



THE CURIOUS INCIDENT OF CANNABIS AND BRAIN-RESEARCH

Michal Gruberger, PhD

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Brain and Cannabis



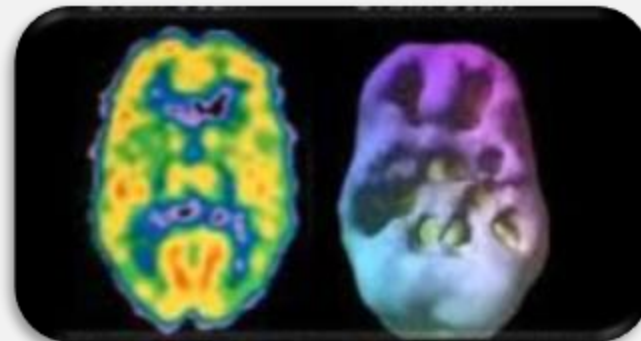
What was:
The BIG BIG
gap



What is:
Affect,
behavior,
cognition



What will be:
Brain is back



Cannabis plants were arranged across the body of a middle-aged man before his burial in Turpan, China, around 2,500 years ago.



CANNABIS IN ONE SLIDE

CB1+2 RECEPTORS:

- Unlike Alcohol, Cannabis resembles an endogenous substance

- Thus, in the brain, Cannabis interrupts neural activity **regulation & flow**

- “When it rains, it pours” principle

Endocannabinoid system

The Endocannabinoid system contains of two receptors, called CB1 and CB2. these receptors are found on cell surfaces and impact various biological processes.

CB1

Located in the brain, central nervous system, and many other parts of the body.

CB2

Found throughout the body on cells associated with our immune system.

CBD interacts with CB1 and CB2 receptors for many effects still being studied.



CB1

CB1 Receptors target:

- Motor activity
- Thinking
- Motor co-ordination
- Appetite
- Short term memory
- Pain perception
- Immune cells

CB2

CB2 Receptors are much broader than CB1 and influence most of the body

- Gut
- Kidneys
- Pancreas
- Adipose tissue
- Skeletal muscle
- Bone
- Eye
- Tumours
- Reproductive system
- Immune system
- Respiratory tract
- Skin
- CNS
- Cardiovascular system
- Liver



WHAT WAS: THE BIG BIG GAP

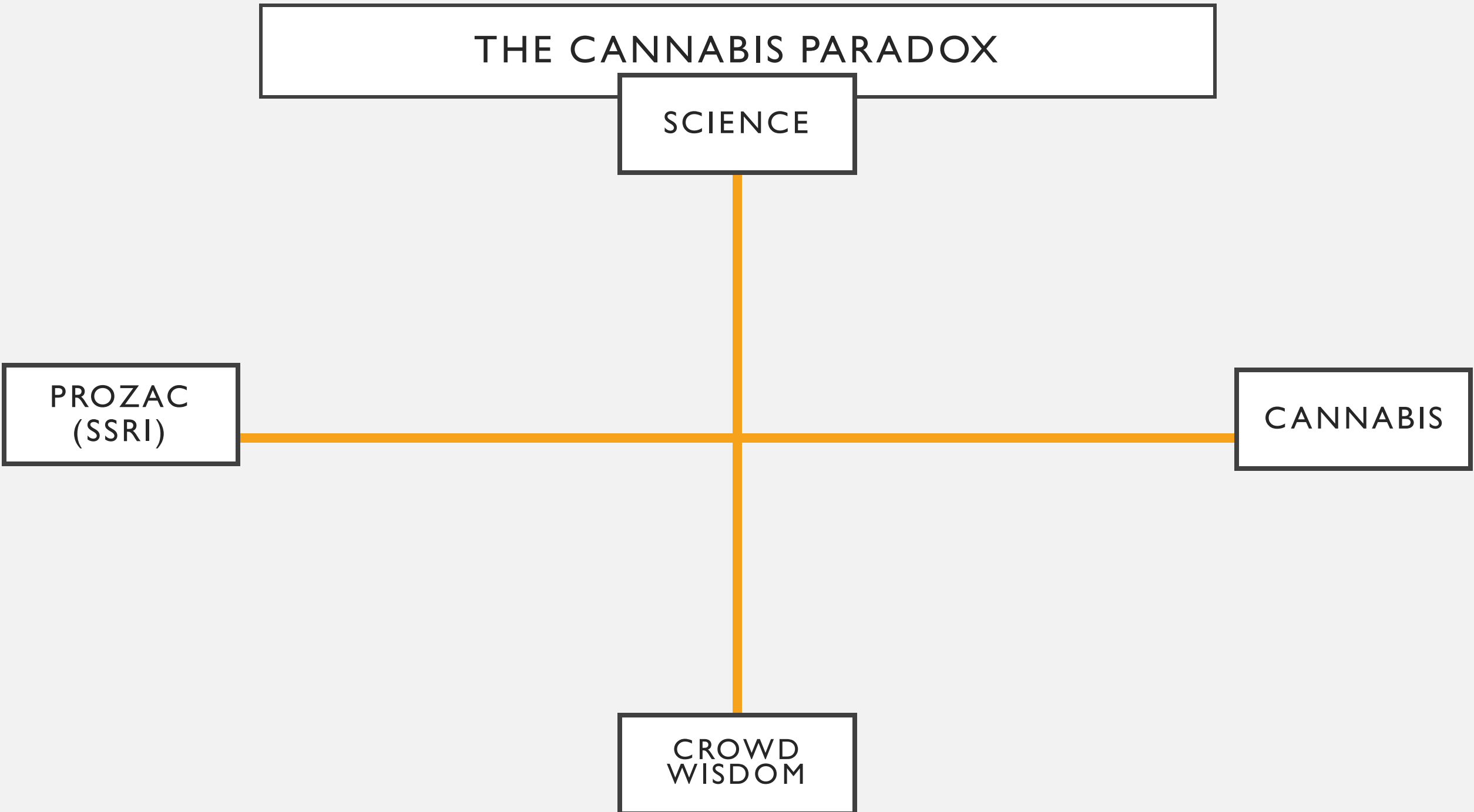
THE CANNABIS PARADOX

SCIENCE

PROZAC
(SSRI)

CANNABIS

CROWD
WISDOM



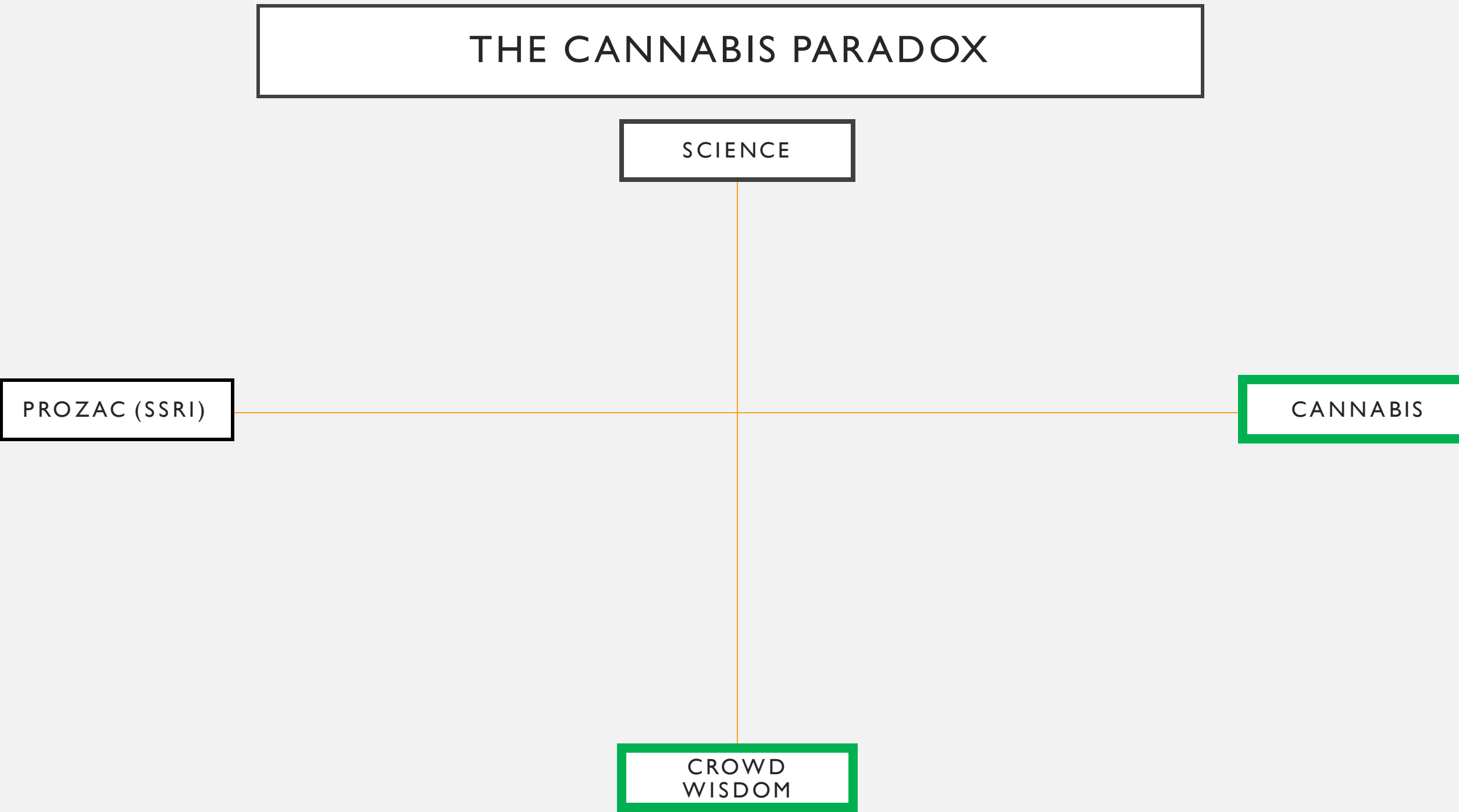
THE CANNABIS PARADOX

SCIENCE

PROZAC (SSRI)

CANNABIS

CROWD
WISDOM



THE CATHERINE JACOBSON CASE

SCIENCE

CANNABIS



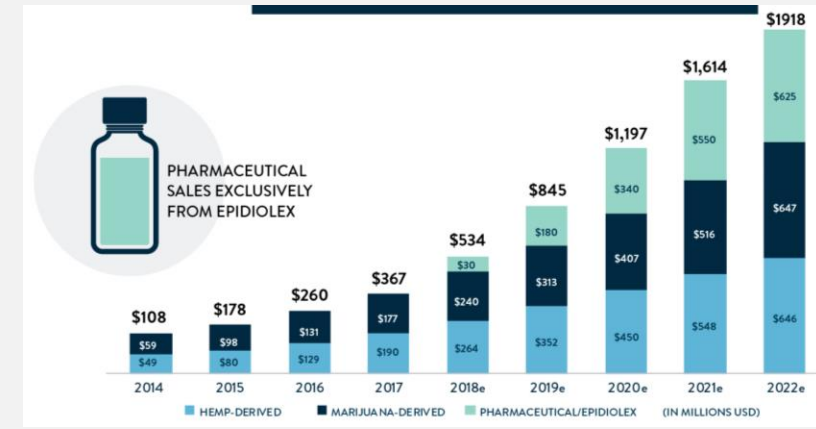
2012



2013



2018



2022

CROWD WISDOM

"It's this completely unprecedented situation; I don't think there's another product out there that's a wellness drug, a pharmaceutical drug for severe disease and a recreational drug."

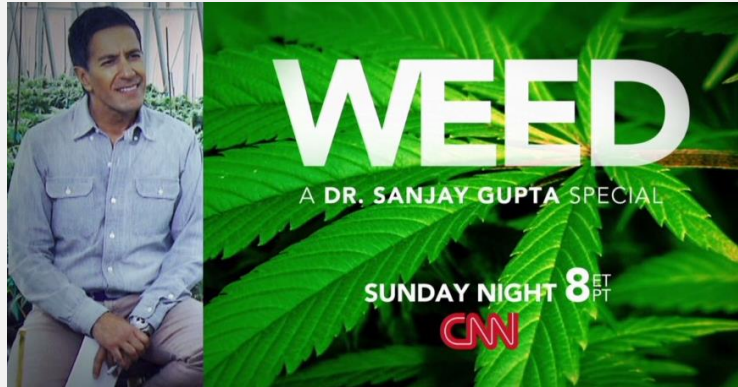
PATIENT ZERO: CHARLOTTE FIGI

SCIENCE

CANNABIS



2011



2013



3001



CROWD WISDOM

PATIENT ZERO: CHARLOTTE FIGI

SCIENCE

CANNABIS



- Currently serves over 55,000 clients worldwide
- 6000 new inquiries each month

Founded by Page Figi and Heather Jackson

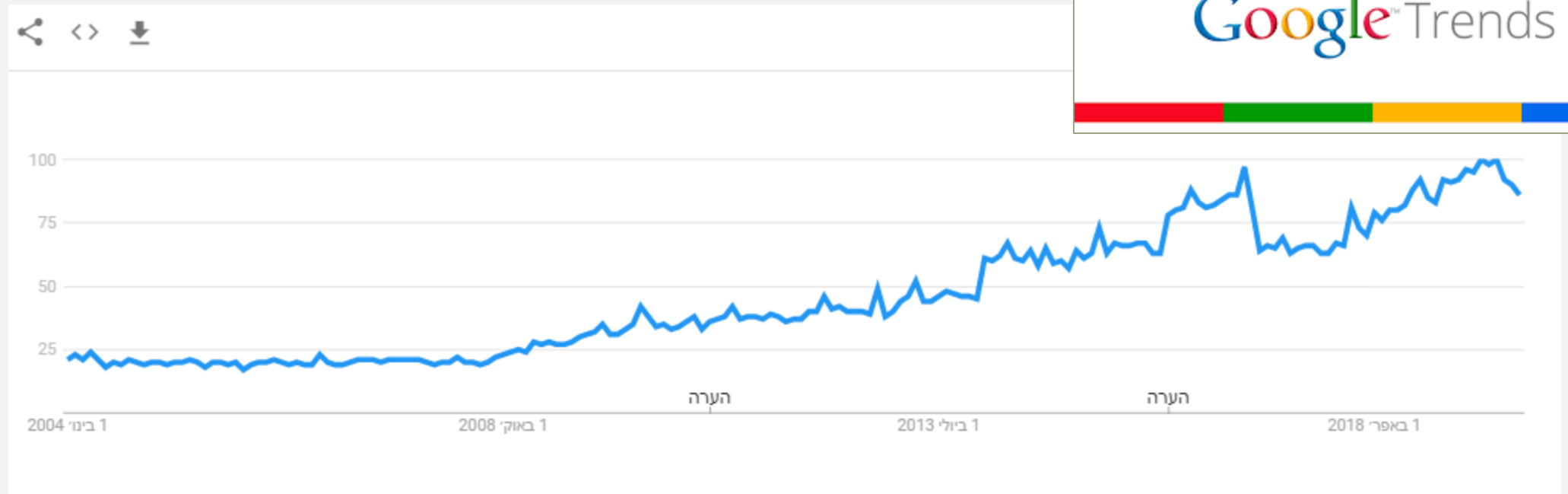


CROWD WISDOM

CANNABIS: GOOGLE TRENDS

SCIENCE

CANNABIS



CROWD WISDOM

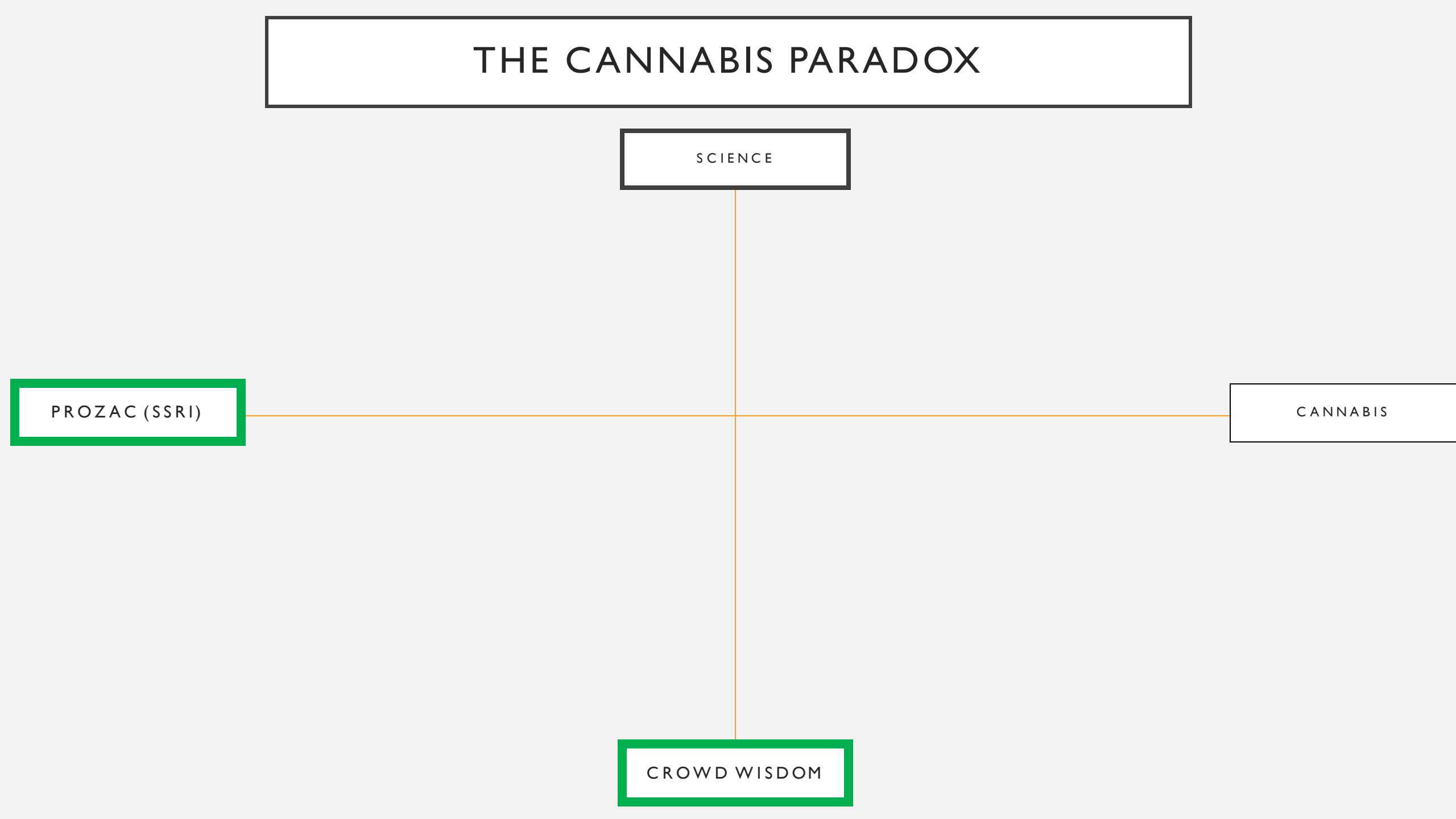
THE CANNABIS PARADOX

SCIENCE

PROZAC (SSRI)

CANNABIS

CROWD WISDOM



PROZAC IN CROWD WISDOM?

SCIENCE

CANNABIS

PROZAC (SSRI)

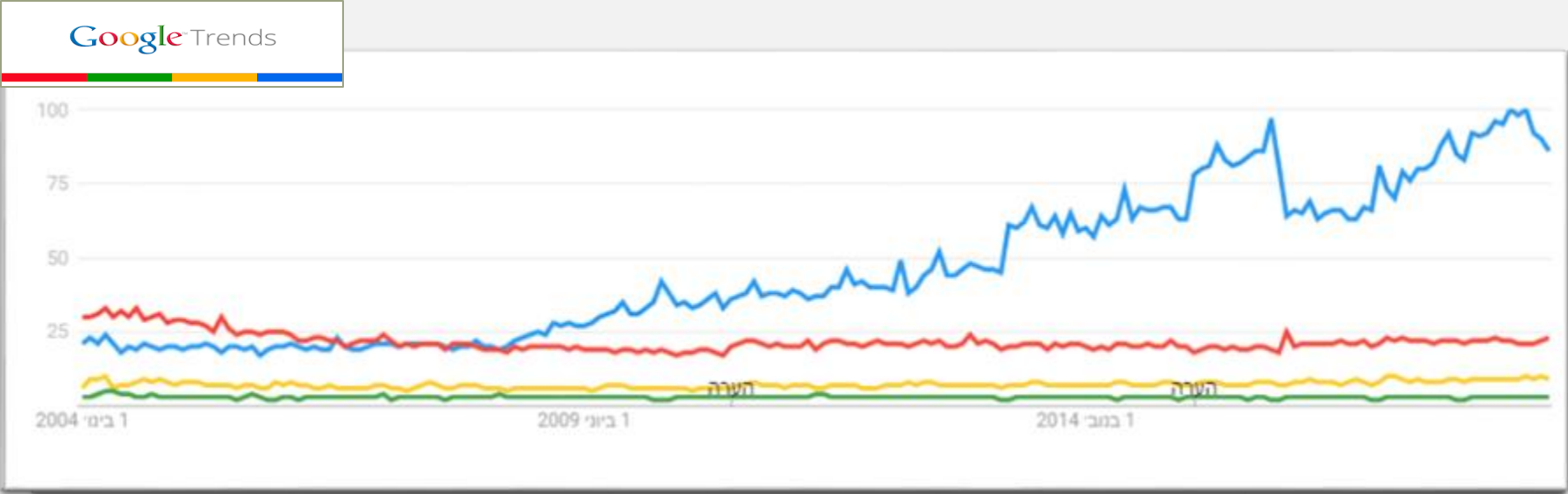
Cannabis

Prozac

SSRI

Pain killer

CROWD WISDOM



THE CANNABIS PARADOX

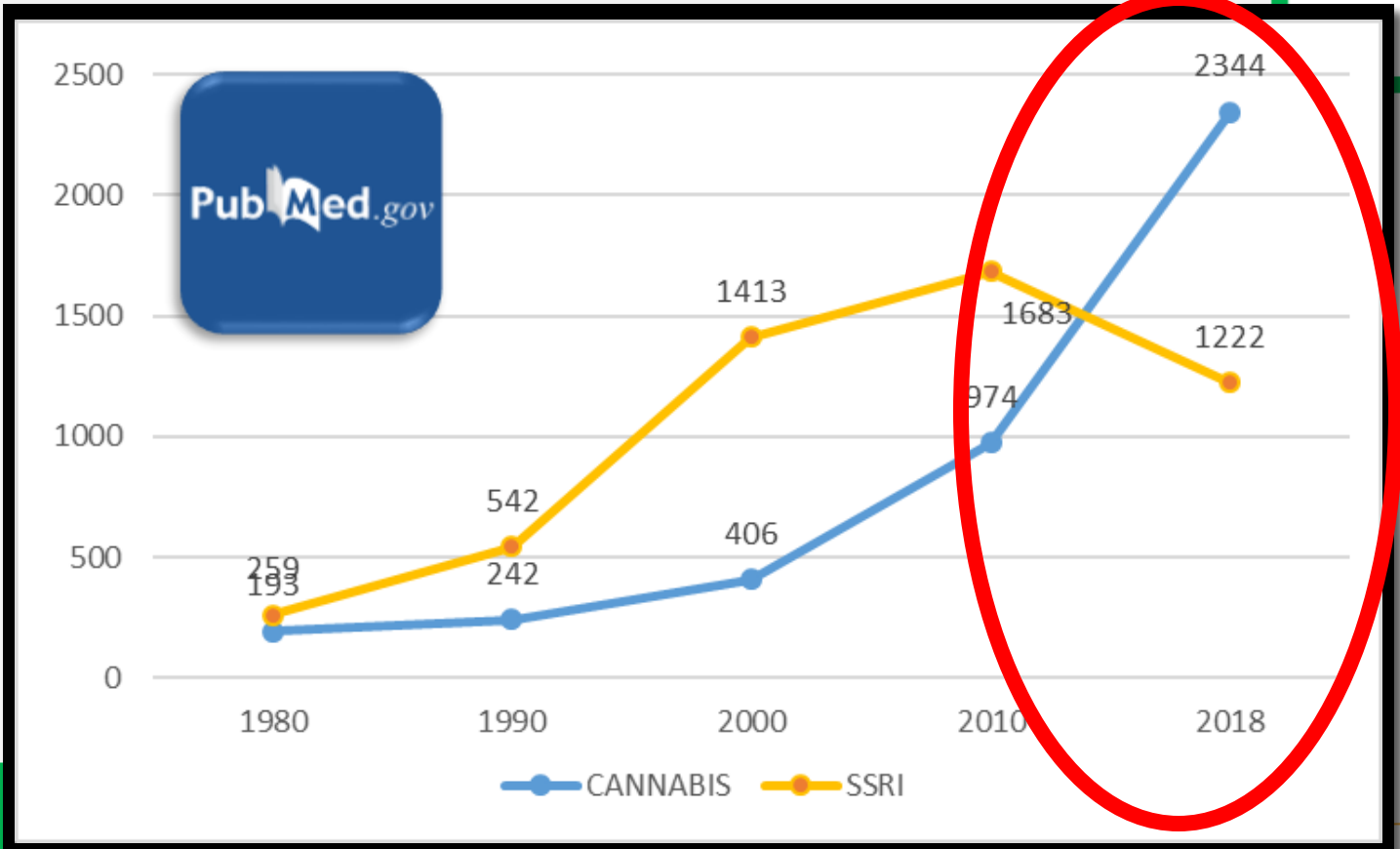
SCIENCE

PROZAC (SSRI)

CANNABIS

CROWD WISDOM

SCIENTIFIC INTEREST: PROZAC VS. CANNABIS



SCIENCE

PROZAC (SSRI)

CANNABIS

CROWD WISDOM

THE CANNABIS PARADOX

SCIENCE

PROZAC (SSRI)

CANNABIS

CROWD WISDOM

2019 “LANCET” META-ANALYSIS

SCIENCE

- 83 eligible studies
- n=3067

Articles

Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis



Nicola Black, Emily Stockings*, Gabrielle Campbell, Lucy T Tran, Dino Zagic, Wayne D Hall, Michael Farrell, Louisa Degenhardt*

Interpretation There is scarce evidence to suggest that cannabinoids improve depressive disorders and symptoms, anxiety disorders, attention-deficit hyperactivity disorder, Tourette syndrome, post-traumatic stress disorder, or psychosis. There is very low quality evidence that pharmaceutical THC (with or without CBD) leads to a small improvement in symptoms of anxiety among individuals with other medical conditions. There remains insufficient evidence to provide guidance on the use of cannabinoids for treating mental disorders within a regulatory framework. Further high-quality studies directly examining the effect of cannabinoids on treating mental disorders are needed.

CROWD WISDOM

2019 REGULATION IN ISRAEL

חוזר המשנה
למנהל הכללי



משרד הבריאות

קנביס רפואי

חוברת מידע ומדריך רפואי



IMCA - Israeli Medical Cannabis Agency
סוכנות ישראלית ממשלתית לקנביס רפואי

כתיבה ועריכה:

מגרי יובל לנרשפט', בעז אלבר' (M.Sc.), פרופ' רפאל משולם, פרופ' ארנון אפק

היחידה לקנביס רפואי (יק"ר), לשכת המשנה למנכ"ל, משרד הבריאות

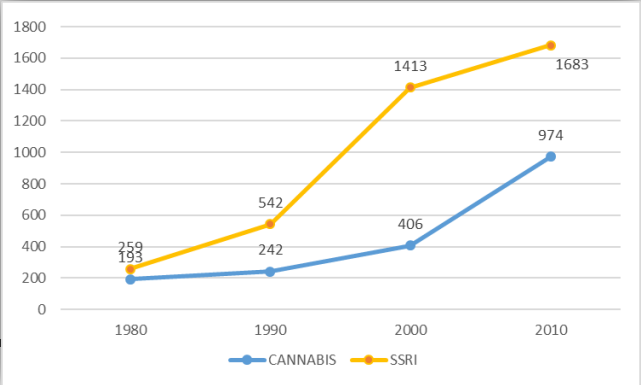
עדכון טיוטה 3 - מאי 2019

הרקע הקליני לקביעת משטר מינון
מושכל של מוצרי קנביס רפואי:

מינון THC (מ"ג/יום)	דרך מתן	מספר מטופלים	המחקר
7.1	עישון	21	Ware, 2010
7.7	Volcano	18	Abrams, 2007
18.5	Volcano	39	Wilsey 2008, 2013
33.6	Volcano	16	Wallace, 2015
5.0	MDI	8	Eisenberg, 2014, 2019*

THE CANNABIS PARADOX

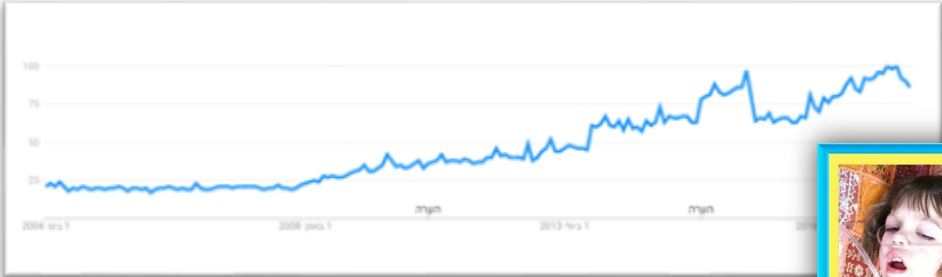
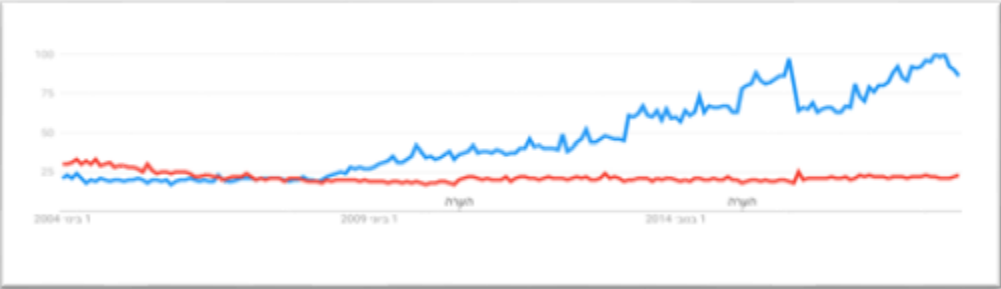
SCIENCE



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PROZAC (SSRI)

CANNABIS



CROWD WISDOM



HOW MANY PEOPLE? (IN THE USA)

Antidepressants



???

Cannabis



34.4 million adults
took antidepressants in 2013-4

Source: National Health and Nutrition Examination Survey
<https://www.nytimes.com/2018/04/07/health/antidepressants-withdrawal-prozac-cymbalta.html>

Almost **37 million** Americans
used marijuana last year (2018)

Source: *Annals of Internal Medicine*
<https://www.fool.com/investing/2018/09/01/nearly-37-million-americans-used-marijuana-in-2017.aspx>
<https://annals.org/aim/article-abstract/2698115/smoking-vaping-use-edibles-other-forms-marijuana-among-u>

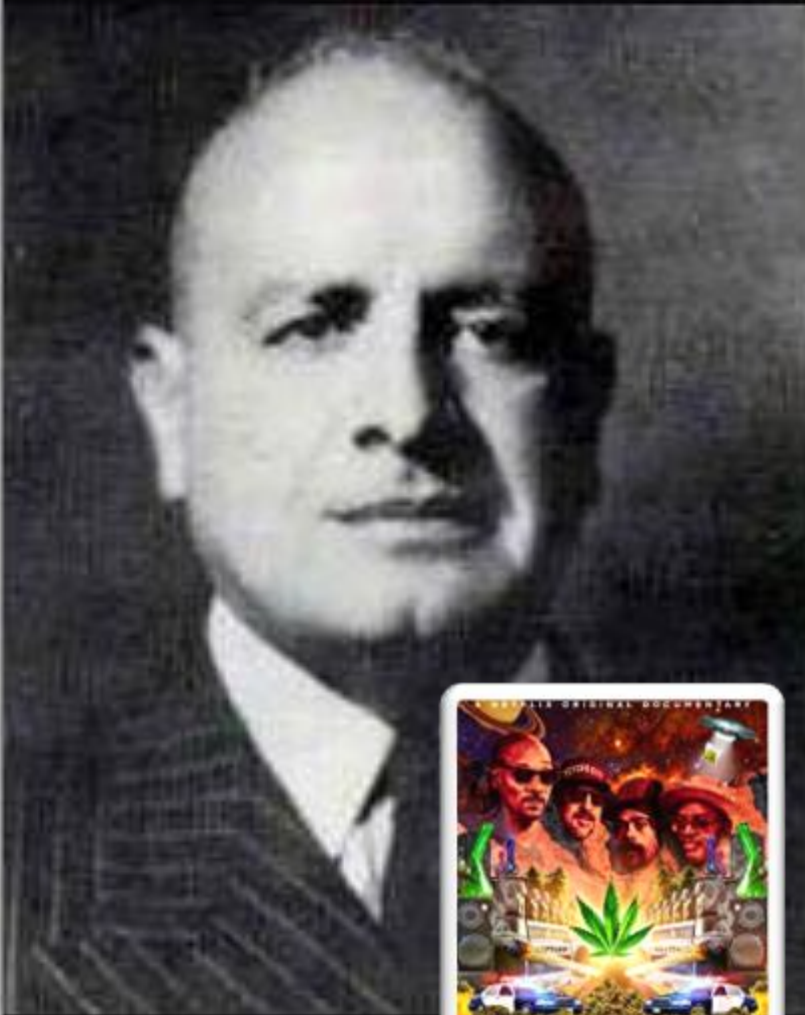
147m people using it annually (globally)
Source: World Health Organization
https://www.who.int/substance_abuse/facts/cannabis/en/

THE CANNABIS PARADOX: WHY?

FIRST US "DRUG CZAR" HARRY ANSLINGER

"There are 100,000 total marijuana smokers in the US, and most are Negroes, Hispanics, Filipinos and entertainers. Their Satanic music, jazz and swing, result from marijuana usage. This marijuana causes white women to seek sexual relations with Negroes, entertainers and any others."

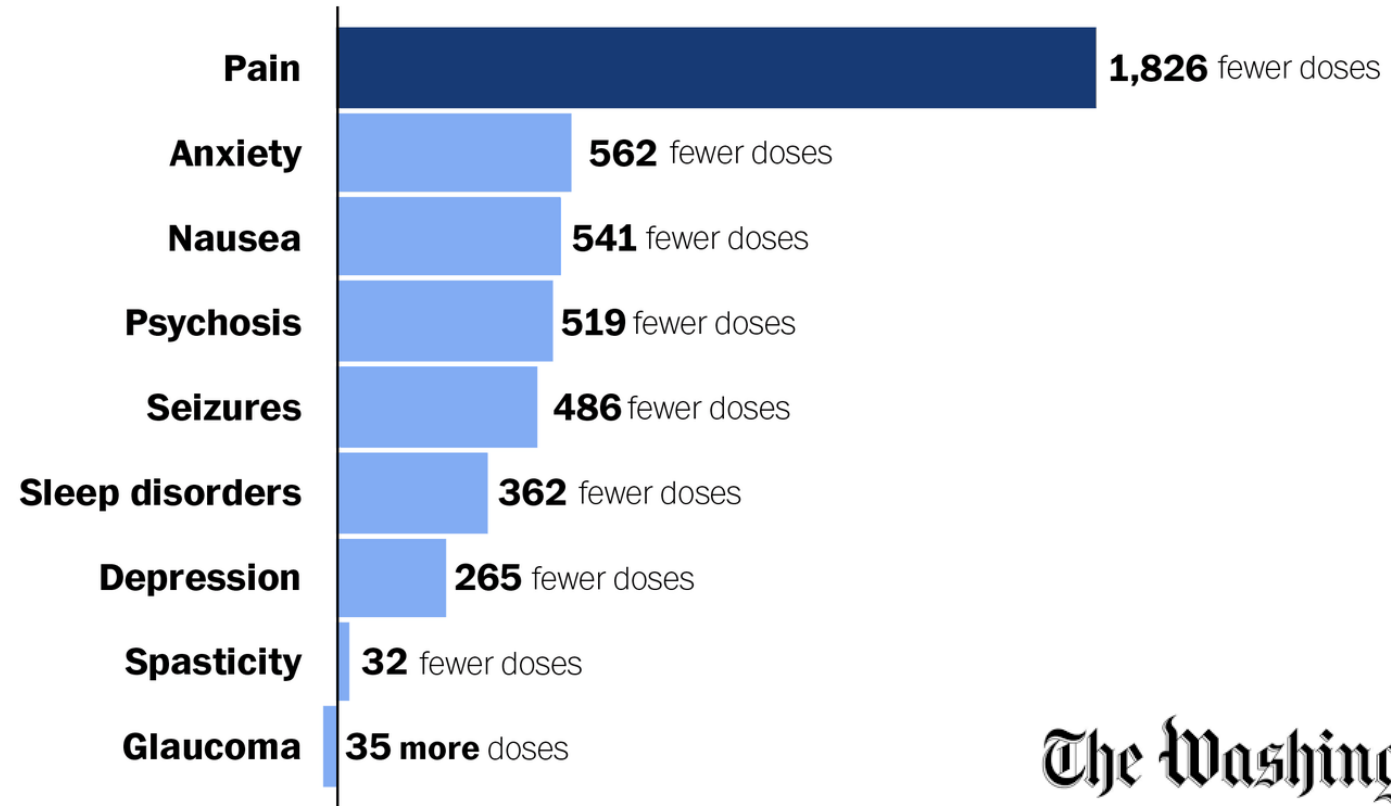
"Reefer makes darkies think they're as good as white men."



THE CANNABIS PARADOX: REALLY WHY?

Fewer pills prescribed in medical pot states

Difference between annual drug doses prescribed per physician in medical marijuana states, and in states without medical marijuana laws, by drug category



The Washington Post

THE SCIENCE OF MARIJUANA

HOW THC AFFECTS THE BRAIN

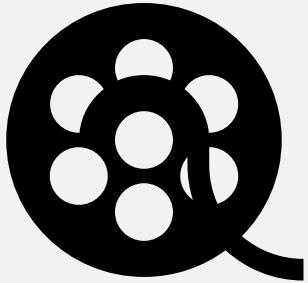


WHAT IS: AFFECT, BEHAVIOR,
COGNITION

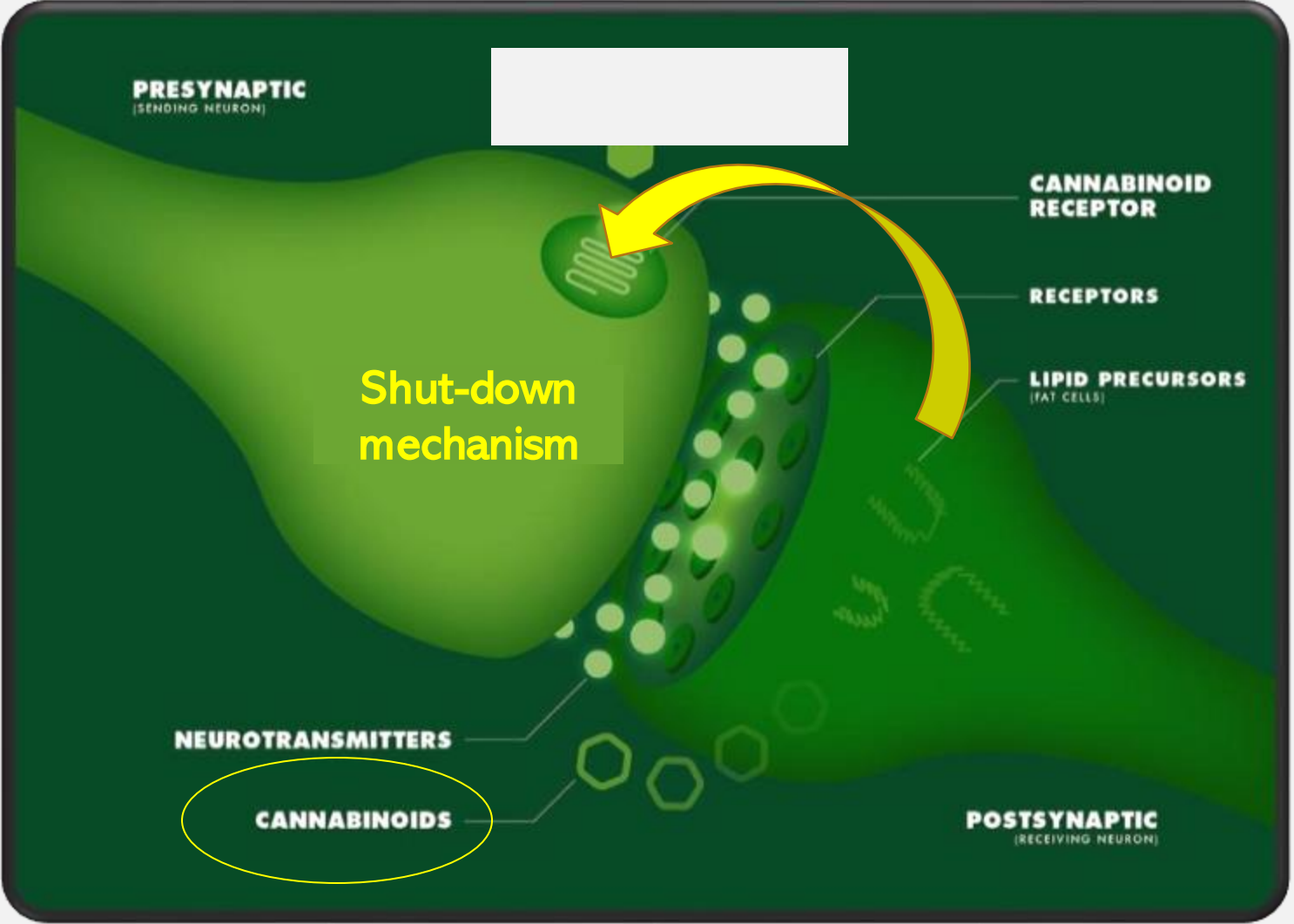
NEURAL MECHANISM MADE SIMPLE

7 FACTS

NEURAL MECHANISM MADE SIMPLE



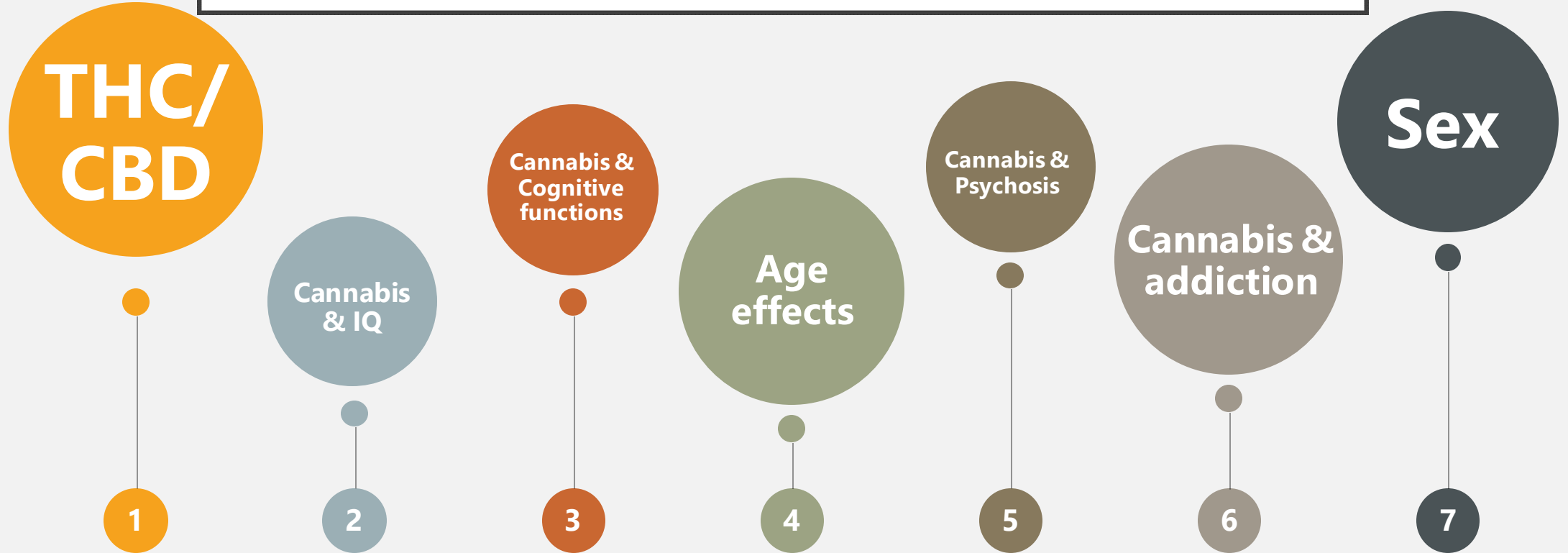
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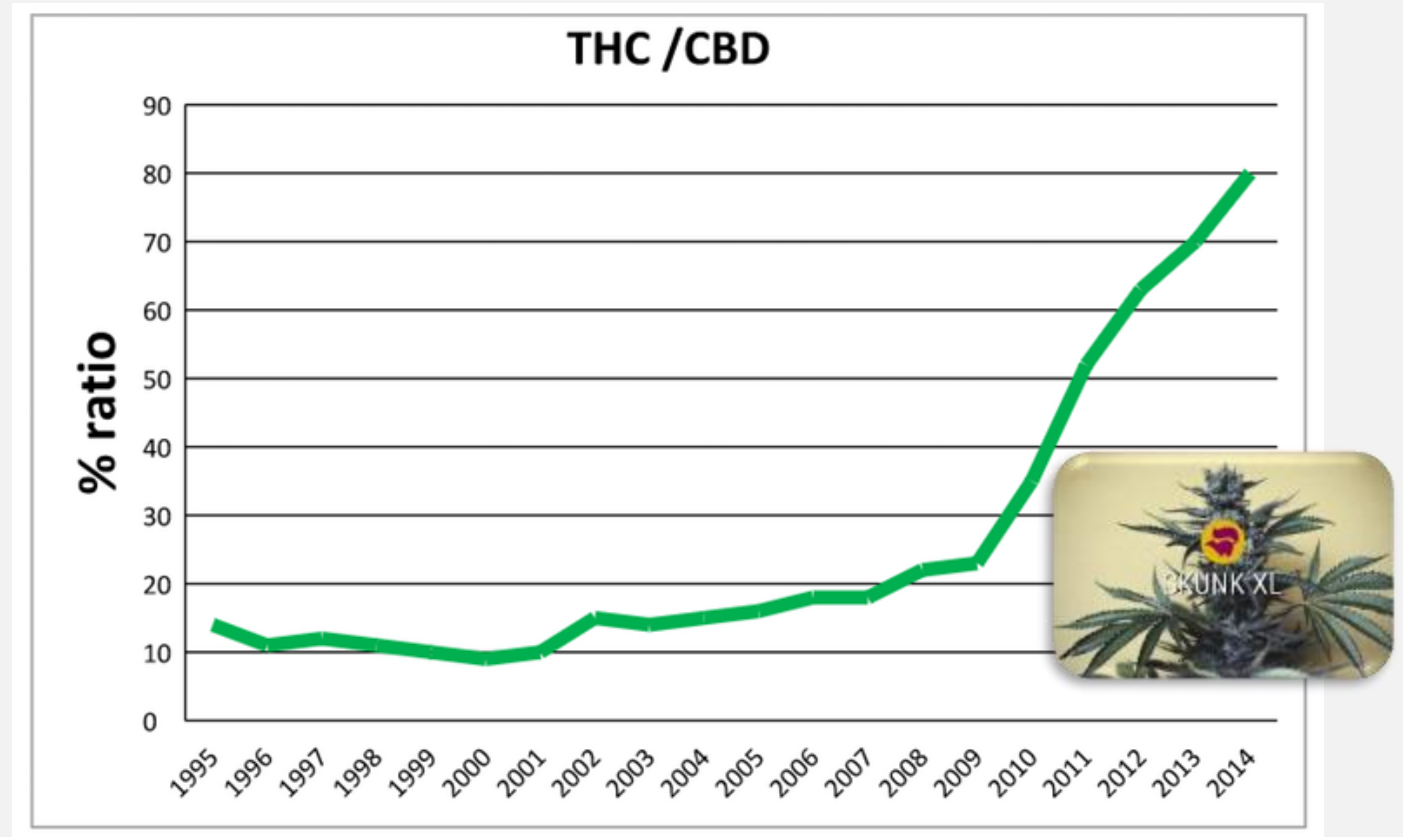
- Strong experiences
- High arousal = uplifted / stressed
- Attention, memory, coordination etc.

7 FACTS



FACT I: RISE IN THC COMPONENT

- Rise in THC, but hardly in CBD
- Thus, studies from decades ago are less relevant (NZ study)
- In the United States, the cannabis that the National Institute of Drug Abuse supplies to researchers for experiments generally has **less than 4% Δ^9 -THC**, and so findings from these experiments have limited implications for modern-day cannabis users.



<https://theconversation.com/is-cannabis-really-getting-stronger-62574>



FACT TWO: CANNABIS & IQ



FACT TWO: CANNABIS & IQ

1

New Zealand, 2012

-6 IQ points

Born at 1972, 1973

Baseline at 7-13

Measurement at age 38

Adolescent dependency
= most decline

Remained apparent even
if mild users

2

UK, 2016

No relation

Born at 1991, 1992

Measurement at 15-16

Only 3% of
participants used
Cannabis regularly

3

US, 2016

No relation

Monozygotic and
dizygotic twins

Discordant for cannabis
use

Measurement at 17-20

Only 3% of twin pairs
had one who used
Cannabis regularly

FACT 3: CANNABIS AND COGNITIVE FUNCTIONS

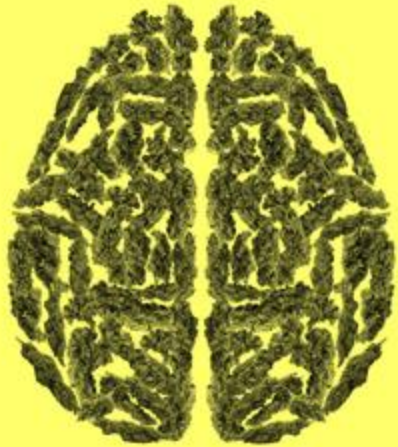
Function

Which?

When?

Supporting evidence

- Animal models



DRUNK VS. STONED:

https://www.youtube.com/watch?v=yJJRVleE3_Q

Addicted

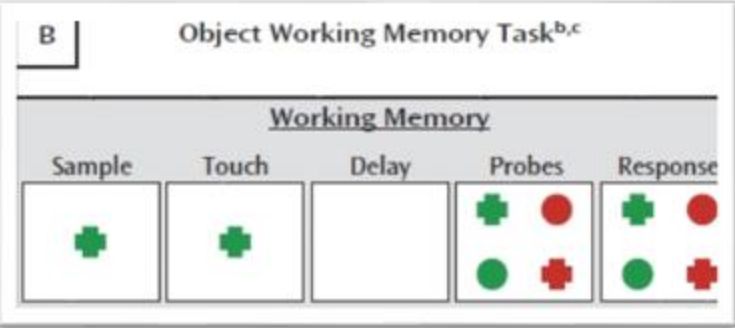
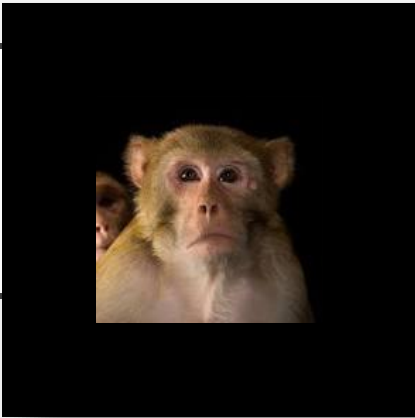
ALVVATS

FACT 4: AGE EFFECTS

The age-related effects of cannabis use on cognitive function depends on **the maturational state** of the neural circuits that are affected by the drug



FACT 4: AGE EFFECTS



Object working memory



Spatial working memory



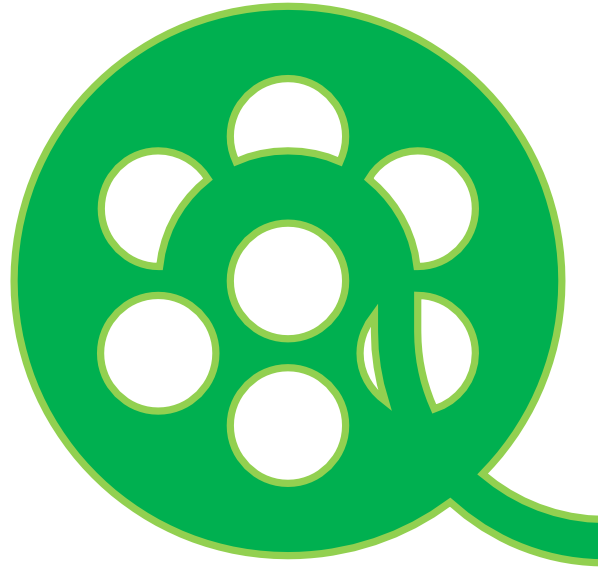
1,2 per day
5 days per week
6 months



...after object working memory, but not on an object working memory task⁴⁷. Thus, the persistent effects of Δ^9 -THC on cognition in animals are more evident when exposure coincides with the developmental stage during which cannabinoid-affected neural circuits are actively maturing.

Similarly, there is also accumulating evidence in humans that neurocognitive function and aspects of brain architecture are more disrupted by cannabis when individuals start using it during adolescence, although there is a scarcity of direct comparisons with adult users. Some structural imaging studies in adolescent

Verrico, C. D., Gu, H., Peterson, M. L., Sampson, A. R., & Lewis, D. A. (2014). Repeated Δ^9 -tetrahydrocannabinol exposure in adolescent monkeys: persistent effects selective for spatial working memory. *American Journal of Psychiatry*, 171(4), 416-425.

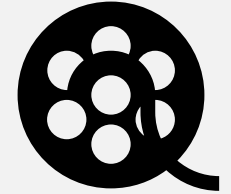


FACT 5: CANNABIS AND PSYCHOSIS

FACT 5: CANNABIS AND PSYCHOSIS

- Nearly 2,000 studies have been published on this topic since 1962
- The Short answer: Yes
 - earlier first episode
 - twice as likely to get psychotic
- But:
 - the vast majority of people who use cannabis do not develop psychotic disorders
 - many people diagnosed with such disorders have never used cannabis

FACT 5: CANNABIS AND PSYCHOSIS

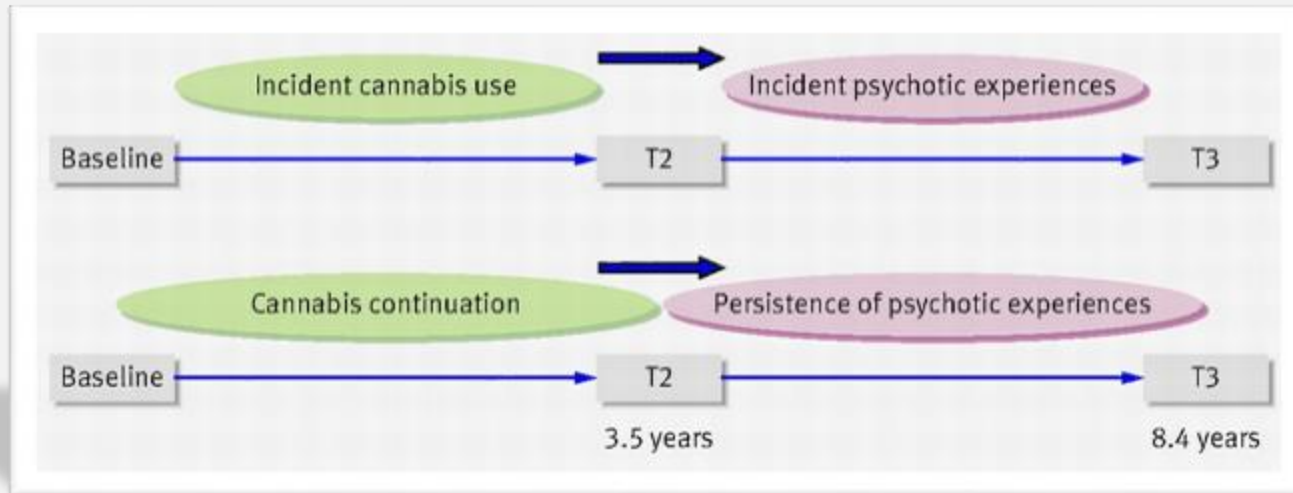


BMJ

RESEARCH

Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study

Rebecca Kuepper, research psychologist,¹ Jim van Os, professor,¹ visiting professor,² Roselind Lieb, professor,^{3,4} Hans-Ulrich Wittchen, professor,^{3,5} Michael Höfler, research statistician,² Cécile Henquet, lecturer⁶



15

N=1923
aged 14-24 at baseline



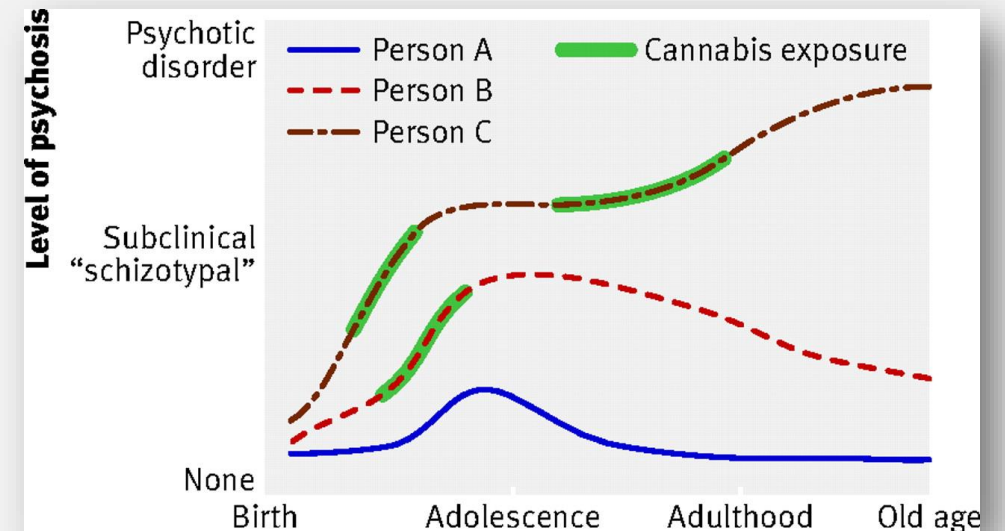
18.5



26.9

RISK FACTORS:

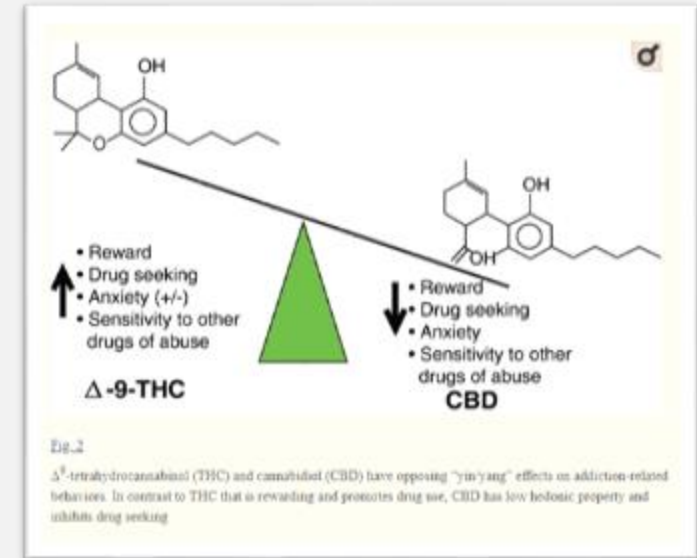
- The type of Cannabis
- Predisposition to psychosis



FACT 6: CANNABIS AND ADDICTION

- Addiction is 9 times more likely than psychosis
- Vulnerability factors:
 - Concurrent tobacco use
 - Early adolescent use
 - Frequent (daily) use
 - Males (83%!) > females (more and faster)
 - THC > CBD

- The Gateway Theory



THE GATEWAY THEORY

Forward Gateway

- ✓ **High frequency & adolescent onset >> Gateway**
- ✓ **Twin study rules out genetic and environmental factors**
- ✓ **Rats studies – THC induces later opiate and cocaine self-administration**



Reverse Gateway

- ✓ **Cannabis is mixed with nicotine in Joints**



- ✓ **Nicotine addiction**



FACT 7: CANNABIS AND SEX



1. An informal poll by **Psychology Today** showed that 67% of respondents felt cannabis **enhanced their sex lives**.

2. 20% claimed it depended entirely on the circumstances at the time of consumption.



3. In a 2009 study by the Australian Research Centre in Sex found a correlation between **orgasming too quickly** and frequent cannabis use in men.

A Santa Barbara study pointed out that cannabis **disrupts a consumer's concept of time**. So, what feels like 10 minutes may be, in fact, only 30 seconds.



FACT 7: CANNABIS AND SEX



3. According to the Mayo Clinic, regular cannabis consumption is one cause of **gynecomastia in men**. This phenomenon is linked to cannabis' effect on testosterone.



4. Back to crowd wisdom:
<https://www.youtube.com/watch?v=M3h0PjSKZJ0>



7 FACTS

More
THC

1

THC
flood

Cannabis
& IQ

2

We're
not sure

Cannabis &
Cognitive
functions

3

Mainly
memory

Age
effects

4

Developm-
ental
phases are
most
vulnerable

Cannabis &
Psychosis

5

Confirmed
!!!

Cannabis &
addiction

6

Confirmed
!!!

Sex

7

It's
complicated

**WHAT WILL BE:
BRAIN IS BACK**

THE CLINICAL & EMPIRICAL BARRIAR

Cannabis



Patient



Outcome



RI.MIND

HARNESSING BRAIN DATA

Revolutionizing the Cannabis market by Replacing
Anecdotal Data with Evidence Based Actionable
Information to deliver Personalized Therapeutic
solutions



elminda

Taking
a BNA™
Test

RiMind leverages Elmind Ltd ground-breaking brain-analysis technology, to personalize cannabis as medicine and solve the information problem associated with the field !



CE & FDA APPROVED TECH



US President Obama



Japan Prime Minister Abe



China Vice Chairman Wang



Pioneering Technology



50 most Innovative Companies

BNA

Functional Imaging Report

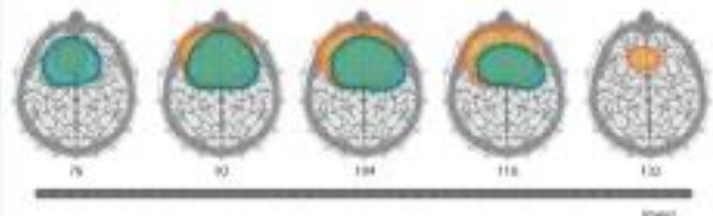
©MindA | 1

Patient Ref: **BLAST18** | Birth Date: **Age 1948** | Gender: **Male**
Age: **69.8** | Age range: **65-75**

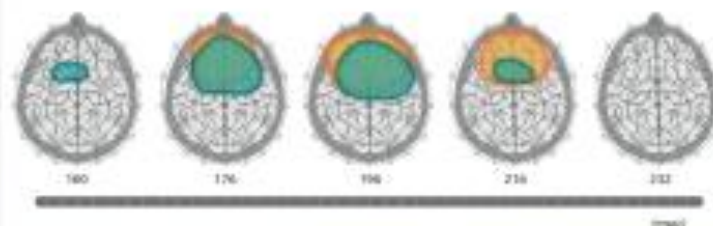
Report Date: **Jan 25, 2018** | Task Name: **Adjusted Auditory Oddball**
Acquisition Site: **CCM 06** | Acquisition Date: **Jan 25, 2018**



Auditory Processing
Sustained Attention



Filtering of Information



The Underlining Technology

Brain Network Analysis (BNA™)

AI Cloud Based Platform-as-a-Service For Brain Analysis



Mapping

INSPECTION

Record brain electrical activities by performing various cognitive tasks associated with visual and auditable responses

Analyzing

AI BASED ANALYTICS

Use AI & ML technology to analyze activities and compare them to an ever-growing data-base to extract and isolate patterns associated with certain brain functions

Enhancing

FUNCTIONAL COGNITIVE REPORT

Actionable physician, patient and consumer-analytics APPS, for disease management & personalization of nutraceuticals and cannabis

We Create Actionable Visualization of Your Brain Functions in Response to Cannabis

68-year-old Male
BNA location: Anxiety
 : Wife's concern
Background:
 Left work, concern about the future !
Recommendation: Cannabis, Sativa or Sativa Hybrid strain to improve uplifted effect, reduce stress and increase concentration

MOOD

UPLIFTED	35%
STRESS	35%
EMOTIONAL CONTROL	35%

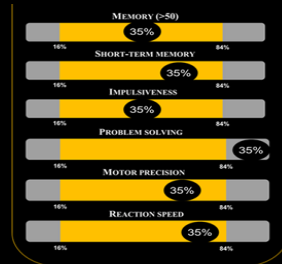
PERCEPTION

ALERTNESS	35%
CONCENTRATION	35%
NOISE FILTERING	35%

BRAIN PERFORMANCE

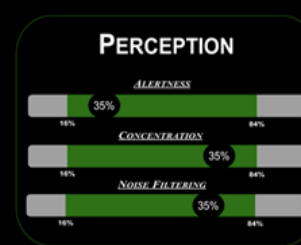
MEMORY (0-50)	35%
SHORT-TERM MEMORY	35%
IMPULSIVENESS	35%
PROBLEM SOLVING	35%
MOTOR PRECISION	35%
REACTION SPEED	35%

BRAIN PERFORMANCE



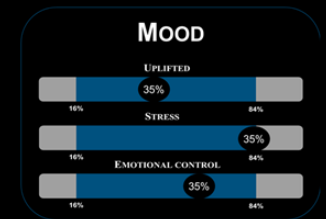
- Memory
- Problem solving
- Motor Precision
- Reaction speed
- Impulsiveness

PERCEPTION



- Alertness
- Concentration
- Noise Filtering

MOOD



- Uplifted
- Stressed
- Emotional control

RiMind Solutions are focused on two complimentary verticals

Data Driven Research & Data Driven Treatment

Data Driven Research



Vertical 1:

Clinical R&D & Drug Development

*Generating clinical data on how cannabis effect brain -
for drug development and verifications of claims*



Data Driven Treatment



Vertical 2:

Prescription & Use: Support & Service

*Personalize Actionable information & recommendation
per strain per disease for both physicians and users*



PERSONALIZED CANNABIS TREATMENT;
RUN EMPIRICAL RESEARCH



>>





THE END

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