by exhaustion of motor system, they may exacerbate day and night symptoms, leading to a further reduction in physical strength, and worsening quality of life.

Moreover, sleep disorders, typically sleep breathing disorders, but also sleep fragmentation, and insomnia, especially when associated with reduction of sleep duration [46], represent an independent risk factor for cardiovascular mortality, mostly when sleep reduction and sleep fragmentation are strongly associated [47], as we have observed in our cohort of subjects affected by ALS. Thus, treating sleep fragmentation by using sleep hygiene, cognitive-behavioral (CBT) protocol for insomnia, and eventually any antidepressants with sedative effects (e.g. trazodone, mirtazapine), that improve rapidly sleep quality [48,49], might be helpful in ameliorate SE, with consequent reduction of fatigue and diurnal sleepiness.

Therefore, sleep is often altered in patients affected by ALS, even in early stage of disease, and it worsens with progression of the illness; thus, evaluation of sleep in patients affected by ALS should be mandatory in diagnostic iter, in order to early identify and adequately treat any sleep disorders, especially sleep breathing disorders and early nocturnal hypoventilation, with the final aim of raise quality of life, and eventually prolong life expectancy.

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REFERENCES

1. Williams DB, Windebank AJ. Motor neuron disease (amyotrophic lateral sclerosis). Mayo Clin Proc. 1991; 66: 54-82.
2. Chiò A, Silani V. Italian ALS Study Group. Amyotrophic lateral sclerosis care in Italy: a nationwide study in neurological centers. J Neurol Sci. 2001; 191: 145-150.
3. Sclerosis L. The Amyotrophic Lateral Sclerosis Functional Rating Scale. Assessment of activities of daily living in patients with amyotrophic lateral sclerosis. The ALS CNTF treatment study (ACTS) phase I-II Study Group. Arch Neurol. 1996; 53: 141-147.
4. Zarei S, Carr K, Reiley L, Diaz K, Guerra O, Altamirano PF, et al. A comprehensive review of amyotrophic lateral sclerosis. Surg Neurol Int. 2015; 6: 171.
5. van der Graaff MM, de Jong JMB V, Baas F, de Visser M. Upper motor neuron and extra-motor neuron involvement in amyotrophic lateral sclerosis: a clinical and brain imaging review. Neuromuscul Disord. 2009; 19: 53-58.
6. Ahmed RM, Newcombe RE, Piper AJ, Lewis SJ, Yee BJ, Kiernan MC, et al. Sleep disorders and respiratory function in amyotrophic lateral sclerosis. Sleep Med Rev. 2016; 26: 33-42.
7. Hetta J, Jansson I. Sleep in patients with amyotrophic lateral sclerosis. J Neurol. 1997; 244: 7-9.
8. Lo Coco D, Mattaliano P, Spataro R, Mattaliano A, La Bella V. Sleep-wake disturbances in patients with amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry. 2011; 82: 839-842.
9. Gaig C, Iranzo A. Sleep-disordered breathing in neurodegenerative diseases. Curr Neurol Neurosci Rep. 2012; 12: 205-217.
10. Miller RG, Jackson CE, Kasarskis EJ, England JD, Forshew D, Johnston W, et al. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2009; 73: 1218-1226.

11. Borghero G, Pugliatti M, Marrosu F, Marrosu MG, Murru MR, Floris G, et al. ATXN2 is a modifier of phenotype in ALS patients of Sardinian ancestry. Neurobiol Aging. 2015; 36: 1-5.

12. Borghero G, Pugliatti M, Marrosu F, Marrosu MG, Murru MR, Floris G, et al. Genetic architecture of ALS in Sardinia. Neurobiol Aging. 2014; 35: 12.

13. Brooks BR, Miller RG, Swash M, Munsat TL, World Federation of Neurology Research Group on Motor Neuron Diseases. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. Amyotroph Lateral Scler Other Motor Neuron Disord. 2000; 1: 293-299.

14. Brooks BR. El Escorial World Federation of Neurology criteria for the diagnosis of amyotrophic lateral sclerosis. Subcommittee on Motor Neuron Diseases/Amyotrophic Lateral Sclerosis of the World Federation of Neurology Research Group on Neuromuscular Diseases and th. J Neurol Sci. 1994; 124: 96-107.

15. [No authors listed] The Amyotrophic Lateral Sclerosis Functional Rating Scale. Assessment of activities of daily living in patients with amyotrophic lateral sclerosis. The ALS CNTF treatment study (ACTS) phase I-II Study Group. Arch Neurol. 1996; 53: 141-147.

16. Cedarbaum JM, Stambler N, Malta E, Fuller C, Hilt D, Thurmond B, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). J Neurol Sci. 1999; 169: 13-21.

17. Hillel AD, Miller RM, Yorkston K, McDonald E, Norris FH, Konikow N. Amyotrophic lateral sclerosis severity scale. Neuroepidemiology. 1989; 8: 142-150.

18. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991; 14: 540-545.

19. Vignatelli L, Plazzi G, Barbato A, Ferini-Strambi L, Manni R, Pompei F, et al. Italian version of the Epworth sleepiness scale: external validity. Neurol Sci. 2003; 23: 295-300.

20. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999; 131: 485-491.

21. Gassino G, Cicolin A, Erovigni F, Carossa S, Preti G. Obstructive sleep apnea, depression, and oral status in elderly occupants of residential homes. Int J Prosthodont. 2005; 18: 316-322.

22. Hedner J, Grote L, Bonsignore M, McNicholas W, Lavie P, Parati G, et al. The European Sleep Apnoea Database (ESADA): report from 22 European sleep laboratories. Eur Respir J. 2011; 38: 635-642.

23. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989; 28: 193-213.

24. Curcio G, Tempesta D, Scarlata S, Marzano C, Moroni F, Rossini PM, et al. Validity of the Italian version of the Pittsburgh Sleep Quality Index (PSQI). Neurol Sci. 2013; 34: 511-519.

25. Stiasny-Kolster K, Mayer G, Schäfer S, Möller JC, Heinzel-Gutenbrunner M, Oertel WH. The REM sleep behavior disorder screening questionnaire--a new diagnostic instrument. Mov Disord. 2007; 22: 2386-2393.

26. American Academy of Sleep Medicine. International classification of sleep disorders. 3rd Edn. Darien, Am Acad Sleep Med. 2014.

27. Allen RP, Picchietti DL, Garcia-Borreguero D, Ondo WG, Walters AS, Winkelman JW, et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria - history, rationale, description, and significance. Sleep Med. 2014; 15: 860-873.

28. Allen RP, Picchietti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. Sleep Med. 2003; 4: 101-119.

29. Trenkwalder C, Allen R, Hogl B, Paulus W, Winkelmann J. Restless legs syndrome associated with major diseases: A systematic review and new concept. Neurology. 2016; 86: 1336-1343.

30. Walters AS, LeBrocq C, Dhar A, Hening W, Rosen R, Allen RP, et al. Validation of the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome. Sleep Med. 2003; 4: 121-32.

31.

32. Puligheddu M, Congiu P, Aricò D, Rundo F, Borghero G, Marrosu F, et al. Isolated rapid eye movement sleep without atonia in amyotrophic lateral sclerosis. Sleep Med. 2016; 26: 16-22.

33. Crofts HS, Wilson S, Muggleton NG, Nutt DJ, Scott EA, Pearce PC. Investigation of the sleep electrocorticogram of the common marmoset (Callithrix jacchus) using radiotelemetry. Clin Neurophysiol. 2001; 112: 2265-2273.

34. Arnulf I, Similowski T, Salachas F, Garma L, Mehiri S, Attali V, et al. Sleep disorders and diaphragmatic function in patients with amyotrophic lateral sclerosis. Am J Respir Crit Care Med. 2000; 161: 849-856.

35. Ferguson KA1, Strong MJ, Ahmad D, George CF. Sleep-disordered breathing in amyotrophic lateral sclerosis. Chest. 1996; 110: 664-669.

36. Moszczynski AJ, Tandon A, Coelho FMS, Zinman L, Murray B. Mortality associated with periodic limb movements during sleep in amyotrophic lateral sclerosis patients. Einstein (Sao Paulo). 2012; 10: 428-32.

37. Ferri R, Rundo F, Zucconi M, Manconi M, Aricò D, Bruni O, et al. Diagnostic accuracy of the standard and alternative periodic leg movement during sleep indices for restless legs syndrome. Sleep Med. 2016; 22: 97-99.

38. Ferri R. The time structure of leg movement activity during sleep: the theory behind the practice. Sleep Med. 2012; 13: 433-441.

39. Ferri R, Rundo F, Zucconi M, Manconi M, Aricò D, Bruni O, et al. Putting the periodicity back into the periodic leg movement index: an alternative data-driven algorithm for the computation of this index during sleep and wakefulness. Sleep Med. 2015; 16: 1229-1235.

40. Limousin N, Blasco H, Corcia P, Arnulf I, Praline J. The high frequency of restless legs syndrome in patients with amyotrophic lateral sclerosis. Amyotroph Lateral Scler. 2011; 12: 303-306.

41. Lo Coco D, Puligheddu M, Mattaliano P, Congiu P, Borghero G3, Fantini ML, et al. REM sleep behavior disorder and periodic leg movements during sleep in ALS. Acta Neurol Scand. 2017; 135: 219-224.

42. Minz M, Autret A, Laffont F, Beillevaire T, Cathala HP, Castaigne P. A study on sleep in amyotrophic lateral sclerosis. Biomedicine. 1979; 30: 40-46.

43. Ebben MR, Shahbazi M, Lange DJ, Krieger AC. REM behavior disorder associated with familial amyotrophic lateral sclerosis. Amyotroph Lateral Scler. 2012; 13: 473-474.

44. Sforza E, Krieger J, Petiau C. REM sleep behavior disorder: clinical and physiopathological findings. Sleep Med Rev. 1997; 1: 57-69.

45. Elamin M, Phukan J, Bede P, Jordan N, Byrne S, Pender N, et al. Executive dysfunction is a negative prognostic indicator in patients with ALS without dementia. Neurology. 2011; 76: 1263-1269.

46. Javaheri S, Redline S. Insomnia and Risk of Cardiovascular Disease. Chest. 2017; 152: 435-444.

47. Rod NH, Kumari M, Lange T, Kivimaki M, Shipley M, Ferrie J. The

joint effect of sleep duration and disturbed sleep on cause-specific mortality: results from the Whitehall II cohort study. PLoS One. 2014; 9: 91965.

48. Wichniak A, Wierzbicka A, Walęcka M, Jernajczyk W. Effects of Antidepressants on Sleep. Curr Psychiatry Rep. 2017; 19: 63.

49. Wichniak A, Wierzbicka A, Walecka M, Jernajczyk W. Effects of Antidepressants on Sleep. Curr Psychiatry Rep. 2017; 19: 63.

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