Cannabis and Sleep Disturbances

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Objectives

- Stages of sleep
- Anatomy of sleep
- Circadian Rhythm and Sleep/Wake Restorative Process
- Endocannabinoid system
- The role of cannabis and sleep
- Dependency
- Sleep disorders and cannabis

Why is sleep important?

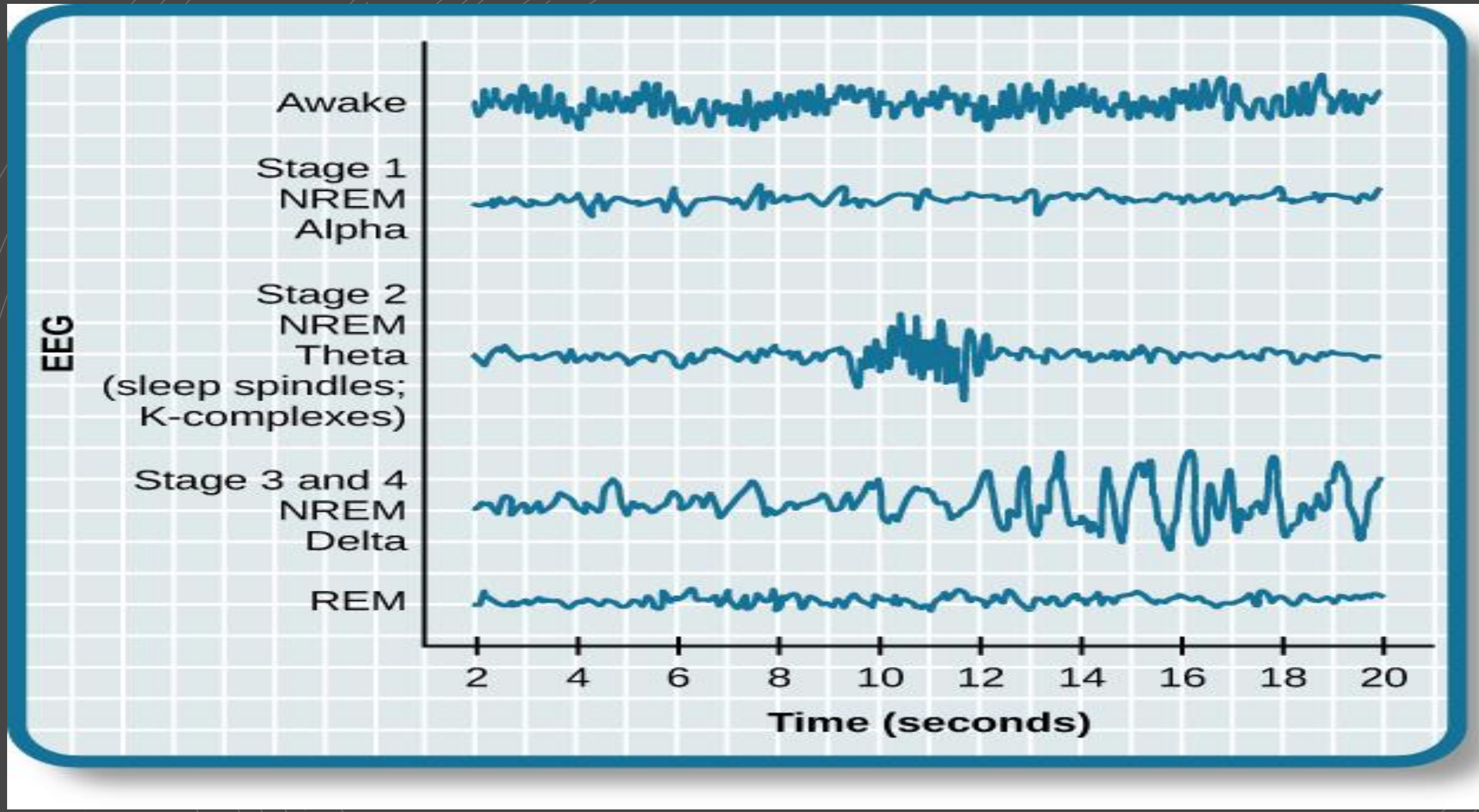
- Sleep plays an important role in several processes
- Memory consolidation
- Diabetes
- Cognitive improvement
- Cardiovascular health
- Weight loss
- Immune system
- Healing processes

Sequences of Sleep Cycles

- The Sequence of Sleep Stages
- Sleep begins in stage 1 and progresses into stages 2,3, and 4.
- Once REM sleep is over, the body usually returns to stage 2 sleep.
- Typically we go through these stages approximately four or five times throughout the night.
- REM stage occurs approximately 90 minutes after falling asleep.
- The first cycle of REM sleep might last only a short amount of time, but each cycle becomes longer.
- REM sleep can last up to an hour as sleep progresses.

4 stages of sleep

- NREM Stage 1
  - Typically lasts between 1 and 10 minutes—you are lightly asleep, and you can quickly return to being fully awake.
  - Hypnic jerk or sense of falling
- NREM Stage 2
  - Usually lasts about 20 minutes, is characterized by a slowing heart rate and a decrease in body temperature. Your body reduces its activity to prepare you to go into a deep sleep.
- NREM Stage 3 or Delta Sleep
  - Starts 35-45 minutes after falling a sleep. As electroencephalograms show, our brain waves slow down and become larger
- REM Stage 4
  - This is the final stage of a standard sleep cycle. The first rapid eye movement (REM) sleep stage lasts around 10 minutes and usually happens after having been asleep at least 90 minutes.


Awake
Stage 1
NREM
Alpha
Stage 2
NREM
Theta
(sleep spindles;
K-complexes)
Stage 3 and 4
NREM
Delta
REM
EEG
2
4
6
8
10
12
14
16
18
20
Time (seconds)

Anatomy of sleep

- **Hypothalamus**, a peanut-sized structure deep and is the control centers affecting sleep and arousal
- **Suprachiasmatic nucleus** (SCN) – clusters of cells that receive information about light exposure directly from the eyes and control your behavioral rhythm (Circadian Rhythms)
- **Brain stem** communicates with the hypothalamus and the brain stem produce a brain chemical called **GABA**, which acts to reduce the activity of arousal centers in the hypothalamus and the brain stem
- **Thalamus** becomes inactive during this time
- **Pineal gland** increases production of **Melatonin**
- **Amygdala**, an almond-shaped structure involved in processing emotions, becomes increasingly active during REM sleep (dreaming)

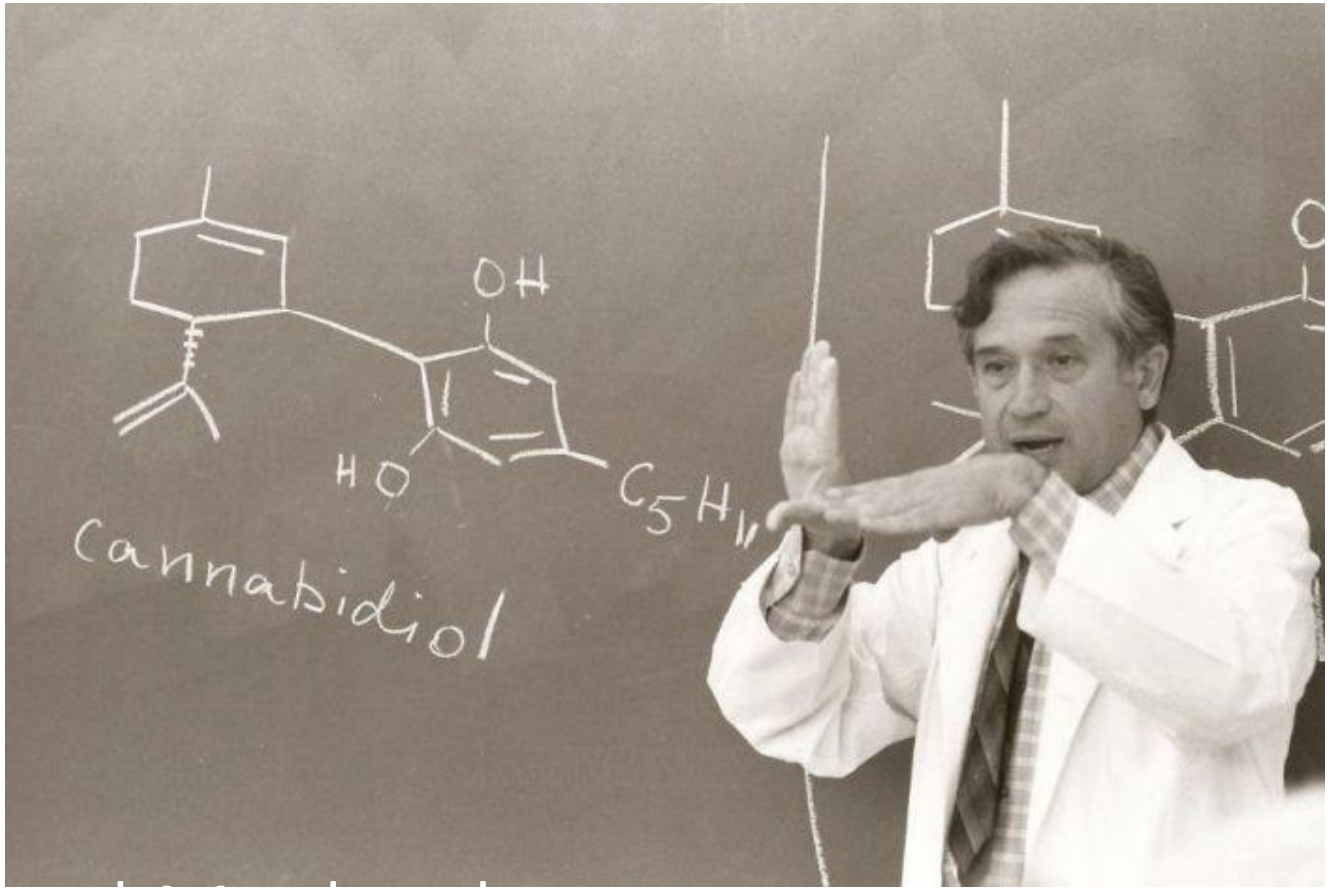
Circadian Rhythm and Sleep/Wake Restorative Process

- Circadian rhythm or biological clock regulates sleepiness and awake cycles
  - Controlled by the Suprachiasmatic Nucleus (SCN) which is controlled by light and darkness via optic nerve
  - Controls hormones (Melatonin) and body temperature
- Sleep/wake homeostasis
  - Tells us that a need for sleep is accumulating and that it is time to sleep.
  - It also helps us maintain enough sleep throughout the night to make up for the hours of being awake.

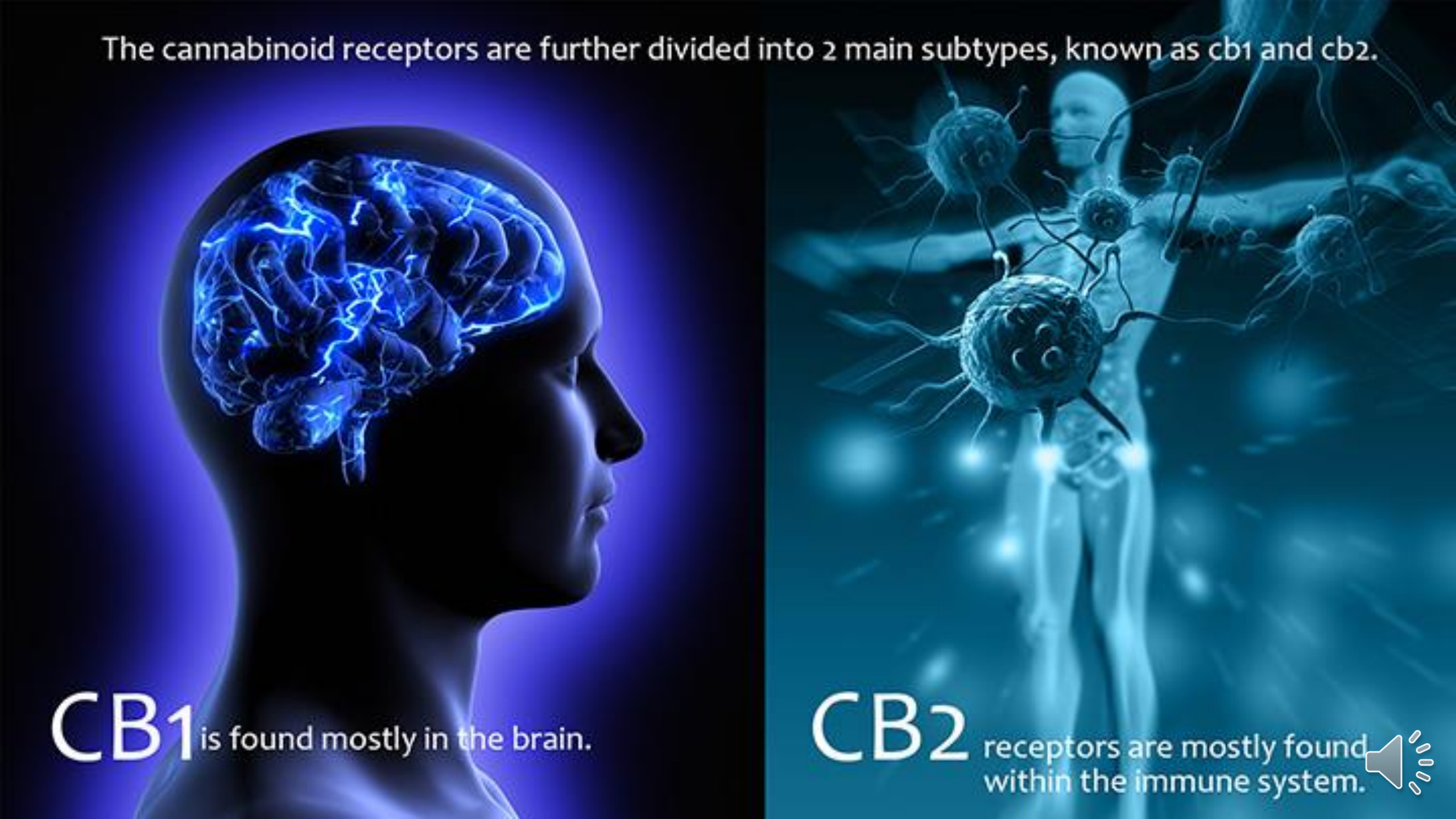
Testing your understanding of cannabis

1. What is the endocannabinoid system?
2. Does cannabis help you sleep?
3. Is cannabis habit forming?
4. What is the major withdrawal symptom of cannabis?
5. Sleep and cannabis relapse. Is this really a problem?
6. What is the role of the Endocannabinoid System on the Circadian Sleep–Wake Cycle?
7. What is the role of CBD on Insomnia/Sleep Quality?
8. Is insomnia a qualifying condition for medical cannabis?

Raphael Mechoulam



The cannabinoid receptors are further divided into 2 main subtypes, known as cb1 and cb2.



CB1 is found mostly in the brain.

CB2 receptors are mostly found within the immune system.

Endocannabinoids: ***Bind CB1 > CB 2***

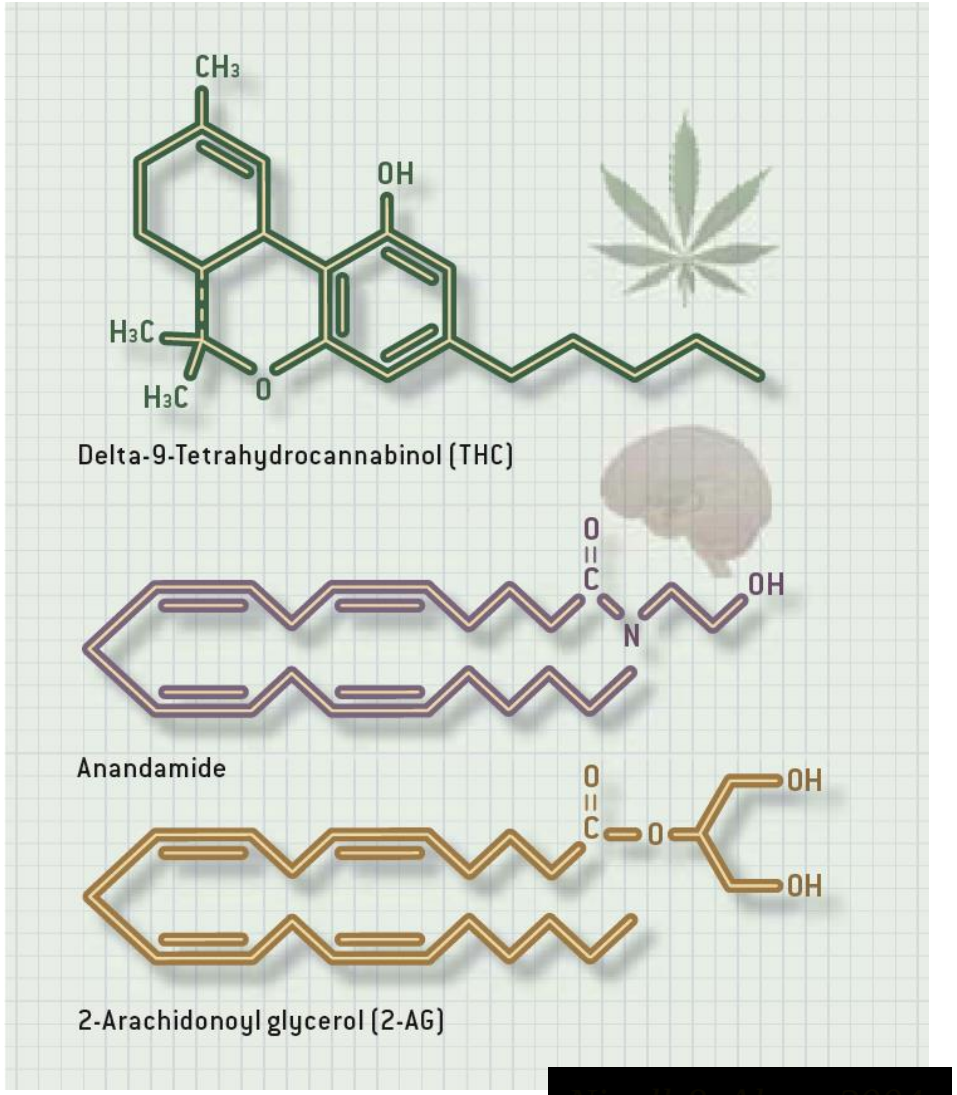
structure, related to prostaglandins

- **Annandamide**

(arachidonyl-ethanolamid)

- **2-Arachidonoyl - glycerol (2-AG)**

more abundant, less potent



Nicoll & Alger, 2004

The role of cannabis and sleep

- 26 states have legalized medical cannabis including the District of Columbia
- 7 states have legalized recreational marijuana
- Cannabis use disorder is on the rise
- Veterans suffering from PTSD use cannabis to relieve symptoms with special emphasis on nightmare reduction using medical cannabis, but the risk of addiction is high
- CBD is commonly used to address anxiety, and for patients who suffer through the misery of insomnia, studies suggest that CBD may help with both falling asleep and staying asleep.

Synthetic Cannabinoids and Natural Pharmaceutical grade

- Based on the potential therapeutic impact, cannabis-based medicine extracts have been developed.
- These extracts are:
  - Synthetic THC
    - Dronabinol or Marinol, and Nabilone or Cesamet)
  - CBD (Cannabidiol)
  - Nabiximols (1:1 CBD/THC, Sativex) which are delivered orally

Impact of Cannabis on Sleep

- Research on cannabis on sleep started in the 1970s and included several studies examining polysomnography (PSG)-based sleep
- Mixed findings and could not replicate some studies
  - Decreases in REM sleep
  - Reduced sleep onset latency
  - Negative impact on sleep quality
    - Habit forming
    - Sleep disturbances when quitting

Sleep and Cannabis Relapse

65% of cannabis users reported poor sleep as the primary reason for lapse/relapse to cannabis during a prior quit attempt

Cannabis Withdrawal and Sleep

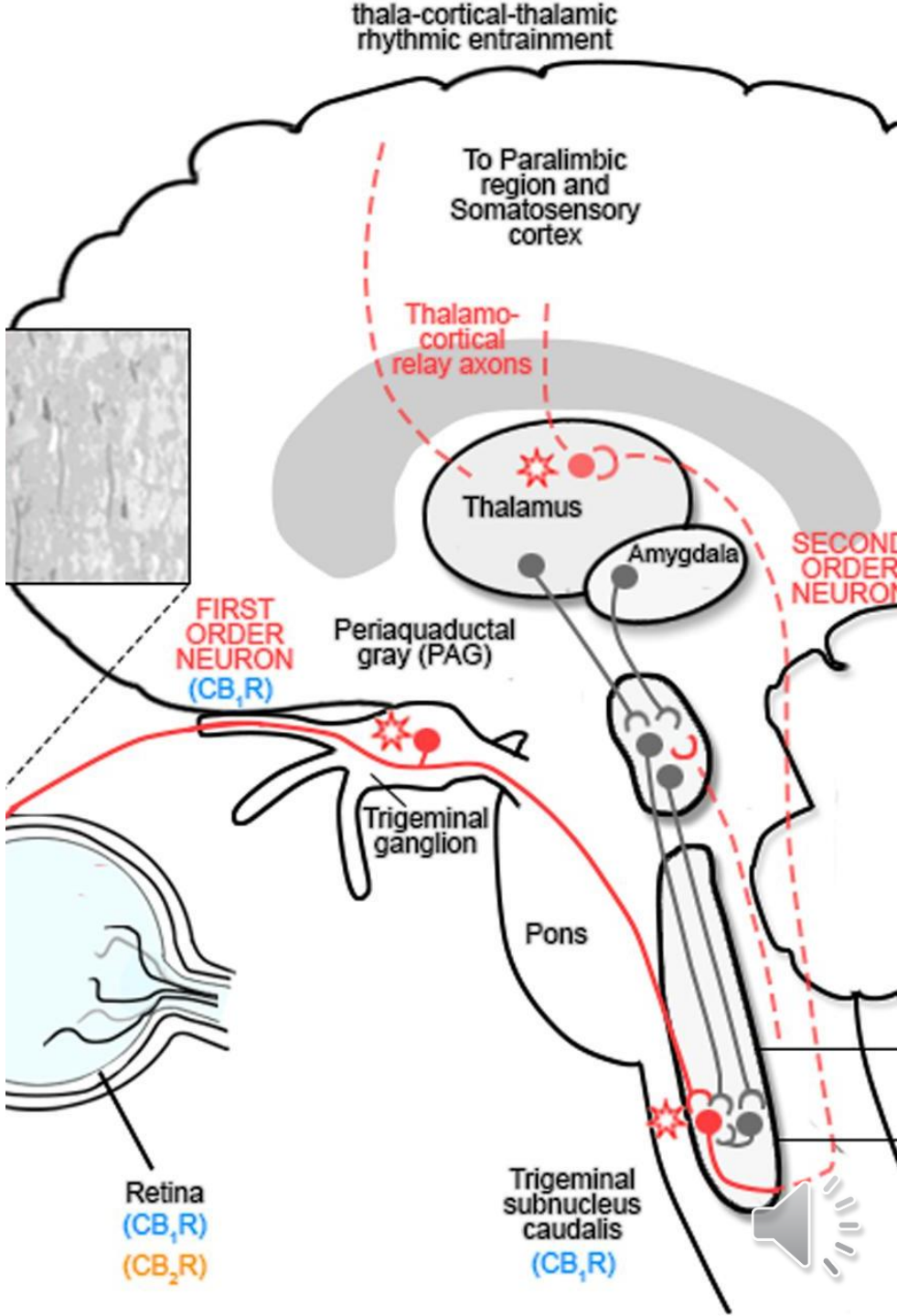
- Approximately 9% of cannabis users become addicted with regular use
- Cannabis withdrawal can last up to 45 days with sleep disturbances being the most common symptom
- Abrupt cannabis cessation among heavy users was associated with:
  - Decrease in total sleep time
  - Decrease in sleep efficiency, and %REM
  - Increases in wake after sleep onset
  - Sleep onset latency
  - Periodic limb movements were observed
- Objective indices of poor sleep have been consistently demonstrated during cannabis withdrawal

The Role of the Endocannabinoid System on the Circadian Sleep–Wake Cycle

ECS is involved in the regulation of the circadian sleep–wake cycle

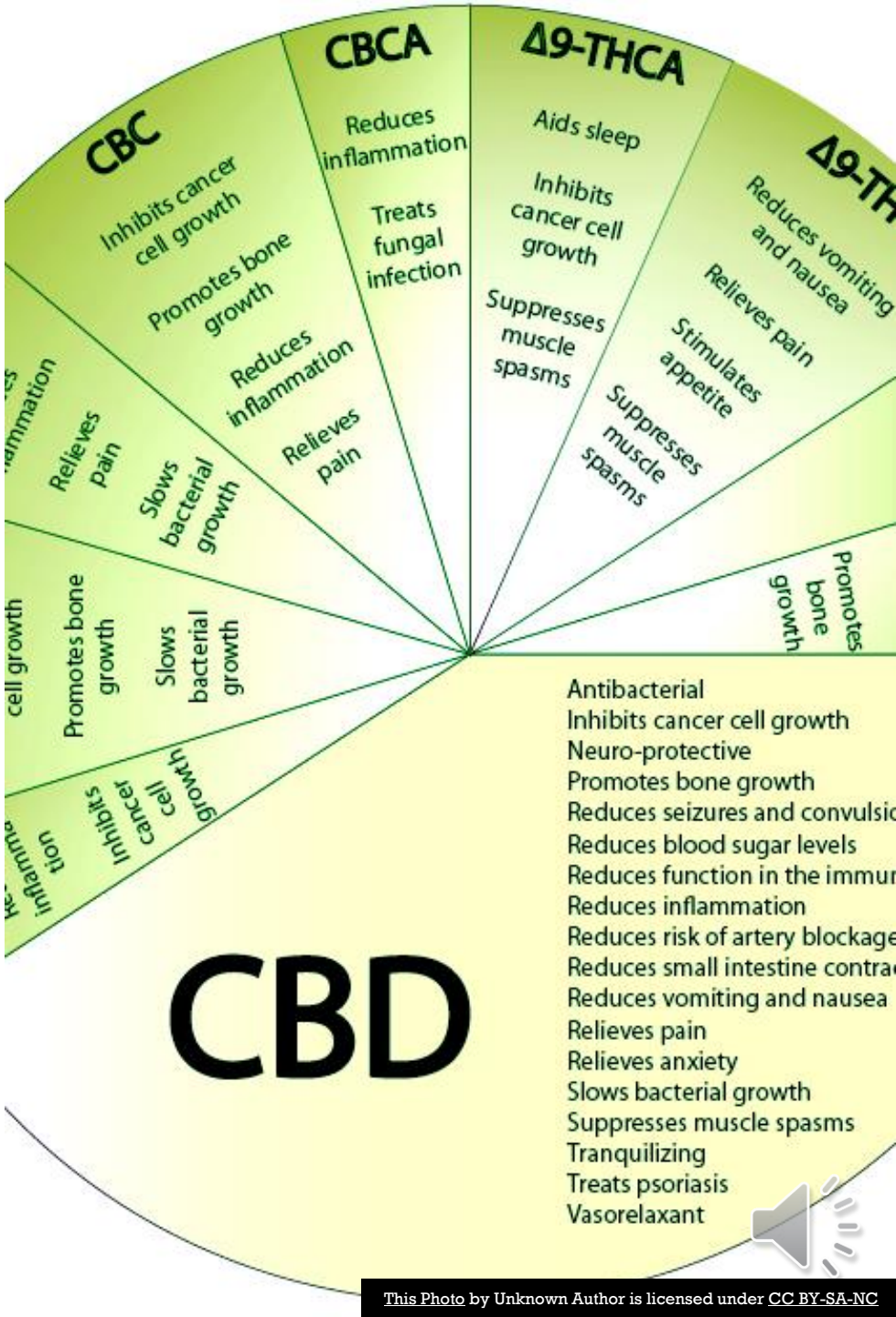
ECS serves as the link between circadian regulation systems (i.e., superchiasmatic nucleus) and the behavioral and physiological processes

Involved in the homeostatic recovery of sleep after non-normal sleep



Effects of Cannabinoids on the Sleep–Wake Cycle

Recent research has demonstrated that the type of cannabinoids (THC, CBD), ratio of cannabinoids, dosage, timing of administration, and route of administration all play a critical role in outcomes.



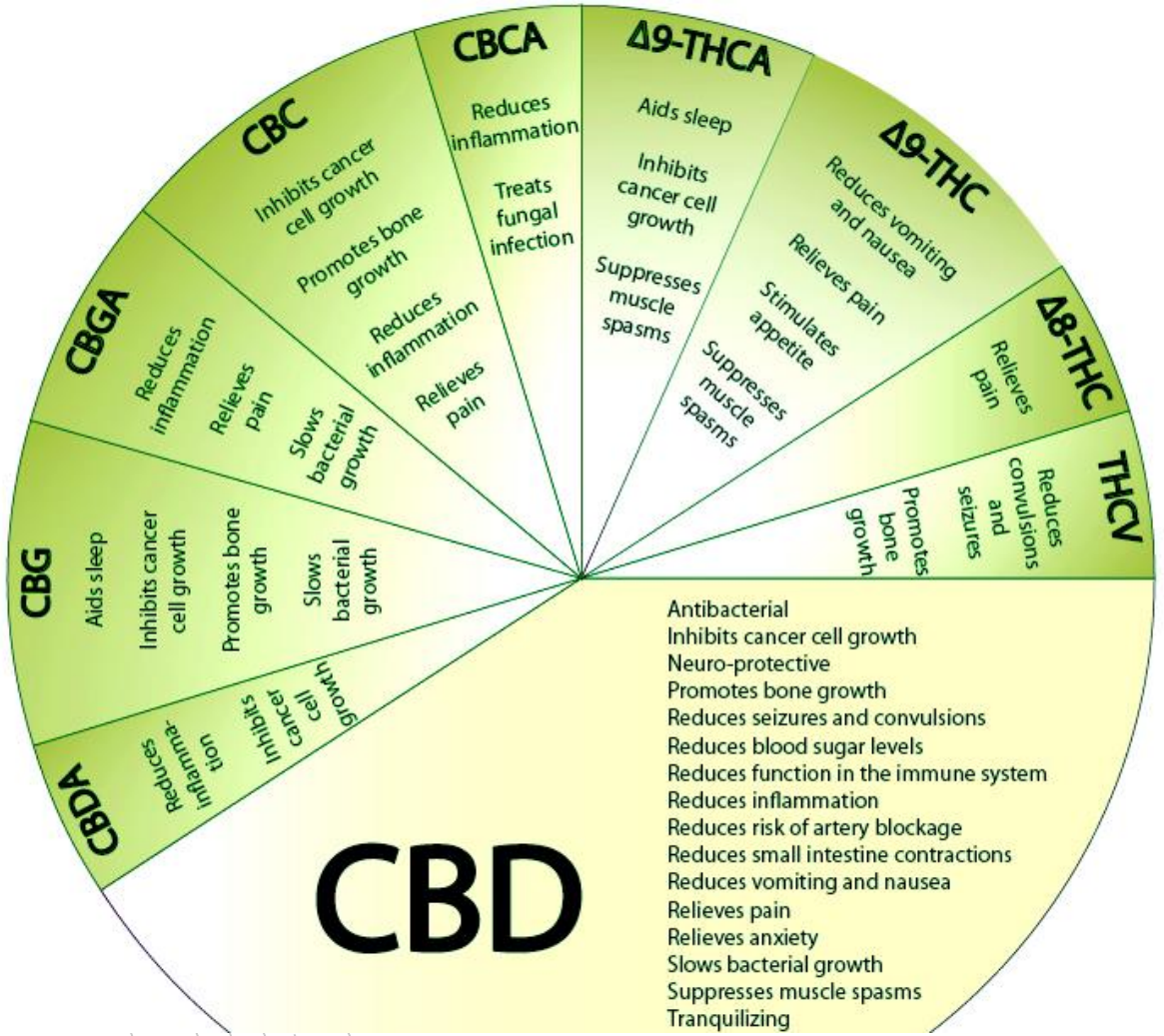
The Role of THC on the Sleep–Wake Cycle

THC administration results in disruption of Circadian Rhythms

Chronic admission of THC leads to tolerance in sleep normal patterns

Dosing is important

- 15mg THC impacted sleep onset, mood, and memory the following day



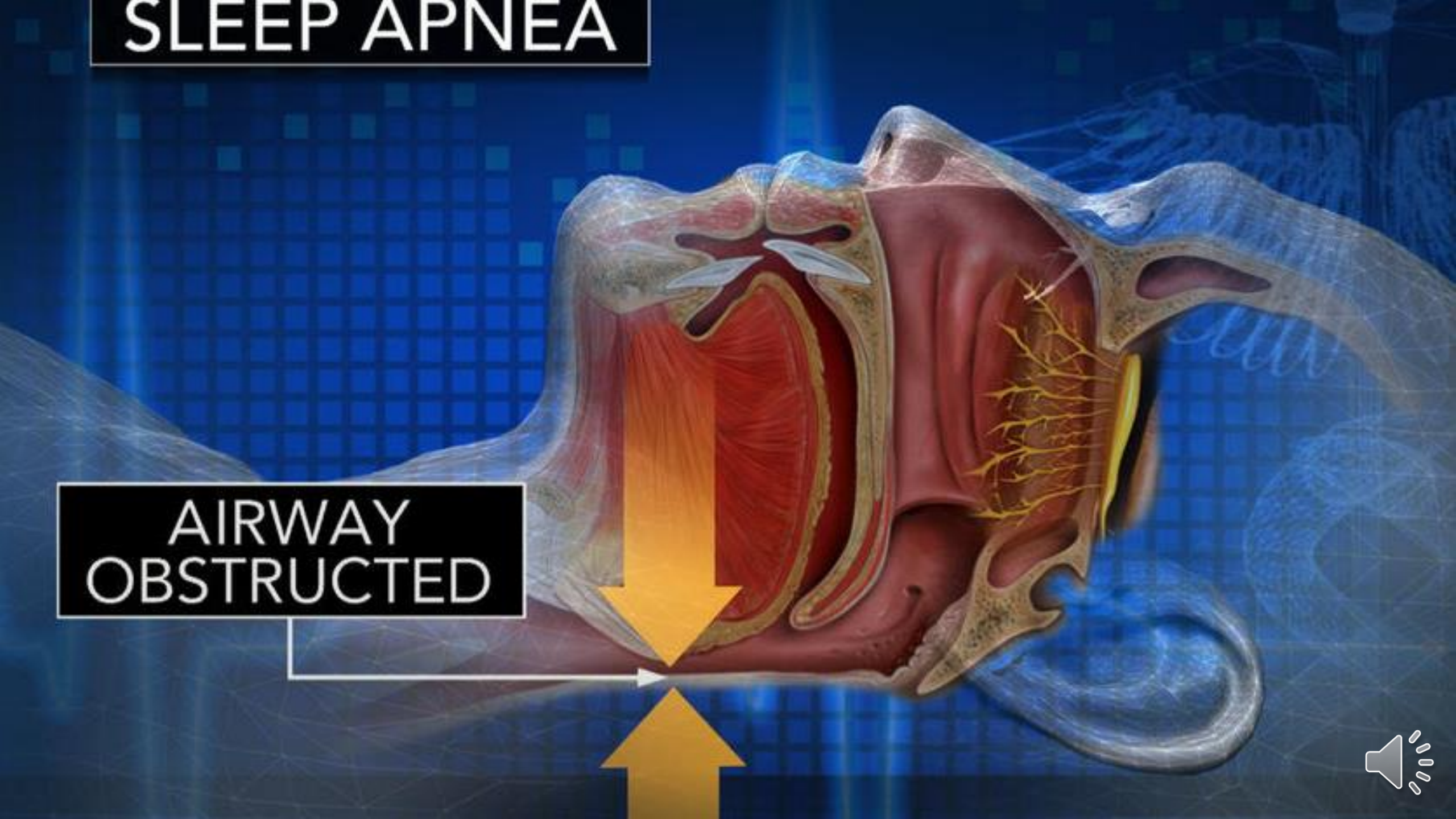
The Role of CBD on the Sleep–Wake Cycle

- CBD has a different affect on sleep patterns versus THC
- Dosing is important
  - Low doses of CBD is stimulating and increased wakefulness
  - Higher doses of 160 mg/day increased total sleep time and decreased the frequency of arousals during the night
  - Increases REM sleep

Insomnia/Sleep Quality

- Prevalence rates of insomnia have increased in recent years that causes significant distress or impairment in functioning
- CBD increased REM sleep
  - Reduced insomnia symptoms and PTSD-related sleep disturbances
  - CBD may impact sleep quality through its anxiolytic effects
  - CBD may decrease stage 3 sleep in young adults
  - THC preparations have been associated with decreased sleep latency

SLEEP APNEA

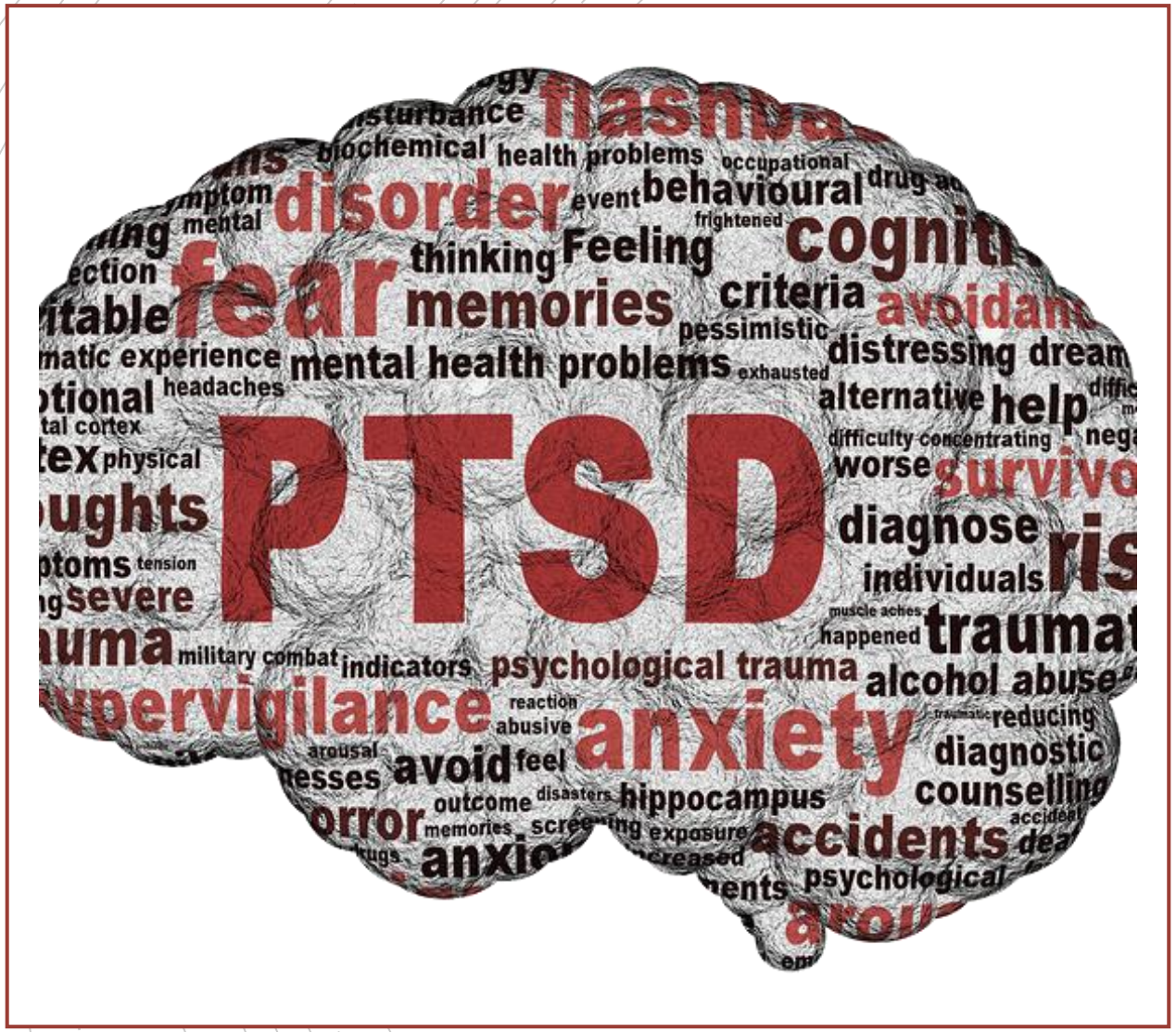


Obstructive Sleep Apnea Slide 1 of 2

- Typical treatment of OSA is CPAP
- THC reduced apneic events, suggesting that the cannabinoid system may function to suppress the Serotonin-Mediated Symptoms of OSA.
- Serotonin is involved in the control of respiration at multiple sites in the central (CNS) and peripheral nervous system (PNS).
- Several studies have investigated the role of serotonin in OSA, with SRIs reducing OSA severity
- Serotonin has been shown to have a tonic (excitatory) effect on the upper airway motor neurons which serve to maintain upper airway patency and reduce apnea.

REM Behavior Disorder

- What is REM Behavior Disorder?
  - Instead of experiencing the normal temporary paralysis of your arms and legs (atonia) during REM sleep, you physically act out your dreams.
  - CBD was used with patients with RBD with Parkinson's Disease
  - CBD suppressed behaviors associated with RBD and was tolerated well by all patients



Nightmares

- Nightmares are associated with posttraumatic stress disorder (PTSD)
- Prasozin, an alpha-adrenergic blocker, is the only current pharmacological treatment for PTSD-related nightmares
- Nabilone (Synthetic THC) produced a reduction in nightmare presence and intensity and increased participants' hours of sleep per night.
- PTSD is one of the diagnoses to obtain medical cannabis prescription

Sleep in Pain Conditions

- Chronic pain affect over 20% of our population and impacts sleep quality
- Sativex, a 1:1 THC/CBD cannabis-based medicine extract, on sleep in chronic pain
- CBD has also been helpful

Daytime Sleepiness

- Excessive daytime sleepiness (EDS) is a common symptom characterized by the urge to fall asleep during the light hours of the day
- Several causes including certain medications, various medical conditions, psychiatric conditions, and sleep disorders such as narcolepsy and OSA
- The negative consequences of EDS which include behavioral, attention, memory, and immune impairment can have a significant impact on quality of life
- Recent work on demonstrates CBD's impact on wakefulness

Summary

- Understanding the relationship of sleep disorders and the use of cannabinoids is in its infancy
- Many people are using cannabis products to help them sleep with little knowledge of rations of THC:CBD and doses
- Cannabis dependency is a real concern as it can lead to fragmented sleep patterns and severe withdrawal symptoms
- More research is needed

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