Clinical evidence in cannabis medicine episode 3

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Cannabis and opioid

Clinical Study Results

- Journal of Psychoactive Drugs 2019, which evaluated data from 1,000 individuals taking legalized cannabis in one state, found that
- among the 65% of individuals taking cannabis for pain,

80% found it was very or tremendously helpful.

82% of these individuals being able to reduce, or halt, taking OTC pain medications

88% being able to halt taking opioids.[35]

- American Academy of Neurology 2019, Annual Meeting revealed that in a preliminary study, investigators at the Dent Neurologic Institute in Buffalo, New York, found that

the cannabis provided elderly patients with relief from chronic pain, sleep disorders, and anxiety related to diseases

such as amyotrophic lateral sclerosis, Parkinson disease, neuropathy, spinal cord damage, and multiple sclerosis.[6]

- Their findings show that medical cannabis is well tolerated in people aged 75 years and older and may improve symptoms such as chronic pain and anxiety.[6]
- Some evidence suggests cannabinoids may diminish opioid requirements for analgesia, although this finding is not conclusive.[36]
- In a systematic review, Nielsen et al evaluated the effect of cannabinoids to reduce opioid requirements for analgesia and found some lower quality studies suggesting a reduction in opioid requirements during coadministration with cannabinoids.
- Higher quality studies, however, failed to confirm an opioid-sparing effect.[36]

Cannabis in Appetite and weight loss

Hypothalamic POMC neurons promote cannabinoid–induced feeding

Marijuana flips appetite switch in brain

Sudden attacks of 'the munchies' triggered by changes in hormone pro-opiomelanocortin (POMC) release by neurons

Appetite and weight loss

Table 1

Clinical Trials With Cannabinoids: Cachexia and Anorexia

DRUG(S)	SUBJECTS	OUTCOME	REFERENCE
Dronabinol and megestrol	Cancer patients	No effect of dronabinol or combination on appetite or body weight	37
Dronabinol	Cancer patients	Increased appetite	38
Dronabinol and megestrol	AIDS patients	No effect of dronabinol or combination on appetite	39
Dronabinol vs placebo	HIV-positive patients	Increased body fat and increased appetite	40
Dronabinol vs placebo	Alzheimer's patients with anorexia	Increased body weight and decrease in disturbed behavior	41
Dronabinol vs placebo	AIDS patients	Increased appetite; stabilized weight	42
Dronabinol vs placebo	Late-stage AIDS patients	Stable body weight for 7 months	43

Dronabinol: taste alterations

Pilot trial to improve taste, smell changes in advanced cancer patients

THC 2.5 mg BID or TID vs placebo x 18 days, n=21

Questionnaires / interviews revealed significant improvement in taste / smell, increased appetite and protein intake

QoL measures found improved relaxation, quality of sleep

Adverse effects same in both groups

TD Brisbois Clarkson et al, *Ann Oncol* 2011; 22: 2086-93

What is the evidence?

Neuroprotection	**Evidence**
Pre-clinical	**+/-**
Clinical	**+**

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Selective Activation of Cannabinoid CB_2 Receptors Suppresses Neuropathic Nociception Induced by Treatment with the Chemotherapeutic Agent Paclitaxel in Rats

Elizabeth J. Rahn, Alexander M. Zvonok, Ganesh A. Thakur, Atmaram D. Khanolkar, Alexandros Makriyannis, and Andrea G. Hohmann

Brief Report

Double-Bli11d .. Placebo control trial Pilot study

Terpenes and appetite

Terpenes and appetite

- Terpenes are the “essential oils of cannabis” and are an element of the plant thought to contribute to and influence the effects a person feels after consuming cannabis. While there is still a ton of research that needs to be done, initial thoughts around terpenes point to the following when it comes to appetite.
- Terpenes thought to increase appetite:
- Myrcene – Also found in thyme, parsley, bayleaf, mango, and lemongrass, Myrcene has musky, herbal, clove, and citrus aromas. You can find high concentrations of myrcene in strains like Green Crack, Alien OG, Northern Lights, and Grandaddy Purple.
- Caryophyllene – Also found in clovers, black pepper, basil, and oregano, Caryophyllene has spicy, peppery, and woody aromas. You can find Caryophyllene is popular strains like Girl Scout Cookies, White Widow, Chemdawg, and Bubba Kush.

Terpenes and appetite

- Limonene – Also found in citrus like lemons, peppermint and rosemary, limonene is a very common terpenes in cannabis. You can find it in strains like Super Lemon Haze, Trainwreck, and Bubba Kush.
- Pinene – Also found in Rosemary, conifer trees, basil, and dill, Pinene is an earthy terpene with aromas of pine, sweetness, and earth. You can find Pinene in strains like Jack Herer, Dutch Treat, Romulan, Blue Dream, and OG Kush.
- Terpenes thought to suppress appetite:
- Humulene – Also found in hops, ginger, sage, and ginseng, Humulene has hoppy, woody, herbal, and spicy aromas. You can find Humulene in strains like White Widow, OG Kush, Sour Diesel, and Headband.

Cannabinoids and appetite

Cannabis increase apatite

- เพราะกัญชา กระตุ้นการหลั่งฮอร์โมนที่ชื่อว่า Ghrelin ซึ่งฮอร์โมนตัวนี้ ควบคุมความรู้สึกหิวอาหาร
- เมื่อ สาร THC กระตุ้นตัวรับ CB1 ทำให้ฮฮร์โมน Ghrelin หลั่งออกมามากขึ้น ทำให้กระตุ้นให้มีความอยากอาหารมากขึ้นนั่นเอง

.

Top Cannabinoids for Appetite

- While terpenes are starting to get some much-needed attention, cannabinoids are still the shining star of marijuana. THC and CBD are the most talked about but there are over 100 cannabinoids that have been identified.
- ในขณะที่ THC ให้ความรู้สึกสบายที่เป็นเอกลักษณ์และออกฤทธิ์ทางจิตสูง แต่ก็คิดว่าจะเพิ่มความอยากอาหารพร้อมกับ cannabinoid ที่ไม่ค่อยมีใครรู้จัก CBG ในทางกลับกันหากคุณต้องการระงับความอยากอาหาร THCV ถือเป็นตัวเลือกที่ยอดเยี่ยม.

Cannabinoids increase appetite:

- THC (Tetrahydrocannabinol) – the main psychoactive cannabinoid in cannabis and found in almost all strains at legal dispensaries.
- CBG (Cannabigerol) – a non-psychoactive cannabinoid that exists in much smaller quantities as compared to THC in cannabis.

Cannabinoids suppress appetite:

- THCV (Tetrahydrocannabivarin) – a very mildly psychoactive cannabinoid. In small doses, it doesn't appear to cause psychoactivity but in large doses, some people report a clear-headed and stimulated high. THCV is believed to provide the benefits of THC without the strong high and with a secondary benefit of appetite suppressant.

Strains and appetite

Top Flower Strains for Appetite

- So now you know the terpenes and cannabinoids that are thought to effect appetite but what about the actual strains? What flower do you choose to stimulate or suppress appetite? Here's a quick list of great choices for either direction you want to go.

Strains thought to increase appetite:

- Pineapple Express – This sativa dominant strain is a cross of the landrace sativa, Hawaiian, and the hybrid, Trainwreck. Expect fruity, floral, and pungent aromas and a strong head and body high.
- Girl Scout Cookies (also known as "GSC") – A super popular hybrid strain with intense euphoric effects. Expect sweet, earthy, peppery aromas delivering a strong balanced high.

Strains thought to suppress appetite:

- Durban Poison – the legendary ladrace strain. Durban Poison gets it's name from the port city of Durban, South Africa from where it was thought to have been first imported into the states in the 1970's. Durban Poison usually has around 1% THCV which is high for any strain. Expect energetic and stimulating effects from this popular sativa.

Endocannabinoids and obesity

- ระบบเอ็นโดแคนนาบินอยด์ เกี่ยวข้องกับระบบการเผาผลาญพลังงาน หรือไขมัน ควบคุม สั่งการ เพื่อให้การทำงานในระบบการควบคุมพลังงานในร่างกายเกิดขึ้นอย่างปกติ
- จากภาพประกอบ เราจะเห็นว่า ระบบเอ็นโดแคนนาบินอยด์ในบทบาทด้านควบคุมระบบพลังงานในร่างกาย มีส่วนตั้งแต่การควบคุมยังระบบประสาทส่วนกลางไปยังระบบประสาทส่วนปลาย และไปถึงการนำควบคุมการเก็บพลังงานในเรื่องอินซูลิน ที่ผมเคยเขียนไปแล้ว
- กระตุ้นให้เซลล์ไขมันขาว เปลี่ยนไปเป็นไขมันน้ำตาล เพิ่มระดับการเผาไขมัน และควบคุมการฝังเก็บไขมันลงในเซลล์ร่างกาย
- ไขมันน้ำตาล คือ ไขมันที่มีไมโตคอนเดรียอยู่เยอะ ซึ่งไมโตคอนเดรียเปรียบได้กับโรงงานผลิตพลังงาน ซึ่งมีเยอะก็ยิ่งจะช่วยเผาไขมันไปใช้มากขึ้น นั่นเอง
- ระบบเอ็นโดแคนนาบินอยด์ยังควบคุมการทำงานของฮอร์โมนที่เกี่ยวข้องกับความต้องการอาหารด้วย เช่น ฮอร์โมนเกรลิน ฮอร์โมนเลปติน เป็นต้น

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Energy balance regulation by endocannabinoids at central and peripheral levels

Carmelo Quarta • Roberta Mazza • Silvana Obici • Renato Pasquali • Uberto Pagotto

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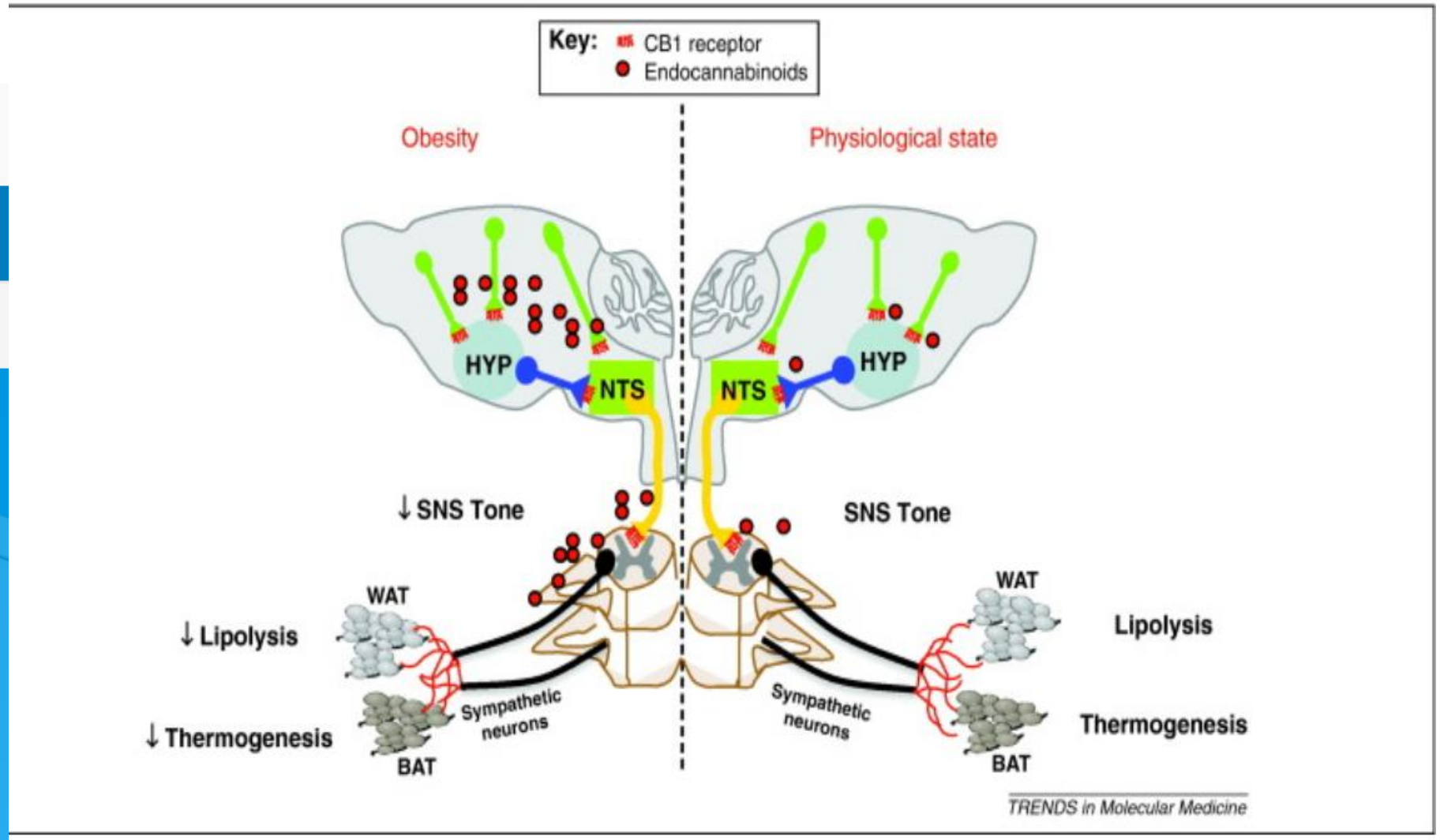
PlumX Metrics



Energy balance regulation by endocannabinoids at central a...

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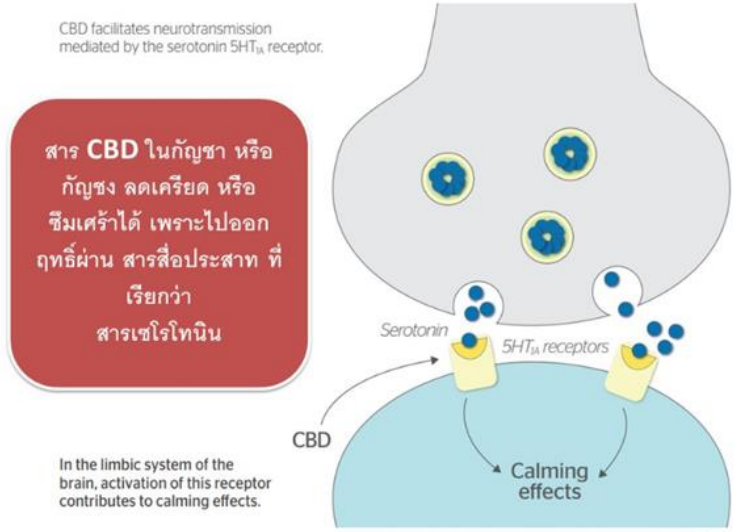
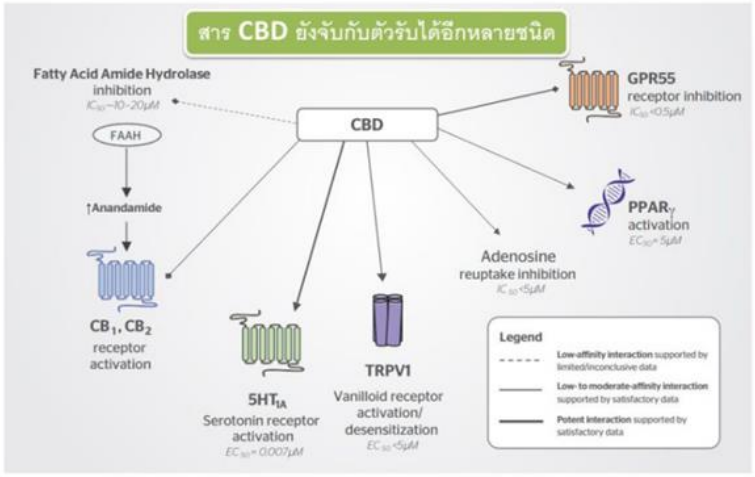
Cannabis and Anxiety

กัญชา กัญชง
แก้โรคเครียด ซึมเศร้าได้?





กัญชา กัญชง จะสามารถแก้โรคซึมเศร้า หรือความเครียดได้หรือไม่นั้น ตามที่เคยมีรายงานของผู้ที่เคยใช้ ก่อนอื่นต้องทำความเข้าใจระบบในร่างกายที่มีส่วนเกี่ยวข้องกับการดูแลสุขภาพของอารมณ์

.

หรือเข้าใจง่ายๆ ก็คือว่า ก่อนจะไปรู้ว่ากัญชา กัญชง สามารถแก้เครียด ลดซึมเศร้าได้ไหม ก็ต้องทำความเข้าใจร่างกายก่อนว่าเวลาที่เครียดหรือซึมเศร้า ร่างกายเกิดอะไรขึ้น มีการทำงานของร่างกายหรือระบบอะไรในร่ากายที่ผิดปกติไป หรือมีสารสื่อประสาทชนิดไหนในร่างกายที่ก่อให้เกิดภาวะเครียด ซึมเศร้า เป็นต้น

.

ปัจจุบันมีการค้นพบว่า สารสื่อประสาทซีโรโทนิน เป็นสารสื่อประสาทที่เกี่ยวข้องกับอารมณ์และความรู้สึกที่เกิดขึ้นในร่างกายของมนุษย์คนเรา และยังพบว่าระบบเอ็นโดแคนนาบินอยด์เป็นระบบที่เกี่ยวข้องกับการทำงานของสารสื่อประสาทซีโรโทนินชนิดนี้ด้วย นั่นหมายความว่า อารมณ์และความรู้สึกของคนเราที่เกิดขึ้น มีระบบเอ็นโดแคนนาบินอยด์เข้ามามีบทบาทสำคัญในการควบคุมหรือปรับสมดุล

.

ภาวะเครียดหรือโรคซึมเศร้า เป็นภาวะที่มีสารสื่อประสาทเซโรโทนินเข้ามาเกี่ยวข้อง และเป็นผลให้มีการใช้ยาเคมีที่มีผลในการควบคุมปริมาณของสารสื่อประสาทชนิดนี้ เพื่อนำมาแก้ไขภาวะของโรคดังกล่าว แต่ด้วยความยาเคมีก็มีอาการข้างเคียง ทำให้การใช้ทางเลือกในกลุ่มสมุนไพรชนิดต่างๆเพิ่มมากยิ่งขึ้น ซึ่งสารไฟโตแคนนาบินอยด์จากกัญชา กัญชง ก็เป็นหนึ่งในสมุนไพรที่มีรายงานการใช้ในอดีตจนถึงปัจจุบัน และพบคุณสมบัติช่วยลดความเครียด ช่วยผ่อนคลาย

.

แต่ด้วยความที่สาร THC ซึ่งพบในกัญชา ก็มักมีคุณสมบัติที่ผลต่อระบบสารสื่อประสาทหลายชนิด และถ้าใช้ไม่เป็นก็จะมีผลทำให้ผู้ที่มีอาการอยู่ก่อนแล้ว มีอารมณ์ที่เปลี่ยนแปลงขึ้นลงได้ง่าย จึงไม่เป็นที่นิยมใช้กันในภาวะนี้ แต่สำหรับสาร CBD ที่พบมากทั้งในกัญชา หรือกัญชง มักให้ผลการเปลี่ยนแปลงในผู้ที่ประสบภาวะเหล่านี้ค่อนข้างดีกว่า หรือให้เข้าใจง่ายๆ คือว่า

.

ถ้าใช้สาร THC ในคนกลุ่มนี้ มักจะกระชากอารมณ์ทั้งขึ้นหรือลงมากกว่าหรือรุนแรงกว่า ทำให้ไม่เป็นที่นิยมใช้ แต่สำหรับ สาร CBD มักจะไม่กระชาก ให้อารมณ์แบบค่อยๆปรับ แบบสุนทรีย์มากกว่า ซึ่งกรณีนี้ คนละอย่าง กับอารมณ์ครึ้มเคลิ้มที่แบบจากการสูบกัญชาที่มีสาร THC นะครับ

.

ในทางการใช้เพื่อประโยชน์ของผู้ที่เครียด หรือ ซึมเศร้า จึงมักแนะนำให้เริ่มต้นด้วยสารไฟโตแคนนาบินอยด์ที่อุดมไปด้วยสาร CBD มากกว่า จะเริ่มที่สาร THC

.

ดังนั้น คำถามที่ว่า ทำไมกัญชา กัญชง จึงจะรักษาภาวะเครียด หรือโรคซึมเศร้าได้ ก็เพราะทั้งในกัญชา กัญชง มีสาร CBD ที่ออกฤทธิ์ไปยังระบบสารสื่อประสาทเซโรโทนิน ซึ่งเป็นสารสื่อประสาทที่สำคัญที่เกี่ยวข้องกับอารมณ์และความรู้สึกที่เกี่ยวข้องกับภาวะโรคดังกล่าว นั่นเอง

12 High-CBD Cannabis Strains to Ease Anxiety

1. Remedy
2. ACDC
3. Lifter
4. Charlotte’s Web
5. Cherry Wine
6. Ringo’s Gift
7. Harle-Tsu
8. Sour Tsunami
9. Elektra
10. Sour Space Candy
11. Suzy Q
12. Critical Mass

12 High-CBD Cannabis Strains to Ease Anxiety

- Cannabis is a go-to remedy for some folks living with anxiety. But not all cannabis is created equal. Some strains can actually bring on or worsen anxiety.
- The key is to choose a strain with a high CBD-to-THC ratio.
- Cannabidiol (CBD) and tetrahydrocannabinol (THC) are the main active compounds in cannabis. They're both similar in structure, but there's one very big difference.
- THC is a psychoactive compound, and CBD is not. It's THC that causes the "high" associated with cannabis, including the anxiety and paranoia that some people experience.
- While not a treatment for anxiety, using high-CBD strains might help ease certain symptoms, especially when combined with other tools, like therapy.
- We combed through Leafly's strain explorer to find 12 CBD-dominant strains worth trying if you're looking for something on the mellower side.
- Keep in mind that strains aren't an exact science. The effects aren't always consistent, even among products of the same strain.

12 High-CBD Cannabis Strains to Ease Anxiety

1. Remedy: Remedy is a 14 percent CBD strain that produces little to no psychoactive effects. It's got a lemon-pine scent. Most users recommend it for its ability to mellow you out without the intense head and body effects of high-THC strains.

2. ACDC: This is another 14 percent CBD strain preferred by people looking to relieve stress, anxiety, and pain without feeling stoned. It contains no relevant amount of THC. The two most common words used to describe its effects are "relaxed" and "happy," according to reviews on Leafly.

3. Lifter: Lifter is a newer player in the cannabis game. It averages around 16 percent CBD with next to no THC. Its aroma is described as "funky cheese with a hint of fuel" (weird flex, but OK). It's uber-relaxing effects won't put a damper on your focus or function.

4. Charlotte's Web: This is one of the best-known high-CBD strains. It contains around 13 percent CBD with little to no THC. It's used in several health and wellness products to help ease anxiety, pain, and depression without any psychoactive effects.

5. Cherry Wine: If you like the smell of wine and cheese, Cherry Wine's your strain. It averages around 17 percent CBD with less than 1 percent THC. According to user reviews, it relaxes your brain and muscles without mind-altering effects.

6. Ringo's Gift: This CBD strain has an average CBD-to-THC ratio of 13:1, but strains as high as 20:1 can be found. Ringo's Gift is a cross of two high-CBD strains: ACDC and Harle-Tsu, which is actually next on our list. Users report a big improvement in anxiety and stress levels after using this strain. Improved sleep is another effect users rave about.

12 High-CBD Cannabis Strains to Ease Anxiety

7. Harle-Tsu: This award-winning strain averages around 13 percent CBD but often tests much higher. It was named best CBD flower at the 2014 Emerald Cup. Lab tests found it to contain 21.05 percent CBD and 0.86 percent THC.This ratio makes it a favorite for people looking to lower anxiety and boost their mood and focus.

8. Sour Tsunami: This was one of the first high-CBD strains ever bred and remains a fan favorite. It has an average CBD:THC ratio of 13:1 or even lower THC. Users report feeling relaxed and happy without that "heavy body" feeling.

9. Elektra: Elektra averages around 16 percent CBD with less than 1 percent THC. Some user reviews say it's tested as high as around 20 percent CBD. Its pungent smoke and aroma get mixed reviews, but people love it for its relaxing effect that doesn't totally wipe you out.

10. Sour Space Candy: This high-CBD strain has some sour notes as far as aroma, but it gets props from people who use it to relieve symptoms of anxiety and depression. Sour Space Candy has an average of 17 percent CBD and only a trace amount of THC.

11. Suzy Q: Suzy Q isn't as high in CBD as some other strains. It comes in at about 11 percent CBD with little to no THC. It's considered a good choice for helping to relax an anxious mind and tense muscles without getting you high or knocking you out.

12. Critical Mass: This strain contains more THC than the others we've listed, making it a good option if you're still looking for a light buzz. It can contain anywhere from 4 to 7 percent THC and 8 to 10 percent CBD. According to user reviews, people who don't generally do well with THC find that this strain relaxes and calms without causing a green out.

What is the evidence?

	Evidence
Insomnia	
Pre-clinical	**-**
Clinical	**++***
Anxiety	
Pre-clinical	**++**
Clinical	**-**

*secondary finding

Cannabinoids and anxiety

Oral cannabinoids used for nausea produces sedation and reduces anxiety

Very low dose cannabis can produce sedation, diminish anxiety without getting high

Cannabidiol can exert anti-anxiety effects, although only demonstrated in acute, experimentally-induced anxiety

Tramer et al, *BMJ* 2001; 323:1-8
Graham and Li, Cannabis and Health, 1976
Bergamaschi et al, *Neuropsychopharmcol* 2011; 36: 1219-26

Psychoneuroendocnnology (2015) 51, 585 - 588

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: .vww.elsevier.com/locateJpsyneuen

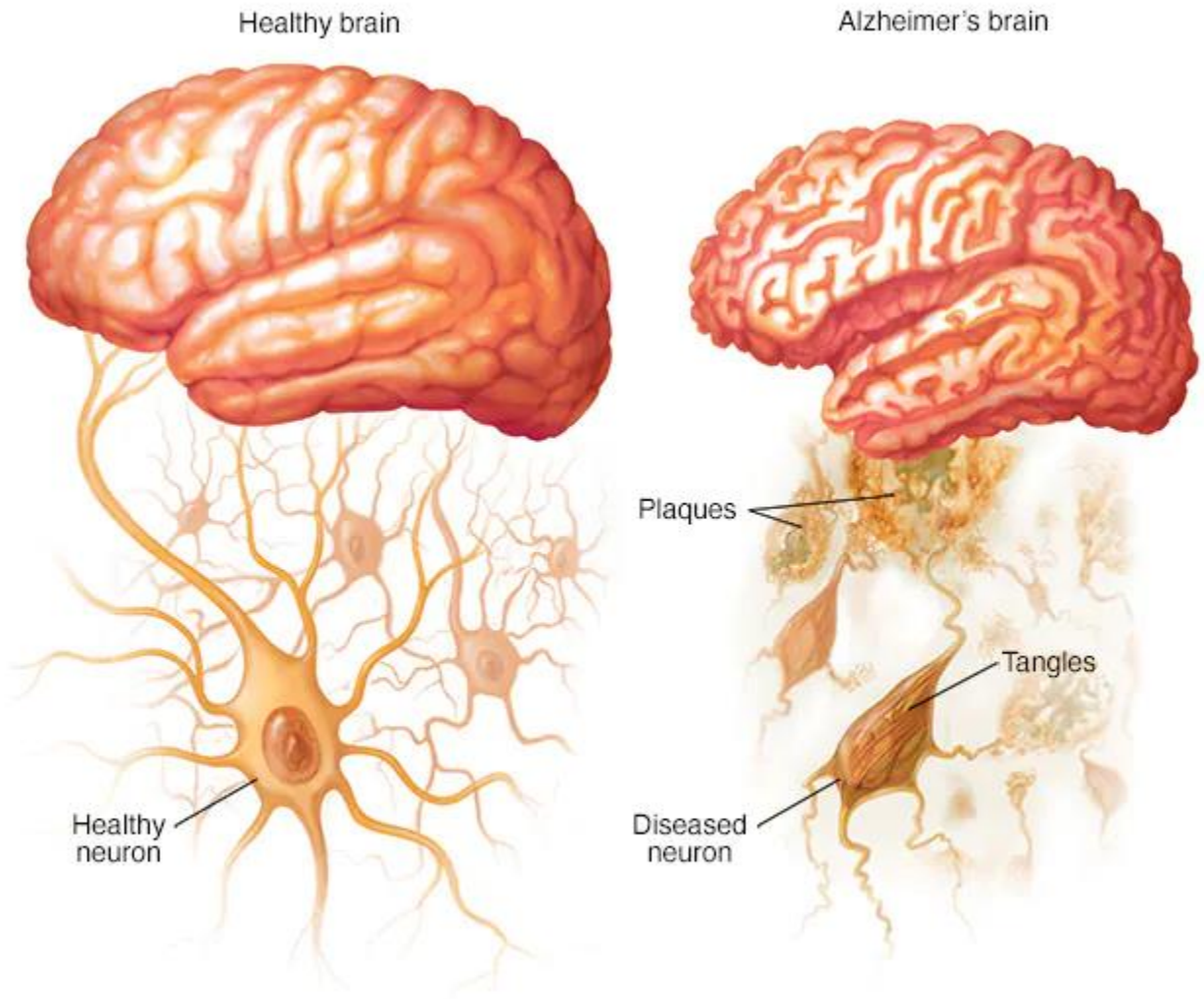
The efficacy of nabilone, a synthetic cannabinoid, in the treatment of PTSD-associated nightmares: A preliminary randomized, double-blind, placebo-controlled cross-over design study

Rakesh Jetly a*, Alexandra Heber a, George Fraser b, Denis Boisvert b

Alzheimer’s disease

Medically reviewed by Seunggu Han, M.D. — Written by Jaime Herndon, MS, MPH, MFA — Updated on February 7, 2022

Alzheimer's disease



Pathophysiology

- The most common cause of dementia with gradual decline of memory, thinking, behavior, and social skills.
- It is a neurodegenerative disease that starts slowly and progressively worsens over time.
- It's characterized by changes in the brain that leads to deposit of certain proteins (amyloid beta) and causes neurodegeneration, neuroinflammation, and the brain to shrink and cell dead.

Mayo Clinic. www.google.com

Risk factors for Alzheimer's disease include:

Age (increasing age is the main risk factor).

Genetics.

Traumatic head injury.

Depression.

Cardiovascular disease and cerebrovascular disease.

High blood pressure.

High cholesterol.

Diabetes.

Smoking.

Obesity.

What is Alzheimer's disease?

- Alzheimer's disease is a progressive form of dementia.
- Dementia is a broader term for conditions that negatively affect memory, thinking, and behavior.
- The changes interfere with daily living.
- Dementia can have a range of causes, such as brain injuries or diseases. Sometimes the cause is unknown.
- Alzheimer's disease accounts for 60 to 80 percent of dementia cases.
- Most people with the disease get a diagnosis after age 65.
- If it's diagnosed before then, it's generally referred to as "younger onset" or "early onset" Alzheimer's disease.
- There's no cure for Alzheimer's, but there are treatments that can slow the progression of the disease.

Alzheimer's facts

- Alzheimer's disease is a chronic (long-term), ongoing condition.
- It is not a typical sign of aging.
- Alzheimer's and dementia aren't the same thing.
- Alzheimer's disease is a type of dementia.
- Its symptoms come on gradually, and the effects on the brain are degenerative, meaning they cause slow decline.
- Anyone can get Alzheimer's disease, but certain people are at higher risk for it.
- This includes people over age 65 and those with a family history of the condition.
- There's no single expected outcome for people with Alzheimer's.
- Some people live a long time with mild cognitive damage, while others experience a more rapid onset of symptoms and quicker disease progression.
- There's no cure for Alzheimer's yet, but treatment can help slow the progression of the disease and may improve quality of life.
- Each person's journey with Alzheimer's disease is different.

Symptoms of Alzheimer's disease

- Everyone has episodes of forgetfulness from time to time.
- But people with Alzheimer's disease display certain ongoing behaviors and symptoms that worsen over time. These can include:
- memory loss affecting daily activities, such as keeping appointments
- trouble with familiar tasks, such as using a microwave
- difficulties with problem-solving
- trouble with speech or writing
- becoming disoriented about times or places
- decreased judgment
- decreased personal hygiene
- mood and personality changes
- withdrawal from friends, family, and community
- These signs don't always mean that a person has Alzheimer's. It's important to see a doctor to determine the cause.
- Symptoms change according to the stage of the disease. In later stages, people with Alzheimer's often have significant trouble with talking, moving, or responding to what's happening around them.

Diagnosing Alzheimer's disease

- The only definitive way to diagnose someone with Alzheimer's disease is to examine their brain tissue after death.
- But a doctor can use other examinations and tests to assess your mental abilities, diagnose dementia, and rule out other conditions.
- The doctor will likely start by taking a medical history.

They may ask about your:

- symptoms
- family medical history
- other current or past health conditions
- current or past medications
- diet, alcohol intake, and other lifestyle habits
- From there, your doctor will likely request several tests to help determine if you have Alzheimer's disease.

Alzheimer's tests

- There's no definitive test for Alzheimer's disease. However, mental, physical, neurological, and imaging tests can help your doctor reach a diagnosis.
- Your doctor may start with a mental status test.

This can help them assess your:

- short-term memory
- long-term memory
- orientation to place and time

For example, they may ask you:

- what day it is
- who the president is
- to remember and recall a short list of words

Next, they'll likely conduct a physical exam. For example, they may:

- check your blood pressure
- assess your heart rate
- take your temperature
- request urine or blood tests, in some cases

Your doctor may also conduct a neurological exam to rule out other possible diagnoses, such as acute medical issues like infection or stroke. During this exam, they will check your:

- reflexes
- muscle tone
- speech

Brain imaging studies

- **Magnetic resonance imaging (MRI) scan.** MRIs can help pick up key markers, such as inflammation, bleeding, and structural issues.
- **Computed tomography (CT) scan.** CT scans take X-ray images, which can help your doctor look for abnormal characteristics in your brain.
- Other tests your doctor may do include blood tests to check for genes that may indicate you have a higher risk of Alzheimer's disease.

Alzheimer's medication

- There's no known cure for Alzheimer's disease.
- However, your doctor can recommend medications and other treatments to help ease your symptoms and delay the progression of the disease for as long as possible.
- For early to moderate Alzheimer's, your doctor may prescribe medications such as donepezil (Aricept) or rivastigmine (Exelon). These drugs can help maintain high levels of acetylcholine in your brain. This can help the nerve cells in your brain send and receive signals better. In turn, this may ease some symptoms of Alzheimer's.
- A newer medication called aducanumab (Aduhelm) is recommended only for those with early Alzheimer's.
- It is thought to reduce the protein plaques that build up in the brain with Alzheimer's.
- However, there are some concerns about whether the drug's potential benefits outweigh its risks.
- To treat moderate to late stage Alzheimer's, your doctor may prescribe donepezil (Aricept) or memantine (Namenda). Memantine can help block the effects of excess glutamate. Glutamate is a brain chemical that's released in higher amounts in Alzheimer's disease and damages brain cells.
- Your doctor may also recommend antidepressants, anti-anxiety medications, or antipsychotics to help treat symptoms related to Alzheimer's. These symptoms vary based on the progression of the disease, and can include:
- depression
- difficulty sleeping at night
- agitation
- hallucinations
- Although the care needs of a person with Alzheimer's will increase over time, the exact symptoms will be different from person to person.

Other Alzheimer's treatments

In addition to medication,

- lifestyle changes can help you manage your condition. For example, your doctor might develop strategies to help you or your loved one:
- simplify tasks
- limit confusion
- get enough rest every day
- use relaxation techniques
- create a calming environment

- a team of healthcare professionals can help you maintain your quality of life at all stages along the Alzheimer's journey. include:
- physical therapist, to help with staying active
- dietician, to maintain a balanced, nutritious diet
- pharmacist, to help with monitoring medications
- mental health professional, who may work with the person with Alzheimer's as well as their caregivers
- social worker, to help with accessing resources and support
- care center, to provide short-term care for someone with Alzheimer's when their caregivers are temporarily unavailable
- hospice care center, to manage symptoms in a comfortable and supportive setting at the end of life
- vitamin E could help slow the loss of functioning in Alzheimer's, especially when taken with medications like donepezil that increase acetylcholine in the brain.
- alternative and complementary therapies

Alzheimer's disease causes and risk factors

- no single cause of Alzheimer's disease, but they have identified certain risk factors, including:
- **Age.** Most people who develop Alzheimer's disease are 65 years of age or older.
- **Family history.** If you have an immediate family member who has developed the condition, you're more likely to get it.
- **Genetics.** Certain genes have been linked to Alzheimer's disease. *Apolipoprotein E (APOE)* is a gene that's been linked to the onset of Alzheimer's symptoms in older adults.
- Having one or more of these risk factors doesn't mean that you'll develop Alzheimer's disease. It simply raises your risk level.
- Other possible risk factors include a history of:
- depression
- smoking
- cardiovascular disease
- previous traumatic brain injury

Alzheimer's stages

- Alzheimer's is a progressive disease, which means the symptoms will gradually increase over time. There are seven main stages:
- **Stages 1–3: Pre-dementia and mild cognitive impairment**
- **Stage 1.** There are no symptoms at this stage. If you have a family history of Alzheimer's and no symptoms, you may wish to talk to a doctor about strategies for healthy aging.
- **Stage 2.** The earliest symptoms appear, such as forgetfulness.
- **Stage 3.** Mild physical and cognitive impairments appear, such as reduced memory and concentration. Learning new skills may become harder. These changes may only be noticeable by someone very close to the person.
- **Stages 4–7: Dementia**
- **Stage 4.** Alzheimer's is often diagnosed at this stage, but it's still considered mild. It's common to notice memory loss and to have difficulty managing everyday tasks.
- **Stage 5.** Moderate to severe symptoms will require help from loved ones or caregivers. This is necessary to ensure that daily needs are being met, such as eating meals and managing the home.
- **Stage 6.** At this stage, a person with Alzheimer's will need help with basic tasks, such as eating, dressing, and toileting.
- **Stage 7.** This is the most severe and final stage of Alzheimer's. There is usually a progressive loss of speech and facial expressions. Movement is likely to become limited.

Prognosis

- People ages 65 and older. with Alzheimer’s typically live for 4 to 8 years Trusted Source after diagnosis, though some live for up to 20 years.

Preventing Alzheimer's (preventive measures.)

- Just as there's no known cure for Alzheimer's,
- health-promoting lifestyle habits are the best tools we have to prevent cognitive decline.

The following steps may help:

- **Try to quit smoking.** If you smoke, quitting benefits your health both immediately and in the long term.
- **Exercise regularly.** Getting active reduces the risk of many conditions, such as cardiovascular disease and diabetes.
- **Keep your brain active.** Try some cognitive training exercises.
- **Eat well.** Eat a balanced diet with plenty of fruits and vegetables.
- **Maintain an active social life.** Friendships, volunteering, and hobbies are likely to benefit your overall health.

CB1 and CB2 pharmacology

- AEA กระตุ้น CB2 ทำให้เซลล์ไฟโบรบลาสท์ของตับถูกทำลาย
- CB2 agonist กระตุ้น CB2 ทำให้เกิด hepatoprotective function (treatment of liver disease)
- ทั้ง CB1 และ CB2 ช่วยปกป้องกระดูก (protective effect of bone loss) ในผู้สูงอายุ (osteoporosis)
- ECS เกี่ยวข้องกับ neurotransmitter ของสมอง

Alzheimer’s disease (AD)

- พบโรคนี้ประมาณ 10% ในคนที่มีอายุ > 80 ปี เป็น most common cause ของ dementia
- เกิดจากพันธุกรรม (genetic) และไม่รู้สาเหตุ (idiopathic etiology)
- มีการลดลงของ CB1 ในสมองของ AD แต่ CB2 เพิ่มขึ้น
- ระดับของ 2-AG เพิ่มขึ้นใน hippocampus แต่ไม่เพิ่มขึ้นในเลือด

Alzheimer's disease (AD)

- อาการ repeat statements and questions over and over
- Forget conversations, appointments or events
- Forget the names of family members and everyday objects
- Get lost in familiar places
- Trouble to find the right words to identify objects, express thoughts or take part in conversation
- นอนไม่หลับ เดินไปมา โกรธ หงุดหงิด ก้าวร้าว ซึมเศร้า วิตกกังวล กระสับกระส่าย
- THC ทำให้พฤติกรรม การกินอาหารและอาการวุ่นวายตอนกลางคืนดีขึ้น

วารสาร
กรมการแพทย์
Journal of the Department of Medical Services

Effectiveness and Safety Evaluation of Medical Cannabis in Alzheimer's disease in Chiang Mai Neurological Hospital

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Chiangmai Neurological Hospital

MAKE A SUBMISSION

LANGUAGE

English

ภาษาไทย

INFORMATION

For Readers

For Authors

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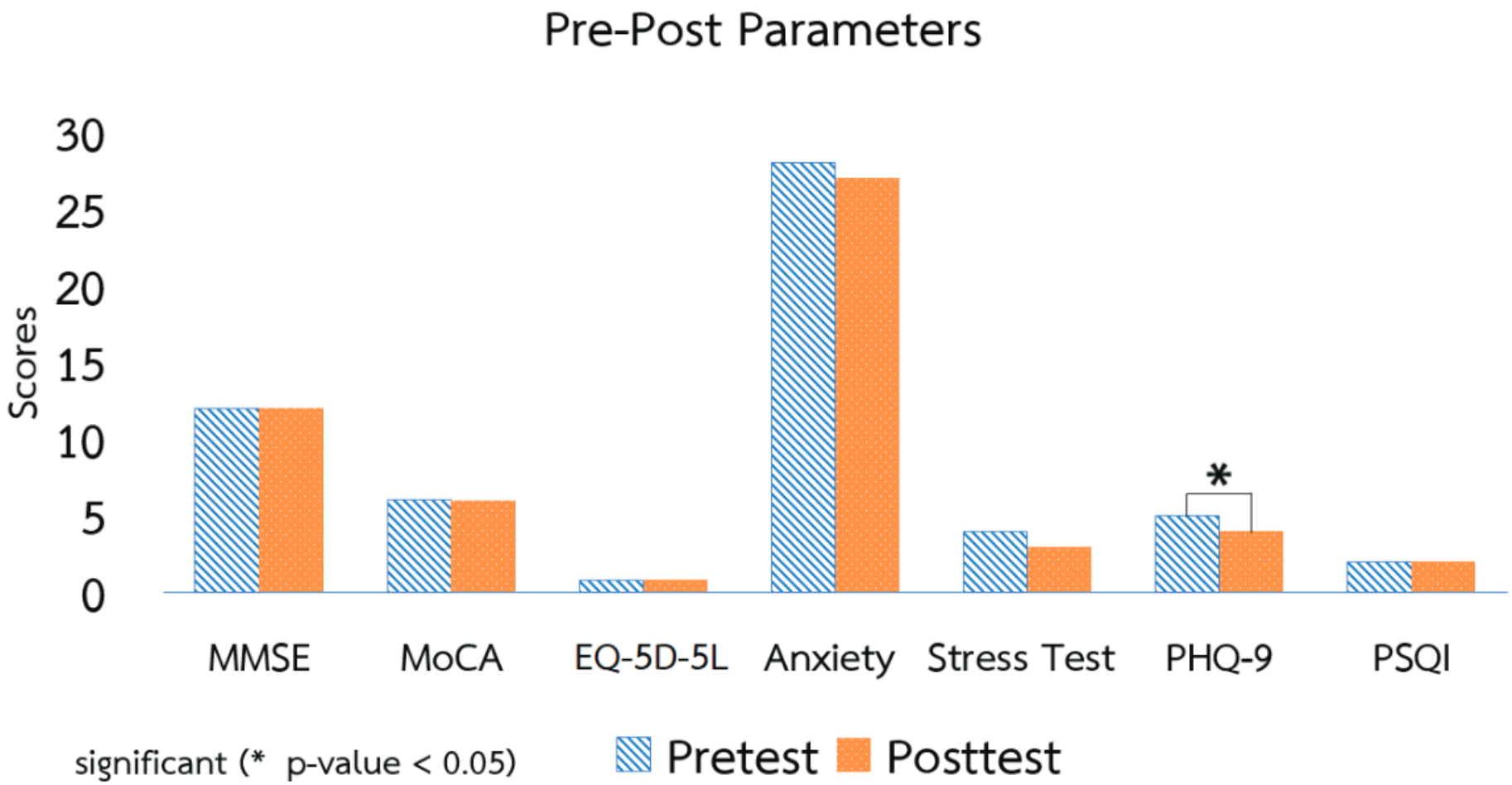
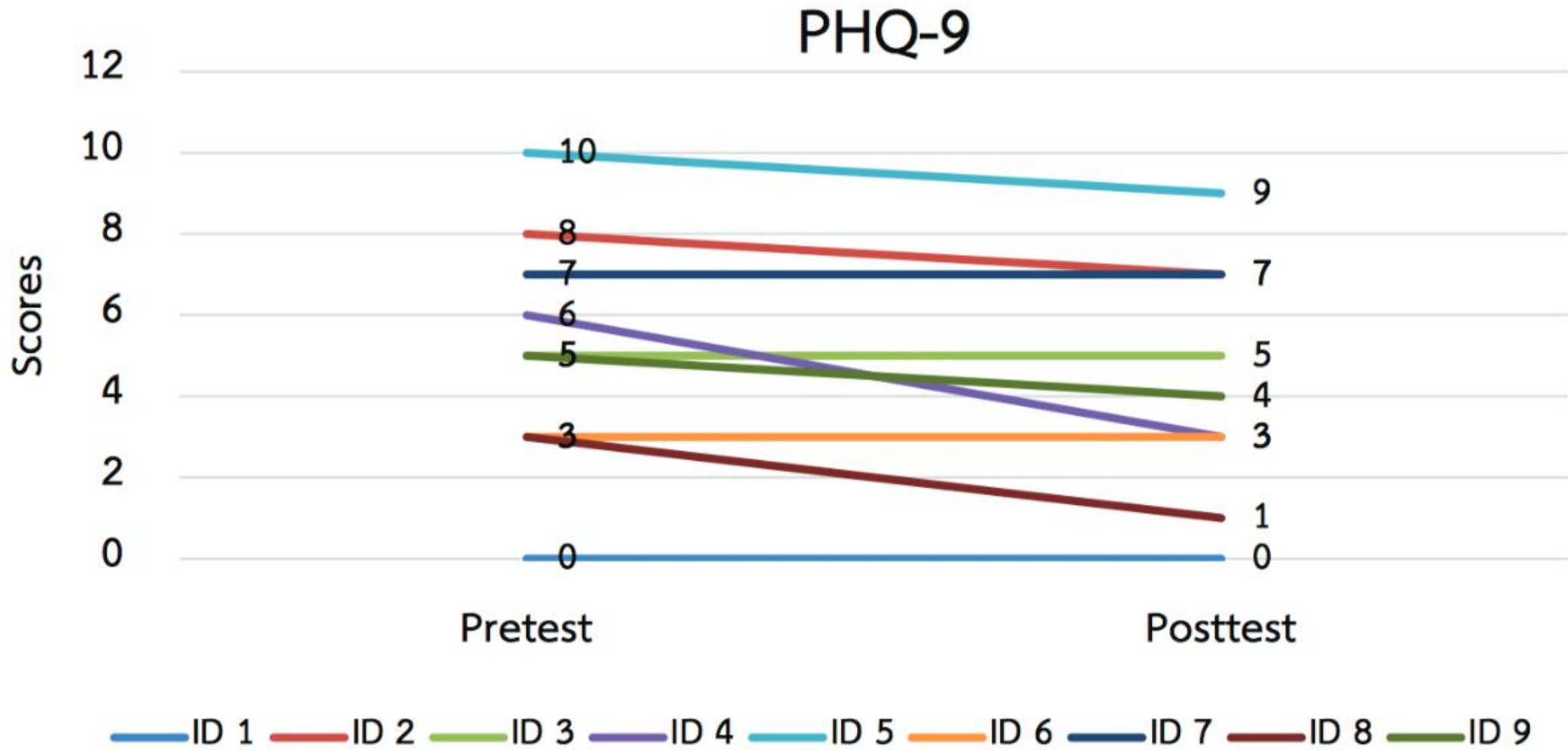


รูปที่ 1 การเปรียบเทียบผลก่อนและหลังการใช้สารสกัดจากกัญชาทางการแพทย์



รูปที่ 2 อาการซึมเศร้า (PHQ-9) เปรียบเทียบก่อนและหลังการรักษา

Journal of Pharmacopuncture

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Review article

A Review on Studies of Marijuana for Alzheimer's Disease – Focusing on CBD, THC

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The results of these studies

- The results of these studies confirmed that CBD activated the peroxisome proliferator-activated receptor-γ(PPARγ) through the Wnt/β-catenin pathway to protect PC12 cells from Aβ neurotoxicity and oxidation stress.
- Increase cell survival.
- Reduce ROS production.
- Reduce lipid peroxidation, inhibit the hyperphosphorylation of tau protein.
- inhibit AChE, and stimulate the neurogenesis of the hippocampus.

Results

- These results implied that the CBD components of cannabis might be useful to treat and prevent AD
- because CBD components could suppress the main causal factors of AD.
- Moreover, it was suggested that using CBD and THC together could be more useful than using CBD or THC alone.

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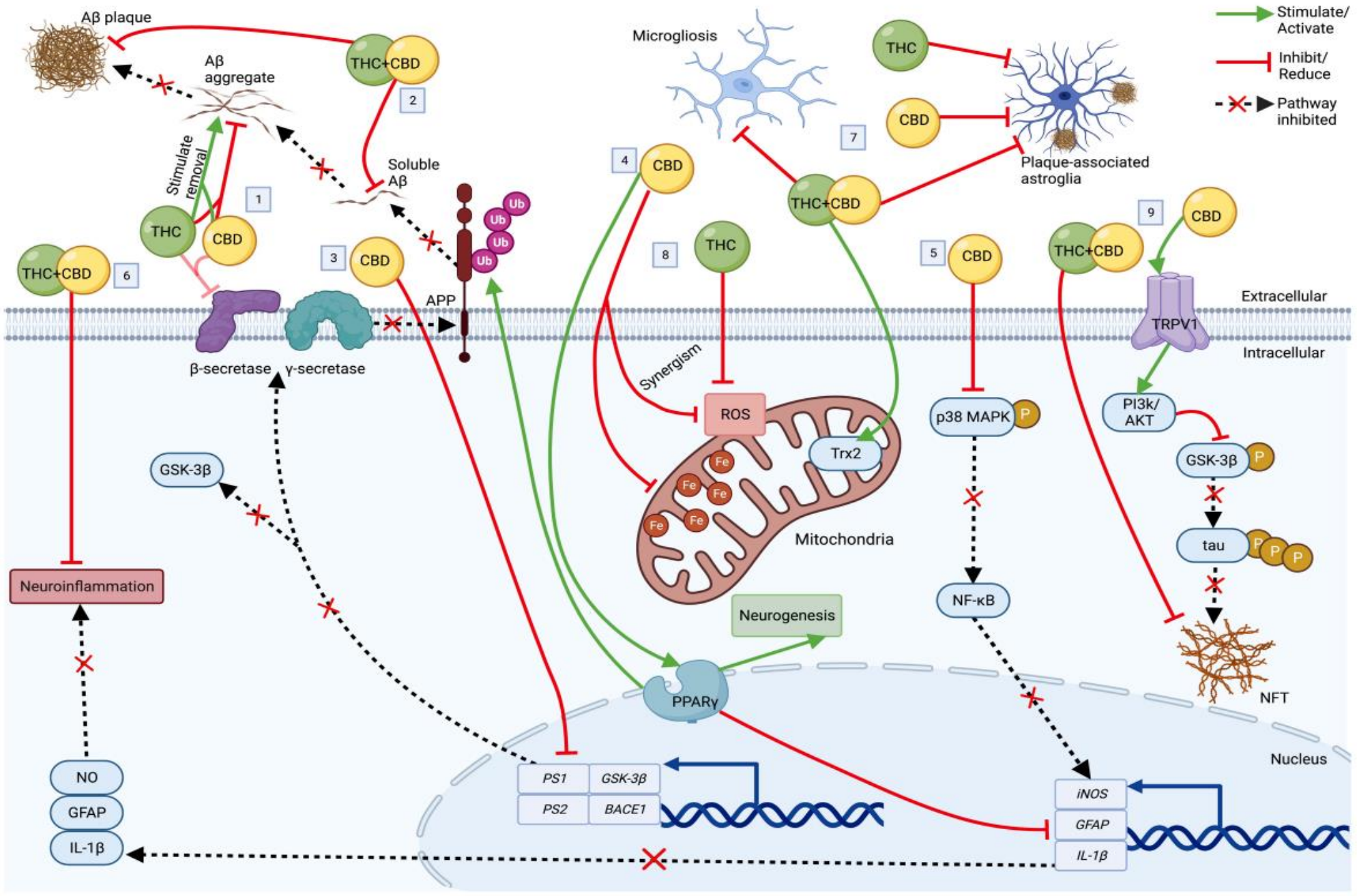
Aβ plaque
Aβ aggregate
THC+CBD
2
Stimulate removal
Soluble Aβ
1
THC
CBD
3
CBD
THC+CBD
6
APP
β-secretase
γ-secretase
Ub
Ub
Ub
Ub
GSK-3β
Neuroinflammation
NO
GFAP
IL-1β
Microgliosis
4
CBD
8
THC
Synergism
ROS
Trx2
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Mitochondria
Neurogenesis
PPARγ
PS1
GSK-3β
PS2
BACE1
7
THC
CBD
THC+CBD
Plaque-associated astroglia
5
CBD
p38 MAPK
P
NF-κB
iNOS
GFAP
IL-1β
9
CBD
THC+CBD
TRPV1
Extracellular
Intracellular
PI3k/ AKT
GSK-3β
P
tau
P
P
P
NFT
Nucleus
Stimulate/ Activate
Inhibit/ Reduce
Pathway inhibited

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Therapeutic properties of multi-cannabinoid treatment strategies for Alzheimer's disease

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Cannabis and Parkinsonism

Parkinsonism

Four main characteristics of disease:

1. Bradykinesia
2. Rigidity
3. Tremor
4. Gait and balance abnormality

คำแนะนำ

การใช้กัญชาทางการแพทย์

Guidance on Cannabis for Medical Use

กรมการแพทย์ กระทรวงสาธารณสุข

ฉบับปรับปรุงครั้งที่ 5 (2565)

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✦ **ผลิตภัณฑ์กัญชาทางการแพทย์น่าจะได้ประโยชน์ (ในการควบคุมอาการ)**

ผลิตภัณฑ์กัญชาประเภทนี้มีหลักฐานทางวิชาการที่มีคุณภาพสนับสนุนมีจำนวนจำกัด[6] ซึ่งต้องการข้อมูลการศึกษาวิจัยเพื่อสนับสนุนต่อไป

อย่างไรก็ตาม ในกรณีที่ผู้ป่วยได้รับการรักษาด้วยวิธีมาตรฐานแล้วไม่สามารถควบคุมอาการของโรคได้ หากจะนำผลิตภัณฑ์กัญชามาใช้กับผู้ป่วยเฉพาะราย[9] ปฏิญญาเฮลซิงกิของแพทยสมาคมโลก (ค.ศ.2013) ข้อ 37[19] ระบุว่ามีความเป็นไปได้หากไม่มีวิธีการรักษาอื่น ๆ หรือมีวิธีการรักษาแต่ไม่เกิดประสิทธิผล ภายหลังจากได้ปรึกษาหารือผู้เชี่ยวชาญและได้รับความยินยอมจากผู้ป่วยหรือญาติโดยชอบธรรมแล้ว แพทย์อาจเลือกวิธีการที่ยังไม่ได้พิสูจน์ หากมีดุลยพินิจว่าวิธีการนั้น ๆ อาจช่วยชีวิตผู้ป่วย ฟื้นฟูสุขภาพ หรือลดความทุกข์ทรมานของผู้ป่วยได้ วิธีการดังกล่าวควรนำไปเป็นวัตถุประสงค์ของการวิจัยโดยออกแบบให้ประเมินความปลอดภัยและประสิทธิผลควบคู่กันไป รวมถึงต้องบันทึกข้อมูลผู้ป่วยทุกราย และหากเหมาะสมควรเผยแพร่ให้สาธารณะได้ทราบ

การใช้ผลิตภัณฑ์กัญชาเพื่อรักษาผู้ป่วยเฉพาะรายและดำเนินการเก็บข้อมูลวิจัยควบคู่กันไป ซึ่งอาจมีรูปแบบการวิจัยในลักษณะการวิจัยเชิงสังเกต (observational study) และ/ หรือ การวิจัยจากสถานการณ์ที่ใช้รักษาผู้ป่วยจริง (actual used research)

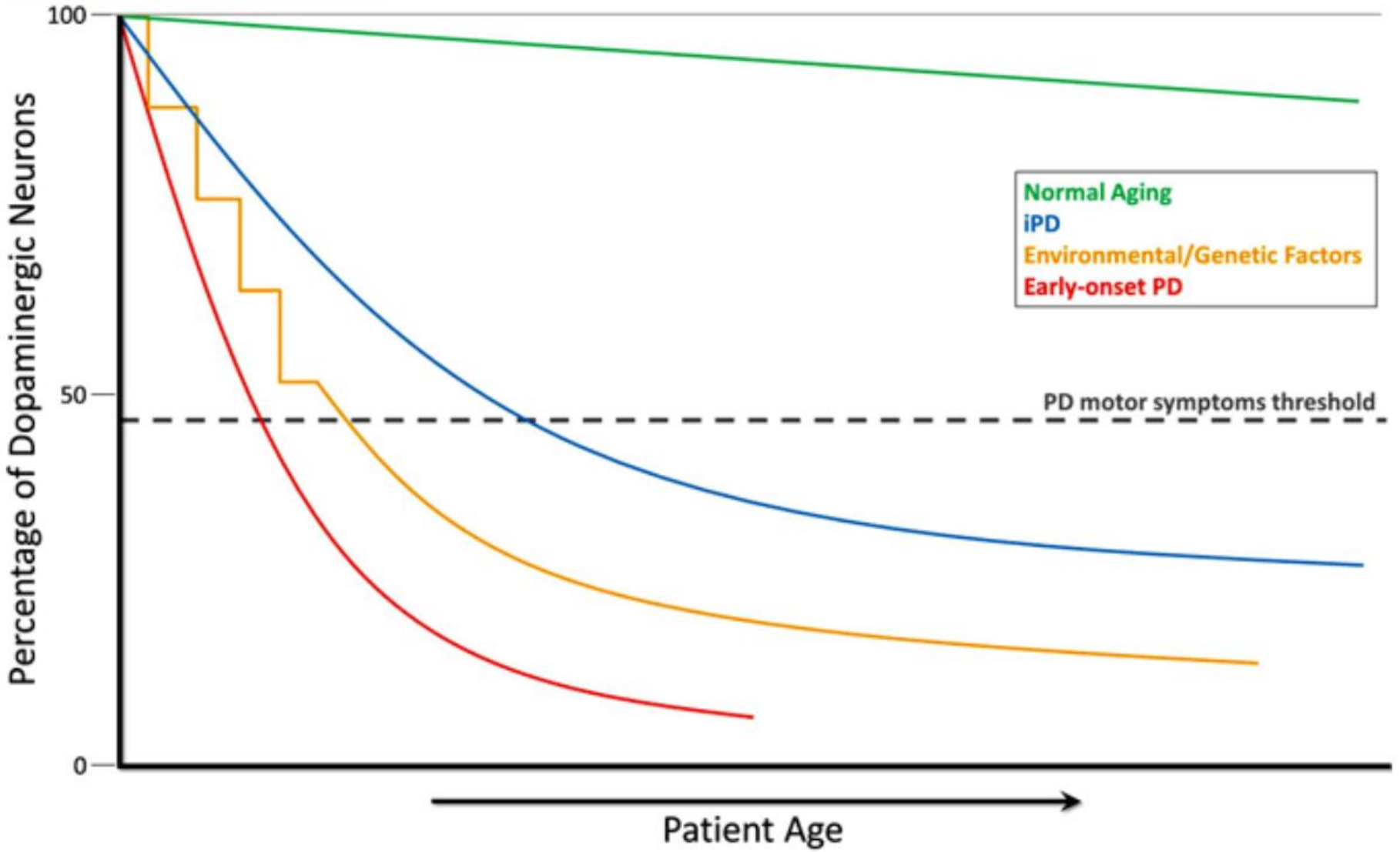
โรคและภาวะของโรคในกลุ่มนี้ อาทิ

1. โรคพาร์กินสัน
2. โรคอัลไซเมอร์
3. โรควิตกกังวลไปทั่ว (generalized anxiety disorders)
4. โรคปลอกประสาทอักเสบ (demyelinating diseases) อื่น ๆ อาทิ neuromyelitis optica และ autoimmune encephalitis

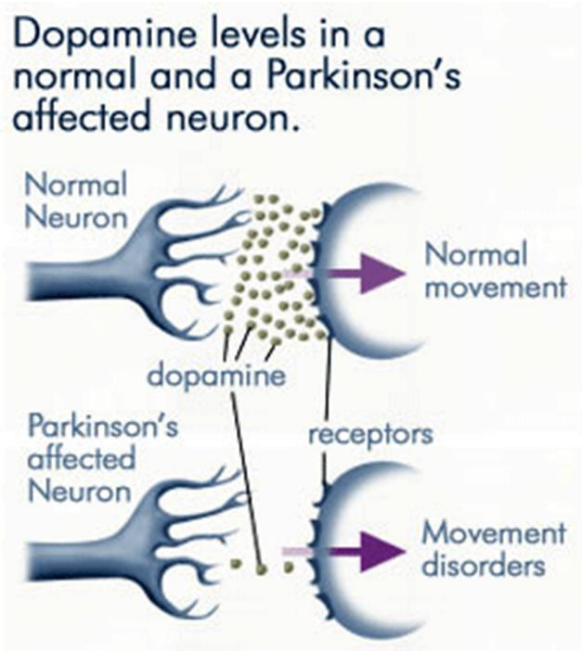
Pathophysiology

- It is a neurodegenerative disease with a progression.
- There is strong evidence that it first affects the dorsal motor nucleus of the vagus nerve and the olfactory bulbs and nucleus, then the locus coeruleus, and eventually the substantia nigra. Cortical areas of the brain are affected at a later stage.
- The loss of dopaminergic neurons in the substantia nigra, resulting in the loss of control of voluntary movements, which manifests as tremor, rigidity, and bradykinesia.

Evolution of Dopamine Depletion in Parkinson's Disease



dopamine receptors on the post-synaptic membrane. Source: anti-agingfirewalls.com.



Effects of Cannabis in Parkinson's Disease: A Systematic Review and Meta-Analysis

Cite

Article type: Systematic Review

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Abstract: The legalization of cannabis in many countries has allowed many Parkinson's disease (PD) patients to turn to cannabis as a treatment. As such there is a growing interest from the PD community to be properly guided by evidence regarding potential treatment benefits of cannabis. This systematic review and meta-analysis aims to compile the best available evidence to help guide patients and their family, clinicians and researchers make informed decisions. A systematic search of the literature was conducted in June 2021. Five randomized controlled studies and eighteen non-randomized studies investigated cannabis treatment in PD patients. No compelling evidence was found to recommend the use of cannabis in PD patients. However, a potential benefit was identified with respect to alleviation of PD related tremor, anxiety, pain, improvement of sleep quality and quality of life. Given the relative paucity of well-designed randomized studies, there is an identified need for further investigation, particularly in these areas.

Keywords: Cannabis, Parkinson's disease, efficacy of cannabis, tremor, UPDRS

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Pros and Cons of Marijuana in Treatment of Parkinson's Disease

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Disclosures can be found in Additional Information at the end of the article

Abstract

Parkinson's disease (PD) is the second most common neurodegenerative disorder of adult onset in the United States. It is a debilitating condition and presents with both motor and non-motor symptoms. Current treatment options are scarce and include replacement of dopamine deficiency with levodopa which targets only motor symptoms of the disorder, does not halt its progression, and is associated with side effects of its own, including dyskinesia. With medical marijuana gaining popularity and being legalized in the United States, we examined the pros and cons of marijuana in the treatment of Parkinson's disease.

Pros and cons

- Pros: Medical marijuana has been observed to improve both motor and non-motor symptoms including bradykinesia, rigidity, tremor, sleep, and pain.
- Cons: It is well known that marijuana can cause impairment in working memory and may have a positive association with depression.

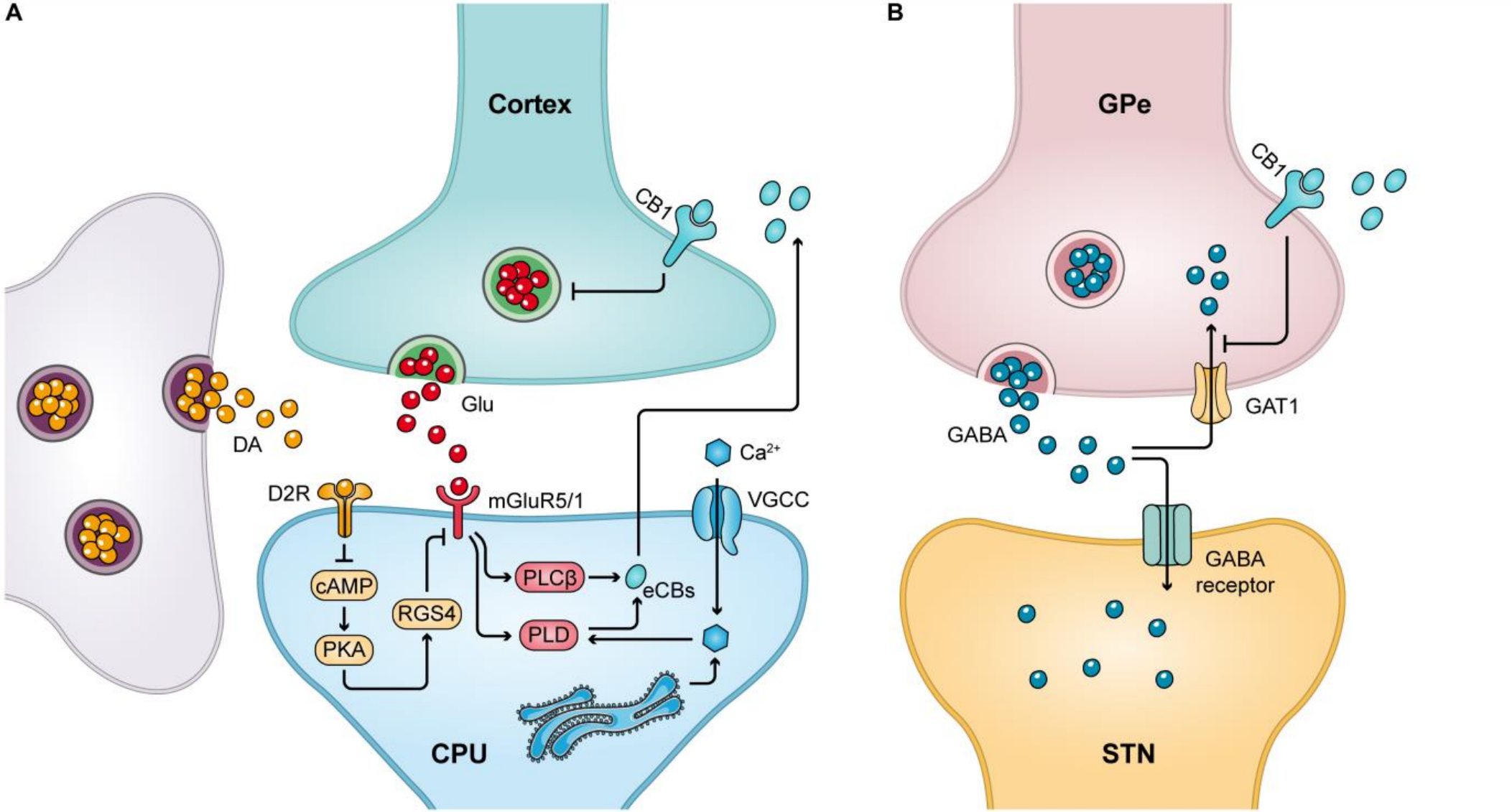

FIGURE 2 | CB1 receptor-mediated retrograde signaling mechanism. **(A)** Release of Glu from the cortical striatal glutamatergic neurons can stimulate the release of eCBs from postsynaptic neurons, which in turn acts on CB1 receptors in the presynaptic membrane to inhibit presynaptic Glu release. Meanwhile, dopaminergic neurons can promote cannabinoid production by decreasing postsynaptic RGS4 phosphorylation levels. **(B)** Stimulation of the presynaptic CB1 receptor in GPe inhibits the reuptake of GABA by GABA transporter protein 1 (GAT1), thereby increasing local GABA levels.

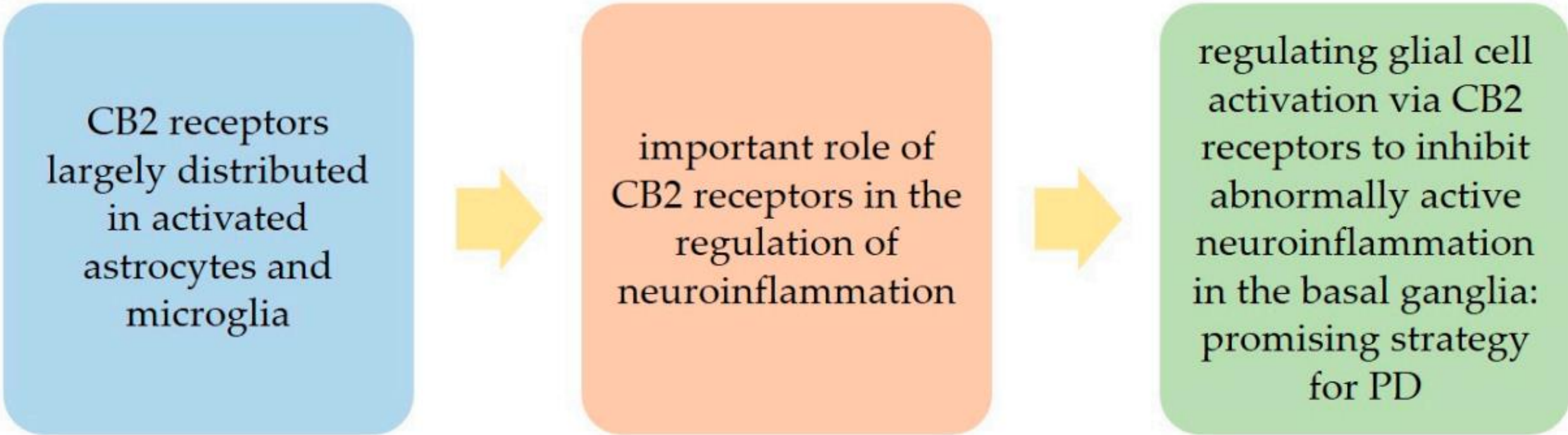

Figure 1. Potential value of the role of the cannabinoid type 2 (CB2) receptors in the regulation of neuroinflammation in Parkinson's disease (PD).

Promising cannabinoid-based therapies for Parkinson's disease: Motor symptoms to neuroprotection

Home > Hydrocarbon > Organic Chemicals > Terpenes > Chemistry > Organic Chemistry > Cannabinoids

Article PDF Available

Promising cannabinoid-based therapies for Parkinson's disease: Motor symptoms to neuroprotection

April 2015 · Molecular Neurodegeneration 10(1):17

DOI:10.1186/s13024-015-0012-0

Source · PubMed

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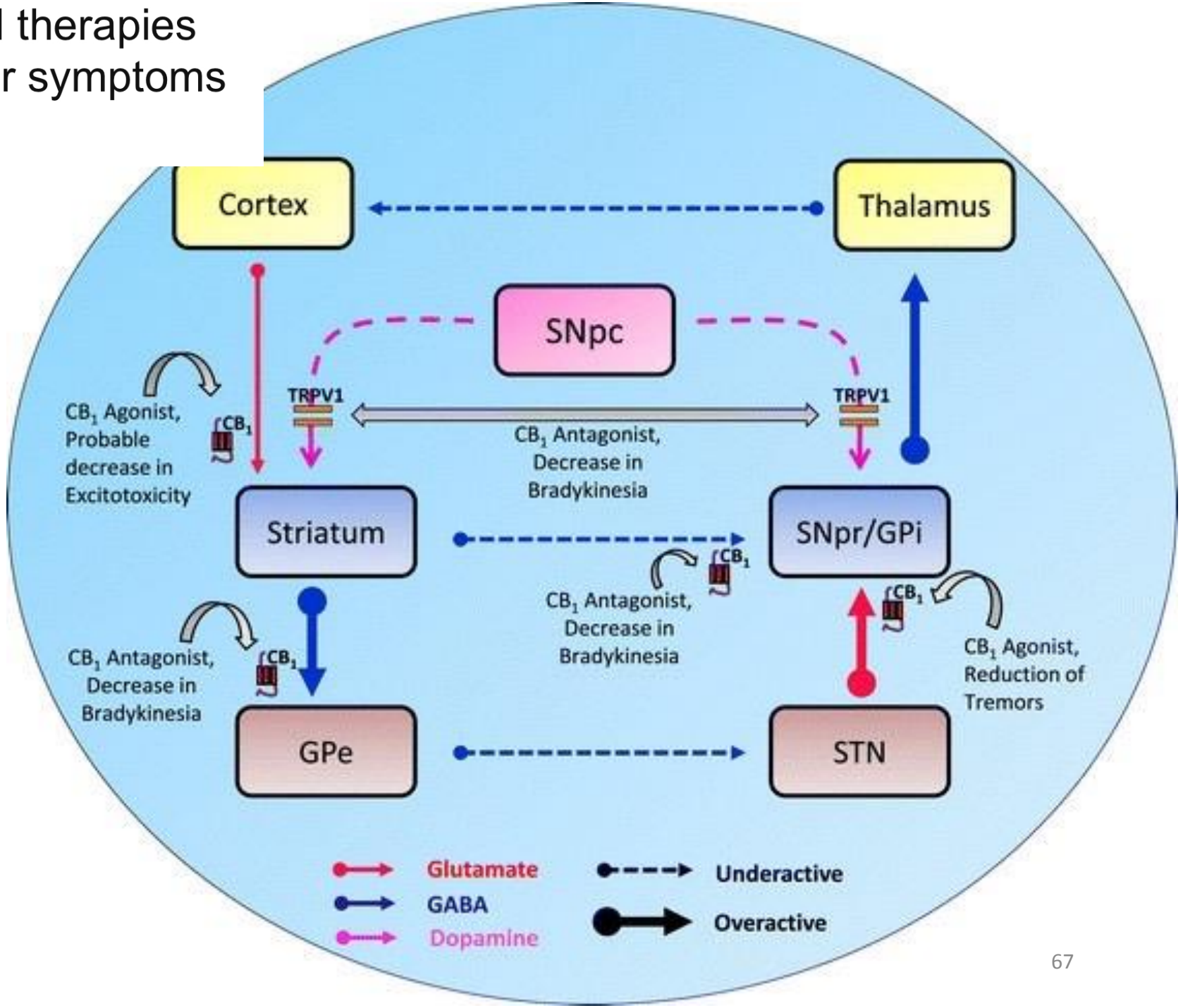
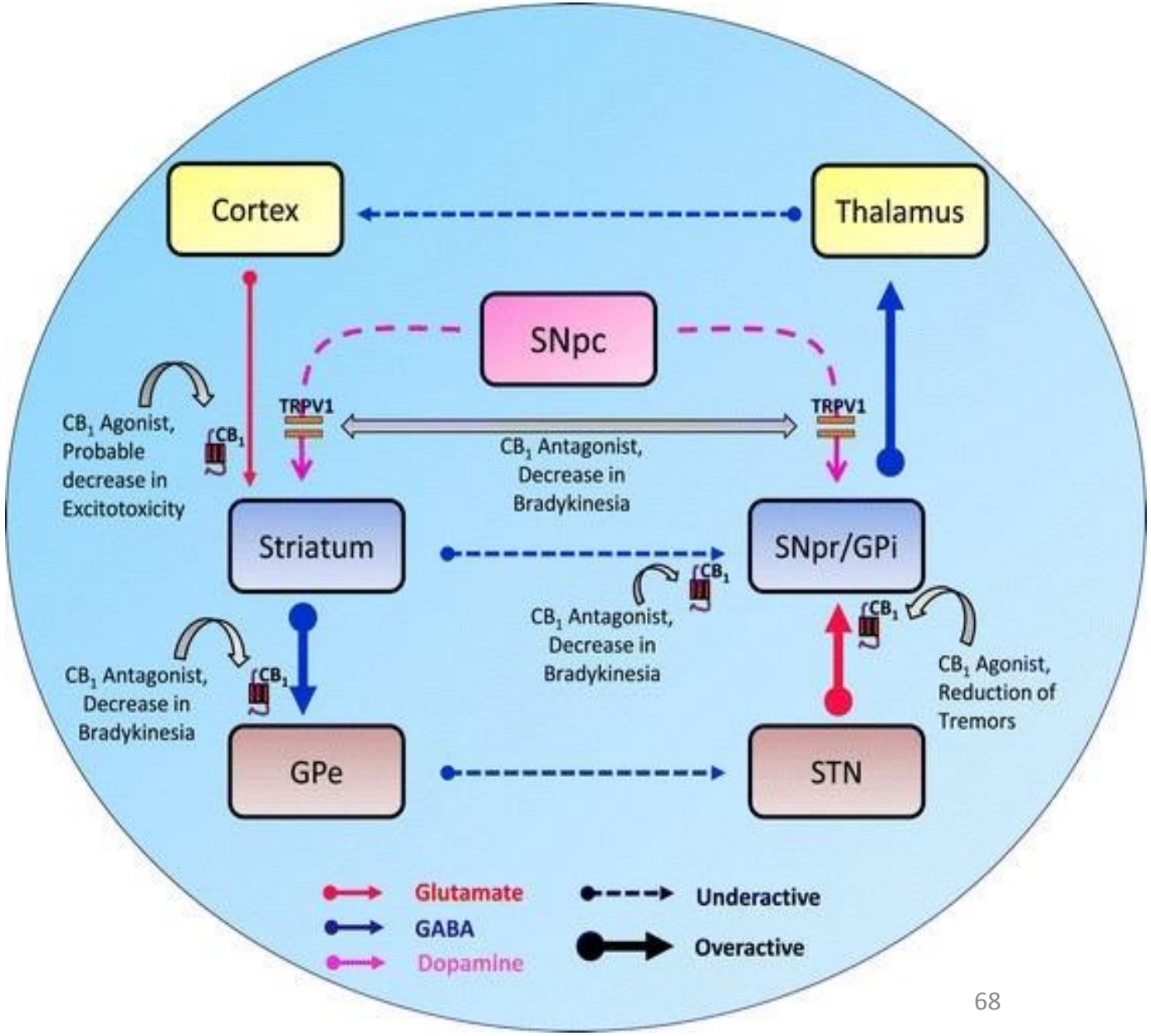


Basal ganglial circuitry in Parkinson's disease (PD) and tentative cannabinoid targets to improve motor disability in PD.

- Progressive loss of dopaminergic innervation in PD causes overactivity of the indirect (inhibitory) pathway, resulting in excess glutamatergic drive to the GPi and SNpr and diminished activity of the inhibitory GABAergic direct pathway, further disinhibiting the activity of the GPi and SNpr.
- As output nuclei (GPi and SNpr) use the inhibitory neurotransmitter GABA, this amplified basal ganglia output leads to extreme inhibition of the motor thalamus which acts as a "brake" on motor activity;
- thus, resulting in the onset of parkinsonian syndrome.
- The neural circuitry above depicts various possible cannabinoid-based targets (CB1, CB2, and TRPV1 receptors) that can be used to mitigate the symptoms observed in PD.

Abbreviations:

- CB1, cannabinoid receptor 1;
- TRPV1, transient receptor potential vanilloid 1;
- GPe, external segment of the globus pallidus;
- GPi, internal segment of the globus pallidus;
- SNpc, substantia nigra pars compacta;
- SNpr, substantia nigra pars reticulata;
- STN, subthalamic nucleus;
- GABA, gamma-aminobutyric acid.



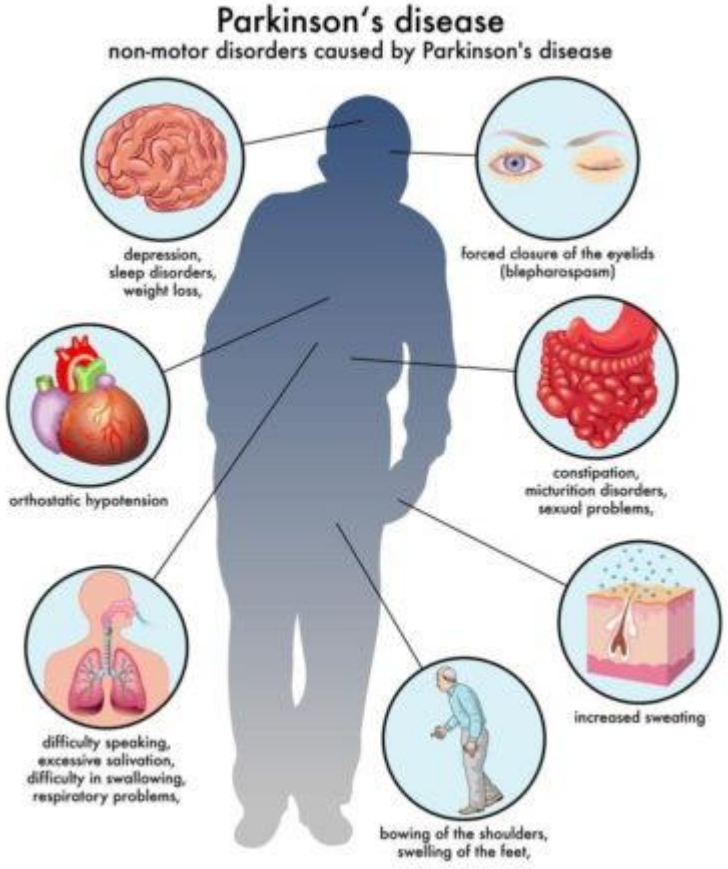
How dose THC work?

- When a person smokes marijuana, THC overwhelms the EC system, quickly attaching to cannabinoid receptors throughout the brain and body.
- This interferes with the ability of natural cannabinoids to do their job of fine-tuning communication between neurons, which can throw the entire system off balance.

https://headsup.scholastic.com

Parkinson’s Disease: What Is It?

- Parkinson’s disease (PD) is a progressive nervous system disorder that affects movement and motor control.
- Symptoms are gradual and often begin with little more than a slight tremor in one hand (asymmetric resting tremor).
- In more advanced stages of the disease, victims may experience cognitive impairment, difficulty walking, masked facial expressions, and trembling of upper and lower extremities.



https://wayofleaf.com/cannabis/ailments/marijuana-strains-parkinsons-disease

Parkinson’s disease (PD)

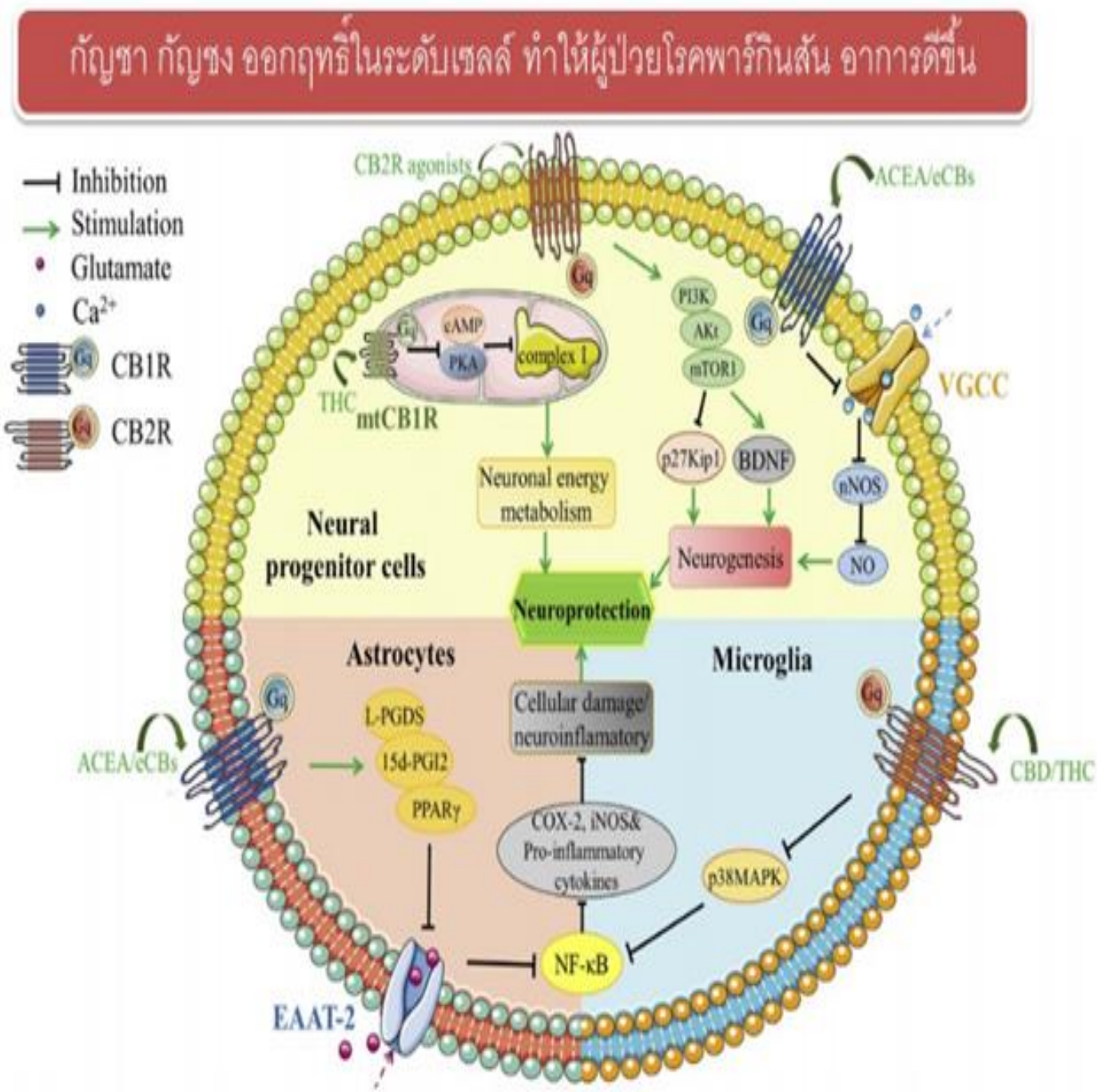
- เป็นโรคความเสื่อมของระบบประสาท neurodegenerative disease ที่พบได้บ่อย
- เกิดจากการเสื่อมตายของเซลล์สมองที่ basal ganglia รวมถึง caudate putamen, globus pallidus interna, substantia nigra
- มีสารเคมีในสมองที่เรียกว่าโดปามีนลดลง
- เกิดอาการสั่น แข็งเกร็ง เคลื่อนไหวช้าและทรงตัวไม่ดี

Parkinson’s disease (PD)

- พบว่ามีการเพิ่มระดับ AEA ใน PD
- และพบระดับ AEA สูงในน้ำไขสันหลังของผู้ป่วย PD ที่ไม่ได้รักษา
- การใช้ cannabinoid receptor agonist and antagonist ยังต้องศึกษากันต่อไปในอนาคต

Cannabis and Pakinsonism

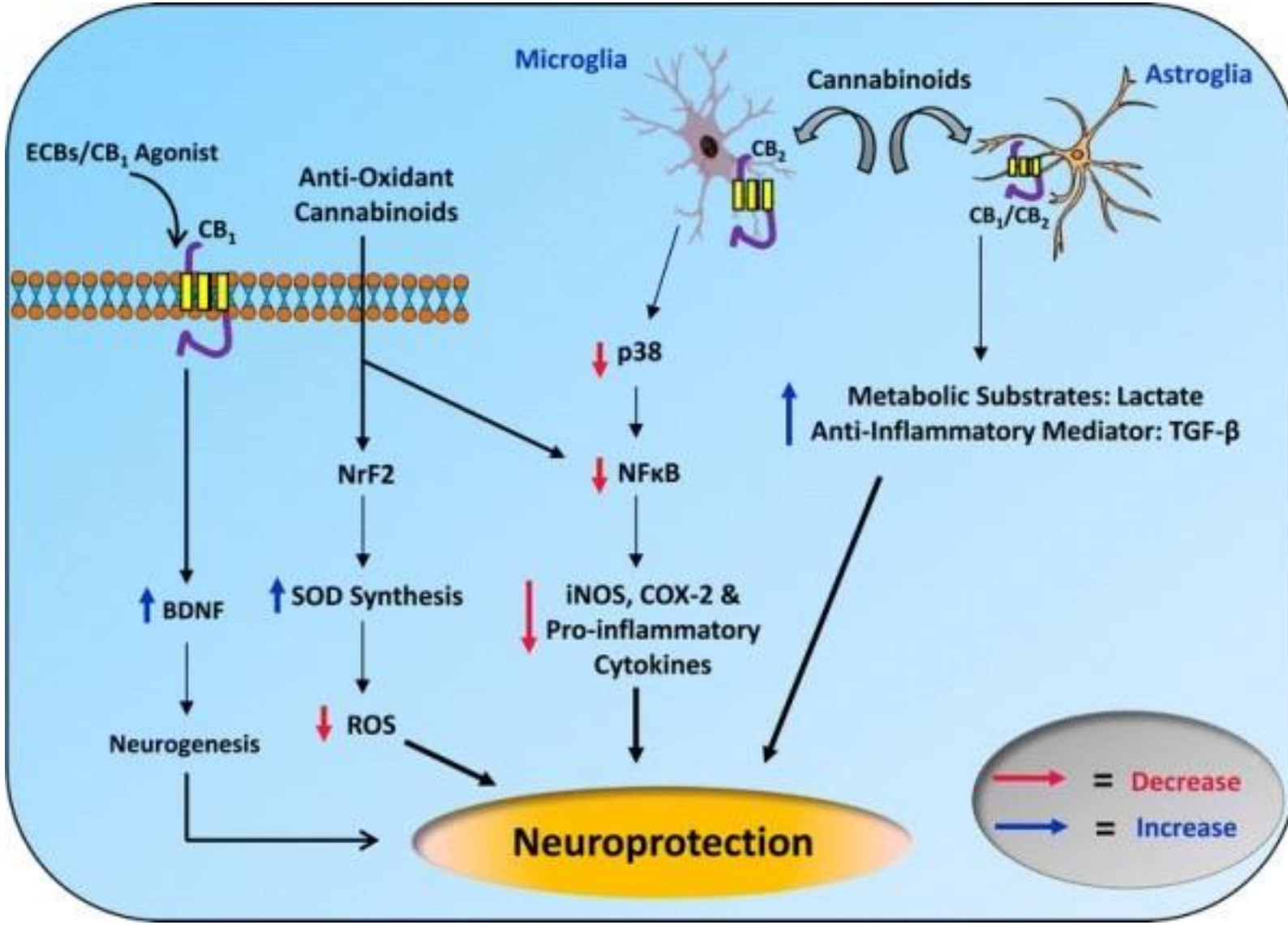
- โดยมีการศึกษาค้นพบว่า การส่งสัญญาณของระบบเอ็นโดแคนนาบินอยด์ที่มีประสิทธิภาพสามารถทำให้การเคลื่อนไหวของร่างกายมีประสิทธิภาพดีขึ้น
- ซึ่งสารสื่อประสาทหลักที่เกี่ยวข้องกับโรคพาร์กินสันนั้น ก็คือ สารสื่อประสาทโดปามีน ซึ่งพบว่า การลดลงของสารสื่อประสาทชนิดนี้หรือความไม่สมดุลในสมองส่งผลให้มีผลต่อการทรงตัวหรือเคลื่อนไหวร่างกาย จึงทำให้เกิดอาการของโรคพาร์กินสัน
- ระบบเอ็นโดแคนนาบินอยด์เช่น AEA และ 2-AG สามารถออกฤทธิ์ ในการส่งสัญญาณที่เกี่ยวข้องกับสารโดปามีนได้ด้วยเช่นกัน
- สารไฟโตแคนนาบินอยด์จากกัญชา ก็มีบทบาทในการควบคุมการทำงานหรือมีผลต่อการทำงานเหมือนระบบเอ็นโดแคนนาบินอยด์ ซึ่งสัมพันธ์กับการควบคุมระบบการเคลื่อนไหวและทรงตัวของมนุษย์ด้วย
- กัญชา กัญชง ยังสามารถลดการอักเสบของเซลล์สมอง ซึ่งเป็นสาเหตุสำคัญที่ทำให้ระบบสารสื่อประสาทในผู้ป่วยพาร์กินสันทำงานผิดปกติไป
- สารไฟโตแคนนาบินอยด์จากกัญชามีคุณสมบัติปกป้องสมอง
- สาร THC และ สาร CBD การกระตุ้นตัวรับ CB1 จะทำให้อาการสั่นของผู้ป่วยดีขึ้น



Probable mechanisms to describe the neuroprotective (independent of the CB1 receptor) action of cannabinoids in PD.

Abbreviations:

- CB1, cannabinoid receptor 1;
- CB2, cannabinoid receptor 2
- BDNF, Brain derived neurotrophic factor;
- ECBs, Endocannabinoids;
- ROS, reactive oxygen species;
- SOD, superoxide dismutase;
- NrF2, nuclear factor erythroid 2-related factor 2
- NFκB, nuclear factor kappa-B;
- p38 mitogen-activated protein kinases;
- iNOS, inducible nitric oxide synthase;
- COX-2, cyclooxygenase-2;
- TGF-β, transforming growth factor beta.



Is cannabis work?

TABLE. Available Evidence of Cannabis Efficacy[6,8,24,26]

Not Enough Evidence to Recommend Routine Clinical Use	No Clear Evidence of Clinical Benefits	Evidence Demonstrates Some Clear Improvement in Symptoms	Available Evidence Supports Improvement in Some Cases
Alzheimer disease	Acute pain	Chemotherapy-induced nausea/vomiting	Seizures
Parkinson disease	Glaucoma	Chronic pain	Cachexia related to HIV/cancer
PTSD	Tremor in MS	Spasticity in MS	Schizophrenia
	Major depression	Generalized anxiety	Psychosis
	Huntington disease	Social anxiety	Sleep disorders

MS, multiple sclerosis; **PTSD**, post-traumatic stress disorder

Pro-resolving anti-inflammation mediators good sleep promoting glimphatic system with less amyloid burden

Neurodegenerative disease
= abnormal proteostasis
= neuroproteinopthy
= misfolded protein disease
= neuroinflammation

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ARTICLE OPEN

Amyloid proteotoxicity initiates an inflammatory response blocked by cannabinoids

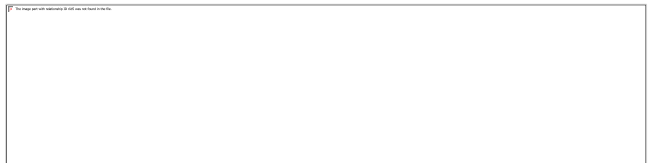
Antonio Currais[1], Oswald Quehenberger[2,3], Aaron M Armando[2], Daniel Daugherty[1], Pam Maher[1] and David Schubert[1]

The beta amyloid (Aβ) and other aggregating proteins in the brain increase with age and are frequently found within neurons. The mechanistic relationship between intracellular amyloid, aging and neurodegeneration is not, however, well understood. We use a proteotoxicity model based upon the inducible expression of Aβ in a human central nervous system nerve cell line to characterize a distinct form of nerve cell death caused by intracellular Aβ. It is shown that intracellular Aβ initiates a toxic inflammatory response leading to the cell's demise. Aβ induces the expression of multiple proinflammatory genes and an increase in both arachidonic acid and eicosanoids, including prostaglandins that are neuroprotective and leukotrienes that potentiate death. Cannabinoids such as tetrahydrocannabinol stimulate the removal of intraneuronal Aβ, block the inflammatory response, and are protective. Altogether these data show that there is a complex and likely autocatalytic inflammatory response within nerve cells caused by the accumulation of intracellular Aβ, and that this early form of proteotoxicity can be blocked by the activation of cannabinoid receptors.

npj Aging and Mechanisms of Disease (2016) **2**, 16012; doi:10.1038/npjamd.2016.12; published online 23 June 2016

Parkinson's Disease Causes

- Scientists have yet to discover a single cause they can concretely attribute to the onset of Parkinson's disease. However, the hallmark of Parkinson's disease is the loss of neurons in the brain responsible for making the chemical dopamine. Once dopamine levels fall, the result is abnormal brain activity, which may result in Parkinson's symptoms.
- It does appear that several factors may play a role in the early onset of Parkinson's disease:
- **Genetics:** There are genetic mutations that can cause this condition. They are rare, barring instances where several family members are affected by Parkinson's. Specific gene variations also increase the risk, but each genetic marker carries a small risk by itself.
- **Toxins:** Excessive exposure to environmental toxins could increase the risk of developing the condition. Examples include exposure to pesticides and herbicides.
- **Gender:** As mentioned above, men are 1.5 times more likely to get Parkinson's than women.
- **Age:** 96% of PD patients are aged 50+.
- **Lewy Bodies:** Clumps of substances found in brain cells may be microscopic markers of PD. While researchers haven't established a concrete link, they believe there is a real correlation between Lewy bodies and PD. Another critical substance is alpha-synuclein. This compound is in all Lewy bodies and appears in a form that cells cannot break down.



What Are the Conventional Medical Treatments for Parkinson's Disease?

- Parkinson's disease is not curable, but medications are on the market designed to help control and manage symptoms. While these drugs can lead to initial improvement, their effect wears off over time. Examples of possible medication options include:
- Carbidopa-levodopa: Doctors feel this is the most effective PD medication. Levodopa is a natural chemical that goes into the brain and converts to dopamine. It is combined with carbidopa because the latter protects levodopa from being converted into dopamine outside the brain.
- Dopamine Agonists: This treatment mimics dopamine effects in the brain.
- MAO B Inhibitors: This set of drugs prevents dopamine breakdown by inhibiting the brain enzyme MOA B, which metabolizes dopamine.
- There are also surgical options to help treat Parkinson's, such as deep brain stimulation (DBS). Like all surgeries, DBS carries risks, such as brain hemorrhage. Few medications provide more than medium-term relief from symptoms. As a consequence, researchers have investigated the potential for cannabis to help PD patients in recent years.

Marijuana for Parkinson's Disease: Highlighting the Effects of a Variety of Strain Types strains-for-Parkinson

1 – Kush Strains: potent marijuana strains that routinely possess very high levels of THC. The Kush high is typically gradual, and some users may not even notice it until they are completely relaxed. Kush strains are also known as big appetite boosters. As the high makes its way down the body, many may feel a tingling sensation that eases tight muscles. All in all, Kush strains are highly sedative strains and are often best used at night. They provide a joyous high that can lighten the mood, relieve stress, and ease tension and spasticity throughout the body.

2 – Citrus Strains: Citrus strains provide a range of sweet, fruity scents and are known for their aromatic terpene profile. Some popular citrus strains include Lemon Tree, Grapefruit, Clementine, and Pineapple Express. citrus-strains In terms of THC content, citrus strains are rarely recommended for novices. They often boast THC content well over 20%, and many report feeling effects within minutes. These strains produce a euphoric head high, and users may experience a whole-body numbing sensation that helps to soothe the muscles.

3 – High-CBD Strains: Across the U.S., individuals are enjoying increased access to high-CBD cannabis strains, some of which even come from hemp. Hemp strains are high in CBD, but possess THC levels of 0.3% or less; meaning they do not produce a high. Also, since hemp is a legal crop under the 2018 U.S. Farm Bill, CBD-rich hemp flower can quite easily be found and purchased in most U.S. states, without the need for a medical cannabis card.

high-cbd-strains As far as potential use among Parkinson's patients, CBD is known to possess a variety of therapeutic benefits, including muscle relief, spasticity relief, and help with sleeping. (Again, it's important to point out that neither hemp nor marijuana is a medically-approved treatment option for PD). Examples of popular high-CBD strains include Harlequin, Harle-Tsu, and Ringo's Gift.

4 – 1:1 CBD/THC Strains: For patients with access to legal medical or recreational cannabis dispensaries, another great medicinal option is strains that boast a roughly 1:1 CBD-to-THC content. cbd-thc-strains These strains pose immense medical potential, and like the high-CBD/low-THC strains, produce much milder intoxicating/mind-altering effects. Popular 1:1 CBD strains include Sweet and Sour Widow, Pennywise, and Cannatonic.

5 – Diesel Strains: Diesel strains include some of the most iconic landrace strains of all time. These are incredibly potent strains which boast immense mind-altering effects. In combination with the intense high that is produced, however, comes tremendous potential for pain and muscle spasm relief. diesel-strain Diesel strains are not recommended for beginner cannabis users – especially those with Parkinson's disease that have little to no experience using marijuana.

Effect of medical cannabis on thermal quantitative measurements of pain in patients with Parkinson's disease

- . 2017 Mar;21(3):486-493. doi: 10.1002/ejp.942. Epub 2016 Oct 10.

- A Shohet 1 2, A Khlebtovsky 1 2, N Roizen 1 2, Y Roditi 1 2, R Djaldetti 1 2

- PMID: 27723182 DOI: 10.1002/ejp.942

- Background: Cannabis can alleviate pain of various etiologies. This study assessed the effect of cannabis on motor symptoms and pain parameters in patients with Parkinson's disease (PD).
- Methods: Twenty patients with PD who were licensed to use cannabis underwent evaluation before and 30 min after cannabis consumption and again after long-term use. Motor function was assessed with the Unified PD Rating scale (UPDRS) by two raters, one blinded. Pain was assessed with the Pain Rating Index (PRI) and Visual Analogue Scale (VAS) of the short-form McGill Pain Questionnaire. Thermal quantitative sensory testing (QST) was performed in 18 patients. The two consecutive QST measurements were validated in 12 cannabis-naïve patients with PD.
- Results: There was a significant decrease from baseline to 30 min after cannabis consumption in mean motor UPDRS score (38.1 ± 18 to 30.4 ± 15.6, $p < 0.0001$), total PRI (27 ± 13.5 to 9.7 ± 11, $p = 0.001$), and VAS score (6.4 ± 2.8 to 3.6 ± 3.1, $p = 0.0005$). Mean cold pain threshold decreased significantly in the more affected limb, but only after exclusion of two patients who consumed cannabis by vaporizer rather than smoking (19.5 ± 5.2 to 15.6 ± 8.7 °C, $p = 0.02$). After long-term (median 14 weeks) exposure, mean heat pain threshold decreased significantly in the more affected limb in all treated patients (43.6 ± 3.5 to 40.9 ± 3.3 °C, $p = 0.05$) and in cannabis smokers (43.7 ± 3.6 to 40.3 ± 2.5 °C, $p = 0.008$).
- Conclusions: Cannabis improved motor scores and pain symptoms in PD patients, together with a dissociate effect on heat and cold pain thresholds. Peripheral and central pathways are probably modulated by cannabis.
- Significance: Quantitative sensory test results are significantly altered following cannabis consumption in patients with PD. Cannabis probably acts on pain in PD via peripheral and central pathways.

Observational Study Clin Neuropharmacol Cannabis (medical marijuana) treatment for motor and non-motor symptoms of Parkinson disease: an open-label observational study

- . 2014 Mar-Apr;37(2):41-4. doi: 10.1097/WNF.0000000000000016.

- Itay Lotan 1, Therese A Treves, Yaniv Roditi, Ruth Djaldetti

- PMID: 24614667 DOI: 10.1097/WNF.0000000000000016

- Objective: The use of cannabis as a therapeutic agent for various medical conditions has been well documented. However, clinical trials in patients with Parkinson disease (PD) have yielded conflicting results. The aim of the present open-label observational study was to assess the clinical effect of cannabis on motor and non-motor symptoms of PD.

- Methods: Twenty-two patients with PD attending the motor disorder clinic of a tertiary medical center in 2011 to 2012 were evaluated at baseline and 30 minutes after smoking cannabis using the following battery: Unified Parkinson Disease Rating Scale, visual analog scale, present pain intensity scale, Short-Form McGill Pain Questionnaire, as well as Medical Cannabis Survey National Drug and Alcohol Research Center Questionnaire.

- Results: Mean (SD) total score on the motor Unified Parkinson Disease Rating Scale score improved significantly from 33.1 (13.8) at baseline to 23.2 (10.5) after cannabis consumption ($t = 5.9$; $P < 0.001$). Analysis of specific motor symptoms revealed significant improvement after treatment in tremor ($P < 0.001$), rigidity ($P = 0.004$), and bradykinesia ($P < 0.001$).

- Conclusions: There was also significant improvement of sleep and pain scores. No significant adverse effects of the drug were observed. The study suggests that cannabis might have a place in the therapeutic armamentarium of PD. Larger, controlled studies are needed to verify the results.

Cannabis and its derivatives for the use of motor symptoms in Parkinson's disease: a systematic review and meta-analysis

- Susan J Thanabalasingam 1, Brandan Ranjith 2, Robyn Jackson 1, Don Thiwanka Wijeratne 3

- PMID: 34104218 PMCID: PMC8161868 DOI: 10.1177/17562864211018561

- Background: Recent changes to the legal status of cannabis across various countries have renewed interest in exploring its use in Parkinson's disease (PD). The use of cannabinoids for alleviation of motor symptoms has been extensively explored in pre-clinical studies.
- Objective: We aim to systematically review and meta-analyze literature on the use of medical cannabis or its derivatives (MC) in PD patients to determine its effect on motor function and its safety profile.
- Methods: We reviewed and analyzed original, full-text randomized controlled trials (RCTs) and observational studies. Primary outcomes were change in motor function and dyskinesia. Secondary outcomes included adverse events and side effects. All studies were analyzed for risk of bias.
- Results: Fifteen studies, including six RCTs, were analyzed. Of these, 12/15 (80%) mention concomitant treatment with antiparkinsonian medications, most commonly levodopa. Primary outcomes were most often measured using the Unified Parkinson Disease Rating Scale (UPDRS) among RCTs and patient self-report of symptom improvement was widely used among observational studies. Most of the observational data lacking appropriate controls had effect estimates favoring the intervention. However, the controlled studies demonstrated no significant motor symptom improvement overall. The meta-analysis of three RCTs, including a total of 83 patients, did not demonstrate a statistically significant improvement in UPDRS III score variation (MD -0.21, 95% CI -4.15 to 3.72; $p = 0.92$) with MC use. Only one study reported statistically significant improvement in dyskinesia ($p < 0.05$). The intervention was generally well tolerated. All RCTs had a high risk of bias.
- Conclusion: Although observational studies establish subjective symptom alleviation and interest in MC among PD patients, there is insufficient evidence to support its integration into clinical practice for motor symptom treatment. This is primarily due to lack of good quality data.

Cannabidiol: pharmacology and potential therapeutic role in epilepsy and other neuropsychiatric disorders

- Orrin Devinsky 1, Maria Roberta Cilio, Helen Cross, Javier Fernandez-Ruiz, Jacqueline French, Charlotte Hill, Russell Katz, Vincenzo Di Marzo, Didier Jutras-Aswad, William George Notcutt, Jose Martinez-Orgado, Philip J Robson, Brian G Rohrback, Elizabeth Thiele, Benjamin Whalley, Daniel Friedman

- PMID: 24854329 PMCID: PMC4707667 DOI: 10.1111/epi.12631

- To present a summary of current scientific evidence about the cannabinoid, cannabidiol (CBD) with regard to its relevance to epilepsy and other selected neuropsychiatric disorders. We summarize the presentations from a conference in which invited participants reviewed relevant aspects of the physiology, mechanisms of action, pharmacology, and data from studies with animal models and human subjects. Cannabis has been used to treat disease since ancient times. Δ(9) -Tetrahydrocannabinol (Δ(9) -THC) is the major psychoactive ingredient and CBD is the major nonpsychoactive ingredient in cannabis. Cannabis and Δ(9) -THC are anticonvulsant in most animal models but can be proconvulsant in some healthy animals. The psychotropic effects of Δ(9) -THC limit tolerability. CBD is anticonvulsant in many acute animal models, but there are limited data in chronic models. The antiepileptic mechanisms of CBD are not known, but may include effects on the equilibrative nucleoside transporter; the orphan G-protein-coupled receptor GPR55; the transient receptor potential of vanilloid type-1 channel; the 5-HT1a receptor; and the α3 and α1 glycine receptors. CBD has neuroprotective and antiinflammatory effects, and it appears to be well tolerated in humans, but small and methodologically limited studies of CBD in human epilepsy have been inconclusive. More recent anecdotal reports of high-ratio CBD:Δ(9) -THC medical marijuana have claimed efficacy, but studies were not controlled. CBD bears investigation in epilepsy and other neuropsychiatric disorders, including anxiety, schizophrenia, addiction, and neonatal hypoxic-ischemic encephalopathy. However, we lack data from well-powered double-blind randomized, controlled studies on the efficacy of pure CBD for any disorder. Initial dose-tolerability and double-blind randomized, controlled studies focusing on target intractable epilepsy populations such as patients with Dravet and Lennox-Gastaut syndromes are being planned. Trials in other treatment-resistant epilepsies may also be warranted. A PowerPoint slide summarizing this article is available for download in the Supporting Information section here.

Pharmacology of Medical Cannabis

- Md Ruhul Amin 1, Declan W Ali 2 3 4

- PMID: 31332738 DOI: 10.1007/978-3-030-21737-2_8

- The Cannabis plant has been used for many of years as a medicinal agent in the relief of pain and seizures. It contains approximately 540 natural compounds including more than 100 that have been identified as phytocannabinoids due to their shared chemical structure. The predominant psychotropic component is Δ9-tetrahydrocannabinol (Δ9-THC), while the major non-psychoactive ingredient is cannabidiol (CBD). These compounds have been shown to be partial agonists or antagonists at the prototypical cannabinoid receptors, CB1 and CB2. The therapeutic actions of Δ9-THC and CBD include an ability to act as analgesics, anti-emetics, anti-inflammatory agents, anti-seizure compounds and as protective agents in neurodegeneration. However, there is a lack of well-controlled, double blind, randomized clinical trials to provide clarity on the efficacy of either Δ9-THC or CBD as therapeutics. Moreover, the safety concerns regarding the unwanted side effects of Δ9-THC as a psychoactive agent preclude its widespread use in the clinic. The legalization of cannabis for medicinal purposes and for recreational use in some regions will allow for much needed research on the pharmacokinetics and pharmocology of medical cannabis. This brief review focuses on the use of cannabis as a medicinal agent in the treatment of pain, epilepsy and neurodegenerative diseases. Despite the paucity of information, attention is paid to the mechanisms by which medical cannabis may act to relieve pain and seizures.

Practical considerations in medical cannabis administration and dosing

- Caroline A MacCallum 1, Ethan B Russo 2

- PMID: 29307505 DOI: 10.1016/j.ejim.2018.01.004

- Cannabis has been employed medicinally throughout history, but its recent legal prohibition, biochemical complexity and variability, quality control issues, previous dearth of appropriately powered randomised controlled trials, and lack of pertinent education have conspired to leave clinicians in the dark as to how to advise patients pursuing such treatment. With the advent of pharmaceutical cannabis-based medicines (Sativex/nabiximols and Epidiolex), and liberalisation of access in certain nations, this ignorance of cannabis pharmacology and therapeutics has become untenable. In this article, the authors endeavour to present concise data on cannabis pharmacology related to tetrahydrocannabinol (THC), cannabidiol (CBD) et al., methods of administration (smoking, vaporisation, oral), and dosing recommendations. Adverse events of cannabis medicine pertain primarily to THC, whose total daily dose-equivalent should generally be limited to 30mg/day or less, preferably in conjunction with CBD, to avoid psychoactive sequelae and development of tolerance. CBD, in contrast to THC, is less potent, and may require much higher doses for its adjunctive benefits on pain, inflammation, and attenuation of THC-associated anxiety and tachycardia. Dose initiation should commence at modest levels, and titration of any cannabis preparation should be undertaken slowly over a period of as much as two weeks. Suggestions are offered on cannabis-drug interactions, patient monitoring, and standards of care, while special cases for cannabis therapeutics are addressed: epilepsy, cancer palliation and primary treatment, chronic pain, use in the elderly, Parkinson disease, paediatrics, with concomitant opioids, and in relation to driving and hazardous activities.

A randomised controlled trial of vaporised Δ 9-tetrahydrocannabinol and cannabidiol alone and in combination in frequent and infrequent cannabis users: acute intoxication effects

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- Access to cannabis and cannabinoid products is increasing worldwide for recreational and medicinal use.
- Two primary compounds within cannabis plant matter, Δ9-tetrahydrocannabinol (THC) and cannabidiol (CBD), are both psychoactive, but only THC is considered intoxicating.
- There is significant interest in potential therapeutic properties of these cannabinoids and of CBD in particular.
- Some research has suggested that CBD may ameliorate adverse effects of THC, but this may be dose dependent as other evidence suggests possible potentiating effects of THC by low doses of CBD.
- We conducted a randomised placebo controlled trial to examine the acute effects of these compounds alone and in combination when administered by vaporisation to frequent and infrequent cannabis users. Participants (n = 36; 31 male) completed 5 drug conditions spaced one week apart, with the following planned contrasts: placebo vs CBD alone (400 mg); THC alone (8 mg) vs THC combined with low (4 mg) or high (400 mg) doses of CBD. Objective (blind observer ratings) and subjective (self-rated) measures of intoxication were the primary outcomes, with additional indices of intoxication examined.
- CBD showed some intoxicating properties relative to placebo. Low doses of CBD when combined with THC enhanced, while high doses of CBD reduced the intoxicating effects of THC.
- The enhancement of intoxication by low-dose CBD was particularly prominent in infrequent cannabis users and was consistent across objective and subjective measures.
- Most effects were significant at $p < .0001$. These findings are important to consider in terms of recommended proportions of THC and CBD in cannabis plant matter whether used medicinally or recreationally and have implications for novice or less experienced cannabis users.Trial registration: ISRCTN Registry Identifier: ISRCTN24109245.

Review > CNS Neurol Disord Drug Targets. 2009 Dec;8(6):432-9.
doi: 10.2174/1871527097898246 42.

Cannabinoids and Parkinson's disease

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Abstract

Cannabinoid-based medicines have been proposed as clinically promising therapies in Parkinson's disease (PD), given the prominent modulatory function played by the cannabinoid signaling system in the basal ganglia. Supporting this pharmacological potential, the cannabinoid signaling system experiences a biphasic pattern of changes during the progression of PD. Thus, early and presymptomatic stages, characterized by neuronal malfunctioning but little evidence of neuronal death, are associated with desensitization/downregulation of CB(1) receptors. It was proposed that these losses may be part of the pathogenesis itself, since they can aggravate different cytotoxic insults

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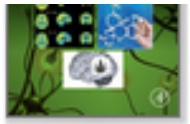

Chapter 3 - Cannabinoids in Parkinson's disease

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In recent years, the endocannabinoid system has emerged as a potential therapeutic target for the treatment of Parkinson's disease (PD). This is based on a number of convergent lines of evidence including the dense localization of components of the endocannabinoid system in brain regions involved in the control of movement as well as evidence of dysregulation of the endocannabinoid system in human PD patients. Moreover, studies in animal