

# Benzodiazepines

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اللهم اجعل علمنا فالماً لوجهك نافعاً  
لأمتك موثقاً إليك لا هارفاً عنك آمين.

# Introduction

Benzodiazepines are a class of medications that act as a central nervous system depressant.

They have a wide variety of uses including anxiolytic effects, or to relieve anxiety; as anticonvulsants, or to manage seizure disorders; as a hypnotic for insomnia; as an anesthetic; and to treat withdrawal syndromes.

They act by enhancing the main inhibitory neurotransmitter gamma-aminobutyric acid, or GABA, by binding to its receptor.

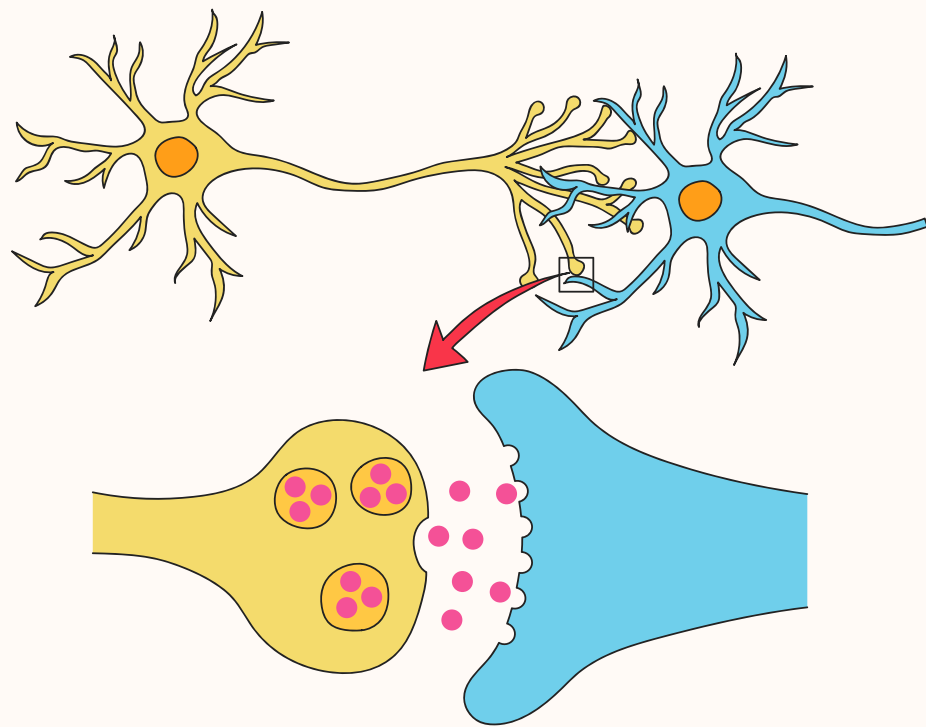


# Neurotransmission

Neurons communicate with each other through neurotransmitters.

When one neuron is stimulated, it'll release excitatory neurotransmitters like glutamate which bind to receptors on the next neuron.

This causes the next neuron to depolarize and release its own excitatory neurotransmitters, propagating the signal throughout the brain. Now, we also have inhibitory neurons that will shut down this chain of events.



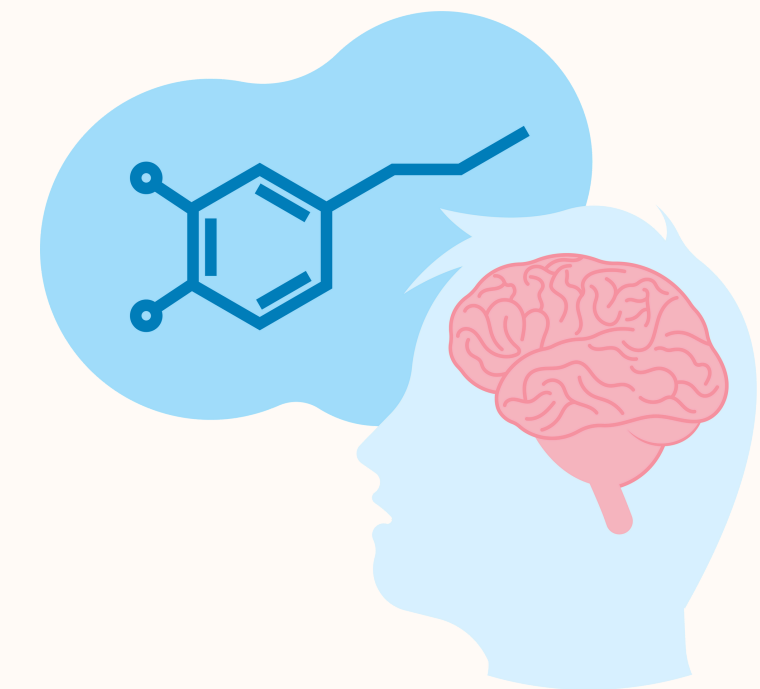
# Neurotransmission

there are cases where neurons in the brain start sending out more excitatory signals than normal. This can occur due to either too much excitation by the excitatory neurotransmitters, or too little inhibition by the inhibitory neurotransmitters like GABA.

Excessive excitatory signals can cause psychiatric disorders like anxiety, and neurological disorders like seizures and epilepsy.

so one way we can decrease the excitatory signals is by enhancing the effect of inhibitory neurons through medication like

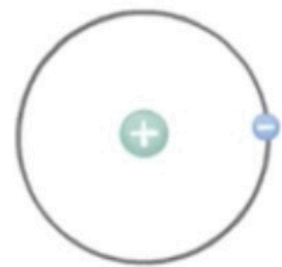
**benzodiazepines.**



# benzodiazepines

## SHORT-ACTING

**A** ALPRAZolam  
**T** TRIAZOLAM  
**O** OXAZEPAM  
**M** MIDAZOLAM



## INTERMEDIATE-ACTING

**T** TEMAZEPAM  
**L** LORazepam  
**C** Clonazepam



## LONG-ACTING

**C** Chlordiazepoxide  
**D** Diazepam  
**(e)** FLURAZEPAM  
**F**



# Mode of action

These medications target the **BZ site of GABAA receptors**

When both benzodiazepine and GABA bind to their separate sites on the receptor, benzodiazepines increase the frequency of Cl<sup>-</sup> channels opening, thereby increasing the influx of Cl<sup>-</sup> ions.

As a result, high intracellular concentrations of Cl<sup>-</sup> ions cause membrane hyperpolarization, which means it's much more difficult for neuron to depolarize and fire off an action potential.

## Note:

(Now, a similar group of medications called **barbiturates** also function by binding to GABAA receptors.

The important distinction is that barbiturates work by increasing the duration of Cl<sup>-</sup> channels opening and unlike benzodiazepines, they can cause the channels to open even in the absence of GABA.)

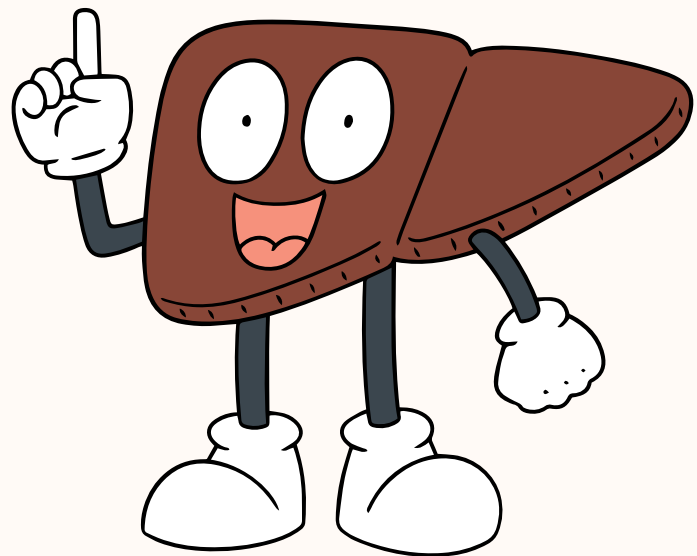


# Metabolism:

Most of these medications are metabolized in the liver by CYP450 enzymes into active metabolites; therefore they should be avoided in individuals with liver impairment.

But, it's important to note that these individuals can use **LORazepam**, **Oxazepam**, and **Temazepam** because they are primarily metabolized by a process known as glucuronidation, This process is not associated with active metabolites and therefore is safe.

**So remember, individuals that drink a LOT, can use LORazepam, Oxazepam, and Temazepam.**



# Effects of drugs



low doses	high doses
<b>Sedation</b>	<b>hypnosis</b>
<b>disinhibition</b>	<b>anesthesia.</b>
<b>anxiolysis</b>	



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# Uses of benzodiazepines



- -Benzodiazepines are very effective anticonvulsants and are considered the treatment of choice for status epilepticus.



- -benzodiazepines are used for anesthesia.



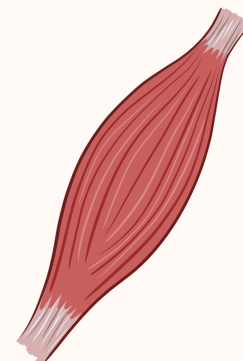
- they are an effective treatment for insomnia, but they decrease REM sleep.



- -Since alcohol and barbiturates also work by targeting GABAA receptors, benzodiazepines can be used to manage their withdrawal symptoms by decreasing their severity.



- -Diazepam can also be used as the second-line treatment for eclampsia, which is a life-threatening complication of pregnancy that is associated with seizures.

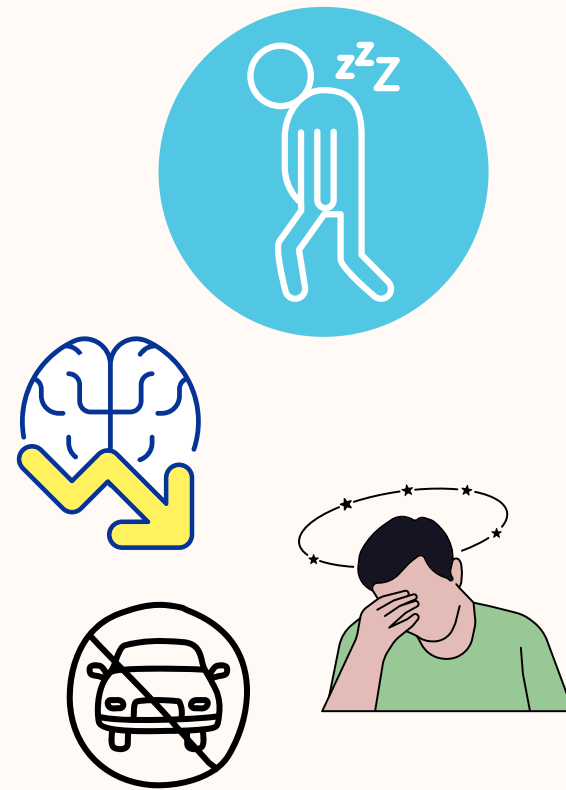


- - they are sometimes used as muscle relaxants to treat spasms, like those caused by cerebral palsy.

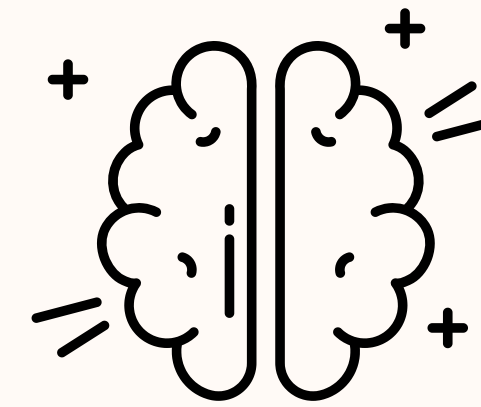


- benzodiazepines are indicated when the neurons get "super excited" and we want to calm them down like in anxiety disorders, or during a panic attack.

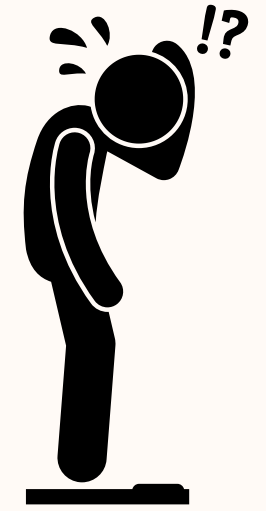
# Side effects :



- drowsiness
- decrease in concentration
- problem solving abilities
- reaction time.
- “Due to this, they should not be taken before driving.”



- Despite being a central nervous system depressant, benzodiazepines can cause paradoxical stimulation in certain parts of the brain, leading to symptoms such as fast speech, excitement, and restlessness.



- anterograde amnesia, which is defined as an inability to form new memories after the administration of the medication.

# Note :

- should be used with caution in the elderly because they can cause ataxia and precipitate falls.
- Drug interactions : when combined with alcohol or other medications that depress the central nervous system, like barbiturates, the depressive effects are additive and can get severe to the point of respiratory **depression and coma**.
- overdose can be managed with **flumazenil**, which acts as a competitive antagonist for benzodiazepines, which means that it binds to the same site as benzodiazepine and blocks its action.

# Overdose

Benzodiazepine overdose is very rarely life-threatening unless associated with the co-ingestion of alcohol, opioids, barbiturates or other respiratory or CNS depressants.

A benzodiazepine overdose can lead to :

- extreme sedation or drowsiness
- confusion and difficulty thinking
- slurred speech
- Hypotonia and hyporeflexia
- Ataxia
- Respiratory depression (benzodiazepines have a wider margin of safety than barbiturates and, consequently, a lower risk of coma and respiratory depression)

**Note** : overdose can be managed with **flumazenil**, which acts as a competitive antagonist for benzodiazepines, which means that it binds to the same site as benzodiazepine and blocks its action.

# Dependence and tolerance:

## Tolerance:

When used chronically, a person can develop tolerance to benzodiazepines, and their effectiveness decreases, which means that they'll need to increase the dose to get the same effects.

This is problematic because benzodiazepines are habit forming and could lead to addiction.

Moreover, short-acting benzodiazepines are associated with a higher addiction potential since they have a shorter half life!

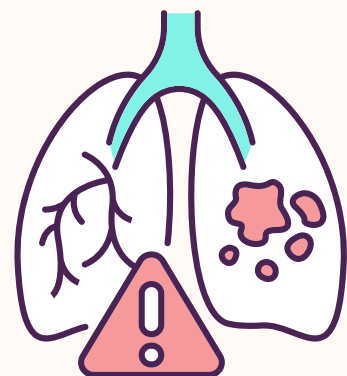
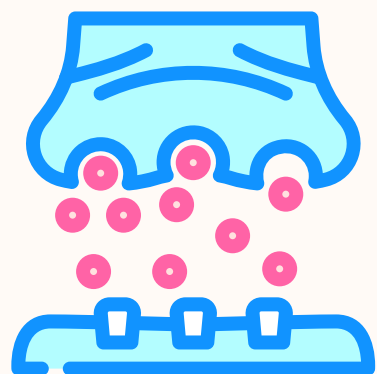
## Dependence

Chronic use also leads to dependence, which means, when the medication is discontinued, the person experiences withdrawal symptoms like insomnia, anxiety, and seizures.

This is less likely to happen when compared to barbiturates, making benzodiazepines the preferred choice.

# Contraindications for benzodiazepines

- Hypersensitivity to benzodiazepines.
- Neuromuscular diseases (e.g., myasthenia gravis ): worsening of myasthenic symptoms.
- narrow-angle glaucoma.
- Respiratory depression (COPD , respiratory failure )
- Drug dependence (alcohol, illicit drug, or prescription medication use).
- Pregnancy (except for the management of eclampsia following unsuccessful magnesium sulfate therapy): ↑ risk of floppy infant syndrome (hypotonia).



Here is the information in a tidy table format:

<b>Short acting (half-life: &lt;6 hours)</b>	
Medication	Characteristics
Midazolam (Versed)	<ul style="list-style-type: none"><li>- Very short half-life</li><li>- Primarily used in medical and surgical settings</li></ul>

<b>Intermediate acting (half-life: 6–20 hours)</b>	
Medication	Characteristics
Alprazolam (Xanax)	<ul style="list-style-type: none"><li>- Treatment of anxiety, including panic attacks</li><li>- Short onset of action leads to euphoria, high abuse potential</li></ul>
Lorazepam (Ativan)	<ul style="list-style-type: none"><li>- Treatment of panic attacks, alcohol and sedative-hypnotic-anxiolytic detoxification, agitation</li><li>- Not metabolized by liver</li><li>- Used with haloperidol in IM formulations to quickly sedate agitated patients</li></ul>
Oxazepam (Serax)	<ul style="list-style-type: none"><li>- Alcohol and sedative-hypnotic-anxiolytic detoxification</li><li>- Not metabolized by liver</li></ul>
Temazepam (Restoril)	<ul style="list-style-type: none"><li>- Because of dependence, rarely used for treatment of insomnia</li><li>- Not metabolized by liver</li></ul>

<b>Long acting (half-life: &gt;20 hours)</b>	
Medication	Characteristics
Diazepam (Valium)	<ul style="list-style-type: none"><li>- Rapid onset</li><li>- Used during detoxification from alcohol or sedative-hypnotic-anxiolytics, and for seizures</li><li>- Effective for muscle spasm</li><li>- Less commonly prescribed to treat anxiety because of euphoria</li></ul>
Clonazepam (Klonopin)	<ul style="list-style-type: none"><li>- Treatment of anxiety, including panic attacks</li><li>- Avoid with renal dysfunction; longer half-life allows for once or twice daily dosing</li></ul>

# Thank you

“ياربِّ برحمتك فرِّج عن إخواننا  
برحمتك نجِّ المستضعفين من المؤمنين  
أفرغ عليهم هبِّراً و يقيناً و أنساً و رحمة وحناناً من لدنك  
اجبرهم و اربط على قلوبهم و آمن روعاتهم و عوّنهم  
اجعلهم في ولايتك و معيتك و عنايتك  
اغفر لهم ذنوبهم و اسرافهم في أمرهم و ثبت أقدامهم و انصرهم على القوم  
الكافرين  
فُذ بأيديهم و سدور ميههم و أنزل عليهم مدداً من عندك  
ثبّتهم و أخلص نيّاتهم و اجعلها في سبيلك و إعلاء كلمتك ، و نهرةً للمستضعفين  
واشف جراحهم و داوي مرّاهم و تقبّل وارحم شهداءهم..  
يا منتقم انتقم من كل مُجرِم ظالم نكّل بعبادك..”

