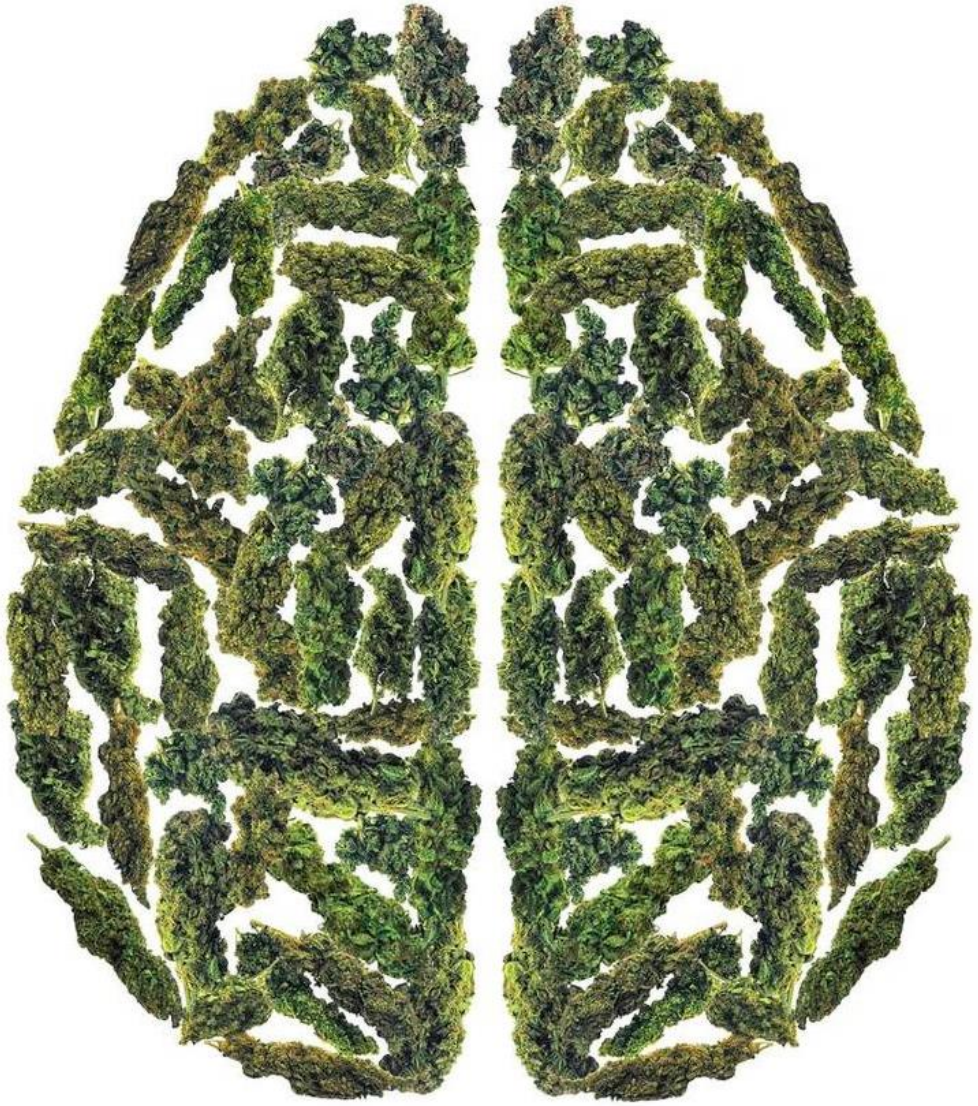
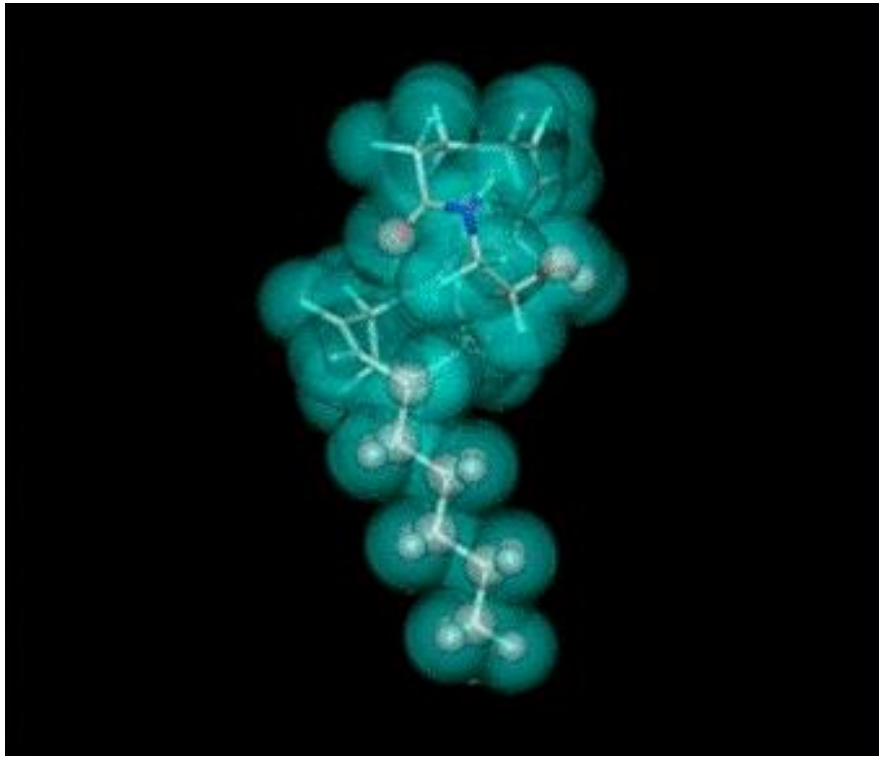
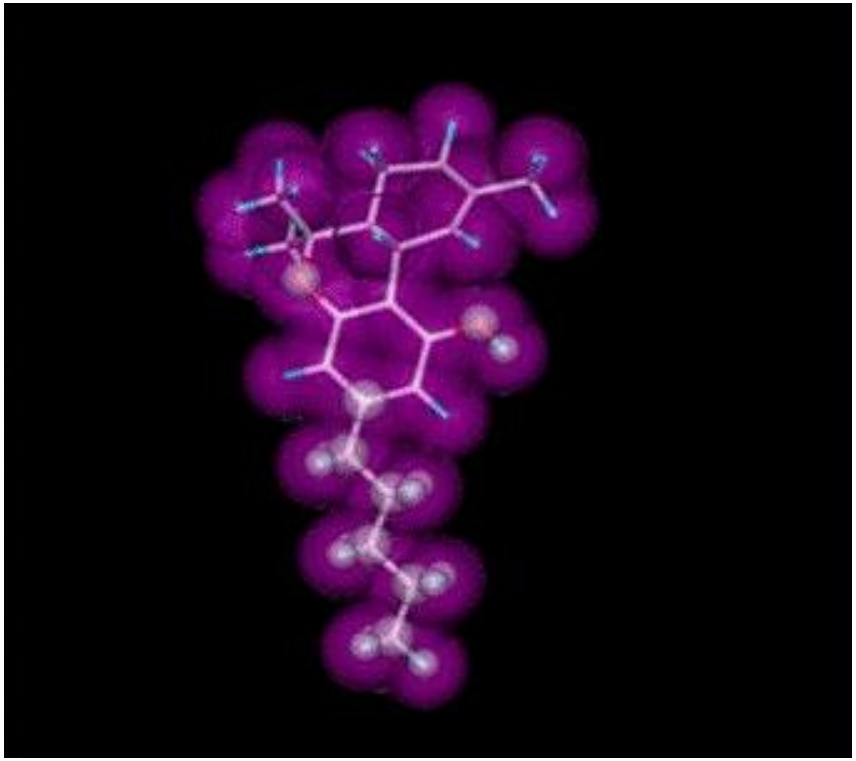
Marijuana's effects on the brain

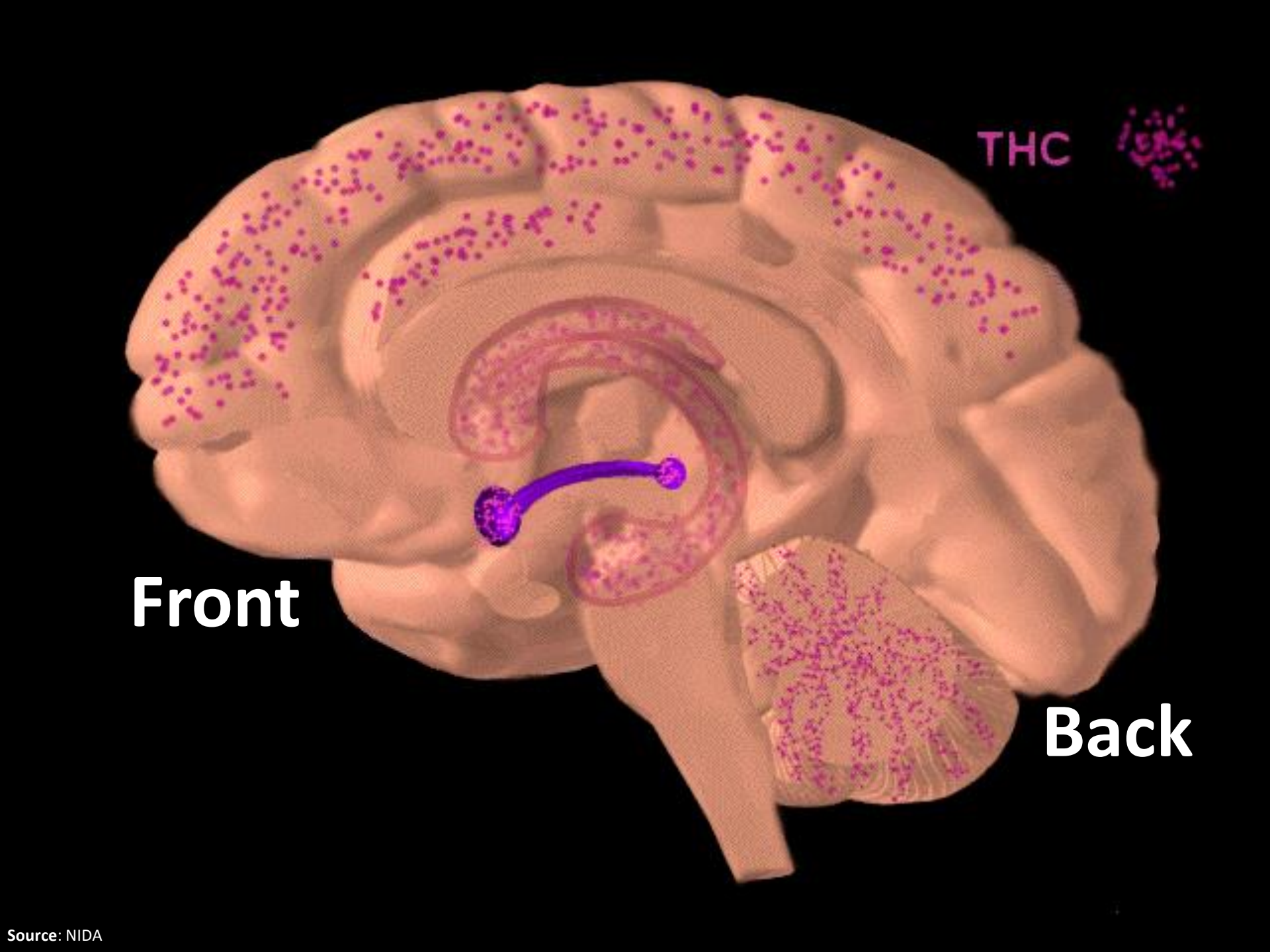


Anandamide



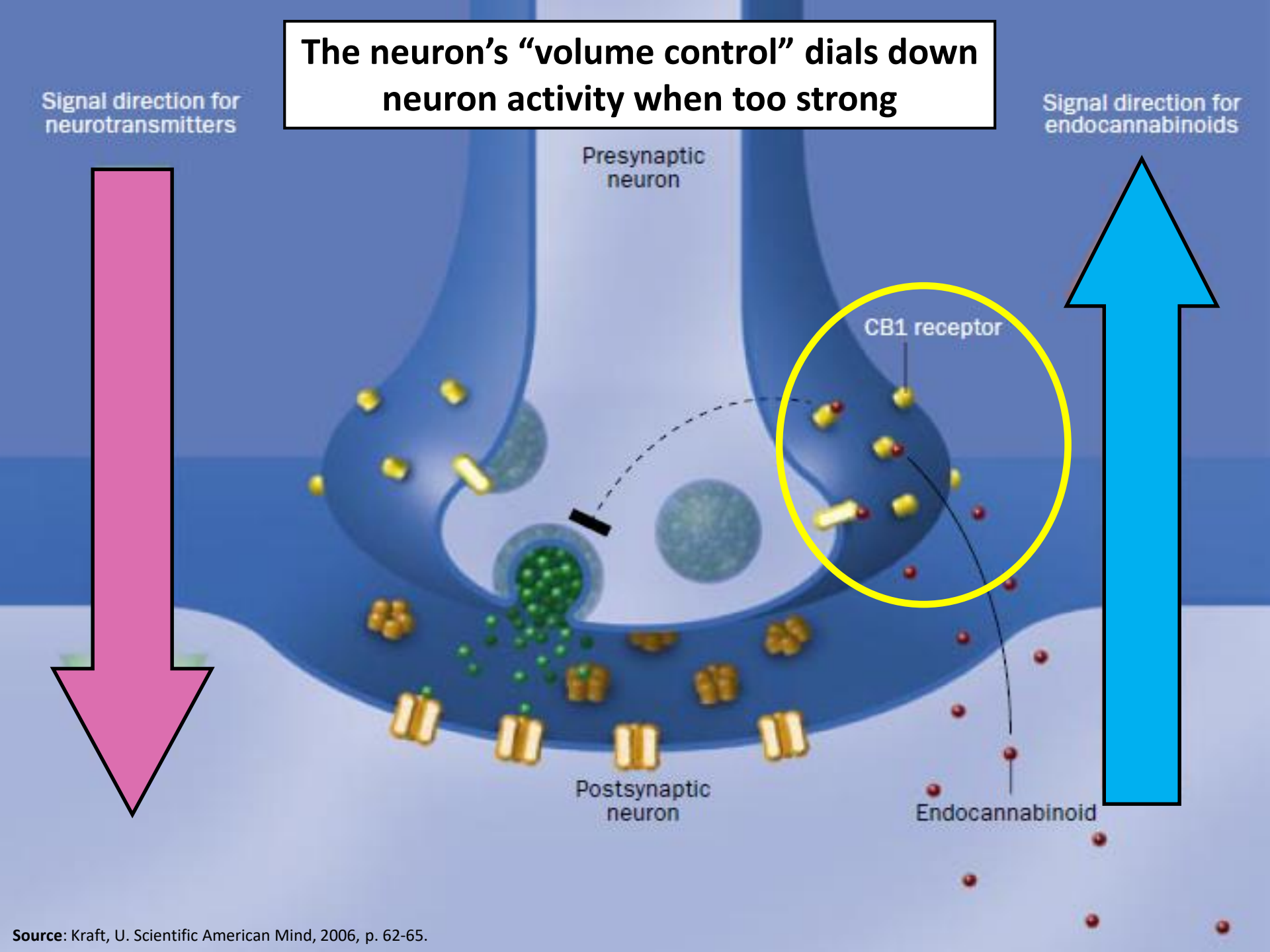
THC





Source: NIDA

The neuron's "volume control" dials down neuron activity when too strong



Source: Kraft, U. Scientific American Mind, 2006, p. 62-65.

Synaptic pruning

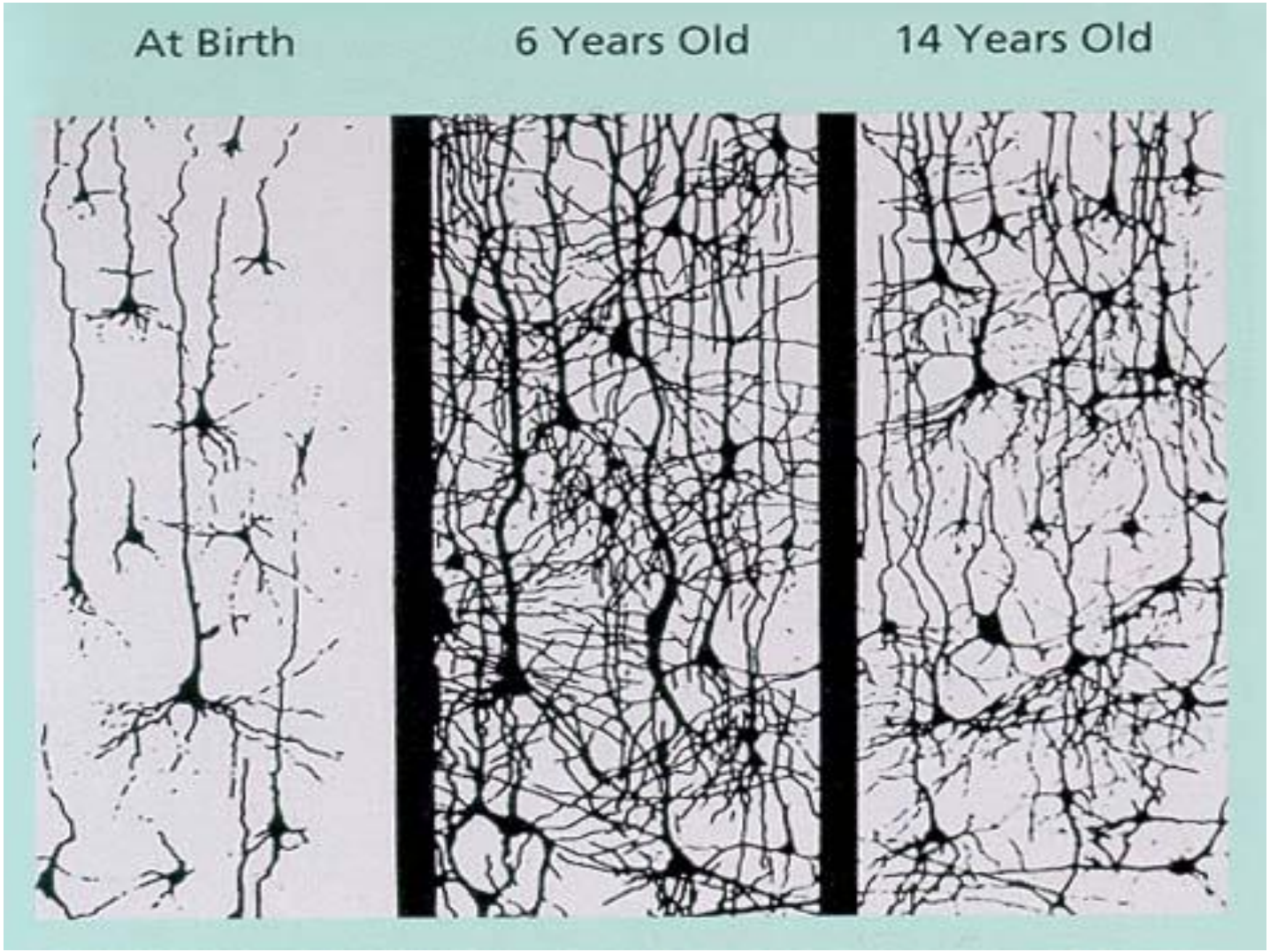


Image retrieved from: http://etec.ctlt.ubc.ca/510wiki/Brain-based_Learning

Receptor binding in brain tissue

Compound	Potency relative to THC
(-)-Delta9-THC	1
Anandamide	.47*

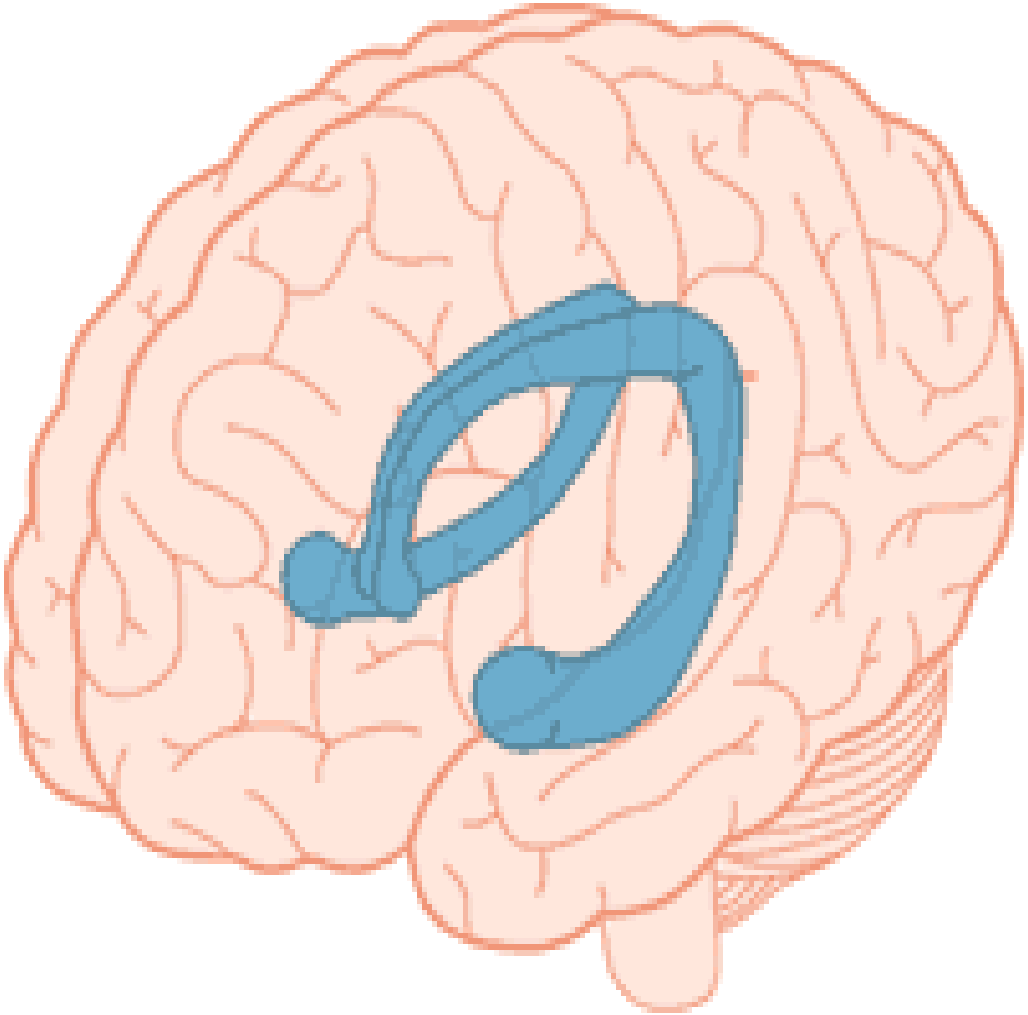
*The affinity of anandamide for cannabinoid receptors ranges from about one-fourth to one-half that of THC. The differences depend on the cells or tissue that are tested and on the experimental conditions, such as the binding assay used.

Source: Joy J, Watson SJ, Benson JJ, eds. Cannabinoids and animal physiology. In: *Marijuana and Medicine: Assessing the Science Base*. Washington, DC: Division of Neuroscience and Behavioral Health - Institute of Medicine. National Academies Press; 1999:288

THC vs. Anandamide

Source: Joy J, Watson SJ, Benson JJ, eds. (1999). Cannabinoids and animal physiology. In: *Marijuana and Medicine: Assessing the Science Base*. Washington, DC: Division of Neuroscience and Behavioral Health -Institute of Medicine. National Academies Press.

Hippocampus and Memory



Source: Iversen L. How cannabis works in the brain. In *Marijuana and Madness*. Ed. Castle & Murray, 2004. Oxford University Press.

Persistent cannabis users show neuropsychological decline from childhood to midlife

Madeline H. Meier[a,b,1], Avshalom Caspi[a,b,c,d,e], Antony Ambler[e,f], HonaLee Harrington[b,c,d], Renate Houts[b,c,d], Richard S. E. Keefe[d], Kay McDonald[f], Aimee Ward[f], Richie Poulton[f], and Terrie E. Moffitt[a,b,c,d,e]

[a]Duke Transdisciplinary Prevention Research Center, Center for Child and Family Policy, [b]Department of Psychology and Neuroscience, and [c]Institute for Genome Sciences and Policy, Duke University, Durham, NC 27708; [d]Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC 27710; [e]Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom; and [f]Dunedin Multidisciplinary Health and Development Research Unit, Department of Preventive and Social Medicine, School of Medicine, University of Otago, Dunedin 9054, New Zealand

Source: Meier et al. Proceedings of the National Academy of Sciences. 2012. Available at: www.pnas.org/cgi/doi/10.1073/pnas.1206820109

The Dunedin Study

N = 1,037

13 yrs (Pre-initiation) **18 yrs** **21 yrs** **32 yrs** **38 yrs**

1 **2** **3** **4** **5**

Assessment ages

Source: Meier et al. (2012). Persistent cannabis users show neuropsychological decline from childhood to midlife. *P Nat Acad Sci* 109(40):E2657–E2664.

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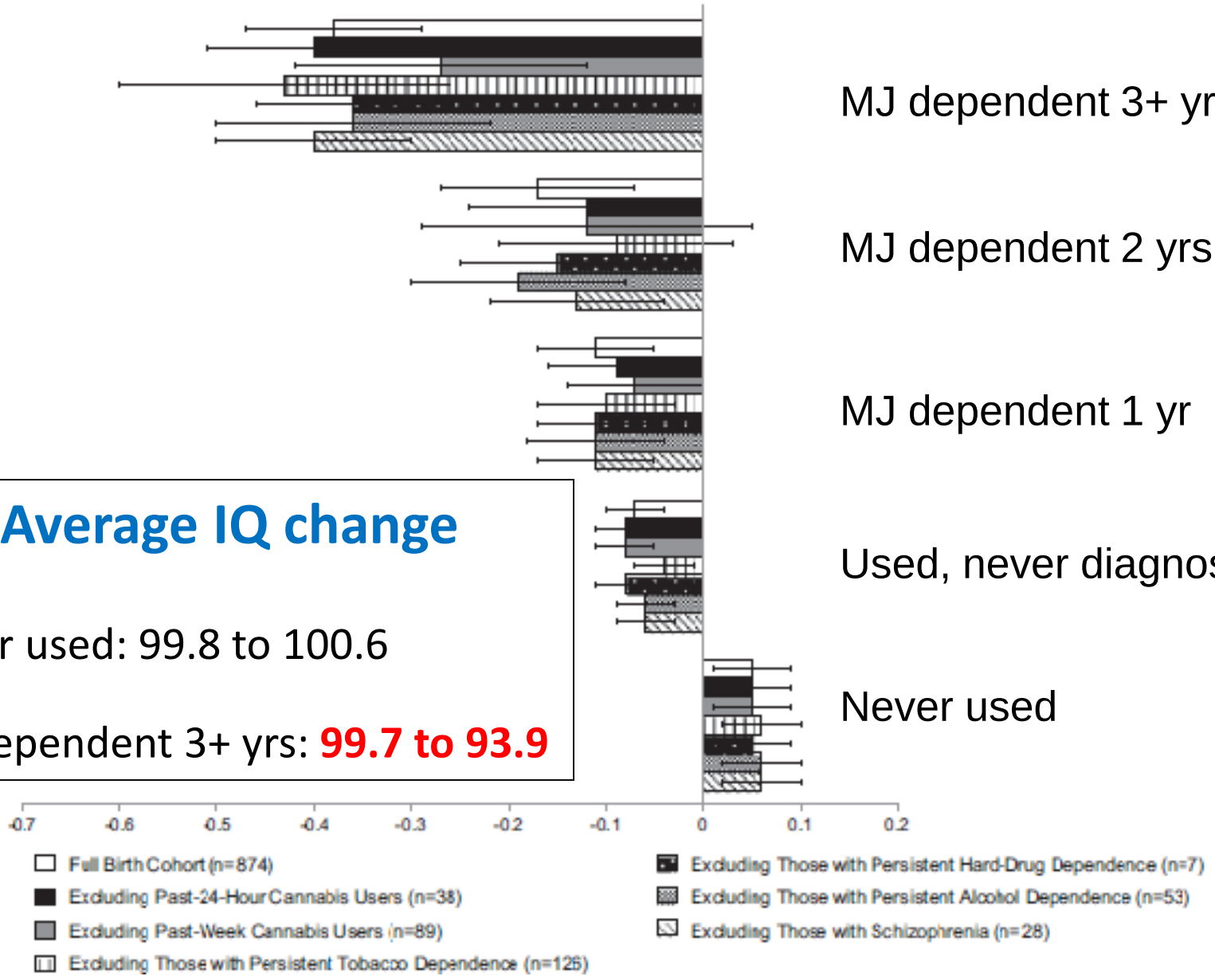


Average IQ change

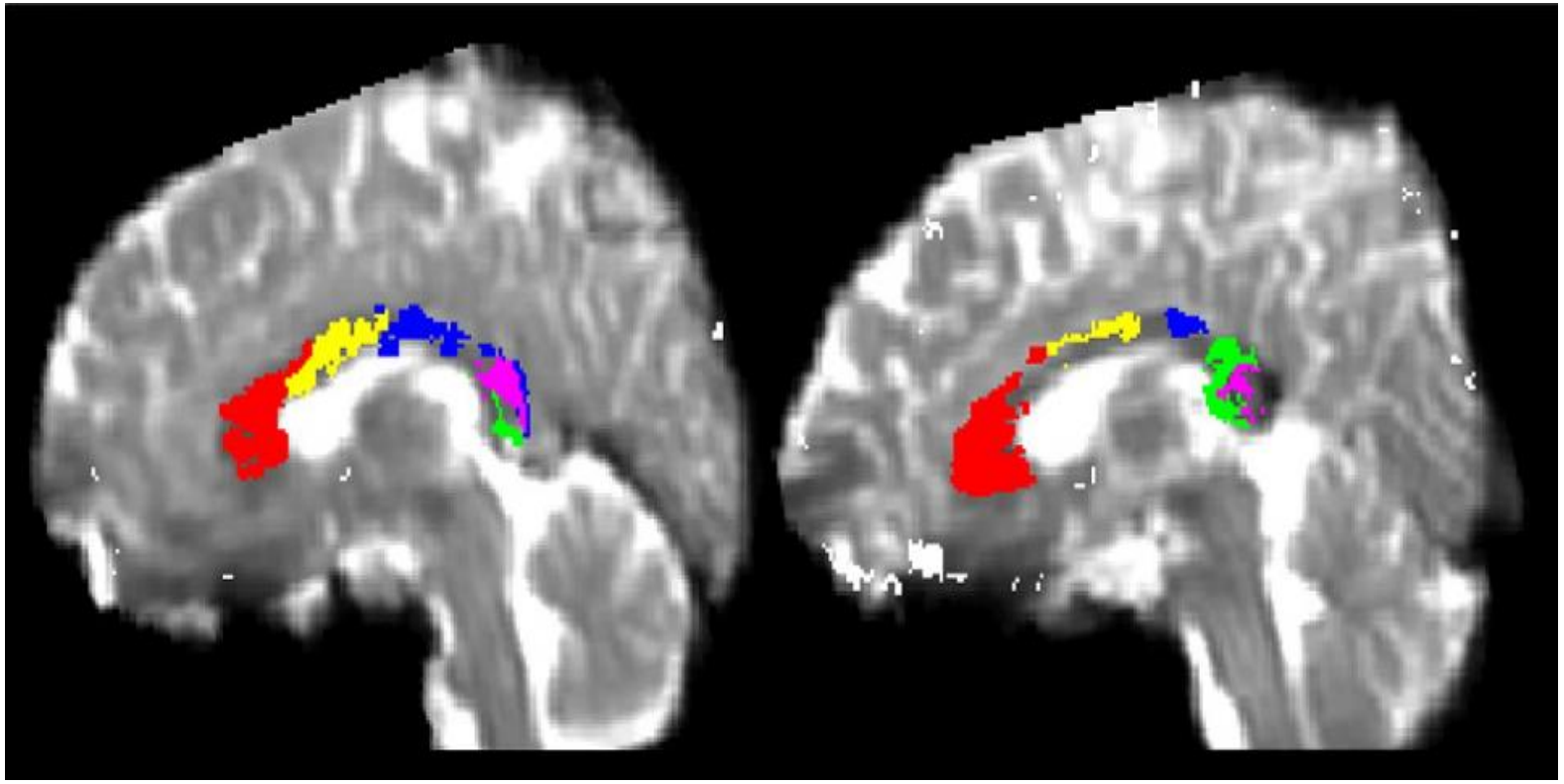
Never used: 99.8 to 100.6

MJ dependent 3+ yrs: **99.7 to 93.9**

Source: Meier et al. (2012). Persistent cannabis users show neuropsychological decline from childhood to midlife. *P Nat Acad Sci* 109(40):E2657–E2664.

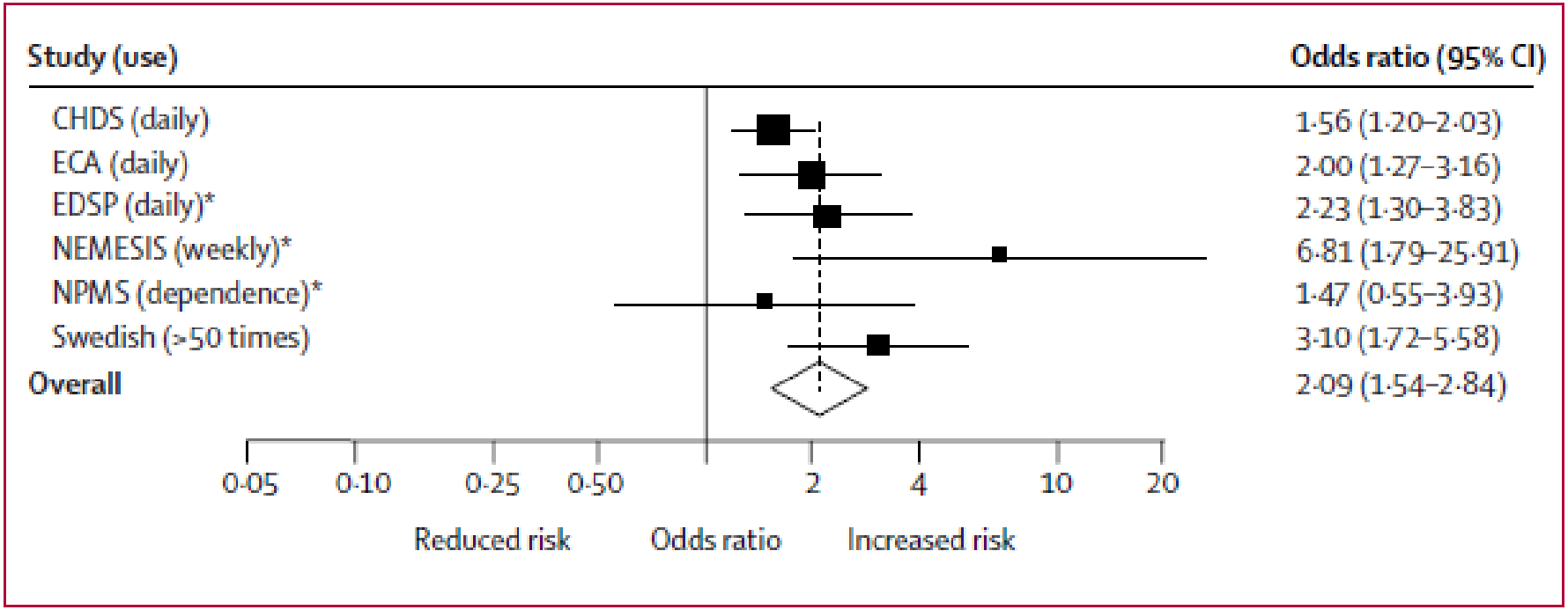
Healthy non-user

Daily MJ user



Source: Arnone D, Barrick TR, Chengappa S et al. (2008). Corpus callosum damage in heavy marijuana use: Preliminary evidence from diffusion tensor tractography and tract-based spatial statistics. *Neuro Image* 41:1067-1074.

Marijuana use and psychotic disorders



A meta-analysis of 6 studies found an increased risk of psychotic outcome among those who used cannabis most frequently compared with non-users (Adjusted Odds Ratio: 2.09, 95% CI: 1.54-2.84).

Source: Moore et al. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet* 370(9584):319–28.

Association between cannabis use and schizoaffective disorder

	# Exposure	# Cases	HR Crude	HR adjusted*
Never used cannabis	39, 978	47	1	1
Ever used cannabis	5,109	12	2.1 (1.1-3.8)	0.8 (0.2-2.9)
>50 times	855	7	7.5 (3.4-16.7)	**7.4 (1.0-54.3)**

*Adjustments for: prior personality disorders at conscription, IQ, disturbed behavior in childhood, social adjustment, risky use of alcohol, smoking, early adulthood socioeconomic position, use of other drugs, brought up in a city. The category "Ever used cannabis" includes all individuals who reported cannabis use, including those who reported ">50 times".

Sources: Griffith-Lendering, Addiction, 108(4), 733-740. Manrique-Garcia, BMC Psychiatry, 12, 112.

Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review

Theresa H M Moore, Stanley Zammit, Anne Lingford-Hughes, Thomas R E Barnes, Peter B Jones, Margaret Burke, Glyn Lewis

Summary

Background Whether cannabis can cause psychotic or affective symptoms that persist beyond transient intoxication is unclear. We systematically reviewed the evidence pertaining to cannabis use and occurrence of psychotic or affective mental health outcomes.

Methods We searched Medline, Embase, CINAHL, PsycINFO, ISI Web of Knowledge, ISI Proceedings, ZETOC, BIOSIS, LILACS, and MEDCARIB from their inception to September, 2006, searched reference lists of studies selected for inclusion, and contacted experts. Studies were included if longitudinal and population based. 35 studies from 4804 references were included. Data extraction and quality assessment were done independently and in duplicate.

The evidence is consistent with the view that cannabis increases risk of psychotic outcomes independently of confounding and transient intoxication effects.

strong. The uncertainty about whether cannabis causes psychosis is unlikely to be resolved by further longitudinal studies such as those reviewed here. However, we conclude that there is now sufficient evidence to warn young people that using cannabis could increase their risk of developing a psychotic illness later in life.

Lancet 2007; 370: 319–28

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Correspondence to: Dr Stanley Zammit, Department of Psychological Medicine, Cardiff University, Cardiff CF14 4XN, UK