



## “To sleep”, “to cough” and “to love’: Uncommon primary headaches

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**Edited by:**  
Marcelo Moraes Valença

**Keywords:**  
Headache  
Sleep  
Cough  
Sexual activity  
Indomethacin  
Valsalva maneuver  
Precipitating factors

### Abstract

#### Introduction

There are some physiological situations in which the individual may experience headache, such as to sleep, to cough and to love. In the first situation, "to sleep", the patient does not have headache when awake, but is awakened by pain during sleep; in the second, the act of "to cough" is a trigger for the onset of pain and finally, "to love," here, meaning sexual intercourse, can be a headache trigger.

#### Objective

To review the epidemiological, pathophysiological aspects and therapeutic management of headaches that arise when sleeping, coughing and having sexual intercourse.

#### Method

A narrative review of literature including case reports and clinical trials were carried out. The articles were systematically obtained and assessed by the authors.

#### Results

Three primary forms considered rare were identified: hypnic headache, primary cough headache and primary headache associated with sexual activity. Hypnic headache occurs only during sleep, predominantly in women after 50 years of age. It was described in 1988 by Raskin, and has a prevalence ranging from 0.07% to 0.22%. Primary cough headache is triggered by coughing or another Valsalva maneuver and is more common in men over 40 years of age. It was first described by Jules Tinel and has a prevalence of 0.4% to 1.2%. Primary headache associated with sexual activity occurs during sexual intercourse. It is more frequent in men after 40 years of age. It was described in the second century of the Christian era, by the Persian physician Avicenna. Its prevalence ranges from 0.9% to 1.6%.

#### Conclusion

Primary headaches in the "to sleep", "to cough", and "to love" group are rare. They predominate in men, after 40 years of age, are of short duration, can be primary or secondary and have a therapeutic response to indomethacin.



## Introduction

There are some physiological situations in which the individual may experience headache, such as to sleep, to cough and to love. In the first situation, "to sleep", the patient does not have headache when awake, but is awakened by pain during sleep;<sup>1,2</sup> in the second, the act of "to cough" is a trigger for the onset of pain;<sup>3</sup> and finally, "to love," here, meaning sexual intercourse, can be a headache trigger.<sup>3</sup>

In ICHD-3, in the group of primary headaches, primary cough headache, primary headache associated with sexual activity and hypnic headache are described, with well-established diagnostic criteria.<sup>4</sup> Despite being called primary headaches, they can be secondary to other pathologies, requiring further investigation.

In this review, we will discuss these unusual forms of headache. Its diagnostic criteria, pathophysiology, differential diagnosis and treatment will be addressed.

### Headaches that occur during sleep

Some headaches occur during sleep or on awakening.<sup>5,6</sup> They are distributed into two groups, primary and secondary, as shown in Table 1.

**Table 1.** Distribution of headaches that occur during sleep

ICHD-3 code	Classification
	<b>Primary</b>
1.1	Nocturnal migraine
3.1	Cluster headache
3.2	Paroxysmal hemicrania
3.3	SUNCT and SUNA syndrome
3.4	Hemicrania continua
4.9	Hypnic headache
	<b>Secondary</b>
5.2	Persistent headache attributed to traumatic injury to the head
6.3	Headache attributed to unruptured vascular malformation
6.4.1	Headache attributed to giant cell arteritis
7.1.4	Headache attributed to intracranial hypertension secondary to hydrocephalus
7.4	Headache attributed to intracranial neoplasia
7.6.2	Post-ictal nocturnal headache
8.2	Medication-overuse headache
10.1.4	Sleep apnoea headache
10.3	Headache attributed to arterial hypertension
10.3.1	Headache attributed to pheochromocytoma
10.7	Headache attributed to other disorder of homeostasis (hypoglycemia)
12	Headache attributed to psychiatric disorder

The first group includes nocturnal migraine and the following trigeminal-autonomic headaches: cluster

headache, paroxysmal hemicranias short-lasting unilateral neuralgiform headache attacks with cranial autonomic injection and tearing (SUNCT) and hemicrania continua. These headaches have similarities in some symptoms and all have good therapeutic response to lithium carbonate.<sup>7</sup>

The second group contains the majority of nocturnal headaches. Among secondary headaches, there are headaches attributed to several causes, such as subdural hematoma, non-ruptured vascular malformation, giant cell arteritis, communicating hydrocephalus, intracranial neoplasia, post-ictal nocturnal headache, medication-overuse headache, sleep apnea headache, nocturnal arterial hypertension, pheochromocytoma, etc.<sup>1,5,8</sup>

Nocturnal migraine. In migraine patients, particularly without aura, headache attacks can occur at any time of the day, including during the night, after sleep onset or when waking up.<sup>9</sup>

**Nocturnal migraine** has not yet been sufficiently validated by scientific studies. However, the experts' experience suggests the existence of a primary headache that arises during sleep or upon awakening and fulfills diagnostic criteria for migraine without aura and not for other primary headaches.<sup>10</sup> Additional scientific evidence are still required for it to be formally accepted and included in the classification of headaches.<sup>10,11</sup>

Due to the use of lithium in cyclic evolution pathologies, Raffaelli started to test it in nocturnal migraine. These patients had an absolute therapeutic response to lithium carbonate, at a dose of 300 to 600 mg/day, in a single dose at night, as in the case of hypnic headache.<sup>11</sup>

**Trigeminal autonomic cephalalgias.** All of these in this group can occur during sleep and awaken the patient, the most studied being cluster headache, whose nocturnal crises range from 50% to 60%.<sup>12</sup> They are accompanied by autonomic manifestations and have specific treatments, such as cluster headache, which is responsive to oxygen and sumatriptan; and paroxysmal hemicrania and continuous hemicrania that is treated with indomethacin.<sup>4</sup>

**Hypnic headache.** This headache always occurs during sleep, causing the patient to wake up.<sup>4,13</sup> It is the real sleep headache. It is a rare primary recurrent headache with a prevalence ranging from 0.07% to 0.22%.<sup>1</sup> There is predominance in women (69% versus 31%) and characteristic of middle age and old age. There are no cranial autonomic symptoms or restlessness and responsiveness to lithium, at a dose of 300 mg to 600 mg, at bedtime.

Hypnic headache was first described by Raskin, in 1988.<sup>13</sup> This author published a series of cases that described a new



type of headache that affected elderly patients during sleep. In all patients, the headache resolved with the use of lithium carbonate.<sup>13</sup>

It is believed that there is a hypothalamic dysfunction, especially due to the decrease in the activity of the suprachiasmatic nucleus, which is the biological clock responsible for the circadian rhythm. This nucleus has a functional proximity to the raphe and pineal gland nuclei. As a result of the decrease in the activity of the suprachiasmatic nucleus, there is a decrease in the release of serotonin and melatonin. Decreased serotonin release leads to decreased modulation of the suprachiasmatic nucleus; and decreased melatonin secretion, leading to decreased modulation of nociceptive circuits. This pathophysiology explains why lithium improves hypnic headache. Lithium increases serotonergic neurotransmission in the hypothalamus and melatonin secretion.<sup>6,14-17</sup>

The successful treatment of hypnic headache, both abortifacient and prophylactic, is based on case reports or series, as no randomized clinical trial has been performed. Due to the short duration of pain, it is difficult to administer an abortive treatment. Despite this difficulty, some drugs have been tested, even in a few patients, and the results are not encouraging. The best responses were with caffeine, alone or associated with analgesics. Prophylactic treatment is based on the continuous use of drugs, before bed, to prevent the occurrence of headache attacks during sleep. Lithium is still the drug of choice.<sup>1</sup>

Secondary nocturnal headaches resolve with removal of the underlying cause and most have a diagnostic biomarker. Below, we will make brief comments about them.

Sleep apnea headache is characterized by occurring on awakening with duration of less than four hours. Its

diagnosis is made through polysomnography.<sup>4</sup> Headache attributed to giant cell arteritis appears at any time of day, but worsens during the night and is associated with other systemic clinical manifestations.<sup>18</sup> Usually, in patients with chronic subdural hematoma, the onset of headache is at night or upon awakening and worsens in the morning.<sup>19</sup> Headache attributed to intracranial neoplasia has characteristics of migraine or tension-type headache, but occurs at night or upon awakening in association with vomiting.<sup>20</sup> Patients with epileptic seizures during sleep may experience post-ictal nocturnal headache.<sup>4</sup> Headache is the main symptom of communicating hydrocephalus and is characterized by the daily occurrence, usually when waking up.<sup>21</sup> Headache attributed to pheochromocytoma occurs during the night or as soon as the patient wakes up.<sup>22</sup> There is a case report describing nocturnal headache in a patient with hypoglycemia.<sup>23</sup>

### Headaches that occur during coughing

Cough is a defense reflex of the airways under physiological conditions, but it can be part of the clinical picture of several pulmonary, cardiac and gastrointestinal diseases. There are three relationships between cough and headache: 1) Cough is associated with headache, for example, in pulmonary infectious conditions; 2) Cough can worsen headache, as in migraine; and 3) Rarely, cough can trigger headache attacks.<sup>4</sup>

Headache triggered by cough was first described in 1932 by the French physician Jules Tinel (1879-1952) and was considered an alarming symptom. In 1956, Charles Symonds (1890-1978) reported 21 patients with cough headache, without any intracranial lesion, now known as primary cough headache.<sup>24</sup> However, this headache can be primary or secondary.

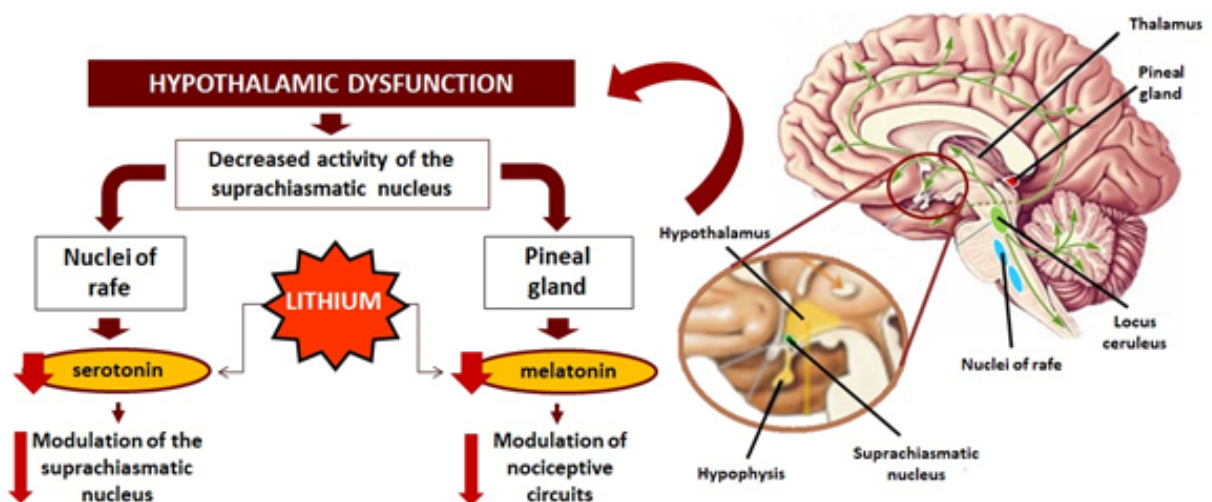


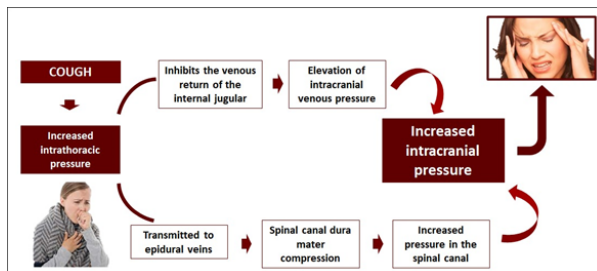
Figure 1. Pathophysiology of hypnic headache.



In the primary form, there is no intracranial lesion. It is a rare headache, occurring in 0.4% to 1.2% of the population.<sup>25-27</sup> It is more common in men after age 40. It is characterized by being bilateral, having a dull character and of moderate intensity. The onset of pain is sudden, lasting from one second to hours. It is caused by coughing or another Valsalva Maneuver.<sup>4</sup> Diagnosis of primary cough headache requires the absence of any other intracranial pathology.

The secondary form is much more frequent and is present in approximately 11% to 59% of the population. It is due to several neurological diseases, such as Chiari type I malformation, platibasia, chronic subdural hematoma, arachnoid cyst, dermoid tumor, and meningioma, among others.<sup>28</sup> The neuroimaging exam is essential for its diagnosis.

From a pathophysiological point of view, cough headache arises from increased intracranial pressure [Fig 2]. During coughing, there is an increase in intrathoracic pressure. Consequently, two situations occur: 1) inhibition of venous return from the internal jugular veins, causing an increase in intracranial venous pressure; and 2) the increase in intrathoracic pressure is transmitted to the epidural veins, leading to compression of the spinal canal dura mater, with increased pressure in the spinal canal. These two situations culminate in increased intracranial pressure, resulting in headache.<sup>29</sup>



**Figure 2.** Pathophysiology of primary cough headache.

Treatment of the secondary cough headache is by removing the underlying process. In primary cough headache, indomethacin is still the most consistent treatment. This drug was first used to treat cough headache in 1981 in a double blind, placebo-controlled study in patients resistant to other preventives. There was a therapeutic response between one and four weeks and the effect was sustained through 18 months of follow-up.<sup>30</sup>

The dose of indomethacin ranges from 25mg to 250 mg a day.<sup>30</sup> Other drugs such as acetazolamide and propranolol are cited.<sup>31,32</sup> Some studies report dural puncture and non-invasive vagus nerve stimulation as alternative treatments.<sup>25,33</sup>

Cough headache has a good prognosis, as it is a self-limited condition, lasting months to a few years. The therapeutic response occurs within a few weeks.

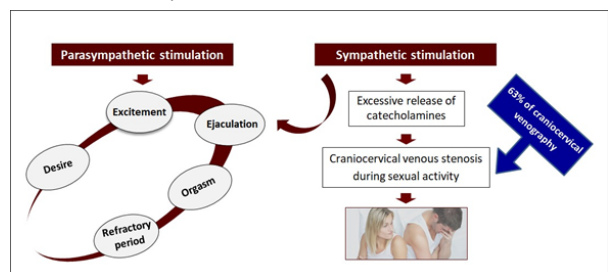
### Headache that occurs during sexual intercourse

“To love” can cause headaches. The expression “to love” here means sexual intercourse, either with another partner or during masturbation. This unusual headache was first described in the century II, after Christ, by the Persian physician Avicenna and is considered one of the oldest headaches.<sup>24</sup> It is classified as primary or secondary to an underlying process of other pathologies.

Diagnostic criteria for primary headache associated with sexual activity are described in ICHD-3. It only occurs during sexual activity. The onset of pain occurs with sexual excitement, it increases in intensity at the moment of orgasm, lasting from one minute to 24 hours.<sup>4</sup>

According to recent studies, primary headache associated with sexual activity predominates in middle-aged men and its prevalence ranges from 0.9% to 1.6%.<sup>34-36</sup> However, the true prevalence of this headache is not known, due to the scarcity of studies and difficulty for patients to express their symptoms out of embarrassment.

The pathophysiology of primary headache associated with sexual activity is unknown, but some authors believe that it is due to sympathetic activation.<sup>37</sup> In sexual physiology, there is participation of the sympathetic and parasympathetic autonomic nervous system [Fig. 3]. During arousal and erection there is parasympathetic activation; and in ejaculation and orgasm there is sympathetic activation. There is excessive release of catecholamines, leading to craniocervical venous stenosis during sexual activity, which would culminate in pain. This venous stenosis was seen in 63% of craniocervical venographies.<sup>38</sup> For this reason, sexual headache is responsive to beta-blockers.



**Figure 3.** Pathophysiology of primary headache associated with sexual activity.

Despite being considered a primary headache, all patients who present this headache must necessarily undergo neuroimaging tests to exclude secondary causes. It may be a symptom of an underlying process of intracranial pathologies. In the differential diagnosis, subarachnoid hemorrhage, rupture of cerebral aneurysm, cervical arterial dissection and arteriovenous malformation should be considered.<sup>3,37,39</sup>



After the onset of headache, the patient will need an acute treatment and the most used drugs are indomethacin and triptans.<sup>37,40</sup> There is also preemptive treatment, in which indomethacin is used 30-60 minutes before sexual activity. In 40% of patients, the pain resolves if the patient stops sexual activity before reaching orgasm.<sup>3</sup>

In prophylaxis, the most consistent treatment is beta-blockers, which are used in the same dose as for migraine prophylaxis. Prophylactic treatment is indicated when the patient has more lasting headache attacks and with a tendency for the disease to become chronic. Duration of treatment should be 3 to 6 months.<sup>37,41,42</sup>

## Conclusion

We conclude that primary headaches in the "to sleep", "to cough", and "to love" group are rare. They predominate in men, after 40 years of age, are of short duration, can be primary or secondary and have a therapeutic response to indomethacin

**Contribution authors:** All authors had the same contribution.

**Funding:** No.

**Conflict of interests:** The authors report no conflict of interest.

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