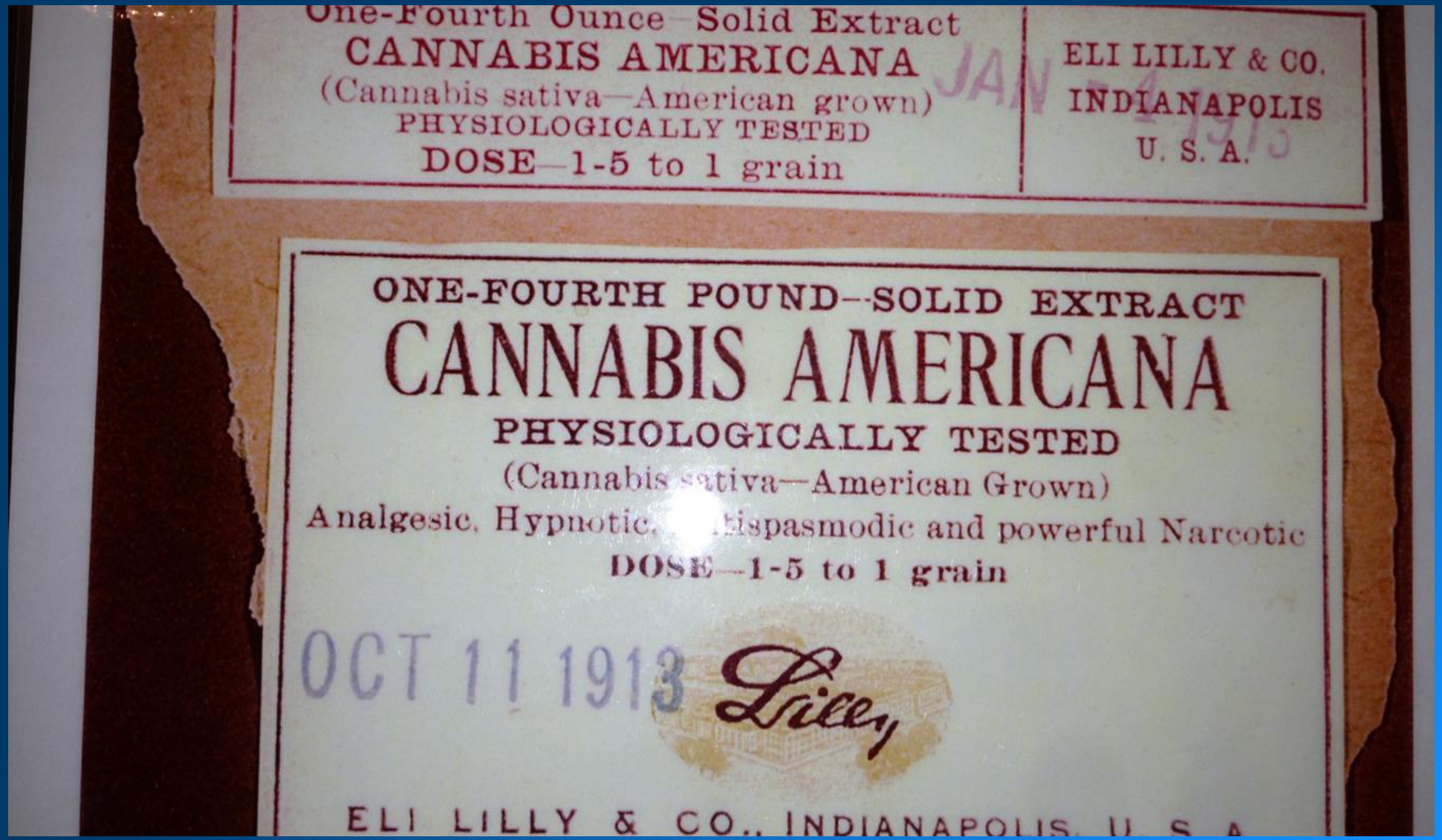
UNITED NATIONS
Office on Drugs and Crime

Cannabis Use For Non-Medical Purposes

Gilberto Gerra
Chief
Drug Prevention and Health Branch

Cannabis: not a new medicine



Substances contained in cannabis

483 known compounds
in the plant:

tetrahydrocannabinol (THC)

84 other cannabinoids:

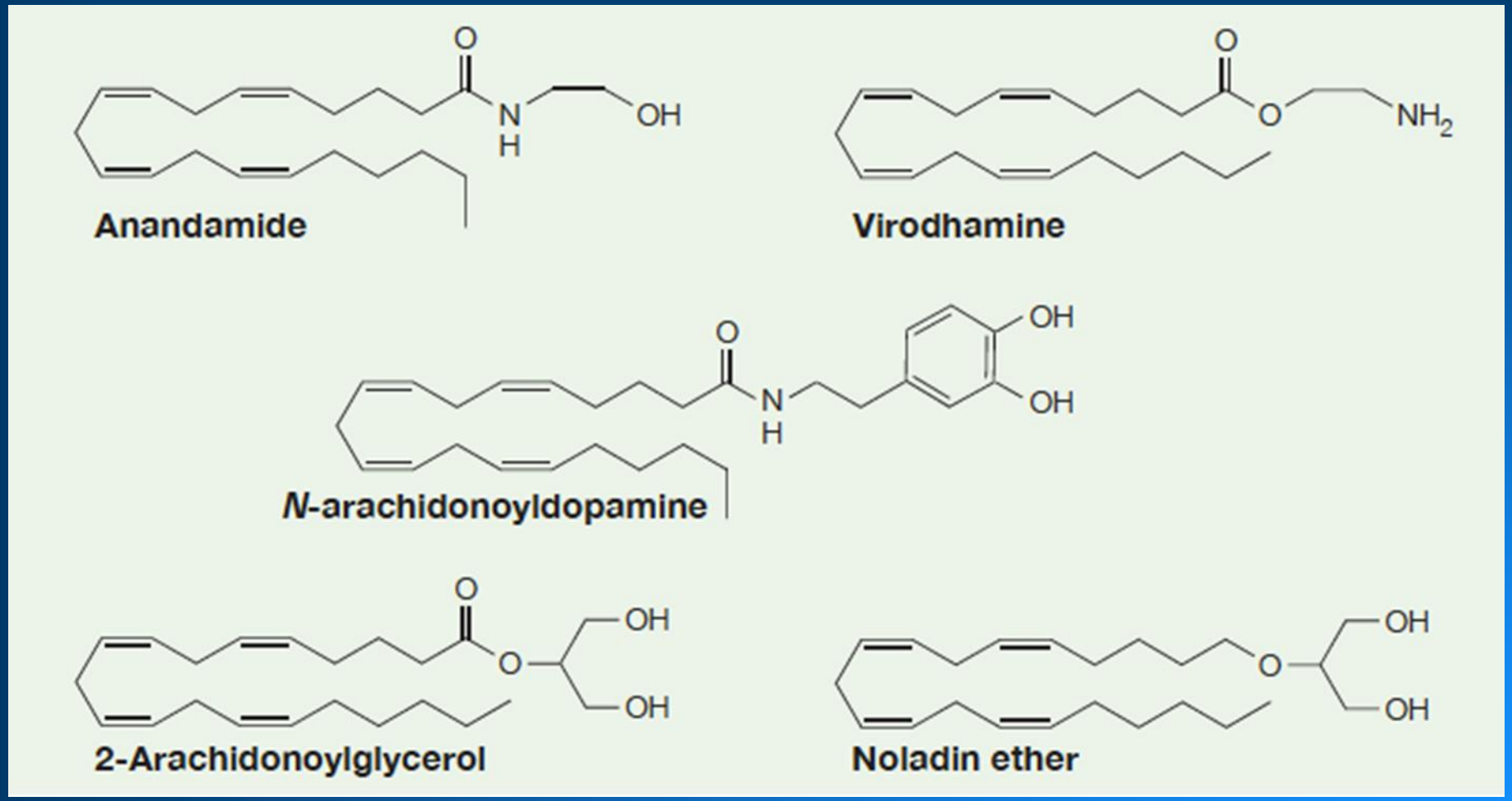
cannabidiol (CBD)
cannabinol (CBN)
tetrahydrocannabivarin (THCV)
cannabigerol (CBG)

Lots of media information

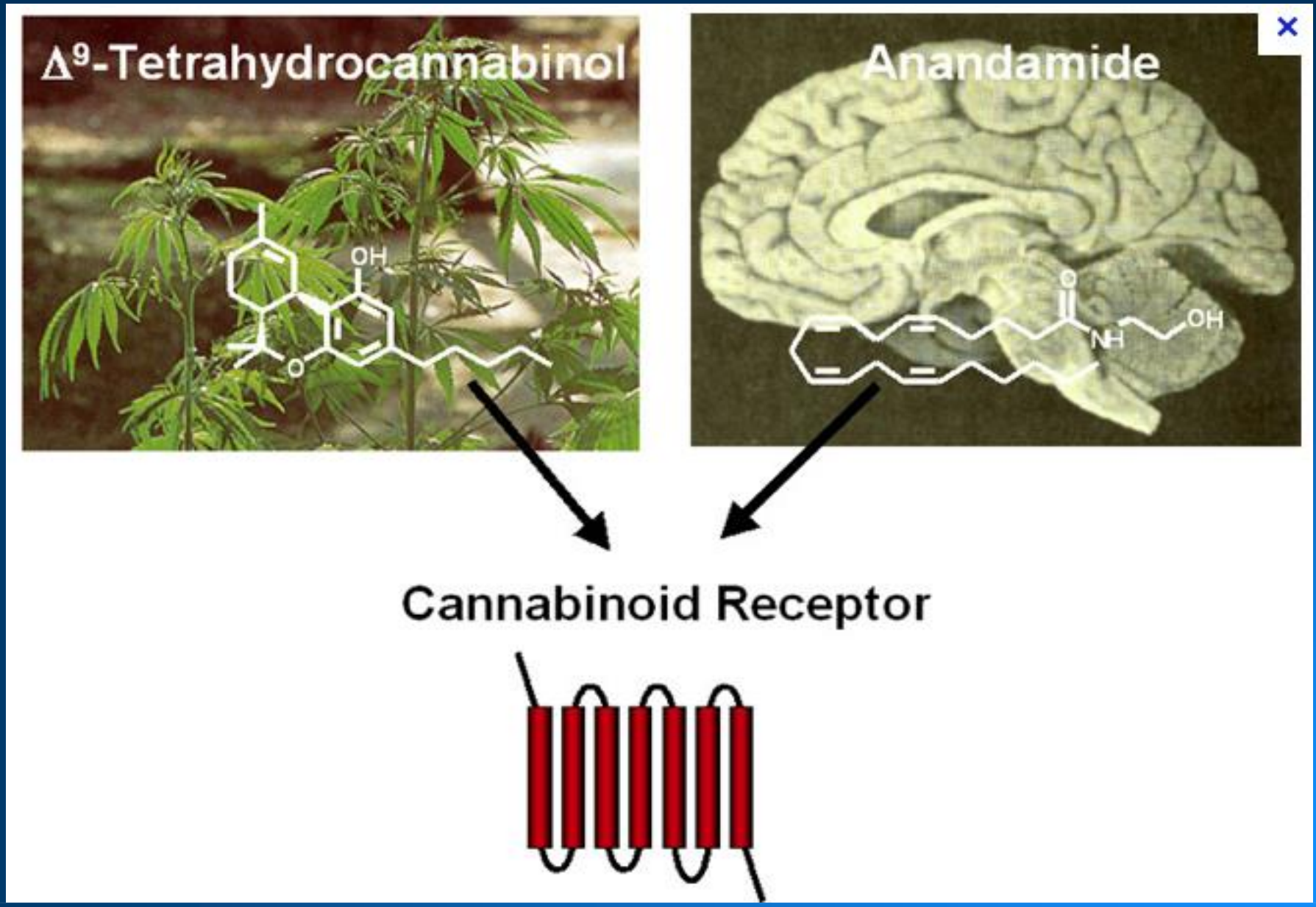
Lots of anecdotal information

Petition: allow veterans diagnosed with PTSD use of medicinal cannabis nationwide.

The endogenous cannabinoids

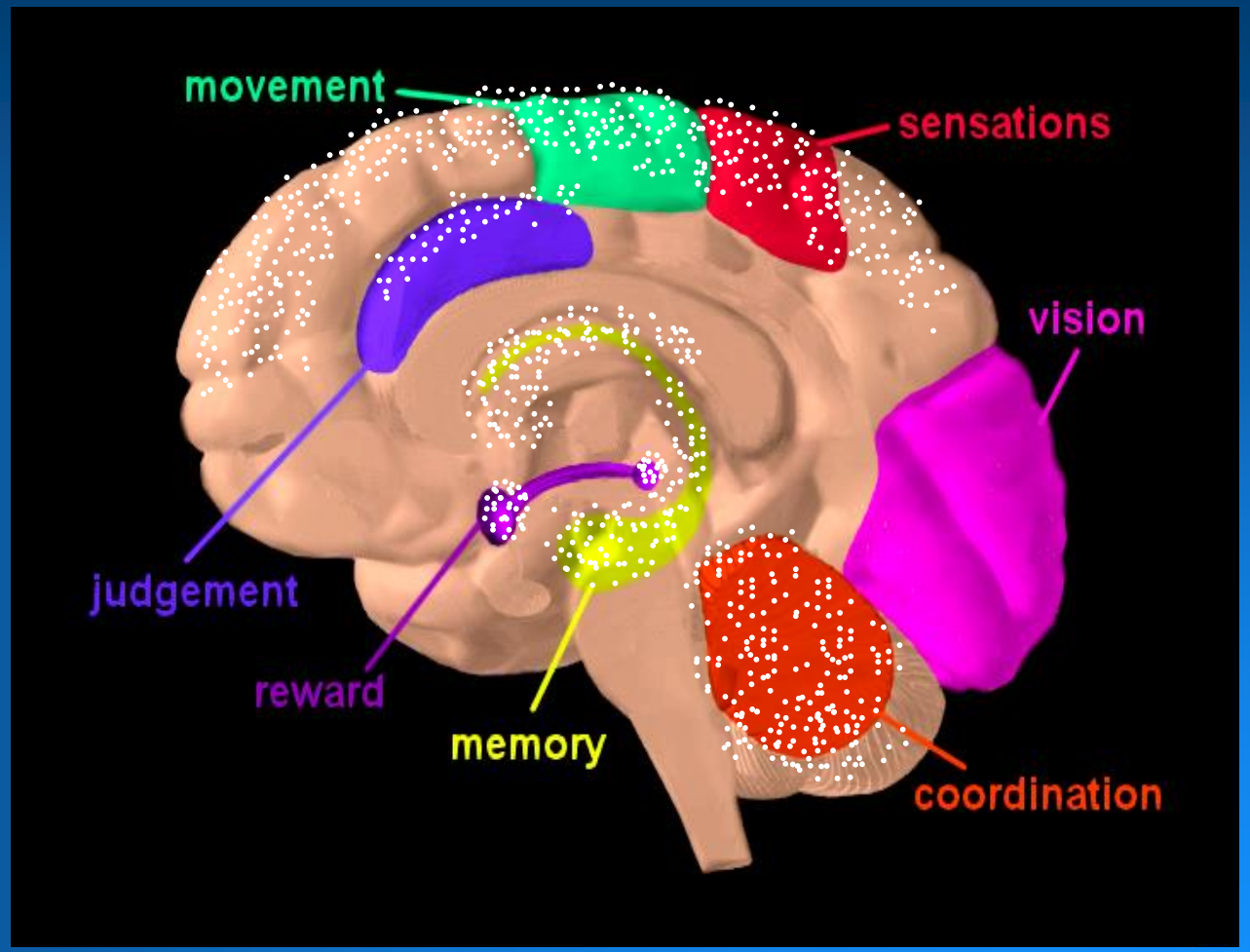


Piomelli, Nature Rev. Neurosci., 2003


Δ9-Tetrahydrocannabinol
OH
O
Anandamide
O
NH
OH
Cannabinoid Receptor

Cannabinoid Receptors Are Located Throughout the Brain and Regulate:

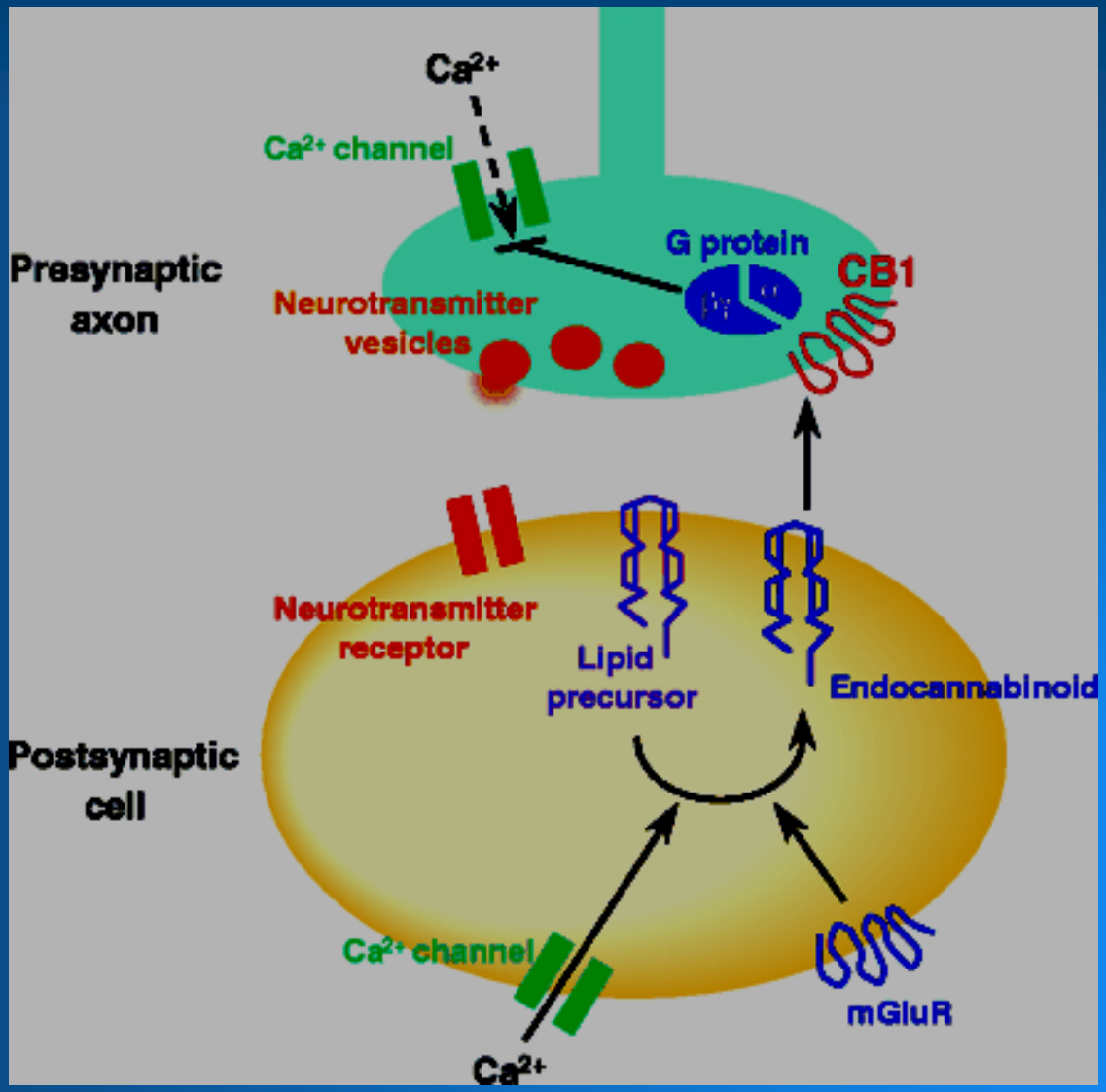
- Brain Development
- Memory and Cognition
- Motivational Systems & Reward
- Appetite
- Immunological Function
- Reproduction
- Movement Coordination
- Pain Regulation & Analgesia



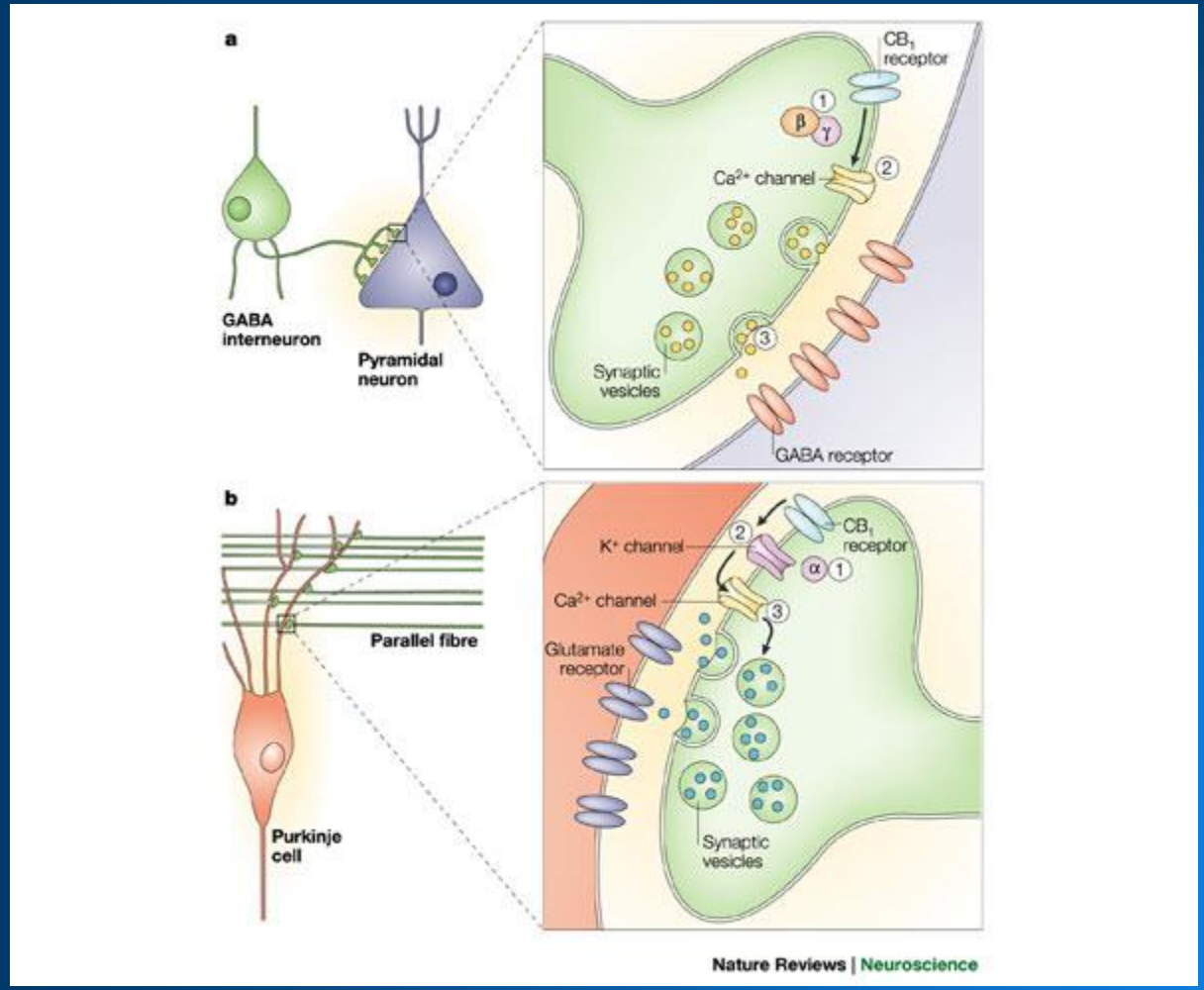
Distribution of Brain CB1 Receptors

- Hippocampus – Memory and Learning
- Amygdala – Novelty, Emotion, Appetitive Behaviour
- Basal Ganglia & Motor Cerebellum – Real Time Coordination, Selective Attention and Time Sense
- Nucleus Accumbens - Reward Mechanisms
- Cortex & Frontal Lobe - Executive Function, Judgment, Synthesis, Evaluation

Retrograde Signaling & the Cannabinergic System



Pre-synaptically located CB1 cannabinoid receptors regulate GABA Release from Axon Terminals

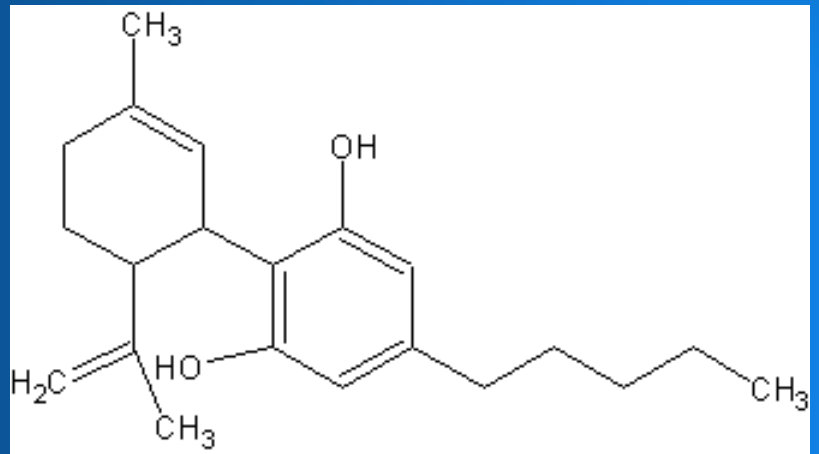


Katona et al., 1999
Hájos et al., 2001
Piomelli et al., 2003

Cannabidiol Reduces the Anxiety Induced by Simulated Public Speaking in Treatment-Naïve Social Phobia Patients

Mateus M Bergamaschi[1,2,3], Regina Helena Costa Queiroz[2,3], Marcos Hortes Nisihara Chagas[1,3], Danielle Chaves Gomes de Oliveira[1,3], Bruno Spinosa De Martinis[3,4], Flávio Kapczinski[3,5], João Quevedo[3,6], Rafael Roesler[3,7], Nadja Schröder[3,8], Antonio E Nardi[3,9], Rocio Martín-Santos[3,10], Jaime Eduardo Cecílio Hallak[1,3], Antonio Waldo Zuardi[1,3] and José Alexandre S Crippa*[,1,3]

Neuropsychopharmacology (2011), 1–8
© 2011 American College of Neuropsychopharmacology. All rights reserved 0893-133X/11 $32.00



Cannabidiol

Psychopharmacology (Berl)
Cannabinol and cannabidiol exert opposing effects on rat feeding patterns.
Farrimond et al., 2012.

Δ(9)-tetrahydrocannabinol-induced
- Increase in food consumption

Cannabinol
- increase in appetitive behavior and food intake

Cannabidiol
- reduction in food intake

an alternative to psychotropic Δ(9)-tetrahydrocannabinol-based medicines since cannabidiol is considered to be non-psychotropic.

Neuro Endocrinol Lett.

Clinical endo-cannabinoid deficiency revisited: can this concept explain the therapeutic benefits of cannabis in migraine, fibromyalgia, irritable bowel syndrome?

underlying
endo-cannabinoid deficiencies
play a role
in migraine, fibromyalgia,
irritable bowel syndrome

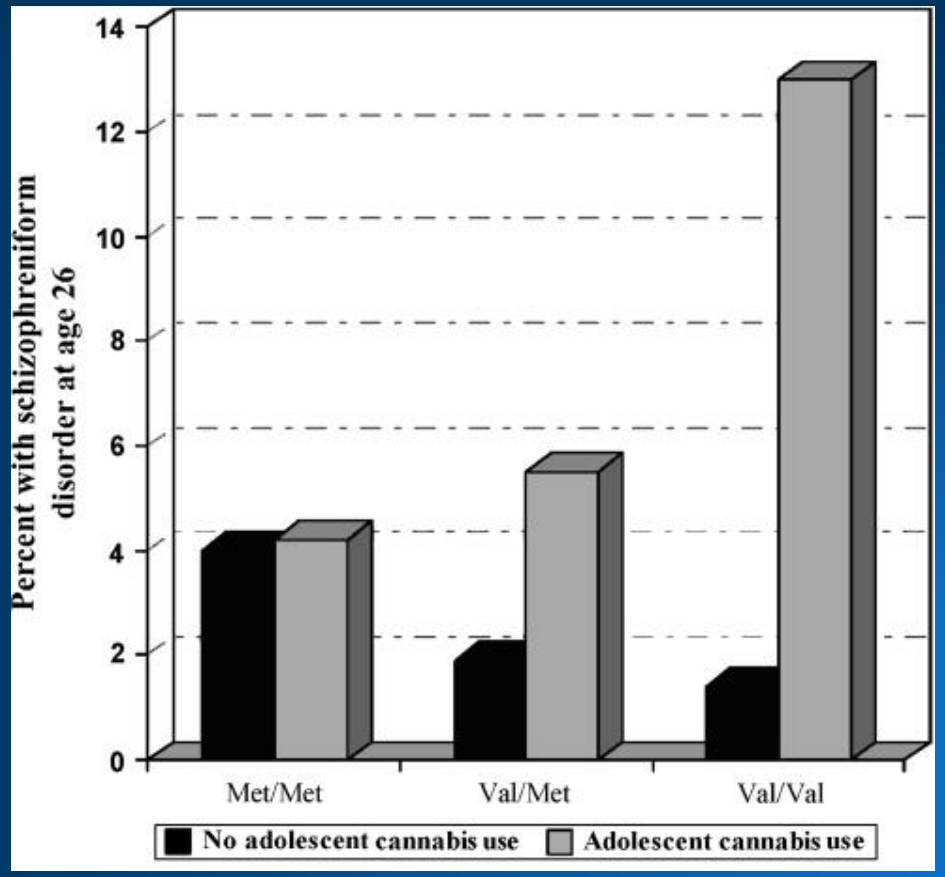
Smith and Wagner, 2014

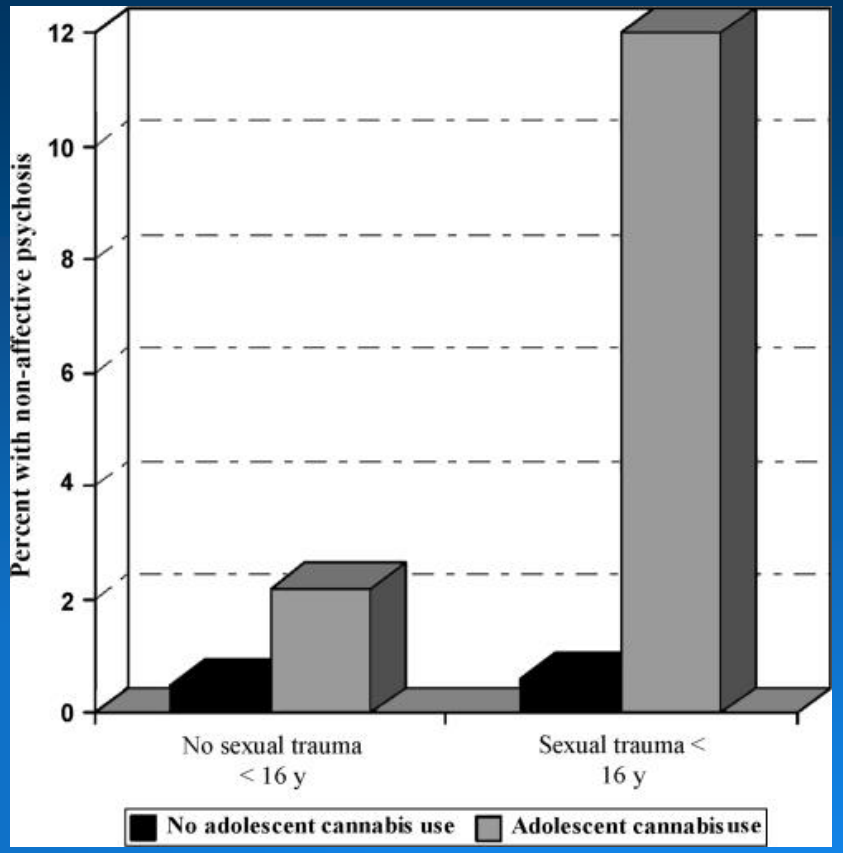
Biol Psychiatry.
Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction.
Caspi et al., 2005

A functional polymorphism
in the catechol-O-methyltransferase (COMT) gene
moderated the influence of adolescent cannabis use
on developing adult psychosis

COMT valine158 allele
psychotic symptoms
if they used cannabis

COMT methionine allele
no such adverse influence





Schizophr Bull.

Gene-environment interplay between cannabis and psychosis.

Henquet et al., 2008

The epidemiological literature in the past 20 years shows that regular cannabis use induces:

- risk of accidents

- dependence

- poor psychosocial outcomes

- mental health problem in adulthood

Some researchers still argue that these relationships are explained by shared causes or risk factors

Hall, 2014

One in six teenagers who regularly smoke the drug become dependent on it

Cannabis doubles the risk of developing psychotic disorders (schizophrenia)

Cannabis users do worse at school

Heavy use in adolescence appears to impair intellectual development and memory.

One in ten adults who regularly smoke the drug become dependent on it

Cannabis users are more likely to go on to use harder drugs

Driving after smoking cannabis doubles the risk of a car crash

Smoking it while pregnant reduces the baby's birth weight

Hall, Addiction 2014

Adverse health effects of marijuana use.

Volkow et al., N. Engl J Med., 2014

Acute psychosis
Chronic psychosis
Depression
Anxiety
Suicidal thoughts
Personality disturbances
Lack of motivation

Eur Arch Psychiatry Clin Neurosci (2012) 262:47–57
DOI 10.1007/s00406-011-0223-5

ORIGINAL PAPER

Psychobiological responses to unpleasant emotions in cannabis users

Lorenzo Somaini · Matteo Manfredini · Mario Amore · Amir Zaimovic · Maria Augusta Raggi · Claudio Leonardi · Maria Lidia Gerra · Claudia Donnini · Gilberto Gerra

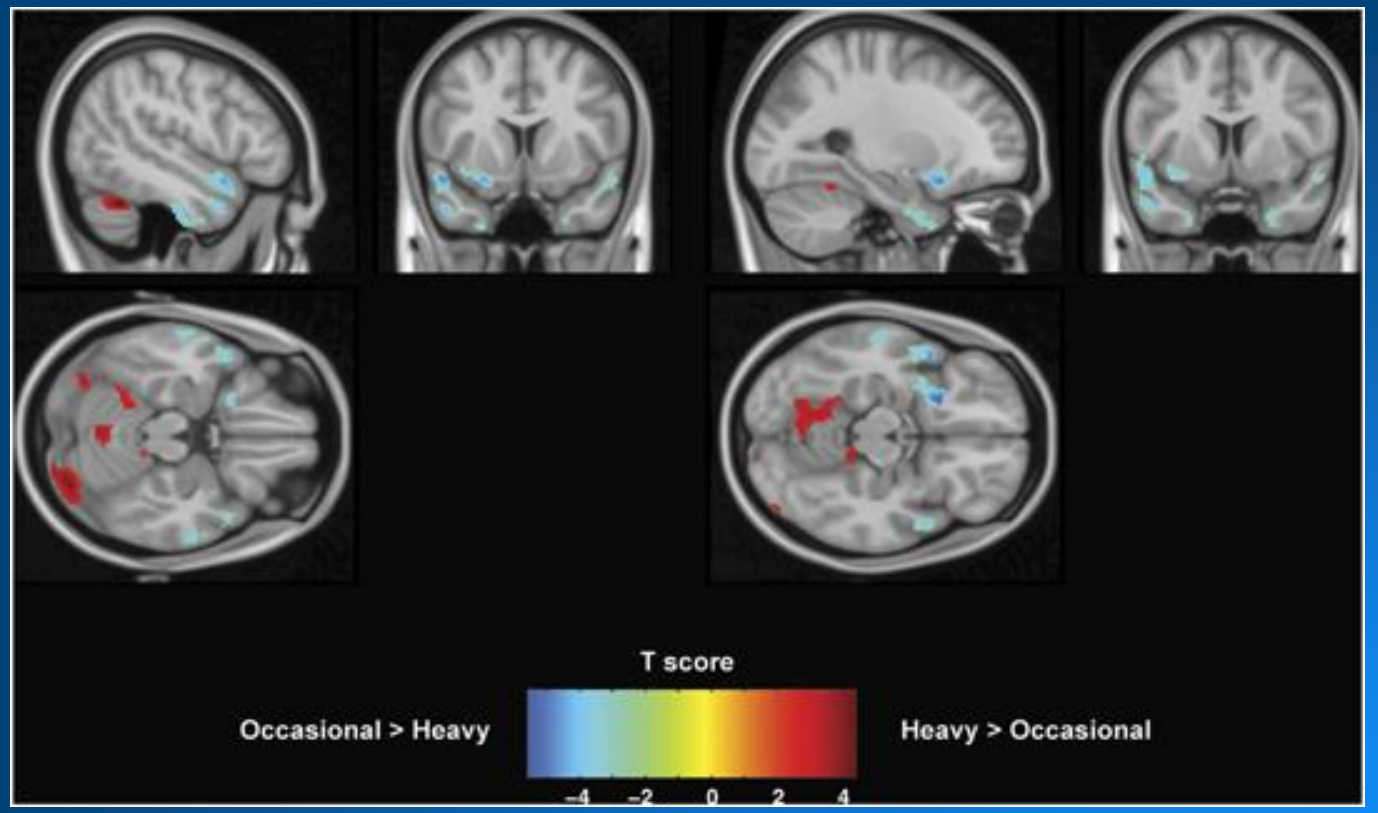
lower levels of arousal in response to negative emotions
compared to abstinent cannabis users and controls

a persistent hyperactivity of hypothalamus-pituitary-adrenal (HPA) axis

impaired hormonal reaction to negative emotions, in comparison with healthy subjects.

reduced sensitivity to negative emotions

Neuropsychopharmacology **39,** 2041–2048
Long-Term Effects of Cannabis on Brain Structure
Battistella et al., 2014



Cold color bar shows regions where gray matter volume
is lower in regular smokers compared with occasional ones.

Cannabis and schizophrenia

Shared risk factors:
parallel development
of co-occurring disorders

Causal model: in vulnerable
or non-vulnerable population

Self-medication model

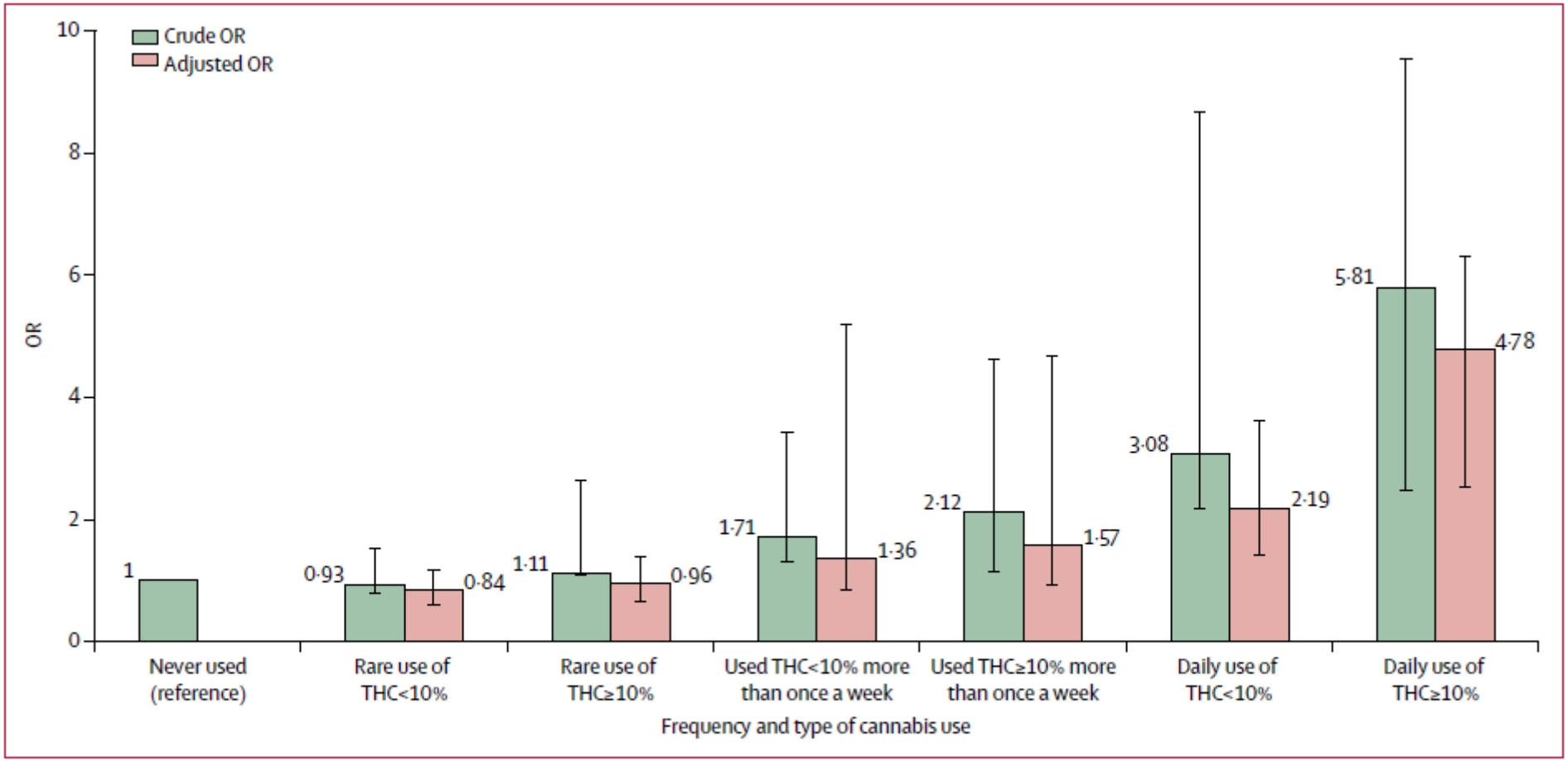
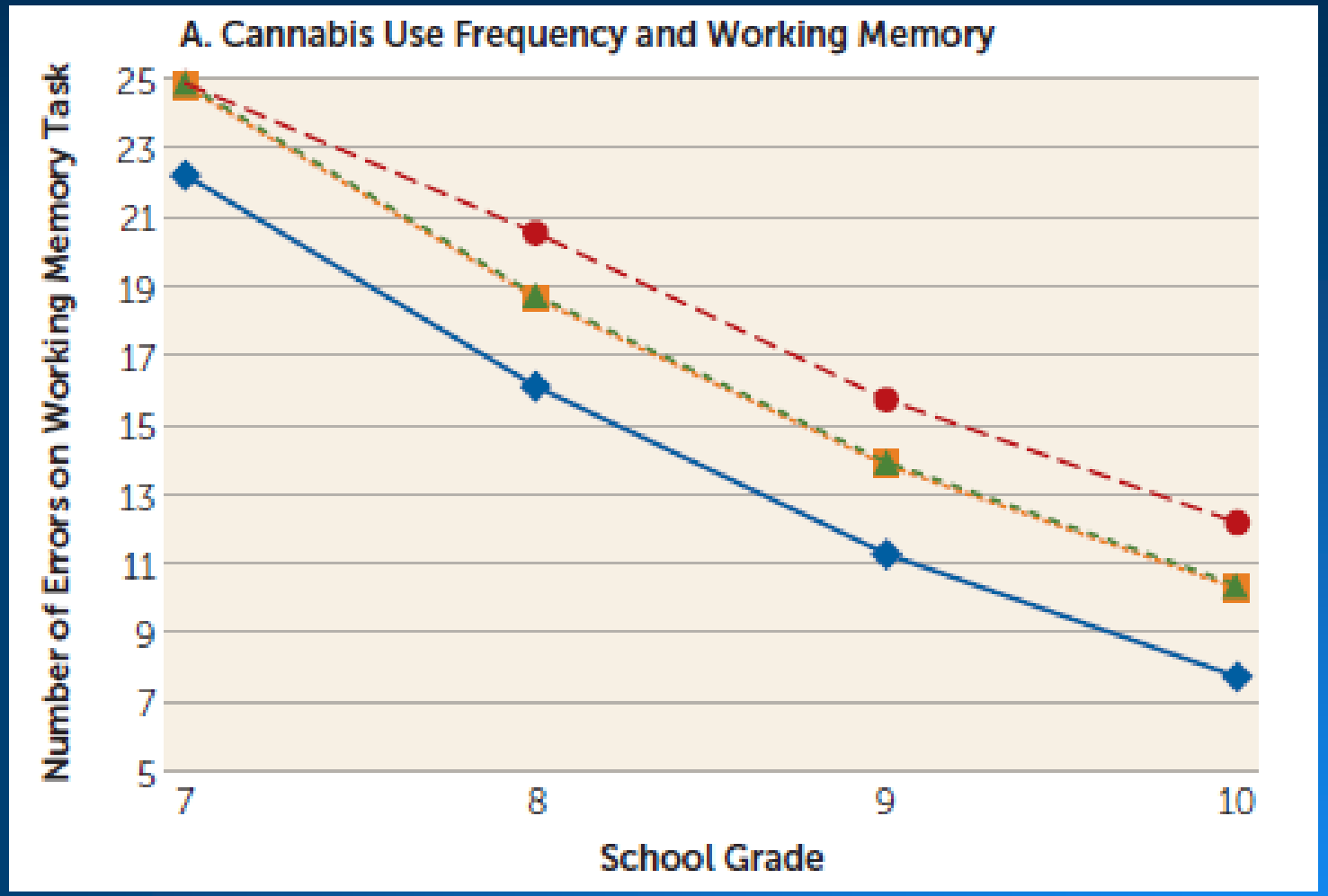
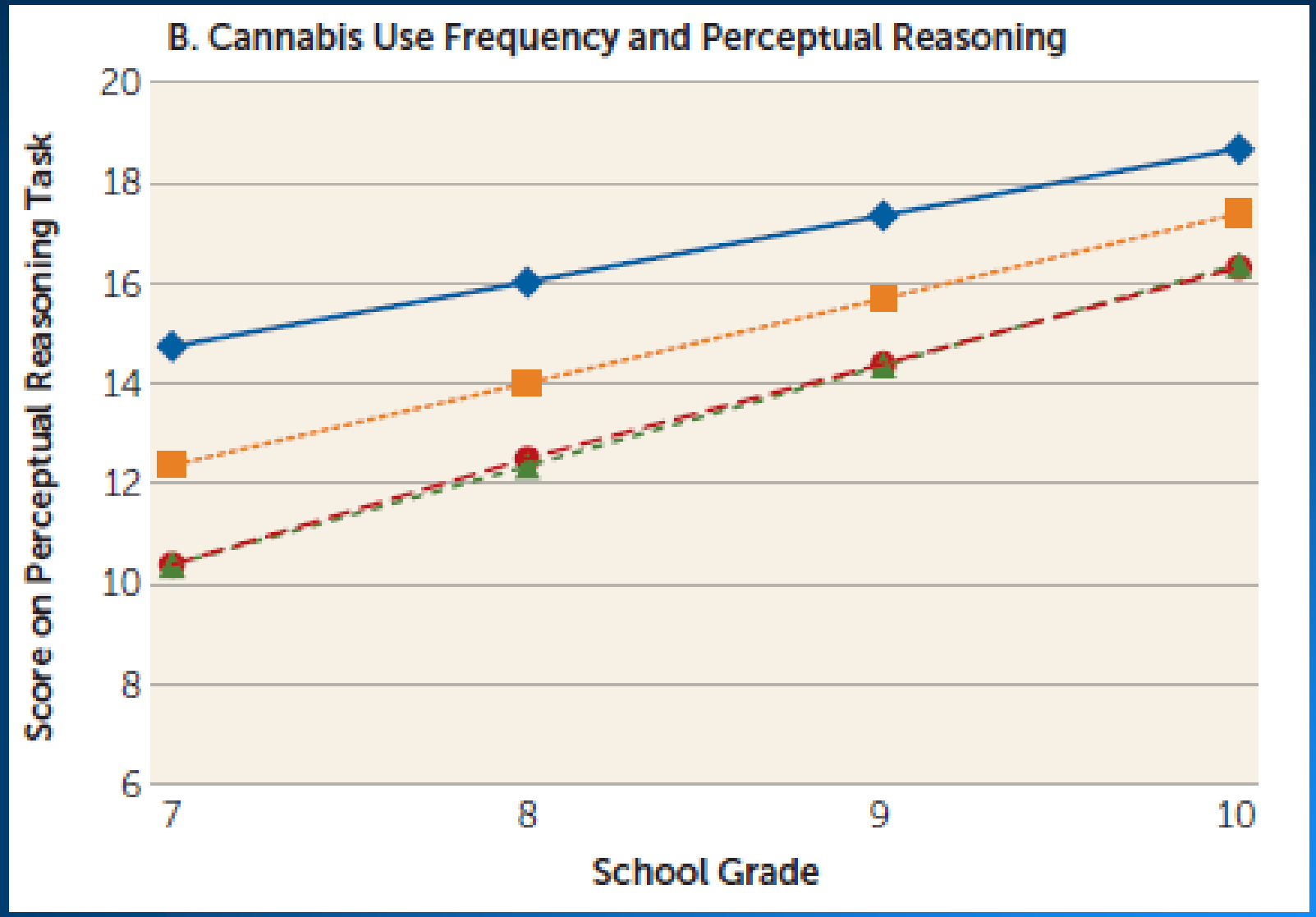


Figure 1: **Crude and fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in the whole sample**
Crude ORs are adjusted only for age, gender and ethnicity and fully adjusted ORs are additionally adjusted for level of education, employment status, and use of tobacco, stimulants, ketamine, legal highs, and hallucinogenics. Error bars represent 95% CIs. OR=odds ratio.

Di Forti et al., Lancet 2019



Morin et al., 2018



Morin et al., 2018

Minorities with lower socioeconomic status had higher prevalence of ever using marijuana and incidence of past year initiation as compared with affluent social groups.

(Forman-Hoffman et al., 2017)

A decrease of cannabis use has been evidenced among youth from affluent families, in contrast to youth from low family affluent status, with heavier use pattern

(ter Bogt et al., 2014)

In terms of consumption of cannabis and other controlled drugs,
the unemployed and students with low educational level ('Hauptschule´: vocational school) emerged as high-risk groups (Henkel and Zemlin, 2016).

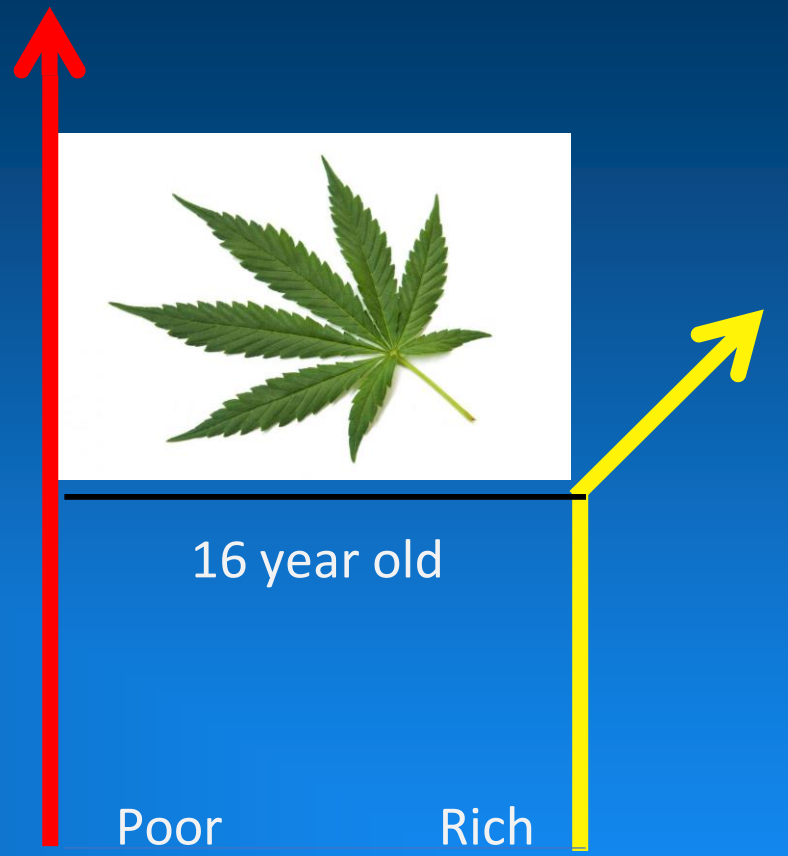
low educational level
=
risk

high educational level
=
resilience

Adolescent from high socioeconomic status
try cannabis (episodic experimenting)
more often than young people
from lower socioeconomic status.

However, cannabis regular use,
with the risk of being affected
by **cannabis use disorders**, associated
with a lower socioeconomic status,
bad school results, early school leaving.

Young people from high socioeconomic status dispose of greater sociocultural resources to master and regulate their consumption



(Beck et al., 2013)

Socioeconomic status and parental education in vulnerability for substance use disorders

Gilberto Gerra, Elisa Benedetti, Giuliano Resce, Sabrina Molinaro

The sample (Males = 24,136; Females = 26,300)
28 out of the 35 countries that participated in 2015 ESPAD data collection

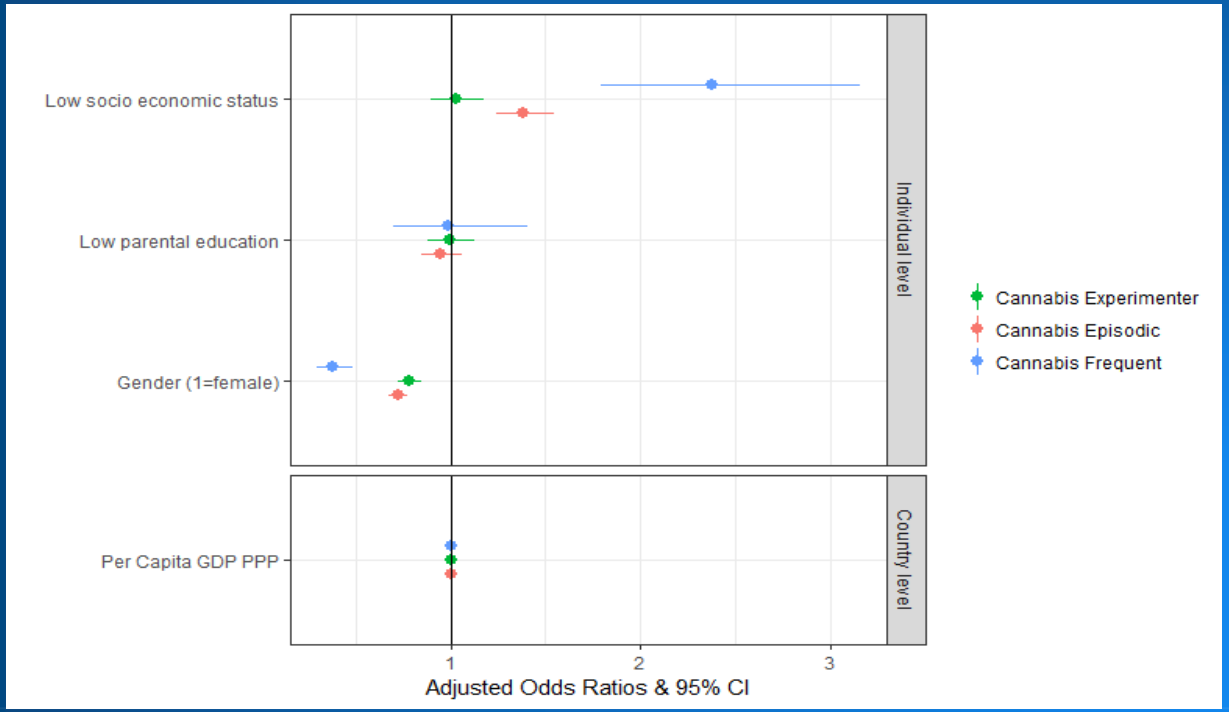
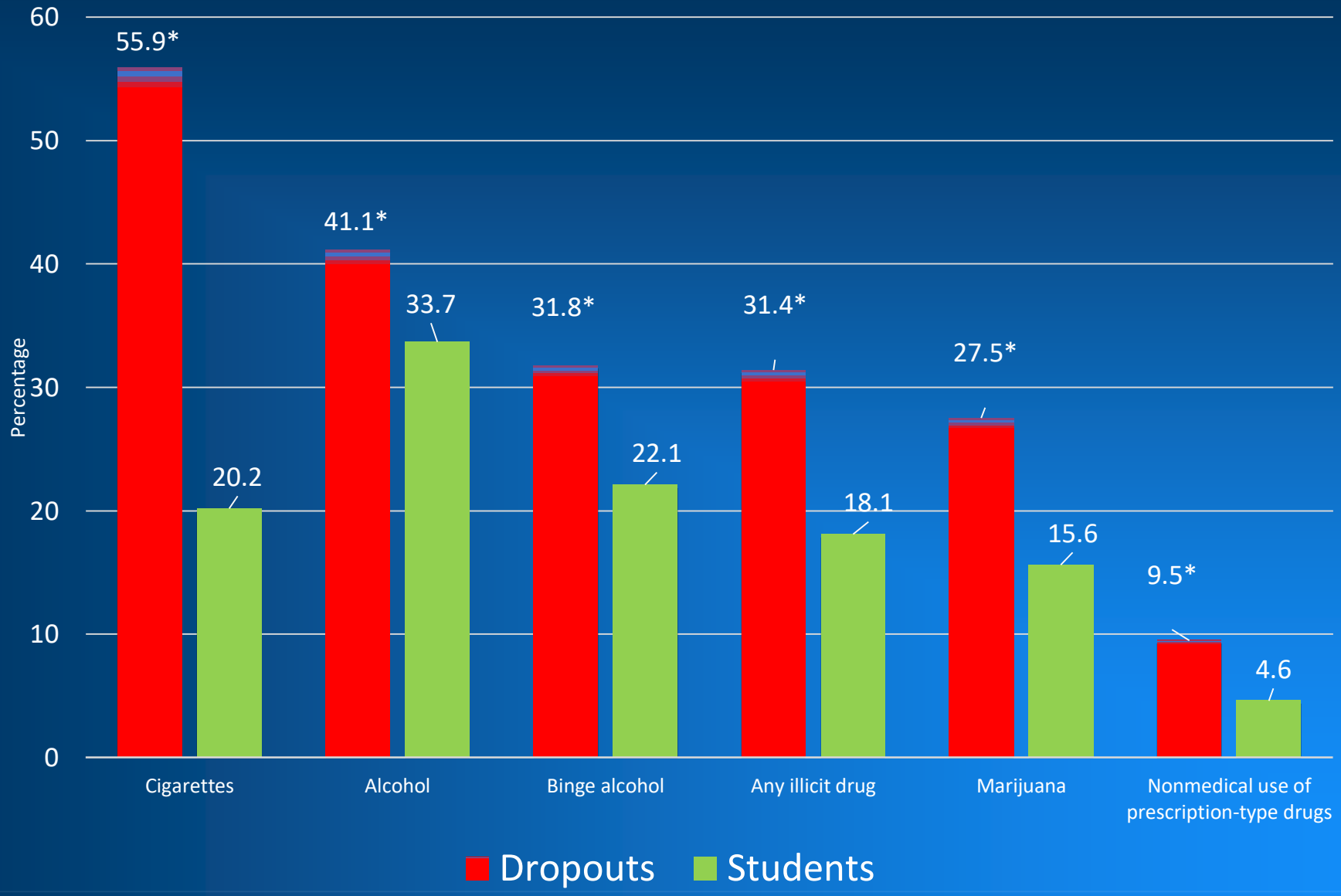


Figure 1. Past month substance use among youth in schools and youth that have dropped out of school (12th grade aged youth)



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