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CLINICAL REVIEW

# Comorbidity between sleep apnea and insomnia

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SUMMARY

The association between insomnia and sleep apnea has received little attention from health professionals in the past few decades. However, recent studies have shown a high prevalence of insomnia complaints in patients with objectively diagnosed obstructive sleep apnea (OSA) syndrome. In this paper we have reviewed data published on different aspects of this association: the clinical profile of sleep-disordered breathing (SDB)-plus, the nature of the association, the role in the onset of insomnia played by OSA itself and other comorbidity factors such as depression or the restless leg syndrome. Finally, we have reviewed data and hypotheses on the metabolic implications of OSA and insomnia, and we speculate on the role that hypothalamic–pituitary–adrenal axis hyperactivity may play in a hypothetical interrelation between OSA and insomnia. The apparent paradox implied by this clinical association reveals the need for interdisciplinary training for physicians who treat both types of disorders.



## Introduction

The association between obstructive sleep apnea (OSA) syndrome and chronic insomnia is likely to have significant clinical relevance and raises several physiopathological questions. This relationship may seem paradoxical because daytime sleepiness is the most characteristic clinical feature of OSA.[1–4] Although the International Classification of Sleep Disorders[5] includes OSA in the differential diagnosis of insomnia, there is little in the literature on this subject.

In recent decades, scientists have paid very little attention to this relationship. However, some published data point out the consistency of this association: a high prevalence of OSA in the elderly population with insomnia,[6] greater presence of clinical features of insomnia in females with OSA than in males,[7,8] or the fact that OSA patients with insomnia appear to suffer less hypoxia and sleepiness than OSA patients with no insomnia complaints.[7]

The presence of insomnia in OSA patients raises certain issues. We need to specify the clinical profile of this association and its impact on OSA severity in order to optimize detection and treatment. In this review, we analyze these issues and review the nature of this association, as well as the roles of OSA and psychiatric and physical comorbidity in the causality of insomnia. This is a multifaceted problem and although there are sleep disorder specialists who are qualified in treating the two disorders, we would suggest that there should be multidisciplinary training for doctors (lung specialists, ENT specialists, psychiatrists, general practitioners) who often treat just one of these disorders.

The data and hypothesis concerning hypothalamic–pituitary–adrenal (HPA) axis hyperactivity in OSA and insomnia suggest that it could be an interactive link between the two processes.

## Association between insomnia and OSA

### *Concurrent insomnia/OSA*

The first reference to the OSA–insomnia association was published in 1973.[9] In 2001, Krakow et al.[10] used the term sleep-disordered breathing (SDB)-plus to refer to patients presenting OSA and chronic insomnia simultaneously, and they estimated that these patients represent 50% of the total number of OSA patients. Another study published the same year estimated that 24.2% of patients with an objective diagnosis of OSA were also diagnosed with insomnia.[11] Both studies were retrospective, and neither of them used validated instruments to assess the presence of insomnia, which might have caused over- or underestimations. Soon afterward, a prospective study that documented insomnia complaints using validated scales estimated that 39% of the patients had both OSA and insomnia.[12] Subsequent data (Table 1), including those from a recent review of a series of our own,[13] have confirmed similar figures ranging from 42% to 54.9%.[14,15] It should not be surprising that the insomnia–OSA association may be especially marked amongst elderly patients, given that age is a risk factor for both processes.[6,16]

The above-mentioned studies were mostly retrospective and used different methodologies. We believe that more studies

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**Table 1**
Percentage of patients with insomnia complaints, with respect to the total from the sample, in different published studies and in one sample of our own. The sums of percentages of various insomnia types are not equal to the percentage of SDB-plus because some patients had several types of insomnia.

| Author/year | *n* | SDB-plus | Breakdown of insomnia complaints | | | |
|---|---|---|---|---|---|---|
| | | | Onset | Maintenance | EMA | Onset + Maintenance |
| Krakow et al.[10] | 231 | 50% | 22% | 25.5% | | |
| Smith et al.[12] | 105 | 39% | | | | |
| Krell et al.[14] | 255 | 54.9% | 30.4% | 38.8% | 31.4% | |
| Chung et al.[15] | 157 | 42% | 6% | 26% | 19% | |
| Benetó et al.[13] | 175 | 46.3% | 4.6% | 25.1% | | 16.6% |

SDB: sleep-disordered breathing, EMA: Early morning awakening.

providing reliable epidemiological information are needed to confirm the high frequency of this association.

### *Clinical profile of SDB-plus*

The first study on this association, carried out by Krakow et al.,[10] described a sample of SDB-plus patients with no differences in age, gender or body mass index (BMI), compared to SDB-only patients (OSA without insomnia complaints). The severity of OSA (min SaO2 and OSA/upper airway resistance syndrome (UARS) ratio) and snoring pattern was similar in both groups. The insomnia patients presented a lower total sleep time, greater sleep latency and less sleep efficiency, objectively measured. Moreover, these patients presented more psychiatric disorders such as anxiety disorders (post-traumatic stress, panic attacks) and depression, cognitive–emotional symptoms such as attention and memory problems, irritability, hostility, frustration and claustrophobia, mental symptoms such as racing thoughts and ruminations, anxiety and fear, and physical symptoms such as indigestion, pain, restless legs and trouble breathing, which are known to interfere negatively with sleep, and resulted in an increased use of sedatives and psychotropic medication. They also reported more complaints compatible with restless leg syndrome (RLS). The authors suggested that the high prevalence of insomnia could be determined by the significant presence of psychiatric comorbidity. The authors speculated that insomnia could make it more difficult for patients to adapt to continuous positive airway pressure (CPAP) therapy, and they recommended implementing this treatment together with pharmacological and cognitive behavioral measures to correct insomnia. This publication constituted a turning point with regard to the clinical relevance of the insomnia/OSA association, as it detected that this association is more frequent than initially thought, and that it probably produces greater distress in patients. In another publication, Smith et al.[12] conducted a prospective study with a sample of 105 patients, using validated questionnaires to assess sleep- and mood-related variables. Their data showed that SDB-plus patients presented higher levels of depression, anxiety and stress than SDB-only patients. Concepts and attitudes about the immediate and long-term negative consequences of insomnia, and the need for control of insomnia were similar in both groups. The subjective data obtained by means of sleep diaries and objective findings using polysomnography revealed a higher degree of nocturnal sleep alterations in the SDB-plus patients, and this was also observed in Krakow's study.

Another retrospective study published subsequently,[14] showed that there were no differences with regard to age or body mass index (BMI) between patients with or without insomnia. However, a significant association with insomnia was found in females, psychiatric disorders, chronic pain, symptoms suggestive of RLS and sleep jerking.

In summary, according to the bibliographical data, there are three main features that characterize SDB-plus: more alterations in nocturnal sleep, a significant presence of psychological disorders, psychiatric disorders such as depression, and an association with other sleep disorders like RLS.

### *Impact of insomnia in OSA*

In the previously mentioned studies there is some discrepancy regarding whether the presence of insomnia in OSA implies increased severity. Krakow et al.[10] did not find any relevant differences in severity of OSA (min SaO2 and OSA/UARS ratio) and snoring pattern between SDB-plus and SDB-only patients. In a retrospective series of 175 consecutive patients recently referred to our laboratory for an objective diagnosis of OSA using polysomnography, no significant differences were found with regard to the AHI (apnea–hypopnea index) between SDB-plus and SDB-only patients.[13]

Conversely, Smith et al.[12] found a positive correlation between the presence of insomnia and increased OSA severity. In another study, it was observed that insomnia complaints were significantly more frequent among patients with mild OSA, specifically, 81.5% of the patients with an AHI $< 10$, as opposed to 51.8% in patients with an AHI $\geq 10$.[14]

Although some studies distinguish between sleep-onset and sleep-maintenance insomnia complaints,[10,13–15] only one study makes a distinction between them according to their impact on OSA. Patients with sleep-onset insomnia presented lower AHIs and less daytime somnolence objectively measured with the Multiple Sleep Latency Test (MSLT), whereas the patients who reported sleep-maintenance insomnia presented higher AHIs and higher levels of objective daytime somnolence.[15]

Data concerning the impact of insomnia on the severity of OSA are scarce and contradictory. Those indicating increased severity would agree with the observation that chronic and acute sleep deprivation increases the AHI.[17–19] However, there is no evidence that sleep loss in insomnia is the same as in sleep deprivation experiments, although the fact that a different physiopathological mechanism is involved does not necessarily imply that any sleep loss in insomnia will not have repercussions. More data and research are needed to explain whether or not insomnia makes OSA more severe.

In the published studies, no data are available to support the hypothesis that the presence of insomnia in OSA complicates its diagnosis and hinders the treatment of patients. The treatment in these cases should consider both pathologies, and it should be complemented with specific pharmacological and cognitive behavioral measures for the treatment of insomnia. In this respect, there is only one publication on a series of 19 chronic insomnia patients with SDB who were treated with both cognitive behavioral therapy (CBT) and SDB treatment (CPAP, oral appliances, or bilateral turbinectomy), producing positive results. Figures for Insomnia Severity Index, Functional Outcomes of Sleep Questionnaire, and Pittsburgh Sleep Quality Index improved markedly with CBT followed by SDB treatment; self-reported insomnia indices also improved, and self-reported SDB therapy compliance was high.[20]

Regarding gender, only one study found a significant relationship between SDB-plus and females.[14] Therefore, more evidence is needed to confirm these findings, which support the data showing a possible different clinical expression of OSA in females, with a predominance of insomnia, the use of sedatives, depression, generalized obesity and complaints of fatigue rather than somnolence.[21–23] We believe that more attention should be paid to SDB-plus in the female population, given the risk of under-diagnosing OSA, especially in premenopausal females, since excessive diagnostic emphasis on sleepiness symptoms implies a risk of not considering other symptoms such as fatigue, tiredness or insomnia.[21,22] The occurrence of OSA in these females is considered to be low, and even irrelevant, despite the incidence data (4.9%)[24] and a worse survival rate in females than in males with similar age characteristics.[25]

No specific data have been found as to whether the OSA/insomnia association increases patients' cognitive symptoms compared to OSA alone.

*Nature of the insomnia–OSA relationship*

Some studies have suggested that although insomnia complaints in OSA are quite frequent, they are not caused by it, and they are probably more closely related to other coexisting factors, such as depression or RLS.[10,14] Another study gave the same opinion with regard to sleep-onset insomnia, but it presented OSA itself as the cause of the sleep-maintenance insomnia.[15]

Obviously, more studies should be conducted to collect evidence about the nature and causality of SDB-plus, as several questions have been raised for which there are no definitive answers.

If insomnia and OSA were independent, we would not expect a high incidence of comorbidity. However, since they are two of the most prevalent sleep disorders, the frequent presence of both disorders in the same patient should not be surprising. But are they just two coinciding processes with no relationship between them? Or, on the contrary, does this coincidence have some physiopathological consequence?

It has been suggested that this relationship is not a mere coincidence and that it works in both directions: OSA favors the development of insomnia through a psychophysiological conditioning process in response to repeated awakenings, developing dysfunctional sleep behaviors. Conversely, insomnia could exacerbate OSA through an unknown mechanism that alters the upper airway muscle tone caused by sleep fragmentation itself and by frequent changes in phase with superficial NREM sleep predominance.[10] The high incidence of OSA in patients with post-traumatic stress disorders[26] has caused speculation about whether insomnia that develops after a psychic trauma may produce an increase in arousals and superficial NREM in phase 1, thus increasing the instability of the upper airway,[27,28] with the subsequent appearance of respiratory effort-related arousals (RERAs) that could progress toward hypopnea or even apnea in patients with other OSA risk factors.[29,30]

With regard to the question of why some patients with repeated apnea have insomnia and others do not, it has been proposed that psychophysiological insomnia and OSA show the juxtaposition of two sleep fragmentation physiopathologies that together produce a continuous disorder ranging from excessive somnolence symptoms to difficulties in getting to sleep.[31] The authors' interpretation is that some factors producing insomnia and/or somnolence would intervene in this "continuum" and make the pendulum swing one way or the other. In this regard, it seems reasonable to consider the importance of individual vulnerability, which would explain why some patients develop insomnia and others do not. Several factors may determine this vulnerability, and they remain unidentified. Aspects such as age, gender, intensity of respiratory events, comorbidity with psychiatric disorders and other sleep disorders, such as RLS, periodic limb movement or those resulting from physical diseases, should be studied in order to determine their exact contribution to insomnia complaints in these patients.

The other question is why do some patients with OSA, with or without insomnia complaints, present daytime somnolence, and others do not? If somnolence is an inherent consequence of the physiopathology of OSA, it should always be present to some degree. It is hard to understand why a certain percentage of patients with OSA do not have excessive daytime sleepiness, and even have problems getting to sleep at night. It is obvious that not all of the factors responsible for excessive somnolence in OSA have been identified. However, there has been speculation about the contribution of intermittent hypoxemia,[32,33] the AHI[34] and sleep fragmentation.[35] Likewise, other factors, such as obesity, diabetes, depression, and subjective estimations of nocturnal sleep loss,[36] have also been suggested. The fact that there are patients with severe OSA who present clinical profiles of chronic insomnia, limited nocturnal sleep and an absence of daytime sleepiness raises new physiopathological questions, such as the influence of each patient's true sleep requirements prior to the appearance of OSA.

## Metabolic factors and activation of the hypothalamic–pituitary–adrenal (HPA) axis could be a link between insomnia and OSA

One possible relevant aspect that has not been emphasized in the aforementioned studies is metabolic and endocrine involvement in both insomnia and OSA, which could represent a hypothetical link between the two conditions.

*Metabolic factors*

In recent years, information has been compiled that relates OSA with the development of metabolic syndrome components, such as obesity, dyslipidemia, high blood pressure (HBP), glucose intolerance, insulin resistance and the induction of an inflammatory state. However, a causality relationship has not yet been fully demonstrated.[37] Obesity is the most common predisposing factor for OSA,[38] and it plays a very relevant role in the relationship between OSA and metabolic syndrome, due to the fact that it is the main cause of glucose intolerance and insulin resistance. The mechanisms that produce this predisposition to glucose intolerance and insulin resistance in OSA are unknown. They are probably related to continuous and intermittent hypoxemia and sleep fragmentation, through processes such as the activation of the HPA axis and the increase in both sympathetic activity and inflammatory mediators like IL-6, TNF-$\alpha$ and leptin (Fig. 1).[39,40]

One interesting recent hypothesis suggests that OSA does not only facilitate the development of metabolic syndrome, but it is also yet another manifestation of this metabolic syndrome. This idea, which strengthens the concept of the interaction and reciprocity of these processes, means that OSA could be considered more as a systemic disease than as a local anomaly. In the context of obesity, it would constitute a vicious circle, in which a bidirectional and progressive flow would be established between apnea, sleepiness, inflammation and insulin resistance. In this way, OSA would predispose to metabolic syndrome, and this syndrome, in turn, would affect respiratory control mechanisms, thus facilitating OSA progression, subsequently aggravating metabolic syndrome.[41] Experimental studies carried out in animal models support this hypothesis by confirming that diabetes mellitus can lead to severe depression of the respiratory control mechanisms and that insulin resistance is an important factor leading to the occurrence of apnea.[42–44] It would be important to confirm whether or not respiratory control is impaired by diabetes in humans with OSA (Fig. 2).

In contrast to the extensive research on the endocrine and cardiovascular effects of OSA, the possibility that chronic insomnia could produce the same kind of effects has not been explored.[45] The presence of certain specific diseases was compared in two patient samples, insomniacs and non-insomniacs. Significant differences were found with regard to HBP, with figures of 43.1% and 18.7%, respectively, and in relation to diabetes mellitus, with figures of 13.1% and 5.0%, respectively.[46]

Chronic sleep deprivation is considered a possible direct risk factor for the development of metabolic syndrome, and an indirect risk factor through obesity.[37] In a recent review, Spiegel et al.[40] described the hypothetical mechanisms through which acute and chronic sleep loss would induce metabolic alterations. Acute sleep deprivation, on the one hand, would induce both an increase in

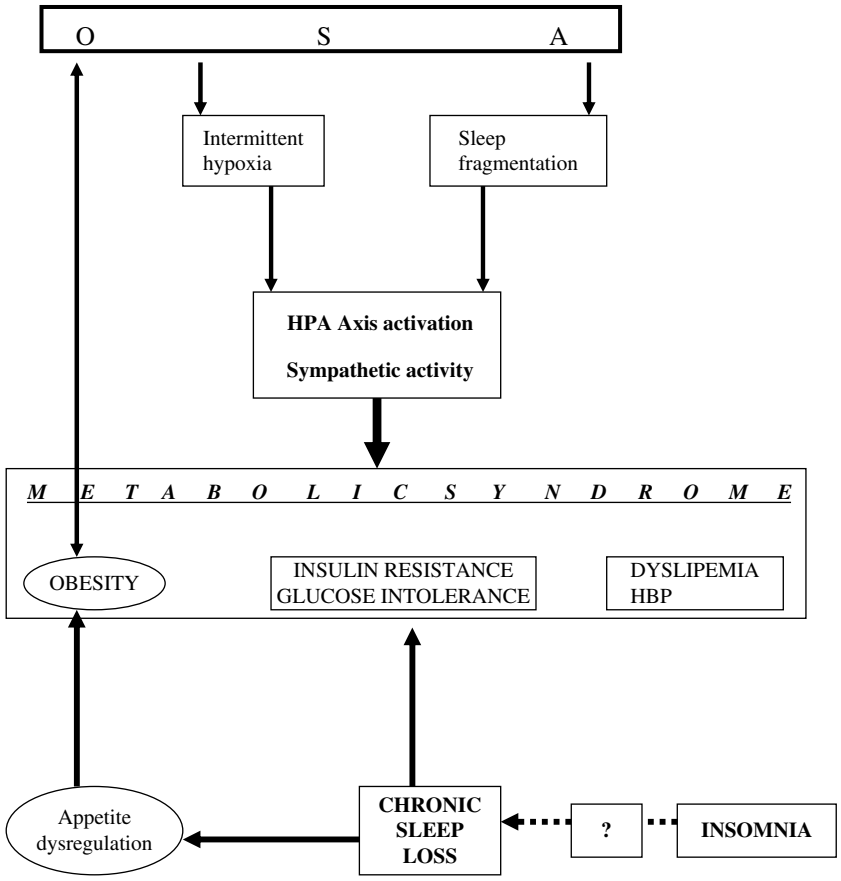


**Fig. 1.** OSA/metabolic syndrome relationship. Sleep fragmentation and intermittent hypoxia may cause HPA axis activation and sympathetic activity which could cause insulin resistance and glucose intolerance. Obesity may predispose to OSA and, in turn, may be facilitated by appetite dysregulation secondary to sleep loss. The question is if in some cases of insomnia there is a sleep loss mechanism which induces metabolic alteration.

glucose blood levels and a decrease in insulin levels, which would lead to glucose intolerance. Chronic sleep deprivation, on the other hand, would not affect glucose levels, but it would increase insulin levels, which would lead to a state of insulin resistance. Weight gain and obesity, favored by appetite dysregulation, and influenced by leptin and ghrelin alterations, would also contribute to this resistance (Fig. 1).[40]

The question that arises is whether chronic sleep deprivation and sleep fragmentation can be assimilated to insomnia. Insomnia's complex physiopathological mechanisms probably differ from

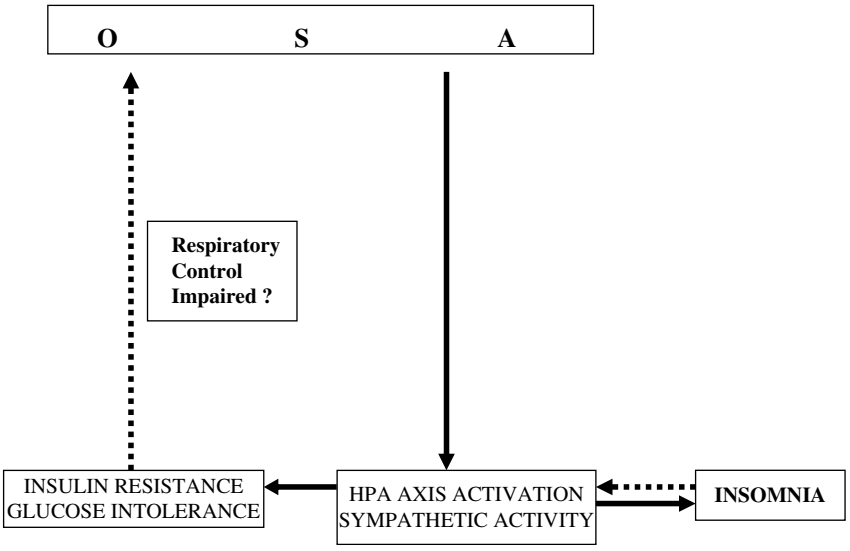


**Fig. 2.** Activation of the HPA axis produced by OSA may, in turn, be a cause of insomnia. The issue is to find out if insomnia produces HPA activation and if it leads to OSA through an increase in insulin resistance and glucose intolerance.

mere sleep deprivation, but a fragmentation of and reduction in the quantity of sleep cannot be ruled out in many insomnia cases. A recent study observed that in a sample of 722 men and 764 women between 53 and 93 years of age, insomnia complaints were significantly more frequent among subjects with a total amount of sleep of less than 6 h, and they were especially significant in those who slept less than 5 h per night. The same study observed an increase in the odds ratios adjusted for glucose intolerance and diabetes mellitus in subjects who slept 6 h or less per night, regardless of whether or not they had insomnia complaints.[47] Similar data have been observed among Japanese workers when evaluating the relationship between the quantity and quality of sleep and the risk of developing diabetes. Sleep-onset and sleep-maintenance complaints were observed with greater frequency in subjects who slept less than 6 h per night, and an increased risk of developing diabetes was associated more with difficulties in falling sleep than with its duration.[48] In another study with 11 young insomniacs without depression (six men and five women), compared to 13 control subjects with no sleep alterations, an increase in ACTH and cortisol secretion was observed, with no modification in the circadian rhythm. Nevertheless, the fact that these increases were produced at nightfall and during the first half of the night suggests that they could be influenced by the sleep loss.[45] These studies are not conclusive, but they suggest an association between insomnia complaints and a reduction in sleep quantity, which should be further investigated.

### *The HPA axis may be a link between insomnia and OSA*

The activation of the HPA axis and its impact on metabolic syndrome could be the common place where insomnia and OSA interact reciprocally, through a process in which other factors, such as a certain predisposition and the possible influence of physical and psychic comorbidity, would play a role.

Results of various studies relate insomnia to an activation of the HPA axis and the sympathetic system.[49–51] The observation that the activation of the HPA axis produces sleep fragmentation, and this fragmentation, in turn, produces increases in the cortisol levels, suggests a model of initiation and perpetuation of severe chronic insomnia, as a vicious circle is established between cause and effect (Fig. 2).[50,51]

A recent review emphasizes the importance of HPA axis hyperactivity as a cause of insomnia and a consequence of OSA. OSA would produce an activation of HPA axis through a mechanism of autonomous activation, awakening and arousal. The activation of the HPA axis would play a relevant role in the secondary production of insulin resistance and HBP in untreated OSA. The authors suggest that OSA, through the activation of HPA axis, is a risk for the development of metabolic syndrome and other hypercortisolemic states, such as insomnia and depression (Fig. 2).[52] Although there is still no scientific evidence, a synthesis of the above-mentioned aspects reveals that it is not far-fetched to intuit the existence of reciprocal links between insomnia and OSA, with a relevant role played by the HPA axis:

- In normal conditions, sleep plays a role in the regulation of glucose metabolism.
- Acute and chronic sleep deprivation, as well as sleep fragmentation, increase sympathetic and HPA axis activity. Sleep deprivation and sleep fragmentation are present in OSA and in various behavioral sleep alterations, among which insomnia could possibly be included.
- Activation of the HPA axis may alter the regulatory balance of glucose, through insulin resistance and glucose intolerance processes.[37,39,40]
- OSA produces an activation of the HPA axis, which could lead to the development of depression and insomnia.[52] At the same time, depression is cause of insomnia. In the opposite sense, insomnia would produce an activation of the HPA axis and the sympathetic nervous system (SNS),[50,51] both of which can facilitate a state of insulin resistance.[39,40]

In any case, this theoretical construction undoubtedly requires further research in order to confirm its validity.

### *Future research*

Possibly the most solid piece of data that can be extracted from all the above is the fact that insomnia complaints frequently coexist with OSA. The methodological limitations of the studies published on this topic indicate the need to unify the criteria for performing new studies.

The first issue is to define the clinical characteristics of the OSA–insomnia association, specifying its objective limits. This step would enable us to determine the dimension of the problem, optimize diagnostic detection and evaluate the effectiveness of treatments. There is general consensus on the diagnostic criteria of OSA, although some aspects continue to be discussed, such as the definition of various respiratory events and the cutoff points on the AHI.[5] Various criteria and definitions of insomnia and its subtypes have been formulated. Criteria that define insomnia as a disorder with impairment of sleep and waking functions should be used. Using symptoms only, such as sleep-onset or sleep-maintenance difficulties, for sample selection, appears to be a suboptimal research practice.[53] The use of research diagnostic criteria (RDC) for insomnia[54] and quantitative insomnia diagnostic criteria[55] has recently been proposed. The RDC were developed by a commissioned work group of the American Academy of Sleep Medicine. They established criteria to identify subjects with insomnia and to differentiate between nine subtypes of insomnia. The application of the RDC would make it possible to standardize research. Moreover, the RDC have the advantage of coinciding with the insomnia disorder listed in the ICSD-2[5] and with the Clinical Modification of the International Classification of Diseases, 10th edition (ICD–10–CM).[56] Many unresolved questions remain, and a lot of work is needed in order to obtain information about the issues raised, by:

- Carrying out prospective studies with homogeneous methodological designs about insomnia prevalence in clinical samples of OSA and in high risk populations prior to the onset of OSA,
- Determining whether the coexistence of insomnia aggravates the OSA process in the following aspects: association with a higher AHI, further developed OSA over time, greater cognitive and performance impact and decrease in the effectiveness and compliance to CPAP,
- Evaluating the effectiveness of CPAP/CBT combined treatment,
- Evaluating the possible causal relationship between OSA and insomnia, for which it is important to obtain information about the chronological sequences in the onset of both processes,
- Evaluating the contribution of other comorbidity factors apart from OSA in the development of insomnia, such as depression and RLS:
  - Neuroendocrine and metabolic aspects:
  - Metabolic and cardiovascular consequences (diabetes mellitus, obesity, HBP) of insomnia, by means of studies on comorbidity. Evaluation of sleep loss as a possible factor involved in this process, by studying the number of sleep hours in chronic insomniacs with and without OSA.

- Investigation of the hypothesis that OSA could be a manifestation or consequence of metabolic syndrome. Research on the possible alteration in respiratory control produced by diabetes mellitus in humans with OSA.

## Sleep disorders require an interdisciplinary approach

The fact that a large percentage of patients with OSA can present intense symptoms of chronic insomnia, and that these patients can have greater difficulty in adapting to and tolerating CPAP therapy, raises the following issues:

- the need for doctors who deal with OSA to extend their knowledge on insomnia, in order to ensure correct diagnosis and treatment,
- the need for doctors who treat insomnia to extend their knowledge on sleep-related respiratory disorders, so that they can be effectively detected.[10,57]

This association between insomnia and OSA is a good example of the interdisciplinary nature of sleep and its disorders. Undoubtedly, extensive knowledge on sleep, not limited to a specific area, is required of doctors who are to manage the insomnia/OSA association. Nevertheless, the issue of training and education in sleep medicine is controversial,[58] despite the obvious lack of information of many doctors who address sleep-related problems.[59,60]

Far from intending to cause controversy, exclusive and reductionist positions are not justified when tackling a problem that requires rigor and teamwork. For too long we have been unaware of the high frequency of complaints of insomnia and reduction in total sleep in the 24-h cycle in patients with OSA.

### Practice points

- Chronic insomnia complaints are very frequent among patients with sleep apnea.
- The presence of chronic insomnia in patients with sleep apnea is accompanied by high levels of depression, stress and other sleep disorders.
- The presence of insomnia may mask clinical presentation, especially in women, thus impeding adaptation to CPAP therapy.
- The relationship between sleep apnea and insomnia may not be a mere coincidence and, therefore, there may be causality interactions through an increase in HPA axis activity.

### Research agenda

In the future, we need to:

- Establish the definitive clinical criteria of insomnia and OSA, to facilitate methodologically uniform and reliable prevalence studies.
- Evaluate the negative impact of insomnia on the severity of OSA: AHI, cognitive disorders and difficulty of treatment.
- Evaluate the contribution of the different comorbidity factors (depression, RLS) to the development of insomnia in OSA.
- Gather information about the metabolic aspects of OSA and insomnia, in order to assess their involvement in the interaction between the two processes.

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