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Drug Therapy for Anxiety and Insomnia

The clinical manifestations of these disorders are similar and overlapping; that is, daytime anxiety may be manifested as nighttime difficulty in sleeping because the person cannot “turn off” worries, and difficulty in sleeping may be manifested as anxiety, fatigue, and decreased ability to function during usual waking hours.

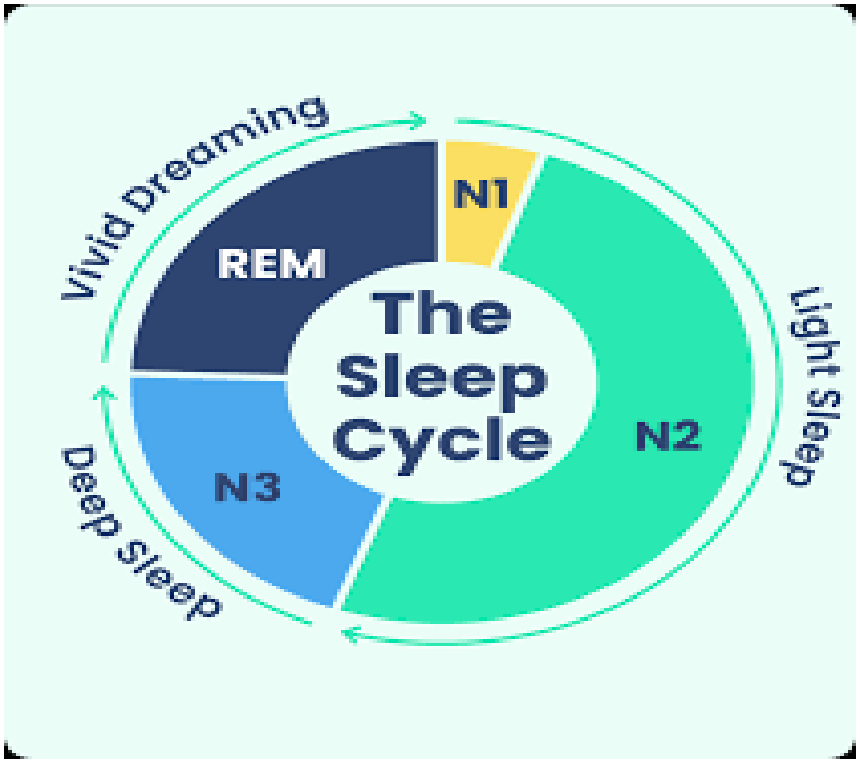
Pathophysiology

anxiety disorders is imbalances among several neurotransmission systems. A simplistic view involves an **excess** of excitatory neurotransmitters (e.g., norepinephrine) or a **deficiency** of inhibitory neurotransmitters (e.g., gamma-aminobutyric acid [GABA]).

GABA is the major inhibitory neurotransmitter in the brain and spinal cord. Gamma-aminobutyric acid A ($GABA_A$) receptors are attached to chloride channels in nerve cell membranes.

Sleep is a recurrent period of decreased mental and physical activity during which a person is relatively unresponsive to sensory and environmental stimuli. Normal sleep allows rest, renewal of energy for performing activities of daily living, and alertness on awakening

Insomnia , prolonged difficulty in going to sleep or staying asleep long enough to feel rested, is the most common sleep disorder. Insomnia is said to be chronic when it lasts longer than 1 month



The 4 Stages of Sleep

NREM Stage 1

- transition period between wakefulness and sleep
- lasts around 5 to 10 minutes

NREM Stage 2

- body temperature drops and heart rate begins to slow
- brain begins to produce sleep spindles
- lasts approximately 20 minutes

NREM Stage 3

- muscles relax
- blood pressure and breathing rate drop
- deepest sleep occurs

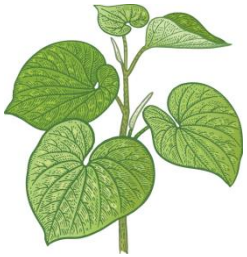
REM Sleep

- brain becomes more active
- body becomes relaxed and immobilized
- dreams occur
- eyes move rapidly

When a person retires for sleep, there is an initial period of drowsiness or sleep latency, which lasts about 30 minutes. After the person is asleep, cycles occur approximately every 90 minutes during the sleep period. During each cycle, the sleeper progresses from drowsiness (stage I) to deep sleep (stages III and IV). These stages are characterized by depressed body functions, non-rapid eye movement (non-REM), and nondreaming, and they are thought to be physically restorative. Activities that occur during these stages include increased tissue repair, synthesis of skeletal muscle protein, and secretion of growth hormone. At the same time, there is decreased body temperature, metabolic rate, glucose consumption, and production of catabolic hormones. A period of 5 to 20 minutes of **REM**, dreaming, and increased physiologic activity follows stage IV.

Herbal Supplements Commonly Used to Reduce Anxiety and Insomnia

Kava (kavalactones)



This supplement is derived from the root of a shrub found in many South Pacific islands

Melatonin

This **Endogenous** hormone is produced by the pineal gland, an endocrine gland in the brain.

Exogenous preparations are produced synthetically and may contain other ingredients. Melatonin products are widely available. Recommended doses on product labels usually range from 0.3 to 5mg

Valerian

This herb is a perennial flowering plant, and the root has been used for centuries as a treatment for anxiety and insomnia

Drug Therapy

The main drugs used to treat insomnia are the **benzodiazepines** and the **nonbenzodiazepine** hypnotics

Benzodiazepines

are widely used for anxiety and insomnia and are also used for several other indications. These drugs have **a wide margin of safety** between therapeutic and toxic doses, and they are rarely fatal, even in overdose, unless combined with other CNS depressant drugs, such as alcohol.

- **Diazepam** (Valium) is the prototype benzodiazepine
- **Alprazolam** (Xanax) is administered orally to reduce anxiety and panic disorders
- **Chlordiazepoxide** (Librium) is most commonly administered for the control of withdrawal symptoms related to acute alcoholism

Nonbenzodiazepine sedative– hypnotic agents

People may receive them prior to diagnostic or surgical procedures or take them nightly.

Eszopiclone

is the first oral nonbenzodiazepine hypnotic to receive FDA approval for long-term use (≤12 months).

Ramelteon

a melatonin agonist, is used for the long-term treatment of insomnia characterized by difficulty with sleep onset.

Drug Therapy for Seizure Disorders

Epilepsy

Sudden, abnormal, hypersynchronous firing of neurons is characteristic of epilepsy. Signs and symptoms of seizure activity lead to the diagnosis. On the electroencephalogram (EEG), abnormal brain wave patterns are present.

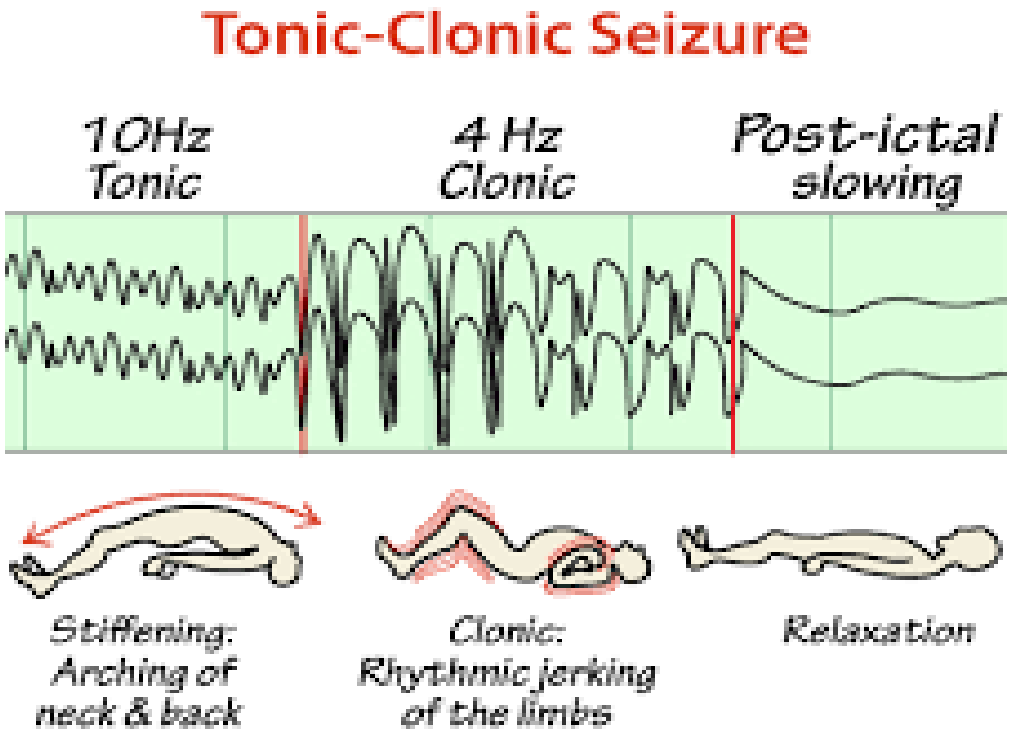
Epilepsy classify seizures as **partial** or **generalized**.

Partial seizures begin in a specific area of the brain and often indicate a localized brain lesion such as birth injury, trauma, stroke, or tumor.

Generalized seizures are bilateral and symmetric and have no visible point of origin in the brain.

The most common type is the **tonic–clonic** or major motor seizure.

- **The tonic phase** involves sustained contraction of skeletal muscles; abnormal postures, such as opisthotonos; and absence of respiration, during which the person becomes cyanotic.
- **The clonic phase** is characterized by rapid rhythmic and symmetric jerking movements of the body



Drugs Administered for Seizures (Antiepileptic Drugs)

Phenobarbital is the prototype AED of the barbiturate class. Since its development in 1912, it has been used as an antiepileptic or sedative

Benzodiazepines

Drugs belonging to this class have a broad range of uses; they may act as antidepressants, antiepileptics, or skeletal muscle relaxants. The benzodiazepines potentiate the effects of GABA by increasing the attraction to the receptor sites

- **Diazepam**
- **Clobazam**
- **Clonazepam**
- **Clorazepate**

Gamma-aminobutyric acid Structural analogs

Gabapentin (Neurontin) for treatment of partial seizures. In May of 2002, the FDA approved it for treatment of postherpetic neuralgia pain.

Pregabalin (Lyrica) is administered for partial-onset seizures, postherpetic neuralgia, neuropathic pain, and neuropathic pain associated with diabetes

Tiagabine (Gabitril) is an adjunctive therapy for partial seizures

Vigabatrin (Sabril) received FDA approval for treatment of infantile spasms and as adjunctive therapy in adults who experience refractory focal seizures

Hydantoins

The prototype antiepileptic of the hydantoin class is **Phenytoin**
The oldest and most widely used AED, it is often the initial drug of choice, especially in adults. In addition to using it to treat seizure disorders, prescribers sometimes order it for cardiac dysrhythmias

Iminostilbenes

The AEDs classified as the iminostilbenes include the prototype **Carbamazepine** (Tegretol).
Oxcarbazepine (Trileptal) has two mechanisms of action that block the voltage-sensitive sodium channels to stabilize the excitability in the brain and control the seizure spread.

Drug Therapy for Parkinson's Disease

Parkinsonism is a chronic, progressive, degenerative disorder of the central nervous system (CNS) characterized by resting tremor, bradykinesia, rigidity, and postural instability. Manifestations of Parkinson's disease also may occur with other CNS diseases, brain tumors, and head injuries. Drugs that deplete dopamine stores or block dopamine receptors, including the older antipsychotic drugs (phenothiazines and haloperidol), reserpine, and metoclopramide, can produce movement disorders such as secondary parkinsonism (which also involves **extrapyramidal reactions .**Treatment can be pharmacologic, nonpharmacologic, and/or surgical

The first symptom of Parkinson's disease is often a resting tremor that begins in the fingers and thumb of one hand ("pill-rolling" movements

Drugs Administered for the Treatment of Parkinson's Disease

- **Dopamine receptor agonists**

Levodopa (L-dopa), the original prototype dopamine receptor antagonist, was developed in the 1960s. It is routinely administered with the drug carbidopa

Levodopa–carbidopa (Sinemet)

Amantadine hydrochloride is an antiparkinson and antiviral agent. . It increases the dopamine release in the nigrostriatal pathway of patients with Parkinson's disease.

Apomorphine hydrochloride is an antiparkinson agent administered for " **off time** ," or "off" episode

Bromocriptine mesylate (Parlodel)is an ergot derivative that directly stimulates dopamine receptors in the brain

Catechol-*o*-methyltransferase Inhibitors

Tolcapone is the prototype COMT inhibitor. COMT plays a role in brain metabolism of dopamine and metabolizes approximately 10% of peripheral levodopa. By inhibiting COMT, tolcapone increases levels of dopamine in the brain and relieves symptoms more effectively and consistently


thank you