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***SLEEP DISTURBANCES CAN INFLUENCE
THE OUTCOME OF PATIENTS WITH
MULTIPLE SCLEROSIS***

Perugia, 14 dicembre 2018

Dott.ssa Laura Buratti
Clinica Neurologica Ancona



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sleep disorders and Multiple Sclerosis |

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SLEEP AND MULTIPLE SCLEROSIS

- Sleep disturbances are common in multiple sclerosis
- Alterations in sleep macro- and microstructure have been described in polysomnographic studies in a large percentage of patients
- Obstructive sleep apnea, restless legs syndrome and insomnia (common sleep disorders in the general population) are even more common in patients with MS

Sleep-Disordered Breathing in People with Multiple Sclerosis: Prevalence, Pathophysiological Mechanisms, and Disease Consequences

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Sleep Med Rev. 2015 Aug;22:15-22. doi: 10.1016/j.smrv.2014.10.002. Epub 2014 Oct 12.

Restless legs syndrome in multiple sclerosis.

Sieminski M¹, Losy J², Partinen M³.

⊕ Author information

Abstract

Restless legs syndrome (RLS) is a sleep-related sensory-motor disorder characterized by unpleasant sensations in the lower extremities. According to m... prevalence of RLS in MS patients compared to MS patients without RLS. Presence of RLS MS patients. Iron deficiency and chronic inflammation may be factors contributir between the course and treatment of MS and RLS requires further prospective :

Curr Neurol Neurosci Rep (2016) 16: 50
DOI 10.1007/s11910-016-0649-2



DEMYELINATING DISORDERS (DN BOURDETTE AND M CAMERON, SECTION EDITORS)

Sleep Disorders in Multiple Sclerosis

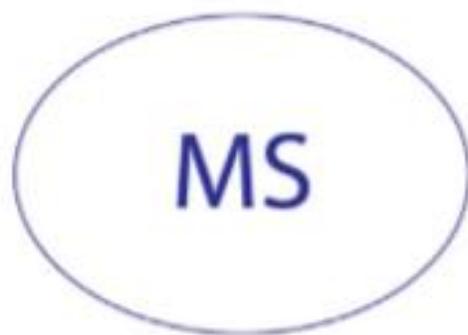
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Sleep-Disordered Breathing in People with Multiple Sclerosis: Prevalence, Pathophysiological Mechanisms, and Disease Consequences

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Inflammation

Demyelinating lesion

Inflammation

Intermittent hypoxia

Consequences

Fatigue and Sleepiness

Neurocognitive impairment

Depression

Falls risk

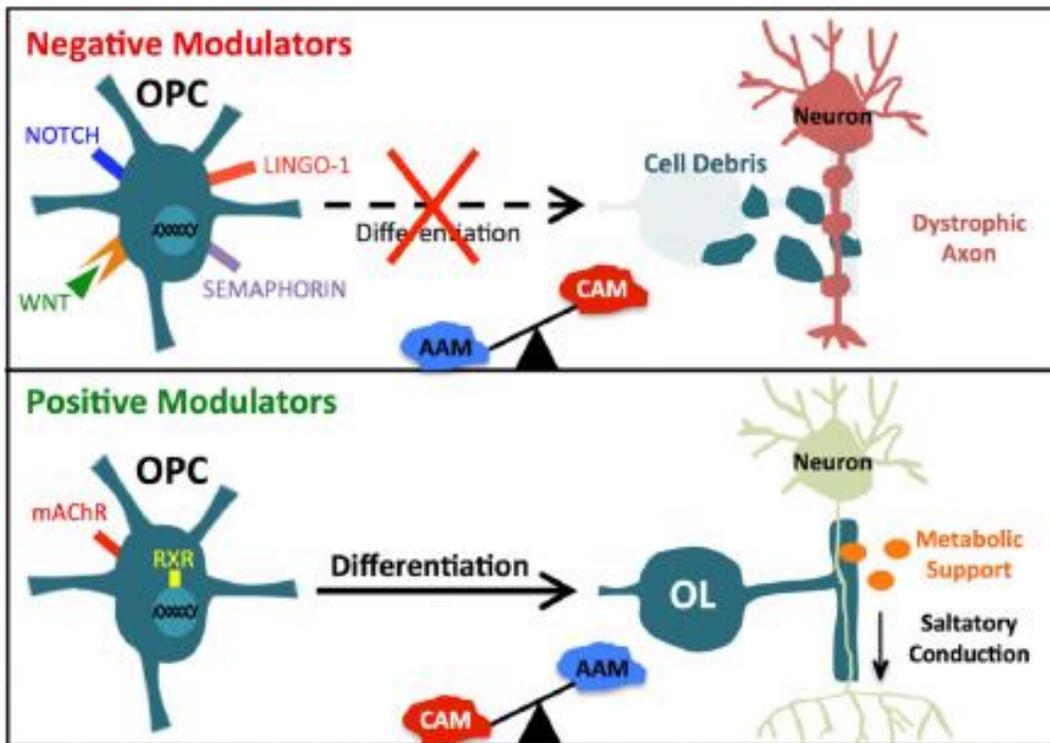


OPCs

Cellular/Molecular

Effects of Sleep and Wake on Oligodendrocytes and Their Precursors

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- Myelin production is a key function of oligodendrocytes
- Oligodendrocyte precursor cells (OPCs) are responsible for the production of new myelin in healthy brain (rapidly recruited to prime the recovery processes in response to injuries)
- proliferation of OPCs is negatively impacted by wake but doubles during sleep whereas their differentiation is enhanced by wake

Oligodendrocyte regeneration: its significance in myelin replacement and neuroprotection in multiple sclerosis

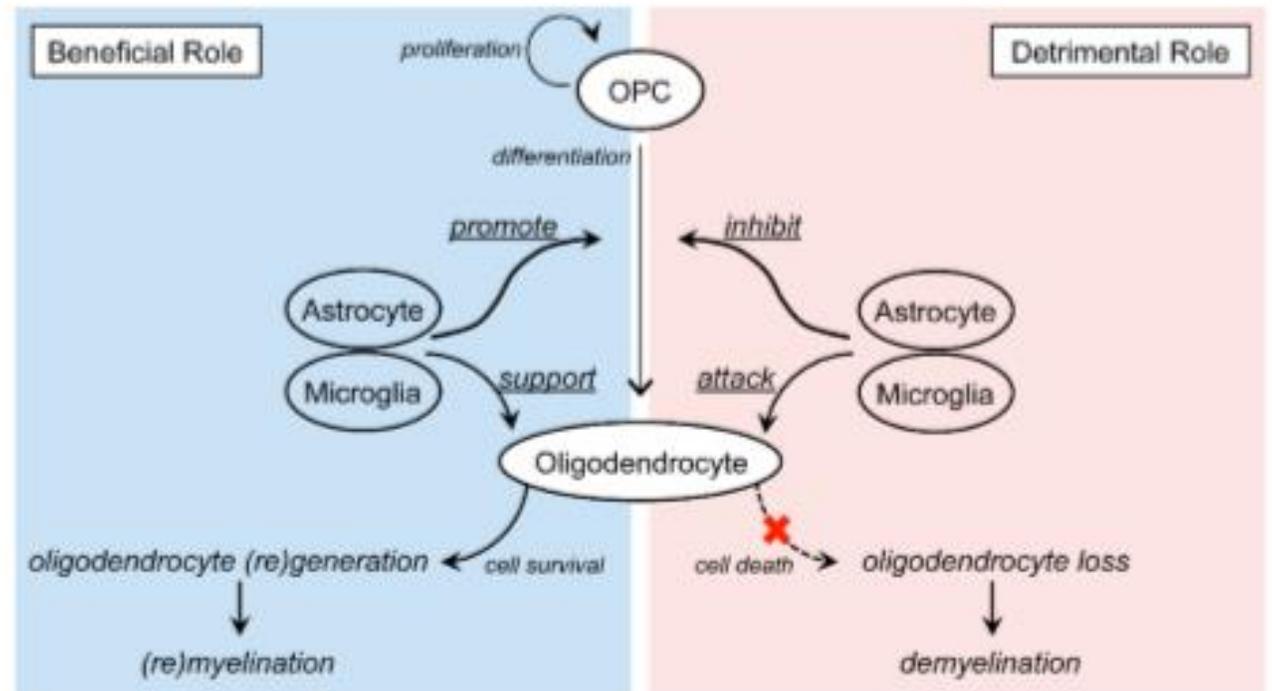
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CEREBRAL GENIC EXPRESSION (WAKE/SLEEP)

- cerebral genic expression significantly changes from sleep to wake
- several transcripts involved in the production and maintenance of membranes, including myelin, show higher levels during sleep



OPCs AND BIOLOGICAL CHANGES

Several biological changes, differently expressed during wake and sleep, can influence OPCs activities

For example, glutamatergic transmission that is higher in wake than in sleep, can inhibit OPC proliferation and affect their ability to produce myelin through AMPA-mediated excitatory currents

HYPOTHESIS

The demonstrations supporting the role of sleep in some oligodendrocyte functions, including myelination, and in the proliferation of new immature oligodendrocytes, suggest that in some clinical conditions, characterized by oligodendrocyte dysfunction, sleep alterations could influence patients' prognosis

AIM OF THIS STUDY

to evaluate possible correlations between sleep quality and MS course, in order to verify whether quality of sleep could be used as a prognostic factor and then open new treatment possibilities.

White matter abnormalities have been demonstrated in some sleep disorders: OSAS and RLS

METHODS

PATIENTS were recruited from subjects attending the Multiple Sclerosis Center of the Neurological Department at the University Hospital of Ancona, Italy over a 6-month period (January 2017–June 2017)

INCLUSION CRITERIA: age <50 years; Relapsing-Remitting form of MS; years from disease onset >3 and ≤5 years; Expanded Disability Status Scale (EDSS) score ≤4.5; availability of accurate medical recordings in the three years preceding the inclusion in the study including at least one medical assessment and a brain and spinal MR examination per year.

THERAPY: first-line treatment with interferon; for relapses all patients had a standard therapy protocol within 24 hours from symptoms' onset with intravenous methylprednisolone 1000 mg/day for 5 days .

EXCLUSION CRITERIA: patients with psychiatric symptoms and cognitive deficits

SLEEP QUALITY assessed using the Pittsburgh Sleep Quality Index (PSQI), a self-administered questionnaire used to evaluate previous month's quality of sleep. It contains 19 self-rated questions and 5 facultative questions; good sleepers (PSQI <5) and bad sleepers (PSQI ≥5).

MAIN VARIABLES OF DISEASE COURSE

- disease duration from MS onset;
- number of relapses during the three years preceding the inclusion in the study;
- relapse duration
- number of days of MS activity calculated as duration in days of each relapse x number of relapses;
- EDSS (baseline EDSS, entry EDSS);
- age and sex;
- number of lesions documented at MR (baseline and entry).

BASELINE CHARACTERISTICS OF THE SAMPLE

<i>Continuous Variables</i>	N	Minimum	Maximum	Mean	SD
EDSS (baseline)	40	0	3.0	1.038	0.7876
EDSS (entry)	40	1.0	4.5	2.188	1.0960
Number of MS lesions (baseline)	40	2	7	3.60	1.533
Number of MS lesions (entry)	40	2	18	6.83	3.137
Number of MS relapses	40	1	4	2.13	0.992
Mean duration of MS relapses (days)	40	3	22	9.90	3.699
Number of days of MS activity	40	3	52	22.03	14.766
PSQI at entry	40	1	13	5.40	3.128
Age	40	25	48	35.63	6.562
<i>Dichotomous Variables</i>	n	Percent			
Female sex (%)	26	65,0%			
PSQI \geq 5 (%)	20	50,0%			

COMPARISON OF BASELINE CHARACTERISTICS OF THE SAMPLE WITH T-TEST

		N	<u>Mean</u>	SD	SEM	P		
	EDSS (baseline)	PSQI < 5	20	1.150	0.8445	0.1888	0.373	
		PSQI ≥ 5	20	0.925	0.7304	0.1633		
	EDSS (entry)	PSQI < 5	20	1.775	0.9386	0.2099	0.015	
		PSQI ≥ 5	20	2.600	1.1074	0.2476		
	Number of lesions (baseline)	PSQI < 5	20	3.75	1.682	0.376	0.543	
		PSQI ≥ 5	20	3.45	1.395	0.312		
	Number of lesions (entry)	PSQI < 5	20	4.95	1.638	0.366	0.000	<i>MULTIVARIATE MODELS</i>
		PSQI ≥ 5	20	8.70	3.181	0.711		
	Number of relapses	PSQI < 5	20	1.50	0.607	0.136	0.000	
		PSQI ≥ 5	20	2.75	0.910	0.204		
	Duration of relapses (days)	PSQI < 5	20	7.60	3.169	0.709	0.000	
		PSQI ≥ 5	20	12.20	2.628	0.588		
	Number of days of activity	PSQI < 5	20	10.85	5.174	1.157	0.000	
		PSQI ≥ 5	20	33.20	12.564	2.809		

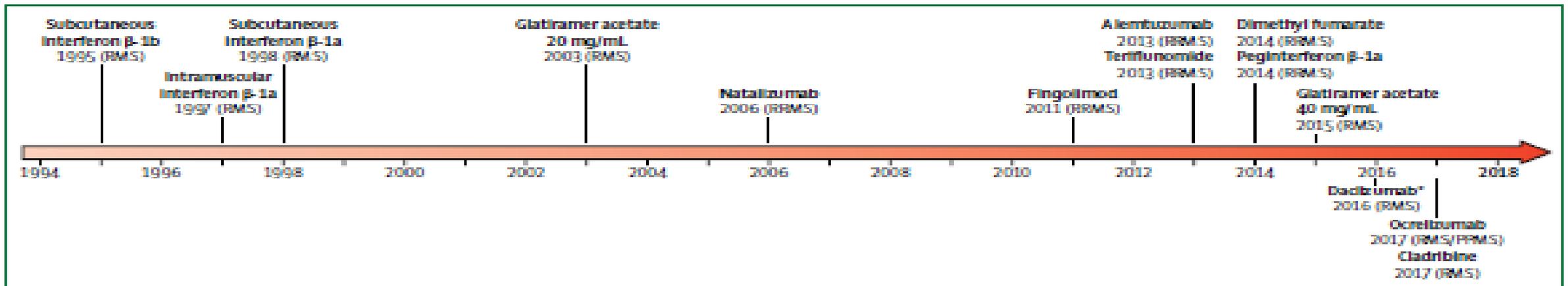
These observations were confirmed after correction for age, sex, baseline EDSS and baseline number of MS lesions in multivariate models for MS relapses, mean duration of MS reactivations and mean days of MS activity.

DISCUSSION

- In spite of their frequency, potential pathogenetic role in different clinical conditions and social implications, sleep disturbances usually are not systematically and carefully investigated in the clinical setting and thus, they are often underestimated
- Pathophysiologic considerations strongly support the relevant role played by a correct sleep hygiene on structural and functional recovery processes.
- OPCs (5-8% of the adult nervous system glial population primarily involved in the repair processes after white matters damages) proliferative activity is increased during sleep and results significantly reduced after sleep deprivation.
- an alteration in sleep quality can have negative influences on remyelination processes and then, on the recovery capacities after a MS relapses.

HIGHLIGHTs

- Sleep disturbances are common in MS;
- Poor sleep quality may affect the efficiency of remyelination processes;
- We found that poor sleep quality negatively influences the clinical evolution of MS;
- Sleep quality assessment may be useful for the management of MS patients.



MANY THANKS to

