Narcolepsy, Narcolepsy Psychophysiology Sleep / Wakefulness Disorders and Medical Treatment of Narcolepsy and New Studies Light Orexin Sleep Studies Done on Top of Alertness on the Meta - Analysis

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ABSTRACT

We need to know in order to understand the sleep disorder narcolepsy, sleep and wakefulness, sleep, sleeping,"said Claperede on the body is a function of the strength of will automatically be delayed for a while, but when a higher level of fatigue would be defeated and the people succumb to sleep."

Protection of biological instinct as a condition of sleep and the body representing the De Sanctic A.Forel, O, and P Wogt Janet has a different interpretation, and finally a study of brain cells during sleep, shrinking cracks between neurons and thus the expansion of fluids through here allows the brain to cleanse, Research also is likely to lead to diseases of the brain in the direction of these toxic proteins opinions of arındırılamamasının say...

The main question that researchers are looking for answers , especially the vulnerable despite the drop were caused by animals slept. The largest effect on the brain's ability to repair, and memory, sleep learning is already known. But experts to sleep lightly "cleaning" function that thinks.

Due to the limited amount of energy that the brain can spend the researchers have to choose one of two functions: awake and aware, or in sleep and cleaning.

Keywords: Narcolepsy, Orexin

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Narcolepsy

Description

Physiological mechanisms of sleep and wakefulness to sleep in 1948-50 Dr.Magoun that the animal experiments, the brain stem centers (along the spinal cord) to the brain and central to the bulb starts Pons showed that the cell group is called the mixed cell group reticular Formation , Formation of reticular alertness providing the upper part of the autonomic nervous system, in that it comprises .

Reticular Formation is a barrier to reach the brain cortex is also eying live sleep by blocking the impulses from the outside, preserves sleep. If some of the important factors that affect sleep and wakefulness reticular Formation

• Instincts

• Vision, hearing, smell,

• Pain stimuli

• Adrenaline, noradrenaline secretion

Vary physiologically during sleep that the body provides the autonomic nervous system controls the autonomic nervous system, the endocrine glands and organs allows you take control of the autonomic nervous system, the parasympathetic centers for sleep and changes in the body is starting to fall asleep and starts to sleep .

• Eyes closed

• The pupils become smaller

• Muscles relax

• Slow heart rate

• Metabolism slows down

decreased rate of body fluids during sleep, body temperature, decreased heart rate and decreased the amount of breathing, physiological, and every day they live with the various periods of sleep phenomenon in which we live.

Sleep is quite complex, is a complex process. Day / night vigilance and life 1/3 thirds of the molecular mechanism of sleep Despite still sleep and sleep / wake regulation of, and research continues on there are unknowns.

Sleep / wake period , such as neurotransmitters, neuromodulators , and some are controlled by a complex network system . And acetylcholine in the brain monoamine systems may play a role in the regulation of sleep thinking of the relationship. As I mentioned above, an ongoing system for Spinal Cord began bulb .

In studies of narcolepsy , excessive daytime sleepiness, cataplexy and rapid eye movement sleep and is characterized by "chronic sleep disorder is defined as" disease, narcolepsy Orexin Narcolepsy is a sleep-wake cycle in patients with CSF orexin, a neuropeptide levels were too low to be detected. Orexin the emergence of the role of the sleep-wake cycle, sleep physiology research and new ideas and new ways of the instrument will benefit.90 % of people diagnosed with narcolepsy and cataplexy in orexin deficiency described in the story.

Orexin A and orexin B, pre-pro orexin gene is produced and newly discovered neuropeptide orexin are cells containing the lateral hypothalamus. OX1 and OX2 orexin receptor identified two after the discovery of OREXINS. The functional significance of the newly defined orexin system in animals and man are found out quickly. If abnormalities in the level of orexin dogs, humans and mice, caused by the narcolepsy indicated. The most important function OREXINS on regulation of normal sleep. Orexins sleep cycle, regulating the activity of the cholinergic and monoaminergic systems. Defined outside of sleep and pharmacological / neurochemical system that functions on the regulation of food intake, energy homeostasis, neuroendocrine and autonomic nervous system activity is by acting. Sleep,temporary loss of consciousness, especially the nervous sense of organic activities and the resulting reduction in voluntary muscle movements regular , temporary , periodic and psychophysiological condition. Endanger the lives of a variety of animals in research in many pathophysiological processes faced with sleepless Upon release seen, a lot of sleep and rest in the lives of animals has been demonstrated that the process (1,2). The most widely accepted model for the layout of the formation and neuroanatomical sleep; cholinergic (acetylcholine and so on.) And monoaminergic (serotonin, epinephrine, norepinephrine, dopamine, etc.). Inhibitory neurons containing relations between the two-sided model (1.3) .

Electrophysiological studies; sleep is not stagnant show that the process (1,2). sleep are five different periods: one, seizure each other every 90 minutes, followed by rapid eye movement (REM) period, and the other non- rapid eye movement (NREM) period. This is to include the definition of periods is done, sleep and wakefulness, "among the five sleep period" is said to be in the periodic transitions (4). As a symptom of sleep problems encountered in almost every disease. The contribution of the developing technology, and over the years the studies have led to significant " sleep medicine " is being collected under the title. When considering recent years, sleep disorders and disorders are classified in different tables described (4). This study will focus on the sleep disorder narcolepsy, which is one of the diseases and the orexin- 3 (75-83) 77 will be informed about the roles in this disease.

Narcolepsy

Narcolepsy: Occurring at any time of the day the irrepressible need to sleep with equally strong apparent illness, chronic sleep disorder known as the "narcolepsy" disease Westphal in 1877, while in 1880, was described by Gelineau. United States of America (USA) diagnosis in patients with Sleep.

Disorders According to the board, and this for three months, continue to have excessive daytime sleepiness, cataplexy story; Sleep paralysis; hipnagogik to the presence of hallucinations and fragmented sleep, which will be held with polysomnographic testing and HLA- DQB1 * 0602 genetic screening diagnosis. Narcolepsy in patients with recently diagnosed in these patients because of the low levels of orexin, orexin levels are put on by looking at (5,6). Cerebrospinal fluid (CSF) and not to the routine analysis of the orexin or plasma orexin Although they are not included in the diagnostic criteria , are considered to be a method that can be used in the diagnosis of narcolepsy (7-10).

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Prevalence and Incidence

Known as a symptom of the disease 0.74/100.000/yıl incidence of cataplexy associated with narcolepsy, narcolepsy without cataplexy in the incidence 1.37/100.000/yıl is. As a result of a meta- analysis study 25-50/100.000 stated that the prevalence of narcolepsy (11). In a study conducted in five European countries, the prevalence of the disease was found to be 47/100.000. According to his work within the confines of their own countries, the prevalence of the disease in Japan, 590/100.000, 1-40/100.000 Hong Kong , Italy, 40/100.000 , 40/100.000 in Saudi Arabia, Israel, as the 0.23/100.000 been determined (12).

Gender is an important factor in the incidence of the disease is not found in the same frequency in men and women (13). First symptoms adolescent term (15-25 years), 70% of the development rate of 80 (14,15). Stories from the 1940s that familial genetic predisposition to narcolepsy is intended for patients (13,16) . Narkolepsili number of patients with familial history of recent studies examined the rate of 4.3 % in Japan , the United States 6%, France 7.6%, Canada 9.9% was found (16).

Pathophysiology and etiology

Pathophysiology of the disease is not known as yet clear, but animal studies narcolepsy cholinergic and monoaminergic neurotransmitter systems may arise from the imbalance between specified. Descending monoaminergic tons, cholinergic hyperactivity and REM cholinergic abnormalities with hypersensitivity and therefore consists of insomnia (16,17).

Symptoms

Two major symptoms of narcolepsy, excessive daytime sleepiness (EDS) and cataplexy. Excessive daytime sleepiness: The patients to sleep during the day, depending usually takes two hours. Sleep, may take up to an hour or more, depending on environmental factors. Patients with REM sleep period. These sleep attacks during the day, talking while driving may or standing. Patients also experience sleep divisions, but it does not feel that they sleep in the process of sleeping 78 (18,19). EDS, is seen in 90 % of patients (2)

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Narcolepsy

Cataplexy: Emotional factors decrease the formation of muscle tone of the patients . Approximately 60 to 100 % of all patients, pediatric cataplexy observed in 80 % of cases 13,18,19). Other first- degree relatives and family studies narcolepsy cataplexy 10-40% more than those encountered (20). Kataplektic events has been reported that patients often either laughing or nervousness. Patients, cataplexy, light-headedness, aphasia, dizziness, defined as an inability to move the knees locked and arms (20,21). Other symptoms: Hipnagogik EDS and cataplexy in patients with symptoms such as hallucinations, as well as (sensory or visual), and sleep paralysis are observed.

Sleep paralysis of the arms, legs and head , such as shortness of breath , and even where there is an inability to move. 40-60% of patients Narcolepsy hypnagogic hallucinations, sleep paralysis is observed in the rate of 17-80 % (18,22). With all of these studies, patients showing symptoms of 15-25% were obtained (19).

If other symptoms in patients with cardiovascular disorders Narkolepsy. Waking autonomic nervous system dysfunction due to an increase in heart rate and blood pressure changes observed in hi- dungeon. Especially during the heart rate may increase the number of cataplexy reported (23). Guilleminault et al., In their study of patients with narcolepsy, a healthy night's sleep, the second and third periods in the control group did not change in blood pressure, but found that the increase in the number of heart beats during cataplexy (24).

Narkolepsy risk of occurrence of cardiovascular disease in a change in the level of the neuropeptide other than changes in energy homeostasis, would create a non-insulin dependent diabetes, obesity and develop the results (25).

Narcolepsy, is a disease affecting the safety and quality of life of patients, all the above as well as the physiological symptoms of psychological problems in patients was found to be (26,27) . Because of these problems concern the patients, to trust yourself, psychosocial problems, such as being referred to as lazy lives (28,29).

Treatment

Social activities in order to control the patient's symptoms, treatment becomes very important. If direct treatments, symptoms and / or frequency can be reduce. Modafinil, tricyclic antidepressants, SSRIs, MAO inhibitors, etc.). And other psychiatric include applications (30,31) .

Narkolepsy drug use at the beginning of treatment (methylphenidate) is a central nervous system stimulant drug called tasting medicine belonging to the class system and cortex activation by activating the brain stem is thought to exert its stimulant effect . Dose systemic availability due to extensive first-pass metabolism, but 30% (11-51 %) is the rapid and extensive biotransformation of methylphenidate. main metabolite, de-esterified, a-phenyl - 2 - piperidine acetic acid for about 2 hours after administration of methylphenidate in the plasma, the unchanged substance 30 - 50 times higher than those climax reaches concentrations. a-phenyl - 2 - piperidine acetic acid is approximately two times the half-life and mean systemic clearance half-life of methylphenidate, 0.17 L / h / kg.

Modafinil enhances wakefulness, alpha 1 - adrenergic agonist effects of modafinil center stimulation. Any receptors directly, though how different pharmacological properties of sympathomimetic amines such as amphetamine and methylphenidate had similar effects on alertness provider. In the studies, modafinil high-frequency delta and theta wave activity increases alpha waves and reduces mental excitement his effect was shown to be compatible with the overall increase .

Appropriate pharmacological concentrations of modafinil sleep / awake on the most effective receptors (noradrenaline, serotonin, dopamine, GABA, Adonazin ,histamine -3 ,melatonin, or benzodiazepine receptors included) connected. Also the activity of MAO-B and II-V does not inhibit fosfodiestaz .

Orexin

Locations Orexin about 1998, the beginning of the body, definition and two independent research groups, both in the dorsal and lateral hypothalamus neuronal hypothalamic neuropeptide described in perikarya. Orexin A and orexin B in about 1998, towards the end of these two neuropeptides is defined as the orphan G protein - matched previously known

(75-83) 79 receptors (GPCRs) are identified as the endogenous ligand and pre-pro orexin OREXINS than anywhere outside the OX1R (orexin receptor 1) and OX2R (orexin receptor 2), respectively. Closely related orphan G protein matched OX1R Orexins and OX2R'yi activate receptors (32-34). Orexins stimulate food intake in rats, animals were fasted for orexin mRNA hunger laid out and prepro orexin mRNA level in proportion to the rise in food consumption increased. All of these peptides within the framework of Greek "appetite", meaning "orexis" because the word was given the name orexin. Terminology for secretins hypothalamic hypocretin -gu settlement was thought to be similar (hypocretin) can be used as (32.35). Orexin A and orexin B is a single polypeptide pre-pro OREXINS leading breeds. Pre-pro orexin gene on chromosome 17q21 in humans are built. Orexin A 33 amino-acid, orexin B is a peptide of 28 amino acids. 46% of orexin A, orexin B is similar to the spelling of the amino acid (36). Kernels suprachiasmatic nusleus orexin receptors in humans, the pituitary gland and peripheral tissues (heart, liver, kidney, lung), but there are very few testes and intestine (37,38). Rat brain pre-pro orexin mRNA perifornikal , under the influence of the lateral and dorsal neurons in the hypothalamus (17,39). Nakabayashi et al-expiration study his performed-pro mRNA for orexin, kidney, adrenal gland, pancreas, placenta, stomach, ileum, colon and colorectal epithelial cells -ing was identified. This result also suggests that orexin A construction human peripheral tissues (40). Orexin endocrine cells in the pancreas were found to be clearly identified, but wherein functional importance (41). According to the orexin B, the orexin A greater amount of tissue and blood are (35). Orexin neurons are located in different regions of the brain. More lateral hypothalamus, perifornikal hypothalamus, the arcuate nucleus and paraventricular hypothalamic nucleus and outside of it, in the cerebral cortex, the thalamus medial structures of the limbic system and the brain stem seen in (8). Orexin neurons in the brain regions where damage or neurodegenerative diseases (Huntington 's disease, Guillain-Barre syndrome, Parkinson's disease, etc.) may result in the loss of these neurons (8,42).

On the Functions of Sleep and Sleep Disorders Orexin

Locus koreuleus, tuberomamiler kernel, the core of the sleep- wake cycle dorsotegmental pontine and lateral parts of the orexin - IR nerve fibers in the brain during sleep are effective OREXINS see (34). Espana et al. by Huang et al., the lateral ventricle of rats by short-term infusion of orexin electroencephalographic (EEG) and electromyographic (EMG) changes identified increased wakefulness, work - ing as a result of their location in the brain OREXINS reported as affected by psychiatric and neurological disorders (43,44).The transition to REM sleep to wakefulness with orexin neurons active, deep sleep, Narcolepsy and Orexins experiencing a more Lancelot 2002

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Active at 80 (45.46). Martinez ark.rats their study and have high levels throughout the day than during the night and wakefulness orexin oreksinin oscillation found that release less (47). Neuromodulator orexin system sleep / wake activity of the cholinergic system in order, that is associated with monoaminergic systems and controls. Orexin studies (particularly orexin A) injection in some parts of the brain monoaminergic neurons in rats was found to increase the rate. Monoaminergic tone signals, a decrease in loss of orexin, so the sleep / wake cycle was caused by a change (48-52). Chronic disease, narcolepsy, sleep disorder narcolepsy Orexins Various studies have shown the possible roles of oreksinin pathology (8,53). Compared to healthy subjects, 85% of patients narkolepsili - 95 reported that less than 93% of orexin neurons (54-56). Due to loss of orexin neurons in patients with Nishino his

studies that the decrease in orexin A, but the type of doberman dogs narkolepsili that there was a genetically orexin neuron degeneration (32). Molecular genetic studies conducted on mice and dogs, and humans as a result of the histopathological analysis narkolepsili plasma and CSF of patients with low levels of orexin A, orexin and / or orexin receptors may cause incapacity narcolepsy reported (17.57 to 59). Pre -pro orexin deficiency narcolepsy generated in mice similar to human behavioral tendencies, sleep / wake disorders, and orexin deficiency is observed period (17,46). OX2R'yi caused by a mutation of the gene encoding " type of canine narcolepsy " in 1973-1974 identified patients (16,38,46). Narcolepsy in dogs and humans later in the " canine " is not related narkolepsy orexin A was found to ocur incapacity . Subsequent comes to the environmental factors in patients with narcolepsy have been reported. Studies of psychological stress, irregular sleep time and sleep time , sleep / wake process of change, divorce, accident, disease, and environmental factors such as pregnancy has accelerated the emergence of the disease in people (16,53). Landing, that environmental factors influence disease in monozygotic twins is seen in 25% of the disease in 31 understands that the only one of the twins (13,16,59) .

Narkolepsy patients due to environmental factors or other than the creation of genetically orexin deficiency that the inflammation may lead to loss of orexin neurons showed a study by Gerashchenko and Shiromani (60). In this study on a regular basis for 30 days hypothalamus lipopolysaccharide in rats infused lateral and lateral hypothalamic orexin levels 30 days after the decrease was 29.7%.

Narkolepsy orexin deficiency occurring in patients as a result of all these reasons, patients with cholinergic hyperactivity, so cataplexy, sleep paralysis and hallucinations are hipnagogik. Dopaminergic hypoactivity in the patients with excessive daytime sleeping and behavioral disorders (75-83) 81 is observed (61). All these results clearly indicate the role of narcolepsy OREXINS .

CONCLUSION AND RECOMMENDATIONS

In our country, the prevalence of narcolepsy is not known how high or low it is a very good reason why a growing number of sleep clinics is still very low due to the fact. This data can be included among the health policies of our country and one of the issues that must be addressed, and there is also increasing the number of sleep laboratories should be improved in terms of the system shows that those who are. Ignoring the socio- economic problems of the patients, as well as a lack of sleep, I often sleep in the "nap" as a central place for the detection and diagnosis of knowledge and / or lack of possibility to go to these centers to place in our country makes it difficult to diagnose the disease.

Which is a chronic sleep disorder narcolepsy just "take a nap" for the disease to know whether GPs, specialist doctors and all health workers of other branches of the health community awareness and traffic next to the driver's license examination, a standard procurement system health checks , and traffic police should be added to such a disease may be due to this reason many good teaching to avoid the fatal accident will be life saving and safety brochures about the community and the public hospitals are prepared and / or distributed within the reach of people, yet informative newspaper articles and articles written about the disease, television / radio programs, and to diagnosis of the places recommended to be placed centers. In this way, a society informed at the first appearance of symptoms and diagnosis is understood that the sleep disorder narcolepsy, a simple thought to be easier.

Should be based on a multidisciplinary approach to treating patients with sleep disorders such as narcolepsy. This subject matter expert doctors, psychologists, nurses, social workers and dietitians work in cooperation for the treatment of diseases. Treatment of narcolepsy should be increased on future work. Orexin cell transplant to treat patients in the future, gene therapy and pharmacological agents should be considered a short-term and low- dose injection of orexin.

This is to be made for the development of treatment methods and a detailed long-term studies will, in practice, it will take time to obtain results.

Remembered that patients with low levels of plasma and CSF orexin low levels Narcolepsy to do, other recent studies related to the neuropeptide orexin, hormones, amino acids and fatty acids in the analysis of the different dimensions of the disease will be important.

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