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***Cannabis & the Endocannabinoid System: What every nurse should know***

***Activity Expiration date: December 31, 2021***

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THIS PRESENTATION IS BROKEN DOWN INTO  
THREE PARTS. ALL 3 PARTS MUST BE REVIEWED  
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1. **ENDOCANNABINOID PHYSIOLOGY**

2. ENDOCANNABINOID PHARMACOLOGY

3. CANNABIS CLINICAL USES & IMPLICATIONS

# Cannabis (Medical Marijuana) & the Endocannabinoid System – PART 1

What Every Nurse Should Know

Dr. Hong Truong, D.O.

I hope that this lecture serve everyone in introducing the ECS and Cannabis medicine.

The objective of the lecture is to help anyone get started in having a good discussion with their patients in regards to the pros and cons of using medical cannabis.



# Learning Outcomes

1. Define the primary physiologic functions of the endocannabinoid system
2. Explain the differences between phytocannabinoids (plant based) & endocannabinoids (internal)
3. Apply the pharmacokinetic properties of endocannabinoids to patient education scenarios
4. Identify nursing interventions to promote patient safety with medical cannabis usage

Here are the objectives we will try to tackle.

- I will be talking about about the ECS system: We will talk about the purpose and the neurobiology of the system. We will also see how cannabis is involved with this system.
- I will talk about the pros and cons of cannabis medicine.
- I will also get into the the pharmacokinetics and pharmacodynamics of THC
- Throughout the lecture I will also sprinkle in some clinical pearls that would be helpful in your practice.



# Endocannabinoid System

Why the hype? Why does it seem to help with everything?

What is the runner's high? Is it just endorphins?

Cannabis is becoming more and more popular in the mainstream again. Is it true that it can treat so many diseases? How can we not be skeptical with anything claiming so many benefits?

To answer the question about the validity of cannabis used as a medicine we must start off with investigating the ECS. Afterwards hopefully we can have a pretty good theoretical basis for why cannabis seems to be so helpful.

Exercise seems to be the best medicine but have we do some people enjoy the effects of exercise? What is the underlying mechanisms? Why do people can get addicted to it? For the longest time I had always thought it was just an endorphins rush. Never really put much thought if there was another system. Some argue there might be another mechanism involved.



# Intro to the Endocannabinoid System

## Cannabis been around

- a. Dated to 2700 BC recorded Chinese medical texts - "Da Ma"
- b. 1800's British doctors documented use for appetite stimulation, muscle relaxation, anticonvulsant, analgesic, and hypnotic properties
- c. 1854 United States Dispensary
- d. 1900's fell out of favor because of unreliable results.
  - i. Marihuana Tax Act of 1937 banned use and Sale
- e. 1980's Researchers in US discovered cannabinoid receptors. 1990's an Israeli researcher discovered endogenous cannabinoids - Thus the ECS system

Here is a broad overview about cannabis in our history. It has been around for a very long time and it seems to have changing sentiments from being useful to not being useful to being useful again.

Just a side story in Chinese Medical Text one of the most famous figures in Chinese medicine performed the first surgeries in China with the help of cannabis. His name was Hua Tuo and is known as a "divine healer" The Chinese call cannabis as "da ma" emphasis is in the character ma which means to numb.

Another interesting point I wanted to point out is if we have information about the ECS system why is not taught in our medical education?

# What is the ECS responsible for?

Helps the body maintain homeostasis and helps the body combat inflammation - Key Point

Cannabinoid  
Receptors



Endocannabinoids



Metabolic Enzymes

Let us dive right in to the ECS and let us break down its components for discussion. At the end we will put it all together. This system seems to be located in basically all animals and the main purpose that take away is: homeostasis/inflammation

I like to talk in big concepts. Today we will focus on the receptors and the endocannabinoids. Many of us here have studied physiology and are familiar with the principle of the lock and key. For our purpose, we have cannabinoid receptors serve as the lock and the endocannabinoid serve as the key.

ECS Purpose: homeostasis/fight inflammation



# Terminology

Agonists: binds to and activates a receptor

Antagonist: Diminishes the effect of an agonist

These are just terms to brush up on our basic science:

Agonist binds and activates

Antagonist blocks at the receptor

# Cannabinoid Receptors

Helps the body maintain homeostasis and helps the body combat inflammation

Cannabinoid  
Receptors



Endocannabinoids



Metabolic Enzymes

On to the cannabinoid receptors



# Cannabinoid Receptors

Located on the the surface of numerous cell types -> diverse number of physiological effects

Where the receptors are located is a major determinant of what the particular effect will be.

## Location, Location, Location!

Remember the question I posed at the beginning. Is it all hype? Is cannabis the panacea of all medicine?

So here is a major concept to help explain why we get make a theoretical basis why cannabis has such a wide possibility of therapeutic options.

Generally, when there is a receptor there will be some type of action.

So the cannabinoid receptors are located almost the entire body we know there are many types of reactions.



## Endocannabinoid System: Cannabinoid receptors

G protein-coupled receptor - Located almost everywhere in the body: Key Point

CB 1 - expressed in the CNS (brain + spinal cord)

Brain- basal ganglia, hypothalamus, amygdala

Heart, uterus, testis, **skin**, small intestine

CB2 - immune system spleen, gastrointestinal system, **skin**

There are 2 well known studied receptors CB1 and CB2  
Classified as G protein receptor

You can See CB1 - expressed in the CNS and the CB2 can be located in the immune system organs.

Most locations actually have a ratio of CB1 and CB2 receptors.



## Endocannabinoid System: Cannabinoid receptors

Keep it simple in your mind:

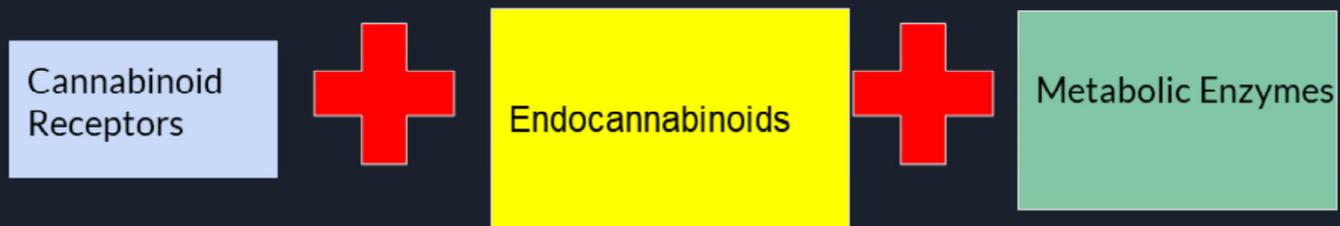
CB 1 - CNS - Brain and Nervous Tissues - > mental and perceptual influences

CB2 - everywhere else-> Immune system and pain control

So this is a slide to keep in mind

# Endocannabinoids

Helps the body maintain homeostasis and helps the body combat inflammation



When there is a lock hopefully we can find the key  
Lets go to the endocannabinoids



## Endocannabinoids - Humans did not evolve this system to just enjoy the plant

Endogenous cannabinoids - 2 well known and studied

Anandamide (AEA) - “blissfulness”; partial agonist of CB1 and CB2

2-AG (2-arachidonoylgerol)

most abundant,  
concentrated in the CNS  
full agonist to the CB1, and CB2 receptor

For those who are wondering - We did not develop an ECS so we can go around enjoying the plant.

We ourselves do produce what we call endogenous cannabinoids.  
There are 2 well known studied: AEA and 2-AG

Anandamide was named after a Sanskrit word meaning “blissfulness” - I think it is pretty appropriate. However, the real work horse of the body is 2-AG



# Anandamide

First discovered 1992 - Raphael Mechoulam

Sanskrit ananda “inner bliss or tranquility”

Lipophilic

Fatty acid amide hydrolase (FAAH) degrades anandamide into  
Ethanolamine and arachidonic acid

Research is trying create and find therapeutic options with **FAAH inhibitors**

Need to give credit to the Israeli researcher Raphael Mechoulam.

Some takeaways from this slide is to note that cannabinoids are lipophilic - meaning fat loving. That means clinically it can be absorbed through skin. It likes to take in the adipose tissues.

One of the building blocks have these molecules require arachidonic acid. Generally it is well known the arachidonic acid pathway will result in pro-inflammatory metabolites. In conventional medicine this is where Cox-inhibitors like NSAIDs come in to block this pathway. So how is ECS capable of being anti-inflammatory? We have a pathway to shunt arachidonic acid to become endogenous cannabinoid that are anti-inflammatory.

FAAH - I just want to mention here that all systems usually have some type of recycling mechanism. FAAH is the enzyme that helps in the process of breaking down. Currently researchers are trying to create FAAH inhibitors to prolong the cannabinoids in our system.



## 2- AG

Discovered 1995

Most abundant endocannabinoid in the human body

CNS

More influential to CB1 and CB2 receptor (full agonist)

Some call it the “work horse”



## If we make them, why do we even need the plant?

Endocannabinoid Deficiency Syndrome - is it a real thing?

We have enzymes (FAAH) that degrades our endocannabinoids. => short lived

Phytocannabinoids last longer in our bodies

Reading on the subject matter there is a very popular hypothesis out there that most clinical disease has to do with a Endocannabinoid Deficiency.

In theory the premise is either people are born with a bad system or the disease process overwhelmed the ECS system. When the body is not in homeostasis or can not contain the inflammation we have disease.

So that brings us to the important question how does the plant version work compared to the ones we make.

Key concept: phytocannabinoids last longer in our bodies.



# Phytocannabinoids

2 most studied:

THC

CBD

Honorable mention:

Beta-caryophyllene

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400+ compounds in a cannabis plant

In the conventional pharmaceutical we try to only have the active ingredient. I usually describe it as like listening to music performed by a soloist.

Cannabis medicine is like herbal medicine. You will be listening to a band or orchestra. In some ways it is like herbal medicine.

There are over 400+ compounds in a cannabis plant. THC and CBD are the most well studied so at this point we will discuss them for now because although there are many compounds but they are the major players or “diva” of the group.



# THC - $\Delta$ - 9 - Tetrahydrocannabinol

Psychoactive compound - Recreationally used to create the “high” sensation

Attaches to CB1 receptors; partial activation; “dimmer switch”

## What happens in the body:

Mentally: impaired reaction time, memory, and judgement and triggers ,  
appetite stimulation, hallucinations

Physically : red and dry eyes, reduced intraocular pressure, dry mouth, muscle  
relaxation, accelerated heart rate, changes in feet and hand temperature  
perception

Just wanted to highlight that Delta symbol. You may see it on the labeling as Delta 9

Also want to skip forward to a point about the confusion in the cannabis labeling right now.

At times you may see THCA and THC listed. Sometimes you may see THCA listed at 20% and THC is listed at 0%

THCA, is the proform of THC or the acid form. is the raw cannabis form = non psychoactive

THC is created by decarboxylation process/heating

As you can use a number of body and physiological changes can occur with THC

This is the compound people are trying to use for recreational purpose in the black market.



## Cannabidiol (CBD)- You will be seeing it everywhere

Cannabis compound effects without the psychoactivity

Made famous with possible results in seizure control

Competes with THC at the CB1 receptor therefore can reduce psychoactivity of THC

CBD inhibits FAAH which will allow more AEA and 2-AG

Cannabis sold online/stores - Advise patient that labeling could be 30% less in actual content

So everyone is all talking about CBD. CBD is CBD whether it comes from the hemp or marijuana plant. This is to support the point where I stated cannabis medicine is like herbal medicine. There are other compounds that support the CBD and THC.

The analogy I tell to patients is that THC is the accelerator and cbds are the brakes. You need both to drive a car in real life,

At the CB1 receptor he competes with THC so that reduces the psychoactivity. CBD also has other functions like inhibiting FAAH. As we recall researching are trying to create FAAH inhibitors so the endogenous cannabinoids we produce stay longer in our system

Advise patients that things sold at stores are not really tested. News articles report that what is labeled is actually 30% less in actual content.



# Beta-caryophyllene

Atypical cannabinoid

It is a Terpene

Full CB2 agonist - target for inflammation, pain, atherosclerosis, and osteoporosis

BCP low boiling point - best used orally or topically

It provides the distinctive flavor/scent: spiciness of black pepper, cloves, hops, and rosemary

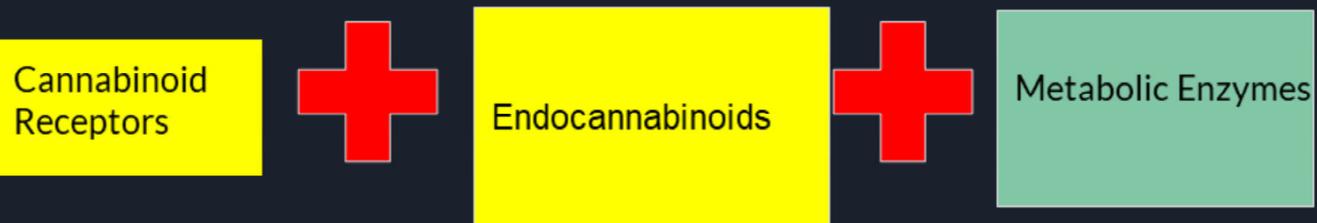
So the ECS can be triggered by other substances than cannabinoids.

Beta-Caryophyllene naturally found in black peppers, rosemary and other herbals can act on the receptors.

This one happens to act on the CB2 receptors.

# Endocannabinoids

Helps the body maintain homeostasis and helps the body combat inflammation

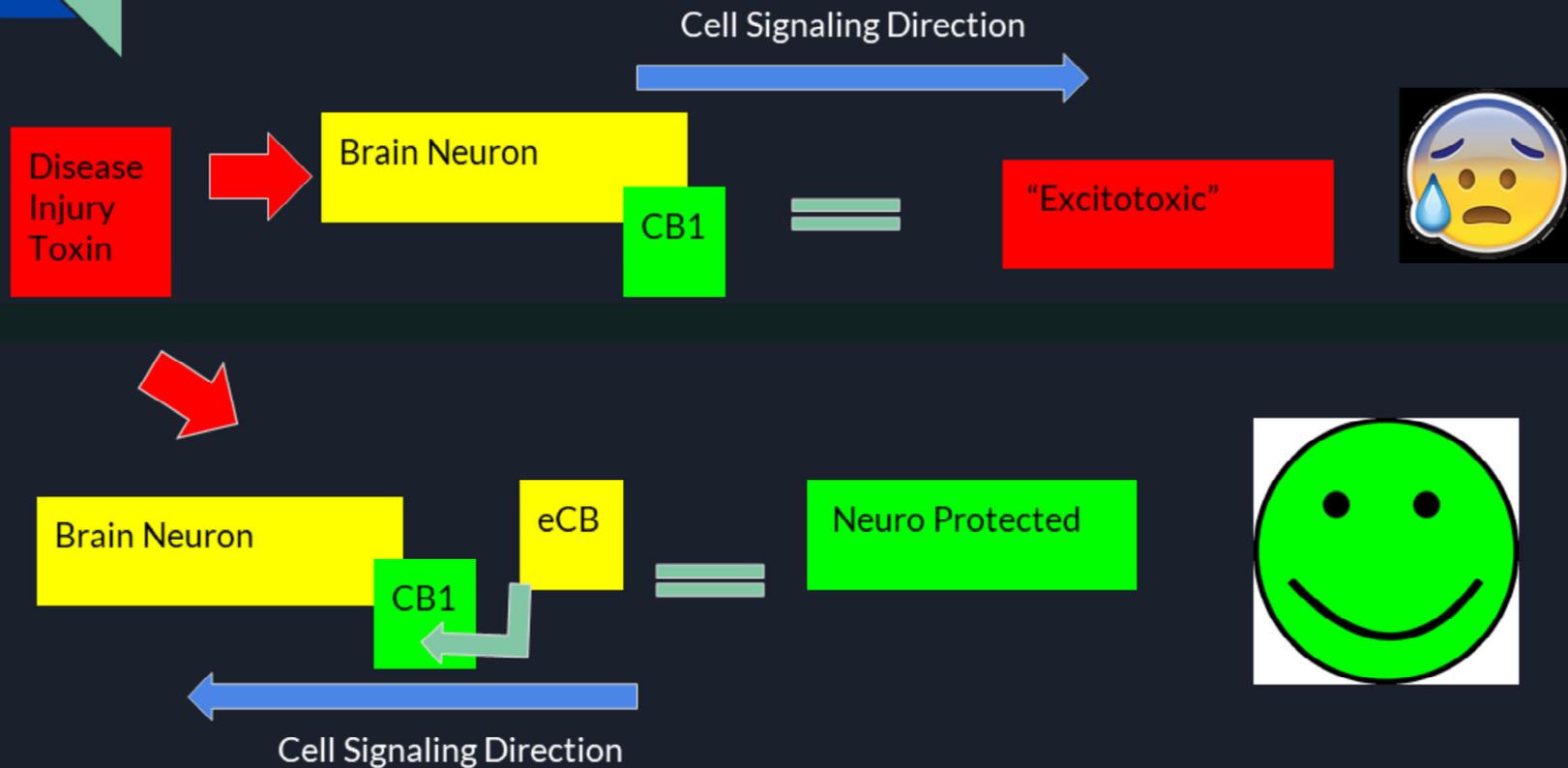


Let's put it all together

We talked about the locks and the keys.

Now let's put it all together.

# Purpose of the ECS? - Homeostasis



Alright, lets put it in a disease state context.

We can have disease, injury toxin, etc.

At the type if we don't control the injury then we have the potential for excitotoxicity.

However, we have an ECS

So the purpose is to reduce the severity of the injury.



## RECAP

Endocannabinoid system helps with homeostasis and helps control inflammation

Location of receptors will determine effects

Endocannabinoids work by dampening the neuroelectrical signalling: retrograde transmission

Phytocannabinoids work stronger and longer than endogenous Cannabinoids

**Other compounds/chemicals can work on the CB receptors - Terpenes**

**Cannabinoids can also work on other types of cell receptors**

So that is a crash course to the ECS  
Here are the key highlights to remember



END OF PART 1

PROCEED TO PART 2