Sleep Physiology

Abdul-Monaf Al-Jadiry,

MD; FRCPsych,

Professor of Psychiatry

Normal Human Sleep

The brain has 3 major states of activity as recorded by the "Electroencephalograph (EEG)":

- **Wakefulness:**
  - **Facilitated by "Ascending Reticular Activating System (ARAS)" & Posterior Hypothalamus.**
  - **EEG demonstrates low voltage fast activity of mixed alpha (8-13 Hz) & beta (>13 Hz) frequencies.**
- **Non-Rapid Eye Movement Sleep (NREM-sleep)**
- **Rapid Eye Movement Sleep (REM-sleep)**

Normal Human Sleep

- Sleep can not be localized to a single neurotransmitter or anatomic location within the brain.
- Sleep cycles consist of 70-120 minutes cycles of NREM & REM sleep.
- Suprachiasmatic nucleus function as a pacemaker for most circadian rhythms and is involved in the sleep-wake cycle.

Normal Human Sleep, Key points

- **Wakefulness** is maintained by activation of the ascending reticular activating system involving several. Neurotransmitters implicate include: glutamate, acetylcholine and the monoamines.

- **NREM sleep** onset is associated with a reduction in activation of the ascending reticular activating system and an increase in neural activity within the ventrolateral pre-optic area, anterior hypothalamus and basal forebrain.

Normal Human Sleep, Key points

- **REM sleep is triggered by activation of cholinergic neurons in the laterodorsal and pedunculopontine tegmental nuclei.**
- **The suppression of motor activity in REM sleep is rated by glutamate-mediated activation of descending medullary reticular formation.**
- **Cycles of NREM and REM sleep alternate throughout the night in a predictable manner.**
- **Ageing is associated with difficulty in maintaining sleep and more frequent arousals.**

Electroencephalograph (EEG)”:

- Electroencephalography (EEG) is the recording of electrical activity along the scalp.
- EEG refers to the recording of the brain's spontaneous electrical activity over a short period of time, usually 20–40 minutes, as recorded from multiple electrodes placed on the scalp.

Electroencephalograph (EEG)":

Alpha waves have a frequency of 8 to 12 cycles per second.

Alpha waves are present only in the waking state when the eyes are closed but are mentally alert.

Alpha waves go away when eyes are open or during concentration

Beta waves have a frequency of 13 to 30 cycles per second.

These waves are normally found when the person is alert or have taken high doses of certain medicines, such as benzodiazepines.

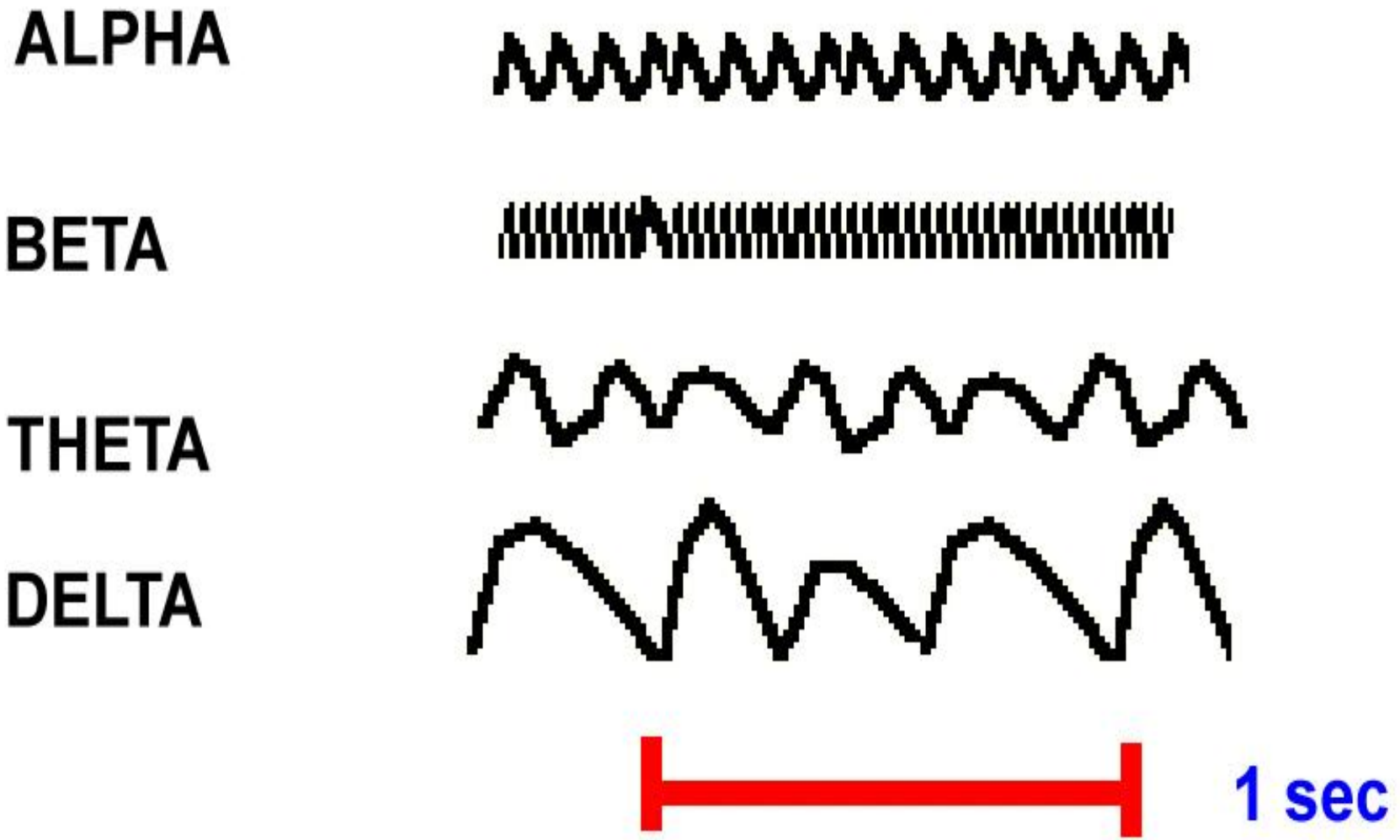
Electroencephalograph (EEG)":

Theta waves have a frequency of 4 to 7 cycles per second.

These waves are normally found only when asleep or in young children.

Delta waves have a frequency of less than 3 cycles per second.

These waves are normally found only when asleep or in young children.


ALPHA
BETA
THETA
DELTA
1 sec

Normal Human Sleep

- **Normal sleep is divided into:**
  - **non–rapid eye movement (NREM) and**
  - **rapid eye movement (REM) sleep.**
- **NREM sleep is further divided into progressively deeper stages of sleep:**
- **stage N1**
- **stage N2**
- **Stage N3 & N4 (deep or delta-wave sleep).**

Normal Human Sleep

- **Stage R sleep (REM sleep) has tonic and phasic components:**

➢ **The phasic component is a sympathetically driven state characterized by rapid eye movements, muscle twitches, and respiratory variability.**

➢ **The tonic component is a parasympathetically driven state with no eye movements.**

Normal Human Sleep

- Waking usually transitions into light NREM sleep.
- NREM sleep typically begins in the lighter stages N1 and N2, and progressively deepens to slow wave sleep as evidenced by higher-voltage delta waves.
- N3 & N4 (slow wave sleep) is present when delta waves account for more than 20% of the sleep EEG.
- REM sleep follows NREM sleep and occurs 4-5 times during a normal 8-hour sleep period.

Normal Human Sleep

- The first REM period of the night may be less than 10 minutes in duration, while the last may exceed 60 minutes.
- The NREM-REM cycles vary in length from 70-100 minutes initially to 90-120 minutes later in the night.
- Typically, N3 & N4 sleep is present more in the first third of the night, whereas REM sleep predominates in the last third of the night.

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Functions of Sleep

1. Homeostatic restoration of tissues
2. Energy conservation
3. Thermo regulation
4. Discarding irrelevant memories from the sensory-overloaded brain and consolidation of perceptual & implicit memory
5. Protection against predation by remaining aloof from predators

NREM Sleep

The EEG differentiated 4 stages of non-REM Sleep:

- **Stage I:**
  - **Theta activity (4-7 Hz).**
  - **EMG demonstrates decreased tonic activity.**
  - **Slow rolling of eyes.**
- **Stage II:**
  - **Theta activity + sleep spindles (brief bursts of 12-14 Hz) + K complexes (high amplitude, slow frequency, electronegative wave followed by electropositive waves).**
  - **Decreased muscle tone.**
  - **Rare eye movement.**

Non-REM Sleep

- **Stage III & IV (Slow-Wave-Sleep):**
  - **Deepest stages of sleep**
  - **Occurs in the first 2 NREM periods**
  - **Epochs of sleep consisting of greater than 20% & 50%, respectively, of high voltage in the delta band (0.5-3.0 Hz)**
  - **Atonia**
  - **No eye movements**
- **NREM Sleep is driven by:**
  - **basal forebrain.**
  - **area around the solitary tract in the medulla.**
  - **and dorsal Raphi nucleus (serotonergic cells).**

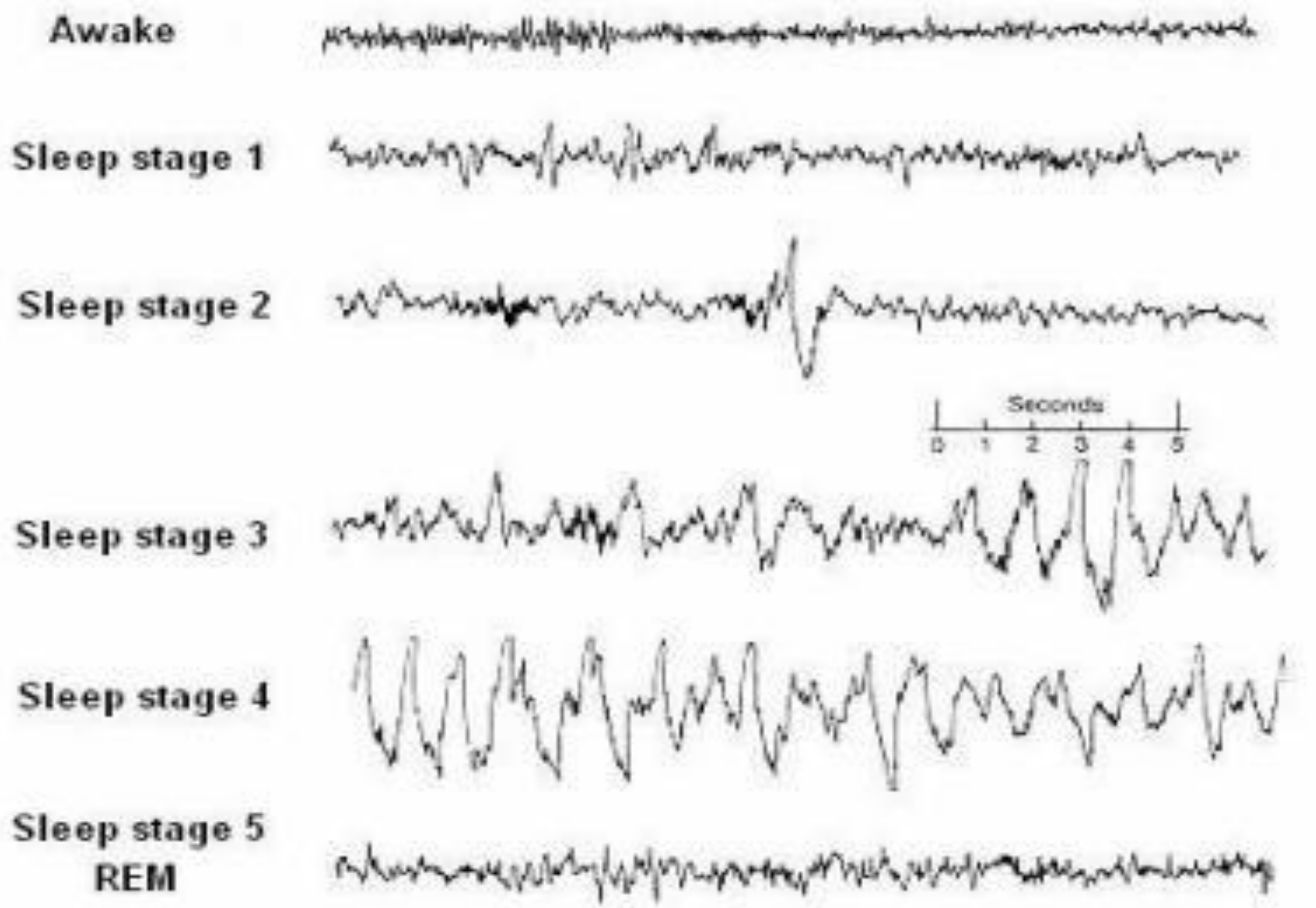
REM-Sleep

- **Brain becomes electrically & metabolically activated.**
  - **Cerebral Blood Flow increased.**
  - **Generalized muscle atonia.**
  - **Penile and clitoral engorgement.**
- **Occur in phasic burst accompanied by fluctuation in respiratory and cardiac rate**
- **Affectively charged, vivid dreams associated with activities of the amygdalae.**
- **Polysomnography (EEG, EOG, EMG) demonstrates eye movements.**

REM-Sleep

- **REM periods in the first half of the sleep period are brief and lengthen in successive cycles.**
- **Controlled by 2 antagonistic systems:**
  - **REM "off" cells: Raphi nucleus [Serotonergic], locus ceruleus [noradrenergic] & nucleus peribrachialis lateralis [noradrenergic].**
  - **REM "on" cells: [cholinergic cells] in the mesencephalic medullary and pontine region.**

EEG wave form



Development & Sleep Stages

- **The baby at birth sleeps 20 hours**
- **Differentiation of REM & NREM sleeping occur at age 3-6 months**
- **During first 3 years of life: sleep-wake rhythm develops from ultradian to circadian patterns with principal sleep phase occurring at night**
- **Puberty & Adolescence: large percentage of REM & decrease in stage III & IIII NREM (slow wave sleep)**
- **Age 20-60 years: gradual and slight decline in sleep efficiency and total sleep time**
- **Old age: light and fragmented sleep with gradual disappearance of slow wave sleep.**

Impact of Sleep Disorders

1. Poor job performance
2. Accidents
3. Impaired physical well being
4. Increased use of alcohol
5. Mood change
6. Fatigue
7. Muscle aches
8. Impaired attention and concentration

Sleep Assessment

I. Pittsburgh Sleep Quality

A self rating instrument useful for measuring subjective sleep quality:

Napping **Stimulants**

Hypnotics **Alcohol**

Diet **Diurnal activity**

Number of arousals

Perceived length of sleep time

Day time mood

Alertness

Sleep assessment

II. Polysomnography

- **The principal diagnostic tool in the field of sleep medicine.**
- **Provides data on:**

- **Sleep continuity**
- **Sleep architecture**
- **REM sleep physiology**
- **Sleep related respiratory impairment**
- **Oxygen desaturation**
- **Cardiac arrhythmias**
- **Periodic movements**

Sleep assessment

III. Nocturnal penile tumescence

IIII. Temperature

IV Infrared video monitoring

V. The multiple sleep latency test (MSLT):

- The most objective & valid measure of excessive sleepiness.
- Average sleep latency of less than 5 minutes indicates a pathological degree of sleepiness associated with a high rate of sleep episode during the wake period and decrements in work performance.
- Detection of sleep onset REM periods in MSLT has become a corner stone in the diagnosis of narcolepsy.

Sleep-Wake Disorders

- **Individuals with sleep-wake disorders present with sleep-wake complaints of:**

  - **Dissatisfaction regarding the quality, timing and amount of sleep.**
  - **Daytime distress and impairment**
  - **depression, anxiety and cognitive changes.**

- ***Persistent sleep disturbances are established risk factors for the subsequent development of mental disorders and substance use disorders.***

Classification of Sleep-Wake Disorders

1. Insomnia disorder
2. Hypersomnolence disorder
3. Narcolepsy
4. Breathing –Relate sleep disorders
5. Circadian- Rhythm sleep-wake disorder
6. Parasomnias:
   - Non-REM sleep arousal disorder
   - Night mare disorder
   - REM sleep disorder
   - Restless-legs syndrome
7. Substance/Medication-Induced sleep disorders

Insomnia Disorder

- **Difficulty initiating or maintaining sleep Lasting at least one month.**
- **Prolonged sleep latencies.**
- **Decreased sleep efficiency.**
- **Extremely light sleep.**
- **Easily affected by noise, temperature fluctuation and anxiety.**
- **Can be chronic causing chronic fatigue, muscle ache and mood disturbances.**
- **Treatment: Sleep hygiene Relaxation, behavior modification, stimulus control, sleep restriction therapy, biofeedback.**

Avoid hypnotic use.

Stimulus control therapy for insomnia

- **The main goal in stimulus control therapy is to reduce the anxiety when attempting to go to bed.**
- **A set of instructions designed to reassociate the bed/bedroom with sleep and to re-establish a consistent sleep schedule are implimented.**
- **The schedule include:**

1) Going to bed only when sleepy

2) Getting out of bed when unable to sleep

3) Using the bed/bedroom only for sleep

4) Arising at the same time every morning

5) Avoiding naps.

Sleep Restriction Therapy for Insomnia

- Keeping a track of sleep patterns with a sleep log.
- Sleep log includes records of bedtime, sleep time, time spend in bed, and getting up time.
- Based on this, the average amount of sleep time calculated to determine the amount of time needed to spend in bed.
- Accordingly, time in bed should be restricted.
- Once sleeping 85 percent of the time spend in bed, the time in bed increased by 15 minutes at intervals until the time in bed stabilizes.
- Taking naps during the day not allowed

Hypersomnolence disorder

- **Characterized by excessive nocturnal and daytime sleepiness despite a main sleep period lasting at least 7 hours.**
- **A prolonged main sleep episode of more than 9 hours sleep that is non restorative or unrefreshing.**
- **Recurrent periods of sleep within the same day**
- **Difficulty being fully awake after abrupt awakening.**

Treatment: stimulants (Methylphenidate)

Narcolepsy

- **Recurrent periods of an irrepressible need to sleep, lapsing into sleep, or napping occurring within the same day.**
- ***Caused by the loss of the hypothalamic neurons producing hypocretin (a protein neurotransmitter involved primarily in the circadian timing of sleep and wakefulness)***
- **Must have been occurring at least 3 times per week over the past 3 months.**
- **Episodes of cataplexy (brief sudden loss of muscle tone) precipitated by laughter or joking**
- **Hypocretin deficiency in the CSF**

Treatment: Stimulants

Breathing Related Sleep Disorders

Sleep disorders characterized by sleep disruption that is caused by a sleep–related breathing disturbance (apneas, hypoapneas, and oxygen desaturation), leading to excessive sleepiness, insomnia, or hypersomnia:

1. **Obstructive sleep apnea**
2. **Central sleep apnea**
3. **Mixed type (Mixed obstructive central apnea)**
4. **Sleep related hypoventilation**
5. **Circadian rhythm sleep-wake disorders**

Obstructive sleep apnea

- **Caused by cessation of air flow through the nose or mouth in the presence of continuing chest breathing movements (lasting 10-20 Secs), resulting in decrease in arterial oxygen saturation and transient arousal, after which respiration resumes normally.**
- **An age related disorder, typically occurs in middle-aged, overweight men (pickwickian syndrome).**
- **Main symptoms are: loud snoring with intervals of apnea, extreme daytime sleepiness and sleep attacks, morning headaches, morning confusion, depression, and anxiety.**
- **Treatment : Nasal continuous positive airway pressure (CPAP)**

Central sleep apnea

- **Cessation of air flow secondary to lack of respiratory effort (no airway obstruction).**
- **Observed breathing pauses during sleep, lack of abdominal and thoracic movement for 10 Secs or longer.**
- **The term refers to two breathing disorders:**

➢ **Cheyne -Stokes respiration**

➢ **Periodic breathing.**

- **common in elderly patients with heart or neurological conditions that affect their ability to breath properly.**

- **Treatment : Mechanical ventilation or nasal continuous positive airway pressure (CPAP)**

Sleep-Related Hypoventilation

- **Episodes of decreased respiration associated with elevated CO2 levels.**
- **Occurs as a result of pulmonary disorder, neuromuscular or chest wall disorder, medications use or obesity.**
- **Impaired ventilation that appears or greatly worsens only during sleep**
- **Treatment : Mechanical nasal ventilation**

Circadian Rhythm Sleep Disorders

- **A persistent or recurrent pattern of sleep disruption that is primarily due to an alteration of the circadian system or to misalignment between the endogenous circadian rhythm and the sleep-wake schedule required by an individual's physical environment or social or professional schedule.**
- **Presents with either insomnia or hypersomnolence**
- **Associated with significant medical comorbidity and impairment in psychosocial functioning.**

Common Circadian Rhythm Sleep Disorders

Delayed Sleep Phase Syndrome (DSPS):

- A disorder of sleep timing.
- DSPS results in falling asleep very late at night and have difficulty waking up in time for work, school, or social engagements.

Advanced Sleep Phase Syndrome (ASPD):

- A disorder in which a person goes to sleep earlier and wakes earlier than desired.
- ASPD results in symptoms of evening sleepiness, going to bed earlier and waking up earlier than desired .

Common Circadian Rhythm Sleep Disorders

Jet Lag or Rapid Time Zone Change Syndrome:

- **Excessive sleepiness and a lack of daytime alertness in people who travel across time zones.**

Shift Work Sleep Disorder:

- **Affects people who frequently rotate shifts or work at night. Associated with:**
  - **A higher injury rate of 2-3 times**
  - **GI, cardiac and reproductive disorders**
  - **Increase in RTA**

Parasomnias

- **Adverse events represent partial arousal from various sleep stages.**
- **Parasomnias involve intrusions of wake behavior into NREM sleep or REM sleep behavior.**
  - **Non-REM sleep arousal disorder**
  - **Night mare disorder**
  - **REM sleep disorder**
  - **Restless-legs syndrome**

NREM Sleep Disorder

- **Recurrent episodes of incomplete awakening from sleep, usually occurring during the first third of sleep episode accompanied by either one of the following:**

➢ **Sleep walking**

➢ **Sleep terrors**

Sleep Walking

- **Repeated episodes of rising from bed during sleep and walking about; can be awakened only with difficulty.**
- **While sleep walking, the individual has a blank, staring face.**
- **The individual is relatively unresponsive to the efforts of others to communicate with him.**
- **No or little dream imagery is recalled**
- **Amnesia for the episode is present**

Sleep Terror

- Repeated episodes of abrupt terror arousals from sleep, usually in babies, and beginning with a panicky scream.
- There is intense fear and signs of autonomic arousal, (mydriasis, tachycardia, rapid breathing, and sweating).
- The individual is relatively unresponsive to the efforts to comfort him others to communicate with him; and can be awakened only with great difficulty.
- No or little dream imagery is recalled.
- Amnesia for the episode is present.

Nightmare

- **Repeated occurrences of extended, extremely dysphoric, and well-remembered dreams that usually involve efforts to avoid threats to survival, security, or physical integrity and that generally occur during the second half of the major sleep episode.**
- **On awakening from the dysphoric dreams, the individual rapidly becomes oriented and alert**
- **Treatment: stimulants, regular bedtime, scheduled daytime naps**

REM Sleep Disorder

- **Repeated episodes of arousal during sleep associated with vocalization and/or complex motor behaviors.**
- **REM sleep without atonia.**
- **Arises during REM sleep, more frequent during the later portions of the sleep period.**
- **Upon wakening the individual is completely awake and alert**
- **Treatment: clonazepam and carbamazepine.**

Restless Leg Syndrome (RLS)

- **An urge to move the legs during sleep.**
- **Usually accompanied by or in response to uncomfortable and unpleasant sensations in the legs (deep parasthesias in calf muscles).**
- **Can be extremely distressing.**
- **Associated with anemia, pregnancy, uremia.**
- **Treatment: BDZ, dopaminergic medication, baclofen ,carbamazepine, Clonidine.**

Thank You