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Breathing Sleep Disturbances and Migraine: A Dangerous Synergy or a Favorable Antagonism?

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1. Introduction

Sleep and headache are two realities known to be linked in a bidirectional way [01]. Clinical research correlates specific headache diagnoses and sleep disorders with chronobiologic patterns and sleep processes, implicating that common anatomic structures and neurochemical processes are involved in the regulation of both sleep and headache. Sleep and pain perception share several structures, such as the thalamus, the hypothalamus, and a number of mesencephalic, pontine and bulbar nuclei, some of which are also involved in breathing regulation.

The respiratory parameters during sleep at night may play a important role in modifying susceptibility to various pathological conditions, including headache. Morning headache was found to be more frequent among Obstructive Sleep Apnea Syndrome (OSAS) patients with a direct relationship with the severity of the sleep breathing disorder: apnoea hypopnoea index (AHI) has been found higher in OSAS patients with morning headache compared with those without morning headaches and also mean oxygen saturation value (SpO2) during total sleep time has been found significantly lower in OSAS patients with morning headache [02]. Furthermore, it has been observed that morning headache may be largely resolved with nasal continuous positive airway pressure.

The relevance of respiratory disturbances during sleep in subjects with primary headaches has not been clearly evaluated.

Additionally, in a previous study we found that subjects with headache, and particularly those with headache-related cutaneous allodynia, had alterations in sleep behaviour [03].

Consequently, a possible link between sleep behavior disturbances, respiratory disorders during sleep and primary headaches may be hypothesized.

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2. Objective

Based on the above reported background, we designed a study to investigate the possible relationships between nocturnal breathing disturbances and headache, particularly migraine, with and without allodynia.
The aims of the study were:

- to evaluate the prevalence of different kinds of headache in a population of subjects who underwent cardiopulmonary monitoring during sleep for presumed respiratory problems;
- to assess the frequency of allodynia among patients with headache in this population;
- to evaluate the possible relationships between the presence of headache - and of allodynia - and the respiratory parameters that reflect oxygen saturation during sleep (AHI, SpO2, T<90%).
- to compare sleep behavior parameters (sleep latency, frequency of awakenings and subjective perception of sleep quality) in subjects without headache and in headache patients, grouped by different diagnostic types.
- to compare the respiratory parameters that reflect oxygen saturation during sleep in these groups and
- to examine any relationship between headache, subjective sleep behavior and breathing quality during sleep.

3. Materials & methods

Population

We enrolled a sample of 302 subjects (225 men and 77 women) presenting consecutively at the Unit of Pneumology of the Luigi Sacco Hospital of Milan, for a full cardiopulmonary monitoring during sleep.

Methods

- History of headache was evaluated in each subject, and headache diagnosis was clinically made according to the ICHD-II criteria.
- The presence of allodynia was assessed by a set of semistructured questions, that had been used by our group in previous studies [04, 05]. This tool investigates if the patient experiences abnormal scalp sensitiveness and/or discomfort during headache episodes and which activities are able to enhance this symptom, such as touching head skin, combing hair, brushing hair, wearing glasses, and so on.
  Patients were asked to give written yes/no responses to written questions as follows: (1) Has the patient experienced abnormal scalp sensitivity or discomfort during headache attacks? If yes, does this abnormal sensitivity or discomfort arise from (a) touching head skin; (b) touching hair; (c) combing hair; (d) brushing hair; (e) wearing glasses; (f) using a hair-band, curlers or elastic for forming a ponytail; (g) lying with head resting on the pain side? Patients replying yes to the first question and at least to one of questions (a-f) were considered to have headache-associated allodynia
- Sleep behavior was evaluated through semi-structured ad hoc questionnaire exploring the mean latency of sleep onset (more or less of 30 min), the frequency of nights with nocturnal wake-up (<2 or >3 nights/month) and the subjective perception of sleep quality (satisfied/not-satisfied).

- Full cardiopulmonary monitoring with SaO2, T90 and AHI determination, was performed by SOMNO check ® effort (WEINMANN) that includes: a nasal respiratory device to reveal air flow and snoring, a pulse oxymeter to measure SaO2 and cardiac rate, an abdominal and a thoracic belt for the inductive thoraco-abdominal pletismography, and a gyroscopic body position detection device.

Statistics

Student T test with Bonferroni correction was used to compare mean ages, mean AHI, mean T<90% and mean SpO2, between groups (subjects with or without headache, with or without allodynia).
Chi square test was applied to compare the distribution of different sleep behavior aspects between different diagnostic groups.

4. Results

Among the enrolled subjects, 198 did not suffer from headache (mean age 60.3 ± 12.7 years, 159 men and 39 women) and 104 had history of headache (mean age 51.4 ± 12.3 years, 66 men and 38 women) of which 67 migraineurs (Mig - mean age 50.8 ± 14.9 years, 37 men and 30 women) and 37 with tension type headache (TTH - mean age 51.4 ± 13.3 years, 29 men and 8 women).
Out of 104 subjects with headache, 50 were allodynic. Allodynia was found in 41 out of 67 migraineurs and in 9 out of 37 patients with tension type headache.

Headache and allodynia distribution in the sample

In our population, headache was present in 34.4% of the studied subjects (104 out of 302 individuals, of which 67 with migraine and 37 with tension type headache) and allodynia during pain attacks was present in 48% of headache patients (50 out of 104 subjects). Allodynia was more frequent among migraineurs (41 out of 67) than in tension type patients (9 out of 37).
After grouping by gender, headache was present in 29,3% of men and in 49,3% of women. Migraine was found in 30 out of 39 female headache patients (30 out of 116 enrolled women, 25% of the female cohort) and in 37 out of 159 male patients with headache (37 out of 225 observed men, 16% of the male population studied). Headache distributions in the different groups are shown in Table 1.

		n°	M/F	M (%)	F (%)	Mean age (years)
Total sample		302	225/77	75	25	57,0
Without headache		198	159/39	80	20	60,3
104 with headache	migraine	67	37/30	55	45	50,8
	tension type headache	37	29/8	78	22	51,4

Table 1. Presence of headache in subjects who underwent a full cardiopulmonary monitoring for presumed respiratory problems during sleep.

Respiratory sleep parameters in different diagnostic groups

As summarized in Table 2, respiratory parameters among subjects with headache were always better than in subjects without headache.

The Apnea Hypopnea Index, that expresses the number of episodes of apnoea per hour, was 23.3 among subjects without headache and 13.8 in the headache group ($p<0.01$), without significant differences between different kinds of headache (14.2 in migraineurs and 13.1 in the tension type group).
Blood oxygenation during sleep was significantly better among headache patients (mean SpO_2 94.4% and T90 6.3%) with respect to controls (mean SpO_2 92.9% and T90 14.7%).
No differences were found between allodynic and non allodynic headache patients also with regard to specific diagnostic groups.

	n°	**AHI Apnea Hypopnea Index** (events/hour)	**SpO_2** (mean oxygen saturation) (%)	**T<90%** % of time with SpO_2 < 90% (%)
Subjects without headache,	198	23.3	92.9	14.7
Headache subjects (Mig+TTH)	104	13.8	94.4	6.3
Allodynic headache subjects	50	15.6	94.5	6.2
Non-allodynic headache subjects	54	12.1	94.3	6.4
Subjects with TTH	37	13.1	93.9	8.9
Allodynic TTH subjects	9	15.9	93.5	10.5
Non-allodynic TTH subjects	28	12.1	94.0	8.5
Subjects with Mig	67	14.2	94.7	4.8
Allodynic migraineurs	41	15.6	94.7	5.3
Non-allodynic migraineurs	26	12.0	94.7	4.0

Table 2. Distribution of respiratory parameters among the different groups

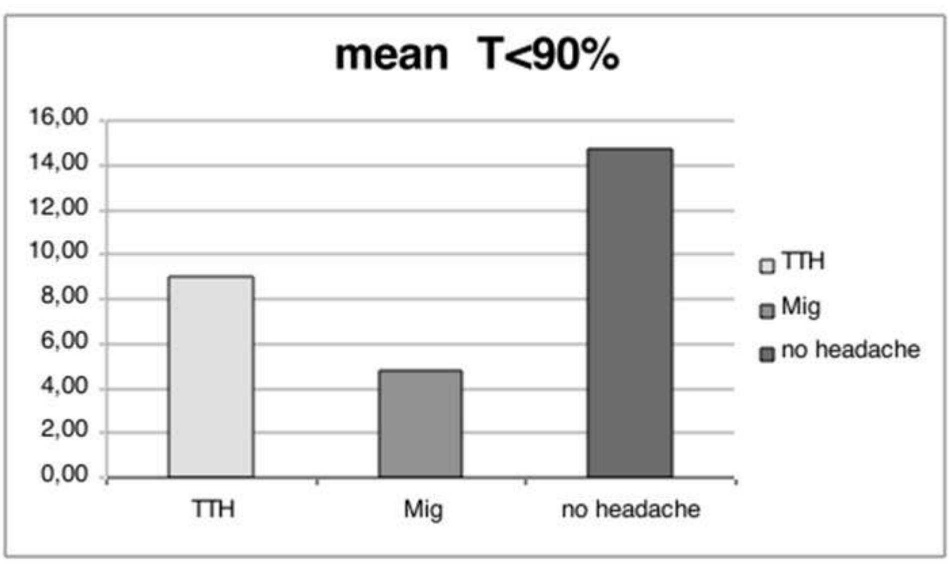

Fig. 1. Blood oxygenation was better among migraineurs. In this diagnostic group, the time period with SpO_2 < 90% was globally significantly shorter than in the other groups.

Sleep behavior in different forms of headache

As previously observed, allodynic subjects with headache, especially if migraineurs, complain of difficulties in falling asleep and of frequent awakenings that disrupt their nocturnal sleep. Tabs 3a, 3b and 3c summarize sleep characteristics in different groups of patients.

subjective satisfaction	no headache n° (%)	headache n° (%)	mig n° (%)	TTH n° (%)	allodynic subjects n° (%)	not allodynic subjects n° (%)	mig with allodynia n° (%)	mig without allodynia n° (%)	TTH with allodynia n° (%)	TTH without allodynia n° (%)
Satisfied	111 (56)	37 (36)	17 (25)	20 (54)	11 (22)	26 (48)	6 (15)	11 (42)	5 (56)	15 (54)
not satisfied	87 (44)	67 (64)	50 (75)	17 (46)	39 (78)	28 (52)	35 (85)	15 (58)	4 (44)	13 (46)
tot.	198	104	67	37	50	54	41	26	9	28

Table 3a. Sleep behavior: subjective perception of sleep quality (satisfied/not-satisfied). Migraineurs – particularly allodynic ones – have a worse perception of their sleep quality with respect to subjects without headache (chi2 test - $p < 0.01$ in both cases).

Sleep latency	no headache n° (%)	Headache n° (%)	mig n° (%)	TTH n° (%)	allodynic subjects n° (%)	not allodynic subjects n° (%)	mig with allodynia n° (%)	mig without allodynia n° (%)	TTH with allodynia n° (%)	TTH without allodynia n° (%)
<30 minutes	159 (80)	72 (69)	42 (63)	30 (81)	30 (60)	42 (78)	22 (54)	20 (77)	8 (89)	22 (79)
>30 minutes	39 (20)	32 (31)	25 (37)	7 (19)	20 (40)	12 (22)	19 (46)	6 (23)	1 (11)	6 (21)
tot.	198	104	67	37	50	54	41	26	9	28

Table 3b. Sleep behavior: sleep onset latency. Migraineurs – particularly allodynic ones – take more time to fall asleep with respect to subjects without headache (chi2 test - $p < 0.01$ in both cases).

Nocturnal awakenings	no headache n° (%)	headache n° (%)	mig n° (%)	TTH n° (%)	allodynic patients n° (%)	not allodynic patients n° (%)	mig with allodynia n° (%)	mig without allodynia n° (%)	TTH with allodynia n° (%)	TTH without allodynia n° (%)
<2 nights/month	70 (39)	26 (25)	16 (24)	10 (27)	7 (14)	19 (35)	4 (10)	12 (46)	3 (33)	7 (25)
>3 nights/month	120 (61)	78 (75)	51 (76)	27 (73)	43 (86)	35 (65)	37 (90)	14 (54)	6 (67)	21 (75)
tot.	198	104	67	37	50	54	41	26	9	28

Table 3c. Sleep behavior: nocturnal awakenings. Migraineurs – particularly allodynic ones – wake more frequently during night with respect to subjects without headache (chi2 test - $p < 0.01$ in both cases).

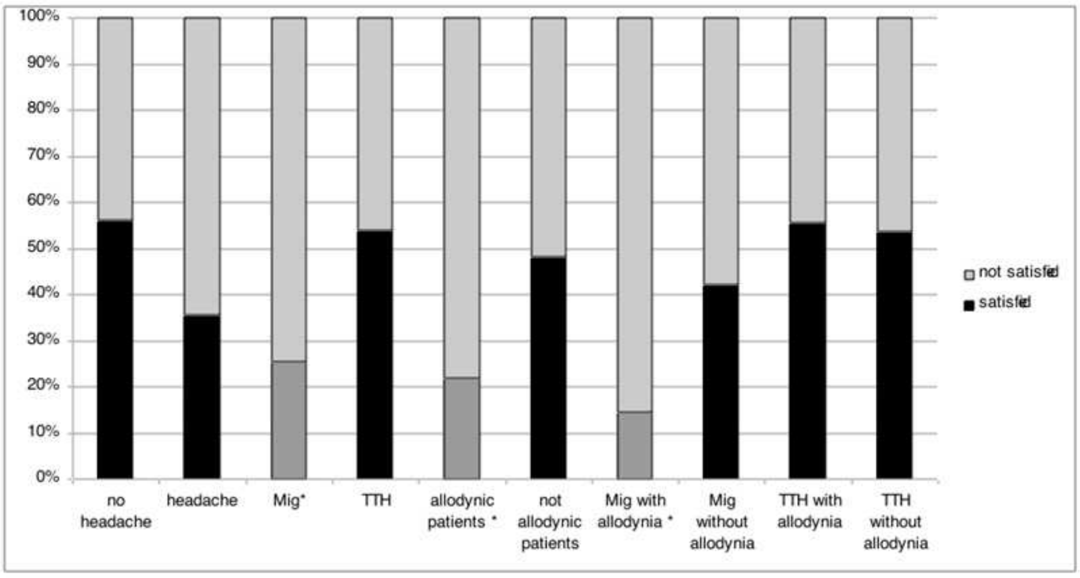

Fig. 2. Migraineurs, particularly if allodynic, are less satisfied about their subjective sleep quality.

Respiratory sleep parameters in different sleep behavior groups

As showed in tables 4a, 4b and 4c, both subjects with and without headache were grouped by sleep behaviour characteristics (satisfaction, sleep latency and presence of nocturnal awakenings). No differences in terms of respiratory parameters were found comparing, in both headache and headache-free groups, subjects satisfied vs not satisfied, subjects with short vs long sleep latency and patients with frequent vs sporadic awakenings.

	AHI	SaO2 media	T<90%
Headache subjects - satisfied by their sleep	11,4	94,6	5,4
Headache subjects - not satisfied by their sleep	15,1	94,2	6,8
Controls - satisfied by their sleep	23,3	93,1	12,8
Controls - not satisfied by their sleep	23,4	92,6	16,5

Table 4a. Sleep behavior: subjects grouped by subjective perception of sleep quality. Respiratory parameters among different groups. No significant differences between satisfied and not-satisfied in both headache and non-headache group with regard to respiratory parameters during sleep.

	AHI	SaO2 media	T<90%
Headache subjects with short sleep latency	15,6	94,3	6,8
Headache subjects with long sleep latency	9,6	94,5	4,2
Controls with short sleep latency	26,0	92,8	14,3
Controls with long sleep latency	14,8	93,7	17,7

Table 4b. Sleep behavior: subjects grouped by sleep onset latency. Apnea episodes (AHI) are meanly more frequent among subjects with rapid sleep onset in both headache and non-headache subjects (no difference after Bonferroni correction). No differences in term of blood oxygenation.

	AHI	SaO2 media	T<90%
headache subjects with sporadic nocturnal awakenings	10,6	94,8	5,1
headache subjects with frequent nocturnal awakenings	15,0	94,2	6,8
controls with sporadic nocturnal awakenings	20,6	93,0	13,2
controls with frequent nocturnal awakenings	25,3	92,8	15,1

Table 4c. Sleep behavior: subjects grouped by presence of nocturnal awakenings. Respiratory parameters do not significantly differ among groups.

5. Discussion

The study gave to somewhat unexpected results. Namely, the evidence of the significant difference observed between headache and non headache subjects in terms of mean AHI ($p < 0.01$), SpO2 ($p < 0.01$) and T <90% ($p < 0.01$) with better respiratory parameters among headache sufferers, particularly amongst the migraineurs. In fact, when we had planned the study, we were looking for possible endogenous elements able to induce and/or transform headache and we hypothesized that a sleep breathing disturbance might be one of this factors. On the contrary, it emerged that headache patients have a better respiratory condition during sleep, also in allodynic cases.

The analysis of sleep behavior in different groups showed that migraineurs took more time to fall asleep and awake more frequently during night with a reduced global sleep satisfaction. In conclusion, if compared to controls, migraineurs seem to sleep worse but to breathe better.

However, the hypothesis that there is an allostatic function of migraine and allodynia could also be made: the presence of these conditions might inhibit deep sleep, and thus avoid prolonged apneas. The observation that allodynic patients complain of a poor subjective satisfaction by sleep with frequent awakenings and difficulties in starting sleep may be the time when an allostatic load (episodic migraine) becomes an allostatic overload (allodynic migraine), or it may correspond to a further allostatic adjustment to maintain an equilibrium: migraine is “sufficient” until the metabolic unbalance is such, that allodynia is needed. Allodynia is more frequently observed among subjects with chronic/transformed migraine, but it is also present in a large portion of episodic migraineurs. Probably transformed migraine is the true manifestation of the overwhelmed allostatic capacity of migraine (allostatic overload) while the presence of allodynia is still a marker of a functional modification.

Overall, using an allostatic perspective, migraine may be considered a functional strategy to maintain equilibrium and to reverse situations potentially dangerous for the hyperexcitable and hypoenergetic migraineurs brain [08]. Transformed migraine may than represent the failure of this strategy (allostatic over-load), without the capacity to counteract the energetic unbalance.

Allodynia (the perception of pain by non-painful stimuli) is largely considered as a marker of migraine transformation, but the observation that it is frequently present also among episodic migraineurs, offers another possible way to interpret this symptom. Allodynia may be an additional manifestation of migraine in an extreme effort to correct a metabolic or energetic or homeostatic disequilibrium, nocturnal sleep related blood oxygenation included.

To explore this unexpected hypothesis, we grouped both headache and non-headache subjects by sleep subjective satisfaction, sleep latency, and presence of awakenings. Comparing groups (headache subjects with short vs long sleep latency, with frequent vs sporadic awakenings and satisfied vs non-satisfied) no significant difference emerged, at least after Bonferroni correction. Probably the relatively small cohort dimension may have influenced the analysis.

The fact that patients with chronic headaches have a high prevalence of sleep complaints is well documented [09] and a high frequency of headache among patients with pathological breathing during sleep is well defined [02], but in the transitional phase toward sleep breathing disturbances, allodynia may be a useful para-physiological modification instead of a symptom of migraine transformation/chronification.

6. Conclusions

Our convenience data found that migraineurs seem to sleep worse but to breath better than headache free patients. The possible mechanism or mechanisms underlying this observation are not clear, but an allostatic mechanism has been proposed which can be tested in future studies.

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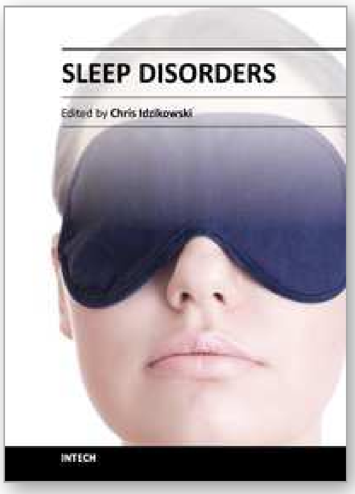

Sleep Disorders

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For progress to be maintained in a clinical field like sleep medicine, unimpeded, unrestricted access to data and the advances in clinical practice should be available. The reason why this book is exciting is that it breaks down the barriers to dissemination of information, providing scientists, physicians, researchers and interested individuals with a valuable insight into the latest diverse developments within the study of sleep disorders. This book is a collection of chapters, which can be viewed as independent units dealing with different aspects and issues connected to sleep disorders, having in common that they reflect leading edge ideas, reflections and observations. The authors take into account the medical and social aspects of sleep-related disorders, concentrating on different focus groups, from adults to pregnant women, adolescents, children and professional workers.