

## Study of the Impact of Chronic Sleep Disorders on the Immune System and its Diagnostic Criteria

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**Abstract:** According to WHO, every 3rd patient who consults a therapist complains of long-term (more than 1 month) problems falling asleep, daytime sleepiness, and frequent awakenings at night. This symptomatology indicates the development of a pathology such as chronic insomnia in a person.

Epidemiological studies have shown that people with sleep problems are at increased risk of developing immune and chronic inflammatory diseases. Since sleep disorders and poor sleep quality are common disorders in the general population, it seems important to recognize them as serious health problems. The exact relationship between immunity and sleep remains unclear; however, it can be assumed that it is formed due to the stress of others and changes in circadian rhythms (often due to, for example, shift work). Studies show that drugs used to treat chronic inflammatory diseases, such as steroids or monoclonal antibodies, have a more complex effect on sleep than those that occur when symptoms of the disease subside. Interestingly, the relationship between sleep and immunity appears to be bidirectional; that is, sleep may affect the course of immune diseases such as inflammatory bowel disease. Thus, proper diagnosis and treatment of sleep disorders are crucial for the patient's immune system and, indeed, health. This review reviews the epidemiology of sleep disorders and immune disorders, the associations between them, and their current treatment and new perspectives on therapy.

**Key points:** sleep, psychoneuroimmunology immunity, insomnia, obstructive sleep apnea, insomnia.

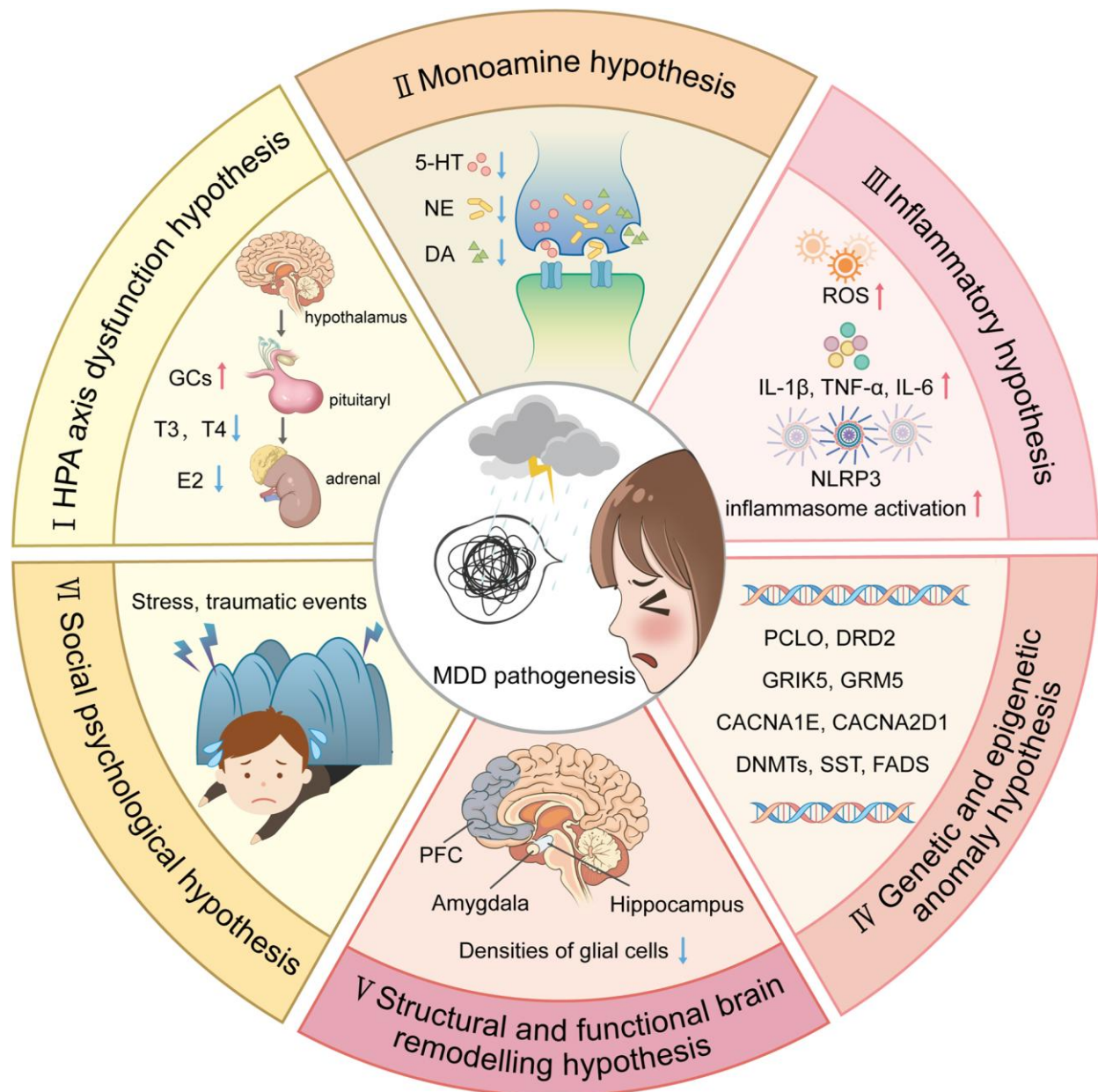
### Introduction

“Sleep disorder” is a term that encompasses a wide range of chronic disorders related to sleep and wakefulness. Several classifications are in use; the International Classification of Diseases, 11th edition, lists a group of disorders or syndromes such as hypersomnias, insomnia disorders, parasomnias, obstructive sleep apnea (OSA), and others [ 1 ]. Many socioeconomic determinants, such as income, employment, education, and marital status, are thought to influence the risk of sleep disorders [ 2 ]. Shift work, which is common in highly developed countries, is also associated with sleep disorders [ 3 ].

Changes in sleep schedules due to social and work demands may increase the prevalence of sleep disorders, which may increase the risk of developing diseases such as fibromyalgia, chronic fatigue syndrome, systemic lupus erythematosus (SLE), inflammatory bowel disease (IBD), or rheumatoid arthritis (RA) [4, 5].

The purpose of this narrative review is to summarize knowledge on the topic of possible links between sleep disorders and immune dysfunction, as well as to explore the pathophysiological basis of this relationship.

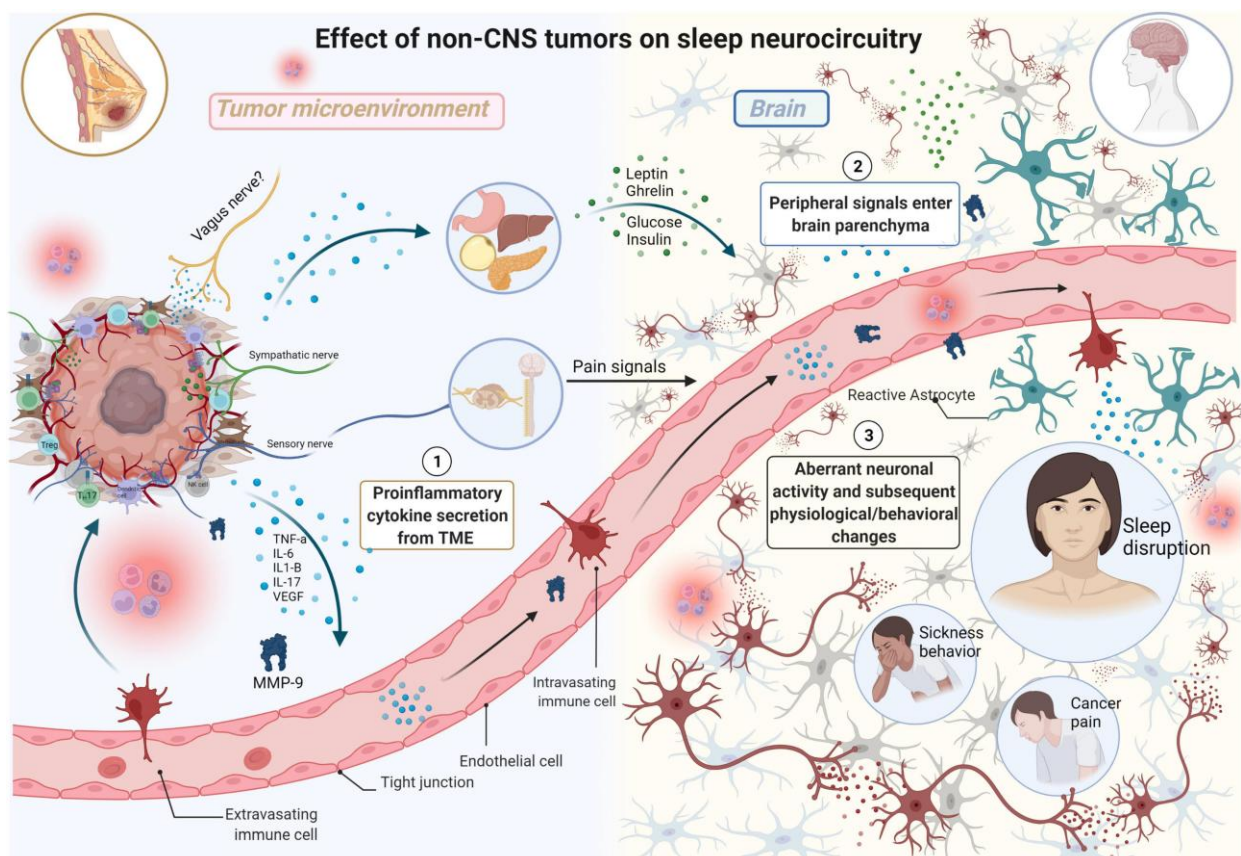
**Materials and methods of research.** Causes of chronic insomnia in women include problems with the cardiovascular system and urinary tract. Sometimes sleep disorders are diagnosed in people with mental disorders. These include not only diseases with a pronounced psychopathic clinical picture, but also phobic disorders, neurasthenia, etc.



Hormonal disorders, brain damage, gastrointestinal diseases, and dermatological pathologies can also cause sleep disorders. Sleep deprivation was associated with low levels of leptin, an appetite-suppressing hormone produced by adipose tissue, and high levels of ghrelin, an appetite-stimulating peptide ( Taheri et al., 2004 ). Another study - a small randomized, crossover clinical trial - also found that sleep restriction was associated with low leptin and high ghrelin levels ( Spiegel et al., 2004 ). The findings suggest that hormonally mediated increases in appetite may help explain why short sleep is associated with obesity. Several mediating mechanisms have been proposed, including the effect of sleep deprivation on the sympathetic nervous system and/or hypothalamic hormones (Spiegel et al., 2004), which also affect appetite. It is characterized by prolonged sleep deprivation. Despite the urgent need to rest, the person is unable to sleep for a long time if he or she is sleepy. On average, it takes 7 to 10 minutes to fall asleep. If sleep does not occur within this time, then we can talk about the first signs of insomnia. Usually the patient experiences this condition on the eve of an important event. When the excitement passes and the emotional background stabilizes, the problems with falling asleep disappear

**Results:** There is a dose-response relationship between sleep deprivation and obesity: the shorter the sleep, the greater the risk of obesity, usually measured by body mass index (BMI)—weight in kilograms divided by height in meters squared. While most studies have been cross-sectional, one prospective study was a 13-year cohort study of nearly 500 adults. By age 27, people with short sleep duration (less than 6 hours) were 7.5 times more likely to have a higher body mass index, after controlling for confounding factors such as family history, physical activity level, and demographic factors (Hasler et al., 2004). Another study, a large population-based study of over 1,000 adults, found a U-shaped relationship between sleep duration and BMI, as measured by polysomnography. Adults who slept 7.7 hours had the lowest BMI; those who slept shorter and longer had progressively higher BMIs. The U-shaped association also holds for other health outcomes, such as heart attacks. The effects of sleep deprivation diminish with age. The study also sought to explore the physiological mechanisms behind the link between sleep duration and BMI. By measuring two hormones associated with appetite, the study found that sleep deprivation increases appetite. Sleep deprivation was associated with lower levels of leptin, a hormone produced by adipose tissue that suppresses appetite, and higher levels of ghrelin, a peptide that stimulates appetite (Taheri et al., 2004). Another study—a small randomized, crossover clinical trial—also found that sleep restriction was associated with lower leptin and higher ghrelin levels (Spiegel et al., 2004). The findings suggest that hormonally mediated increases in appetite may help explain why short sleep is associated with obesity. Several mediating mechanisms have been proposed, including effects of sleep deprivation on the sympathetic nervous system and/or hypothalamic hormones (Spiegel et al., 2004), which also influence appetite.

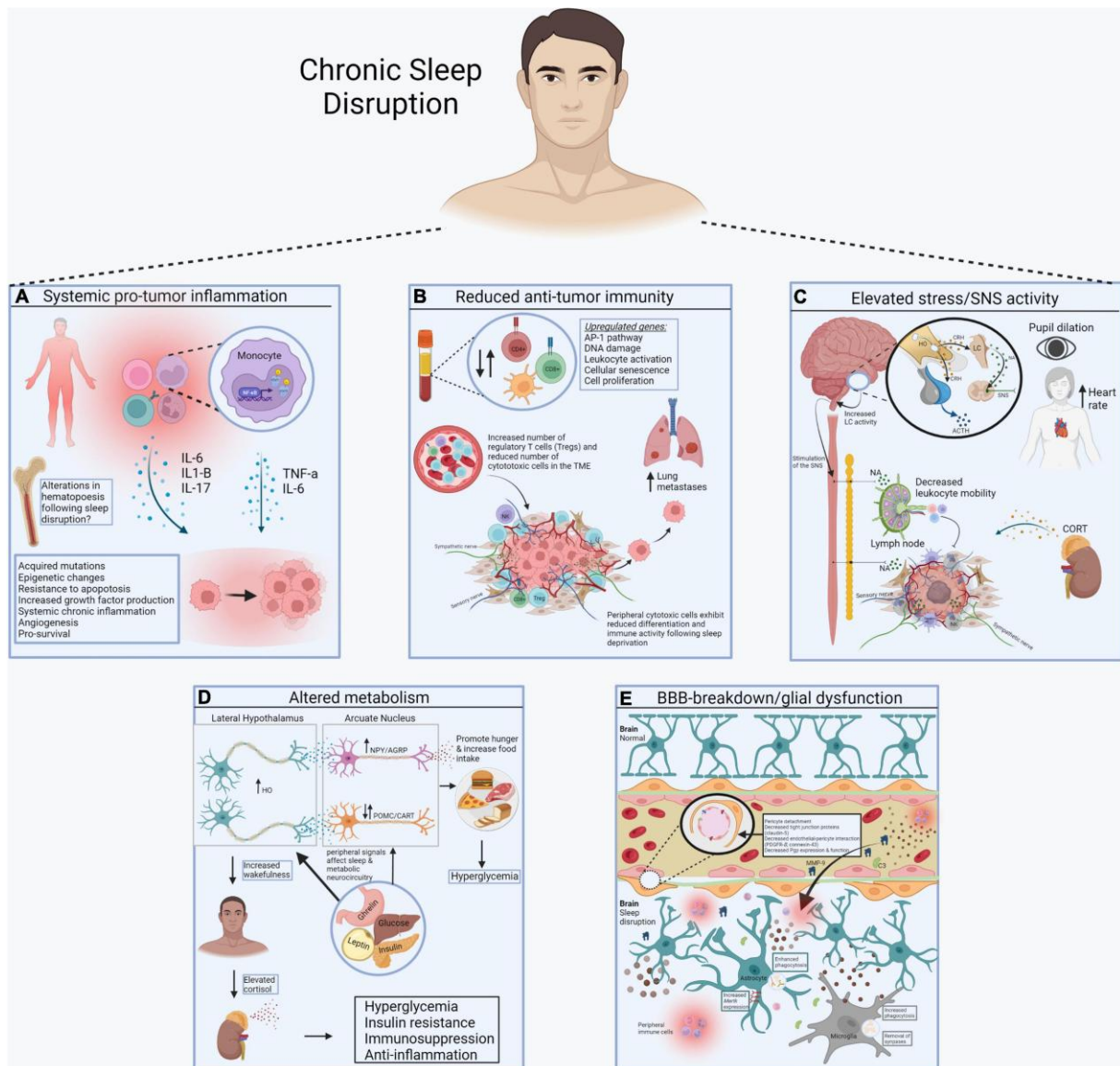
Night rest is very important for the body and is one of the main mechanisms for restoring vitality. In the moments of awakening, a person receives a huge amount of information through his external receptors. After falling asleep, they are “turned off” and the central nervous system “switches on” to analyze the information received. By the way, it is these processes that explain “prophetic” dreams. There is nothing abnormal in this phenomenon, it is simply the processing of information that a person may not have paid attention to during the day and its representation in the form of vivid images.



At night, the production of melatonin, which is responsible for regulating biological rhythms, is activated. This hormone also ensures uninterrupted metabolic and recovery processes. If melatonin is not synthesized in sufficient quantities, a person experiences serious health problems.

Sleep disorders occur for various reasons. Sometimes such a deviation is short-term, but if the pathology lasts for several months, then we are talking about the development of a disease such as chronic insomnia. Insomnia also includes sleep disorders that occur more than 3 times a week.

If you feel that your life or the lives of your loved ones are like running in a vicious circle: increased activity in the evening - problems falling asleep - shallow and intermittent sleep - difficulties waking up in the morning - daytime drowsiness, impaired concentration, you need to seek urgent medical attention, because there is a 95% chance that you have chronic insomnia.



### Certain categories of patients are at higher risk of developing the disease:

Women. Hormonal fluctuations during the menstrual cycle, as well as disruptions during menopause, increase the likelihood of anxiety conditions that interfere with normal sleep.

Individuals over 60 years of age. Age-related changes in sleep structure, an increased need for rest, concomitant pathologies of various pathogenesis, and the development of pain syndromes can lead to chronic insomnia.

People prone to psycho-emotional disorders. Many diseases, including depression and neurosis-like conditions, PTSD, bipolar disorder, can lead to problems falling asleep. Chronic insomnia and

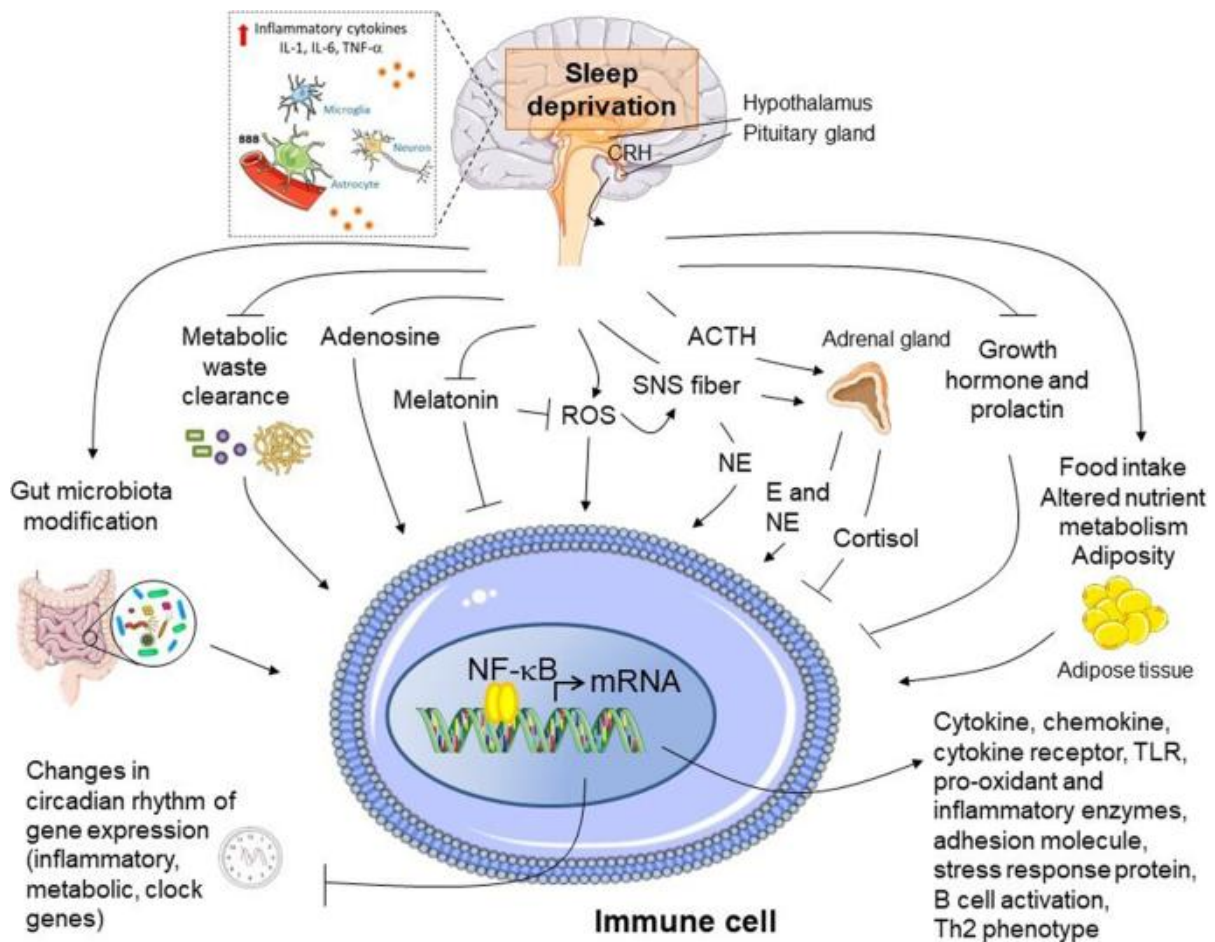
inability to fall asleep with very early awakenings (4-5 hours) are one of the main symptoms of depressive disorder.

Patients who are constantly under stress. Severe shocks, such as a serious illness or the death of a loved one, as well as other life problems, can cause temporary or chronic insomnia. Financial difficulties, increased intellectual or physical stress do not allow the body to fully rest and are risk factors for sleep disorders.

Individuals who work at night or on a rotating schedule. An unregulated workday with constant overtime keeps a person stressed for a long time. Chronic stress sooner or later leads to sleep problems.

## Symptoms

If you identify one or more of the symptoms on the list, you may suspect the development of chronic insomnia in yourself or your loved ones:



- waking up without an alarm clock (as a result, the night's rest time is significantly reduced, a person rests less than 6 hours);
- It takes at least 30 minutes to fall asleep;
- frequent awakenings at night (the total duration of the waking period is half an hour or more);
- severe drowsiness and fatigue during the day.

Over time, long-term sleep disorders lead to constant headaches. A person becomes irritable and emotionally unstable. If left untreated, apathy and depression develop, the patient does not want to do work or household chores, begins to be indifferent to his appearance and health.

## The main causes of chronic insomnia are:

- poor sleep hygiene (uncomfortable sleeping position or bed, uncomfortable temperature or lighting in the room);

- b. regular exposure to stress factors;
- c. increased physical or intellectual stress in the evening;
- d. noise (even if the patient assures that extraneous sounds are not distracting, such a background interferes with proper rest);
- e. change of time zones (acute insomnia occurs during a single long flight, which passes for some time without medical intervention, but regular trips sooner or later end in chronic insomnia);
- f. Constantly spending time on a personal computer, phone, tablet;
- g. abuse of caffeine and energy drinks.

Post-insomnia disorders. A sleep disorder characterized by painful awakening in the morning, even if a person has slept well all night. The main symptoms of chronic insomnia of the post-insomnia type: weakness in the morning, unwillingness to open your eyes after waking up, daytime drowsiness. Causes of the disorder: lack of vitamins and minerals, emotional stress, late bedtime.

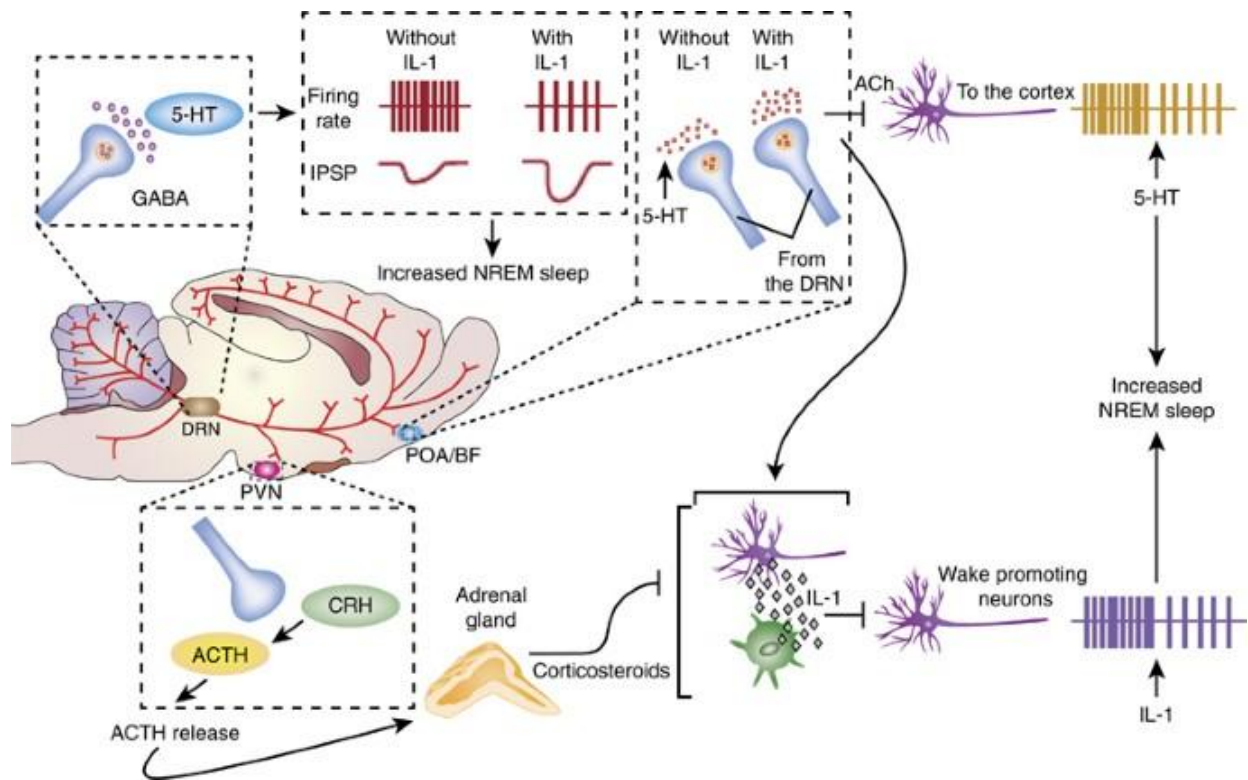
Intrasomnic disorders. The patient experiences insomnia after falling asleep, he suddenly wakes up at night and can no longer fall asleep. As a result, sleep is superficial and light (resembles sleep). The main causes of this type of insomnia are thyroid pathologies, high blood sugar, snoring, and mental disorders.

### **Complications of the disease**

The consequences of chronic insomnia are very dangerous for human health and negatively affect the quality of life. Without appropriate therapy, the patient may experience the following complications:

- a. memory problems;
- b. weakened immunity;
- c. malfunction of the digestive system (chronic sleep apnea sufferers are often diagnosed with colitis, stomach ulcers, and gastritis);
- d. neurological diseases;
- e. exacerbation of chronic pathologies;
- f. increased blood pressure;
- g. swelling;
- h. learning difficulties;
- i. pathologies of the cardiovascular system;
- j. endocrine diseases;
- k. psychoemotional disorders;
- l. decreased performance;
- m. fatigue.

With the development of chronic insomnia, the likelihood of gaining excess weight due to metabolic disorders increases. Due to an unbalanced diet and intolerance to physical exercise, it is very difficult for a person to get rid of the added weight. The patient has no strength left to play sports.



If you cannot fall asleep quickly, wake up often at night, your sleep is disturbed and disturbed even by minor irritants (dim light, quiet sounds), and during the day you experience severe drowsiness, pressure fluctuations, tachycardia, and headaches - seek urgent help from a specialist.

First, you need to undergo an examination by a therapist who will help determine the cause of insomnia and possible pathologies that may lead to the disorder. If necessary, the patient is additionally examined by a somnologist or psychotherapist (if depression is suspected).

Under no circumstances should you self-medicate by taking sleeping pills in large quantities or using other questionable methods.

By doing this, you will only exacerbate the problem, which will lead to a more difficult and longer recovery later.

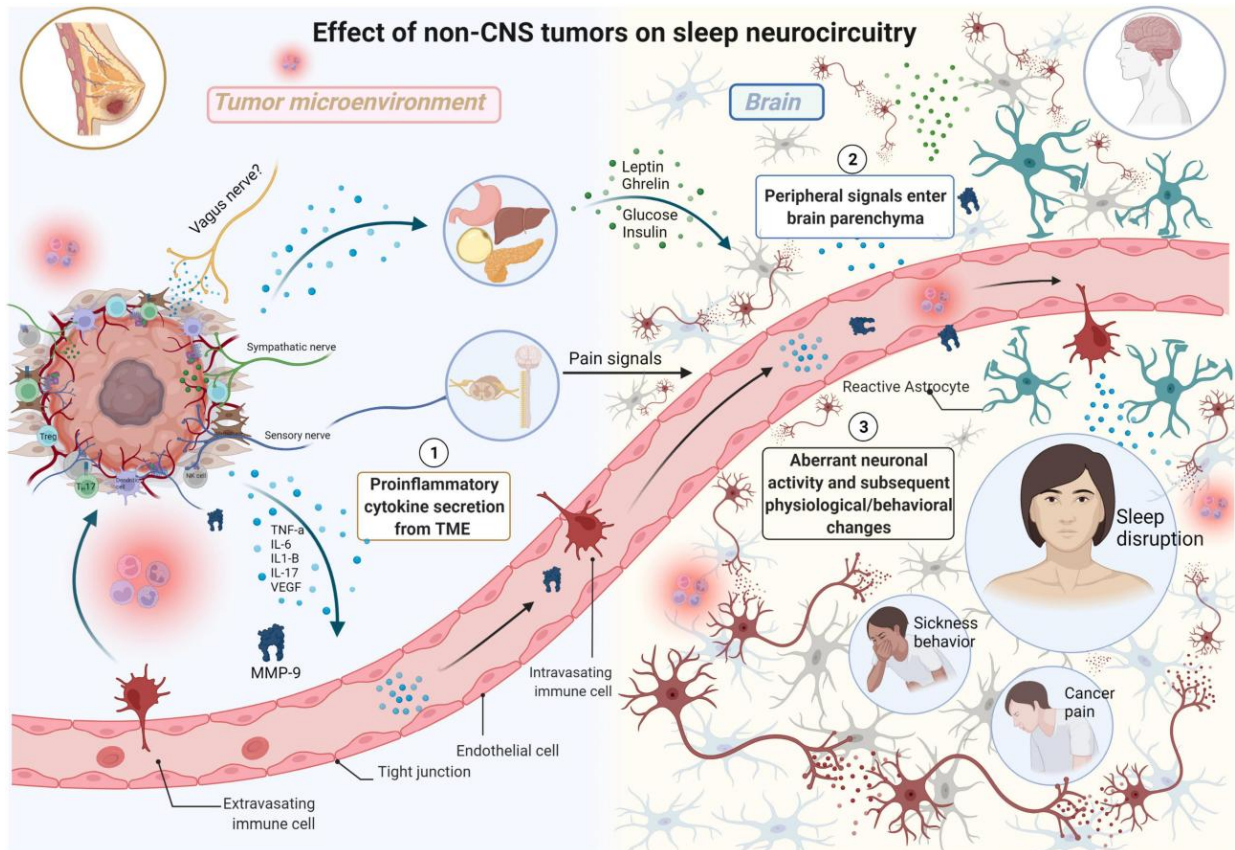
## Treatment

Treatment of chronic insomnia is usually done on an outpatient basis. A stay in the clinic is only recommended during a detailed diagnosis, which includes a polysomnographic examination, tests, and a questionnaire to rule out mental disorders.

Non-drug treatments (used in the absence of organic diseases) are often more effective than the use of drugs. The most common method of dealing with sleep disorders is cognitive behavioral psychotherapy. It focuses on:

- teach the patient the rules of sleep hygiene (following a pre-established routine, giving up the phone and tablet before bedtime, resting during the day);
- increase emotional resistance to stress;
- explaining the importance of proper rest (patients often sacrifice sleep for household chores or work);
- teaching relaxation techniques (helps relieve excessive arousal and anxiety).
- If psychotherapy does not have the expected effect, the patient is prescribed a course of pharmacotherapy. There are many drugs that have a strong sedative and hypnotic effect. Depending on the severity of the deviation, the following drugs are used:

- f. benzodiazepines (due to the high risk of developing addiction and the gradual weakening of the therapeutic effect, they are prescribed for a short period of time - a maximum of 20 days);
- g. non-benzodiazepine sleeping pills, antihistamines (have a symptomatic effect, do not affect the cause of the disorder);
- h. drugs containing artificially synthesized melatonin analogues (recommended for severe jet lag);
- i. herbal sedatives (prescribed for moderate anxiety, the drugs are 100% safe and do not cause drowsiness, can be taken simultaneously with a course of psychotherapy).



Treatment of chronic insomnia in adults requires a lot of time and effort. In order not to deal with a serious disorder later, it is necessary to think about preventing its development. Experts give several recommendations for the prevention of insomnia:

- a. ventilate the room before going to bed;
- b. be active during the day, try not to lie down even for a short rest;
- c. avoiding intellectual activity and discussing problems before going to bed;
- d. keep a routine and go to bed at the same time;
- e. Avoid drinking caffeinated and energy drinks;
- f. do not drink alcohol or strong tea before going to bed;
- g. eliminate unnecessary noise and light sources;
- h. follow a diet (don't go to bed hungry, but don't overeat);
- i. take a walk before going to bed;
- j. If you feel stressed, do breathing exercises.

The comfort of the bed is of great importance. The bed should be wide and comfortable. If you have back problems, then buy an orthopedic mattress instead of a regular one. The bed should not have

any foreign odors. If you still can't fall asleep within half an hour, get up and do something useful, for example, read a book or drink herbal tea.

**Conclusion:** Many studies show that the greater the level of sleep deprivation, the greater the apparent negative impact (although the difference is not statistically significant). Another common finding is that negative impacts are associated with shorter or longer sleep durations, compared with 7 to 8 hours of sleep. This type of association is often described as a U-shaped relationship. However, it is important to note that most of these studies are observational in nature and therefore cannot draw firm conclusions about cause and effect. The associations observed in some studies may be subject to various types of bias, such as temporal (or “reverse causality”) bias, in which sleep loss may be a manifestation or symptom of the underlying disease. The latter is most often found in cross-sectional studies, but can also affect associations observed in cohort studies, especially if they are relatively short-term and/or the disease under investigation has a long preclinical phase. The following discussion and, where possible, support the plausibility of potential physiological mechanisms behind epidemiological associations and actual causal relationships.

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