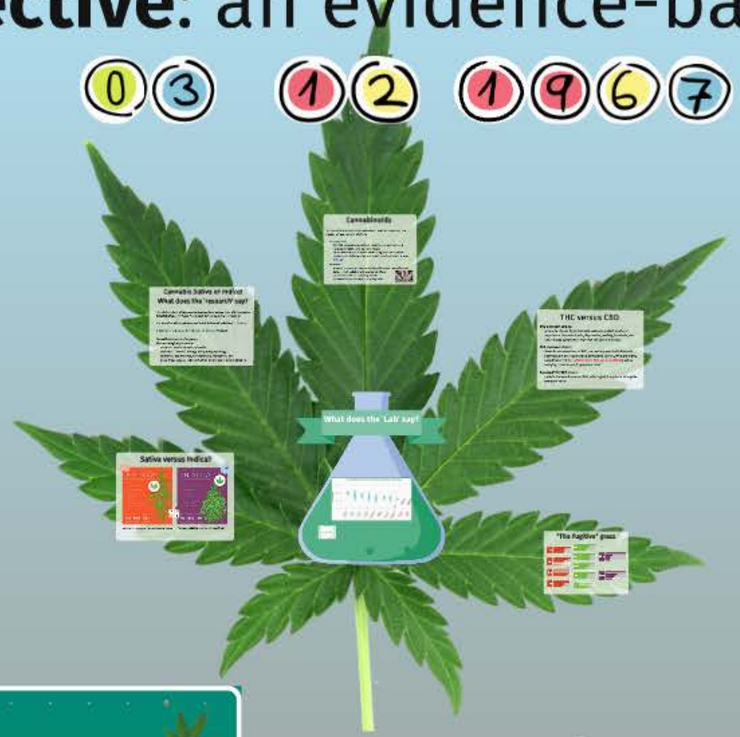
The challenging Cannabis health benefits from a clinical pharmacology perspective: an evidence-based vision

SAMA CONFERENCE 2019



SOUTH AFRICAN MEDICAL ASSOCIATION
UNITING DOCTORS FOR THE HEALTH OF THE NATION

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Clinical Researcher

SAMA The Challenging Cannabis

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Cannabinoids

The cannabis is comprised of hundreds of chemical compounds that create a unique harmony of effects

- Cannabinoids:
  - THC (Δ9-tetrahydrocannabinol) – Feel hungry and high, and relieves symptoms like pain and nausea
  - CBD (Cannabidiol) – is a non-intoxicating, used to alleviate anxiety, pain, inflammation, and other 'promising' medical uses!
- Terpenes:
  - aromatic compounds, responsible for distinctive cannabis aroma
  - Limonene (citrus scent) – relaxing effects
  - Pinene (pine scent) – cooling effect

Cannabis *Sativa* or *Indica*! What does the 'research' say?

"The clinical effects of the cannabis chemicals have nothing to do with the plant or its leaflets shape." Dr Russo (Neurologist, Cannabis psychopharmacologist)

"And all sativas will energize you, and not all indicas will sedate you" – Mandel

If Sativa vs. Indica isn't Predictive of Effects, What is?

- **Cannabinoids** versus **Terpenes**
- **Pharmacological properties**
  - chemical profile of each cannabis,
  - individual (human) biology and pathophysiology,
  - tolerance, dependence, tachyphylaxis, resistance, and
  - dose, frequency, co-administration and route of administration

THC versus CBD

THC-dominant strains:
- primarily chosen by individuals seeking a potent euphoric experience (to control pain, depression, anxiety, insomnia, and CNS-related symptoms). High risk for adverse effects

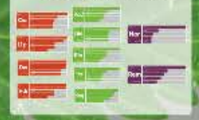
CBD-dominant strains:
- Limited concentrations of THC, and widely used by individuals seeking pain and neurological symptoms control, who are highly sensitive to THC (or suffered from THC adverse effects), while enjoying 'clear-headed' symptom relief

Balanced THC/CBD strains:
- contain balanced levels of THC, offering mild euphoria alongside symptom relief

What does the 'Lab' say?

Sativa versus Indica?

"The Fugitive" grass



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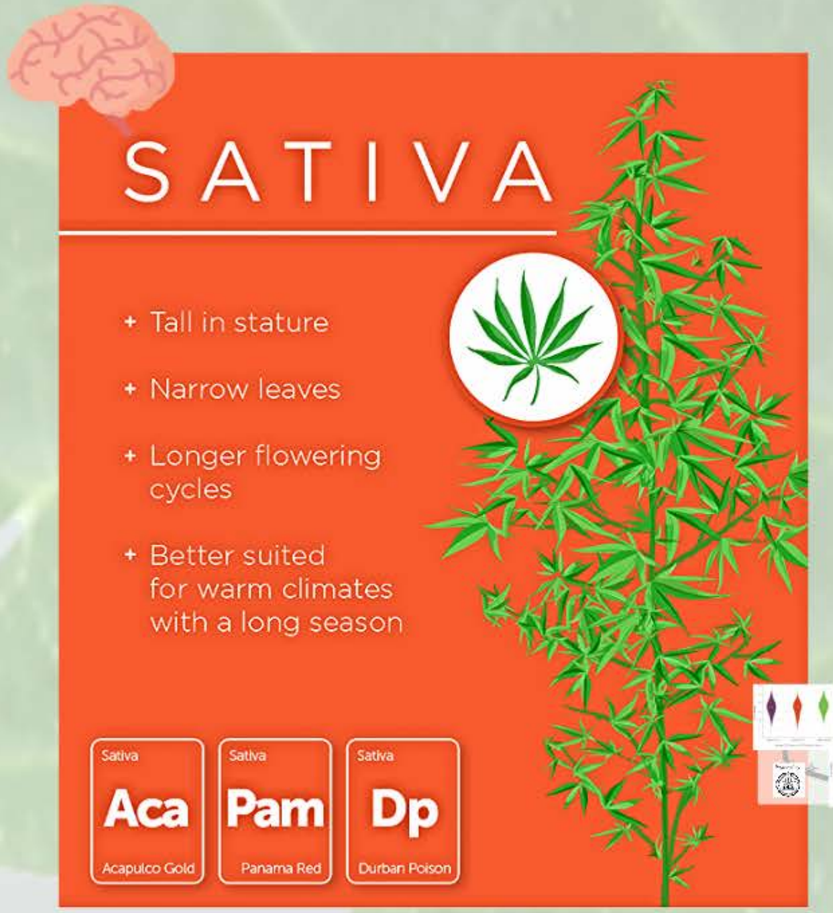

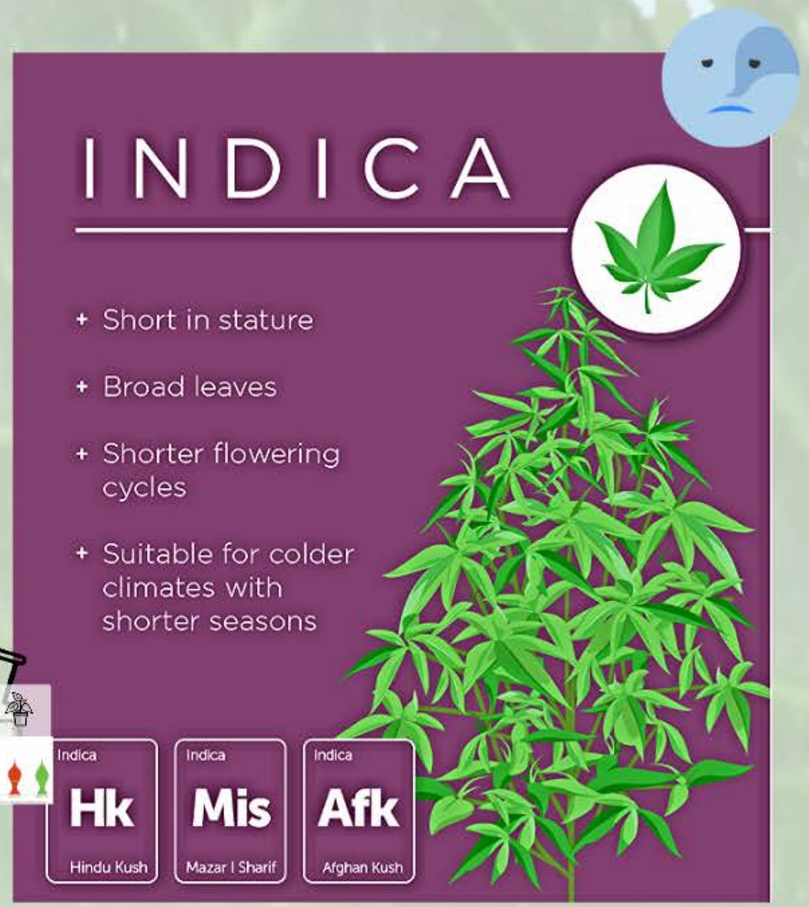

Uplifting CNS effects, pair well with physical activity

Physically sedating, possible adverse effects?

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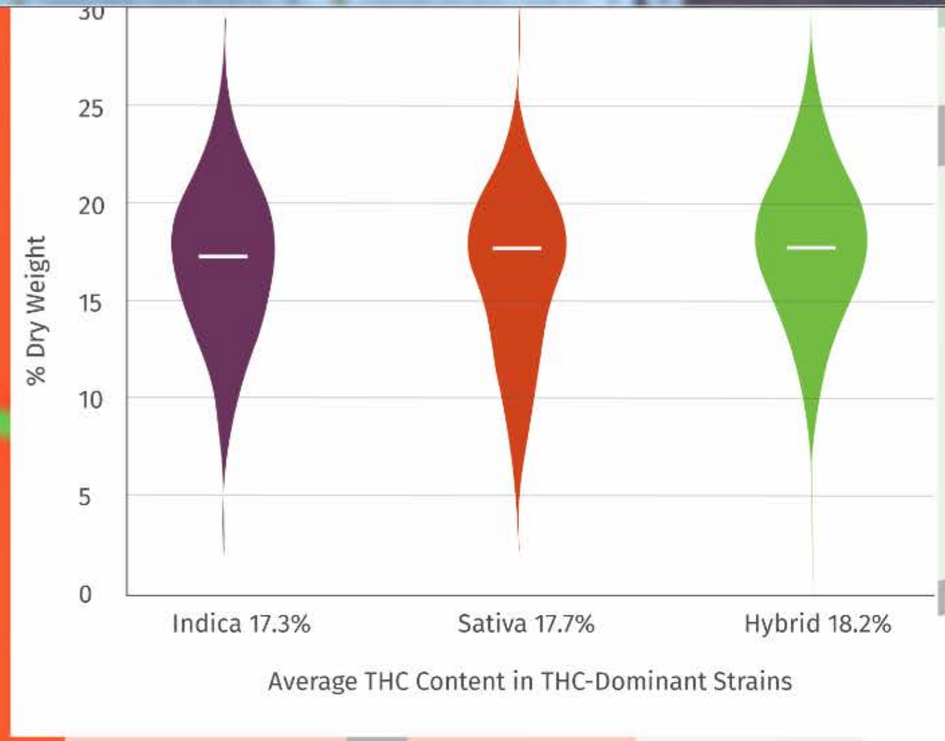

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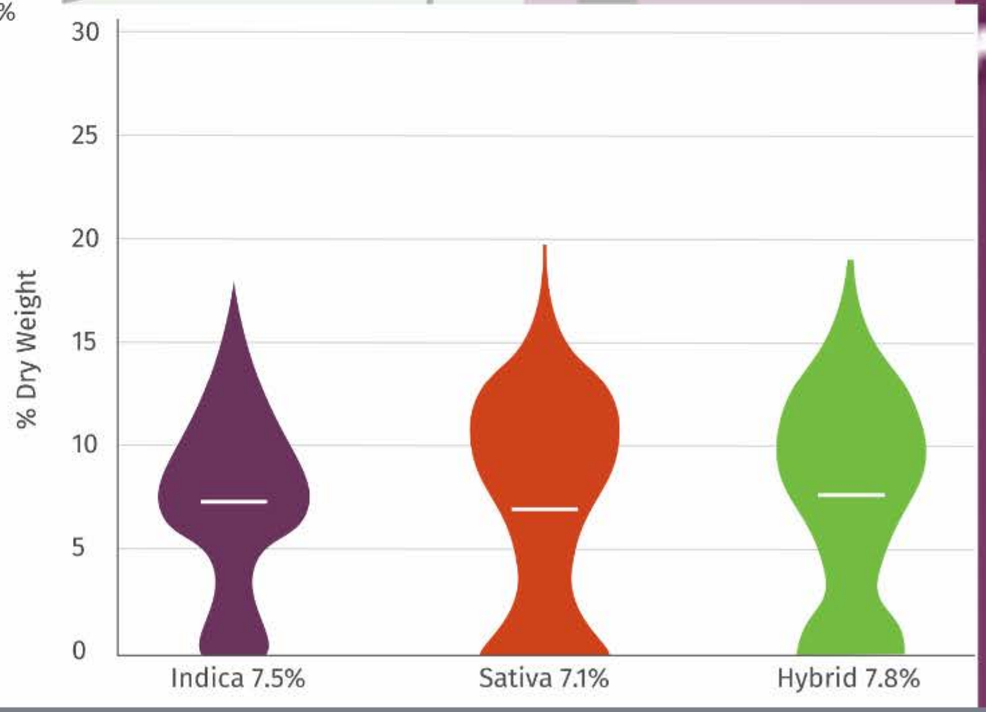

Indic

Cannabis *Sativa* or *Indica*! What does the 'research' say?

"***The clinical effects of the cannabis chemovar have nothing to do with the plant or its leaflets shape***." (*Dr Russo: Neurologist; Cannabis psychopharmacology*)

"***not all sativas will energize you, and not all indicas will sedate you***" - Placebo?

If Sativa vs. Indica Isn't Predictive of Effects, **What Is?**

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- **Pharmacological** properties:
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  - **CBD** (cannabidiol) = is a less-intoxicating , used to alleviate anxiety, pain, inflammation, and other 'promising' medical uses?
  - **Others?**
- **Terpenes:**
  - aromatic compounds, responsible for distinctive cannabis smell
  - Gelato = **kief**: sedating and energizing effects
  - Linalool (*cinnamon*) = relaxing effects
  - Pinene (sideritis: ironwort) = alerting effect

delta-9-tetrahydrocannabinol (**THC**)

Cannabidiols (**CBD**)

Cannabigerols (**CBG**)

Cannabichromenes (**CBC**)

Cannabinol (**CBN**)

cannabinodiol (**CBDL**)

cannabicyclol (**CBL**)

cannabielsoin (**CBE**)

cannabitriol (**CBT**)

more!!.

THC versus CBD

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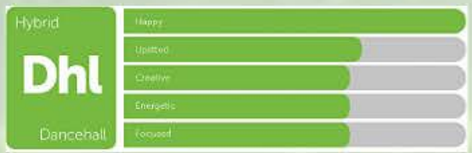

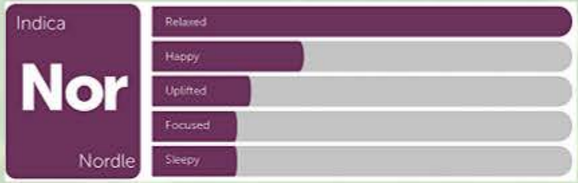

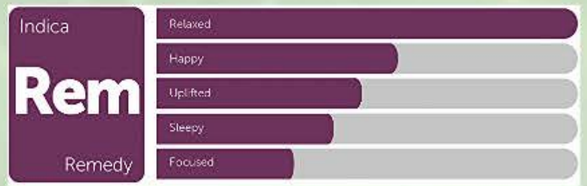

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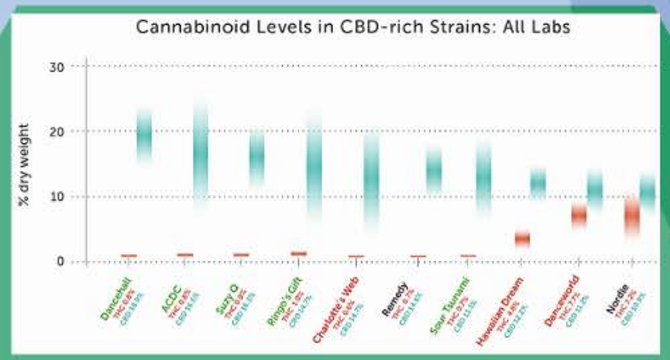
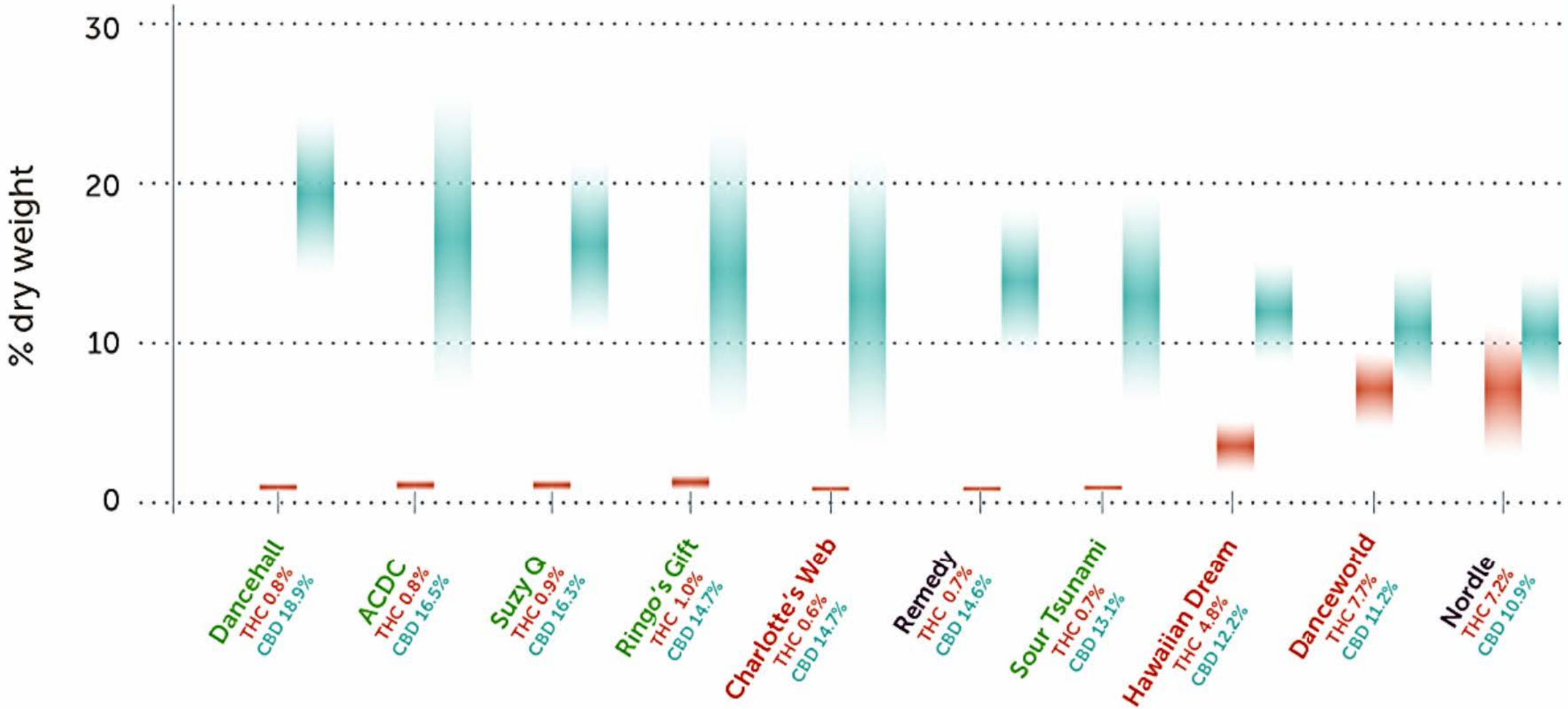


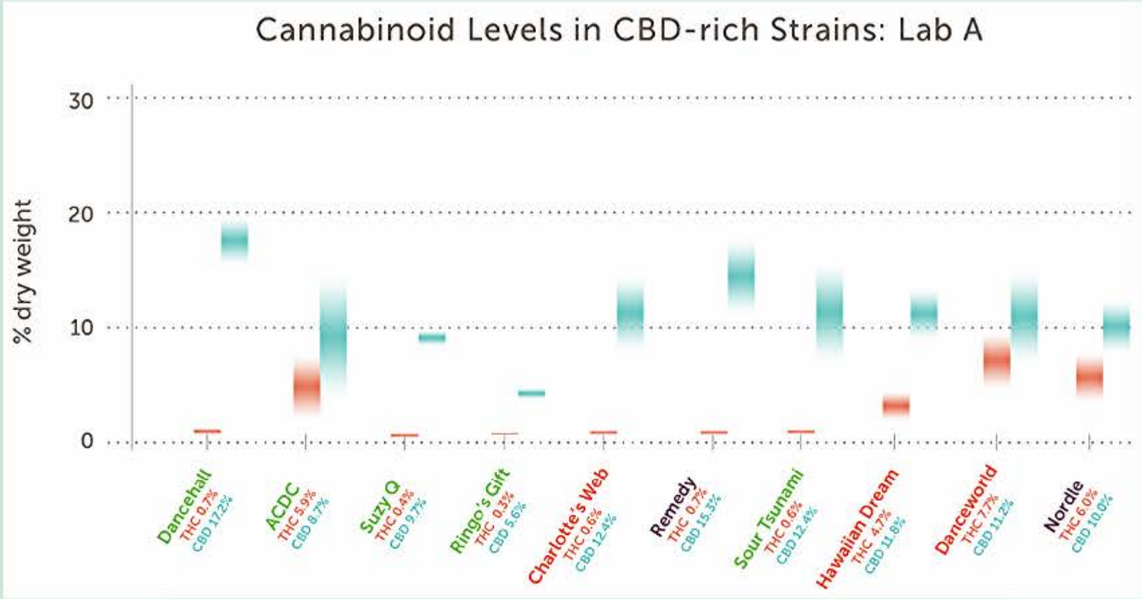
Cannabinoid Levels in CBD-rich Strains: All Labs



ACDC

THC 5.9%

CBD 8.7%



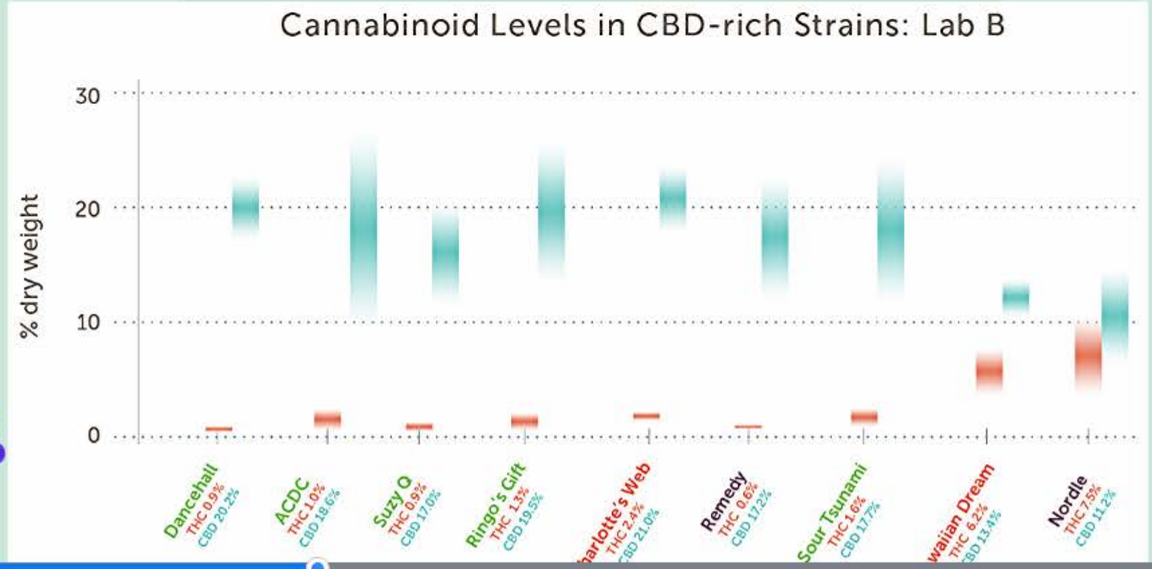
genetics

growth

ACDC

THC 1.0%

CBD 18.6%



assay

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The 'Cannabis' Road Ahead

(1000 km) Evidence-based vision

Identify the main ingredient

CBD/THC balanced strains

- natural
- hybrid
- synthetic

Measured units not percentage/ratio

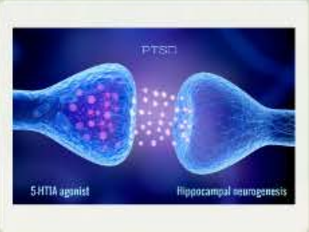
- mcg, mg, g

Well-tolerated, preferred route of administration

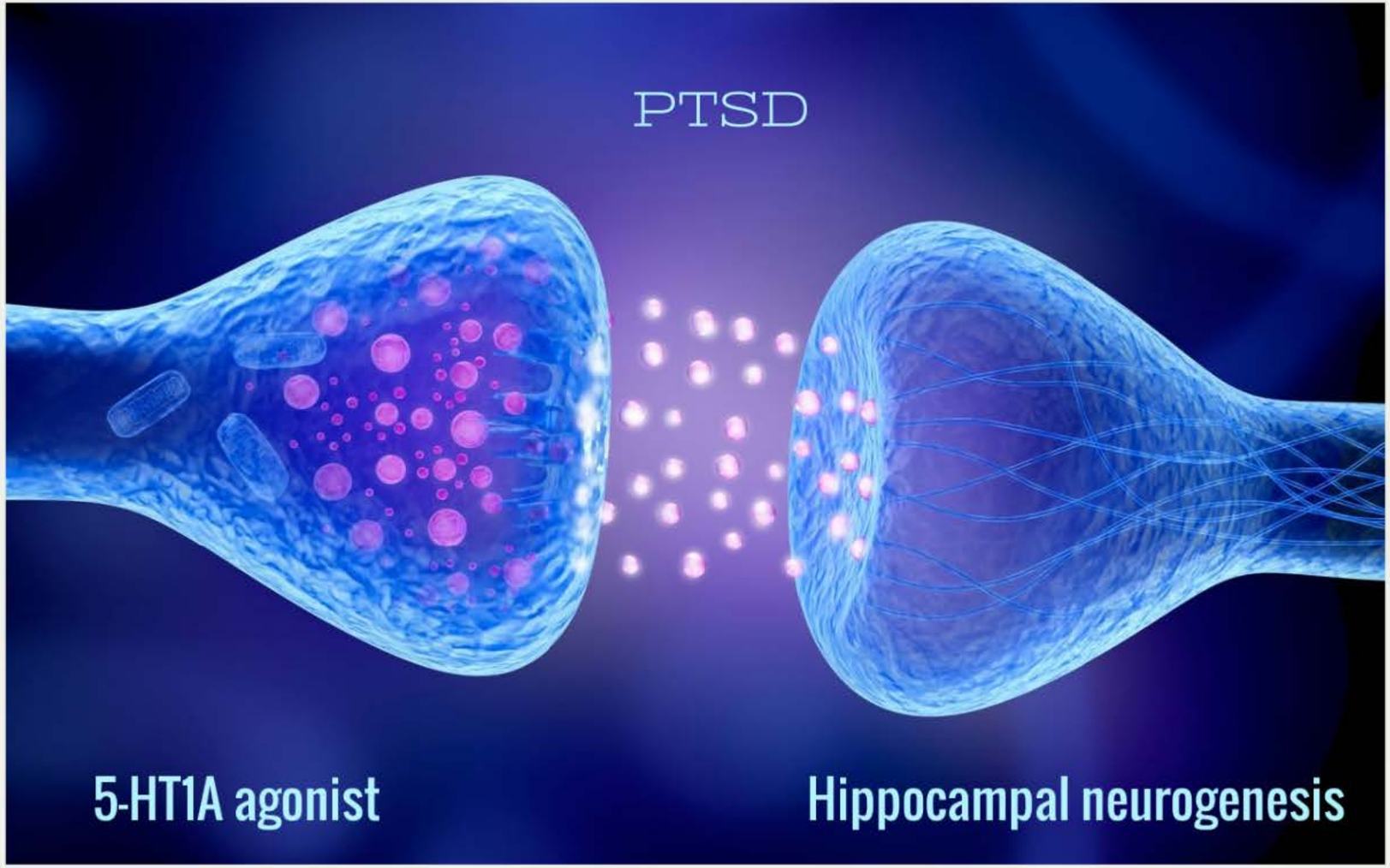
- oral: tablet, capsule, powder (Kief), gum
- liquid: syrup, drops, oil (RSO)

List the major 'therapeutics'

- Psychomotor retardation:
  - mood disorders (depression), anxiety (PTSD), insomnia



- Neurodegenerative disorders:
  - Parkinson's, MS/MND, Alzheimer's, Huntington's
- Anti-inflammatory and analgesic:
  - acute (trauma), chronic (RA, OA), cancer
- Seizure disorder:
  - Epilepsy


PTSD
5-HT1A agonist
Hippocampal neurogenesis

Understand the Endo-cannabinoid system

Partial agonist at (CB1)

CB1 receptor: **Ananadamide**

retrograde endocannabinoid neurotransmitter

Rat: synthetic THC = DA release?

Withdrawal: activation of CRF in basal ganglia = generally mild

short t1/2, and low Vd

Clinical trials

Better understanding

Generalisability

Placebo-effect

Efficacy and safety

Healthcare system trust

Learn from others

St. John's Wort:

- introduced as healthy (dietary) supplement
- Identifiable ingredient:
  - *Hypericum perforatum*

Therapeutic efficacy confirmed by RCTs and systematic reviews

Verdict: more effective than placebo and similar in effectiveness to low-dose TCAs in the short-term treatment of mild to moderately severe depression

Invest on current evidence

Clinical research

Epilepsy

REVIEW

Evidence for cannabis and cannabinoids for epilepsy: a systematic review of controlled and observational evidence

Emily Stockings,[1] Dino Zagic,[1] Gabrielle Campbell,[1] Megan Weier,[1] Wayne D Hall,[2,3] Suzanne Nielsen,[1] Geoffrey K Herkes,[4] Michael Farrell,[1] Louisa Degenhardt[1]

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - REVIEW ARTICLE

Check for updates

Evidence for the use of cannabinoids in Parkinson's disease

Carsten Buhmann[1] · Tina Mainka[2] · Georg Ebersbach[3] · Florin Gandor[3,4]

- There are a growing number of uncontrolled trials and case reports that suggest beneficial effects of cannabinoids in patients with .....
- Due to large variety of substances investigated, the varying routes of intake, differing doses and time courses make it difficult to compare data

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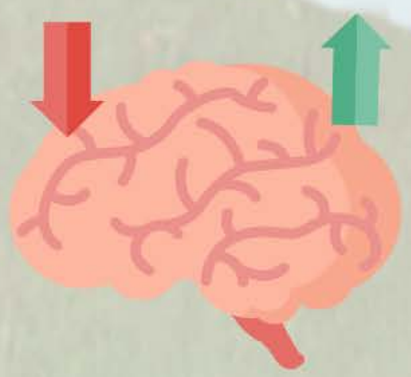
Requirements

- Investors
- Healthcare system
- Clinical research experts
- Dispensing system
- Adverse reactions reporting system (pharmacovigilance)
- Legal team
- Community leaders
- Media (pre-filtered, unbiased)
- Awareness campaigns
- Database

Gateway Drug

The use of a psychoactive drug can be coupled to an increased probability of the use of further drugs = **Gateway-IN**



Cannabis as **Gateway-OUT**?

Opioid dependence:

- Methadone (*agonist*)
- Naltrexone (*antagonist*)
- Buprenorphine (*agonist*/*antagonist*)

Challenge what you see!

disbelief, fear and uncertainty

Thank
You!