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BREATHING DISORDERS DURING SLEEP

National Institutes of Health
National Heart, Lung, and Blood Institute

"You Can Snore Your Life Away."

This sounds more like a joke than a warning. But, in fact, habitual loud snoring is the most common symptom of breathing disorders that occur during sleep. The person who snores not only sleeps restlessly, but also is at risk for serious disorders of the heart and lungs. Snoring can therefore be lifethreatening because it can lead to high blood pressure, irregular heart beats, heart attacks, and sudden death.

Normal breathing must continue at all times whether awake or asleep. The act of breathing is an automatic, highly regulated mechanical function of the body. In healthy sleeping individuals, most muscular and neural activities will slow or even shut down but respiration goes on under a neuromuscular "auto pilot." However, if something goes wrong with the auto pilot during sleep, breathing may become erratic and inefficient.

Understanding Sleep

Sleep is a complex neurological state. Its primary function is rest and restoring the body's energy levels. Repeated interruption of sleep by breathing abnormalities such as cessation of breathing (apnea) or heavy snoring, leads to fragmented sleep and abnormal oxygen and carbon dioxide levels in the blood. Excessive daytime sleepiness and various disorders of the heart, lungs, and the nervous system result.

In the 1950's scientists realized that sleep is not just a quiet state of rest. In fact, two stages of sleep occur with distinct physiological patterns-rapid-eye-movement sleep (REM), and non rapid-eye-movement sleep (NREM) or deep sleep. In normal sleep, REM occurs about 90 minutes after a person falls asleep. The two sleep stages recur in cycles of about 90 minutes each, with three non-REM stages (light to deep slumber) at the beginning and REM towards the end. The amount of sleep needed by each person is usually constant although there is a wide variation among individuals.

How sleep occurs and how it restores the body are not well understood. Scientists originally believed that sleep occurs because the brain lapses into a passive resting state from lack of stimulation. Another theory proposed that sleep occurs when the body generates and accumulates sufficient amounts of a "sleep-inducing substance." However, research now suggests that sleep results when specific changes in brain function occur. By studying brain waves, scientists can define and measure various degrees, levels, and stages of sleep.

Sleep consists of a rhythmic combination of changes in physiological, biochemical, neurophysiological and psychological processes. When the rhythm is disturbed or the individual processes are abnormal during sleep, a variety of sleep-related disorders may result.

Sleep-Related Disorders

Sleep-related complaints appeared regularly in medical literature in the beginning of the 19th century. However, from 1900 to the mid-1960s little was published in scientific journals about the "sleepy patient" except for an occasional report on the normal or abnormal aspects of sleep physiology. Recent developments of research techniques in neurobiology, molecular biology, molecular genetics, physiology, neuropsychiatry, internal medicine, pulmonary medicine, and cardiology have allowed scientists to study the details of sleep. As a result, there has been an explosion in interest in understanding sleep and "sleep disorders."

Some sleep-related disturbances are simply temporary inconveniences while others are potentially more serious. Sleep apnea is the major respiratory disorder of sleep. Other serious sleep-related disorders are narcolepsy and clinical insomnia. "Jet lag syndrome,"

caused by rapid shifts in the biological sleep-wake cycle, is also an example of a temporary sleep-related disorder. So are the sleep problems experienced by shift workers. Sleep apnea is the condition of interrupted breathing while asleep. "Apnea" is a Greek word meaning "want of breath." Clinically, sleep apnea, first described in 1965, means cessation of breathing during sleep.

Narcolepsy is a neurological disorder whose main symptoms in uncontrollable, excessive sleep, regardless of the time of day or whether the person has had enough sleep during the previous night. The other features of this disorder can include brief episodes of muscle weakness or paralysis caused by laughter and anger (cataplexy), paralysis for brief periods upon awakening from sleep (sleep paralysis), and dreamlike images at sleep onset (hypnagogic hallucination). Narcolepsy, which may affect several members of the same family, is a life-long condition. Medications help to reduce the symptoms but do not cure the disease.

Insomnia is the commonly experienced difficulty in falling asleep, remaining asleep throughout the night, and the inability to return to sleep once awakened. Its causes may be physical or psychological and it may occur regularly or only occasionally.

Even a partial list of all the disorders caused by or associated with disturbed sleep adds up to some 70 items. The costs to society due to loss of productivity, industrial accidents and medical bills are estimated to be over $60 billion. These staggering statistics led to the creation by the U.S. Congress in 1988 of a National Commission of Sleep Disorders Research. This group is charged with task of developing a blueprint for a national effort to reduce the medical and economic consequences of sleep disorders.

Likely Candidates for Sleep-Related Disorders

Some of the people most likely to have or to develop a sleep-related disorder include:

- adults who fall asleep at inappropriate times and places (e.g., during conversation, lecturing, driving) and who exhibit nighttime snoring
- elderly men and women
- postmenopausal women
- people who are overweight, or have some physical abnormality in the nose, throat, or other parts of the upper airway
- night-shift workers
- people who habitually drink too much alcohol
- blind individuals who tend to develop impaired perception of light and darkness and have disturbed circadian rhythms, the cycles of biologic activities that occur at the same time during each 24 hours
- people with depression and other psychotic disorders.

Sleep and Breathing Disorders

In 1944, the important observation was made that ventilation (exchange of air between the lung and environment) normally decreases during sleep. Even in "normal" people, breathing patterns during sleep may show a few irregularities. For example, a person might experience an average of seven breathing pauses of up to 10 seconds per night without any associated symptoms or problems. However if the breathing irregularities are accompanied by reduced oxygen supply to tissue (hypoxia) and repeated loss of sleep, these people are at risk of developing more serious problems.

Sleep Apnea

Sleep apnea is the most common sleep disorder in terms of mortality and morbidity, especially in middle-age men. Perhaps the best known sleep apnea "patient" is Charles Dickens' Fat Joe in The Posthumous Papers of the Pickwick Club, the overweight, red-faced boy in a permanent state of sleepiness, who snored and breathed heavily. The term "Pickwickian" syndrome is now used to describe patients with the most severe form of sleep apnea that is associated with reduced levels of breathing even during the day.

Sleep apnea occurs in all age groups and both sexes, but seems to predominate in males (it may be underdiagnosed in females) and in African Americans. The Association of Professional Sleep Societies estimates that as many as 20 million Americans have this condition. The conditions associated with sleep apnea are a cascade: apnea, arousal, sleep deprivation, and excessive daytime sleepiness. Each is related to the frequency of the prior condition.

Like obesity with which it is often associated, the clustering of sleep apnea in some families suggests a genetic abnormality. Ingestion of alcohol and sleeping pills increases the frequency and duration of breathing pauses during sleep in people with or without sleep apnea.

Because of serious disturbances in their normal sleep patterns, patients with sleep apnea feel sleepy during the day and their concentration and daytime performance suffer. The common consequences of sleep apnea range from annoying to life-threatening. They include personality changes, sexual dysfunction and falling asleep at work, on the phone,

or driving.

Symptoms of Sleep Apnea

Patients with sleep apnea have many repeated involuntary breathing pauses during sleep. The length of the breathing pause can vary within a patient, and among patients, and can last for 10 seconds to 60 seconds. Fewer than 30 such breathing pauses during a 7-hour sleep, or shorter breathing pauses, are not considered indicative of sleep apnea. Most sleep apnea patients experience 20 to 30 "apneic events" per hour, more than 200 per night. These pauses may occur in clusters.

The breathing pauses are often accompanied by choking sensations which may wake up the patient, intermittent snoring, nighttime insomnia, early morning headaches, and excessive daytime sleepiness, although not all patients, for some reason, complain of daytime sleepiness. During the apneic events, a person may turn blue from low blood oxygen levels.

Other features of sleep apnea include slowing down of heart beat below 60 beats per minute (bradycardia), irregular heart beat (cardiac arrhythmias), high blood pressure (both systemic and pulmonary arterial), increase in red cells in the blood (polycythemia), and obesity. The absence of restful sleep may cause deterioration of performance, depression, irritability, sexual dysfunction, and defects in attention and concentration.

Types of Sleep Apnea

Scientists have distinguished three types of sleep apnea: obstructive, central, and mixed. However, since all three types can have the same symptoms and signs, a sleep evaluation is needed to tell the difference among them.

Obstructive Sleep Apnea (OSA) is the most common type. During OSA efforts to breath continue but air cannot flow out of the patient's nose or mouth. The patient snores heavily and has frequent arousals (abrupt changes from deep sleep to light sleep) without being aware of them.

OSA occurs when the throat muscles and tongue relax during breathing and partially block the opening of the airway. When the muscles of the soft palate at the base of the tongue and the uvula (the small conical fleshy tissue hanging from the center of the soft palate) relax and say, the airway becomes obstructed marking breathing labored and noisy. Airway narrowing may also occur due to overweigh, possibly because of the associated increases in the amount of tissue in the airway.

The reduction in oxygen and increase in carbon dioxide which occur during apnea cause arousals. With each arousal, a signal is sent to the upper airway muscles to open the airway; breathing is resumed with a loud snort or gasp. Although arousals serve as a rescue mechanism and are necessary for a patient with apnea, they interrupt sleep, and the patient ends up with less restorative and sleep than normal individuals.

Central Apnea occurs less frequently than obstructive apnea. There is no airflow in or out of the airways because efforts to breathe have stopped for short periods of time. In central apnea, the brain temporarily fails to send the signals to the diaphragm and the chest muscles that maintain the breathing cycle. It is present more often in the elderly than in younger people but often goes unrecognized.

In central apnea, there is periodic loss of rhythmic breathing movements. The airways remain open but air dose not pass through the nose or mouth because activity of the diaphragm and the chest muscles stops. Patients with central apnea may not snore and they tend to be more aware of their frequent awakenings than those with obstructive apnea.

In Mixed Apnea, a period of central apnea is followed by a period of obstructive apnea before regular breathing resumes. People with mixed apnea frequently snore.

Snoring and Sleep Apnea

Snoring is a sign of abnormal breathing. It occurs when physical obstruction causes fluttering of the soft palate and the adjacent soft tissues between the mouth, external orifices of the nose (nares), the upper part of the windpipe (trachea), and the passage extending from the pharynx to the stomach (esophagus).

Snoring always occurs with obstructive sleep apnea. When diagnosing sleep disorders, obstructive sleep apnea is excluded if snoring is not a symptom. All snorers do not necessarily have sleep apnea; however, because they almost certainly have some physical obstruction in their airways, they may develop sleep apnea.

The prevalence of snoring is greater in the older population and apparently peaks in 60-year-old men and women, declining in older individuals. Men seem to snore more than women. Men also are more likely to develop sleep-disordered breathing. It is estimated that nearly half of all males over 40 snore habitually. Snoring is also more common in overweight people.

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A visit to the doctor is not necessary when a person snores unless some of the other symptoms of sleep disordered breathing also occur. However, since snoring is an annoying or irritating symptom with some negative social aspects, many people have sought a "cure" for it. More than 300 devices have been patented in the U.S. which claim to control snoring. Many of these devices were developed even before medical scientists found out that heavy snoring is a potential marker of sleep apnea.

Sleep Apnea and the Heart

Sleep apnea and snoring seems to increase the likelihood of having a variety of cardiovascular diseases. These include high blood pressure, ischemic heart disease (a condition caused by reduced blood supply to the heart muscle), cardiac arrhythmias (abnormal heartbeat rhythm), and cerebral infarction (blood clot in the brain). It is not unusual for patients with sleep apnea to be mistakenly treated for primary heart disease because cardiac arrhythmias may be more prominent than the breathing disturbances.

Nearly 50 percent of sleep apnea patients have high blood pressure. Patients with the most severe sleep apnea seem to have the highest blood pressure levels and are also more likely to have trouble controlling their blood pressure than patients who do not have sleep apnea. No one knows whether a cause and effect relationship exists between high blood pressure and sleep apnea. If it does exist, the ways these conditions interact is unknown.

Snoring alone does not appear to be a risk factor for heart disease. Only when snoring occurs with sleep apnea or obesity does it seem to be associated with these conditions.

Sleep Apnea in Infants

Before a baby is born, the mother's breathing takes care of its respiratory needs. Although the unborn baby's lings are filled with fluid and are not ready to take in air, its respiratory muscles make breathing motions, as if "training" to take on the responsibilities of breathing after birth.

As soon as birth occurs, the normal newborn baby begins a continuous pattern of periodic breathing characterized by a succession of apneas followed by regular breathing. Apneas occasionally lasting longer than 10 to 15 seconds are common during the newborn period. Apneas are more frequent and longer in premature newborns than in full-term infants. The frequency of apnea decreases with age during the first 6 months of life.

Babies turn blue during sleep and appear limp may be undergoing episodes of insufficient breathing. They should be checked for a sleep-related disorder.

Sleep Apnea and Sudden Infant Death Syndrome

Sleep apnea is sometimes implicated in sudden infant death syndrome (SIDS), also called crib death. About 10,000 infants die every year in this country for SIDS. Scientists do not know the reasons for these deaths but sleep apnea may play a role because these babies die when they are asleep and show no evidence of trauma. On autopsy, pinpoint hemorrhages are sometimes noted in the thoracic cavity which may be caused by lack of oxygen prior to cardiac arrest and vigorous respiratory movements.

Diagnosis of Sleep Apnea

The general physician may sometimes recognize sleep apnea, but specialists in neurology, psychiatry, pulmonary medicine and cardiology may be needed for accurate diagnosis and management. Diagnosis of sleep apnea is difficult because disturbed sleep can cause various other diseases or make them worse. Several major medical centers now have pulmonologists, neurologists, and psychiatrists with specialty training in sleep disorders on their staff. Although an evaluation for sleep apnea can sometimes be done at home, it is more reliable if it is done in a sleep laboratory.

A variety of tests can be used to diagnose sleep apnea. These include pulmonary function tests, polysomnography, and the multiple sleep latency test. Physicians continue to try to develop other simple and economic procedures for the early diagnosis of sleep apnea.

Pulmonary function tests taken by sleep apnea patients may show normal results unless the patient has a coexisting lung disease. To make a definitive diagnosis of sleep apnea, the physician may order an all-night evaluation of the patient's sleep stages, and of the status of breathing and gas exchange during sleep.

Polysomnography is a group of tests that monitors a variety of functions during sleep. These include sleep state, electrical activity of the brain (EEG), eye movement (EOG), muscle activity (EMG), heart rate, respiratory effort, airflow, blood oxygen and carbon dioxide levels. Other tests may be ordered depending on a particular patient's needs. Polysomnography sometimes helps to distinguish between different sleep disorders. These test are used both to diagnose sleep apnea and to determine it severity.

The Multiple Sleep Latency Test is done during normal working hours. It consists of

observations, repeated every 2 hours, of the time taken to reach various stages of sleep. In this test, people without sleep apnea take more than 10 minutes to fall asleep. On the other hand, patients with sleep apnea or narcolepsy fall asleep fairly rapidly. When it takes the patient an average of less than 5 minutes to fall asleep, it is considered pathological sleepiness. There is thus some uncertainty in the diagnosis if the sleep latency period (speed of falling asleep) is between 5 and 10 minutes. This test is important because it measures the degree of excessive daytime sleepiness and also helps to rule out narcolepsy, which is associated with onset of REM sleep (dream sleep) in many of the naps.

Treatment of Sleep Apnea

More than 50,000 patients are treated each year for breathing disorders of sleep. Physicians tailor therapy to the individual patient based on medical history, physical examination, and the results of laboratory tests and polysomnography.

Patients with sleep apnea can help themselves by trying avoid doing anything that can worsen the disease. Sleeping in improper positions can increase the frequency of apnea. Use of alcohol suppresses the activity of the upper airway muscles so that the airway is more likely to collapse. Sleeping pills and sedativehypnotic drugs suppress arousal mechanisms and prolong apneas. Moving to high altitudes may aggravate the condition because of low oxygen levels. Overweight sleep apnea patients should lose weight.

Because the exact mechanism responsible for obstructive sleep apnea is not known, there is still no treatment that directly addresses the underlying problem. In most cases, medications have not proved successful. Surgical procedures are effective only 50 percent of the time because the exact location of the airway obstruction is usually unclear.

Since patients with sleep apnea usually have significant family and work problems, the treatment should include strategies that will help them cope with these problems. Education of the patient, family, and employers is sometimes needed to help the patient return to an active normal life.

Position Therapy

In mild cases of sleep apnea, breathing pauses occur only when the individual sleeps on the back. Thus using methods that will ensure that patients sleep on their side is often helpful.

Nasal Continuous Positive Airway Pressure (CPAP)

CPAP is the most common effective treatment for sleep apnea. In this procedure, the patient wears a mask or a pillow over the nose during sleep and pressure from an air compressor forces air through the nasal passages. The air pressure is adjusted so that it is just enough to hold the throat open when it relaxes the most. The pressure is constant and continuous. Nasal CPAP prevents obstruction while in use but apneas return when CPAP is stopped.

The major disadvantage of CPAP is that about 40 percent of patients have difficulty using it for long periods of time. Irritation and drying in the nose occur in some patients. Facial skin irritation, abdominal bloating, mask leaks, sore eyes, and headaches are some of the other problems. Because many patients stop using nasal CPAP due to the discomfort arising form exhaling against positive pressure, the search goes on for more comfortable devices. Modifications of CPAP in the treatment of sleep apnea are currently being defined.

One device, which some patients find more comfortable, is the bilevel positive airway pressure (BiPAP). Unlike CPAP where the pressure is equal during inhalation and exhalation, BiPAP is designed to follow the patient's breathing pattern. It lowers the pressure during expiration and maintains a constant inspiratory pressure.

The ramp system, a modification of CPAP, allows the pressure to be applied only when the patient goes to sleep, increasing pressure slowly over a 30-minute period. The purpose of the ramp system is to make CPAP more comfortable.

Nocturnal Ventilation

Patients can be ventilated non-invasively during sleep with positive pressure ventilation through a CPAP mask. This technique is now used in patients whose breathing is impaired to the point that their blood carbon dioxide level is elevated, as happens in patients with obesity-hypoventilation syndrome and certain neuromuscular disease.

Pharmacologic Therapies

No medications are effective in the treatment of sleep apnea. However some physicians believe that mild cases of sleep apnea respond to drugs that either stimulate breathing or suppress deep sleep. Acetazolamide has been used to treat central apnea. Tricyclic antidepressants inhibit deep sleep (REM) and are useful only in patients who have apneas in the REM state.

Oxygen administration sometimes benefits patients without andy side effects. However, the role of oxygen in the treatment of sleep apnea is controversial and it is difficult to predict which patients will respond to oxygen therapy.

Dental Appliances

Dental appliances which reposition the lower jaw and the tongue have been helpful to some patients with obstructive sleep apnea. Possible side effects include damage to teeth, soft tissues, and the jaw joint.

Surgery

Some patients with sleep apnea may require surgical treatment. Useful procedures include removal of adenoids and tonsils, nasal polyps or other growths, or other tissue in the airway, or correction of structural deformities. Younger patients seem to benefit from surgery better than older patients.

Tracheostomy

Tracheostomy is used only in patients with severe, life-threatening obstructive sleep apnea. In this procedure a small hole is make in the windpipe (trachea) below the Adam's apple. A T-shape tube is inserted into the opening. This tub stays closed during waking hours and the person breathes normally. It is opened for sleep so that air flows directly into the lungs, bypassing any upper airway obstruction. Its major drawbacks are that it is a disfiguring procedure and the tracheostomy tube requires proper care to keep it clean.

Uvulopalatopharyngoplasty (UPPP)

UPPP is a procedure used to remove excess tissue at the back of the throat (tonsils, adenoids, uvula, and part of the soft palate). This technique probably helps only half of the patients who choose it. Its negative effects include nasal speech and backflow (regurgitation) of liquids into the nose during swallowing. UPPP is not considered as universally effective as tracheostomy but does seem to be a cure for snoring. It does not appear to prevent mortality form cardiovascular complications of severe sleep apnea.

Some patients whose sleep apnea is due to deformities of the lower jaw (mandible) benefit from reconstruction of surgical advancement of the mandible. Gastric stapling procedures to treat obesity are sometimes recommended for sleep apnea patients who are morbidly obese.

Treatment of Patients with Coexisting Lung Diseases

Asthma, chronic bronchitis, emphysema, or other lung diseases can cause breathing problems during sleep. Patients with these diseases may be frequently awakened by cough, aspiration of secretions, choking sensations, and apnea-like sleep disturbances. The treatment in these cases depends on whether the sleep disturbances are due to lung disease or sleep apnea.

Pathophysiology of Sleep and Breathing:

Highlights of the National, Heart, Lung, and Blood Institute Programs

Sleep

The modern era of sleep research started in the mid-1950's with the discovery that sleep is not a homogeneous phenomenon. Rather it fluctuates cyclically between two distinct sequential stages of sleep.

The first sleep stage is variously called synchronized sleep, slow sleep, slow-wave sleep, quite sleep, or nonrapid-eye-movement (NREM) sleep. In this state the EEG is dominated by large-amplitude slow waves; body functioning generally slows: there are slow, rolling eye movements; the pupils constrict; the respiratory and heart rates decline; blood pressure decreases; and total body oxygen consumption is reduced. It is believed that NREM sleep is a recuperative state.

The second state of sleep is called synchronized sleep, fast sleep, fast-wave sleep, dream sleep, or rapid-eye-movement (REM sleep. The EEG is synchronized, with low-voltage fast waves and there are intermittent eye movements. It is also called paradoxical sleep because of the paradox that the EEG in this sleep stage is similar to that in wakefulness or light sleep, although this is deep sleep in terms of arousability. During REM sleep, central-nervous-system (CNS) activity generally increases, and body system are variously activated and inactivated in a complex physiological pattern. The normal adult spends some 15 to 20 percent of the sleeping hours in REM sleep; this percentage decreases with aging. In contrast, the human fetus of 30 weeks spends 80 percent of its sleep in REM sleep. This declines to 50 percent at term. The amount of quiet sleep (NREM) increases for 50 to 60 percent by 3 months and to 70 percent between 6 and 23 months.

At the biochemical level, hormone-like prostaglandins and cytokines, which are intercellular messengers found in the brain, are implicated in the mechanisms that control

sleep. Some speculate that a balance between prostaglandin D2 which increases sleep, and prostaglandin E2 which increases wakefulness, may be involved in the controlling mechanism. The prostaglandins produce their effects when injected into the preoptic area of the hypothalamus, an area responsible for temperature regulation. This may explain the link between sleep and fall in temperature, and also may unify the neurophysiological and biochemical mechanisms of sleep.

Interleukin-1 is localized in the brain in areas associated with control of sleep, and is believed to play a sleep regulatory role. The amount of interleukin-1 in cerebrospinal fluid fluctuates in parallel with the normal sleep/wake cycle.

There is no clear biological answer to the fundamental question of why we sleep. A wide variety of medical and psychiatric illnesses and factors related to age and gender can pathophysiological sequelae. A major goal of sleep research is the characterization of the etiology and pathophysiology of the causes and effects of disturbed sleep.

Breathing

The two major components of breathing are inspiration and expiration. Inspiration is an active process involving contraction of the diaphragm, external intercostal, and in certain circumstances, accessory muscles. It serves to increase intrathoracic volume, decrease intrapleural pressure and allow exchange of air and carbon dioxide within the alveoli of the lungs. Oxygen is transported from the alveoli to the pulmonary bloodstream by passive diffusion and is made available to tissues. Expiration, on the other hand, is a relatively passive process, requiring little or no contraction of the muscles during quiet breathing. A main function of the breathing process is to bring about the exchange of oxygen and carbon dioxide and other gaseous products from biological system.

At birth, the baby switches from dependence on placental gas exchange to air breathing. At the moment of birth there is also a switch from intermittent breathing efforts of the fetal stage to sustained breathing efforts. Since the infants' respiratory muscles are not well-equipped to sustain high workloads, respiratory muscle fatigue is a problem for premature infants, and apneic episodes requiring intervention occur in at least 50 percent of surviving infants weighing less than 1,500 grams.

Breathing disorders during sleep occur either when there are deficiencies in neurally generated rhythmic respiratory efforts or when there is normal generation of rhythmic efforts but mechanically impeded airflow in upper airways. Metabolic and behavioral control systems in the brain are believed to be the control mechanisms for sleep and breathing. The metabolic system that responds to changes in carbon dioxide and oxygen seems to exert its major influence over NREM sleep. On the other hand, the behavioral control system is involved in voluntary respiratory activities and appears to influence REM sleep; many of the ventilatory changes that occur in REM sleep are similar to the behavioral ventilatory activities such as swallowing, voluntary breath holding, and hyperventilation.

Subjects without any clinical problems may exhibit obstructive or central apnea during periods of REM sleep. Although severe changes in respiratory behavior often occur during the REM sleep, sleep apnea can occur in both NREM and REM sleep. However, sleep staging in patients with severe sleep apnea syndrome is difficult because of severe sleep fragmentation. Thus it is difficult to define the relative importance of abnormal respiration detected during REM or NREM sleeps.

Research Highlights

A recent basic research advance of potential clinical implication relates to the application of modern three dimensional medical imaging techniques to the study of pathogenesis of sleep apnea. Magnetic resonance imaging (MRI) and ultrafast X-ray computed tomography (CT) of the upper airways, combined with computer graphics and reconstructions, have begun to provide exquisite details of the geometry of the upper airway. These approaches now permit identification of the precise anatomical sites of collapse or areas of abnormal compliance to determine if the problem is in a specific area or is a more generalized multifocal abnormality. This information will impact on the treatment options, particularly if there is more diffuse involvement since this wold predict failure of localized surgical procedures.

Only 50 percent of patients with sleep apnea undergoing uvulopalatopharyngoplasty benefit from this procedure. Investigators are exploring ways to identify those patients most likely to benefit from this procedure. A small scale clinical trial conducted to determine predictors of success for UPPP revealed that 86 percent of patients who had documented (by fiberoptic endoscopy) preoperative nasopharyngeal obstruction at the level of the soft palate, showed significant improvement in the number of apneas, arousals and in the cumulative time in apnea-hypopnea following surgery. In contrast, only 18 percent of the patients who had a collapsing segment in regions of the pharynx other than the soft palate showed any improvement following UPPP. This is the first prospective clinical study to demonstrate that closure of the passive pharynx at the level of the soft palate predicts a favorable surgical outcome.

An important opportunity for research on the pathophysiology and treatment of sleep apnea has open up with the finding that the English bulldog seems to be a suitable animal model of sleep apnea. This model is permitting the study of the regularly occurring periodicities in neural activity of the upper airways and the inspiratory muscles, and the role of neural mechanisms in the genesis of sleep apnea. Studies with this model revealed that the consequences of intermittent apnea (sleepiness or hypox emia) serve to increase the magnitude and frequency of neural inhibitory activity, thereby worsening the apnea.

Other studies exploring new treatments for obstructive sleep apnea in animals and humans have identified buspirone, a hypnotic agent as a potentially effective drug for sleep apnea. Buspirone seems to increase ventilation in both anesthetized and awake rats and cats without producing the traditional respiratory depressive effect. In a small scale, controlled clinical trial, this drug decreased sleep apnea and improved respiratory status in the patients receiving the drug.

Associations between snoring, hypertension, heart disease, and stroke raise the possibility of common factors and/or causal relationships between sleep apnea and cardiovascular disorders. Such links may be related to biochemical factors such as insulin, catecholamine, or cortisol that are increased in stress. Sleep apnea may itself be a stress that produces hormonal imbalances that lead to the hypertensive state. Alternately obesity, sleep apnea, and other cardiovascular risk factors may share common metabolic pathways and therefore may be genetically determined. These relationships are being explored by studying families with a history of sleep apnea and/or sudden infant death syndrome as well as by studying racial and genetic differences in the prevalence of sleep apnea-related illnesses.

Research Opportunities

Since 1986, the Division of Lung Diseases, National Heart, Lung, and Blood Institute, has been engaged in a concerted national program in cardiopulmonary disorders in sleep designed to fill critical gaps in the understanding of the pathogenesis, diagnosis, treatment, and prevention of sleep-disordered breathing. Some research areas of current emphasis include the following.

1. Natural history of sleep apnea with the goal of determining the magnitude of the problem and designing the most effective therapy.
2. Scientific basic for the influence of age, gender, ethnicity, smoking obesity, and snoring on the development of sleep apnea.
3. Assessment of the severity of sleep apnea and defining the relationships of disease severity, response to treatment and prognosis.
4. Cellular and molecular basis of the role of hypoxia in excessive daytime sleepiness and sleep apnea.
5. Cardiovascular consequences of sleep apnea and the underlying neural cellular and respiratory mechanisms.
6. Improved therapeutic modalities for sleep apnea when associated with blood pressure, asthma, chronic heart failure, angina pectoris, chronic pulmonary disease and stroke.

For More Information

Additional information about breathing-related sleep disorders and other disorders of sleep can be obtained form your local sleep disorders center and the following sources:

Unites States
American Sleep Apnea Association
P.O. Box 3893
Charlottesville, VA 22903

The American Sleep Disorders Association 604 Second Street Southwest
Rochester, MN 55902

Association of Sleep Disorders Centers
P.O. Box 2604
Del Mar, CA 92014

AWAKE NETWORK
P.O. Box 534
Bethel Part, PA 15102

American Narcolepsy Association
P.O. Box 1187
San Carlos, CA 94070

Narcolepsy Network
155 Van Brackle Rd.
Aberdeen, NJ 07747

National Heart, Lung, and Blood Institute (NHLBI) Communications and Public Information Branch 9000 Rockville Pike

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(Other institutes at NIH that have information about sleep disorders include the National Institute of Neurological Disorders and Stroke, National Institute od Child Health and Human Development, National Institute of Mental Health, National Institute on Aging. The address for each is 9000 Rockville Pike, Bethesda, MD 20892.)

Centers for Disease Control and Prevention 1600 Clifton Road, NE
Atlanta, GA 30333

International
Sleep Apnea Research Association, Inc.
65 Kitchener Avenue
Earlwood NSW 2206
Australia

Sleep Apnea Society of Alberta
Faculty of Nursing
University of Calgary
2500 University Drive NW
Calgary, Alberta T2N 1N4

Nederlandse Vereniging Van Slaap Apnoe Patienten De Nye Oanliz 25
9084 AN GOUTOM
The Netherlands

British Sleep Society
Sleep Disorder Clinic
Leicestershire General Hospital
Leicester, LE5 4PW
United Kingdom

Glossary

Adenoids	Gland-like tissue growths in the nose above the throat which obstruct breathing when swollen.
Airway obstruction	Narrowing, clogging or blocking of the air passages to or in the lung.
Apnea	Cessation of breathing.
Arousal	An abrupt change from deep sleep to a lighter stage of sleep which may or may not lead to awakening.
Cardiac arrest	Sudden cessation of cardiac function.
Cardiac arrhythmia	Variation in the normal rhythm of the heartbeat.
Circadian rhythm	Natural daily fluctuation of physiological and behavioral functions.
Cor pulmonale	Heart disease secondary to lung disease.
CPAP	A mechanical ventilator used to deliver continuous positive airway pressure.
Dyspnea	Difficult or labored breathing.
Diaphragm	The major respiratory muscle that participates in the act of breathing. The diaphragm separates the chest and abdominal areas.
Edema	Abnormal amount of fluid in body tissues.
Hemorrhage	Escape of blood from blood-carrying tissue.
Hypoxia	A state in which there is oxygen deficiency.
Hyperventilation	A state in which abnormally fast and deep respiration results in the intake of excessive amount of oxygen into the lung and reduced carbon dioxide levels in the blood.
Hypoventilation	A state in which there is an insufficient amount of air entering and leaving the lung to bring oxygen to the tissues and eliminate carbon dioxide.
Ischemic heart disease	Heart disease from restricted blood supply due to obstruction in blood vessels.

Nares	Openings in the nasal cavities-nostrils.
NonREM sleep	A nonuniform series of four stages of sleep which occur early in the night and are characterized by the absence of movement and slow wave brain activity. NREM generally preceded the first REM period.
Polysomnography	The continuous recording of a number of physiological functions and events during sleep.
Prostaglandins	A group of fat-derived chemicals involved in the regulation of a number of body functions.
Pulmonary function tests	Tests to measure the degree of damage to the lung; the most common tests measures, using a devise called the spirometer, the ability of the lung to move air into and out of the lung.
Rapid eye movement	A stage of sleep in which dreaming is associated with mild involuntary muscle movements. Adults cycle in and out of REM at about 90 minute intervals. REM occupies 20 percent of total sleep.
Sleep fragmentation	Interruption of a sleep stage by awakening or appearance of another sleep stage.
Sleep hygiene	Conditions and practices that promote effective and continuous sleep, e.g., regular bedtime and arise time; restriction of alcohol, coffee etc.
Sleep latency	Time measured from "lights out" or bedtime to actually falling asleep.
Tracheostomy	Surgical insertion or a tube into the airway through the neck to maintain an opening for the outside air to enter the lungs.
Ventilation	The process of exchange of air between the lungs and the atmospheric air leading to exchange of gases with blood.

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